INCISIONAL AND CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

RISK FACTORS, MANAGEMENT AND OUTCOMES
NEW DEVELOPMENTS IN MEDICAL RESEARCH

Additional books in this series can be found on Nova’s website under the Series tab.

Additional e-books in this series can be found on Nova’s website under the e-book tab.
INCISIONAL AND CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

RISK FACTORS, MANAGEMENT AND OUTCOMES

ROOSEVELT COLLINS
EDITOR

New York
# CONTENTS

<table>
<thead>
<tr>
<th>Preface</th>
<th>vii</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chapter 1</strong></td>
<td>1</td>
</tr>
<tr>
<td>Incisional Hernias: Risk Factors, Prevention and Management</td>
<td>Fabrizio Ferranti</td>
</tr>
<tr>
<td><strong>Chapter 2</strong></td>
<td>19</td>
</tr>
<tr>
<td>Biomolecular Basis of Incisional Hernias</td>
<td>Manu Kaushik, Jasneet Singh Bhullar and Vijay K Mittal</td>
</tr>
<tr>
<td><strong>Chapter 3</strong></td>
<td>31</td>
</tr>
<tr>
<td>Incisional Hernia with Loss of Abdominal Domain</td>
<td>Valentin Oprea and Florin Buia</td>
</tr>
<tr>
<td><strong>Chapter 4</strong></td>
<td>67</td>
</tr>
<tr>
<td>Preoperative Techniques for the Management of Giant Hernias</td>
<td>Karla Verónica Chávez-Tostado</td>
</tr>
<tr>
<td><strong>Chapter 5</strong></td>
<td>83</td>
</tr>
<tr>
<td>Intraabdominal Pressure Modification in “Component Separation” Technique for Repair of Incisional Hernia</td>
<td>Marco Mazzocchi, Valentina Sorvillo and Luca A. Dessy</td>
</tr>
<tr>
<td><strong>Chapter 6</strong></td>
<td>97</td>
</tr>
<tr>
<td>Incidence, Risk Factors and Repair of Incisional Hernia Formation After Abdominal Organ Transplantation</td>
<td>Laszlo Piros</td>
</tr>
<tr>
<td><strong>Chapter 7</strong></td>
<td>113</td>
</tr>
<tr>
<td>Right Sided Congenital Diaphragmatic Hernia: Diagnostic, Prognostic and Therapeutic Implications</td>
<td>Aneela Bidiwala, John Bishara and Sathyaprasad Burjonrappa</td>
</tr>
<tr>
<td><strong>Index</strong></td>
<td>131</td>
</tr>
</tbody>
</table>
Incisional hernia (IH) represents a postoperative abnormal orifice or weakness in the abdominal wall through which normally contained viscera protrude beneath the skin. This book examines the risk factors, prevention methods, and management options for incisional hernias. It also provides a biomolecular basis of IH; discusses the loss of abdominal domain; examines preoperative techniques for the management of giant hernias; studies intraabdominal pressure modification in “component separation” techniques for the repair of incisional hernias; reviews the incidence, and repair of IH after abdominal organ transplantation; and finally, provides an overview of the diagnostic, prognostic and therapeutic implications of right sided congenital diaphragmatic hernias (CDH).

Chapter 1 - Incisional hernia is one of the most common complications of abdominal surgery with an incidence reported in the literature of 3% to 35%. Different etiologies have been hypothesized, including wound infections, obesity, older age, steroid treatment, and diabetes. Many authors also believe that biological factors such as genetic connective tissue disorders play a role in the pathogenesis of the incisional hernia. Side by side with these factors, the type of laparotomy and suturing techniques have long been recognized as relevant conditions predisposing the development of this complication. In this respect, transverse abdominal incision is associated with a lower incidence of incisional hernia when compared with vertical incision. The optimal strategy of abdominal wall closure has remained an issue of ongoing debate and, to date, the optimal technique and material for abdominal fascia closure remains controversial. The repair of incisional hernia continues to be a challenging problem and various methods of repairs have been proposed. Each technique has its drawbacks and there are still controversies as to the best treatment. Traditionally, primary open suture repair is reserved for patients with small hernia defects, but the technique yields a high recurrence rate. In the last few decades, the introduction of prosthetic mesh has improved the results of hernia repairs and nowadays mesh is used in almost all patients who undergo incisional hernia repair. Laparoscopic approach has grown in popularity over the years and has become a widely used operative technique for treating incisional hernia. This minimally invasive approach has several potential advantages over open mesh repair, including a quicker return to normal activities, less postoperative pain, and a lower incidence of wound related complications. However, some studies have not definitely confirmed these advantages and have not shown significant difference in the recurrence rates between laparoscopic and open repair. In conclusion, the best treatment of incisional hernia is still under scrutiny. Laparoscopic incisional hernia repair is technically feasible, reliable, and
effective in many cases, but large and complex incisional hernias are best treated using open surgery.

Chapter 2 - “The history of hernia repairs and failures is, in many ways, the history of general surgery itself”. Over the years, the practice of Hernia repair has progressively evolved from tissue reconstruction to the modern era of mesh repair but, surprisingly the cumulative incidences for recurrence of both incisional and inguinal hernia repairs has displayed a linear rise. The causal etiology of incisional hernia is of fundamental relevance not only while selecting the optimum repair technique but also in other therapeutic approaches and methods. A number of studies have shown that formation of incisional hernia is associated with the wound closure technique. However, over the years a number of investigators have stressed upon the role of biological factors in modulating the repair process at the biomolecular level. Molecular research provides increasing evidence supporting involvement of connective tissue in abnormal wound healing with impaired scarring resulting in development of incisional hernias. Hence a deeper insight is necessary to understand the role of connective tissue derangement leading to these hernias which should include an in depth analysis of biomarkers indicating the collagen activity in the wound matrix.

Chapter 3 - Despite improvements in surgery, incisional hernias are still too frequent a complication of laparotomy, ranging in incidence from 2% to 50%. Many of these hernias will have a complex course due to the progressive enlargement of the abdominal wall defect. When the presence of a significant amount of bowel becomes too large and the hernia becomes irreducible, the condition is referred to as an incisional hernia with a loss of domain (IHL). Historically, the bowel and other displaced viscera were said to have lost the right of domain or lost the right of domicile. This review is intended to elucidate the definition, why and how such hernias evolve and how to manage the difficult problems which can ensue. Only in the last four years has the concept of loss of domain been defined and recognized by the European Hernia Society as a clinical problem which has become a therapeutic challenge to surgeons and patients. Local and systemic pathophysiology, indications and contraindications to surgery as well as the prevalent modalities offered by the literature will be presented, augmented with the authors’ own experience. It will become evident that, in fact, hernias attended by loss of domain, should ideally be the preserve of a dedicated, interdisciplinary team made up of an experienced surgeon, reanimator, cardiologist and pneumologist.

Chapter 4 - The term “giant hernia” describes various clinical scenarios that are characterized by a ventral hernia of great size, with some degree of loss of domain and inability to achieve muscle closure with conventional techniques. The definition, the diagnosis and the surgical technique are not standardized and there are no randomized clinical trials or guidelines on giant hernias, thus the planning and surgical approach must be individualized carefully.

To succeed in the abdominal wall reconstruction procedure, the authors must optimize the patient’s respiratory, circulatory and immune system. In a second stage, the abdominal wall must be prepared by means of 3 different techniques: Progressive pneumoperitoneum to provide expansion of the abdominal wall, intrrafascial tissue expanders to make a gradual enlargement of the parietal tissue in a controlled manner, and mioaponeurotic relaxation with Botulinic toxin A, that elongates the lateral abdominal wall, leading to a reduction in the defect size.
Each of these techniques has several and different advantages, they can be used in combination with one another with a high rate of success.

Chapter 5 - Between 5 and 11% of abdominal surgeries are complicated by incisional hernias. The repair of these massive ventral hernias continues to be challenging for surgeons. The repair of these defects should ideally be tension-free, provide dynamic muscle support, and prevent eventration.

Surgical options are open primary repair, open repair with mesh, laparoscopic repair, or autologous tissue transfer or mobilization. Primary repair is rarely successful, with recurrence rates ranging from 18% to 62%. If synthetic mesh is added, recurrence rates dramatically drop to 2%-32%. Therefore reconstruction using pre-peritoneally placed prosthetic material is still the most frequently used technique. Anyway the increased risk of infection in case of wound complications and the rigidity of the abdominal wall are relative contraindications against the use of prosthetic materials.

An interesting alternative to traditional mesh are acellular dermal matrix, porcine intestinal mucosa and porcine dermal, used safely and effectively to successfully repair incisional hernias wherever the use of traditional permanent prostheses would not be safe.

An already standard technique, introduced in 1990 by Ramirez, Ruas and Dellon is the “components separation technique” characterized in bridging the fascial gap without the use of prosthetic material. The technique is based on the enlargement of the abdominal wall surface by separation and advancement of the muscular layers, thus allowing regaining to up to 10 cm of unilateral advancement.

A remarkable evaluation to be made is as the reconstruction with the component separation allows reducing the intra-abdominal pressure.

Normal intra-abdominal pressure in adults is less than 10 mmHg, whilst intra-abdominal pressure values over 15 mmHg are indicative of intra-abdominal hypertension. Prolonged increased intra-abdominal pressure over 20 mmHg is known to cause serious conditions such as acute renal failure, pulmonary impairment and reduced blood flow to the gastro-intestinal organs. In addition a vicious circle begins and increased intra-abdominal pressure causes elevation of the diaphragm, which is in turn followed by increased intra-thoracic pressure, and there is evidence suggesting that increased intra-thoracic pressure results in increased intra-cranial pressure and functional obstruction of the cerebral venous outflow via the jugular venous system.

The abdomen has a dynamic muscular wall that can accommodate marked variations in volume, which are accompanied by changes in intra-abdominal pressure. Repair of the incisional hernia causes extrinsic compression of the abdominal content and elevation of intra-abdominal pressure, especially in the first day after surgery. However intra abdominal pressure slowly decreases the days after surgery and stands on physiological values.

Chapter 6 - Patients undergoing abdominal solid organ transplantation have an increased risk of developing incisional hernia. The risk is higher following larger abdominal transplant surgery, such as liver (OLT) or simultaneous pancreas kidney transplantation (SPK). However, kidney recipients are also susceptible to hernia formation. Organ recipients are placed on immunosuppressive therapy after transplantation to prevent rejection of the new graft. It’s more frequently associated with impaired wound healing causing significant risk for developing incisional hernia. Transplant candidates are at increased risk given their baseline organ dysfunction too, just like end-stage renal disease (ESRD), liver cirrhosis or type 1 diabetes. The Ventral Hernia Working Group Grading System categorizes immunosuppressed
patients into the Grade 2 (comorbid) group including patients who have comorbidities that increase the risk for surgical site infection (SSI). Surgical site infection is a significant risk factor for hernia formation and the risk of SSI is even higher in immunocompromised patients who do not have the ability to respond normally to an infection due to a weakened immune system caused by immunosuppressive drugs. Data in the literature indicates that the mTOR-inhibitor sirolimus inhibits wound healing and several previous studies showed that high dose steroids and sirolimus cause higher rates of hernia formation. Hernia formation after kidney transplantation ranges from 1.6-18% in the literature. The use of MMF, obesity, age and female gender are risk factors. Hernia formation after liver transplantation ranges from 1.7-32.4%. Acute rejection (treated with steroids), postoperative thrombocytopenia, and Mercedes type incision, use of sirolimus and MMF, male gender, a higher BMI, and a MELD score greater than 22 are risk factors in liver recipients. Rates of incisional hernia after pancreas transplantation are also high, ranging from 13 to 34.8%. High-dose immunosuppression owing to immunogenicity of the pancreas leads to considerably impaired wound healing. Strategies focusing on prevention and early treatment of SSI and the appropriate choice of immunosuppressive agents may help to decrease the risk of incisional hernia formation following abdominal organ transplantation. If hernias develop, repairing the incisional hernias and using mesh in solid organ transplant recipients are safe methods in experienced hands.

Chapter 7 - The incidence of congenital diaphragmatic hernia (CDH) is approximately 1 in 2000-5000 live births. In the majority of fetuses with CDH, the defect is located on the left (85%), whereas right–sided (15%) and bilateral (<1%) defects are less frequent. The etiology of CDH is unknown, however, 2% of cases have been noted to be familial and another 15% of patients have associated chromosomal abnormalities. In CDH, the degree of lung hypoplasia is a major determinant of survival. Pulmonary hypoplasia results in respiratory insufficiency and pulmonary hypertension.

Right sided CDH (R-CDH) is a highly variable defect with many similarities to Left sided CDH (L-CDH), but with potentially important distinctions. R-CDH occurs through the defect resulting from failure of the anterior pleuropertitoneal membrane to fuse with the sternum and costal cartilages during embryogenesis. Controversy exist in regards with worse prognosis of RCDH as compared to left side, as review of literature reveals conflicting data.

There are several theoretical explanations suggest that impact of RCDH might be worse. First, right lung normally accounts for 57% of total fetal lung volume and any compromise on its development may have a larger clinical impact. Second liver herniation through diaphragm is more frequently seen in right sided defects, because of anatomic adjacency of the right lobe. The size of defect necessary to permit herniation of liver on the right side is likely to be substantially larger than left sided defects hence associated with poor outcome.

However, the underlying pathophysiology needs to be investigated further. Diagnosis of CDH can be made prenatally or postnatally after birth. Right sided defects appeared more difficult to detect prenatally compared with left sided defect partly due to the echogenicity of the liver. In recent years new ventilation strategies such as nitric oxide, gentle ventilation, high frequency oscillatory ventilation, and extracorporeal membrane oxygenation (ECMO) therapy were introduced and improved post natal prognosis.

The concept has changed from performing emergency repair to delaying repair for at least 24-48 hrs to allow for clinical stabilization and a fall in pulmonary vascular resistance.
Surgery can be delayed for up to 7-10 days. There is no evidence that timing of surgery influence survival. Repair of CDH can be performed effectively using different surgical approaches such as thoracic approach, abdominal approach or VATS or laparoscopic technique. Surgical repair may be more challenging in R-CDH because of near universal liver herniation as well as potential for anatomical anomalies uniquely associated with right sided defect.

This results in increase in morbidity in right sided vs. left sided survivors. To date, recognized prognostic factors for post natal outcome in newborns with CDH include pulmonary hypoplasia, intra-thoracic liver herniation, associated anomalies, prenatal diagnosis, low birth weight and prematurity.

Long term pulmonary morbidity in CDH consists of impaired obstructive and restrictive lung function from altered lung structure and underdeveloped pulmonary vessels.
Chapter 1

**INCISIONAL HERNIAS: RISK FACTORS, PREVENTION AND MANAGEMENT**

*Fabrizio Ferranti*  
Division of General Surgery-San Paolo Hospital,  
ASL RM/F Civitavecchia, Rome, Italy

**ABSTRACT**

Incisional hernia is one of the most common complications of abdominal surgery with an incidence reported in the literature of 3% to 35%. Different etiologies have been hypothesized, including wound infections, obesity, older age, steroid treatment, and diabetes. Many authors also believe that biological factors such as genetic connective tissue disorders play a role in the pathogenesis of the incisional hernia. Side by side with these factors, the type of laparotomy and suturing techniques have long been recognized as relevant conditions predisposing the development of this complication. In this respect, transverse abdominal incision is associated with a lower incidence of incisional hernia when compared with vertical incision. The optimal strategy of abdominal wall closure has remained an issue of ongoing debate and, to date, the optimal technique and material for abdominal fascia closure remains controversial. The repair of incisional hernia continues to be a challenging problem and various methods of repairs have been proposed. Each technique has its drawbacks and there are still controversies as to the best treatment. Traditionally, primary open suture repair is reserved for patients with small hernia defects, but the technique yields a high recurrence rate. In the last few decades, the introduction of prosthetic mesh has improved the results of hernia repairs and nowadays mesh is used in almost all patients who undergo incisional hernia repair. Laparoscopic approach has grown in popularity over the years and has become a widely used operative technique for treating incisional hernia. This minimally invasive approach has several potential advantages over open mesh repair, including a quicker return to normal activities, less postoperative pain, and a lower incidence of wound related complications. However, some studies have not definitely confirmed these advantages and have not shown significant difference in the recurrence rates between laparoscopic and open repair. In conclusion, the best treatment of incisional hernia is still under scrutiny.

*Corresponding author: Fabrizio Ferranti. E-mail: fabrizio.ferranti@fastwebnet.it.*
Laparoscopic incisional hernia repair is technically feasible, reliable, and effective in many cases, but large and complex incisional hernias are best treated using open surgery.

**INTRODUCTION**

Incisional hernia is one of the most common complications after abdominal surgery. More than 2 million laparotomies are performed annually in the United States [1] resulting in an incisional hernia rate of between 20% and 35% [2, 3, 4]. It is the most common indication for reoperation by a 3:1 ratio over adhesive small bowel obstruction [5]. Approximately 100,000 patients undergo incisional hernia repair annually in the United States [6]. Because of its high frequency, incisional hernia represents a social problem and a cost in terms of health care expenditure with a total estimated cost of 3.2 billion dollars yearly [7].

Several predisposing factors have been implicated in the development of the disease. Some of them are patient-related and others, of greater importance, are surgeon-related [3, 8, 9, 10, 11]. The quality of surgical technique is considered an important factor because incisional hernias are the only abdominal hernias that are iatrogenic in their origin [12]. There is also strong evidence that the disease may be associated with abnormal collagen metabolism and distinct genetic expression profile [13, 14, 15].

The natural history of incisional hernia involves its gradual enlargement over time. Patients typically present with an abdominal bulge and complain of discomfort [16]. Patients are also disconcerted by the cosmetic appearance in an already scarred abdomen. Moreover, incisional hernia has a detrimental effect on respiration and postural maintenance, which have a profound impact on the patient’s quality of life [10, 17, 18]. Incarceration or strangulation of the bowel in the hernia sac may occur in 3-10% of cases, and in patients in whom bowel resection is performed postoperative, the mortality rate is about 20% [19, 20, 21]. For these reasons elective operation should be the treatment of choice [22].

The repair of incisional hernias is a challenging problem and controversy exists regarding the ideal treatment. Despite the development of numerous techniques, incisional hernia recurrence rates range from 3% to 60% with an average of 25%, with considerable morbidity and mortality [23, 24, 25]. It has also been noticed that recurrences occur more rapidly than the initial hernia developed [26].

In the last few decades, the introduction of prosthetic materials and the “tension free repair” concept have improved the results of incisional hernia repair [27, 28]. Moreover, the laparoscopic approach, since its introduction in 1993 [29], has rapidly gained acceptance as an efficacious and reliable technique. The minimally invasive approach seems to have several advantages over the open approach, including a lower incidence of recurrence and fewer wound complications [30, 31].

The aim of this chapter is to review the etiology, risk factors, and prevention of the incisional hernia and analyze the outcomes and complications of the different surgical techniques employed for the treatment of the disease.
**Etiology and Risk Factors**

Many risk factors are regarded as responsible for the development of incisional hernias, including abnormal collagen and protease metabolism [32, 33, 34], obesity, smoking, aneurysmal disease, malnourishment, corticosteroids treatment and diabetes [3, 8, 12, 27, 35, 36]. All of the risk factors may contribute to incisional hernia, but no single factor is regularly associated with the disease [37]. Moreover, surgeon-related technical aspects are considered of great importance [38] because, as mentioned earlier, incisional hernias are the only abdominal hernias that are iatrogenic [12].

Biologic factors may play an important role for the development of the disease. Tissue from patients expressed immature collagen, increased amounts of collagen III and increased tissue matrix metalloprotease levels [39]. Furthermore, morphologic changes are present not only in the fascial tissue, but also in the hernia sac, skin specimens and scar tissue surrounding explanted meshes [40]. It has also been noticed that variations in gene expression may predispose either to primary or incisional hernias. Microarray analysis of skin and fascia of patients affected by incisional hernia have shown distinct gene expression profiles compared with those of normal patients [13]. Therefore, it has been suggested that the study of gene expression profiles may be used to stratify, preoperatively, patients into different groups at risk for incisional hernia development [13].

About 40% of obese patients who undergo open gastric bypass develop an incisional hernia [40]. Increased recurrence rates are also seen in overweight patients after repair of incisional hernia [41]. The recurrence is related to BMI and as the BMI increases so does the recurrence rate [42]. A decrease of 10% in incisional hernia development after bariatric operations has been reported when double-stranded PDS suture is used in closing laparotomy [43].

Smoking, reducing both blood and tissue oxygen tension, adversely influences healing of surgical wound [44]. It has been found that smokers who undergo abdominal surgery are at great risk for wound infection and incisional hernia [45, 46]. Thus, smoking cessation at least 4 weeks before scheduled surgery is advisable [47].

Patients who are malnourished or catabolic, such as in the systemic inflammatory response syndrome (SIRS) show impaired wound healing [40] and increased risk for both wound dehiscence and incisional hernia [42]. A serum albumin level less than 3.0 gr/dl is the most valuable predictor of poor surgical results and increased postoperative complications [48].

Perioperative glycemic control is beneficial for regular wound healing [49] and a glucose level of 140 mg/dl to 160 mg/dl seems to be the optimal glycemic range in the postoperative period [50]. Hyperglycemia has been shown to alter chemotaxis, phagocytosis and oxidative burst, which prevent the early killing of bacteria that entered the wound during surgery [51].

Wound infection is commonly reported as the most significant risk factor [9]. In patients who develop wound infection, incisional hernia incidence is reported in 23% of cases [8]. However, other studies did not find any correlation between the two phenomenons [38, 52]. Wound infection may delay the progression of acute wound healing process into the fibro-proliferative phase, where rapid gains in strength occur [53].
Steroids also have a detrimental effect on regular wound healing processes. It has been proved that steroids reduce the inflammation phase and inhibit collagen synthesis and wound contraction [54].

Aneurysmal disease has also been considered a risk factor for development of incisional hernia [2, 55, 56]. Patients who are operated on for abdominal aortic aneurysm (AAA) develop incisional hernias in 28.2% of cases [55]. It has been assumed that a pathologic extracellular matrix metabolism may predispose to dilated aorta and hernia [57]. However, when the quality of the abdominal wall closure technique is taken into account, the rate of incisional hernia is similar in patients operated on for AAA and in those operated on for other diagnoses [58].

Other predisposing factors are surgeon-related, such as the type of abdominal incision, the method of wound closure, the quality of suture, and the choice of suture material.

Many studies suggest that transverse incisions have a lower rate of incisional hernia than midline incisions [3, 8, 59]. A study found a 10.5% incisional hernia rate after midline incisions compared with a 7.5% rate after transverse laparotomy and a 2.5% rate after paramedian incisions [60]. It has been supposed that collagen architectural structure may play a role because collagen bundles in the abdominal wall are oriented transversally [61, 62]. Thus, transverse incision is more stable as it encircles tissue collagen bundles rather splitting them [40]. Growing evidence supports the theory that incisional hernias may be the result of the mechanical disruption of laparotomy, occurring during the acute phase of the healing process [40, 63]. It is assumed that incisional hernia develops during the early postoperative period, the main mechanism being separation of aponeurotic edges [37]. It is well established that the interactive bio-mechanical process, with sequential cellular and molecular elements of tissue repair, is activated during acute wound healing [15]. Mechanical signals related to intrinsic and extrinsic wound loads activate the mechanical pathway healing process with subsequent effect on fibroblast activity and collagen deposition [14]. Thus, even a mechanical wound failure alone may alter the normal healing pathway by reducing the biological signals, selecting an abnormal population of fibroblasts and ultimately impairing the fibroblast repair function [15, 64].

The tension on the suture line is a crucial factor that contributes to a regular healing process of laparotomy. In fact, the main mechanism of wound dehiscence is the suture cutting through the suture-holding tissue, with development of small defects in the suture line, which may evolve into protrusion and ultimately into incisional hernia [65]. It has been proved that in high-tension sutures the rate of incisional hernias is higher than in low-tension sutures because the soft tissue included in a tight suture is more compressed and necrotic than with low-tension sutures [66]. There is also strong evidence that the suture length (SL) to wound length (WL) ratio correlates strongly with laparotomy dehiscence [67]. A low rate of incisional hernia is found when the SL to WL ratio is 4 or more [68]. Moreover, closing abdominal walls with large, rather than with small stitches, is associated with a high rate of incisional hernias [69]. Based on these results, laparotomy should be closed with many small stitches at close intervals placed 5 to 8mm from the wound edge [65, 70].

Continuous versus interrupted closure in abdominal wound closure remains controversial. Continuous suture produces a stronger wound, is more rapid and spreads the tension equally over the wound length [71, 72]. However, many studies [73, 74, 75] reveal no significant difference in incisional hernia rate between continuous or interrupted suture. Mass closure versus layered closure also represents a matter of debate. It is presumed that closing the
wound in a single layer produces better results than a layered closure [76]. Furthermore including the peritoneum into the suture line does not increase the tensile strength and may contribute to the formation of postoperative adhesions [77].

The suture material is an important factor for incisional hernia prevention, because sutures contribute to wound strength for at least 6 weeks [62]. Slow absorbable monofilament suture material has shown the best results compared with quickly absorbable materials [78, 79] or nonabsorbable sutures, which may act as a saw in the fascia and may predispose to late incisional hernia formation [10].

In summary, many factors play a role in the development of incisional hernias but fundamentally, this complication occurs when the laparotomy fails to heal. The underlying mechanism is a combination of inadequate surgical techniques and the biology of wound-healing defects.

**TREATMENT**

Hard data about the natural course of incisional hernias are rarely reported in the literature [80]. However, it is well known that incisional hernias will continue to enlarge over time and about 10% of patients will present with incarceration or strangulation [4, 81] with subsequent high morbidity and mortality [82]. For these reasons, the presence of an incisional hernia is, itself, an indication for surgical treatment [16].

No ideal repair exists and several techniques have been proposed. Primary suture of the defect was employed especially in the early experience of incisional hernia repair. The most simple primary closure technique involves using continuous or interrupted sutures to approximate the edges of fascial defect. The technique should be performed only for small incisional hernias with fascial defects less than 4 cm in diameter and using non-absorbable suture [35, 61]. However, even if primary repair is limited to the treatment of small fascial defects, the procedure yields a high recurrence rate ranging from 25% to 63% [9]. Component separation technique (CST) is a type of primary suture in which relaxing incisions in the external oblique aponeurosis allows for movement of the rectus muscle on each side [83]. This approach has been advocated for large incisional hernias and in patients with wound contamination [84]. Recurrence after CST has been reported in 16% of patients after mean 12-52 months’ follow-up, and approximately 20% develop local complications such as skin necrosis and wound infection [85].

High recurrence rates associated with primary suture techniques have led to an increased application of a large variety of prosthetic mesh [17, 28]. Their systematic use led to a 50% decrease in hernia recurrence frequency [9] and nowadays a mesh is used in almost all patients who undergo incisional hernia repair [27]. Prosthetic mesh may be placed in different abdominal locations, either by traditional open approach or laparoscopically [86, 87, 88]. With an open approach, the prosthetic mesh can be placed above, (overlay), below (underlay) or in both sides of the fascia (inlay) [16]. Aforementioned terms are sometimes used without clarity and add difficulty in comparing different techniques [85]. However, there is compelling evidence that underlay positions (including intraperitoneal, properitoneal and retro-rectus location) are superior to other positions because they exploit the principle of
Pascal’s law [17, 89]. In laparoscopic approach, the mesh is always placed in underlay-intraperitoneal position [90].

Open overlay technique can be performed with or without primary closure of the fascia. Proponents of the former approach use the mesh to reinforce a primary closure, suturing a polypropylene mesh to the anterior rectus sheath [86]. The advantage of this approach is that contact between the underlying visceras and the prosthetic mesh is avoided. Disadvantages include a repair under tension and mesh infection when the wound becomes infected [25]. Onlay technique without closing fascial defect has the advantage of less tension on the repair, but exposes the mesh directly to intra-abdominal contents with the risk of erosion and fistulation of the prosthetic material into the gastrointestinal tract [16].

The retro-rectus mesh repair was primarily described by Stoppa [91] during the 1990s. This repair involves placing a polypropylene mesh to overlap the defect and keeping the hernia sac as a buffer between the mesh and intra-abdominal contents. Above the umbilicus, the dissection is carried out above the rectus fascia and underneath the rectus muscle, while below the arcuate line the dissection is performed in the preperitoneal space. A large polypropylene mesh is placed and secured with partial or transfixing sutures. The technique yields a recurrence rate less than 10%, while mesh infection is reported in 5-10% of cases and mortality is 1.8% [82, 88, 91]. Since the advent of bilayer prosthesis, intraperitoneal mesh repair has become a common approach. Its main advantage is that intraperitoneal location of the mesh allows for the largest overlap on the defect and a better tissue ingrowth [10]. The technique can be performed either laparoscopically or by a traditional open approach [88, 93]. The latter technique involves opening the hernia sac, dissecting adhesions from the abdominal wall, and placing the mesh with the non-adhesive surface facing against the abdominal contents. Fixation of the mesh prosthesis can be performed in different ways. Some [10] secure the mesh only to the fascial edges, others [94] fix the mesh to the posterior abdominal wall with partial or full thickness sutures. Restoration of the abdominal wall is performed by midline fascial approximation [28].

**Laparoscopic Repair**

Laparoscopic approach, since its introduction in the early 1990s [29], has become an important option for the treatment of incisional hernia. The technique seems to offer several advantages over the open approach including low risk of wound infection [94, 95], shortened hospital stay [96, 97], lower costs [98], and low recurrence rate [99, 100]. However many meta-analysis [96, 101, 102], comparing the outcomes of the two approaches include not just the incisional hernias but also primary ventral hernia repairs as well. Focusing on studies comparing the two techniques exclusively for incisional hernia, only 6 Randomizes Controlled Trials [94, 103, 104, 105, 106, 107] were found and no studies showed differences between the two procedures. An unquestionable benefit of laparoscopic repair is the ability to evaluate the abdominal wall fully permitting identification of remote or “Swiss-cheese” defects that might be missed with an open approach and predispose to a hernia recurrence [16, 108]. Several contraindications exist for the laparoscopic repair such as cardio-respiratory disease, strangulated hernias, “hostile” abdomen, and contaminated operative field [109]. Laparoscopic repair requires placing the mesh directly onto the peritoneum of the anterior abdominal wall [110]. Accessing the abdomen can be accomplished by either an open or
closed technique and both access methods are suitable. It is important to locate the first trocar as far from the hernia as possible, in order to avoid intestinal injuries. Adhesiolysis is performed with minimal use of cautery and the margins of the hernia defect are cleaned circumferentially to allow adequate room for prosthetic overlap. Content of the hernia sac is gradually reduced into the abdomen and the hernia sac itself is left in situ [90]. Mesh is inserted through a trocar site and fixed to the abdominal wall. Major controversy exists regarding the method of mesh fixation especially as regards the advisability of employing transfascial sutures along with tacks, or using tacks alone [111]. It has been demonstrated that additional transfascial suture fixation reduces the recurrence rate from 9% to 4% [112, 113]. However, several studies [99, 110, 114] have been shown that tacks only fixation is also a suitable technique with a recurrence rate of 4.4%. Recently, new fixation devices such as glue and staples have been developed with the advantage of less postoperative pain [115].

There is controversy surrounding the importance of restoration of dynamic abdominal wall function in the laparoscopic approach due to its technical difficulty with this procedure. However, reconstruction of the abdominal wall is advisable because it avoids bulging phenomenon and allows restoration of a dynamic abdominal wall with better functional and cosmetic results [116, 117].

**COMPICATIONS OF INCISIONAL HERNIA REPAIR**

Seroma is one of the most common complications in both laparoscopic and open incisional hernia repair [118]. Because the hernia sac is left in situ and drains are not used in laparoscopic approach, this complication is seen more often in the minimally invasive approach [16, 119]. The presence of seroma is so frequent that if it is carefully searched for, it can be detected in almost all patients. For this reason many surgeons [120] do not consider seroma itself as a complication unless they become symptomatic or persist beyond 6-8 weeks [30, 119]. Up to 80% of seromas are asymptomatic and resolve spontaneously by 90 days [121]. However, aspiration of seroma may be considered in patients with pain or in case the seroma persists after 3 months of observation [30].

Bowel injury is a severe, potentially lethal complication, which may occur during adhesiolysis. The incidence of iatrogenic enterotomy is 7.2% in open hernia repair and 9% in laparoscopic procedure [105]. Others [30, 122] have reported a lower frequency of bowel injury in laparoscopic repair with an incidence ranging between 1% and 3%. Prompt recognition of the injury is critical because the mortality in unrecognized bowel injury is 7.7% higher than in uncomplicated incisional hernia repair [112]. If an enterotomy occurs during an open repair, bowel injury is repaired and the hernia defect should be closed primarily [30]. The management of bowel injury during laparoscopic repair is controversial and different options are available, depending on the extent of contamination and injury, and on the surgeon’s experience. If gross contamination is present, the best treatment is to perform an immediate laparotomy and repair the hernia primarily [123]. If the bowel injury and contamination are limited, the enterotomy may be treated laparoscopically and the hernia defect repaired with mesh immediately [124]. An alternative is to repair the bowel injury and delay the hernia repair until after a period of inpatient administration of antibiotics [125]. In case of missed enterotomy, if there is a high index of suspicion, the patient should be taken to
the operating room without delay, and if contamination is found the mesh must be explanted, intestinal enterotomy repaired, and a primary abdominal wall closure performed or, alternatively, a biologic/absorbable mesh may be implanted [30, 110].

