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Molecular Factors of Failure in Incisional Hernia Surgery

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Rezumat

Factori moleculari de eșec în chirurgia herniilor incizionale

Herniile incizionale apar la fel de frecvent ca și acum 20 de ani, chiar dacă utilizăm tehnologii moderne în termeni de sutură. Tehnici chirurgcale, fie reparații primare sau intervenții după eșecul reparării primare sunt caracterizate prin rate ridicate de recurență. Utilizarea plaselor a devenit esențială în repararea tuturor tipurilor de hernii - inghinale, ventrale sau incizionale. Implantarea de plasă este o procedura relativ bine codificată chirurgical. Dar chirurgia este doar primul pas în procesul de vindecare. Implantarea plasei produce un răspuns puternic, cu mecanisme hematologice: absorbția de proteine, activarea complementului, coagularea, activarea trombocitelor, activarea neutrofilelor și mecanisme tisulare: proliferarea, aderența, fibroza. Ratele de recurență sunt în mod constant mai mici atunci când sunt utilizate procedee alloplastice și o varietate de plase au fost dezvoltate în acest scop. Cum aceste plase sunt încorporate de către organismul uman și modul în care limitele biomecanice ale peretelui abdominal sunt restaurate este încă subiect de dezbatere pentru chirurgi. Studiile histopatologice și progresul în designul și tehnologia materialelor sunt cheile pentru rezolvarea aceastei probleme. De asemenea, studiile histopatologice ar trebui să stabilească materialul pentru reparație personalizat în funcție de biologia fiecărui pacient. Această lucrare încearcă să analizeze factorii de eșec în chirurgia herniei incizionale, diferiți de erorile procedurilor chirurgicale. Complicațiile pot fi evitate sau reduse printr-o selecție adecvată a tipului de plasa utilizat în mod particular pentru fiecare caz în parte și printr-o tehnică chirurgicală meticuloasă. Herniile incizionale sunt considerate în acest moment un fenomen biologic progresiv, nu doar unul strict tehnic, nu "pur și simplu o gaură de perete abdominal", care trebuie bine suturată.

Cuvinte cheie: incizională, hernii, plasă, colagen, reparații

Abstract

Incisional hernias occur as frequent as they did 20 years ago even if we use modern technologies in terms of suture. Sutures techniques, either primary repair or applied after failure of primary repair are characterized by high rates of recurrence. Using the hernia mesh has become mandatory in repairing of all types of hernias - inguinal, ventral or incisional. Implantation of the mesh is a relatively well-coded surgical procedure. But surgery is only the first step in the process of healing. Implantation starts a strong response with haematological mechanisms: protein absorption, complement activation, coagulation, platelet activation, neutrophil activation and tissue mechanisms: proliferation, adhesion, fibrosis. Recurrence rates are consistently lower when replacement meshes are used and a variety of meshes have been developed for this purpose. How the mesh is embedded by the human body and how the biomechanical limits of the abdominal wall are restored is still a subject of debate for surgeons. Histopathological studies and progress in design and materials are the only keys to solve this problem. Also pathological studies should determine the right material for personalized repair according to each patient's biology. This paper attempts

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to analyze the molecular failure factors in incisional hernia surgery, different from errors in surgery procedures. Complications can be avoided or reduced by an appropriate selection of the type of place in a particular case, and by performing a meticulous technique. Incisional hernias are considered at this moment a biological progressive phenomenon, and not only a strictly technical one, a "simple hole in the abdominal wall" that has to be firmly sutured.

Key words: incisional, hernias, mesh, collagen, repair

Introduction

Implantation of a mesh is a relatively well-coded surgical procedure. But surgery is only the first step in the process of healing. Implantation determines a strong response with haematological mechanisms: protein absorption, complement activation, coagulation, platelet activation, neutrophil activation and tissue mechanisms: proliferation, adhesion, fibrosis.

Despite the better results in terms of hernia relapse noted by many studies it seems that using surgical mesh just delays the relapse of hernias with 2 to 4 years (1,2). Incisional hernias occur almost as frequent as they did 20 years ago even if we use modern technologies in terms of suture.