Significant persistent postoperative pain is a rare complication that occurs more often in laparoscopic repair with an incidence of 1%-3% [126, 127]. The pain, which is muscular in nature, is related to mesh fixation using transfascial suture. If the pain is intense, conservative treatment such as non-steroidal anti-inflammatory drugs or local anesthetics injection may be useful [119, 128].

Mesh infection is a severe complication that occurs more often in open approach than in laparoscopic repair with an incidence, respectively, of 8.2% and 1.1% [94, 129]. If a mesh infection is suspected and abdominal CT imaging reveals fluid collections and extensive inflammatory reaction, an open abdominal operation is required, and if the diagnosis is confirmed at exploration, the mesh is explanted [102, 130]. In patients with limited mesh infections and prosthetic materials other than ePTFE, a conservative treatment may be accomplished, with percutaneous drainage, local wound care, and prolonged antibiotics treatment [131, 132].

Incisional hernia recurrence is variable, as reported in the literature, and the reason may be that until 2014 most of meta-analysis reported on studies in which data on primary ventral hernias and incisional hernias were pooled [133]. Analysis of surgical repairs for specific type of hernias has shown that incisional hernia presents the highest recurrence rate (6.3%) compared with primary ventral hernia (2.3%) [133]. Furthermore, several studies [31, 134] have shown better results for laparoscopic incisional hernia repair with an incidence of recurrence of 3.1%, compared with open procedures in which the recurrence is 12.1%. However, as mentioned earlier, some meta-analysis showed no significant difference in recurrence rates between the two techniques with a reported incidence of 3.4% and 3.6%, respectively [102, 135].

Other factors have been shown to increase the risk of recurrence such as obesity, size defect mesh overlap, and previous repairs [30]. It is known that recurrences commonly occur at the mesh margin so a mesh overlap of 3-5 cm is required [112, 136]. Furthermore, the mesh should cover not only the fascia defect but also the entire abdominal incision [137]. The recurrence rate also increases with the size of the hernia defect and those greater than 10 cm have the highest risk of recurrence [138].

Finally, patients with a BMI less than 40 have a recurrence rate of 3.5% compared with 9.4% in patients with a BMI greater than 40 [139].

Cost may be considered a relative disadvantage to the laparoscopic approach. Operative room supply costs can be greater with laparoscopic repair than with the open approach ($2237 versus $664) and the operative time was longer as well (149 versus 89 minutes) [98, 140]. However, overall effective costs seem to be advantageous for laparoscopic repair and the lower cost with minimally invasive approach is attributed to fewer intensive care admissions, shorter hospital stays and reduced morbidity compared with the open approach [92, 98].
CONCLUSION

Incisional hernias remain a challenging problem with associated significant morbidity. There is a lack of consensus among surgeons regarding optimal treatment. The introduction of prosthetic mesh has improved the results of incisional hernia repair, lowering the recurrence rate. The laparoscopic approach is a well-accepted and effective option and its potential advantages such as reduced postoperative pain, shorter hospital stay, and fewer wound complications are enticing. However, there is still an important role for the traditional open approach, primarily in patients who present contraindications to a laparoscopic repair and in those with large parietal defects.

REFERENCES

Incisional Hernias: Risk Factors, Prevention and Management


[87] Temudon T, Siadati M, Sarr MG. Repair of complex or recurrent ventral hernia by using tension-free intraparietal prosthetic mesh (Stoppa Technique): Lessons learned from our initial experience (fifty patients). *Surgery* 1996;120(4):738-743;discussion 743-744.


[103] Navarra G, Musilino C, De Marco ML, Bartolotta M, Barbera A, Centorrino T. Retromuscular sutured incisional hernia repair: a randomized controlled trial to


Chapter 2

BIOMOLECULAR BASIS OF INCISIONAL HERNIAS

Manu Kaushik¹, Jasneet Singh Bhullar²,* and Vijay K Mittal¹

¹Department of Surgery. Providence Hospital and Medical Centers, Southfield, MI, US
²Department of Colorectal Surgery. University of Minnesota, Minneapolis – St.Paul, MN, US

ABSTRACT

“The history of hernia repairs and failures is, in many ways, the history of general surgery itself”. Over the years, the practice of Hernia repair has progressively evolved from tissue reconstruction to the modern era of mesh repair but, surprisingly the cumulative incidences for recurrence of both incisional and inguinal hernia repairs has displayed a linear rise. The causal etiology of incisional hernia is of fundamental relevance not only while selecting the optimum repair technique but also in other therapeutic approaches and methods. A number of studies have shown that formation of incisional hernia is associated with the wound closure technique. However, over the years a number of investigators have stressed upon the role of biological factors in modulating the repair process at the biomolecular level. Molecular research provides increasing evidence supporting involvement of connective tissue in abnormal wound healing with impaired scarring resulting in development of incisional hernias. Hence a deeper insight is necessary to understand the role of connective tissue derangement leading to these hernias which should include an in depth analysis of biomarkers indicating the collagen activity in the wound matrix.

Keywords: incisional hernia, biomolecular causes, collagen defects, ventral hernia, hernia

* Corresponding author: Jasneet Singh Bhullar MD, MS, Department of Colorectal Surgery, University of Minnesota Minneapolis - St Paul, MN, 55114, USA, Email- drjsbhullar@gmail.com.
INTRODUCTION

The first historical evidence on abdominal wall hernia are found in the reports from 14th century BC Egyptian papyrus and later in Hippocratic manuscripts of the 2nd century BC [1]. Unlike the other hernia forms, incisional hernias are unique that they are most commonly contributed by the surgeons themselves. Of all surgical incisions, at least 10-15% will develop hernia in time leading to nearly 150,000 patients requiring repair of ventral hernias per year in the United States [2]. The number is expected to decrease over the coming years secondary to extensive application of minimally invasive techniques for various abdominal operations. Technical aspects involved in wound closure are seen to be a common etiology, but the discussion should also include the concept of the biological factors influencing incisional hernia formation.

EPIDEMIOLOGY AND RISK FACTORS

Incisional hernias occur secondary to failure in the healing of the abdominal wall. It is believed that factors causing increased propensity towards developing an Incisional hernia are mostly iatrogenic, however over the years various previous and ongoing studies have stressed on the importance of the role of biological factors in the causation of such hernias of the abdominal wall. Table 1 illustrates a broad classification of factors contributing to Incisional Hernia formation.

<table>
<thead>
<tr>
<th><strong>Patient Factors</strong></th>
<th><strong>Iatrogenic</strong></th>
<th><strong>Biological</strong></th>
<th><strong>Genetic</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ageing</td>
<td>Inadequate fascial bites</td>
<td>Decreased collagen I/III ratio</td>
<td>Ehler Danlos Syndrome</td>
</tr>
<tr>
<td>Smoking</td>
<td>Increased tension over fascial edges</td>
<td>Fibroblasts disruption</td>
<td>Marfans Syndrome</td>
</tr>
<tr>
<td>Pulmonary-COPD</td>
<td>Tight sutures</td>
<td>Increased MMP’s</td>
<td>Osteogenesis Imperfecta</td>
</tr>
<tr>
<td>Previous Hernias</td>
<td>Broken Sutures</td>
<td></td>
<td>GREMLIN I gene</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Laparoscopic trocar site defects (&gt;10mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Co-morbidities-carcinomas, cirrhosis</td>
<td>Surgical site infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Intra-abdominal pressure-Obesity, Pregnancy, Ascites</td>
<td>Operative time&gt;2.5 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroid use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolonged ileus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MMP- molecular metallo-proteinases.
**Risk Factors for Incisional Hernias**

Various risk factors have been identified in order to prevent incisional hernias. However, the exact etiology of the development of such hernias is still not well understood and has been considered to be a combination of various multi-factorial processes. The factor considered to be of utmost importance is the surgical technique used for the closure of the abdomen. Inadequate fascial bites, tension on the fascial edges, a tight closure are few of the established technical causes. An early development of an incisional hernia post-operatively indicates the contribution of local factors like infection, suture tension, broken sutures, etc. Increased age can result in deficient or poor wound healing of the post-operative tissue and can result in hernia formation as well. Surgical site infection is also a dominant contributor to the causation of incisional hernias. It increases the risk to as high as 80%. Factors increasing intra-abdominal pressure like obesity, ascites, and pregnancy can act as major risk factors. In obese patients, fat can mask the tissue layers and hence increase the chances of developing a seroma or post-operative wound infection. Co-morbidities like carcinomas, liver cirrhosis and other chronic wasting disorders affect wound healing comprehensively and increase the risk of developing an incisional hernia. Pulmonary disorders like COPD and chronic smoking can result in vigorous coughing leading to fascial disruption. The modern era has seen the increased use of laparoscopic surgery for many abdominal surgeries. Inability to close the fascial defects more than 10-15 mm at the trocar sites can also predispose to hernia formation.

Imbalances in collagen metabolism and disruption of fibroblasts during healing have been considered to be the leading biological causes of hernia formation. Other factors like smoking, obesity, malnutrition, immunosuppression, surgical site infection and connective tissue and other genetic conditions have been widely studied and proven to be the major factors for developing incisional hernia.

**The Biology of Incisional Hernias**

The abdominal wall is a complex combination of soft tissue structures that provides the dual functions of maintaining the upright posture and free movement of the torso and also forms a protective barrier for the internal viscera by the communion of skin, subcutaneous tissue, fascia, muscles and the peritoneum. All surgical procedures targeting the viscera will have to wound the abdominal wall and it can be safely said that it becomes a common site of surgical morbidity. Herniation of the intra-abdominal structures through sites of potential weakness in the abdominal wall is becoming fairly common making abdominal hernia repairs the most common surgical operations performed in the United States with approximately one million cases annually [2]. Nearly 700,000 operations are for inguinal hernia, with an additional 100,000 for umbilical, epigastric, Spigelian, and flank hernia repairs [2, 3]. Over the years, the practice of Hernia repair has progressively evolved from tissue reconstruction to the modern era of mesh repair but, surprisingly the cumulative incidences for recurrence of both incisional and inguinal hernia repairs has displayed a linear rise. The history of hernia repairs and failures is, in many ways, the history of general surgery itself [2].
The causal etiology of incisional hernias is of fundamental relevance not only while selecting the optimum repair technique but also in other therapeutic approaches and methods. Some might question the supremacy of the technique implied by the surgeon for the repair while others might blame the patient’s anatomy. This ongoing debate has led to a number of hypothesis and arguments. Usually, hernias of the abdominal wall are regarded as a mechanical defect which has to be closed technically. In the history of general surgery, even the most experienced surgeons, irrespective of the utilized method of repair have constantly faced recurrences even after using the most meticulous repair possible. As a consequence, the general idea remains that the causation of incisional hernias involves a spectrum of a number of complex factors other than the operative technique itself. Patients with hernia and in particular those with incisional hernia are likely predisposed for recurrent hernia formation [5].

**Mechanism of Incisional Hernia Formation**

Incisional hernias are the most common cause of re-operation in abdominal surgery patients. There is increasing evidence that majority of incisional hernia result from laparotomy wound failure. A number of studies have shown that formation of incisional hernia is related to the wound closure technique. However, over the years a number of investigators have stressed on the role of biological factors in modulating the repair process at the bio-molecular level.

Molecular biological research provides increasing evidences of the involvement of connective tissue in abnormal wound healing along with impaired scarring resulting in the development of incisional hernias. A deeper insight is necessary to understand the role of connective tissue derangement leading to these hernias which should include an in depth analysis of biomarkers indicating the collagen activity in the wound matrix. A number of previous and ongoing studies support the statement that fascial separation is a phenomenon that is commonly observed in the early post-operative period when the wound tensile strength is minimal and leads to a delayed presentation of an abdominal wall herniation [7].

**ROLE OF COLLAGEN**

Collagen is the predominating structural component of the fascial planes and defects in the collagen metabolism can lead to delayed or even incomplete healing. Healing of a midline incision involves a complex interplay of countless mediators and an extensive interaction with collagen. Collagen possesses a long half-life in comparison to various growth factors and cytokines, hence offering the most reasonable explanation of the complex scarring and healing process [5]. Thinner collagen fibrils, an imbalance of type I collagen in relation to type III collagen, and increased levels of the collagen degrading matrix metalloproteinases (MMPs) have been reported in patients with inguinal and incisional hernias[8, 9, 10]. Abnormal collagen metabolism with formation of immature collagen isoforms was an early biological mechanism proposed for development of primary and incisional hernias [11, 12]. In recent years the studies on incisional hernias have shifted their focus to the concepts of
Biomolecular Basis of Incisional Hernias

Turnover of collagen in patients presenting with incisional hernias. Defects in collagen metabolism have been studied to play a pivotal role.

Loss of tissue structure and strength are the fundamental basis of incisional hernia formation. Fascial defects following midline incisions can be caused following replacement of fascial planes with scar tissue over time. This disruption of normal architecture can induce the expression of abnormal structural collagen which might explain the rising incidence of recurrent incisional hernias requiring surgical repair. It is an established proposal that the incidence of Incisional hernia increases with each attempt at repair [6].

Table 2. Different Types of Collagen

<table>
<thead>
<tr>
<th>Types</th>
<th>Location</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Skin, Tendon, Vascular ligature, viscera, Fascia, Bone</td>
<td>Resistance to tension</td>
</tr>
<tr>
<td>II</td>
<td>Cartilage, nucleus pulposus, notochord, vitreous body, cornea</td>
<td>Resistance to intermittent pressure</td>
</tr>
<tr>
<td>III</td>
<td>Reticular fibres, uterus, blood vessels, spleen, Lymph nodes</td>
<td>Structural maintenance in expansible organs</td>
</tr>
<tr>
<td>IV</td>
<td>Basal lamina, epithelium, glomeruli, lens capsule</td>
<td>Support and Filtration</td>
</tr>
<tr>
<td>V</td>
<td>Cell surfaces, hair, placenta</td>
<td>Tensile strength</td>
</tr>
</tbody>
</table>

So far 28 types of Collagen have been studied. Collagen can be divided into 5 major types as described in Table 2. The interstitial matrix is composed mainly of the combination of collagen I and III and small amounts of collagen V. It has been seen that collagen V facilitates the assembly and arrangement of collagen I fibers. In a recent study patients with three types of hernias were studied: Primary unilateral inguinal hernia, multiple hernias (>3 hernias), and incisional hernias. It was seen that in patients with incisional hernias, the turnover of type V collagen was decreased and the turnover for type V collagen was increased when compared with hernia free controls [14].

Collagen and metalloproteinase form the cornerstone of healing for any wound irrespective of its anatomical location. They largely influence the balance between the degradation and the healing processes of the tissue. A number of studies found reduced levels of matrix metalloproteinases, in patients with incisional hernia by application of western blot analysis [14]. Klinge et al. postulated that the decrease in the ratio of collagen I/III is because of concomitant increase in collagen III in the patients with incisional hernias/recurrent hernias [15]. Hence the quality of the parent tissue is of major significance and the primary determinant of the resultant tissue strength and stability [16]. Samples of tissues in patients with recurrent incisional hernias show an imbalance between collagen I/III ratio [17] as well as similar changes in the procollagen III/I mRNA ratio in the skin [18]. This ratio can be considered as a reliable predictor of wound healing. Type I collagen of all known variants is responsible for the mechanical strength of the resultant tissue secondary to its high tensile properties. Alterations of the collagen composition may occur secondary to alteration in collagen synthesis as well as turn over which in turn increases the elasticity of the resultant tissue. Collagen hemostasis is controlled by a degradation system, which is constituted by
molecular metalloproteases and there is a direct link between MMP-2 and collagen gene expression as collagen binding to discodin domain receptor II regulates MMP-2 gene transcription [19]. The MMPs are enzymes which are known to play a major role in the healing and remodeling of the extra cellular matrix. They often reflect the binding potential of the collagen to the surface molecules during regeneration. The MMP gene in human encodes for around 25 homologous enzymes that play a role in cleaving the collagen molecules [20]. Literature repeatedly stresses on the imbalances in the different types of collagen, but there is a need to study the interplay and role of various biochemical markers underlying these variations. MMP 2 has gained importance after various studies on tumor invasion. It is expressed in increased amounts by tumor cells and an increased MMP 2 concentration is seen near sites of tumor spread [21]. MMP-2 is also known as gelatinase A, a 72 kDa peptidase located in the 16q13 genomic region [1]. MMP activity is regulated by a number of factors such as regulation of gene expression, zymogen activation and inhibition of active enzymes by inhibitors such as alpha 2 macroglobuline and tissue inhibitors of MMP (TIMP’s) [22, 23]. Within the abdominal wall damaged collagen fibers are repaired through the sequelae of proliferation and remodeling [24].

**FIBROBLASTS**

In the initial phases of wound healing, fibroblasts populate the wound site by the process of proliferation which in turn is driven by an inter-play of growth factors and various mediators. Defects have been studied in the kinetic properties of fibroblasts cultured from laparotomy wounds and biopsies of hernia sites from rat models of incisional hernia by Franz et al. These defects led to an imbalance in collagen hemostasis and ultimately forming defective tissue with low tensile strength and hence low durability. Some studies used in vitro primary based culture systems to examine the fascial biopsies in patients with Incisional hernias. [25]. A microbiological and ultrastructural analysis of such samples showed fibroblast loss secondary to caspase activated apoptotic processes leading to alteration in the cytoskeleton and cell structure of the incisional hernia fascia. The fibroblasts displayed changes compatible with degenerative or auto-phagic processes and an increased sensitivity to apoptotic factor promoting cell death and tissue rupture [26].

The importance of the role of fascia was understood years after the advent of hernia repair techniques and it was established that this fiber layer grants structural integrity and strength to the tissue healing. The fascia is largely dependent on the quality of the extracellular matrix, which is invariably maintained by the fibroblasts and the apoptosis of fibroblasts leads to a low strength foundation of the healing fascia invariably increasing the incidence of incisional hernias post abdominal surgeries. The malicious alliance of pro inflammatory and proteolytic molecules, within the incisional hernia fascia modulated the fibroblast phenotype resulting in stable changes in the basic cellular machinery which will invariably impeded and modify the regeneration of the violated extracellular matrix [25]. The process of tissue regeneration / wound healing is an extensive process and shown in Figure 1.
Pioneer researchers of the past have described Incisional hernias to be a connective tissue disorder [26, 27]. Disorders such as Ehler Danlos syndrome, Marfans and Osteogenesis imperfecta are considered to have a high risk of developing Incisional hernia. In a micro-array based study by Calaluce et al. [28], showed distinct gene expression profiles in the skin of patients with recurrent incisional hernia. It also showed an association between GREMLIN1 and incisional hernia formation.

Ehler Danlos syndrome is an inherited collagen disorder and is frequently undiagnosed in the patients presenting for abdominal surgeries and repairs. A retrospective study by Girotto et al. to study the patients presenting with recurrent abdominal wall herniation with one or more prior repairs with mesh or autologous tissues concluded that patients with Ehler Danlos Syndrome were at an increased risk of failure of abdominal closure secondary to defects in collagen [29]. They reported gynaecological procedures to be the most common initial surgeries.

Fibrillin 1 has a major role in maintaining connective tissue stability [30 - 32]. Fricke et al. studied the role of fibrillin 1 gene mutations in the causation of incisional hernias [18]. They studied tissue biopsies of 22 patients (9 females and 13 males) and concluded that Scar samples of muscle fascia represented a reduction in fibrillar reactivity and some alteration in the distribution of fibrillin with presence of clots, thicker bundles and abrupt directional changes when compared to the non-scar tissue of patients without hernia. Fibrillin -1 acts as a reservoir for transforming growth factor beta 1 (TGF beta 1) via latent TGF beta -1 binding protein which binds to microfibrillar structures and fixes TGF Beta 1 [33]. Microfibrils with fibrillin-1 promote the development of elastic fibers which inturn provide mechanical support to the healing tissue. Disturbed cellular interactions lead to a deranged aggregation and damaged polymerization of fibrillin 1 monomers leading to the development of unstable
microfibrillar polymers. Fibrillin 1 defects can also be seen in various microfibrillopathies [32] and further studies are needed to further understand the relation between these mechanisms and incisional hernia formation.

INCISIONAL HERNIA AND THE LAPAROSCOPIC SURGEON

The modern era of General surgery has witnessed an extensive application of laparoscopic techniques for various abdominal surgeries. Laparoscopy is not only minimally invasive but is associated with less post-operative pain and shorter hospital stay. The first known report of port site hernia was reported by Tonouchi et al. [34]. Port site herniation is a known complication but it’s becoming more significant following the expansive implication of laparoscopy for surgeries. A number of factors have been considered responsible for port site herniation over the years. Table 2 summarizes some of the known risk factors for incisional hernia formation after laparoscopic procedures.

Table 3. Risk factors for port site incisional hernia formation

<table>
<thead>
<tr>
<th>Risk factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patient factors</td>
<td>Obesity</td>
</tr>
<tr>
<td></td>
<td>Preexisting hernias</td>
</tr>
<tr>
<td>2. Location of trocar</td>
<td>Umbilical (most common)</td>
</tr>
<tr>
<td>3. Operative factors</td>
<td>Port size &gt;5mm</td>
</tr>
<tr>
<td></td>
<td>Extension of port size, manipulation and reinsertion of port</td>
</tr>
<tr>
<td></td>
<td>Drain through port site</td>
</tr>
</tbody>
</table>

The location of the hernia formation varies but Umbilical incisional hernias have been demonstrated by numerous studies [35, 36]. However other trocar sites are also involved but the incidence is relatively lower in comparison to the umbilicus [37]. Certain patient factors like preexisting umbilical hernias have also been noted to be of vital importance. Nasser et al. reported 12% of patients undergoing laparoscopic cholecystectomy had a preexisting umbilical and para-umbilical defects of which around 83% were asymptomatic [37]. Obesity is a known risk factor for causation of incisional hernias in patients who undergo laparoscopic surgeries. Studying an incisional hernia on an obese patient can be challenging but there is plenty of supportive literature to understand and establish the correlation [38].

Operative risk factors like trocar diameter more than 5 mm have been known to be associated with port site incisional hernias [39 - 41]. Certain reports have also shown that manipulation and re-insertion of ports can lead to herniation [38]. Also certain surgeons tend to extend the port incision for the extension of the gall bladder during cholecystectomies and this invariably acts as a contributor towards the development of incisional hernias [42]. Placing of drains through the port site can also be an etiological factor for hernias [43].
CONCLUSION

Incisional hernia is one of the most common complication seen after laparotomy. The failure of various surgical approaches and techniques has prompted extensive research for understanding the pathophysiology behind the causation of incisional hernias. A number of known risk factors have been studied and described over the past few decades. It has been concluded that collagen metabolism has a strong correlation with the development of incisional hernias. Biomolecular research is providing increasing evidence of the involvement of connective tissue in abnormal wound healing along with impaired scarring resulting in hernia formation. More research is suggested to understand the role of biomolecular factors affecting collagen metabolism in the wound matrix which in turn leads to incisional hernias.

ACKNOWLEDGMENT

The chapter was reviewed by Gokulakkrishna Subhas MD, Department of Colorectal Surgery. Robert Wood Johnson – Rutgers University, New Jersey, USA.

REFERENCES


[18] Fricke, M; Langer, C; Brunner, E; Sakai, L; Fuzesi, L; Reinhardt, D; Quondamatteo, F. Fibrillin 1 in incisional hernias: an immunohistochemical study in scar and non scar regions of human skin and muscle fasciae. *J Anat.*, 2008 May, 212(5).


[21] Salameh, JR; Talbott, L; May, W; Gosheh, B; Parminder, JS. Role of Biomarkers in Incisional hernias. *American surgeon*, vol. 73, 561-68.


[30] Dietz, HC; Cutting, GR; Pyeritz, RE; Maslen, CL; Sakai, LY; Corson, GM; Puffenberger, EG; Hamosh, A; Nanthakumar, EJ; Curristin, SM. Marfan syndrome caused by a recurrent de novo missense mutation in the fibrillin gene., 1991 Jul 25, 352(6333), 337-9.

[31] Pereira, L; Andrikopoulos, K; Tian, J; Lee, SY; Keene, DR; Ono, R; Reinhardt, DP; Sakai, LY; Biery, NJ; Bunton, T; Dietz, HC; Ramirez, F. Targetting of the gene encoding fibrillin-1 recapitulates the vascular aspect of Marfan syndrome. Nat Genet., 1997 Oct, 17(2), 218-22.


[35] Coda, A; Bossotti, M; Ferri, F; Mattio, R; Ramellini, G; Poma, A; Quaglino, F; Filippa, C; Bona, A. Incisional hernia and fascial defect following laparoscopic surgery. Surg Laparosc Endosc Percutan Tech., 2000 Feb, 10(1), 34-8.


[39] Shafer, DM; Khajanchee, Y; Wong, J; Swanström, LL. Comparison of five different abdominal access trocar systems: analysis of insertion force, removal force, and defect size.


Chapter 3

INCISIONAL HERNIA WITH LOSS OF ABDOMINAL DOMAIN

Valentin Oprea*, MD, PhD, and Florin Buia, MD
Department of General Surgery,
Constantin Papilian Emergency Military Hospital, Cluj-Napoca, Romania

ABSTRACT

Despite improvements in surgery, incisional hernias are still too frequent a complication of laparotomy, ranging in incidence from 2% to 50%. Many of these hernias will have a complex course due to the progressive enlargement of the abdominal wall defect. When the presence of a significant amount of bowel becomes too large and the hernia becomes irreducible, the condition is referred to as an incisional hernia with a loss of domain (IHLD). Historically, the bowel and other displaced viscera were said to have lost the right of domain or lost the right of domicile. This review is intended to elucidate the definition, why and how such hernias evolve and how to manage the difficult problems which can ensue. Only in the last four years has the concept of loss of domain been defined and recognized by the European Hernia Society as a clinical problem which has become a therapeutic challenge to surgeons and patients. Local and systemic pathophysiology, indications and contraindications to surgery as well as the prevalent modalities offered by the literature will be presented, augmented with our own experience. It will become evident that, in fact, hernias attended by loss of domain, should ideally be the preserve of a dedicated, interdisciplinary team made up of an experienced surgeon, reanimator, cardiologist and pneumologist.

INTRODUCTION: INCIDENCE OF INCISIONAL HERNIAS

An incisional hernia (IH) is defined as a postoperative, abnormal weakness or orifice in the abdominal wall, through which normally contained viscera protrude beneath the skin. The herniated visceral mass is always enveloped by a serous sac in continuity with the parietal

*Corresponding author: V. Oprea. E-mail:opreacv31@gmail.com, tel: 00 40 745608567.
peritoneum [1, 2]. Most of the masses present as a bulge underneath the area of the postoperative scar. The main reason for the presentation of these patients is usually a visible bulge, a mass palpated at examination or confirmed through imaging techniques.

Despite the considerable improvements in surgical know-how (innovations, suture materials, suturing techniques, mesh, and laparoscopy), the incidence of incisional hernia, recurrences and complications remains high. The frequency of these appear to be on the rise due to more complex, extensive surgeries in an older, higher risk patient group, an increasing population and longer life expectancy. All these factors underline the fact that the topic is one of major medical and economic importance [3, 4]. The attendant morbidity and mortality of IH must never be underestimated. Mortality following elective repair has been reported to be as high as 5.3% [5]. Complications of a serious nature: adhesions, bowel obstruction, intestinal fistulas, loss of domain can wreak havoc in a patient’s quality of life [6, 7]. In addition, cosmetic appearances can be most unrewarding.

The true incidence of IH with associated loss of domain is difficult to determine as evidenced by the wide range of the published data in the literature. The published incidence of primary IH depends on the methodology, the length of the follow-up, the objectivity of the clinical examination but also on the study of the patients’ characteristics. The longer the follow-up, the higher the incidence of IH as reported recently by Fink et al. [8]. They concluded that a one year follow-up in the detection of IH was not sufficient and that 3 years should be a mandatory requirement. According to Muysons et al. the incidence of IH after 23.8 months is 12.8% but the rate can be as high as 69% in a prospective follow-up of high risk patients [9]. An estimated range of incidence of IH has been observed to be between 2% and 30%; this complication can be doubled in the presence of infection following laparotomy [10, 11, 12, 13].

The number of IH repairs has been escalating annually while the recurrence rate has remained constant [4]. The estimation of the incidence of IH is a challenge fraught with dramatic swings between over and under-estimations. In the US, 4-5 million laparotomies are performed with an optimistic estimation of 400,000 to 500,000 cases of IH, annually. On a yearly basis, 200 000 IH are repaired with associated costs (societal: employers, patients, hospital and lost productivity). From 2008 to 2009, approximately 381 000 cases of IH were reported with an expected annual increase of 1-2% [3, 14, 15, 16].

Flum reported a 3.7% annual increase in the incidence of IH repair per 100,000 population in the state of Washington [17]. The growth rate may simply be the result of an increase in the frequency of abdominal procedures and Flum predicted that 153 000 cases of IH were likely to develop. Rutkow, in the same year reported 105 000 IH repairs at a cost of $ 2.5 billion [18]. In a 5 year span (2001-2006) Poulose in the US reported an increase of 22% in the incidence of IH (126,548 to 154,278) at a cost of $ 3.2 billion [19]. In Italy, a similar increase in IH repairs from 1999 to 2003, was calculated at 20% [20].

**LOSS OF DOMAIN: WHAT IS IT?**

Hernia defects are not all alike. They differ in their anatomic complexity but also in their associated co-morbidities and surgical history [21]. It will be important to clearly define these entities in order to avoid misinterpretations.
According to the European Hernia Society (EHS), IH must be classified depending on location, size (the width of the defect being more important than its surface area) and the number of previous repairs [22]. The hernia gap is the leading parameter for tailoring IH surgery [3, 22]. Many of the IH - 21% according to Stoppa - are IH which are difficult to repair but also time consuming [5]. Stoppa labeled them complex hernias and since then, a large number of herniology scholars have recently described what characterizes a complex hernia [23]. A constant and most frequent feature of an IH is its large size. Such a large hernia accompanies an abdominal wall defect, with a width greater than 10-15 cm [1, 2, 24]. Atrophy of the muscular wall, a large amount of visceral content permanently outside the abdominal cavity within a sac forming a secondary abdominal cavity has come to define IH with loss of domain (IHLD) or simply loss of domain (LD) [2, 11, 23, 24].

Despite the substantial literature covering IH, loss of domain itself has been poorly singled out because of the paucity of clinical data which invariably has come from limited series from surgeons whose interest in this discipline is highly focused and specific. The first report of IHLD dates back to 1943. Goni-Moreno pointed out that the loss of domain meant the inability of the abdominal cavity to reintegrate the externalized viscera without increasing the intra-abdominal pressure (IAP) beyond the critical pressure of 15 mm Hg [14]. Chevrel on the other hand, defined IHLD as an IH with an irreducible sac and contents because of adhesions, with a defect larger than 10-15 cm in width and larger than an area of 100-225 cm$^2$ [2]. Lastly, Kingsnorth defined loss of domain as the clinical picture whereby more than 20% of the abdominal content lies outside the abdominal cavity [25].

Rosen proposed a multi-factorial classification for IHLD which differentiated a hernia defect as large or small, the presence or absence of infection and the size of the hernia sac with its externalized contents [26]. These patients can then be classified in two groups: Group 1: non-contaminated with small defects and large sacs or massive defects with massive sacs; Group 2: contaminated with small defect and massive sacs or massive defects with huge sacs. The second group, those patients with enterocutaneous fistulas, infected meshes and stomas are deemed difficult and challenging situations often with limited options.

The initial clinical examination of an irreducible hernia is an important step in the evaluation of the IH but is insufficient even while a clear diagnosis is established [27]. This is because an irreducible IH may be of a size which will permit re-integration without exceeding the capacity of the abdominal cavity to adapt to that re-integration [28, 29]. The axiom which suggests that “you know it when you see it” no longer applies to the evaluation of IHLD. All attempts to assess the degree of herniated viscera dates back to the 1950s when Kather and Neto advocated a calculation of the volume of a hernia sac with tape and pelvimeter, thus computing the volume of the resulting ellipse [28].

A new parameter for evaluation and classification of LD was introduced by Ammaturu and Bassi [30]. Considering the shape of the anterior abdominal wall to be somewhat of an irregular hexagon, the surface of the abdominal wall (SAW) was obtained by multiplying the length of the inter-iliac line with that of the length along the xypho-pubic line. The surface of the wall defect itself (WDS) was also calculated using a computerized model. A SAW/WDS ratio of 15 and under was considered to be a prognostic sign of early post-operative complication due to inordinate tension. The ratio correlated with intra-abdominal pressure (IAP). Unfortunately, the method turned out to be complex and was not adopted as a useful adjunct to evaluation.
Tanaka et al. evaluated prospectively 23 patients with IHLD through the use of abdominal computed tomography (ACT) between 2001 and 2008 [31]. They concluded that the ACT provided reliable objective data for the calculation of the volumes of the hernia sac, the abdominal cavity but also the necessary volume of gas needed for insufflation in a progressive preoperative pneumoperitoneum (PPP). The abdominal cavity and the hernia sac could be considered to be ellipsoid structures. Measuring the cranio-caudal, transverse, and antero-posterior diameters of the abdominal cavity (A,B,C) and hernia sac (a,b,c) the volumes could be calculated using a simplified formula \((\text{Vol} = 0.52 \times A \times B \times C)\). Based on the relationship between abdominal cavity volume (ACV) and hernia sac volume (HSV) the volume ratio (VR) \(\frac{HSV}{ACV}\) was calculated. Without specifying how this value was arrived at, a cutoff ratio of 25% for VR was established. A volume ratio (VR) greater than 25% was considered to be significant prognostic reading for LD.