In general, the role of intraparietal prosthetic implant is to provide mechanical strength to weakened fascial structures. Surgical meshes are designed to withstand tension forces acting on the abdominal wall. Moreover, ideally, the mesh should facilitate hernial defect healing by encouraging the incorporation of connective tissue and strong collagen tissue into the mesh.

The advantage of modern meshes with large pores is represented by embedding tissue to grow through the mesh; also, large pores can create a thinner scar, more integrated, with better biomechanic properties. Finally, it creates a more elastic scar for the patient (3). In addition, the most recent technological advances have enabled the use of proper materials that were developed in several different types of mesh, which allow an adequate support to the abdominal wall.

This new type of mesh - which became known as "light weight" or "low-mass" offers a combination of thin filament, larger pores and a percentage of absorbable material which offer the possibility to be more closely aligned with the physiological properties of the abdominal wall.

Material and Methods

The present study attempts to compare in terms of relapse the rate and quality of life of patients, various types of meshes in various surgical procedures for incisional hernias (eventrations), and also analyse how the mesh is incorporated in the abdominal wall. We analyzed the results in terms of biomechanics as well.

We analyzed a total of 62 patients admitted to our clinic and operated on throughout a period of 5 years. All patients were operated on by the same surgical team, adapting the type of mesh used in the surgical technique depending on the type of hernia. In the selection process of the mesh and of how to position it we analyzed the biological status of the patient but also the associated his/her comorbidities. Were used the 4 most utilized categories of existing meshes at this time.

Results

Patient age ranged from 27 to 68 years with a mean of 48.5 years. 40 of the patients were males. Rate of obese patients in the study group was 59.6% (37 patients with BMI > 40 kg/m^2). All 62 Patients tolerated the procedure well, without intraoperative complications. There were six cases of postoperative complications. No myocardial infarction or pneumonia was recorded. One patient suffered a pulmonary embolism and was treated with anticoagulants (*Table 1*).

Most complications were minor, with only 7 patients requiring re-hospitalization for management. 3 patients had deep wound infection defined as purulent leakage. It wasn't necessary to remove the mesh and all were managed successfully with antibiotics and wound cleansing. There was no evidence of infection, including in those with purulent leakage. Wound cultures were not routinely performed in patients with suspected seroma in the absence of clinical signs of infection. 7 patients experienced postoperative bowel slowdown phenomena, problem solved in all cases by specific medication. 5 patients had chronic abdominal pain. (*Table 2, Table 3*)

By analyzing the factors that influence the healing process after laparotomies, it seems that wound infection is in most cases the cause of accidents of parietal postoperative scarring and that these accidents are conditioned by time of onset and duration of infection, clinical severity and its forms of manifestation. Mesh materials for abdominal wall hernia repair are probably the most common surgically implanted biomaterials in medicine. Since the introduction of synthetic

Table 1. *Characteristics of incisional hernias*

Characteristics	Number (%)
Supraumbilical	48(77.41%)
Umbilical	12(19.35%)
Infraumbilical	2(3.22%)
Recurrent	24(38.7%)
Incarcerated	14(22.58%)

Table 2. *Complications*

Complication	No/rates
Haematoma	2(3.22%)
Infection	3(4.83%)
Seroma	5(8.06%)
Postoperative small bowel slowdown	7(11.29%)
Chronic abdominal pain	5(8.06%)
Recurrence *	5(8.06%)

*recurrence rate after 24 months of follow up

Table 3. *Risk factors associated with recurrence*

Factors	No/rates
Diabetes	8(12.9%)
Chronic pulmonary obstructive disease	17(27.41%)
Benign prostate hyperplasia	14(22.58%)
Obesity	37(57.67%)
Cirrhosis	2(3.22%)
Smoking	39(62.9%)
Chronic steroid use	3(4.83%)

materials in surgery by Usher, our understanding of mesh biology developed continuously.

In general, the ideal mesh is characterized by low cost, functionality, improved intraoperative handling, sterility or even anti-infectivity characters and optimized biocompatibility. In addition, the relevant parameters of evaluation are the amount of material, tensile strength, flexural strength and elasticity. Especially for laparoscopic repair, pore size plays a key role. During our study the types of mesh available to us were: polytetrafluoroethylene (PTFE: Gore-Tex), polyethylene (Mersilene, Parietex), polypropylene (Marlex, Prolene, Atrium, SurgiPro), light weight polypropylene and polyglactin mesh (Vypro I / II), polypropylene and polyglecaprone (UltraPro).

Polytetrafluoroethylene mesh (used in 18 cases) is characterized by very small pore size (1-6 microns) and therefore acts as a foil without colonization of tissues. Although ensuring sufficient mechanical stability, to date, there is little information about long-term degradation. Due to low adhesion, it is probably the first choice for intraperitoneal placement of the prosthesis (laparoscopic repair). However, due to the small size of the pores, bacterial colonization rate may be high, leading to higher infection rates compared with other materials (4,5). Therefore, removal of prosthesis in cases with infection is sometimes necessary. Another disadvantage of this mesh is the high cost.

Polyethylene meshes (used in 3 cases) have good mechanical stability and produce only limited adhesions. With multicore design, and light weight these type of mesh have reasonable flexibility. Degradation, leading to reduced mechanical stability after 10 years, seems to be a problem with polyethylene meshes. Moreover, hydrolytic decay was found to be responsible for catalyzing persistent infections. Finally, it was also reported that patients with polyethylene mesh implants have a higher incidence of complications, delay in wound healing. Seroma are common and relapse rates are higher compared to polypropylene mesh (6). To summarize, due to loss of stability and reported related complications polyethylene mesh does not seem to be fully suitable for permanent strengthening of the abdominal wall.

Polypropylene mesh (38 cases) has a reasonable good mechanical stability and elasticity. So far, long-term degradation has not been reported. Polypropylene meshes are less prone to infection and can even be left in place in case of infection (7,8). After a pronounced inflammatory reaction at first, in most cases there is a relatively long reaction time and "weak" chronic foreign body reaction. Postoperative seroma occurs in 14.5-45% of cases, which is why drainage is recommended (*Fig. 1 A,B,C*).

In order to avoid the drawbacks of large amounts of material, such as foreign body strong reaction, a reduced polypropylene mesh material was proposed. Investigations on the tensile strength of the abdominal wall led to the conclusion that common polypropylene meshes are oversized, leading to the development of low-weight mesh (used in our study in 3 cases). Thus, polyglactin filaments were added to increase resistance to bending and to improve intraoperative handling. Due to the large size of the pores, it maintains a high level of flexibility, even when integrated into scar tissue. In addition, as shown by Klinge et al, tissue response is characterized by a significant reduction of inflammation and fibrosis, leading to a physiological integration, and to the formation of scar mesh instead of a rigid plate. Consequently, postoperative

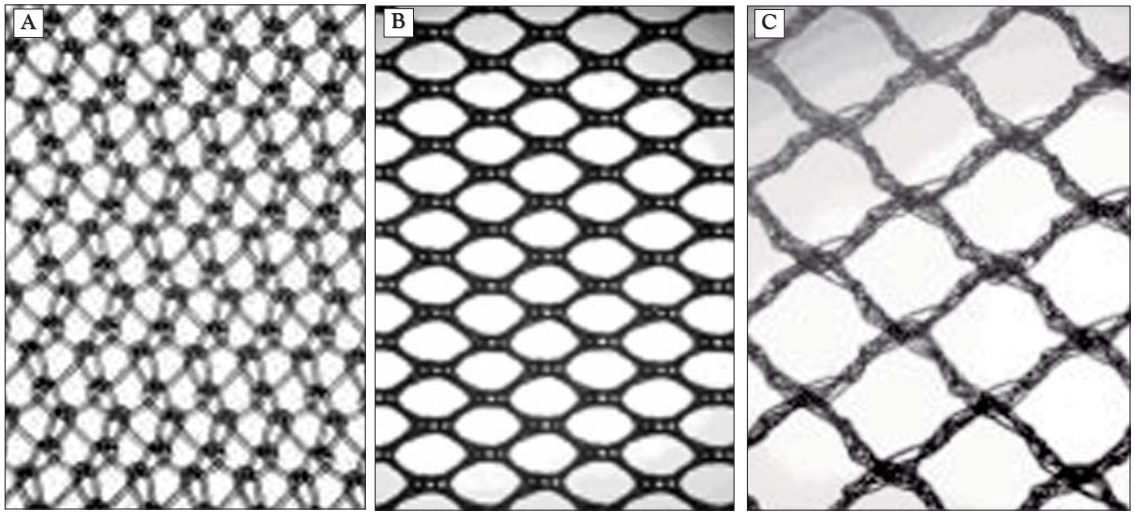

Figure 1. *Used mesh materials from left to right: polypropylene mesh, polyester mesh (Mersilene), material-reduced composite mesh made of polypropylene and absorbable polyglecaprone. Magnification 12.5x*