By measuring these same volumes but adding a new parameter, a peritoneal volume (PV) (which results from the summation with ACV), Sabbach et al. calculated the ratio between HSV and PV. They concluded that a ratio larger than 20% was predictive of too tense a fascial closure [32].

Considering that both the hernia sac and the abdominal cavity are not exact geometric figures, deAranjo et al. measured the volumes of rat kidneys and spleen by water dislocation (direct method) and mathematical resolution (indirect method) [28]. No statistical difference was found between the two methods. The authors felt that they had confirmed the method of ACT evaluation.

**LOSS OF DOMAIN: HOW DOES IT APPEAR?**

Even when the incidence of IH is high, not all hernias result in a loss of abdominal domain. In its natural history the tendency of IH is to undergo progressive traction by the lateral muscles with the consequent enlargement of the herniated mass [24, 33]. As Flament et al. stated, the natural course of an IH takes about two years before the defect stabilizes [34]. It takes that period of time before most patients accept the inevitability of surgery so that the evolution of IH in its natural course, leading to loss of domain, is quite rare but not impossible! Most IHLD are the consequence of abdominal catastrophes: burst abdomen, extensive infections of the abdominal wall including chronic mesh infections, extension of primary or secondary tumors [35, 36].

*A burst abdomen* (open abdomen, acute postoperative abdominal wound dehiscence, acute wound failure) is a severe, potentially life threatening complication of abdominal surgery, consisting of an acute mechanical failure with rupture of a wound and separation of the abdominal fascial edges [37, 38, 39]. Intra-abdominal organs protrude through the wound. The overlying wound edges may not have separated (type I burst abdomen) or they may have separated (type II) revealing an evisceration [40].

The reported incidence of burst abdomen varies between 0.2 and 5% of all laparotomies, with a slight increase to 7% in specific populations undergoing emergency operations or peritonitis [37, 39, 41, 42]. The last century has seen no improvement in the incidence of burst abdomen (Table 1) [43, 44].
The burst abdomen can be associated with a significant morbidity and high mortality rate, from 4 to 56% [41, 45]. Cöl reported a strong correlation between the number of risk factors present for abdominal wound dehiscence and mortality rate: 30% for 7 risk factors and 58% for 8 risk factors [46]. Presentation of a burst abdomen is typically around the 8th postoperative day, ranging from 5 to 14 days; detection of a serious or sero-sanguineous wound exudate prior to dehiscence is reported in 84% of the cases. If the dehiscence is complete, about 2/3 of patients in our experience (unpublished data), the bowel is edematous and protrudes outside the abdominal cavity. Frequently, it is associated with fascial necrosis and infection. A specific sign for early detection of wound disruption is a low skin temperature about the wound. What does it mean? Possibly delayed epithelial recovery, reduced presence of inflammatory cells and reduced collagen production [45].

Intra-abdominal infection is present in up to 40% of the patients. The presence of contamination and infection imposes a difficult and challenging problem for the surgeon.

Table 1. Incidence of burst abdomen

<table>
<thead>
<tr>
<th>Period</th>
<th>Number of Laparotomies</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1900-1940</td>
<td>71,000</td>
<td>0.4%</td>
</tr>
<tr>
<td>1950-1983</td>
<td>20,000</td>
<td>0.59%</td>
</tr>
<tr>
<td>1985-1998</td>
<td>18,000</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

Surgical treatment becomes a must when complete dehiscence occurs but consistent guidelines on the course to follow are yet to be established. Conservative management of the burst abdomen is a viable option in small defects, when the condition of the patient is poor, or if there is a high risk of bowel injury. For these patients, the incidence of loss of domain is 100%.

Suturing has traditionally been the most common treatment option for a burst abdomen. It is not the optimal technique because of its 50% or higher incidence of recurrence, its high mortality (60%) and high recurrence rate IH [47]. Closure with a running, slowly absorbable monofilament suture could be a sound option for younger patients with few co-morbidity issues in whom the cause of the rupture has been purely a matter of technique: slippage of knots, broken sutures, etc. [44]. Retention sutures are marred by high recurrence rates and are painful [3].

Patients with large defects which would result in tension when closed, need a mesh repair. But studies are inconsistent on the use of synthetic meshes especially in the presence of infection. Van’t Riet et al. reported a series of 18 patients with abdominal wall defects repaired with mesh in the presence of infection [39]. 15 patients (77%) developed a mesh infection with 18 different bacteria identified from the abdominal cavity. Mesh was removed from 8 patients with a global mortality of 56%. In survivors, the rate of recurrence of IH was 63%.

There is no convincing evidence to support a preference for in-lay, on-lay or sub-lay position of the mesh. All meshes can be used whether they are absorbable or non-absorbable. The use of polypropylene mesh implies a high complication rate in a septic environment [39]. For patients with large defects and intra-abdominal infections, the best option appears to be a multistage repair accepting the fact of a planned ventral hernia (see below).

The use of negative pressure wound therapy may be a valid option. Heller reported on 13 patients with a successful primary fascial closure in 9 [46].
Convincing evidence regarding an ideal management of burst abdomen is sadly lacking, with so many issues yet to be studied, this discipline is in dire need of dedicated talent.

The open abdomen is a strategy used to avoid or treat an abdominal compartment syndrome, severe abdominal trauma, abdominal sepsis, or mesenteric ischemia. It has reduced the mortality in both traumatic and non-traumatic abdominal catastrophes but has also created a challenging clinical problem [49]. Even with the recent, temporary, abdominal closure techniques, after resolution of the primary intra-abdominal pathology, the fascial edges may not come together. The result is a large abdominal wall defect which may be difficult to manage [50]. The skin, also, may not be enough to cover the defect. In such a situation, a planned ventral hernia is a management strategy in which the viscera are covered with split thickness skin grafts [40]. In these cases, a hernia is a favorable outcome which can be repaired when it is safe, possible, and tolerated by the patient.

Brandl et al. recently reported a large series of 209 patients with open abdomen, treated by negative wound pressure and delayed fascial closure [51]. Mortality was 21% (44 patients) and planned ventral hernia was used for 7% of the survivors (12 patients). In 21 patients the abdominal wall defect was larger than 15 cm in width. The authors reported that 35% of patients with an open abdomen developed an incisional hernia in a median follow-up of 26 months. Kaplan-Meyer analysis estimates an IH rate of 52% to 66% at 3 and 5 years respectively.

In 1994, Fabian et al. reported on the staged management of acute abdominal wall defects which ended with a planned ventral hernia repair and loss of substance from 10 to 25 cm in width [51]. After resolving the intra-abdominal pathology, an absorbable mesh was placed over the bowel for an average of 14 days (range: 3 to 30) in 91 patients. 12% developed enteric fistulas, most of them mesh-related. After mesh removal split thickness skin grafts were placed over the bowel creating a planned ventral hernia. Similar algorithms and results were reported later [52]. The method has many disadvantages: a two staged procedure is costly and increases the risk of enterocutaneous fistulas. Skin grafts are not stable and can ulcerate. The resulting abdominal wall defect is difficult to manage and has a high complication and recurrence rate. Cheatham et al. reported that the method significantly decreased perception of physical, social and emotional health [53].

The infected mesh contaminated hernias are often the product of multiple recurrences, contain enterocutaneous fistulas or have infected materials [54]. After removal of the infected material and take down of the fistula, the surgeon is often faced with a large defect. If a biological ‘mesh’ is not available a multistage approach could yield a favorable outcome.

Necrotizing soft tissue infection is a rare but potentially fatal broad spectrum of infectious processes that include but are not limited to necrotizing cellulites, necrotizing fasciitis, and myonecrosis [55]. Usually, they are polymicrobial infections caused by mixed aerobic and anaerobic flora (Streptococcus spp, Staphylococcus spp, Peptostreptococcus, Bacteroides, Clostridium, Enterobacteriaceae) [56, 57]. The reported incidence is 0.40/100.000 adults with a male to female ratio of 3:1. Mortality is very high (60-70%) and of the survivors, most will develop large and complex abdominal defects.
LOSS OF DOMAIN - WHY OPERATE?

In the last 50 years, major research on IH focused on improvement of surgical techniques, meshes and quality of life. More than 4000 peer reviewed papers were published. Despite this large body of work, very little evidence based data are available on the natural course or indications for IH repair [1, 58]. Little appears to be known about the actual complaints or symptoms from the patients before surgery. It is assumed that they are present in almost 1/3 of patients but what they are is rarely reported [59]. While the surgical treatment of an asymptomatic IH may be argued, in an IHLD that argument disappears and surgery is almost always, a must. The natural history of IH is a gradual increase in size according to Laplace’s law. As IH enlarges, complications occur and these become part of its natural history [34].

IHLD must never be simply considered a “hole” in the abdominal wall. In 1973, Rives properly named it “incisional hernia disease” because of the dangers of the externalization of viscera and the presence of serious complications [60]. In this condition, we are dealing with a complex patient and a complex hernia [23]. All these defined characteristics make IHLD different from ventral hernia or uncomplicated IH [14].

Generally speaking, patients with IHLD have a poor quality of life resulting from a combination of muscular disturbances, chronic gastrointestinal pathology and psychosocial issues. The abdominal wall of these patients is invariably compromised, quantitatively and qualitatively due to the loss of muscular and fascial tissue [29]. Those functions of the abdominal muscles are presented in Table 2.

Table 2. Abdominal Muscle Functions

<table>
<thead>
<tr>
<th>Flat muscles:</th>
<th>Increase IAP to facilitate defecation, micturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>External oblique</td>
<td>Stabilize trunk</td>
</tr>
<tr>
<td>Internal oblique</td>
<td>Tensor of the abdominal wall</td>
</tr>
<tr>
<td>Transversus abdominis</td>
<td>Flexor of the vertebral</td>
</tr>
<tr>
<td>Rectus abdominis muscle</td>
<td>Stabilizes the pelvis during walking</td>
</tr>
<tr>
<td></td>
<td>Protects viscera</td>
</tr>
</tbody>
</table>

The “primum movens” of all disabilities is the absence of the structural integrity of the abdominal wall, the mechanical resistance of the trunk secondary to the lateral muscular retraction of the flat abdominal muscles and significant external protrusion of viscera.

The absence of the normally functioning abdominal muscles leads to the restriction of daily activities which in turn, worsen the overweight. The lack of activity of the anterolateral abdominal group of muscles is a major hindrance to the back muscles which are not counterbalanced by the abdomen. As a consequence, the spine is strained into a dorsal kyphotic accentuation and postural reflex contraction of the vertebral musculature. Back pain becomes a major symptom for which no statistics on prevalence are supplied in the literature [14, 26].

As a result of the absence of activity and purpose, the muscle fiber loses its contractile ability and becomes shorter [2]. A defect as large as ¼ of the abdominal circumference leads to retraction of the composite layer of the abdominal wall (internal oblique muscle and transversus abdominis muscle) by 20% on each side [61]. The internal oblique muscle
develops a pattern similar to that seen in mechanically unburdened muscles: fibrosis, disuse atrophy, changes in muscular fiber composition (see Table 3) [61].

The fibrosis is a result of perimysial type I and type III collagen increased deposition. Mechanical properties are also altered: reduced compliance and shrinkage, increased tissue stiffness.

All these transformations act as a trigger for microstructural and biochemical muscle and fascial alterations. Structural integrity and function of the fascia depends on the quality of its extracellular matrix (ECM) which is synthesized by the resident fibroblasts. The absence of mechanical stresses and strains leads to inhibition of the mechanotransduction mechanism which controls the repair signals. The absence of strain results in decreased cell proliferation and modification of orientation angle of the fibroblasts [62]. These results sustain the study of Rosch et al. who described the controlling mechanisms of differentiation, proliferation and proteolysis [63]. Diaz et al., in human incisional hernia fascial biopsies found thinning of the ECM with significant reduction in fibroblasts density [64]. Also a phenotypic transformation of IH fibroblasts was described; they have a bipolar fusiform shape, reduced cross sectional area, fewer active microfilaments, and a short replication rate. The modifications are reversible after abdominal wall reconstruction because load bearing soft tissue repair faster than non-load bearing and the fibroblast cellularity is increased with increased type I and type III collagen expression as stated by Dubay et al. [61].

**Table 3. Internal oblique muscle development pattern**

<table>
<thead>
<tr>
<th>Decreased type I muscle fibers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased type II a muscle fibers</td>
</tr>
<tr>
<td>Decreased type II b muscle fibers</td>
</tr>
<tr>
<td>Selective atrophy of type II b fibers</td>
</tr>
<tr>
<td>(reduced crossed sectional area from 3916 μ to 2606 μ)</td>
</tr>
</tbody>
</table>

In patients with IHLD, respiratory insufficiency is a major feature. The alterations of the respiratory function are a summation of pathological factors related to extreme obesity, smoking and cardiovascular comorbidities connected to factors induced by the loss of domain: loss of the contribution of the abdominal muscles, decreased IAP and diaphragmatic impairment. Secondary dorsal kyphosis is another contributing factor for respiratory disturbances. In 1973, Rives emphasized the therapeutic problems and physiopathologic respiratory implications of large abdominal IH introducing the term “thoraco-abdominal compartment” to describe the link between the chest and the abdomen [65]. As a consequence of loss of domain with large amount of visceral mass outside the abdomen (“the second abdomen” of Rives), anatomical and functional modifications similar to those of the thoracic trauma, are produced. These complex alterations were named “volet abdominal” or “abdominal shutter.” This leads to a four phases “paradoxical respiration” [66]. Briefly, abdominal wall moves in and out during both inspiration and expiration being unable (together with the diaphragm) to contract against viscera no longer retained. During the inspiration the bowels are forced out.

The result is a major chronic respiratory insufficiency through reduced respiratory compliance (both pulmonary and thoraco-abdominal), increased resistance of the airways, decreased functional residual capacity, and decreased oxygenation. The whole mechanical
work of breathing is altered. In obese patients the presence of IHLD can mask all of these disturbances with an increased vital capacity, and increased residual volume/total lung capacity ratio. Trivellini reported that during the surgical repair of IHLD an increase of IAP leads to respiratory failure [65]. The postoperative increment of the abdominal cavity is associated with inhibition of the diaphragmatic activity with 15% as an adaptive relaxation that enlarges the cavity in a cephalad direction [67]. Also increasing of the IAP leads to an overall increase of the activity of the abdominal muscle by 18%, thus contributing to an increased IAP.

A decreased IAP induces disturbances in pressure within hollow viscera with chronic distension and chronic oedema of the mesentery and visceral wall. The viscera chronically outside the abdomen suffer gravitational chronic stretching and elongation which worsens the oedema. Portal circulation is also influenced and is a contributing factor in venous mesenteric stasis. In association with visceral adhesions and incompetent abdominal wall, all the above mentioned mechanisms lead to a poor bowel function, chronic micturition disorders, chronic abdominal pain and discomfort.

The last important changes are seen on the skin. Usually, secondary to the pressure of the viscera the covering skin becomes extremely thin due to an absence of the subcutaneous fat. Disorders of the subcutaneous circulation determine local ischemia at the top of the bulge with skin ulcers. This becomes a problem because ulcers are always infected and microorganisms are found at the edges of these ulcerations. The treatment is usually conservative with topical antibacterial agents rather than systemic antibiotics [34]. Another dermatological problem is intertrigo, more frequently seen in diabetic patients. Unlike trophic ulcers, which can’t be eliminated, intertrigo is easy to treat and eradicated before surgery.

**LOSS OF DOMAIN – WHEN TO OPERATE?**

_Evaluation of preoperative risk:_ safety is the primary goal in the surgery of IHLD. The surgical procedure could be a major, severe insult to an anatomically, physiologically and psychologically affected patient. The operative risk should be rigidly and objectively assessed to optimize results. A multidisciplinary approach (hernia surgeon, plastic surgeon, anesthesiologist, physical therapist, and nutritionist) will be more efficient and will reduce costs. Preoperative postponement, better preparation, better surgical strategy and technique will lead to better postoperative outcomes. Preoperative evaluation must focus on the patient’s capacity to support a long procedure with a lengthy general anesthesia [68].

The desperate patients who will absolutely want to be operated on (patients with morbid obesity, severe pulmonary disease, oxygen dependence) must be refused surgery because they will not withstand the trauma. “A stable abdominal wall in a dead patient is not a success” [26].

Most patients with IHLD are obese with an average BMI of 38 kg/m². Almost 70% have a BMI greater than 30 kg/m², therefore, weight loss before surgery is primordial (see below). Other frequent comorbidities are smoking (32%), diabetes (15%), and arterial hypertension (41%). Almost half of these patients have 2 or more comorbidities generating the so called “complex patient” or “high risk patient” [21]. Indeed, all these factors are independent variables associated with negative postoperative outcomes such as infections, delayed
healing, skin necrosis, entero-cutaneous fistulas. In a study of Ghazi et al. 28% of high risk patients presented overall complications compared to only 12% in non-risk patients [21]. Patients with comorbidities have a 4-fold increase in the risk of infection and patients with a history of infection have a 41% incidence of infection following hernia repair compared with 12% in those without a history of infection [69-71]. Rates of coexisting systemic disease and ASA scores are significantly higher in IHLD when compared with other hernias [72]. The number of coexisting diseases and ASA score are statistically significant, independent predictors of longer hospital stay.

All patients with IHLD must be examined with an abdominal CT scan. Besides volumetric evaluation of the abdominal cavity and of the hernia sac, tomography offers information about size and location of the abdominal wall defect, about the condition of the residual musculature, fluid collection in the abdominal wall and the presence and location of the prostheses in the abdominal wall. Last but not least, CT can identify the presence of deep seated infections and locate of entero-cutaneous fistulas [27].

Detailed medical history, clinical examination and previous medical and operative reports are essential. Cardiovascular evaluation with a modified Lee test and general status evaluation with ASA score, Goldman index or Physical status Class System are necessary [68]. Nutritional status must be evaluated and revised when necessary. Albumin must be over 3 g/dl because there is an established high association between hypoalbuminemia, morbidity and mortality. Blood glucose levels must not exceed 110 mg/dl and glycosylated hemoglobin must be under 7.

Alcoholic patients must receive thiamine and folate supplements. All septic foci must be eradicated prior to surgery.

Evaluation of the operative risk begins with the results of the pulmonary function tests when vetting a patient for surgery. The aim is to identify latent respiratory insufficiencies in order to prevent an abdominal compartment syndrome (ACS). Minute respiratory volume, the ratio of maximum expiratory flow rate to vital capacity and blood gas determinations (partial oxygen pressure, CO₂ partial pressure, pH and O₂ saturation) are mandatory.

Smoking cessation is a necessity for some period of time in order to optimize pulmonary function, tissue perfusion, and to reduce the rate of postoperative complications. Smokers must be approached differently when assessing their degree of tobacco dependence as evaluated by the Fagerström test for Nicotine Dependence (Table 4).

<table>
<thead>
<tr>
<th>Fagerström scale</th>
<th>Grade of dependence</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1-2</td>
<td>Low dependence</td>
<td>Brief counseling without NRT</td>
</tr>
<tr>
<td>Grade 3-4</td>
<td>Low to moderate dependence</td>
<td>Brief counseling with NRT</td>
</tr>
<tr>
<td>Grade 5-7</td>
<td>Moderate dependence</td>
<td>2-3 weeks counseling with NRT</td>
</tr>
<tr>
<td>Grade 8 +</td>
<td>High dependence</td>
<td>Intensive</td>
</tr>
</tbody>
</table>

NRT – Nicotine Replacement therapy.

Biochemical validation of smoking cessation is mandatory; levels of carbon monoxide (CO) in expired air must to be of the order of 10 parts/million or less to be considered indicative for smoking cessation.
Why must a patient stop smoking? Smoking is, nowadays, the most frequent addiction associated with increased morbidity and mortality. Despite the enormous progress and effort made to control tobacco use, almost 1 billion people worldwide are confirmed smokers [73]. The societal cost of tobacco use has been estimated to be US $96 billion in medical expenses and US $97 billion in lost productivity [74].

A growing body of evidence suggests that smoking is associated with adverse and inferior long-term outcomes in surgery [74-78]. This illustrates a major concern because more than 20% of surgical patients are smokers [76]. More and more data suggests that smoking is an independent factor for surgical outcomes. With all this incriminating data, almost half of the surgeons do not routinely counsel their patients to stop smoking before surgery [74]. Evidence indicates that with physicians’ advice, the rate of abstinence increases [75].

Components of tobacco smoke (nicotine, CO, and 300 more toxic substances) have physiologic effects that induce a hypercoagulable state, vasoconstriction, and thrombogenesis by stimulating the release of cathecolamine which enhance the activity of tromboxane A2 [74, 75]. Carbon monoxide binds hemoglobin and decreases the oxygen-carrying capacity of the blood. The chronic hypoxemic state increases erythropoeisis, red cell aggregation, and thrombogenicity. Pulmonary function is also altered by impaired cilliary function, increased mucus retention, and impaired alveolar macrophage function. Nicotine directly damages the microvasculature by injuring the endothelial cells of small vessels. Detrimental effects to tissue through poor oxygenation impairs the healing and the defense mechanisms of neutrophils. Chronic wound hypoxia is a predictor of wound infection [74]. Connective tissue deposition at the surgical site is altered by decreased fibroblast cell migration, increased cell adhesion and increased activity of metalloproteinases [74, 79].

Table 5. Complication rates in surgical patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration</th>
<th>Outcome</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moller [82]</td>
<td>6-8 weeks</td>
<td>Overall complication rates 52% in smokers versus 18% in ex-smokers</td>
<td></td>
</tr>
<tr>
<td>Sorensen and Jorgensen [83]</td>
<td>2-3 weeks – 60 patients</td>
<td>No difference in overall complication rates in smokers (43%) versus ex-smokers (41%)</td>
<td></td>
</tr>
<tr>
<td>Lindstrom [84]</td>
<td>4 weeks – 117 patients (general surgery and orthopedics)</td>
<td>Any complication within 30 days postoperative; relative risk reduction of 0.51 (95% CI 0.27-0.97)</td>
<td></td>
</tr>
<tr>
<td>Wong [76]</td>
<td></td>
<td>Pulmonary: no difference between 2 weeks versus 2-4 weeks</td>
<td>Wound: risk is lower for over 3-4 weeks versus under 3-4 weeks (p &lt; 0.004); similar risk for over 3-4 weeks versus non-smokers (p = 0.007)</td>
</tr>
<tr>
<td>Mills [77]</td>
<td>Meta-analysis</td>
<td>Total postoperative complications: 22% former versus 32% smokers (p &lt; 0.001)</td>
<td>Pulmonary: 15% former versus 20% smokers (p = 0.003); no statistically significant difference between early and late quitters</td>
</tr>
<tr>
<td>Sorensen [81]</td>
<td>General surgery and orthopedics: 4 weeks; CO and cotinine</td>
<td>Neutrophil count decline by 17% (p &lt; 0.05)</td>
<td>Wound infection rate 12% versus 2% (p &lt; 0.05) Do not affect wound rupture</td>
</tr>
</tbody>
</table>
Preoperative smoking cessation seems to offer important benefits in reducing complications although the minimum duration of abstinence necessary to confer benefits is unknown [77, 78]. However surgery is frequently scheduled within a few weeks from diagnosis and anesthesiologist’s consult, surgery could represent an event that motivates the patient to stop smoking - “teachable moment”. Smokers who stop smoking close to surgery have a higher risk of pulmonary and overall peri-operative surgical complications [80]; patients who stop smoking less than 2 weeks prior to surgery had four times the increased rates of pulmonary complications. These data were confirmed by Wang et al. who confirmed that a short period failed to reduce risks to values as low as in non-smokers [76]. A growing body of literature is beginning to establish that 4 to 8 weeks of abstinence before surgery is the ideal period of cessation which will not increase the complication rate in surgical patients (Table 5).

Hypothetically cessation less than 3-4 weeks before surgery might be beneficial for some patients in whom the time from diagnosis to surgery is short.

All these observations are limited because few studies have any rigid methodological quality, rather they are simply retrospective observational studies based on a qualitative, self-reported status of ex-smoker or nonsmoker.

A more beneficial effect is obtained after specialized counseling and interventional therapy [78].

The intervention can be: 1) intensive – weekly, individual behavioral counseling 4-8 weeks before surgery, with professionally trained smoking cessation counselors. Nicotine replacement therapy (NRT) is tailored to nicotine dependency; 2) medium 2-3 weeks counseling in combination with NRT, and 3) short – brief counseling sessions with or without NRT or NRT without counseling.

Intensive smoking cessation interventions with persistent counseling are more effective. A minimum intervention period of 4 weeks may be necessary to negate the deleterious effects of smoking on surgical outcome [78]. Each additional week of cessation results in an improvement. Randomized trials which successfully introduced smoking cessation and abstinence had significantly decreased the rates of complications; the effect being magnified with longer duration of the cessation [77].

Progressive preoperative pneumoperitoneum (PPP). Pneumoperitoneum implies the injection of atmospheric air or other gas into the abdominal cavity for diagnostic or therapeutic purposes. The procedure was used for the first time in 1931, before the advent of streptomycin for the treatment of cavitary tuberculosis. It was believed that elevation of the diaphragm would bring about varying degrees of lung collapse and thus lead to the collapse of the cavity and subsequent healing [85].

In October 1940, Ivan Goni-Moreno first reported intra-peritoneal injection of oxygen to reduce an incarcerated epigastric hernia [86]. Twelve years later, Berlemont published his experience reporting no death in 17 prepared patients versus 5 deaths in 8 unprepared [87]. Masson and Koontz have shown similar results in their reports (1953, 1954) [88, 89].

The goals of the PPP are to reposition the diaphragm, to make the muscles suppler, and to diminish adhesions between bowel loops [34]. Originally PPP was performed by intermittent per-cutaneous puncture of the abdominal wall followed by air insufflation. For some authors it is still the method of choice [90]. Nowadays the procedure has been extensively modified into several techniques which rely on abdominal computed tomography scan or ultrasound guided insertion of different devices [91].
Under mild intravenous sedation, in the operating room, a catheter is inserted preferably under local anesthesia. For morbidly obese patients epidural anesthesia could be a valid option avoiding unnecessary local infiltration and the risk of subcutaneous infections. A large variety of catheters were tried for PPP induction: pleural drainage catheters, 18 G central line, urethral catheters, surgical subcutaneous implantable ports, surgical peritoneal dialysis and radiologic drainage catheters [91-93]. Beyond the model used it is important that each catheter be provided with 3 valve system in order to maintain the air into the cavity and not to allow air leaks between insufflations. Placement of the device varies according to the surgeon’s preferences: left lower quadrant, Palmer’s point, or any other location outside the external margin of the rectus abdominis muscle. The correct placement is verified by instillation of a few water drops or a few ml of water-soluble radio-opaque contrast. An alternative method for catheter insertion is a 3-4 cm laparotomy through a left or right McBurney’s incision. Once the catheter is directed into the pelvis the peritoneal and aponeurotic incisions are tightly sutured in order to avoid air leaks. The device can be connected to a port or subcutaneously tunneled 5cm from its peritoneal entry. In a recent study of Alyami et al., the procedure is marred by a large number of subcutaneous abscesses (16% of 25 patients) which make the technique risky for surgical repair of IH [91]. In the same study the puncture of the abdominal wall was free of septic complications.

There is no consensus as to the initial volume of the insufflated air. Reported figures vary between 500 to 1000 ml [90, 92, 93]. Goni-Moreno states that the first injection should be done cautiously as there may be some disturbances (diffuse pain, nausea, pain in the shoulder), but these soon disappear. In our experience 500-600 ml represents an optimal volume well tolerated by the patient [93]. The air insufflation is repeated 2 or 3 times a week with injection of 500-2000 ml of atmospheric air at each session. This is preferred to O₂, CO₂, or nitric oxide because it is absorbed more slowly, ensuring the method’s efficacy. It is safe to stop the procedure when the patient feels pain in the shoulder, nausea, or undue tension in the abdomen. Because PPP works by increasing IAP it is recommended to perform the maneuver with the patient fasting in order to avoid vomiting and aspiration. A very tight binder or an abdominal belt maintain elevation of the diaphragm and abdominal pressure [34]. Some authors consider that the air inflates only the hernia sac, but in fact the air occupies the whole abdomen. Prophylaxis and prevention of deep vein thrombosis is essential.

The duration and the amount of insufflated air are patient dependent variables. No concrete recommendations were found in the studied literature concerning duration of PPP; Goni-Moreno stops the procedure when the flanks are bulging which means appropriate clinical elongation of the abdominal wall [86]. Flament recommended 2 weeks of insufflations, 2-3 times a week [34]. Raynor recommends a chest X-ray to estimate the volume created [87]. After Herzage the optimal period for increasing peritoneal cavity volume is at least 30 days. Through dynamic stereography Willis et al. demonstrated that the size of the abdominal cavity no longer increases after 6 to 10 days of insufflation [92]. Personal experience with simple measurements of the abdominal circumference and spirometry led us to consider the patient optimally prepared for surgery when the respiratory flow volume curve is stabilized and when two consecutive measurements remained unchanged (unpublished data). This was on average after 21 days (21.63 ± 5.44 days). Regarding the total amount of insufflated air, it varies from 5 to 18 liters depending on the author’s experience [85-88, 94-96].
The main effect of PPP is the gradual increase in the volume of the peritoneal cavity. Although many authors have surmised this happenstance, the assumption was confirmed recently. Dumont et al., for the first time, demonstrated that PPP progressively stretches the abdominal cavity by increasing the length of the abdominal muscles by 8.3 cm (p < 0.001) [97]. Lardiére-Deguel et al., on CT scan volumetry, showed an increase in the volume of the peritoneal cavity by 49% [98]. Similar results were reported by Sabbagh et al. with an increase of the volume of the abdominal cavity by 2000cc [90]. Besides the musculoaponeurotic elongation, the increasing volume of the peritoneal cavity is achieved by elevation of the diaphragm. The latter is a result of particular importance because PPP produces a marked and stable improvement of the respiratory function [60, 99]. Indeed, Flament reported that chest X-rays confirm this with a 10-15 cm space differential between liver and diaphragm [34]. A stable improvement of the respiratory function in all its components was obtained in our study; the improvement was maintained even after surgery [93]. Contradictory results were obtained by Sabbagh et al. who reported a decrease in all dynamic respiratory function parameters after PPP [90]. Both spirometry and gasometry suffer a statistically significant decrease. Authors believe that PPP induced a restrictive syndrome with impact in 95% of the cases having the same respiratory effect as surgical treatment of IH.

An additional mechanism whereby PPP contributes to the reduction in the size of the hernia, is by a decrease in the volume of the viscera through the lessened oedema of its mesentery and its viscera. Insufflated air induces a peritoneal irritation with capillary vasodilatation followed by an influx of leukocyte and macrophage which promote local immunity. This mechanism seems to be a cutaneous antibacterial protection factor because patients treated with PPP have had a significant reduction in the rate of postoperative surgical site event [86].

Complications of the PPP are related to the puncture of the abdominal wall and the resulting effects of the insufflated air. Perforation of a hollow/solid organ is rare; the absence of viscera within the abdominal cavity could be a valid explanation for the low tendency towards visceral lesions [90]. More frequently, hematomas and/or bruises, and localized infections are encountered. Risk of infection is lowered when the device is placed by puncture. Cutaneous emphysema occurs in nearly all patients and requires no specific therapy. Rarely, a voice change or thickening of the cervical region suggests mediastinal air migration. Systemic complications related to the presence of air in the peritoneum are pneumonia, pulmonary embolism, and myocardial infarction. In a series of 587 patients, Goni-Moren reported 4 cases of deep vein thrombophlebitis with secondary pulmonary embolism, 9 patients with pneumonia, and 3 with myocardial infarction [86].

There are no controlled trials in the literature to suggest the effectiveness of PPP with respect to recurrence of the repaired IH. Raynor et al. described 3 recurrences in 7 patients after a 36 months follow-up while Caldironi et al. only 2 recurrences in 40 patients [87, 96]. On 487 repairs Goni-Moren reported a recurrence rate of 3.6% (14 patients) without specifying the type of hernia and the length of follow-up [86].

Weight loss - why and how? In the western world, obesity is a growing epidemic associated with an increased risk for secondary, serious, chronic medical conditions, complications and sequelae. Most of them are former surgical patients with past, complex procedures in whom a large majority will develop incisional hernias [100]. Perioperative outcomes in these patients are often inferior relative to the general surgical population. In a
large population study, morbidly obese patients experienced more wound, renal, and tromboembolic incidents than normal weight patients for 16 other types of major surgical procedures [101]. Overweight and obese patients experienced similar rate of complications in relation to normal weight patients. This data demonstrate the “obesity paradox” in overweight and obese patients across multiple surgical procedures [101]. Unfortunately we do not have enough data on surgery of the IHLD which, nowadays, is considered to be a major surgical procedure. This lack correlates with the reduced number of medical reports in small series of patients.

The incidence of obesity is high in patients with IH. More exactly, almost 75% of them will have variable degrees of obesity [21]. This high prevalence has significant implications for hernia surgeons. First of all, obese patients are high risk patients as classified by the American Society of Anesthesiology (ASA) as type III or IV. During general anesthesia, Body Mass Index (BMI) is an important determinant of lung volumes, oxygenation, and respiratory mechanics (Table 6) [102]. Not only are alterations present in morbidly obese patients but also in the moderately obese patients and the result is the high cost of the work of breathing.