pain was significantly reduced in these patients. Polyglactin disappears completely after 3 months of implantation, leaving in place slightly corrugated polypropylene filaments. However, despite the clinical benefits, there is still controversy about the use of this type of mesh due to a possible enhancement of infection by the braided interstice structure.

Discussion

Infection, once triggered, profoundly changes the entire healing process, the end result being lack of scarring or an unsightly scar formation, often unaesthetic and almost always with inadequate physical qualities (low resistance), obtained by secondary healing. Such scars represent with predilection the site of future incisional hernias. Virulent germs reduce to annihilation the phagocytic ability of leukocytes and macrophages and divert them from reclaiming their role in the inflammatory focus, an indispensable condition for the appearance of granulation tissue and synthesis of normal collagen in terms of quantity and quality, especially over the first period (7-14 days). Even if subsequently collagen is normalized (or is in excess), fibre quality remains inferior and with inadequate orientation, as happens especially after prolonged suppurations or in the presence of chronic infection around the inadequate sutures (9).

The type of suture material used has a very important role, which by its qualities may favour or not per primam healing. In wound healing, reparative regeneration and organization – repair are based on mechanisms of histogenesis. Regeneration represents the replacement of destroyed tissue through proliferation of neighbouring cells, which have structural and functional qualities similar to those of altered cells. It is, therefore, a recovery in identical tissue as the one found in the epidermis.

Organization and repair require replacement of tissue by conjunctive tissue, resulting in a scar, which is interposed between the edges of the wound, between other structures, starting from dermis. This scar tissue has a unique morphology and biology in relation to the tissue interposed and to the ones it connects to. Scars formed due to granulation tissue and to the collagen synthesized by fibroblasts of the tissue the affected structures, but fail to regain normal morphology. Collagen ensures their continuity, strength and other mechanical properties, allowing their functionality to be as close to normal as possible. For this reason, repair of mesenchymal structures by collagen synthesis is "the keystone" of scarring, this protein retaining the phylogenetic role of "linking cells" (10,11).

In relation to the dynamics of these processes and their importance at a certain time in the evolution of the lesion, three phases of healing are described, called differently depending on the criteria considered [biochemical, pathological and clinical (12,13)]: immediate phase (catabolic, inflammatory, latency) second phase (proliferation and histogenesis, fibroplasia, granulation or collagenesis) and third stage (maturation of scar tissue and then remodelling), all being partially overlapping phases.

The 3 phases are obviously interrelated and present interrelationships leading to a normal healing. The dominant characteristic of a phase precedes and prepares the next phase events.

Per primam surgical wound healing can often be deviated from its normal evolution under the influence of many factors. The interfering mechanisms involved in healing cause changes in the development stages of this process and, frequently, switching to a secondary repair. In both cases, the scar is disturbed, especially registering deficiency disorders and, less often, excess (hypertrophic scars, keloid). Depending on their method of action, these factors are classified into general and local. General factors, dependent on the biological status of patient, indirectly influence, from a distance, through unfavourable conditions, the healing process. General factors and iatrogenic ones, predispose to and often play an aggravating role. Our results showed that the general factors frequently influencing surgical wound healing frequently, especially laparatomies, and which can often be corrected or prevented are: hypoproteinaemia, diabetes, severe anaemia and iatrogenic factors.

Local factors act on the wound itself directly disturbing the intimate mechanisms of healing. Today, it is hard to say which is the real importance of the 2 categories of factors: some give priority to general causes, while others insist on local ones. A related issue is still uncertain regarding timing and the way in which each factor considered separately disrupts healing.