Besides anesthetic high risk, obesity is a significant risk factor for IH recurrence, surgical site occurrences, blood transfusion and 30 days readmission for surgical complications.

<table>
<thead>
<tr>
<th>Table 6. Alterations in breathing mechanisms in obese patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased resistance of the lung</td>
</tr>
<tr>
<td>Increased airway resistance</td>
</tr>
<tr>
<td>Decreased oxygenation</td>
</tr>
<tr>
<td>Reduced respiratory compliance (mainly in lungs)</td>
</tr>
<tr>
<td>Decreased functional residual capacity</td>
</tr>
</tbody>
</table>

There is no doubt that weight reduction is an important factor in patients’ recovery time due to the decreased incidence of perioperative complications. In a study by Cho et al., a dramatic reduction of perioperative complications from 40.7 to 5.5% was observed after 4 weeks of preoperative weight optimization [103]. The incidence of deep vein thrombosis, pulmonary embolism as well as a 5 fold decrease in infection rate have been obtained [14].

Considering all these data, weight loss for obese patients with IHLD is always recommended and should be mandatory. There is no evidence based data for the best approach on weight loss, surgical or otherwise. Both of them are often inaccessible though the goal is sometimes accomplished [100, 104]. There are some reports from dedicated centers with good results on weight loss by conservative means. Shouldice Hospital is a referral center for abdominal wall hernias with a weight reduction program which has been in place used for seven decades. This program limits the amount of carbohydrate intake and encourages fruits and vegetables to a limited total intake of 1500 calories/day. Chan and Chan reported a weight loss of 11 ± 13,1 kg within a 2-6 months period preoperatively, reducing the proportion of obese patients from 35,6% to 13,3% for simple incisional hernias [105]. Surprisingly, the rate of recurrence was not influenced; the rate of SSI was not related to the weight reduction.

A small series of 25 patients with a protein sparing diet associated with a multidisciplinary approach of nutritional counseling and exercises was reported by Rosen et
al. [100]. They obtained a faster and more significant decreases in BMI compared to similar nutritional modifications. The conclusion of the study was that a motivated patient, associated with regular monitoring by a nutritional expert leads to an excellent long term rate of success for preoperative weight optimization. As for smoking cessation, surgery for an obese patient could be a “teachable moment” that must be exploited by the team.

Forced starvation, with its negative impact on collagen formation and wound tensile strength is not advisable. Bariatric surgery for weight loss in patients with IHLD is still a matter of conjecture. Patients with large defects, infections or prior fragments of meshes are not suitable candidates for laparoscopic sleeve gastrectomy (LSG) or laparoscopic Roux “en Y” gastric by-pass (LGBP). For a small number of patients, the simultaneous laparoscopic bariatric procedures and IH repair was reported with a short term follow-up [106-111]. We agree with Angrisani’s opinion to discourage the bariatric procedure because of the increased risk of mesh infection (especially in LGBP) and of the increased risk of recurrence by modification of the hernia/mesh ratio [104]. Delayed repair of the IH is the method of choice. Intra-gastric balloon could be an efficient and safe method for BMI reduction; a mean BMI loss of 4-5 kg/m$^2$ is generally achieved in 75% of patients [104]. Considering the “obesity paradox” we can reduce the target of weightless only to a small percentage below the current patient’s weight. More data are still necessary.

**LOSS OF DOMAIN – HOW TO REPAIR?**

Advances in surgical technique and technology have allowed surgeons to take on more difficult cases and higher risk patients. The abdominal wall has a multitude of functions all of which depend on an established interplay between dynamic muscle layers and a static framework. This interplay allows the maintenance of a constant intra-abdominal pressure which in turn allows support for respiration, locomotion of the trunk, micturition and defecation [21].

To obtain the best outcome in the repair of IHLD we should apply the principles of reconstruction as the basis of an individualized strategy. Meticulous surgical technique, optimal timing, tension-free repair in a clean, well vascularised wound must be the cornerstones of an ideal repair. While planning the correction of a giant incisional hernia, the surgeon is faced with 4 major problems:

1. Identification of loss of domain,
2. Closure of the abdomen,
3. Reconstruction without complications or sequelae (including recurrence), and
4. Elimination of dead spaces resulting from the large dermal flaps [30]. More challenges are added because of the excess displaced abdominal viscera, insufficient lateral musculo-fascial tissue for mesh fixation, impaired mechanisms of the abdominal wall and sometimes presence of infection (mesh infection, wound infection, stomas, and intestinal fistulas) [64, 75].

The ideal surgical treatment respects the principles of: 1. No restriction of the volume of the abdominal cavity; 2. Avoiding an increase of the IAP; 3. Improving compliance of the
chest wall while maintaining unchanged pulmonary function and 4. Minimizing the total mechanical work of the breathing muscles [23]. Despite the numerous surgical techniques available, none can fully respect these goals (Table 7).

A laparoscopic ventral hernia repair can be a valid therapeutic option but only for non-contaminated small abdominal wall defects with large hernia sacs [26]. For large defects with large sacs laparoscopy is not suitable because of the diminished working space and because intraperitoneal mesh does not assure a stable and functional abdominal wall. Sometimes poor cosmetic outcomes can be expected.

Mesh reconstruction becomes a must for IHLD to reduce the recurrence rate of 50%. The mesh ensures a support net for the new reconstructed abdominal wall. It is difficult to answer which is the best placement of the mesh for these patients; further studies are necessary. For large uncontaminated defects (grade I and II in Ventral Hernia Working Group classification – see Table 8) the best option – if it is possible – retrorectus synthetic mesh repair with or without transversus abdominis release (TAR). Mesh will be fixed with full thickness permanent sutures assuring a 2.5 times greater solidity than tack fixation [14]. For grade III and IV, a biologic with or without component separation is the option of choice.

Table 7. Surgical techniques in hernia repair

<table>
<thead>
<tr>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary suture closure</td>
</tr>
<tr>
<td>Laparoscopic repair</td>
</tr>
<tr>
<td>Prosthetic repair (on-lay, sub-lay, in-lay)</td>
</tr>
<tr>
<td>Rives-Stoppa ± Transversus Abdominis Release</td>
</tr>
<tr>
<td>Component Separation ± prosthetic repair</td>
</tr>
<tr>
<td>Endoscopic component separation ± prosthetic repair</td>
</tr>
</tbody>
</table>

Table 8. Ventral Hernia Working Group classification

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Low infectious risk; young patients without comorbidities</td>
</tr>
<tr>
<td>Grade II</td>
<td>Patients with comorbidities which raise infectious risk (smoking, diabetes, malnutrition). There no evidence of wound contamination or active infection</td>
</tr>
<tr>
<td>Grade III</td>
<td>Patients with potentially contaminated wounds: infected seromas, injury to the gastrointestinal tract, history of wound infection</td>
</tr>
<tr>
<td>Grade IV</td>
<td>Patients with infected wounds: septic dehiscense, infected meshes, stomas</td>
</tr>
</tbody>
</table>

Formerly the domain of the general surgeon, the increasing complexity of the abdominal wall defects have drawn on the expertise of the general and reconstructive plastic surgeons. Regardless of the surgeon’s background, their goals in managing complex abdominal wall defects are to restore the structural and functional integrity of the musculofascial system and to provide as table, durable wound while minimizing complications and optimizing aesthetic appearance [112].
Despite the high incidence of defects unsuitable for direct closure, there is little consensus as to the optimal technique for repair. Options include the use of prosthetic mesh, fascia lata or dermal grafts, pedicled or free tissue transfer, and the CST [113].

The management of such defects poses a surgical challenge, particularly since primary repairs have resulted in recurrence rates as high as 50% [114]. The use of synthetic mesh can significantly reduce recurrence rates by up to 20%, but this carries a risk of mesh infection, exposure, and extrusion. It is also contraindicated in the presence of gross contamination or infection [115].

**COMPONENT SEPARATION TECHNIQUE (CST)**

The components separation technique (CST), first described by Ramirez et al., provides tension-free closure of large, full thickness anterior abdominal wall defects with autologous tissue [116]. The CST enables significant advancement of the rectus abdominis, internal oblique, transversus abdominis muscles toward the midline, with preservation of the neurovascular bundles, resulting in a dynamic longstanding repair. It was originally described without the use of prosthetic material. Quoted recurrence rates range from 0% to 30% [114, 117, 118].

As the CST was first described over 2 decades ago, data are now available from large case series and with long-term follow-ups, demonstrating the efficacy of this technique. For instance Dibello et al. reviewed 200 patients who underwent CST and showed a 22.8% hernia recurrence rate for primary CST after a mean follow-up period of 10 months [119]. Another study by Ko demonstrated a 19.8% hernia recurrence rate at a mean follow-up of 4.4 years [120].

Subsequent modifications of the CST have incorporated the use of prosthetic materials, to augment the repair, and this has been shown to further lower hernia recurrence, when compared to CST alone [120]. While concerns remain regarding the risk of infection and extrusion of the mesh, the Ko series did not demonstrate a significant increase in major or minor postoperative complications when a mesh was used [120].

Data from the only prospective, randomized-controlled trial comparing autologous CST hernia repair with prosthetic mesh hernia repair (composite ePTFE/polypropylene mesh), showed a favorable outcome for the CST, given the frequency of wound complications and subsequent loss of the prosthesis in the mesh group [121].

Wound complications such as dehiscence, infection, hematoma, and seroma have been reported in several series and are thought to relate to the undermining of the subcutaneous space, raising of cutaneous flaps, transection of epigastric perforating vessels, and the creation of dead space during the CST [117, 118].

Kingsnorth et al. have suggested that the application of fibrin sealant where skin flaps are dissected past the linea semilunaris may help to reduce the incidence of seroma [122]. In addition, the recent introduction of endoscopic and minimally invasive techniques have been shown to reduce wound complications, possibly by preserving local blood supply and thereby minimizing tissue ischemia [123]. However, with large hernia defects endoscopic techniques are of limited value.
INDICATIONS FOR COMPONENTS SEPARATION

In general, there are two types of patients selected for a component separation procedure: those for whom the procedure is elective, but who will clearly benefit from a restored abdominal wall, and those for whom component separation is the only option.

It is almost counterintuitive, but component separation is best for a young, fit person who has a future cosmetic and functional need of a reconstructed abdominal wall. The second group comprises individuals for whom synthetic mesh is contraindicated, or patients who have a history of infection, require mesh removal and who developed ongoing infections or an entero-cutaneous fistula (Table 9).

The technique is not indicated for small or average size, uncomplicated hernias since these can be repaired with the standard open or laparoscopic techniques.

Table 9. Component separation indications

1. Infected abdominal wall with or without mesh.
2. Patients with hernias who are also having a colostomy reversal.
3. Very large ventral hernias.
4. Multiple defects.
5. Multiple failed attempts at previous repairs.
6. Treatment or prevention of the abdominal compartment syndrome (ACS). May avoid open wound management which usually results in a large ventral hernia and potential skin deficit.

Caution should be exercised in those patients who have scarring from lateral incisions as well as those with stomas since dissection will be restricted and tedious. Also, lateral hernias prevent the use of bilateral fascial transposition and surrounding tissue mobility will be limited by the ribs and iliac crest.

Delaying the operation until any risk factors (obesity, smoking, COPD, malnutrition, steroids) can be eliminated, will greatly improve the outcome of the surgery.

CONTRAINDICATIONS OF COMPONENTS SEPARATION

True contraindications to hernia repair are rare. A subset of minimally symptomatic or asymptomatic patients with very large hernias at very low risk for incarceration may benefit from observation rather than attempted repair. Additionally, in some patients, the cardiopulmonary stress or bleeding risk associated with major surgery may preclude operative management of their abdominal wall defect. Given the risk factors associated with the development of a ventral hernia, many of the potential candidates for repair have significant medical comorbidities. It is incumbent upon the reconstructive surgeon to maintain an awareness of these comorbid conditions, as well as the alterations in physiology caused by the hernia defect or its repair.
Patients with conditions such as chronic obstructive pulmonary disease (COPD), heart disease, or liver failure must be screened preoperatively. Postoperatively, patients with COPD may be difficult or impossible to wean from a ventilator. Intra-abdominal operations involve large fluid shifts and may cause significant cardiovascular stress intra-operatively and postoperatively, with intravascular return of third space volume in the early postoperative period. In addition, patients with liver failure have high morbidity and mortality rates with operations that require general anesthesia and should not undergo elective abdominal wall reconstruction. The risk of such a major operation for patients with the above comorbid conditions must be defined, as these risks may well outweigh any benefits of abdominal wall reconstruction.

Relative contraindications to elective abdominal wall reconstruction/ventral hernia repair include pre-existing conditions that may increase the risk of recurrence (i.e., smoking, mild COPD, obesity, diabetes, ascites, cancer, multiple hernia recurrences, a noncompliant patient).

Although there is no clear consensus on contraindications to component separation, and only a few absolute contraindications, most surgeons point to the need to look at the functional status of the abdominal wall. Previous operations that have significantly damaged the lateral abdominal wall musculature also are contraindications. For example, undergoing a muscle resection when the colon cancer eroded into the lateral abdominal wall may contraindicate a later component separation. Rosen, pointed out the 10-time recurrent hernia patient whose abdominal wall had become fibrotic and noncompliant so that the tissue could not be brought toward the midline.

**Complications**

Even with an exceptional technique, wound complications are not uncommon with the component separation and the incidence of such complications can reach a rate of 25%. Wound complications such as dehiscence, infection, hematoma, and seroma have been reported in several series and are thought to relate to the undermining of the subcutaneous tissues, transection of epigastric perforating vessels, and creation of dead space during the CST [117, 118].

Not surprisingly, drainage is also a significant aspect of postoperative care. In open component separations we uses several large-bore, fluted drains in the subcutaneous space and leave them in until drainage is about 30 cc a day or less, while also warning patients about in situ drains which can be typically left in place for six to eight weeks (unpublished data).

**Surgical Technique**

In the early 1990s, there was no standard way to teach the Component Separation Technique or apply it to patients. However, in 1990, Oscar Ramirez, MD, published a landmark paper which helped resolve much of the technical confusion surrounding component separation [116]. Dr. Ramirez, who was a plastic surgeon at Johns Hopkins...
University School of Medicine in Baltimore at the time, provided a standard description on how to perform the technique of open component separation. He proposed releasing the external oblique aponeurosis, separating the external and internal oblique muscles and incising the posterior rectus sheath. In cadavers, the flap could be advanced 10 cm. Dr. Ramirez and his colleagues concluded that the component separation was suitable for large abdominal wall defects.

Although the approach is more than two decades old, component separation has become one of the most popular topics in hernia repair over the past several years, finally making its way out of academic centers and into operating rooms around the country. The crossover of component separation from plastic surgery to general surgery was another major reason the technique was reintroduced. In terms of technique, the component separation really is the first step of a larger hernia operation or abdominal wall reconstruction.

The component separation method provides an anatomically correct, and an innervated abdominal wall reconstruction as opposed to an adynamic mesh repair by mobilizing the external oblique muscle (EOM). Accidental dissection between the internal oblique and transversus muscles may potentially injure the neurovascular bundles of the rectus muscle and interfere with muscle dynamics. Increased compliance of the abdominal wall is more important than the rate of recovery of wound tensile strength as a mechanical property to predict low hernia recurrence rates. As the size of implanted mesh increases, the abdominal wall becomes less pliable resulting in a rigid, fixed abdominal wall. Shestak et al. found that after components separation in abdominal wall reconstruction, several patients showed a 40 percent improvement in their ability to generate truncal flexion force [124]. Patients with large defects have poor dynamics of the abdominal wall impairing some of their activities of daily living; however, with myofascial medial transposition the mechanics of the abdominal wall improve greatly.

Although component separation has a relatively long history, the technique is still evolving and many issues remain unresolved. Most surgeons who use the operation regularly perform a unique variation of it, refining the open, endoscopic or minimally invasive approaches to better preserve blood supply to the abdominal muscles and thus lower wound complication rates. Surgeons also debate how far one should go laterally, and whether releasing the posterior rectus sheath destabilizes or denervates the rectus abdominis complex. Moreover, the surgeon has a choice between a non-mesh repair and mesh reinforcement with either a synthetic or biological material [125].

The Ventral Hernia Working Group advocates the use of mesh as the recurrence rate is reduced from ranges of 18%-62% to 2%-32% [125]. These wide ranges are partly explained by the varying sizes of hernias in the series [126, 127].

One of the most significant questions is whether hernias repaired using component separation should be reinforced with synthetic or biologic mesh. Generally, most surgeons seem to reinforce with mesh whenever possible, pointing to traditional IH literature on mesh versus primary suture repair.

One possible answer to the question “what is the most appropriate mesh to use” comes from data on a series of 200 component separations performed over a decade ago by Greg Dumanian [128]. In the study, 79% of patients had no mesh reinforcement, 9% were reinforced with AlloDerm (LifeCell) and 12% were reinforced with either regular or soft polypropylene mesh. All primary reinforcement was in the underlay position. Dumanian
found that AlloDerm had the highest incidence of recurrence, followed by “no mesh” repairs. Regular and soft polypropylene had the lowest rates of recurrence.

Although it is considered common sense to reinforce repairs with a biologic mesh when a synthetic one is contraindicated, the use of bioprosthetics can be very expensive. There are no clear-cut answers in the few studies published so far. The general attitude of most surgeons who face the problem, consists in using resorbable meshes such as polyglactin rather than a bioprosthetic.

**ANTERIOR COMPONENT SEPARATION**

Although endoscopic and minimally invasive approaches also work, most general surgeons are now learning open component separation, as described by Dr. Ramirez. This method has a moderate learning curve compared with other methods.

The open technique involves first raising skin flaps from the costal margin down to the inguinal ligament and out several centimeters lateral to the linea semilunaris. The external oblique aponeurosis is then divided 2 to 3 cm lateral to the linea semilunaris from the inguinal ligament up to a distance of about 5 cm above the costal margin. This process is repeated bilaterally. If the medial slide of the muscles is inadequate the posterior rectus sheath is then divided from the costal margin down to the inguinal ligament approximately 1 to 2 cm lateral to the midline, which allows elongation and advancement of the rectus abdominis complex relative to the lateral abdominal wall. Ultimately, the goal of component separation is to restore abdominal wall function while preventing wound complications. This means that preserving the nerves and blood supply to the skin flaps is of paramount importance. The key issue here is the preservation of the epigastric arteries and their perforators.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
<th>When to use</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Wide fascial advancement</td>
<td>• Significant wound morbidity (Necrosis, ischemia, infection, hematoma)</td>
<td>• If skin won’t come to midline</td>
</tr>
<tr>
<td>• Innervated/vascularized repair</td>
<td>• Noncompliant abdominal walls, not much advancement</td>
<td>• Will create a skin flap anyways</td>
</tr>
<tr>
<td>• Improved functional outcomes</td>
<td>• Durability?</td>
<td>• The hernia is so big that the lateral extent of the hernia sac is at the external oblique</td>
</tr>
<tr>
<td>• Closure of wide defects with autologous tissue</td>
<td></td>
<td>• If I don’t want to use mesh, violate the retro rectus plane, or think an onlay is acceptable</td>
</tr>
</tbody>
</table>

**MINIMALLY INVASIVE COMPONENT SEPARATION**

**Sparing of Periumbilical Perforators**

Consensus now appears to exist with regard to the importance of sparing the periumbilical perforators to preserve the integrity of the skin and soft tissue overlying the fascial repair. How to approach the fascial repair itself, however, is the root of much disagreement.
## ENDOSCOPIC COMPONENT SEPARATION (ECS) TECHNIQUE

In 1997 Lowe et al. [127] introduced endoscopic components separation (ECS) and described the application of a balloon technique for subcutaneous dissection and outer exposure of the external oblique aponeurosis, which was divided along the semilunar line with electrocautery. Around the same time modifications of the technique by Mass et al. simplified the endoscopic approach [129].

Further improvement and minimization of the technique was done in 2007 by Rosen et al. by internal exposure of the external oblique in combination with avascular separation of the external and internal oblique components by dissection with an endoscopic balloon, thus avoiding subcutaneous undermining of the skin flaps. Rosen and colleagues showed that there was no statistically significant difference in the amount of abdominal wall mobilization between ECS and OCS.

When performing an ECS, it is most important to enter the proper space. This is best carried out through a 1.5-cm incision below the costal margin along the anterior axillary line. The surgeon must ascertain that he is lateral to the rectus muscle to avoid entering the wrong plane. Using S-retractors and a Kelly clamp, the subcutaneous tissues are bluntly dissected to expose the external oblique aponeurosis which is then incised to expose the internal oblique beneath it. An excellent option, especially for obese patients, is the use of the optical trocar for muscle dissection. This trocar allows quick and easy tissue identification and navigates the abdominal wall layers for controlled entrance between the EOM and IOM.

Sterile lubricant is injected into the opening to facilitate balloon dissection of the space between the muscles. This is performed in a similar fashion as when creating the preperitoneal space in the inguinal TEP repair. Previous experience with the balloon dissector will make this part of the operation an easier transition. The unilateral balloon allows a more controlled dissection than the bilateral balloon; however, this will depend on the surgeon’s preference.

A blunt-tip or structural balloon port is then inserted and the space is insufflated at a pressure of 10 to 12 mmHg.

One 5-mm port is inserted just cephalad to the inguinal ligament and another at approximately the level of the umbilicus at the mid- to posterior axillary line. This will allow adequate longitudinal and transverse dissection. A 30-degree, 10-mm scope is utilized; however, a 5-mm angled scope is also required to alternate trocars.

Approximately 2 cm lateral to the linea semilunaris, using the cautery and sharp dissection, the external oblique aponeurosis is released longitudinally from the level of the costal margin to the inguinal ligament. The same technique is performed on the contralateral side. Closed suction drains are not necessary since the space is essentially avascular.
The muscular complex is then transposed to the midline. On each side approximately 4 cm can be gained in the upper third of the abdomen, 8 to 10 cm in the middle, and 3 cm in the lower third. If additional fascial translation is required, the posterior rectus sheath can be separated from the rectus muscle for a 2 cm additional advancement. It is possible then to close very large abdominal wall defects with minimal morbidity [123].

Reinforcement with mesh (biologic or synthetic) is at the discretion of the surgeon. Whether the mesh is placed in an overlay, underlay, open, or laparoscopic fashion is determined by the surgeon at the time of repair.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Direct access to lateral compartment</td>
<td>• Requires laparoscopic skill set</td>
</tr>
<tr>
<td>• Avoids subcutaneous flap</td>
<td>• Achieves 85% of open release</td>
</tr>
<tr>
<td>• Avoids division of abdominal wall perforators</td>
<td>• No flaps, can be difficult to place mesh</td>
</tr>
<tr>
<td>• Decreases complexity of postoperative wound infections</td>
<td>• Learning curve (helpful to be mentored when beginning technique)</td>
</tr>
<tr>
<td></td>
<td>• Not appropriate for loss of domain, extensive lateral abdominal wall scarring</td>
</tr>
</tbody>
</table>

ECS is associated with lower rates of wound complications because limited subcutaneous dissection is undertaken, thus preserving blood supply from the epigastric vessels to the skin [131, 132]. Many reports have demonstrated the effectiveness and safety associated with the ECS technique for repair of large midline ventral hernias as indicated by the incidence of recurrent herniation and postoperative complications. In contrast, there are no corresponding publications on quality of life (QOL) in these patients following repair of their hernia with this new technique [130, 131, 133-135].

A retrospective review of patients undergoing open or endoscopic CST between 2005 and 2009 was performed by Karem et al. [136]. The review compared patient-related variables, length of hospital stay, wound morbidity, and costs associated with the index operation and encounters within a 6-month period. In a similarly complex group of patients, the total direct costs associated with endoscopic and open CST were similar. Endoscopic instruments made a marginal contribution to the total overall costs, but significant cost contributors were the use of biologic grafts and wound morbidity.

**POSTERIOR COMPONENTS SEPARATION (PCS)**

This posterior component separation technique was first developed in 2006 by surgeons Yuri Novitsky and Michael Rosen. The first publication, in 2012, described this modification of the classic retromuscular Rives-Stoppa technique to facilitate myofascial advancement and mesh placement beyond the lateral borders of the linea semilunaris.

As with the anterior component separation introduced by Oscar Ramirez, MD, in 1990 (external oblique release), division of one of the three lateral abdominal muscles relaxes the abdominal hoop mechanism, allowing for midline advancement to facilitate primary fascial closure. TAR has been shown to provide at least an equivalent myofascial release as the anterior components separation with the added benefits of a greater release at the subxiphoid,
subcostal and suprapubic locations. Areas which are anatomically fixed and limited when an external oblique release is attempted. In practice, TAR allows for both greater release and for the use of a much larger mesh, facilitating closure of the most challenging of cases.

The TA and internal oblique muscles serve as the major contributors to the hoop tension in the lateral abdominal wall, and division of the TA allows for significant advancement of the posterior sheath and midline. Wound morbidity is greatly reduced due to the elimination of subcutaneous flaps, sparing of the periumbilical perforators and preservation of the abdominal wall neurovascular supply. Novitsky and Rosen report that their wound complication rates decreased from 48% to 25% and recurrence rates dropped from 14.3% to 3.6%, comparing TAR with a combined traditional Rives-Stoppa/anterior component separation. With a TAR, much larger pieces of mesh can be placed into the retromuscular position extending bilaterally to the retroperitoneum as needed to allow for the widest overlap possible. Mesh is placed in the well-vascularized retromuscular position, decreasing mesh infections, and excluded from the viscera, thus allowing the use of cost-effective uncoated meshes.

The goal of the TAR procedure is to medialize the rectus muscles, restore the linea alba, and provide a durable and functional repair. Midline fascial closure provides an additional layer of protection from superficial surgical site infection and exposure of the mesh. Medialization of rectus muscles in combination with TAR repositions the muscles tension of the anterior abdominal wall and may actually improve oblique function through positive compensatory changes, as evidenced radiographically by hypertrophy of the rectus and external and internal oblique muscles. Functional studies examining isokinetic and isometric measurements post-TAR demonstrate an improvement in core physiology and quality of life.

Several modifications of the classic retromuscular Stoppa technique to facilitate dissection beyond the lateral border of the rectus sheath were recently reported.

Briefly, the retromuscular space is developed laterally to the edge of the rectus sheath. The posterior rectus sheath is incised 0.5-1 cm medial to the lineasemilunaris to expose the medial edge of the transversus abdominis muscle. The muscle then is divided, allowing entrance to the space anterior to the transversalis fascia. The posterior rectus sheath then is advanced medially. The mesh is placed as a sub-lay and the linea alba is restored ventral to the mesh.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takes advantage of retromuscular dissection plane</td>
<td>Can injure abdominal wall neurovascular supply</td>
</tr>
<tr>
<td>Allows for medialization of both posterior and anterior components</td>
<td>Easy to get in wrong plane</td>
</tr>
<tr>
<td>Closure of defect</td>
<td>Large dead space created</td>
</tr>
<tr>
<td>Avoids subcutaneous flap creation</td>
<td>Technically challenging</td>
</tr>
</tbody>
</table>

Although TAR has been made to look easy by some expert demonstrations, the anatomy must be well understood, and the layers can be both subtle and unforgiving. Accidental disruption of the internal oblique will destabilize the lateral abdominal wall and interfere with the neurovascular bundles, leading to both a very challenging lateral hernia and abdominal pain.
As with the popularization and subsequent decline in the use of transverse rectus abdominis myocutaneous flaps, there are valid theoretical concerns that TAR may eventually create unrecognized morbidity. Exercise physiologists cite that the TA muscle is the one that provides the bulk of the core strength of the flat muscles of the abdomen. It provides stability to the spine, and there may be implications for lower back issues in the future.

Anterior components separation (ACS) creates large lipo-cutaneous flaps to release the external oblique fascia often leading to major wound complications. Posterior components separation (PCS) involves the release of the posterior rectus sheath and transversus abdominis muscles, providing equivalent myofascial advancement with significantly less wound morbidity when compared with ACS and a low recurrence rate. Although further studies are needed, PCS has evolved as an important addition to the armamentarium of surgeons undertaking complex abdominal wall reconstructions. Minimally invasive component separation with inlay bioprosthetic mesh (MICSIB) uses tunnel incisions for external oblique aponeurosis release. It preserves both the rectus abdominis myocutaneous perforator vessels that supply the overlying skin and the connection between the subcutaneous fat and anterior rectus sheath, thereby reducing the subcutaneous dead space while potentially improving the vascularity of the overlying skin flap. Inlay bioprosthetic mesh reinforces the musculo-fascial repair.

Open components separation (CS) has traditionally been a popular method for management of complex abdominal wall hernias. However, it has been associated with significant wound complications.

There are many techniques in AWR which imply component separation. Things are far from clear as seen by the variety of patients who require such techniques, the complexity of defects, conditions under which they occur, the lack of extensive experience in techniques that are quite new, the paucity of cases comprised in the studies until recently, the fact that there are few randomized and prospective trials with results make for difficult comparisons.

The CST is a safe and effective technique, which can be used to treat complex abdominal hernias/defects.

However, most cases should not require component separation and not every patient needs a dynamic abdominal wall. In the patient with comorbidities, obesity, a smoker, patient who has not modified risk factors, an abdominal wall reconstruction should be avoided and expectant management should be practiced for minimally symptomatic hernias. Symptomatic hernias may be best approached in this group with a laparoscopic ventral hernia repair to minimize complications, if possible. Just as many rods lead to Rome there are several other techniques, including the modified Chevrel onlay, which may give the closure needed without entering the abdomen or dividing the TA.

With regard to the overuse of TAR and component separation techniques in general, there has definitely been a shift in hernia repair to routine use. Every surgery (especially with component separations) burns a bridge, and we need to decide if the benefit is worth the cost and if the individual circumstance has been optimized. As with most endeavours in surgery, the most important lesson regarding TAR is not technical; it is the clinical judgment to decide which patients will be helped by the procedure.
REFERENCES


Incisional Hernia with Loss of Abdominal Domain


Incisional Hernia with Loss of Abdominal Domain

No conflict of inters. No disclosures to declare. Both authors equally contributed to conception and writing of the manuscript.

**Biographical Sketch**

*Name:* Valentin Oprea  
*Affiliation:* Department of Surgery Emergency Military Hospital “Constantin Papilian” Cluj-Napoca, Cluj county, Romania  
Chief Division of General surgery  
*Date of Birth:* October 31 1964  
*Education:* “Carol Davila” University of Medicine Bucharest – graduated in 1990  
Fellowship in General Surgery 1990-1994  
Fellow of Surgery 1995-1999  
Senior Consultant in Surgery  
Laparoscopic Surgery – Basic and advanced training course “Iuliu Hatieganu” University of Medicine, Cluj-Napoca  
Doctoral Thesis (PhD) in Surgery 2010 “Iuliu Hatieganu” University of Medicine, Cluj-Napoca  
*Address:* Romania, Cluj County, Cluj-Napoca No 91 Al Vaida-Voevod street  
*Research:* In vivo and in vitro study of polypropylene mesh infections  
Local cellular response on the interface between mesh and human organism  
Systemic inflammatory response after prosthetic repair of complex hernias  
Quality of life after prosthetic repair of incisional hernias  
*Professional Appointments:* Research Director  
*Publications:*  
Chapter 4

PReoperative Techniques for
The Management of Giant Hernias

Karla Verónica Chávez-Tostado, MD
Endocrine Surgery, National Institute of Nutrition Salvador Zubirán,
México City, Mexico
General Surgery Attendant at Hospital General Ajusco Medio,
México City, Mexico

Abstract

The term “giant hernia” describes various clinical scenarios that are characterized by a ventral hernia of great size, with some degree of loss of domain and inability to achieve muscle closure with conventional techniques. The definition, the diagnosis and the surgical technique are not standardized and there are no randomized clinical trials or guidelines on giant hernias, thus the planning and surgical approach must be individualized carefully.

To succeed in the abdominal wall reconstruction procedure, we must optimize the patient’s respiratory, circulatory and immune system. In a second stage, the abdominal wall must be prepared by means of 3 different techniques: Progressive pneumoperitoneum to provide expansion of the abdominal wall, intrafascial tissue expanders to make a gradual enlargement of the parietal tissue in a controlled manner, and mioaponeurotic relaxation with Botulinic toxin A, that elongates the lateral abdominal wall, leading to a reduction in the defect size.

Each of these techniques has several and different advantages, they can be used in combination with one another with a high rate of success.

Introduction

An incisional hernia is a condition that presents with the displacement of internal organs from their normal anatomical site through a defect in the abdominal wall which is developed during scar consolidation after a surgical procedure. This is one of the most common surgical problems since the incidence after a laparotomy is 10-20% [1].
These hernias arise due to several risk factors, the final consequence is the weakening of the abdominal mioaponeurotic structure or the failure of sutures: the support given by the injured abdominal wall gives rise to one or more defects [2]. The first consequence of this anatomical situation is that the resistance of the abdominal wall has decreased, and its capacity solely depends externally on the skin and internally on the peritoneum, and with time, a part of the moving internal organs may slide towards the subcutaneous space through these defects that have developed. The outcome of this is a hernia that, due to several factors that determine the increase in the intra-abdominal pressure (i.e., muscular effort, cough, obesity) eventually increases its size. Incisional hernias can easily become complicated due to adhesions between internal organs and the wall, which cause intestinal obstruction, incarceration and strangulation. Surgical treatment in all patients is mandatory due to these fatal complications [2].

Patients with massive incisional defects are frequently disabled because their hernia is painful, it restricts their movements, generates back pain, affects breathing and significantly decreases life quality. These hernias are regularly not reducible, not because of the defect’s size but because of the loss of domain. Some patients may have chronic obstruction symptoms when their abdominal wall has multiple related defects [3].

**DEFINING GIANT HERNIAS**

The classification of incisional hernias is based upon anatomical and functional criteria and it is considered for its location, the patient’s comorbidities, its risk of postoperative complications and for the space in its maximum diameter of the parietal defect. According to the size of an incisional hernia, it is defined as: small (<10cm wide), big (10-20 cm) and giant (>20cm) [4].

The term giant hernia, or also called massive hernias, describes an entity that is characterized by a big ventral hernia related to multiple and complex clinical situations. The definition, diagnosis and surgical technique are not standardized; each case is unique, so the surgical planning and repair must be carefully selected.

The area of the hernial defect in relation to the intra-abdominal content and the volume of the hernial sac are the most important determining factors for hernia severity and complexity. A characteristic of the majority of giant hernias is the loss of domain, these giant sacs hold most of the internal organs and abdominal content for long periods of time which gives rise to a radical alteration in the anatomical and functional relations of the thoracic wall (rib cage), diaphragm and abdominal wall due to the progressive decrease of the intra-abdominal pressure caused by visceral herniation. In a middle line ventral hernia, the lateral muscles’ tensile strength extends the defect among the rectus muscles in such a way that the normal respiratory function is altered, this generates more herniation of the abdominal content towards the defect and thus, a chronically decreased abdominal cavity [5].

There are multiple formulas in relation to the hernial and abdominal volumes in order to objectively evaluate the loss of domain using scanning measures with CT scans [3].

The giant hernia is characterized for being a complex ventral hernia associated with a great parietal loss, which is so significant that it cannot be repaired with a simple apposition technique like in the rest of the hernias and it is related to:
• Multiple parietal defects.
• Important muscle atrophy of very large muscle areas.
• Relapses after repairs with or without mesh.
• Recurrent bowel obstruction.
• Prior mesh infection.
• Chronic infection of abdominal wall.
• Enterocutaneous fistula.
• Abdominal hypertension.
• Obesity [2].

Figure 1. Patient with giant incisional hernia, with loss of domain, enterocutaneous fistulae, and exposed mesh.

**Preoperative Workup**

When these patients are assessed, it is very important to make a detailed clinical history, a thorough physical examination and routine paraclinical examinations. The initial assessment should be multidisciplinary, including the surgical team, internal medicine, pneumology, dermatology, etc.

The planned outcome should comply with functional and esthetic objectives and the patient’s expectations; his physical activity and longevity are significant issues so the existing different options should be discussed with the patient and assess the tolerance to the same.

Respiratory function tests should be carried out since the reconstruction of the abdominal wall decreases total lung capacity, vital and residual functional capacity [6]. Nutritional assessment is also one of the most significant aspects for abdominal reconstruction since it has been demonstrated that malnutrition affects healing and decrease in tensile strength in tissues; albumin levels below 2g/dL are associated to a prolonged swelling and fibroplasia decrease [6].

The loss of excessive weight is essential in these patients since most of them are overweight and obese, which increases the risk of infections, recurrence and perioperative
complications. Any infection in the patient’s abdominal wall (i.e., ulceration, open wounds, enterocutaneous fistula) should be treated, by means of procedures of drainage, removal of strange objects such as meshes, surgical debridement, topical or systemic antibiotics, etc. The repair in patients with fistulas, recent manipulation or significant swelling due to trauma or infections, should be made until the inflammatory process has decreased.

A history of an intra-abdominal neoplasia is very important, since it complicates the process of abdominal reconstruction; the chemotherapy reduces healing, and radiotherapy damages tissues which can contribute to the surgical site’s swelling and atrophy.

Information about the prosthetic material previously used should be available and this can be presented with extrusion, fistulas or infection. Previous incisions should be analyzed since they indicate an interruption of abdominal vascularization of the area.

Every patient should have an imaging evaluation through CT scans which allows the assessment of the abdominal muscles, the defect size, the volume of the hernial sac, the presence of loss of domain and to rule out other unexpected conditions [7].

Figure 2. Diagnostic and treatment approach algorithm in patients with giant hernia.

**ABDOMINAL PREPARATION TECHNIQUES**

The repair of these hernias with loss of domain is technically difficult, with high morbidity, mortality and recurrence rates. This is a surgical challenge that implies the reduction and repositioning of the hernial content in a sudden way into the abdominal cavity, which can cause intra-abdominal hypertension [8], therefore extreme care and monitoring of the patient is necessary.
The objectives of the surgical management must be: 1. Re-functionalization of the abdominal wall including muscular support, 2. Prevention of visceral eventration and 3. An adequate tissue cover; for this, the aponeurotic apposition of both hernial ends is very important since the restructured wall acts as a primary support, the abdominal continent and prevents an excessive strain on the mesh, so all the techniques available should be used in order to achieve this objectives [9]. The use of prosthetics is required in order to prevent recurrences [8].

There are two surgical strategies for the treatment of abdominal parietal defects that are not suitable for the tension approximation of the tissues:

One option is to bypass the defect, whether with the patient’s native organic tissue, with synthetic products or with a compound material. The second option is to re-approximate the native tissue after several preoperative manipulations that generates abdominal progressive expansion and thus, an adequate hernia continent [9].

Currently there are no standard criteria to select a preoperative method, there are only recommendations with different evidence levels, the most widely used are:

- Progressive pneumoperitoneum: this has been used for 60 years in patients with “loss of domain”.
- Tissue expanders: they consist of implants that gradually expand the musculofascial tissue as a precursor to reconstruct the wall which allows bringing the ends of the defect together, they can be used in the subcutaneous, intermuscular, intramuscular or intra-abdominal space.
- Temporary muscle relaxation: secondary to a flaccid paralysis after an injection of Botulinum toxin type A (BTA).

**PREOPERATIVE PROGRESSIVE PNEUMOPERITONEUM**

The use of preoperative progressive pneumoperitoneum (PPP) for preoperative management of complex hernias started with Dr. Goñi Moreno in 1940 [10]. Afterwards, Herszage, Berlemont, Koontz, Gravez and Martínez Muníve [11] reported its use with some changes. PPP is recommended in patients with big hernias with loss of domain, when it is impossible to return the hernial content otherwise, and when there is a risk of generating respiratory failure or postoperative intra-abdominal hypertension [12].


The main purpose of the procedure is to increase the capacity of the abdominal cavity in order to contain all the hernial volume to perform a successful plasty. The largest series report good results using oxygen, CO₂ or room air.

The procedure consists of locating a scar-free point in the abdomen, preferably in Palmer’s point. A tap is made with a needle or trocar with sterile technique under local anesthesia, and a catheter is placed with Seldinger technique. Once inside the abdominal cavity the patient is insufflated with gas until he presents scapular discomfort or a sensation of abdominal fullness. Insufflation can be performed with an I.V. catheter, a peritoneal
dialysis catheter, or directly with a Veress needle. If a catheter is used it can remain in the intra-abdominal cavity until the surgical procedure.

Intra-abdominal pressure can be measured through a laparoscopic sensor. It is kept under observation and the procedure is repeated every 2 days for at least two weeks. Between each insufflation and surgery, patients should wear an abdominal belt to avoid the air from expanding only the hernial sac. This procedure can be made with inpatient treatment or outpatient treatment with controls in the physician’s office.

Figure 3. Abdominal CT scan of a patient who has been prepared with progressive pneumoperitoneum with a multi-lumen catheter after the insufflation of 2000cc of air.

Figure 4. Final preoperative result of a patient with progressive pneumoperitoneum.
Volumes insufflated in different reports vary around 14.71 liters total, with a range of 1-25 liters per session of insufflated air, in an average of 7-10 days for inguinal hernias and 15-28 days for ventral hernias [12, 14].

The loss of insufflated gas due to absorption and air leak is of approximately 47% since the peritoneum has a great reabsorption capacity, CO$_2$ absorption can be up to 42 L/minute [15].

There is a sustained elongation of the abdominal cavity, but also of the hernial sac, without altering the relation between these two. The procedure does not instantly reintroduce the hernial content, however it increases the possibility to reduce it during the surgical procedure. Also, it allows the visualization of associated or multiple defects that had not been diagnosed in previous examinations.

PPP generates the elongation of muscles in the abdominal wall, which enables the apposition of the aponeurotic ends. In a prospective study, it was observed that the average length of the abdominal rectus increased from 99 to 109 mm ($p<0.05$) and from 100 to 113 mm ($p<0.05$), the length of anterolateral muscles also increased from 198 to 233 mm ($p<0.05$) and from 185 to 210 mm ($p<0.01$) [16].

PPP also gives rise to progressive respiratory adaptation through controlled moderate restriction and it can be considered a tolerance parameter for definite abdominal plasty. This pulmonary preparation is essential in patients with giant hernias due to functional and anatomical issues that patients suffer.

The effects of PPP considering respiratory function, intra-abdominal volume and the length of the muscles in the abdominal wall were compared in a prospective study of 19 patients. The finding was an increase in the intra-abdominal volume of 2,021cc ($p<0.01$) as well as the volume of the hernial sac in 690cc ($p<0.01$) with no difference in the relation between the hernial volume and the abdominal cavity [14]. Regarding the respiratory function, a decrease in the Forced Vital Capacity (FVC) of 25.3% ($p<0.01$) and 29.6% in the FEV1 ($p<0.05$) was found. There were no differences in the FEV1/FVC rate. Total pulmonary volume decreased 15.4% without being significant [14].

In another study by Oprea et al. reported a significant increase in the respiratory parameters (FVC, FEV1, FEV1/FVC) during the preparation with pneumoperitoneum and in the postoperative, compared to basal values [17].

Adhesiolytic effect of the PPP has also been described, which can explain the progressive distribution of the air in the abdominal cavity and the ease of dissection during the surgical procedure [18, 19, 20].

This procedure is not exempt from complications which are secondary to the repeated taps, insufflation intolerance, subcutaneous emphysema and hematoma formation [14]. No cases of mortality have been reported from the use of this technique.

**Botulinic Toxin A**

The temporary muscle relaxation technique secondary to an injection of Botulinum toxin type A (BTA) in the abdominal wall generates muscle paralysis and its resulting relaxation entails a reduction in the hernial defect and helps surgical reconstruction [21], since it allows the advancement of muscle lateral flaps without weakening them in its anatomical structure, it
is a tool that does not permanently weaken the wall and does not generate great postoperative pain.

The botulinum toxin is a product of the *Clostridium botulinum* bacillus; it has several serotypes, type A being the first one to be isolated and purified for clinical use. The neurotoxin blocks the protein complexes within the cholinergic nerve endings producing a block in the muscular and autonomous synapse at the level of the neuromuscular junction; moreover, it performs proteolysis of the necessary receptors for the release of neurotransmitters generating a muscular “chemodenervation”. An atrophy and reduction in the affected muscle mass can be seen in a 31%, being a reversible process with an axonal restructuring. The preoperative use of this toxin is safe because it is highly specific and selective since it acts coming together with high affinity to cellular ecto-receptors that have contact with target neural cells, it only acts in cells that have this receptor [22]. Its clinical effect starts within 3 days with a peak at 2 weeks, recovering nerve function within 3-6 months [23].

The originally described technique [21] consists of the infiltration with 100ui of Botulinum toxin type A in 5 points on each side of the aponeurotic defect: two points in the midaxillary line between the costal margin and the external iliac crest, and three points in the edge of the external oblique muscle. Under sterile conditions and guided by the findings of the CT scans of the internal and external oblique muscles, and with or without guidance with an ultrasound in real time. This is an outpatient treatment. Control imaging tests are performed after 4 weeks and surgery is scheduled. Until now, no complications have been reported in the use of this procedure or in the use of preoperative BTA.

![Figure 5. Infiltration points during the application of TBA. MAL = Medial axillary line. AAL = Anterior axillary line MCL = Medium clavicular line CM = Costal margin IC = iliac crest.](image-url)
The first study that reported the benefits of BTA in the increase of the abdominal cavity was described by Çakmak [24] using rats to prove the paralysis effect as a result of the BTA injection in the abdominal muscles, getting a difference of 21% in the intra-abdominal volume between the experimental and control groups. A prospective study on pigs was performed in 2011 through the application of 150ui of BTA on one side of the abdominal wall randomly, on the other side, isotonic solution was infiltrated as a placebo. Three weeks later both groups were compared and an increase of 49% was reported on the advancement of musclecutaneous flaps on the side with BTA compared to the control group, as well as a 68% of advancement performing a muscular components separation [25].

In 2009, the group of Ibarra et al. [21] carried out a prospective study in 12 patients with giant hernias with previous open abdomen management, applying BTA in 5 points on each side of the abdominal wall guided by electromyography. Imaging tests were performed before BTA and 4 weeks after the same. The comparison of both studies reported a global reduction of the hernial defect of 5.25±2.32cm (p<0.001; 95% CI 3.59-6.91), the primary apposition was achieved in 6 patients, and 6 required muscular component separation (MCS), 16.67% of post-surgical complications was reported. In the 9-week-follow-up, no recurrences were reported.

The use of BTA in patients with open abdomen to decrease the formation of secondary planned ventral hernias through the application of 300ui diluted in 6 points has been reported as well, resulting in a primary apposition rate of 83% with a partial closing supported with resorbable mesh in 6% and a rate of residual hernia of 11% [23].

The technique of preoperative application of BTA enables better conditions to plan the surgery and does not exclude the other additional resources that in the intraoperative would be needed to re-functionalize the wall [22]. However, the dose and the application technique of BTA are not standardized yet, so randomized studies are necessary in order to determine them [26].

**Tissue Expanders**

Hobard and Byrd were the first ones to use the musculofascial expansion techniques using expanders implanted as precursors for the reconstruction of the abdominal wall. They described the expansion of the abdominal fascia in congenital defects in the middle line and in cloacal defects [27] and its use has continued in the pediatric surgery field [28]. Carlson described the expansion technique in the plane between the subcutaneous tissue and the abdominal fascia in patients who received grafts on big-sized defects, with subsequent reconstruction with intraperitoneal mesh [29].

The main advantage of this technique is the recovery of the normal anatomy without an impact on the muscles or neurovascular structures and achieving a strain-free closing. Usually, the lateral abdominal wall is not damaged due to previous surgeries in patients with giant hernias, so it can be safely used for expansion in these patients and can be used in ostomized patients since most stomas are medial to the rectus sheath. The insertion of expanders is easily reproducible; it is an outpatient procedure with minimum anesthetic and surgical risk.
Figure 6. Patient before and after the use of tissue expanders for abdominal wall reconstruction.

Figure 7. Tissue expander removal during the abdominal wall reconstruction procedure.

The expansive forces generated by the implant are applied on the abdominal wall muscles, but as well as on the soft tissues and the abdominal cavity, this is demonstrated by
the protrusion of the hernial sac after the big volume expansion. In some cases, the visceral return to the abdominal cavity during this process is observed.

The ideal position for the expanders is in the interoblique muscle plane, with which an expansion of the myofascial complex, skin and soft tissues is produced. Since the external oblique muscle is the largest and most vascularized of the muscles in the lateral abdominal wall, it is the one that is used as a cover of the expansion, leaving the internal and transverse oblique muscle as a deep and robust layer for the expander. If the expansion was made one plane below the internal oblique muscle, the transversalis fascia would not have enough integrity to allow the expansion underneath the arcuate line which will cause a preperitoneal expansion.

Table 1. Comparison of different methods of abdominal preparation for patients with giant hernia

<table>
<thead>
<tr>
<th>Preoperative Progressive Pneumoperitoneum</th>
<th>Botulinic Toxin A</th>
<th>Tissue expanders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantages</td>
<td>Low cost</td>
<td>Easy reproduction</td>
</tr>
<tr>
<td>Great availability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can be used in combination with other methods.</td>
<td></td>
<td>Can be used in combination with other methods.</td>
</tr>
<tr>
<td>Improvement in respiratory function</td>
<td>Does not alter the functionality or wall anatomy</td>
<td></td>
</tr>
<tr>
<td>Does not alter the functionality or wall anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disadvantages</td>
<td>Difficult to reproduce</td>
<td>High cost</td>
</tr>
<tr>
<td>Possible visceral lesions when introduced</td>
<td>Not available in every center.</td>
<td>Pain when filling the expander.</td>
</tr>
<tr>
<td>Discomfort when insufflating.</td>
<td>Pain due to infiltration</td>
<td>Prolonged time required (1-2 months)</td>
</tr>
<tr>
<td>Can cause intra-abdominal hypertension</td>
<td>Possible anaphylactic reaction</td>
<td>It requires an operating room for placement</td>
</tr>
<tr>
<td>Multiple subsequent visits to insufflate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technical difficulties</td>
<td>Patients with multiple adherences</td>
<td>Ostomized patients</td>
</tr>
<tr>
<td>Obese patients</td>
<td>Obese patients</td>
<td>Irradiated skin</td>
</tr>
<tr>
<td>Irradiated skin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This plane is avascular, it is easily identified and it provides a wide space for the placement of expanders. This space is limited by the inguinal ligament in its inferior border, medially by the lateral border of the rectus sheath, laterally by the mid-axillary line where the neurovascular bundle of the major oblique is found, and its superior limit by the costal margin. Transverse incisions are used on the muscles of the abdominal wall in the rib margin through the external oblique fascia since no nerves or parietal vascular structures are damaged through the blunt dissection of a plane between the external or internal oblique muscle at this point [30].
Expert commentary.

Antonio Espinosa-de-los-Monteros, MD
Plastic Surgery Attendant
National Institute of Nutrition Salvador Zubirán, México City, México.

These days, best outcomes for hernia treatment, in terms of lower postoperative wound complications and lower recurrence rates, are achieved when the muscles are closed together and posterior mesh is placed to reinforce closure.

Giant hernias are inherently complex because they require special techniques to achieve full muscle closure, they are associated with increased postoperative morbidity, and recurrence rates are expected to be higher. To overcome these situations, modern approaches focus on preoperative preparation. This not only refers to improve systemic patient conditions, but also to modify the relationship between abdominal continent (i.e., the abdominal wall) and abdominal content (i.e., the visceral block).

This chapter discusses several techniques that allow us to get a positive impact in this regard. This policy implies a modification on classical trends that used to take patients straight to the operating room to get their problem fixed, regardless of general conditions present. The experience retrieved from those days, has shown us that obesity, smoking, immunosuppression, coagulation disorders, pulmonary restriction, high serum glucose levels, malnutrition, and local infection among others, are modifiable conditions that perpetuate undesirable outcomes that include wound dehiscence, infection, need of prolonged local wound care, multiple trips to the operating room, mesh removal, postoperative bleeding, chronic sinus tracts, extruded mesh, chronic seromas, and ultimately hernia recurrence.

Preoperative computed tomography scan has become an important tool for preoperative evaluation in patients with complex giant hernias. It helps in defining the extent of the defect, as well as the characteristics of abdominal wall muscles, and to obtain local measurements that ultimately have an impact on postoperative prognosis. Today, muscle thickness, intra-abdominal volume, and total abdominal wall length have become modifiable conditions that allow us to prepare challenging patients transitorily in order to be able to perform surgical procedures that are associated to an improved quality of care. In our medical center, patients with extreme obesity and giant hernias undergo transient weight loss with vertical band gastroplasty. Once they have lost weight after few months, open gastroplasty reversal and conversion to a gastric bypass is performed along with abdominal wall reconstruction for ventral hernia repair. This preoperative preparation has allowed us to provide surgical care that has been associated with appropriate and stable results.

Today, a trend towards optimizing patients’ conditions preoperatively exists. This not only is expected to be associated with better immediate postoperative outcomes, but also with improvements in overall physical activity, quality of life, and decrease in hernia recurrence rates. Most of these maneuvers have a transitory impact on overall patients’ conditions. This impact is beneficial for surgical repair of giant hernias, but a relationship between abdominal wall, intra-abdominal content, and systemic conditions exists for patients lives.

Modern studies with long follow-ups (i.e., ten years or more) have shown us that hernia recurrence can occur even several years after surgical repair. Therefore, future directions will have to be focused on developing strategies that provide longer lasting benefits, so that these
positive conditions are not only present during surgical repair to assure the procedure is going to be feasible, but also to provide a scenario that is consistent with stability of results achieved. This policy is likely to involve not only abdominal wall surgeons in overall patient care, but also physical therapists, internists, nutriologists, infectologists, endocrinologists, pneumologists, radiologists, bariatric surgeons, algologists, primary care physicians, wound care nurses, and social workers. Also, this trend will require longer patient follow-ups so that we can have an overall impact in decreasing the development of this disease, in improving the quality of the treatments we provide, and in implementing rehabilitation processes that can be associated with long lasting stability of our care.

In order to perform the exposition of the inter oblique plane, a 5cm-long transverse incision is made in the costal margin in the anterior axillary line, slightly oblique and towards the costal margin; the dissection is made through the subcutaneous cellular tissue, an incision is made in the fascia of the external oblique going downwards following the direction of its fibers. This allows the dissection within an areolar and superficial plane to the fascia of the internal oblique. The expanders are placed vertically in the dissected anatomical space, 250cc are initially infiltrated and the fascia and skin are sutured by planes. Afterwards, 250cc are infiltrated every week to complete 1L according to the patient’s tolerance. This procedure should be made in the operating room and it can be an outpatient treatment.

The implants are removed during the reconstruction surgery of the abdominal wall. These leave a dissected space that can be used to complete a muscular component separation.

However, there are no controlled prospective studies in the use of tissue expanders for the closing of defects of the abdominal wall. It is an invasive, high-cost procedure that includes several visits to the doctor’s office. There are many questions left about the effectiveness of this method since part of the expansion is made towards the intra-abdominal cavity [9].

An intraabdominal increase in volume can be achieved by both tissue expanders and progressive pneumoperitoneum, but the techniques are expensive and time-consuming and have not shown individual superiority in a clinical trial. Combining these methods might be beneficial, but again it requires further investigation.

REFERENCES


Preoperative Techniques for the Management of Giant Hernias


**BIOGRAPHICAL SKETCH**

**Name:** Karla Verónica Chávez-Tostado  
**Affiliation:** Endocrine Surgery, Instituto Nacional De Nutrición Salvador Zubirán. México city, México  
**Date of Birth:** November 15, 1985  
**Education:**  
General medicine: Universidad de Guadalajara, Jalisco, México  
General surgery: Hospital General Dr. Manuel Gea González, México city  
Endoscopic surgery: Hospital General Dr. Manuel Gea González, México city  
Endocrine surgery: Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México city  
**Address:** Vasco de Quiroga No. 15. Tlalpan, D.F. México. PO BOX 14090  

**Research and Professional Experience:**  
Professional Appointments: Attending surgeon, Hospital General Ajusco Medio. México city, México.  

**Publications Last Three Years:**  
(1) Resultado de la aplicación de Toxina Botulínica A en el tratamiento de Hernias incisionales gigantes (Rev Hispanoam Hernia 2014;2(4):145-151 Revista Hispanoamericana de Hernia. ISSN: 2255-2677.  
Chapter 5

**INTRAABDOMINAL PRESSURE MODIFICATION IN “COMPONENT SEPARATION” TECHNIQUE FOR REPAIR OF INCISIONAL HERNIA**

*Marco Mazzocchi¹, Valentina Sorvillo² and Luca A. Dessy²*

¹Department of Plastic and Reconstructive Surgery, University of Perugia, Perugia, Italy
²Department of Plastic and Reconstructive Surgery, “Sapienza” University of Rome, Rome, Italy

**ABSTRACT**

Between 5 and 11% of abdominal surgeries are complicated by incisional hernias. The repair of these massive ventral hernias continues to be challenging for surgeons. The repair of these defects should ideally be tension-free, provide dynamic muscle support, and prevent eventration.

Surgical options are open primary repair, open repair with mesh, laparoscopic repair, or autologous tissue transfer or mobilization. Primary repair is rarely successful, with recurrence rates ranging from 18% to 62%. If synthetic mesh is added, recurrence rates dramatically drop to 2%-32%. Therefore reconstruction using pre-peritoneally placed prosthetic material is still the most frequently used technique. Anyway the increased risk of infection in case of wound complications and the rigidity of the abdominal wall are relative contraindications against the use of prosthetic materials.

An interesting alternative to traditional mesh are acellular dermal matrix, porcine intestinal mucosa and porcine dermal, used safely and effectively to successfully repair incisional hernias wherever the use of traditional permanent prostheses would not be safe.

An already standard technique, introduced in 1990 by Ramirez, Ruas and Dellon is the “components separation technique” characterized in bridging the fascial gap without the use of prosthetic material. The technique is based on the enlargement of the abdominal wall surface by separation and advancement of the muscular layers, thus allowing regaining to up to 10 cm of unilateral advancement.

A remarkable evaluation to be made is as the reconstruction with the component separation allows reducing the intra-abdominal pressure.
Normal intra-abdominal pressure in adults is less than 10 mmHg, whilst intra-abdominal pressure values over 15 mmHg are indicative of intra-abdominal hypertension. Prolonged increased intra-abdominal pressure over 20 mmHg is known to cause serious conditions such as acute renal failure, pulmonary impairment and reduced blood flow to the gastro-intestinal organs. In addition a vicious circle begins and increased intra-abdominal pressure causes elevation of the diaphragm, which is in turn followed by increased intra-thoracic pressure, and there is evidence suggesting that increased intra-thoracic pressure results in increased intra-cranial pressure and functional obstruction of the cerebral venous outflow via the jugular venous system.

The abdomen has a dynamic muscular wall that can accommodate marked variations in volume, which are accompanied by changes in intra-abdominal pressure. Repair of the incisional hernia causes extrinsic compression of the abdominal content and elevation of intra-abdominal pressure, especially in the first day after surgery. However intra-abdominal pressure slowly decreases the days after surgery and stands on physiological values.

Between 5 and 11% of abdominal surgery are complicated by incisional hernias [1-6] and causing serious morbidity due to various factors, including bowel or omental incarceration and strangulation.

The presence of large incisional hernias generate many invalidating symptoms, such as bulging of the abdominal wall, chronic wounds, immobility and back pain, thus requiring surgical treatment [7].

The repair of these substantial ventral hernias has always represented a formidable challenge for the reconstructive surgeon. Not only because such defects are frequently unattractive, but also because of abdominal wall weakness associated with marked contour abnormality and protuberance of abdominal viscera. These sequelae from massive defects often interfere with the patient’s activities of daily living [8].

Many surgeons try to postpone or avoid abdominal wall reconstruction because of the difficulties in management, the high morbidity and the moderately high recurrence rate associated with this procedure.

The traditional approach to incisional hernia repair is an incision via the previous scar, which is usually vertical. However, an approach via a low transverse incision may, in some cases, be considered. Indeed, techniques that have been developed for the surgical approach to abdominoplasty include the use of a transverse lower abdominal incision and the resection of excess skin. Numerous studies, most of which have been gynaecological in nature, suggest as successful pannus resection in conjunction with intra-abdominal procedures [9-14]; very few of these reports have addressed the challenges involved in the repair of incisional hernia [15-18].

The benefits described for this approach are: full exposure of the abdominal wall defects, a surgical approach through known tissue planes, and fascial repair far from the skin incision. By incorporating these aspects into hernia repair, the safety of the procedure is maintained, the recurrence rates are reduced, and the aesthetic outcome is enhanced [19].

Taking into account reconstructive techniques surgeons have many options: open primary repair, open repair with mesh, laparoscopic repair, or autologous tissue transfer or mobilization.

The objectives of abdominal wall reconstruction basically are to restore structural support, provide stable soft-tissue coverage, and optimize aesthetic appearance while
minimizing morbidity and postoperative disability. [21-24] So the repair should ideally be tension-free, provide dynamic muscle support, and prevent eventration. Primary fascial repair satisfies the last two of these three criteria, but cannot be realized in a tension-free environment when the fascial defect is large. Consequently, primary repair is rarely successful, especially in large defects with recurrence rates ranging from 18% to 62%, depending on the size. [21-24] Anyway synthetic meshes settlement reduces significantly recurrence rates to between 2% and 32% [21, 23-26].

Recurrence of incisional hernia is, however, directly related to definite patient comorbidities, defect characteristics, specific repair methods and, most importantly, follow-up time. Not surprisingly, the recurrence rate is related to the size of the hernia, with a 41% recurrence rate for hernias larger than 4 cm, and a 25% recurrence rate for those smaller than 4 cm [27]. The role of primary repair in moderately large hernias is therefore limited. Moreover, numerous efforts have been made to reduce tension, including expansion of the abdominal wall with prosthetic materials. Although techniques that use mesh, or other prosthetic materials, can eliminate tension on the closure, they are not ideal due to the risk of infection, mesh migration, erosion into the bowel and enterocutaneous fistula. Bioprosthetic mesh has clear advantages over synthetic mesh. Healing in bioprosthetic repair sites is due to a regenerative process as different to scar tissue formation of synthetic one. Once remodelled with autologous tissue, there is theoretically no ongoing foreign body response, thereby reducing the risk of chronic infection and subsequent erosion through the skin or viscera. Bioprosthetic mesh adheres significantly less to abdominal viscera, thus allowing it to be placed directly over the bowel. However, little is yet known about the biological and physiological mechanisms of action and long-term outcomes of abdominal wall reconstruction performed with bioprosthetic materials. [28, 29] Another functional drawback of mesh is that since it does not provide dynamic support, problems occur where the static mesh meets the dynamic abdominal wall tissue [30, 31].

The use of autologous tissue to repair abdominal wall hernias has been described in detail. Some examples of autologous tissues suitable either as free or pedicled flaps are tensor fascia lata, sartorius and rectus femoris, functional to close large defects. However, in huge defects, the deficiency of necessary tissue may require the placement of prosthetic material or transposition of autologous material to bridge the fascial gap.

Anyhow reconstruction using pre-peritoneally placed prosthetic material remains the most frequently used reconstruction method. [24] This technique leads to an increased risk of infection in case of wound complications and is a relative contraindication against the use of prosthetic materials in patients with healing defects. Another pitfall of the use of large sheets of synthetic material for hernia repair is the resulting rigidity, non-compliance, a-dynamism of abdominal wall. [32] Moreover, the use of prosthetic material should be, if possible, avoided whenever the interposition of either the peritoneum or greater omentum between the bowel and the prosthesis is impossible.

To overcome this problem biological prostheses have recently become available. These prostheses are useful in contaminated wounds or when the risk of infection is high. Acellular dermal matrix, porcine intestinal mucosa and porcine dermal collagen have been used safely and effectively as an substitute to traditional synthetic meshes to successfully repair hernias in contaminated operating fields [28, 29].

Another valid alternative to the use of prosthetic material was described in 1990 by Ramirez, Ruas and Dellon as the “components separation technique.” [33] This technique is
based on the amplification of the abdominal wall surface by separation and advancement of the muscular layers. This technique allows regaining up to 10 cm per side, thus permitting a tension-free abdominal closure with medialization of the rectus abdominis muscle in large ventral hernias. [20, 34-41] Recent modifications of the original technique, including preservation of periumbilical perforators, have led to decreased wound complications in large hernia repairs. [42] This technique reduce the risk of recurrence and provide a reliable autologous reconstructive option for complex ventral abdominal defects [33, 34, 43-45]. Ger and Dubois reported that innervated and vascularized musculofascial flaps are superior to prosthetic materials or adynamic and devascularized autologous tissue for the repair of large hernia defects. [46] Abrahamsom and Eldar emphasized the importance of recreating the linea alba to provide an anchor for the lateral abdominal wall anteriorly in order to reduce the risk of recurrence [47, 48].

An interesting data to evaluate in all surgical technique is the abdominal pressure either pre and postoperative.

In our experience we evaluated 35 patients from January 2006 to June 2015. The reasons for surgery were recurrent incisional hernia in 23 cases (65.7%) and incisional hernia in the remaining 12 cases (34.3%). Patients underwent previously to surgery included bariatric, bowel resection, cholecystectomy and a variety of obstetric/gynaecological procedures. Within the subgroup of patients with recurrent hernias, the number of prior repairs ranged from 1 to 4 (mean: 1.85). The overall incidence of prior mesh encountered perioperatively was 71.4% (25 cases). The type of mesh that had been used in the previous surgical treatment was composite Prolene/e PTFE dual mesh or Polytetrafluoroethylene-PTFE. The mesh was infected in five cases.

23 patients were women (65.7%) and 12 patients were men (34.3%). The patients’ age ranged between 45 and 79 years (median: 62 years).

The patients’ body mass index ranged from 19.6 to 58.2 kg/m² (mean: 42.9 kg/m²).

Patients had at least one risk factor for recurrence, including morbid obesity (12 patients, 34.3%), diabetes mellitus (10 patients, 28.5%), and recent massive weight loss after bariatric surgery (8 patients, 22.8%). Eight patients (22.8%) had a history of smoking. None of the patients had severe asthma or a chronic respiratory tract disorder.

Preoperative measurements of the defect area were made by means of computed tomography scan. All defects were midline; according to Chevrel’s classification [49], they were supraumbilical (M1) in 5 cases, juxtaumbilical (M2) in 7 cases, subumbilical (M3) in 6 cases and xypho-pubic (M4) in the remaining 17 cases. All the defects were longer than 11 cm transversally and varied in length vertically. According to Chevrel’s classification [49], they were 10 to 15 cm wide (W3) in 18 cases and > 15 cm in the remaining 17 cases (W4). The size of the defects ranged from 108 cm² (11x13 cm) to 499 cm² (24x26 cm), the mean being 325 cm². In two patients, the computed tomography scan highlighted the loss of abdominal domain. In addition, the abdominal viscera in these two patients were predominantly outside the abdominal cavity, the size of the abdominal cavity being substantially reduced because of the lateral contraction of the abdominal wall musculature.

All patients underwent preoperative deep venous thrombosis prophylaxis, with subcutaneous heparin injections and sequential compression devices, and intravenous cephalosporine injection. Our approach was a lower abdominal incision; in addition a vertical incision was added only in the patients with a previous midline scar, resulting in an inverted T
incision (43%). This technique allowed a greater exposure, especially in cases of epigastric hernias.

The position of the low transverse skin incision allows dissection from the normal tissue planes around the hernia toward the fascial edge and hernial sac, thus minimizing the risk of enteric injury. Our suggestion is to grasp with a clamp each end of the skin paddle before avulsion; thus ensuring a good alignment of the superior and inferior skin edges. After panniculectomies were accomplished by excising a large horizontal ellipse with corners based at the bilateral iliac crests. Pannus specimens were sent to the pathology laboratory for weights and gross inspection. The extent of panniculus resection ranged from 850 g to 3250 g, the mean being 1470 g. This primary lipectomy allows optimizing exposure of the hernia sac and the rectus musculature. It’s important to pay attention to elevate the skin flaps only as far as necessary to clearly identify the hernial defect and the semilunar lines in order to preserve as many perforators as possible. In general, attempts were made to limit exposure to the suprapubic/hip incision by means of conservative undermining under the costal margins. The procedure that we performed recreates the linea alba, thereby successfully providing a midline anchor.

After this initial stage abdomen was opened through bilateral incisions in the external oblique fascia just lateral to the semilunar line. The plane is dissected prudently to avoid dissecting down the internal oblique fascia, since the arteries and nerves that supply the abdominal musculature travel deep within this fascia. If it’s impossible to achieve enough mobilization, the posterior sheath of the rectus fascia can be incised to gain further distance. [31] Secondary the posterior side of the abdominal wall was cleaned of adhesions, and bowel resection was performed when necessary (in two cases of bowel adherence and two of “loss of domain.” If a prior prosthetic mesh was identify it was removed.

After assessing the total distance on each side, the surgeon can mobilize tissues, gaining as much as 10 cm in the epigastrium, 20 cm at the waist and 6 cm in the suprapubic region. [33] In all 22 of our patients, we were able to successfully close the fascial defects and avoid the use of permanent mesh.

Component separation was performed in the original method by incising the aponeurosis of the external oblique muscle longitudinally about 2 cm laterally of the rectus sheath, and dissecting the external oblique muscle until the internal oblique fascia was encountered. The external oblique muscle was then elevated to the level of the midaxillary line bilaterally. After debridement of the scar and separation of the tissue from the medial edges of the rectus muscle, the myofascial rectus flaps were advanced. This mobilization allowed primary closure of the hernia defect with minimal tension using interrupted figure-of-eight 0 polypropylene suture. Plication of the midline abdominal wall from the xiphoid to pubis was performed, thereby approximating adjacent fascia over the hernia repair, reinforcing the repair and improving the contour and tone of the lax abdominal wall using uninterrupted 2/0 polydioxanone suture. No mesh was used in any of the cases. Suction drains were used routinely.

If the umbilicus had previously been released from the abdominal wall, it was reattached. The patients were maintained on nothing-by-mouth status postoperatively until the return of bowel function defined by the passage of flatus. Nasogastric tubes were used if extensive intra-abdominal dissection was required as part of the procedure. A pressure dressing was maintained during the immediate postoperative period, and a pressure bandage was kept in place for four weeks.
There are three most reliable methods of indirectly measuring intra-abdominal pressure are gastric, inferior vena cava and urinary bladder pressure measurements. [50-52] In this study, intravesical pressure was measured on account of the simplicity of this measurement in catheterized patients. The first measurement was effectuated following the induction of general anaesthesia, a standard Foley catheter was inserted and the bladder emptied as best as possible by gravity. Upon the return of four muscular twitches, 100 ml of sterile saline was instilled into the emptied bladder and the catheter tubing clamped distally to the aspiration port. A Stryker compartmental pressure monitor (Stryker-Leibinger, Kalamazoo, Mich.) was used to measure intravesical pressure, at the end of expiration, through the catheter aspiration port. Measurements were taken at the following intervals: preoperatively (T0), after hernia repair (T1), after skin closure (T2), postoperative day one (T3). Data collected were analyzed by means of Wilcoxon’s matched pairs signed rank sum test; statistical significance was set at \( p < 0.05 \). Data showed an intravesical pressure increase following muscular repair (T1), when it reached a mean value of 15.14 mmHg, another slight increase following complete skin closure and application of the dressing (T2) (mean value: 15.95 mmHg) and, lastly, a slight drop in intravesical pressure 1 day postoperatively (T3) (mean value: 14.00) (Table I). The difference in intra-abdominal pressure values was highly significant (\( P < 0.01 \)) between T0 and T1, T2, and T3 as well as between T1 and T2, T2 and T3, and T1 and T3 (Table II).

Fifteen patients were completely satisfied with the appearance of their abdomen (score 2), while seven were satisfied with the improvement (score 1). No patients reported an absence of improvement (score 0).

All the patients were extubated on the day of surgery; none required reintubation because of respiratory compromise, while six patients needed oxygen delivered by mask (to maintain saturation above 92%) for more than one hour in the recovery period. The mean intensive care unit stay was 0.3 days (range, 0 to 3).

The average length of hospital stay in the panniculectomy/separation-of-components patients was 8.9 days (range, 5 to 24). Bowel function was the predominant reason for this prolonged hospital stay.

No major early (up to 3 months) complications occurred in patients. The most common minor complication was minor skin necrosis or dehiscence, only requiring local wound care, which occurred in six patients (17.1%). In two of these patients some degree of necrosis and wound separation, which required additional dressing changes, occurred at the T-junction, though neither required reoperation for debridement or closure.

Cellulitis, requiring either intravenous or oral antibiotics, occurred in one patient (3%). Infected fluid collection requiring local wound care and antibiotics occurred in two cases (6%). Seromas formed following drain removal in seven patients (20%), all of which were treated successfully with drain replacement or serial percutaneous drainage.

Follow-up visits were scheduled 1, 3 and 6 months, and then every year after surgery in order to evaluate the presence of complications or hernia recurrence. The mean follow-up time was 26.8 months (range, 12 to 44 months). Hernias recurrence was detected in one of the patients (3%), who had a small (3x4 cm) after 12 months. This hernia recurrence was successfully resolved by means of a secondary procedure. Our recurrence data are interesting compared to the ones reported by Ramirez et al. (recurrence of 8%), [33] Di Bello and Moore (recurrence 8.5%) [34] and Thomas et al. (no recurrences). [44] Probably the issue that influences significantly to the low recurrence rate in our series was the work made to relieve tension on the fascial closure once the edges were sutured. This was realized by using a
second running suture placed on either side of the fascial closure to imbricate the edges. This moved the tension from the closure onto the imbricating suture line and off the fascial closure. The resulting primary fascial coaptation ensures dynamic support of the abdominal wall, thereby minimizing the potential bulge associated with a simple patch closure of prosthetic mesh. Anyway a longer follow-up period is required to more accurately assess the recurrence rate in our series.

Table 1. Intravesical pressure (mmHg)

<table>
<thead>
<tr>
<th></th>
<th>Preop.</th>
<th>Hernia repair</th>
<th>Skin closure</th>
<th>1 Day postop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>17</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>16</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>18</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>19</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>18</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>21</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>11</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>15</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>13</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>9</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>8</td>
<td>14</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
<td>14</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>13</td>
<td>6</td>
<td>12</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>14</td>
<td>10</td>
<td>19</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>15</td>
<td>8</td>
<td>13</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>16</td>
<td>9</td>
<td>19</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>17</td>
<td>10</td>
<td>20</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>18</td>
<td>9</td>
<td>14</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>19</td>
<td>9</td>
<td>15</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>20</td>
<td>7</td>
<td>12</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>21</td>
<td>8</td>
<td>14</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>22</td>
<td>4</td>
<td>10</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>23</td>
<td>8</td>
<td>14</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>24</td>
<td>7</td>
<td>17</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>25</td>
<td>7</td>
<td>15</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>26</td>
<td>8</td>
<td>12</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>27</td>
<td>8</td>
<td>14</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>28</td>
<td>6</td>
<td>12</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>29</td>
<td>9</td>
<td>19</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>30</td>
<td>9</td>
<td>17</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>31</td>
<td>8</td>
<td>17</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>32</td>
<td>6</td>
<td>16</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>33</td>
<td>9</td>
<td>18</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>34</td>
<td>7</td>
<td>15</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>35</td>
<td>8</td>
<td>17</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>MEAN</td>
<td>7,5</td>
<td>15,14</td>
<td>15,95</td>
<td>14</td>
</tr>
</tbody>
</table>
Table 2. Statistical significance of the differences between values was determined by the Wilcoxon test

|                          | M +/- SD (mmHg) |
|--------------------------|-----------------
| Preop (T0)               | 7.5 +/- 2.064   |
| Hernia repair (T1)       | 15.14 +/- 3.371 |
| Skin closure (T2)        | 15.95 +/- 3.124 |
| 1 day postop (T3)        | 14 +/- 3.338    |

M, mean; SD, standard deviation.

<table>
<thead>
<tr>
<th>Wilcoxon test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop (T0) - Hernia repair (T1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preop (T0) - Skin closure (T2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preop (T0) - 1 day postop (T3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hernia repair (T1) - Skin closure (T2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hernia repair (T1) - 1 day postop (T3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Skin closure (T2) - 1 day postop (T3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

p, probability.

No patient developed abdominal wall weakness, lateral herniation or postoperative bowel obstruction.

A physical examination was also conducted at each follow-up visit and the condition of the abdominal wall evaluated by means of an ultrasound examination and CT imaging.

The clinical appearance of the abdomen was subjectively evaluated by patients after surgery. The subjects’ global impression of clinical improvement was recorded using a scale ranging from 0 to 2 (0 = no improvement; 1 = satisfaction with improvement; 2 = complete satisfaction).

An important feature of the component separation technique is that it provides local autologous reconstruction for complex and contaminated wounds. Indeed, autologous reconstruction is the most logical option when an infected or contaminated wound is expected [43, 47, 48]. However, the surgeon should be fully aware of the risks involved in component separation before surgery. The use of this procedure must be taken into account within the context of the patient’s preoperative medical condition and the complexity of the defect.

As the inability to sufficiently expose incisional hernias result in a high recurrence rate, we hypothesise that recurring or recalcitrant hernias may benefit by the creation of a dynamic abdominal wall, and that wide exposure of the entire anterior abdominal wall not only permits the identification of additional areas of weakness and simultaneous hernias, but also reduces the tension created by scar and skin contracture. In addition panniculectomy, a commonly used technique to gain access to the obese abdomen, has yet to be recognised in the literature as an adjunct to the separation-of-parts hernia repair in obese patients [9-14, 18]. According to our experience the combination of these procedures is recommendable in every type of patient. In fact, the poor vascularity of widely undermined skin flaps may be partly responsible for this high complication rate. However, the combination of the component separation technique with an abdominoplasty, in which a part of the skin flaps is resected, may reduce the likelihood of this complication by eliminating the poorly vascularized part. In conclusion panniculectomy decreases tension on the fascial closure, eliminates poorly
vitalized tissue and a portion of the subcutaneous dead space. In the other hand, we recognize that this adjunctive technique creates an additional incision, thus increasing the chance of wound infection or dehiscence.

Conservative pannus resection and the separation-of-parts hernia repair in our series was achieved without either significantly elevating the diaphragm or creating any postoperative ventilation difficulties (the “loss of domain” syndrome), as the intra-abdominal pressure values showed [18].

The extensive undermining that is often needed for effective fascial closure can predispose patients to seroma formation. Seromas are associated with an increased risk of infection, wound dehiscence, flap necrosis and reoperation. From this it follows that placement of multiple suprafascial drains, which we strongly suggest, can reduce the rate of seroma formation. It is important to left drains in place until the skin flap has adhered to the fascia. It may be possible to apply fibrin sealants, which have been used to reduce the incidence of seroma formation following breast surgery, to abdominal wall surgery [53].

Normal intra-abdominal pressure in adults is less than 10 mmHg and intra-abdominal pressure values over 15 mmHg are suggestive for intra-abdominal hypertension [54, 55]. Prolonged increased intra-abdominal pressure over 20 mmHg is known to cause serious conditions such as acute renal failure, pulmonary impairment and reduced blood flow to the gastro-intestinal organs [56-59]. Moreover, increased intra-abdominal pressure causes elevation of the diaphragm, which is in turn followed by increased intra-thoracic pressure, [60] and there is evidence suggesting that increased intra-thoracic pressure results in increased intra-cranial pressure and functional obstruction of the cerebral venous outflow via the jugular venous system [61, 62].

The abdomen has a dynamic muscular wall that can accommodate noticeable variations in volume, accompanied by changes in intra-abdominal pressure. [50, 63] Repair of the incisional hernia causes extrinsic compression of the abdominal content and elevation of intra-abdominal pressure, as observed in our series. It’s interesting to evaluate that, although intra-abdominal pressure increased in all of our patients following repair of the rectus abdominis muscle, and increased even slightly further after complete skin closure and application of the dressing, it remained well below the danger level. Indeed, intra-abdominal pressure was below 20 mmHg in all the patients the day after surgery, and no cases of continued augmented pressure were reported.

Our data highlight the feasibility of combined panniculectomy/separation of components for the correction of incisional hernias. The high salvage rate of multiple recurrent hernias associated with this surgical approach suggests that it should be taken into account when a laparoscopic technique or the use of biomaterials are contraindicated. Therefor we strongly recommend this as the procedure of choice for the autologous tissue reconstruction of massive midline defects of the abdominal wall.

Hernia repair combined with abdominoplasty provides both functional and aesthetic benefits and normally creates a highly satisfied patient base. When surveyed, patients with successful autologous tissue repairs noticed improvements in the appearance and strength of their abdomen, in their postoperative emotional state.

In conclusion, the component separation technique is, in our opinion, an effective, mesh-free method for the repair of large midline hernias.
REFERENCES


Chapter 6

INCIDENCE, RISK FACTORS AND REPAIR OF INCISIONAL HERNIA FORMATION AFTER ABDOMINAL ORGAN TRANSPLANTATION

Laszlo Piros*
Department of Transplantation and Surgery, Semmelweis University, Budapest, Hungary

ABSTRACT

Patients undergoing abdominal solid organ transplantation have an increased risk of developing incisional hernia. The risk is higher following larger abdominal transplant surgery, such as liver (OLT) or simultaneous pancreas kidney transplantation (SPK). However, kidney recipients are also susceptible to hernia formation. Organ recipients are placed on immunosuppressive therapy after transplantation to prevent rejection of the new graft. It’s more frequently associated with impaired wound healing causing significant risk for developing incisional hernia. Transplant candidates are at increased risk given their baseline organ dysfunction too, just like end-stage renal disease (ESRD), liver cirrhosis or type 1 diabetes. The Ventral Hernia Working Group Grading System categorizes immunosuppressed patients into the Grade 2 (comorbid) group including patients who have comorbidities that increase the risk for surgical site infection (SSI). Surgical site infection is a significant risk factor for hernia formation and the risk of SSI is even higher in immunocompromised patients who do not have the ability to respond normally to an infection due to a weakened immune system caused by immunosuppressive drugs. Data in the literature indicates that the mTOR-inhibitor sirolimus inhibits wound healing and several previous studies showed that high dose steroids and sirolimus cause higher rates of hernia formation. Hernia formation after kidney transplantation ranges from 1.6-18% in the literature. The use of MMF, obesity, age and female gender are risk factors. Hernia formation after liver transplantation ranges from 1.7-32.4%. Acute rejection (treated with steroids), postoperative thrombocytopenia, and Mercedes type incision, use of sirolimus and MMF, male gender, a higher BMI, and a MELD score greater than 22 are risk factors in liver recipients. Rates of incisional

* Corresponding author; Laszlo Piros. Department of Transplantation and Surgery, Semmelweis University, Baross u. 23, H-1082 Budapest, Hungary. E-mail: piros666@hotmail.com.
hernia after pancreas transplantation are also high, ranging from 13 to 34.8%. High-dose immunosuppression owing to immunogenicity of the pancreas leads to considerably impaired wound healing. Strategies focusing on prevention and early treatment of SSI and the appropriate choice of immunosuppressive agents may help to decrease the risk of incisional hernia formation following abdominal organ transplantation. If hernias develop, repairing the incisional hernias and using mesh in solid organ transplant recipients are safe methods in experienced hands.

**INTRODUCTION**

The improvement in the success of solid organ transplantation over the past few decades means that it is now a well-accepted mode of treatment for patients with end-stage organ disease. Abdominal organ transplantation includes the kidneys, liver, pancreas, small bowel and combinations of abdominal organs. The most frequently transplanted organs are kidney and liver, which together account for more than 70% of all transplanted organs.

Patients undergoing abdominal solid organ transplantation have an increased risk of developing incisional hernia. The risk is higher following larger abdominal transplant surgery, such as liver (OLT) or simultaneous pancreas kidney transplantation (SPK). However, kidney recipients are also susceptible to hernia formation. Organ recipients are placed on immunosuppressive therapy after transplantation to prevent rejection of the new graft. It’s more frequently associated with impaired wound healing causing significant risk for developing incisional hernia. These complications are dangerous in the organ recipient population, because they can compromise the survival of the transplanted graft. Transplant candidates are at increased risk given their baseline organ dysfunction too, just like end stage renal disease (ESRD), liver cirrhosis or type I diabetes.

In this review we surveyed the literature for reports of risk factors for incisional hernia among liver, pancreas and kidney recipients and the surgical repair of this hernia.

**ROLE OF IMMUNOSUPPRESSION**

The Ventral Hernia Working Group Grading System categorizes immunosuppressed patients into the Grade 2 (comorbid) group including patients who have comorbidities that increase the risk for surgical site infection (SSI) [1]. Surgical site infection is a significant risk factor for hernia formation and the risk of SSI is even higher in immunocompromised patients who do not have the ability to respond normally to an infection due to a weakened immune system caused by immunosuppressive drugs.

Immunosuppression after solid organ transplantation is a combination of different agents. Immunosuppressive drugs can be classified as induction therapies, maintenance therapies and antirejection therapies. At the time of transplantation, induction is generally achieved with high-dose corticosteroids and depleting or non-depleting protein drugs (polyclonal or monoclonal antibodies), followed by the addition of a calcineurin inhibitor and an antiproliferative agent [2]. Induction immunosuppression with currently-used biological agents - either monoclonal (IL-2 receptor antagonists: daclizumab, basiliximab; alemtuzumab - anti CD52, muronomab - anti CD3) or polyclonal (antithymocyte globulin - rATG-
Thymoglobulin) antibodies - is not always used after transplantation. Its goal is to prevent acute rejection during the early post-transplantation period, particularly in patients at a high risk immunologically (i.e., increased number of HLA mismatches, higher panel reactive antibody percentage, presence of a donor-specific antibody, longer cold ischaemia type, black people, etc.) [3].

The standard long-term immunosuppression to avoid graft rejection is usually maintained with a combination of corticosteroids, a calcineurin inhibitor (cyclosporine A or tacrolimus), and an antimitabolite (mycophenolate mofetil) or antiproliferative agent (sirolimus, everolimus) with the goal of decreasing steroid and calcineurin inhibitor (CNI) use. However, this combination may change during the course of an organ transplant recipient's life.

Corticosteroids (prednisolone and methylprednisolone) are generally used for induction and maintenance immunosuppression, as well as for acute rejection by preventing production of cytokines and vasoactive substances, including interleukin (IL)-1, IL-2, IL-6, tumor necrosis factor-α, chemokines, prostaglandins, major histocompatibility class II, and proteases. There are several well-documented adverse effects of corticosteroids, including infections, glucose intolerance, cushingoid features, fattening, osteoporosis, hypertension, hyperlipidemia, peptic ulcer disease to name just a few. Steroid-related infections, diabetes and wound healing inhibition could play a major role in the development of incisional hernia after transplantation. Early corticosteroid withdrawal decreases the rate of infection among transplant recipients [4]. Corticosteroid avoidance, even in a sirolimus-based regimen, results in a marked reduction in wound healing complications and lymphoceles [5].

Calcineurin inhibitors (CNI) are the base agents of most of the maintenance immunosuppression as they are very effective antirejection drugs. Cyclosporine has been a keystone of immunosuppression in organ transplantation since the 1980s [6]. The mechanism of action of this polypeptide of fungal origin and prodrug is that it binds to cyclophilin and this complex inhibits calcineurin phosphatase and T-cell activation by dephosphorylation of inactive nuclear factor of activated T cells (NF-AT). It prevents the production of IL-2 via calcineurin inhibition. Adverse effects of cyclosporin beside infection include nephrotoxicity hyperkalemia, hypomagnesemia, nausea, vomiting, diarrhea, hypertrichosis, hirsutism, gingival hyperplasia, skin changes, hyperlipidemia, glucose intolerance, malignancy, hyperuricaemia and hemolytic uremic syndrome.

Tacrolimus (FK 506) is a macrolide antibiotic and is powerful and selectively active against helper T cells. This agent binds to tacrolimus-binding protein instead of cyclophilin and this active complex inhibits calcineurin with greater potency than the corresponding cyclosporine complex. The mode of action is similar to cyclosporin: preventing the production of IL-2 via calcineurin inhibition. Tacrolimus is a potent and widely used immunosuppressive agent in liver transplantation [6, 7]. Adverse effects are similar to those of cyclosporine but with a lower incidence of hypertension, hyperlipidemia, skin changes, hirsutism, and gingival hyperplasia and a higher incidence of new-onset diabetes mellitus after transplantation (NODAT) and neurotoxicity.

Sirolimus, also called rapamycin, is a macrolide isolated from soil found on Easter Island. Everolimus is a rapamycin analog with a similar mechanism of action and adverse effect profile. The mechanism of action of rapamycin is to bind the cytosolic protein-FKBP12 in a similar way to tacrolimus. In contrast to the previous one, the sirolimus-FKBP12 complex inhibits the mTOR pathway by directly binding the mechanistic target of rapamycin (formerly known as mammalian TOR) complex 1 (mTORC1). This complex inhibits signal 3 by
blocking translation of the RNA and preventing the progression from G1 phase to the S phase of DNA synthesis. It also inhibits IL-2 and other cytokines receptor-dependent signal transduction mechanisms and thereby blocks activation and proliferation of T and B cells, and similarly the proliferation of nonimmune cells and the pathways that could be involved in oncogenesis. The antiproliferative mTOR inhibitors appear to have antitumorigenic effects through the inhibition of angiogenesis and it may also have a role in the treatment of cancer. Sirolimus-based immunosuppressive therapy has been associated with a reduced incidence of malignancy after solid organ transplantation [8].

Adverse effects associated with mTOR inhibitors are thrombocytopenia, anemia, hyperlipidemia, pneumonia, oral ulcers, and diarrhea, but these antiproliferative agents can also cause poor wound healing and dehiscence formation of lymphoceles. The antiproliferative mechanism has a positive effect on tumor development, but a negative effect on wound healing and facilitates SSI and therefore incisional hernia development. Several previous studies showed that high dose steroids and sirolimus lead to higher rates of hernia formation. Valente and colleagues reported that the use of sirolimus, tacrolimus, and prednisone was associated with a greater incidence of lymphoceles, fluid collections, and other consequences of poor wound healing, compared with mycophenolate mofetil (MMF), tacrolimus, and prednisone [9]. Knight and colleagues reported incisional hernia rates of 18% with the use of Sirolimus [10]. Montalti reported a hernia formation rate of 32.4% after liver transplantation and identified Sirolimus as a risk factor along with male gender, higher BMI and higher MELD score [11]. Moreover, sirolimus dose-dependently inhibits vascularization and incorporation of implanted surgical mesh, as showed by Laschke [12]. Immunosuppressed patients should not be treated with sirolimus in cases of incisional hernia repair to promote adequate mesh incorporation.

Among inhibitors of nucleotide synthesis (purine synthesis inhibitors) azathioprine was the first immunosuppressive agent used in organ transplantation. It was synthesized by George Herbert Hitchings and Gertrude Elion in 1957, and at first was used as a chemotherapy drug. The developers of this agent were joint recipients of the 1988 Nobel Prize. Azathioprine is an antimetabolite prodrug that converts 6-mercaptopurine to tissue inhibitor of metalloproteinase, which is converted to thioguanine nucleotides which interfere with DNA synthesis. It is used for maintenance immunosuppressive therapy, however after pervading of cyclosporine it became a second-line drug.

Azathioprine use in transplantation has been widely replaced by mycophenolate mofetil (MMF). Mycophenolate acid reversibly inhibits inosine monophosphate dehydrogenase (IMDH), the enzyme that controls the rate of synthesis of guanine in the “de novo” pathway of purine synthesis used in the proliferation of B and T lymphocytes. Other rapidly dividing cells are able to recover purines via a separate guanosine salvage pathway and are thus able to escape the effect. This agent is used for maintenance immunosuppression. Adverse effects include myelosuppression such as leukopenia, anemia, and thrombocytopenia, and gastrointestinal adverse effects such as nausea, vomiting, and diarrhea. Enteric-coated mycophenolate sodium (EC-MPS) is introduced with fewer reports of gastrointestinal effects. Fikatas [13] and Kahn [14] found the use of MMF to be a risk factor for hernia formation in liver recipients, the latter included Sirolimus as part of their immunosuppressive therapy. Humar and colleagues reported a hernia formation rate of 3.6% after kidney transplantation, and they found that the use of MMF and obesity were both significant risk factors [15]. Interestingly, Smith et al. found that failure to initiate therapy with MMF or calcineurin
inhibitors was associated with a higher risk of hernia formation among kidney, pancreas and liver transplant recipients [16]. Nevertheless, significantly more wound complications were observed with Sirolimus in kidney [17] and heart [18] recipients compared with MMF.

Biologic agents are polyclonal and monoclonal antibodies and are frequently used in transplantation for induction immunosuppressive therapy or treatment of rejection. The most frequently used antibodies for induction therapy are antithymocyte globulin, alemtuzumab, and basiliximab. The selection of the induction therapy is usually based on risk-benefit considerations for each individual patient. Polyclonal antilymphocyte antibodies were first successfully used in organ transplantation in the 1970s. These agents induce the complement lysis of lymphocytes and uptake of lymphocytes by the reticuloendothelial system and mask the lymphoid cell-surface receptors. Preparations include horse antithymocyte globulin (Atgam) and rabbit antithymocyte globulin (Thymoglobulin, ATG). Most regimens involve 5-7 days of intravenous administration of thymoglobulin for induction immunosuppressive therapy or treatment of steroid-resistant cellular rejection or antibody-mediated (humoral) rejection. In conjunction with inhibitors of terminal complement activation, it has been shown to be beneficial in cross-match-positive transplantation. Thymoglobulin causes prolonged leukocyte depletion with a delay of a few months to recover. As polyclonal agents are xenogenic proteins, adverse effects include fever and chills. Other adverse effects are thrombocytopenia, leukopenia, hemolysis, respiratory distress, serum sickness, and anaphylaxis.

In the 1980s monoclonal antibodies emerged as a new class of immunosuppressive agents in organ transplantation. Monoclonal antibodies recognizing CD3- and CD25-positive T cells proved their efficacy, others against CD52 and CD20, are still under investigation. Muromonab-CD3 (OKT3) is a murine monoclonal antibody; it binds to the T cell receptor-CD3-complex on the surface of circulating T cells, initially leading to activation, but subsequently inducing blockage and apoptosis of the lymphocytes. Alemtuzumab (Campath-1H) is a lymphocyte-depleting humanized monoclonal antibody directed against CD52. CD52 is a membrane protein on all B and T cells and most macrophages and natural killer cells. Administration of alemtuzumab results in the rapid and effective depletion of lymphocytes and it may take several months to return to pretransplantation levels. Basiliximab (Simulect) and daclizumab (Zenapax) are chimeric and humanized antimonoclonal antibodies that target the IL-2 receptor (CD25). In clinical practice both are used for induction. These agents bind to the IL-2 receptor α-chain (CD25 antigen) on activated T cells, depleting them and inhibiting IL-2-induced T-cell activation. These two agents have a very low prevalence of adverse effects. Rituximab is an anti-CD20 monoclonal antibody, and it eliminates most B cells and is approved for treating non-Hodgkin B-cell lymphomas, including some posttransplant lymphoproliferative disease (PTLD) in organ transplant recipients. Rituximab is used in combination with maintenance immunosuppressive drugs, plasmapheresis, and intravenous immunoglobulin to suppress antibody-mediated allograft rejection in transplant recipients.

Polyclonal antibodies may have a role in the development of posttransplant incisional hernia. Knight and colleagues showed that the use of Thymoglobulin for induction immunosuppression independently increases the incidence of wound complications among recipients receiving sirolimus-based immunosuppression [10]. The significant T cell-depleting effect of thymoglobulin suggests that these lymphocytes likely play an important role in wound repair mechanisms. Barbul et al. observed in a murine model that anti-T-cell
monoclonal antibody administration decreased the mechanical strength and collagen production in a wound, while CD8 depletion improved wound healing. In conclusion, T cells may play a regulatory role in the wound healing process [19, 20]. Benavides reported that rabbit antihuman thymocyte globulin-induced renal transplants recipients treated with sirolimus, cyclosporine, and steroids show a significantly increased incidence of postoperative incisional hernias, lymphoceles and wound infections compared to recipients receiving basiliximab [21].

**Kidney Transplantation**

Kidney transplantation as a treatment of choice for end-stage renal disease (ESRD) is the most frequently performed abdominal organ transplantation. The standard operation is usually a heterotopic procedure without removal of the native kidneys, placing the graft extraperitoneally into the right or left iliac fossa using the iliac vessels for vascular anastomoses. The right fossa is preferred for primary kidney transplantation in most of the cases, but the left fossa is chosen if a pancreas after kidney (PAK) transplantation is planned or in the case of a secondary transplant. Alternatively, the graft can be placed intraperitoneally using the inferior vena cava and the infrarenal aorta or common iliac artery for vascular anastomoses. This approach is chosen after multiple previous kidney transplantations and during simultaneous pancreas kidney (SPK) transplantation.

For the standard extraperitoneal technique usually curvilinear Gibson incision, J-shaped (“hockey stick”) incision or oblique incision is used. Nanni and colleagues compared the J-shaped and the oblique incisions with regard to the incidence of long-term complications, and they found a lower incidence of hernia formation and abdominal wall relaxation by switching to oblique incision from J-shaped flank incision in kidney recipients [22].

Renal paratransplant hernia is an uncommon and potentially fatal complication of kidney transplantation. Usually it is an iatrogenic surgical complication due to an unnoticed injury of the peritoneum during the extraperitoneal preparation. After surgery bowel loop can herniate through the defect over the kidney graft and incarcerated hernia could even develop which urgent surgical intervention. A meticulous surgical technique during transplantation may help avoid this complication and if a peritoneal defect is noticed, it should be closed immediately [23].

Hernia formation after kidney transplantation is less frequent compared to the other transplanted abdominal organs and it ranges up to 18% in the literature, but it is generally below 10%. Humar and colleagues reported a hernia formation rate of 3.6% of after kidney transplantation, and they found that the use of MMF and obesity were both significant risk factors [15]. Mahdavi et al. found BMI, age and female gender to be risk factors with a rate of 3% [24]. Smith et al. reported a rate of 7% 10 years after kidney transplantation with BMI and SSI as significant risk factors for incisional hernia formation [16]. Knight and colleagues reported incisional hernia rates of 18% with the use of Sirolimus in kidney recipients [10]. It seems that the most important risk factors of hernia development in kidney transplant patients are immunosuppression - especially the use of mTOR inhibitors-, BMI and SSI. Moreover, obesity itself is probably one of the biggest risk factors for incisional wound infection after
transplantation. Repeated reoperations due to posttransplant hemorrhage or urine leak are also risk factors.

LIVER TRANSPLANTATION

Liver transplantation (OLT) is the accepted treatment of choice for several causes of acute or chronic irreversible liver disease. Chronic liver diseases account for the majority of liver transplants, the indications include chronic viral infection (HCV, HBV), alcoholic liver disease (ALD), autoimmune hepatitis, cholestatic disorders, metabolic diseases and selected hepatic malignancies. Hepatocellular carcinoma (HCC) most commonly occurs in the presence of cirrhosis as a result of longstanding chronic liver disease. Liver transplantation (OLT) is the best therapy of choice for early, unresectable HCC. The mTOR inhibitors can be potent immunosuppressive agents after OLT for HCC due to their antiproliferative effect. In these patients the risk of incisional hernia development is therefore theoretically higher. Montalti et al. revealed Sirolimus, male gender, higher BMI, and a MELD score greater than 22 as risk factors for incisional hernia formation in liver recipients [11]. Kahn and colleagues found that end-stage liver cirrhosis, Sirolimus, and MMF are independent significant risk factors [14]. The liver disease itself has a negative impact on wound healing due to hypoalbuminaemia.

The standard surgical procedure is orthotopic transplantation with the removal of the diseased liver. In rare cases heterotopic transplantation can be performed during auxiliary liver transplantation for acute liver failure, with a hemiliver graft implanted temporarily, while the native liver recovers. The standard procedure has three phases: pre-anhepatic (hepatectomy), anhepatic, and post-anhepatic (implantation of the graft). Basically two main techniques are available for the implantation of the liver: standard technique with cross-clamp and removal of the retrohepatic vena cava (with or without veno-venous bypass), and piggy-back technique or side-to-side cavaplasty with caval preservation (with or without temporary portocaval shunt). This procedure requires good exposure, especially for the upper caval anastomoses. Usually a bilateral subcostal incision is made with an extension in the midline toward the xiphoid process. However, an area of relative ischemia at the trifurcation point of this so-called Mercedes type of incision may contribute to impaired wound healing and lead to the development of incisional hernia. The most common site of hernia is at this triple point. Janssens and Piazzese reported that the use of the Mercedes type incision is a risk factor for hernia development ranging from 5 to 17% [25, 26]. Vardanian reported 4.6% incisional hernia rates with exclusive use of the Mercedes type incision [27], while Gastaca reported a 1.7% rate of hernia formation with the use of a bilateral subcostal incision without midline extension. [28] We aim to avoid Mercedes type incision in our Institute, and we prefer simple bilateral or alternatively J-shaped or “hockey stick” incision for liver transplantation or major hepatic surgery.

According to Smith and colleagues, hernias continue to form as long as 10 years after surgery, with one in five patients forming an incisional hernia after liver or pancreas transplantation [16]. Compared to kidney transplantation, hernia formation after liver transplantation tends to be higher, with estimates ranging up to 33%. Smith et al. also showed that obesity is a significant risk factor for liver transplant recipients due to increased
intraabdominal pressure placing mechanical stress on the incision. However, obese patients have an increased risk of SSI [16]. Ascites, if it persists after transplantation, also increases intraabdominal pressure. Moreover posttransplant ascites leaking through the surgical incision facilitates dehiscence of the wound and may need surgical reconstruction.

**PANCREAS TRANSPLANTATION**

The purpose of pancreas transplantation is to ameliorate type 1 diabetes and achieve absolute insulin independence. There are different types of pancreas transplantation. Most of the procedures are simultaneous pancreas-kidney (SPK) transplantations performed on individuals with type 1 diabetes with end-stage renal disease using grafts from the same deceased donor. Pancreas can be transplanted after a previous successful living or deceased donor kidney transplantation (PAK). Simultaneous deceased donor pancreas and live donor kidney (SPLK) can lead to a lower rate of delayed graft function and reduced waiting time.

The indications for pancreas transplantation alone (PTA) are brittle diabetes, severe, frequent hypoglycemia, and hypoglycemia unawareness with normal kidney function.

Pancreas transplantations were initially performed through lower transplant flank incisions opposite the kidney. However, because of the high wound complication rate, most centers now perform pancreas transplants through a lower midline incision. Usually the pancreas is placed into the right and the kidney into the left iliac fossa, using the iliac vessels for vascular anastomoses or alternatively portal venous drainage can be performed. The exocrine secretion of the pancreas graft is usually drained more recently into the small bowel or formerly into the bladder. The incidence of graft pancreatitis, leakage, intraabdominal abscess and sepsis has largely been reduced for now. However, the rate of relaparotomies is slightly higher compared with other transplanted organs owing to technical and infectious problems.

Rates of incisional hernias after pancreas transplantation are also high, ranging from 13 to 35% [16, 29, 30, 31, 32]. Hanish reported BMI as a risk factor [30]. Sampaio and colleagues found that obesity in SPK recipients is associated with an increased risk of posttransplant complications, pancreas and kidney graft losses, and patient death [31]. Obese patients also have a 3-fold higher rate of graft pancreatitis/enteric leak. In light of this, in our department our pancreas program selects non-obese recipients with a BMI of less than 25. Furthermore, obesity is associated with an increased frequency of dehiscence, ventral hernia, intra-abdominal infection, gangrene, necrotizing fasciitis, and repeated laparotomy [30]. In general only a small percentage of pancreas transplant patients may fall into the obese or even overweight category. Moreover, all pancreas recipients are diabetic patients who are at an increased risk of complications from wound healing for several reasons.

High-dose immunosuppression owing to immunogenicity of the pancreas leads to considerably impaired wound healing. Pancreas recipients usually require induction therapy. We believe that perhaps the late side effects of the Thymoglobulin–Sirolimus-Cyclosporin combination we used contributed to the relatively high incidence (35%) of postoperative hernias among our SPK patient group [32]. We experience a lower rate of incisional hernia development after SPK with a recently used Thymoglobulin-Tacrolimus-MMF based immunosuppressive regimen.
INTESTINAL TRANSPLANTATION

Patients with intestinal and parenteral nutrition failure requiring intestinal transplantation often have multigraft failure too. The most common intestinal allografts are: isolated intestinal, combined liver-small bowel and multivisceral transplants. Successful primary closure of the abdominal wall following either combined or isolated intestinal transplantation is not always feasible. Primary closure under tension can lead to fascial ischemia or necrosis, with subsequent dehiscence and it is facilitated by restricted volume of the recipient abdominal cavity, donor-recipient size discrepancies and significant intraoperative edema. Simultaneous abdominal wall transplantation can be utilized to reconstitute the abdominal domain of patients undergoing intestinal transplantation [33, 34, 35]. Under these conditions, intestinal graft recipients are more prone to posttransplant hernia development, however no data was found relating to the incidence of this in the literature.

PREVENTION AND REPAIR

Smith and colleagues found that SSI is the strongest risk factor for hernia formation and with underlying organ dysfunction and immunosuppressive therapy, transplant patients are at increased risk of SSI and, subsequently, incisional hernias [16]. Obese patients already have an increased risk of SSI and it is even higher if the patient is an organ recipient. Prophylaxis with the use of antibiotics starting at the time of transplantation, close monitoring of the wound healing in the postoperative period and aggressive treatment if SSI develops could reduce the risk of incisional hernia formation later on. Encouraging patients who are overweight to lose weight while on the waiting list is highly recommended.

An adequate diet after transplantation supports normal wound healing by providing normal albumin levels. Liver recipients, especially with poor initial function of the graft, may have hypoalbuminaemia and ascites. Treatment with intravenous albumin substitution is of utmost importance in these patients. Pancreas recipients are at increased risk of complications from wound healing due to diabetes, therefore glycemic control is important.

The immunosuppression regimen may be an important and modifiable risk factor for hernia formation. Sirolimus use is associated with a higher incidence of wound healing complications compared to other drugs. On the other hand, mTOR inhibitors are needed in several cases, such as calcineurin nephrotoxicity or posttransplantation lymphoproliferative disease (PTLD). Adequate and individually-tailored immunosuppressive therapy is therefore mandatory. However, temporary switching from one immunosuppressive agent to another is a possible strategy if there are wound healing problems.

One of the well-known benefits of minimally invasive surgery is the small incision and low incidence of hernia development. While open surgery remains the gold standard for abdominal organ recipients, robotic-assisted kidney (RAKT), and even pancreas transplantation have recently been reported [36, 37]. Currently the high cost is the most prohibitive factor for its widespread use. This technique is especially beneficial for obese patients and in the long term should compensate for the initial cost by minimizing surgical complications. Robotic surgery in organ transplantation is a very advanced application of the technique, and a high level of expertise is needed in any surgeon who considers this approach.
Various methods have been employed to repair incisional hernias in transplant patients: primary repair, synthetic mesh, biologic mesh, human acellular dermal matrix, tensor fascia lata grafts, component separation, flaps from the thighs, or a combination of these approaches [13, 29, 38, 39]. Several authors reported successful laparoscopic incisional hernia repair in patients after various abdominal organ transplantations [40, 41]. Most commonly, surgical repair with polypropylene mesh is a simple, safe and effective technique in abdominal organ transplant patients.

CONCLUSION

Owing to the required immunosuppression, organ recipients are prone to wound infections, incisional herniae, and fascial dehiscences. SSI and obesity are significant risk factors for incisional hernia formation following abdominal solid organ transplantation. Strategies focusing on prevention and early treatment of SSI and the appropriate choice of immunosuppressive agents may help to decrease the risk of incisional hernia formation following abdominal organ transplantation. If hernias develop, repairing the incisional hernias and using mesh in solid organ transplant recipients are safe methods in experienced hands.

REFERENCES


Incidence, Risk Factors and Repair of Incisional Hernia Formation …


**Biographical Sketch**

*Name:* László Piros PhD, FEBS  
*Affiliation:*  
Tel.: +36-1-2676000  
Cell phone: +36-20-8258587  
E mail: pirosli666@hotmail.com  
*Date of Birth:* June 6th, 1976  
*Education:*  
1994 graduation at the Czuczor G. Benedictine High School, Győr/ Hungary  
1994-2000 Medical Studies, School of Medicine, Semmelweis University, Budapest/Hungary  
*Address:* Department of Transplantation and Surgery, Semmelweis University, School of Medicine  
Baross u. 23, H-1082 Budapest, Hungary
**Research and Professional Experience:**

2000-2006  
Residence of Surgery, Department of General and Thoracic Surgery Budai MÁV Hospital, *Budapest/Hungary* (general and thoracic surgery)

Department of Anaesthesiology and Intensive Therapy, Árpád Hospital, *Budapest/Hungary* (6 months emergency room)

Department of Traumatology, Árpád Hospital, *Budapest/Hungary* (6 months traumatology)

Department of Surgery, St. Rókus Hospital, *Budapest/Hungary* (9 months general surgery)

Department of Thoracic Surgery, National Korányi Institute of Pulmonology, *Budapest/Hungary* (2 months thoracic surgery)

Department of General and Vascular Surgery, St. Borbála Hospital, *Tatabánya/Hungary* (3 months vascular surgery)

Department of Pediatric Surgery, Semmelweis University, *Budapest/Hungary* (1 month pediatric surgery)

Department of Transplantation and Surgery, Semmelweis University, *Budapest/Hungary* (39 months general, laparoscopic surgery and organ transplantation, experimental studies of kidney transplantation in rats)

2007  
Hungarian National Board Exam of General Surgery

2007  
Fellow in kidney, liver and pancreas transplantation

Department of Transplantation and Surgery, Semmelweis University, *Budapest/Hungary*

2009  
European Diploma in Transplantation Surgery (European Union of Medical Specialists/UEMS, European Board of Surgery/EBS, European Society of Organ Transplantation/ESOT) Module 1/Multi-organ retrieval, Module 2/Kidney Transplantation. *Paris*

2013  
European Diploma in Transplantation Surgery (European Union of Medical Specialists/UEMS, European Board of Surgery/EBS, European Society of Organ Transplantation/ESOT) Module 3/Pancreas Transplantation. *Vienna*

2014  
PhD Diploma, thesis: Examination of factors influencing survival of liver transplantation for hepatocellular carcinoma (The University of Medicine and Pharmacy of Tirgu Mures – Romania)

2014  
Eurotransplant ELIAC membership – supplementary auditor

2014  
Head of the Combined Pancreas – Kidney Transplant Waiting List Committee of Budapest

2015  
European Diploma in Transplantation Surgery (European Union of Medical Specialists/UEMS, European Board of Surgery/EBS, European Society of Organ Transplantation/ESOT) Module 4/Liver Transplantation. *Brussels*

**Professional Appointments:**

Assistant Professor of Surgery in the Department of Transplantation and Surgery, Semmelweis University, Budapest

**Specialization:**

- liver, pancreas and kidney transplantation team
- General surgery, laparoscopic surgery
- Laparoscopic donor nephrectomy
Memberships in scientific societies:

- Hungarian Surgical Society
- Hungarian Society of Transplantation
- Hungarian Association of the Study of the Liver
- European Society for Organ Transplantation
- European Liver and Intestine Transplant Association

Publications:


MARS therapy, the bridging to liver retransplantation – Three case from the Hungarian Liver transplant program. Pócze, B., Fazakas, J., Zádori, G., Görög, D., Kóborti, L., Dabasi, E.,


**ABSTRACT**

The incidence of congenital diaphragmatic hernia (CDH) is approximately 1 in 2000-5000 live births. In the majority of fetuses with CDH, the defect is located on the left (85%), whereas right–sided (15%) and bilateral (<1%) defects are less frequent. The etiology of CDH is unknown, however, 2% of cases have been noted to be familial and another 15% of patients have associated chromosomal abnormalities. In CDH, the degree of lung hypoplasia is a major determinant of survival. Pulmonary hypoplasia results in respiratory insufficiency and pulmonary hypertension.

Right sided CDH (R-CDH) is a highly variable defect with many similarities to Left sided CDH (L-CDH), but with potentially important distinctions. R-CDH occurs through the defect resulting from failure of the anterior pleuroperitoneal membrane to fuse with the sternum and costal cartilages during embryogenesis. Controversy exist in regards with worse prognosis of RCDH as compared to left side, as review of literature reveals conflicting data.

There are several theoretical explanations suggest that impact of RCDH might be worse. First, right lung normally accounts for 57% of total fetal lung volume and any compromise on its development may have a larger clinical impact. Second liver herniation through diaphragm is more frequently seen in right sided defects, because of anatomic adjacency of the right lobe. The size of defect necessary to permit herniation of...
liver on the right side is likely to be substantially larger than left sided defects hence associated with poor outcome.

However the underlying pathophysiology needs to be investigated further. Diagnosis of CDH can be made prenatally or postnatally after birth. Right sided defects appeared more difficult to detect prenatally compared with left sided defect partly due to the echogenicity of the liver. In recent years new ventilation strategies such as nitric oxide, gentle ventilation, high frequency oscillatory ventilation, and extracorporeal membrane oxygenation (ECMO) therapy were introduced and improved post natal prognosis.

The concept has changed from performing emergency repair to delaying repair for at least 24-48 hrs to allow for clinical stabilization and a fall in pulmonary vascular resistance. Surgery can be delayed for up to 7-10 days. There is no evidence that timing of surgery influence survival. Repair of CDH can be performed effectively using different surgical approaches such as thoracic approach, abdominal approach or VATS or laparoscopic technique. Surgical repair may be more challenging in R-CDH because of near universal liver herniation as well as potential for anatomical anomalies uniquely associated with right sided defect.

This results in increase in morbidity in right sided vs. left sided survivors. To date, recognized prognostic factors for post natal outcome in newborns with CDH include pulmonary hypoplasia, intra-thoracic liver herniation, associated anomalies, prenatal diagnosis, low birth weight and prematurity.

Long term pulmonary morbidity in CDH consists of impaired obstructive and restrictive lung function from altered lung structure and underdeveloped pulmonary vessels.

**EPIDEMIOLOGY**

The incidence of congenital diaphragmatic hernia (CDH) has been reported as high as 1 in 2000 births [1]. Approximately 1,000 CDH infants are born in the USA yearly with a prevalence of 2.4 per 10,000 live births [1, 2]. Males compared to females are more likely to have CDH (1.4 to 1.6:1 ratio) and more likely to have right-sided defects [3]. Right sided lesions are rare (10-15%) compared with left sided (85%) [4].

**ASSOCIATED ANOMALIES**

CDH is associated with multiple anomalies. Musculoskeletal and cardiac anomalies are most common, although the patterns of malformation differ in association with right-sided CDH compared to left-sided CDH [5]. CDH can be associated with chromosomal abnormalities (most frequently trisomy 18), and it can present in other syndromes (i.e., Beckwith-Wiedemann, Goldenhar, and others) [6-8].

Aneuploidy is present in 20% of prenatally diagnosed CDH infants, with 70% having an associated structural malformation [9]. In contrast, postnatal diagnosis of CDH has a 35% chance of an associated anomaly. It is speculated that the difference is due to fetal demise and/or termination of pregnancy. Survival of live born infants with isolated CDH (no associated anomalies present) is higher (63% to 77%) than survival of infants born with additional anomalies or aneuploidy (19% to 43%) [5, 10, 11]. In infants with chromosomal
abnormalities survival is low (<10%). Intrauterine fetal demise occur in both isolated (2%) and non-isolated (11%) CDH.

**DIAPHRAGMATIC DEVELOPMENT**

The embryology of the diaphragm is still poorly understood. The diaphragm begins to form during the fourth week of gestation. It fuses from four embryonic components: septum transversum, pleuroperitoneal folds (PPF), the crura, and the body wall mesoderm [12, 13]. The septum transversum migrates dorsally and separates the pleuropericardial cavity from the peritoneal cavity, however there is still communication between the pleural and peritoneal cavities. The septum transversum interacts with the PPF and forms the primitive diaphragmatic structures. Eventually, the septum transversum develops into the central tendon. Two theories exist on how the diaphragm muscularizes. One theory states that the innermost muscle layer muscularizes from the thoracic cavity, while another theory believes it muscularizes from the posthepaticmesenchymal plate [14, 15]. The pleuroperitoneal membranes close and separate the thoracic and abdominal cavities by the eighth week of gestation [16, 17]. Typically, the right side of the diaphragm closes before the left.

There are multiple hypotheses for why CDH develops. One theory suggests a failure of muscularization of the future diaphragm prior to complete closure of the canal [16]. Failure to close the pleuroperitoneal canal allows the abdominal contents to enter the thoracic cavity (also allowing the liver to herniate into the chest).

Exposure to teratogens has been implicated in CDH. These include phenmetrazine, thalidomide, quinine, cadmium, lead, and nitrofen [17-20]. Nitrofen, a herbicide, in particular is known to cause pulmonary hypoplasia, other pulmonary abnormalities, and diaphragmatic defects. Vitamin A deficiency in CDH infants and the effects of vitamin A administration in nitrofen-induced pulmonary hypoplasia have developed new hypotheses that alterations in retinoid-regulated target genes may be responsible for CDH development [21, 22].

**Lung Development**

Lung development is divided into five stages [23]. The *embryonic stage* begins during the third week of gestation with the laryngotracheal groove. The primary lung buds and trachea form from this diverticulum by the fourth week. The primitive lobar structures are seen by the sixth week of gestation.

The *pseudoglandular stage* occurs between the sixth and 16th weeks of gestation with the formation of the main and terminal bronchi. The major branches of the conducting airways are completed by 16 weeks through a process of dichotomous branching, which is initiated early in the embryonic period of lung development [28].

The *canalicular stage* occurs between the 16th and 26th weeks of gestation. The pulmonary vessels and respiratory bronchioles are formed. Late in the canalicular period lung sacculation and alveolarization begins and forms the respiratory bronchiolo, alveolar duct, and alveoli. Type1 pneumocytes and type 2 pneumocyte precursors also appear, and at this
stage, gas exchange is possible. During this stage, the structures for the preacinar region are present. It consists of the trachea, major bronchi, lobar bronchi, and terminal bronchioles.

The saccular stage continues from 26 weeks to term with the maturation of alveolar sacs. Airway dimensions continue to grow and surfactant synthesis starts. The final stage is the alveolar stage beginning at 36th weeks and continues to about eight years of age with a continued increase and development of alveoli.

While the lung develops, the fetal pulmonary vasculature develops occurs in concordance with the associated lung development and follows the pattern of airway and alveolar maturation [28]. Pulmonary arteries and veins form along the tubules and ultimately invade the acinar regions, where capillaries form between the arteries and veins, completing the pulmonary circulation. The pulmonary vasculature develops as these acinar units multiply and evolve during the canalicular stage [28]. The bronchial vasculature arises from the aorta, providing predominantly to bronchial and bronchiolar regions of the lung. A functional unit known as the acinus consists of the alveolus, alveolar ducts, and respiratory bronchioles. During sacculation, a unique pattern of vascular supply forms the capillary network surrounding each terminal saccule, providing an ever-expanding gas exchange area that is completed in adolescence.

CDH was found to have pulmonary hypoplasia in animal models [29]. Lung hypoplasia can occur in virtually all diaphragmatic hernias to a certain degree.

Only a small amount of parenchymal tissue may remain on the ipsilateral side of the defect, but hypoplasia is also seen on the contralateral side. In addition, the pulmonary vasculature appears to be less compliant with abnormally thick-walled arterioles [24]. Surfactant levels are also decreased which may result in immature functioning lungs [25]. Interestingly, the contralateral lung also exhibits the structural abnormalities of pulmonary hypoplasia.

The abnormal fetal pulmonary circulation in CDH fetuses appears to occur in early gestation. The pulmonary arteries muscularizes and the circulation decreases in density per unit of lung parenchyma [26]. The impaired lung growth and development has been speculated to be related to impaired vascular development [27].

Pulmonary hypertension (PHTN) appears to develop in-utero, which may cause a reduction in pulmonary artery growth and proper alveolar development [28].

Prenatal Diagnosis

Majority of the fetuses diagnosed prenatally have fetal demise or die shortly after birth. The overall incidence reported is an underestimation. CDH with additional anomalies are also detected prenatally at a higher rate than CDH in isolated cases [5]. When a prenatal diagnosis of CDH is made a careful work-up and examination into other anomalies should take place to make an appropriate prognostic determination and proper management.

Right-sided defects are more difficult to diagnose, as the herniated fetal liver has a similar echogenicity to fetal lung. Herniated small bowel loops are not easily distinguishable either from lung parenchyma. This misinterpretation on fetal ultrasound (US) may lead to other diagnoses (i.e., cystic lung anomalies). Prenatal detection rates are higher with left-sided than right-sided hernias, and bilateral hernias. This may be due to the distorted anatomy.
Right-sided hernias usually contain the liver, and, because of its volume, this tends to plug the defect and may minimize herniation of other viscera.

The diagnosis of a CDH is often made on a prenatal US examination. US diagnosis is made around the mean gestational age of 24 weeks, but can be made as early as 11 weeks [29].

Polyhydrannios is the most common finding on US and has been reported present in up to 80% with associated CDH. The mechanism of polyhydrannios may be due to obstruction at the gastro-esophageal junction secondary to the stomach herniating into the thorax. Other US findings suggestive of a CDH include the absence of the stomach in the abdomen and the presence of other solid viscera in the thorax.

Several fetal parameters have been proposed in order to predict neonatal outcome in isolated CDH based on lung sizes, position of the liver and pulmonary vasculature status [30]. However, as yet there is no consensus as to which parameter is most accurate and useful in predicting neonatal outcome in these cases.

Currently, the most extensively studied prediction method is determination of intrathoracic liver position and measurement of the area of the contralateral lung as obtained in a transverse section of the fetal thorax [31]. Lung area is expressed as a ratio to the fetal head circumference (LHR). The LHR measurement method uses the longest lung axis and has been noted to correlate with survival. However, LHR increases with gestational age (GA) and it is therefore preferable to use the observed to expected normal mean LHR (o/e-LHR) for GA to obtain a GA-independent prediction of postnatal survival [31].

Predicting survival of CDH fetuses based on LHR has been statistically supported: 100% survival with LHR > 1.35, 61% with LHR between 1.35–0.6, and no survival with LHR < 0.6 in one series. Although fetal ultrasound is the most reliable modality for prognosis, its inconsistent utilization and inter-rater variability has created variable results.

US can be limited by the poor acoustic contrast between fetal lung and herniated viscera, position of the fetus, and operator experience. As a result, prenatal magnetic resonance imaging (MRI) evaluation is being used with increasing frequency when US detects a complex fetal anomaly and is ideally suited for fetuses with a diaphragmatic hernia [32-34]. MRI can readily determine liver position in relation to the diaphragm and detect herniated liver into either hemithorax.

It may also be used to more accurately assess lung volume and perhaps correlate with outcome.

A number of studies comparing LHR or the o/e-LHR and lung volume measurement on magnetic resonance imaging (MRI) have shown good correlation between these two measurement techniques, with inconsistencies mainly due to the variable size of the ipsilateral lung, side of the defect and GA at assessment [35-39].

In left-sided CDH the prenatal measurement of LHR is a good marker for indirectly assessing pulmonary hypoplasia, if LHR is corrected for GA. In right-sided CDH, despite correcting for GA, LHR does not seem to predict pulmonary hypoplasia, possibly because the small numbers of cases make statistical inference impossible. Whether direct measurement of lung volume by fetal MRI, can indirectly assess pulmonary hypoplasia in left and right-sided CDH remains to be determined.

Large volume CDH studies are limited, as they had only small numbers of right-sided CDH patients. The available data which have compared the management and outcome of
right-sided CDH vs. left-sided CDH are inconsistent. One study reports that right-sided CDH carries disproportionately high mortality and morbidity [40]. Several studies report the presence of liver herniation is a predictive of poor outcome [41-44].

There is still disagreement regarding prediction of poor outcome as another study reports that right-sided CDH was not associated statistically with poor neonatal outcome [12]. The herniated liver, reduced lung sizes and decreased vascularity are factors related directly to the neonatal outcomes in isolated CDH independent of the side of the defect. Perhaps future research can clear up misconceptions.

**Postnatal Diagnosis**

After birth, signs and symptoms of CDH is various. Respiratory symptoms in an infant with a CDH are determined by the severity of pulmonary hypoplasia and pulmonary arterial hypertension. The most severe cases develop respiratory distress at birth, whereas most infants present within the first 24 hours of life. The symptoms of respiratory distress may include cyanosis, gasping, chest retractions, and poor respiratory effort. The signs of CDH are a scaphoid abdomen and an asymmetric distended chest. The asymmetry is caused gastrointestinal distension. Increasing distension will lead to increasing respiratory compromise, difficulty ventilating the infant and cause decreased venous return with right sided CDH or cardiac output by mediastinal compression by left sided CDH. Findings on auscultation may not be present due to the small size of the infant’s chest.

The diagnosis of a CDH can be confirmed by a plain chest radiograph that demonstrates loops of intestine in the chest. The chest radiograph shows angulation of the mediastinum and a shifting of the cardiac silhouette into the contralateral thorax. Although minimal aeration of the ipsilateral chest may be noted, chest radiographs are unreliable for estimating the degree of pulmonary hypoplasia. As stated above, once the diagnosis of a CDH is confirmed, additional evaluation should be carried out to search for associated anomalies.

Although most CDHs present in the first 24 hours of life, 10% to 20% of the infants with this defect present later [45, 46]. These infants usually have mild respiratory illnesses, chronic pulmonary disease, pneumonia, effusion, empyema, or gastric volvulus. CDH is invariably associated with abnormal intestinal rotation and fixation, some children may present with intestinal obstruction or volvulus. Right sided CDH is often more difficult to diagnosis. Minimal features, such as intestinal and gastric herniation, may not be seen. The herniated right lobe of the liver can be mistaken for a right diaphragmatic eventration. Occasionally, CDH may be completely asymptomatic and is only discovered incidentally [47, 48]. Older patients who present later in life have a much better prognosis due to milder or absent associated complications.

**Treatment**

The concept of treatment for CDH has been changed due to recent advances in the management. Advances in medical management and postnatal care are based on targeting the primary mechanism of pathophysiology and correcting the disorder with respect to
physiology rather than anatomy. These include gentle ventilation (concept based on minimizing lung injury), high frequency ventilation (preserves end expiratory volume and avoids alveolar over distension), and treatment of pulmonary hypertension with inhaled nitric oxide therapy and extracorporeal membrane oxygenation (ECMO). These changes have been shown to improve survival.

The focus of surgical treatment has also changed from emergency surgery at presentation to surgical closure of defect after stabilization of the patient. Advances in surgical management include introduction of fetal interventions, laparoscopic repair, and lung transplantation.

Supportive Care

Fetuses with CDH should be delivered at a tertiary care center due to access to a neonatologist, pediatric surgeon and ECMO. Most centers plan for delivery at 38-39 weeks with low threshold to convert to cesarean delivery if there are signs of fetal distress.

Initial post natal therapy is targeted at resuscitation and stabilization of infant. An infant with CDH should be intubated immediately at delivery. Bag-masking is avoided because it leads to gastrointestinal distension and compression of the lung that make ventilation more difficult. A nasogastric tube is essential to decompress the stomach and bowel and aid with lung expansion.

Mechanical Ventilation

Over the period of years mechanical ventilation strategies have trended towards less aggressive approaches with the goal of maintaining oxygenation while limiting the risks of ventilator induced lung injury. Utilization of standardized protocols for postnatal CDH care and ventilator management has shown improvement in overall survival rates [49, 50].

Strategies directed towards “gentle ventilation” reduce iatrogenic injury to hypoplastic lungs. Ideally peak airway pressures should be limited to less than 25 cmH$_2$O. Antonoff et al. introduced a standardized protocol involving ventilation strategies on veno-arterial (VA) ECMO which include conventional synchronized intermittent mandatory ventilation (SIMV) with a respiratory rate of 10 breaths per minute, positive end-expiratory pressure (PEEP) of 12 cm H$_2$O, peak inspiratory pressure (PIP) of 25 mm Hg, and fraction of inspired oxygen (FIO$_2$) of 0.40, with the PEEP being lowered to 8 cm H$_2$O upon lung clearance. For operative repair, ventilator settings are adjusted to a rate of 60 breaths per minute, PIP of 25 mm Hg, PEEP of 6 cm H$_2$O, and an FIO$_2$ of 0.80. These new treatment strategies substantially improved survival to discharge (67% preprotocol vs. 88% postprotocol; $P = .015$). Among ECMO patients, survival was increased up to 82% [49].

All the reported standardized protocols share the use of lung-protective strategies including use of low ventilation pressures, reduced oxygen saturation goals, and permissive hypercapnia while maintaining normal acid-base balance. Blood pressure support should be provided in order to maintain arterial mean blood pressure levels thereby minimizing any right to left shunting [49-52].
Extracorporeal Membrane Oxygenation

Extracorporeal Membrane Oxygenation (ECMO) remains the mainstay of treatment of severe CDH. It is used to stabilize the CDH infant during the time of maximal pulmonary vascular reactivity when standard therapy fails. Proposed indications for ECMO use include inability to maintain preductal oxygen saturations >85%, peak inspiratory pressures requirements >28 cm H₂O, mean airway pressure >15, pressor-resistant hypotension, inadequate oxygen delivery based on persistent metabolic acidosis or rising serum lactate level, or inability to wean from FiO₂ 100% in the first 48 h of life [53, 54].

Data from study done by Benjamin and colleagues suggest that patients with R-CDH have higher ECMO utilization and also benefit from ECMO. In this study, 54% of patients required ECMO support with overall survival rate of 74% [55]. The rate of ECMO utilization rate as well as the survival rate in this study were higher than expected when compared to prior studies [40, 56-58]. However, the most recent multicenter study done by Duess and colleagues did not find significant difference in the need of ECMO utilization from R-CDH to L-CDH [59]. More studies are needed in future to confirm these findings. While considering ECMO, the cost effectiveness should also be kept in mind as there will be subsets of babies with severe pulmonary hypoplasia in which all available treatment strategies maybe futile [60]. Pre-ECMO PCO₂ is one of predictors of poor outcome. In a retrospective review, Hoffman et al. utilized predictive equations in patients with CDH requiring ECMO. The finding was significant as there were no survivors in cases when pre-ECMO PCO₂ could not be brought down to 70 [61].

Due to predictably worse postnatal outcomes associated with severe fetal CDH, Ex Utero Intrapartum Therapy (EXIT) to ECMO has been proposed as a treatment strategy for severe CDH. This is an alternative lung protective management strategy in which ECMO support is initiated at birth as part of an ex utero intrapartum treatment (EXIT) procedure. EXIT to ECMO allows for aggressive postnatal management while avoiding the predictable barotrauma, hypoxia, acidosis and hemodynamic instability. Initial studies have shown a 64% survival rate after EXIT to ECMO [62]. However, when studied in a small series of infants with <15% predicted lung volume, there was no survival benefit in the EXIT to ECMO group compared to standard postnatal ECMO group (33% vs. 50% survival) [63]. At present, there are no absolute predictors of outcome of severe pulmonary hypoplasia with CDH and ECMO remains an important treatment modality for preoperative stabilization.

Surgical Management

The concept in surgical management has changed from performing emergency repair to delaying repair for at least 24–48 hours to allow for clinical stabilization and a fall in pulmonary vascular resistance [64]. Depending on the clinical condition of the patient, surgery can be delayed for up to 7–10 days. Surgical repair is delayed until pulmonary hypertension is significantly improved or resolved. Criteria for timing of surgical repair may include the following: absence of shunting episodes, ventilator settings FiO₂ <0.5, PIP <25, MAP <12 which allows for postsurgical escalation if needed, the infant being off ECMO or ready to come off ECMO, normal acid–base balance, and resolution of anasarca [52]. Hence the mean age of repair remains variable [65, 66]. There is no evidence that timing of surgery
influence survival, however, associated conditions (cardiac defects and renal failure) and initial blood gases are significant factors that influence survival [67].

**Operative Approach**

Generally, repair of congenital diaphragmatic hernia can be performed via an open repair procedure or by using a minimally invasive technique.

The open repair can be performed either by a transthoracic or transabdominal approach. Transthoracic approach is preferred for a right-sided hernia because it allows better visualization of the diaphragmatic foramen and adhesions around the pleura and pericardium. With a Morgagni hernia, the transthoracic approach provides wide exposure and easy repair of hernia sac [68]. It also provides a better access to the hernia sac in obese patients [69].

The transabdominal approach is technically better for repairing bilateral and complicated hernias. With the transabdominal approach, it is easier to reduce the content of the hernia and repair the sac [70]. However, the transabdominal approach is mandatory if there are complications (e.g., strangulation, incarceration, or perforation with peritonitis) as it is strongly recommended that the entire abdominal cavity be inspected in all cases of peritonitis [69-71].

Surgical repair is more challenging in R-CDH because of near-universal liver herniation as well as the potential for anatomical anomalies uniquely associated with right-sided defects [72-77]. These operative challenges are implied by the increased requirement for prosthetic material (76% vs. 41%) and abdominal wall (38% vs. 19%) repairs in R-CDH vs. L-CDH diaphragm. However recurrence did not statistically differ between right and left survivors in review done by Fisher et al. [40].

The routine use of chest tubes after CDH repair to drain pleural fluid has been abandoned. Tube thoracotomy should only be used for postoperative chylothorax or pleural fluid causing hemodynamic compromise.

**Minimally Invasive Technique**

Laparoscopic repair is a safe and excellent way to confirm diagnosis and repair the uncomplicated hernia of Morgagni [72-75]. However the R-CDH is difficult to repair by the laparoscopic approach because of the large friable liver impeding access to the defect. Thoracoscopic approach has an advantage of flexibility and more choices in the selection of an extrathoracic ligation method and allowing the surgeon to make a proper incision and precise repair of the defect [76]. Shah et al. advocated thoracoscopic approach for neonatal Bochdalek, and Marhuenda et al. advocated laparoscopic approach for Morgagni hernia [77, 78]. During Minimally invasive surgery technique, the patient’s PCO₂ typically rises. Although increases in CO₂ absorption during MIS are generally well tolerated in infants, infants with CHD demonstrate greater changes in end tidal CO₂ (etco₂) and impaired elimination of CO₂ during thoracoscopy and laparoscopy. Hypercapnia and the associated acidosis results in increased pulmonary shunting and for patients with moderate to severe pulmonary hypertension this can precipitate pulmonary vasospasm and intraoperative instability. Due to the aforementioned reasons thoracoscopic repair of CDH is reserved for
cases with a small defect and mild pulmonary hypertension. In patients requiring concomitant congenital cardiac anomaly repair a trans-sternal approach can be used.

Surgical repair typically involves primary or patch closure of the diaphragm. Primary repair is performed when there is sufficient diaphragm to approximate without tension. Patch closure with either prosthetic mesh or autologous graft is used to achieve tension free repair in large CDH [71]. The need for patch repairs has been shown to be an independent predictor of mortality and is associated with secondary outcome measures of morbidity including the need for oxygen at discharge and duration of ventilation [79].

Different prosthetic materials, including polypropylene mesh, PTFE patch (Teflon), expanded ePTFE, Dacron and autologous tissues such as fascia and muscle flaps have been used. Prosthetic materials demonstrated a wide variety of characteristics with individual benefits; however none has been described as an ideal prosthesis. Patients who underwent patch repair have been noted to be significantly more likely to develop increased risk of recurrence and small bowel obstruction than patients who had a primary repair [80].

Robotic repair of diaphragmatic hernia has been described as being safe, although the long-term outcomes of these repairs are yet to be evaluated. Both Morgagni and Bochdalek hernia have all been successfully repaired via the use of robotic instruments [81, 82]. Van Meurs et al. performed lung transplantation on a patient with congenital diaphragmatic hernia who continued to deteriorate after delayed repair despite apparent resolution of pulmonary hypertension [83]. There has been no other report of lung transplantation for the treatment of congenital diaphragmatic hernia in the literature following this paper.

**Fetal Intervention**

Fetal surgery has been explored in experimental studies and has been applied clinically. In experimental studies, prenatal tracheal occlusion has been shown to induce lung growth with reduction of herniated viscera and a dramatic improvement in lung compliance and gas exchange [43]. Fetal surgery has revolutionized from open surgical repair to tracheal occlusion techniques: open surgical tracheal occlusion (TO), endoscopic external tracheal occlusion, and endoscopic endoluminal tracheal occlusion. A substantial improvement in outcome and 35% survival of patients has been reported with fetal endoscopic tracheal occlusion (FETO) [43, 85], though it is still associated with a high incidence of premature rupture of membranes and preterm delivery in severe congenital diaphragmatic hernia [43].

**Outcomes**

There is a limited published literature on the outcomes of R-CDH and moreover there are significant dissimilarities in outcomes. Survival rates for CDH vary between institutions. These differences in outcome are partly due to the low incidence of disease in a single institute and partly due to the variation in individual institute with respect to ventilation strategies, criteria for ECMO and operation timing. In terms of mortality of R-CDH in comparison to L-CDH, the current literature is contradictory. Some authors have reported higher, as well as lower survival rates comparatively, whereas other has found no differences in RCDH vs. LCDH [5, 59, 86].
Fisher et al. found that there was a trend towards a decrease in survival among neonates undergoing repair of right sided defects. Survival in R-CDH compared with L-CDH was 55% vs. 77%. In addition, increase utilization of extracorporeal membrane oxygenation up to 40% for right-sided as compared to 15% for left-sided cases was noticed. The use of diaphragmatic patch and abdominal wall prosthesis were also higher in right-sided hernias. No significant differences were detected in right-sided vs. left-sided recurrences. In this largest single institution series, right-sided CDH carries a disproportionately high morbidity and mortality and prenatal diagnosis was the only factor predictive of R-CDH survival [40]. Similar findings are reported in a population based study conducted by Colvin et al. in Western Australia, stating increase mortality in infants with R-CDH [87].

A multicenter study including three European tertiary pediatric surgical centers shows that prenatal diagnosis and patch repair was associated with an increased mortality rate in R-CDH. However, the morbidity following repair of R-CDH was not significantly different from that in L-CDH in survivors [59].

A 25 five year review on R-CDH done by Jani and colleagues in a tertiary care center, RCDH was associated with high mortality (50%), prolonged length of stay and other anomalies. Low five minute Apgar score, and high alveolar-arterial gradient were significant predictors of mortality [88].

**Long Term Morbidity**

The improved survivals of infants with severe CDH have led to the need for improved management and follow up of long-term morbidities. CDH survivors have a higher incidence of respiratory, neurologic, gastrointestinal, and nutritional difficulties [89-92].

Respiratory difficulties ranges from asthma-related difficulties and propensity for pulmonary infections to chronic pulmonary hypertension. CDH survivors demonstrate delays in neurocognitive and language skills [92] and up to a one month delay in structural brain development as seen on MRI [93]. Almost all CDH patients have gastroesophageal reflux requiring medical treatment and some go onto require fundoplication. Higher metabolic demands also contribute to nutritional deficiencies and poor growth with up to 56% of patients below the twenty-fifth percentile for weight [90].

Large volume CDH studies are limited due to small numbers of R-CDH. Available data comparing management and outcome of right sided vs. left sided CDH are inconsistent. These differences are due to compilation of data from multiple institutes with multiple treatment strategies. Multi-institutional studies with a standardized protocol, along with a large number of subjects, comparing the various outcomes including mortality, morbidity and associated malformations of RCDH and LCDH are needed.

**REFERENCES**


Right Sided Congenital Diaphragmatic Hernia


INDEX

A

A burst abdomen, 34, 35
abdominal shutter, 38
acid, 92, 100, 119, 120
acidosis, 120, 121
acute rejection, 99
acute renal failure, ix, 84, 91
adhesions, 5, 6, 32, 33, 39, 41, 42, 68, 87, 121, 128
adverse effects, 99, 100, 101
airways, 38, 115
albumin, 11, 69, 105
alcoholic liver disease, 103
alveolar macrophage, 41
alveoli, 115, 116
alveolus, 116
Ammaturo and Bassi, 33
anaphylaxis, 101
anatomy, 22, 55, 75, 77, 94, 116, 119
anemia, 100
anesthesiologist, 39, 42, 79
aneuploidy, 114
aneurysm, 4, 12
angiogenesis, 100, 125
angulation, 118
antibiotic, 99
antibody, 99, 101
antigen, 101
aorta, 4, 102, 116
apoptosis, 24, 101
arterial hypertension, 39, 118
arteries, 52, 87, 112, 116
arterioles, 116
artery, 102
ascites, 21, 50, 104, 105b
aspiration, 7, 43, 88
asthma, 123
asymptomatic, 7, 26, 37, 49, 118
atrophy, 38, 70, 74
auscultation, 118
autoimmune hepatitis, 103
azathioprine, 100

B

bacillus, 74
back pain, 68, 84
bacteria, 3, 35
barotrauma, 111, 120
bilateral, x, 49, 53, 87, 103, 113, 116, 121
biomarkers, viii, 19, 22
biomaterials, 91
birth weight, xi, 114
births, x, 113, 114
BJS, 57
bleeding, 49, 78
blood, ix, 3, 23, 40, 41, 45, 48, 51, 52, 53, 54, 84, 91, 119, 121
blood flow, ix, 84, 91
blood pressure, 119
blood supply, 48, 51, 52, 53, 54
blood transfusion, 45
blood vessels, 23
body image, 57
body mass index (BMI), x, 3, 8, 39, 45, 46, 86, 97, 100, 102, 103, 104
bone marrow transplant, 112
bowel, viii, 2, 7, 9, 31, 32, 35, 36, 39, 42, 69, 84, 85, 86, 87, 90, 98, 102, 104, 105, 116, 119, 122
bowel injury, 7
bowel obstruction, 2, 9, 32, 69, 90, 122
brain, 123, 129
branching, 112, 115
breast augmentation, 95
breathing, 39, 45, 47, 68
bronchioles, 115, 116
<table>
<thead>
<tr>
<th>E</th>
<th>G</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECM, 38</td>
<td>gangrene, 104</td>
</tr>
<tr>
<td>edema, 105</td>
<td>gastrocentomy, 46</td>
</tr>
<tr>
<td>effusion, 118</td>
<td>gastroesophageal reflux, 123</td>
</tr>
<tr>
<td>electrocautery, 53</td>
<td>gastrointestinal tract, 6, 47</td>
</tr>
<tr>
<td>electromyography, 75</td>
<td>gastroscisis, 95</td>
</tr>
<tr>
<td>elongation, 39, 43, 44, 52, 73, 77</td>
<td>gelatinase A, 24</td>
</tr>
<tr>
<td>embryogenesis, x, 113, 124</td>
<td>gene expression, 3, 24, 25</td>
</tr>
<tr>
<td>embryology, 115</td>
<td>general anesthesit, 39, 45, 50, 88</td>
</tr>
<tr>
<td>emotional health, 36</td>
<td>general surgeon, 47, 52</td>
</tr>
<tr>
<td>emotional state, 91</td>
<td>general surgery, viii, 12, 19, 21, 22, 41, 51, 110</td>
</tr>
<tr>
<td>emphysema, 44</td>
<td>genes, 115</td>
</tr>
<tr>
<td>empyema, 118</td>
<td>genetics, 29, 124</td>
</tr>
<tr>
<td>end stage renal disease (ESRD), ix, 97, 98, 102, 104</td>
<td>gestation, 115, 116</td>
</tr>
<tr>
<td>Endoscopic Component Separation, 53</td>
<td>gestational age, 117</td>
</tr>
<tr>
<td>endothelial cells, 41</td>
<td>gingival, 99</td>
</tr>
<tr>
<td>enlargement, viii, ix, 2, 31, 34, 67, 83</td>
<td>glycosylated hemoglobin, 40</td>
</tr>
<tr>
<td>enzymes, 24, 100</td>
<td>Goni-Moreno, 33, 42, 43, 44</td>
</tr>
<tr>
<td>epidemic, 44</td>
<td>growth, 9, 22, 24, 32, 116, 122, 123, 125</td>
</tr>
<tr>
<td>epigastrium, 87</td>
<td>growth factor, 9, 22, 24</td>
</tr>
<tr>
<td>epithelium, 23</td>
<td>growth rate, 32</td>
</tr>
<tr>
<td>erosion, 6, 85</td>
<td>guanine, 100</td>
</tr>
<tr>
<td>etiology, viii, x, 2, 19, 20, 21, 22, 28, 61, 113</td>
<td>HBV, 103</td>
</tr>
<tr>
<td>Eurotransplant, 110</td>
<td>HCC, 103</td>
</tr>
<tr>
<td>evolution, 34, 127</td>
<td>healing, x, 3, 4, 5, 12, 20, 21, 22, 23, 24, 25, 27, 28, 40, 41, 42, 59, 69, 70, 85, 97, 99, 100, 102, 105</td>
</tr>
<tr>
<td>examinations, 69, 73</td>
<td>health, 2, 57</td>
</tr>
<tr>
<td>exercise program, 62</td>
<td>health care, 2</td>
</tr>
<tr>
<td>external oblique, 5, 51, 52, 53, 54, 56, 74, 77, 79, 87</td>
<td>heart disease, 50</td>
</tr>
<tr>
<td>extracellular matrix, 4, 24, 28, 38</td>
<td>hematoma, 44, 48, 50, 52, 73</td>
</tr>
<tr>
<td>extrusion, 48, 70</td>
<td>hemoglobin, 41</td>
</tr>
<tr>
<td>exudate, 35</td>
<td>hemolytic uremic syndrome, 99</td>
</tr>
<tr>
<td>fascia, vii, 1, 3, 5, 6, 8, 13, 21, 24, 25, 28, 38, 48, 55, 56, 75, 77, 79, 87, 91, 94, 111, 122</td>
<td>hemostasis, 23, 24</td>
</tr>
<tr>
<td>fetal demise, 114, 116</td>
<td>hepatocellular carcinoma, 110, 112</td>
</tr>
<tr>
<td>fetal distress, 119</td>
<td>herbicide, 115</td>
</tr>
<tr>
<td>fetus, 117, 125</td>
<td>hernia, vii, viii, ix, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 31, 33, 34, 35, 36, 37, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 59, 60, 63, 64, 67, 68, 70, 71, 75, 77, 78, 79, 80, 81, 84, 85, 86, 87, 88, 90, 91, 92, 93, 94, 97, 98, 100, 102, 103, 104, 105, 106, 107, 109, 110, 111, 121, 122, 124, 128</td>
</tr>
</tbody>
</table>
laparoscopic surgery, 21, 29, 110
laparoscopy, 26, 32, 47, 80, 121
laparotomy, vii, viii, 1, 3, 4, 5, 7, 9, 11, 12, 13, 22, 24, 27, 28, 31, 32, 43, 57, 59, 67, 104
layered closure, 4
lead, 22, 25, 26, 39, 42, 56, 100, 103, 104, 105, 115, 116, 118
leakage, 104
leaks, 43
lesions, 44, 77, 114, 129
leukopenia, 100, 101
life expectancy, 32
ligament, 52, 53, 77
liver cirrhosis, ix, 21, 97, 98, 103
liver disease, 103
liver failure, 50, 103, 112
liver transplantation, x, 97, 99, 100, 103, 107, 108, 110, 111, 112
local anestesia, 43, 71
local anesthetic, 8
loss of domain, viii, 31, 32, 33, 34, 35, 38, 46, 53, 54, 57, 58, 67, 68, 69, 70, 71, 80, 87, 91
low risk, 6, 49
lumen, 72
lung function, xi, 114
lung transplantation, 119, 122, 129
lymphocytes, 100, 101
lymphoid, 101
lysis, 101
macrophages, 101
magnetic resonance imaging (MRI), 117, 123, 125, 126, 129
malignancy, 99, 100, 107
malnutrition, 21, 47, 49, 69, 78
Marfan syndrome, 29
matrix, viii, ix, 3, 11, 19, 22, 23, 24, 27, 28, 61, 83, 85, 93, 106, 109
matrix metalloproteinase, 11, 22, 23, 28, 61
measurements, 43, 55, 78, 86, 88, 95, 117
mechanical stress, 38, 104
mechanical ventilation, 119
mediastinum, 118
melitus, 86, 99, 112
membership, 110
mesentery, 39, 44
mesh, vii, viii, ix, x, 1, 5, 6, 7, 8, 9, 10, 11, 14, 15, 16, 19, 21, 25, 32, 34, 35, 36, 46, 47, 48, 49, 51, 52, 54, 55, 56, 57, 58, 59, 63, 64, 65, 69, 71, 75, 78, 79, 83, 84, 85, 86, 87, 89, 91, 93, 98, 100, 106, 108, 109, 122
mesh infection, 8
mesoderm, 115
meta-analysis, 6, 8, 13, 14, 16, 61, 64
metabolic, 12
metabolic acidosis, 120
metabolic syndrome, 62
metabolism, 2, 3, 4, 11, 21, 22, 27
metalloproteinase, 23, 100
methylprednisolone, 99
microorganisms, 39
migration, 41, 44, 85
Minimally Invasive Component Separation, 52
MMP-2, 24
MMPs, 20, 22, 24, 28
models, 24, 116, 124
modifications, 38, 46, 48, 53, 55, 64, 86
molecules, 24, 28
monoclonal antibody(ies), 98, 101, 102
monomers, 25
morbidty, xi, 2, 5, 8, 9, 14, 21, 29, 32, 35, 40, 41, 50, 52, 54, 55, 56, 59, 64, 70, 78, 84, 85, 109, 114, 118, 122, 123, 128, 129
morphology, 57, 125
mortality, 2, 5, 6, 7, 16, 32, 35, 36, 40, 41, 50, 70, 73, 118, 122, 123, 124, 128
mortality rate, 2, 16, 35, 50, 123
mRNA, 12, 23
mTOR inhibitors, 100, 102, 103, 105
mucosa, ix, 83, 85
mucus, 41
multiple myeloma, 112
muscle atrophy, 69
muscle mass, 74
muscle relaxation, 71, 73
muscles, 21, 34, 37, 38, 42, 44, 47, 48, 51, 52, 53, 54, 55, 56, 62, 68, 70, 73, 74, 75, 76, 77, 78, 80, 81, 93
mutations, 25, 29
mycophenolate mofetil, 99, 100, 107
myelosuppression, 100
myocardial infarction, 44
nasogastric tube, 119
natural killer cell, 101
nausea, 43, 99, 100
necrosis, 5, 35, 40, 88, 91, 105, 112
necrotizing fasciitis, 36, 104
necrotizing soft tissue infection, 36
Index

neonates, 123
nephrectomy, 110, 111, 112
nerve, 74
neurotoxicity, 99
neurotransmitters, 74
neutrophils, 41
nicotine, 11, 41, 42
nitric oxide, x, 43, 114, 119
nodes, 23
non-smokers, 41, 42
non-steroidal anti-inflammatory drugs, 8
notochord, 23
Novitsky, 15, 54, 55, 63, 93
NRT, 40, 42
nucleotides, 100
nutrition, 11, 105
nutritional deficiencies, 123

O

obesity, vii, x, 1, 3, 8, 21, 38, 39, 44, 45, 46, 49, 50, 56, 68, 78, 86, 92, 97, 100, 102, 103, 104, 106
obstruction, ix, 68, 84, 91, 117
occlusion, 122, 126
OCS, 53
oedema, 39, 44
omentum, 85
oncogenesis, 100
open overlay technique, 6
operations, 3, 20, 21, 34, 50
optimization, 45, 46
oral antibiotics, 88
organ transplantation, vii, ix, 97, 98, 99, 100, 101, 102, 105, 106, 107, 109, 110
organism, 65
organs, ix, 23, 34, 67, 68, 84, 91, 95, 98, 102, 104
osteogenesis, 20, 25
osteoarthritis, 99
outpatient, 15, 72, 74, 75, 79
overlay, 5, 6, 54
overweight, 3, 37, 45, 69, 104, 105
oxygen, 3, 39, 40, 41, 42, 71, 88, 119, 120, 122

P

pain, vii, 1, 7, 8, 9, 16, 26, 37, 39, 43, 55, 74
pancreas, ix, 97, 98, 101, 102, 103, 104, 105, 108, 109, 110, 111, 112
pancreas transplant, x, 98, 103, 104, 105, 109, 110
pancreas transplantation, x, 98, 103, 104, 105, 109, 110
pancreatitis, 104
paradoxical respiration, 38
paralysis, 71, 73, 75, 81
parenchyma, 116
pathogenesis, vii, 1, 27, 124
pathology, 36, 37, 87, 125
pathophysiology, viii, x, 27, 31, 114, 118
pathway, 4, 99, 100
pelvis, 37, 43
peptic ulcer disease, 99
peptidase, 24
perforation, 121
pericardium, 121
peritoneal cavity, 43, 44, 115
peritoneal volume, 34
peritoneum, 5, 6, 21, 32, 44, 68, 73, 85, 102
peritonitis, 34, 121
pH, 40
phagocytosis, 3
phenotype, 24
phosphorylation, 12
physical activity, 69, 78
physical therapist, 39, 79
physiological mechanisms, 85
physiology, 49, 55, 119
placenta, 23
planned ventral hernia, 35, 36, 75
plasmapheresis, 101
plastic surgeon, 39, 47, 50
pleura, 121
PLS, 58
pneumonia, 44, 100, 118
polyclonal antibodies, 101
polyhydramnios, 117
polymerization, 25
polymers, 26
polypeptide, 99
polypropylene, 6, 13, 14, 35, 48, 51, 65, 79, 87, 93, 106, 109, 122
population, 4, 27, 32, 44, 98, 123, 124, 127, 129
posterior component separation, 54
postoperative outcome, 39, 78
postoperative pain, vii, 1, 7, 8, 9, 74
post-transplant, 99
prednisone, 100
pregnancy, 21, 114
prematurity, xi, 114
preoperative risk, 39
preservation, 48, 52, 55, 86, 94, 103
preterm delivery, 122
prevention, vii, x, 2, 5, 11, 43, 49, 94, 98, 106
prognosis, x, 78, 112, 113, 114, 117, 118
progressive preoperative pneumoperitoneum (PPP), 34, 42, 43, 44, 62, 65, 71, 73, 80, 81
Index

proliferation, 24, 38, 100
prophylaxis, 86
propylene, 108
prostheses, ix, 40, 83, 85
prostheses (es), prosthetic materials, 48, 83, 85, 86, 122, 123
protection, 44, 55
proteinase, 27
proteins, 11, 12, 28, 101
proteolysis, 38, 74
PTFE, 16, 86, 122
pubis, 87
pulmonary arteries, 116
pulmonary artery, 116
pulmonary circulation, 116
pulmonary embolism, 44, 45
pulmonary function test, 40
pulmonary hypertension, x, 113, 119, 120, 121, 122, 123
pulmonary vascular resistance, x, 114, 120
purines, 100
quality of life, 2, 10, 32, 37, 54, 55, 57, 78
radiotherapy, 70
Ramirez, ix, 13, 29, 48, 50, 52, 54, 63, 83, 85, 88, 93
receptor, 12, 24, 74, 98, 100, 101
recognition, 7
reconstruction, viii, ix, 7, 10, 12, 19, 21, 38, 46, 47, 50, 51, 56, 63, 64, 67, 69, 70, 73, 75, 76, 78, 79, 80, 81, 83, 84, 85, 90, 91, 93, 94, 104, 112
recovery, 35, 45, 51, 75, 88
rectus abdominis, 43, 48, 51, 52, 56, 63, 91, 94
rectus femoris, 85
recurrence, vii, viii, ix, 1, 2, 3, 5, 6, 8, 9, 11, 19, 21, 27, 28, 32, 35, 36, 44, 45, 46, 47, 48, 49, 50, 51, 52, 55, 56, 57, 69, 70, 78, 83, 84, 85, 86, 88, 90, 93, 121, 122
regeneration, 24
Registry, 106, 127
rehabilitation, 79
rejection, ix, 97, 98, 99, 101
relaxation, vii, 39, 67, 73, 102
renal failure, 112, 121
repair, vii, viii, ix, x, xi, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14, 15, 16, 17, 19, 20, 21, 22, 23, 27, 28, 32, 33, 35, 37, 38, 39, 43, 46, 47, 48, 49, 51, 52, 53, 54, 55, 56, 57, 58, 60, 61, 62, 63, 64, 65, 68, 70, 78, 81, 83, 84, 85, 86, 87, 88, 90, 91, 92, 93, 94, 98, 101, 106, 108, 109, 114, 119, 120, 121, 122, 123, 124, 127, 128, 129
resection, 2, 9, 50, 84, 86, 87, 91
resistance, 37, 38, 45, 68
resolution, 34, 36, 120, 122
resource utilization, 10, 14, 60
respiration, 2, 38, 46
respiratory failure, 39, 71
respiratory insufficiency, x, 38, 113
respiratory rate, 119
response, 3, 60, 65, 85, 112
restructuring, 74
retro-rectus mesh, 6
risk, vii, ix, 2, 3, 4, 6, 8, 10, 11, 21, 25, 26, 27, 32, 35, 36, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 56, 57, 60, 62, 68, 69, 71, 75, 83, 85, 86, 87, 91, 93, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 127
risk factors, vii, x, 2, 3, 10, 21, 26, 27, 35, 49, 56, 57, 60, 68, 93, 97, 98, 100, 102, 103, 106, 107
Rives, 37, 38, 47, 54, 55, 57, 60, 62, 65
RNA, 100
Rosen, 14, 16, 33, 45, 50, 53, 54, 55, 57, 58, 60, 62, 63, 64, 93, 106
scar tissue, 3, 23, 25, 85
secretion, 9, 104
sensation, 71
sensitivity, 24
sensor, 72
sepsis, 36, 104
septum, 115
Seroma, 7, 16, 53
serum, 3, 78, 101, 120
serumalbumin, 3
severe asthma, 86
side effects, 104
signal transduction, 100
signals, 4, 38
signs, 118, 119
smoking, 3, 11, 21, 38, 39, 40, 41, 42, 46, 47, 49, 50, 61, 78, 86
smoking cessation, 3, 11, 40, 42, 46, 61
Sparing of Periumbilical Perforators, 52
spine, 37, 56
spleen, 23, 34
<table>
<thead>
<tr>
<th>Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI, x, 45, 97, 98, 100, 102, 104, 105, 106</td>
</tr>
<tr>
<td>stability, 23, 25, 56, 79</td>
</tr>
<tr>
<td>stabilization, x, 114, 119, 120</td>
</tr>
<tr>
<td>stasis, 39</td>
</tr>
<tr>
<td>sterile, 71, 74, 88</td>
</tr>
<tr>
<td>sternum, x, 113</td>
</tr>
<tr>
<td>steroids, x, 4, 49, 97, 100, 102</td>
</tr>
<tr>
<td>stomach, 117, 119</td>
</tr>
<tr>
<td>strangulated hernia, 6</td>
</tr>
<tr>
<td>stress, 49, 50</td>
</tr>
<tr>
<td>stretching, 9, 39</td>
</tr>
<tr>
<td>structure, xi, 4, 23, 24, 68, 73, 114</td>
</tr>
<tr>
<td>subcutaneous emphysema, 73</td>
</tr>
<tr>
<td>subcutaneous tissue, 21, 50, 53, 75</td>
</tr>
<tr>
<td>suprapubic, 55, 87</td>
</tr>
<tr>
<td>surface area, 33</td>
</tr>
<tr>
<td>surfactant, 116</td>
</tr>
<tr>
<td>surgical debridement, 70</td>
</tr>
<tr>
<td>surgical intervention, 102</td>
</tr>
<tr>
<td>surgical technique, viii, 2, 5, 21, 37, 46, 47, 67, 68, 86, 94, 102</td>
</tr>
<tr>
<td>surgical techniques, 2, 5, 37, 47</td>
</tr>
<tr>
<td>survival, x, xi, 98, 110, 113, 114, 117, 119, 120, 121, 122, 123, 124, 126, 127, 128, 129</td>
</tr>
<tr>
<td>survival rate, 119, 120, 122</td>
</tr>
<tr>
<td>survivors, xi, 35, 36, 114, 120, 121, 123, 129</td>
</tr>
<tr>
<td>suture, vii, 1, 3, 4, 5, 7, 8, 10, 11, 12, 13, 16, 21, 32, 35, 47, 51, 59, 63, 87, 89, 93</td>
</tr>
<tr>
<td>swelling, 69, 70</td>
</tr>
<tr>
<td>“Swiss cheese”, 6</td>
</tr>
<tr>
<td>symptoms, 37, 68, 84, 118</td>
</tr>
<tr>
<td>synapse, 74</td>
</tr>
<tr>
<td>syndrome, 3, 25, 44, 91</td>
</tr>
<tr>
<td>synthesis, 4, 23, 28, 100, 116</td>
</tr>
<tr>
<td>the volume ratio, 34</td>
</tr>
<tr>
<td>therapeutic approaches, viii, 19, 22</td>
</tr>
<tr>
<td>therapy, ix, x, 11, 35, 40, 42, 44, 97, 98, 100, 101, 103, 104, 105, 106, 111, 114, 119, 120</td>
</tr>
<tr>
<td>thoraco-abdominal compartment, 38</td>
</tr>
<tr>
<td>thoracotomy, 121</td>
</tr>
<tr>
<td>thorax, 117, 118</td>
</tr>
<tr>
<td>thrombocytopenia, x, 97, 100, 101</td>
</tr>
<tr>
<td>thrombophilia, 44</td>
</tr>
<tr>
<td>thrombosis, 43, 45</td>
</tr>
<tr>
<td>TIMP, 24, 28</td>
</tr>
<tr>
<td>tissue, viii, ix, 3, 4, 6, 12, 19, 21, 22, 23, 24, 25, 36, 37, 38, 40, 41, 46, 48, 49, 50, 52, 53, 59, 63, 67, 71, 76, 79, 81, 83, 84, 85, 86, 87, 91, 92, 94, 100, 116</td>
</tr>
<tr>
<td>tissue perfusion, 40</td>
</tr>
<tr>
<td>tobacco, 40, 41</td>
</tr>
<tr>
<td>tobacco smoke, 41</td>
</tr>
<tr>
<td>toxic substances, 41</td>
</tr>
<tr>
<td>toxin, viii, 67, 71, 73, 74, 81</td>
</tr>
<tr>
<td>trachea, 115, 116</td>
</tr>
<tr>
<td>transection, 48, 50</td>
</tr>
<tr>
<td>transformations, 38</td>
</tr>
<tr>
<td>transforming growth factor (TGF), 25, 29</td>
</tr>
<tr>
<td>transplant recipients, x, 98, 99, 101, 103, 106, 107, 109</td>
</tr>
<tr>
<td>transverse section, 117</td>
</tr>
<tr>
<td>transversus abdominis, 37, 47, 48, 55, 56</td>
</tr>
<tr>
<td>trauma, 36, 38, 39, 70</td>
</tr>
<tr>
<td>treatment, vii, x, 1, 2, 3, 5, 6, 7, 8, 9, 12, 13, 15, 16, 35, 37, 39, 42, 44, 46, 57, 59, 61, 64, 68, 70, 71, 72, 74, 78, 79, 80, 84, 86, 98, 100, 101, 102, 103, 105, 106, 108, 112, 118, 119, 120, 122, 123, 126, 127, 129</td>
</tr>
<tr>
<td>trial, 11, 12, 13, 14, 15, 48, 61, 64, 79, 92, 93, 106</td>
</tr>
<tr>
<td>trisomy, 114</td>
</tr>
<tr>
<td>tuberculosis, 42</td>
</tr>
<tr>
<td>tumor(s), 24, 34, 99, 100, 112</td>
</tr>
<tr>
<td>tumor cells, 24</td>
</tr>
<tr>
<td>tumor development, 100</td>
</tr>
<tr>
<td>tumor invasion, 24</td>
</tr>
<tr>
<td>tumor necrosis factor, 99</td>
</tr>
<tr>
<td>type 1 diabetes, ix, 97, 104</td>
</tr>
<tr>
<td>tyrosine, 12</td>
</tr>
</tbody>
</table>

T cell receptor, 101
T cells, 99, 101, 102
T lymphocytes, 100, 107
TBA, 74
teachable moment, 42, 46
techniques, vii, viii, ix, 1, 2, 5, 6, 8, 13, 14, 15, 20, 24, 26, 27, 32, 36, 42, 47, 48, 49, 56, 64, 67, 71, 75, 78, 79, 84, 85, 103, 111, 117, 122
tensile strength, 5, 22, 24, 46, 51, 68, 69
tension, ix, 2, 3, 4, 6, 14, 20, 21, 23, 33, 35, 43, 46, 48, 55, 58, 71, 83, 85, 86, 87, 88, 90, 105, 122
tensor fascia lata, 85, 106
the components separation technique, 48
the intra-abdominal pressure, ix, 33, 68, 83, 91
The open abdomen, 36
the second abdomen, 38
ultrasound, 42, 74, 90, 116, 117, 125, 126
umbilical hernia, 26, 29
underlay, 5, 14, 51, 54
urinary bladder, 88
urinary tract, 112
uterus, 23
vascular surgery, 110
vascularization, 70, 100, 107
vasculature, 116, 117
vasoconstriction, 41
vasoconstriction, 41
vein, 43, 44, 45, 112
ventilation, x, 91, 114, 119, 122, 126
Ventral Hernia Working Group, ix, 47, 51, 64, 97, 98, 106
vessels, xi, 41, 48, 50, 54, 56, 102, 104, 114, 115
viral infection, 103
viscera, vii, viii, 6, 21, 23, 31, 33, 36, 37, 38, 39, 44, 46, 55, 84, 85, 86, 117, 122
vitamin A, 115, 125
vitamin C, 11
volet abdominal, 38
volvulus, 118
weakness, vii, 21, 31, 84, 90
weight loss, 39, 44, 45, 46, 63, 78, 86
weight reduction, 45, 63
wound dehiscence, 3, 4, 11, 12, 28, 34, 35, 59, 78, 91
wound healing, viii, ix, 3, 4, 13, 19, 21, 22, 23, 24, 25, 27, 63, 97, 98, 99, 100, 102, 103, 104, 105, 106, 107, 108
wound infection, vii, 1, 3, 5, 6, 11, 21, 41, 46, 47, 54, 60, 91, 102, 106
xiphoid process, 103