Although a few experimental studies made it possible to determine certain specific actions of some of these factors, most of them have complex effects, interfering with several mechanisms and phases, both directly and potential. An additional difficulty in assessing the role played by one or more of these factors is the fact that they are often associated and therefore, enhance each other's effects.

For most researchers and clinicians, local factors hold the primary role in wound healing disturbance and, therefore, they are called determinants.

Severe hypoproteinaemia significantly increases inflammatory oedema in focal lesions by decreasing plasma colloid-osmotic pressure, delaying granulation tissue formation and causing deficits in collagen synthesis. Diabetes, a widespread disease, delayed healing only in unbalanced cases (14). Action in this case is indirect, favouring infection and reducing local irrigation due to angiopathy, which leads to poor oxygenation affecting all phases of healing. Severe anaemia accompanying hypovolaemia decreases the amount of O_2 needed to repair and creates ideal conditions for the development of anaerobic germs. Moderate anaemia without hypovolaemia is compatible with normal healing. Corticosteroids can delay and even block scarring through multiple actions, which interest the whole process. The main action of corticosteroids is anti-inflammatory (as they are usually indicated), but due to their effect on catabolism and on protein anabolism, they suppress proliferation and epithelial angiofibroblastic processes that require high mitotic activity. Corticosteroids intervene directly on collagen synthesis and promote infection by inhibiting the inflammatory reaction. As a result of these actions, in the case of primary sutured incisions, scarring is delayed, with poor resistance to "breakout force", which explains the frequency of incisional hernias. Fear of nefarious action of corticosteroids is more

justified, as doses are higher and when their administration is made preoperatively, intraoperatively and during the first 3-4 days after surgery (in full inflammatory phase) (15). Cortisone therapy is often required in emergency surgery, when collapsed hemodynamics are involved. Their negative effects can be encountered both after parenteral administration and after topical application, in which case, corticosteroids can be used (but with caution) for prevention of hypertrophic and keloid scars. Prevention and control of the shortcomings of corticosteroids are possible through concomitant administration of vitamin A, which is a major antagonist of the adverse inflammatory reaction, proliferation and collagen synthesis, but not of the retractile influence.

Any surgical wound has a high microbial pollution, but infections occur in the presence of predisposing factors that increase germ virulence or decrease the body's defence.

Basically, in terms of microbial factor, the contamination degree has predictive importance for the risk of infection, predicted more than 100 years ago by Volkman ("it is not the penetration of germs that is important, but their number") (cited by 8). Experimentally it was found that a low contamination degree, less than 105 bacteria / gram of tissue, is compatible with primary healing, unless local and general aggravating factors are involved, while overcoming the quantitative limits causes a high frequency of infections, proportional to the number of germs, reaching up to 40-100% of cases.

The importance of general factors is proved by the fact that germ pollution under 105 / gram of tissue is not followed by infection, as a result of the effectiveness of natural mechanisms of defence. All causes that suppress these mechanisms contribute to the development of infection, even if the contamination is well below the mentioned limit.

In line with the widespread use of surgical mesh, most studies have reported excellent results, with recurrence rates of less than 10%. Examination of the literature shows that the results were independent of the mesh and the surgical technique. In addition, in 2003, in one retrospective study, Flum et al analyzed data from 10,822 patients operated on for incisional hernias by simple suture or by alloplastic procedures (16). 5 years postoperatively, 14% of patients experienced at least one relapse, compared with 11% after mesh repair. Lowest rates described by Flum et al could be due to the fact that many patients who have suffered a relapse did not have surgical reintervention.

However, the most striking fact is that all studies have found an unexpectedly growing incidence of relapses over the years, not only in the suture group, but in the mesh group as well (17,18). The recurrence rate shows a nearly linear curve. Comparing to simple suture, procedures with mesh implants seem only to delay recurrence for 2 or 4 years, respectively in some patients with multiple relapses.

These data show that the development of incisional hernia recurrence is not primarily a technical problem (19). As a consequence, the only plausible explanation is that the phenomenon is biological. It seems that retromuscular preaponevrotic placement of the mesh is the optimal position, due to collagen thickness and fibre number (*Fig. 2, 3*).

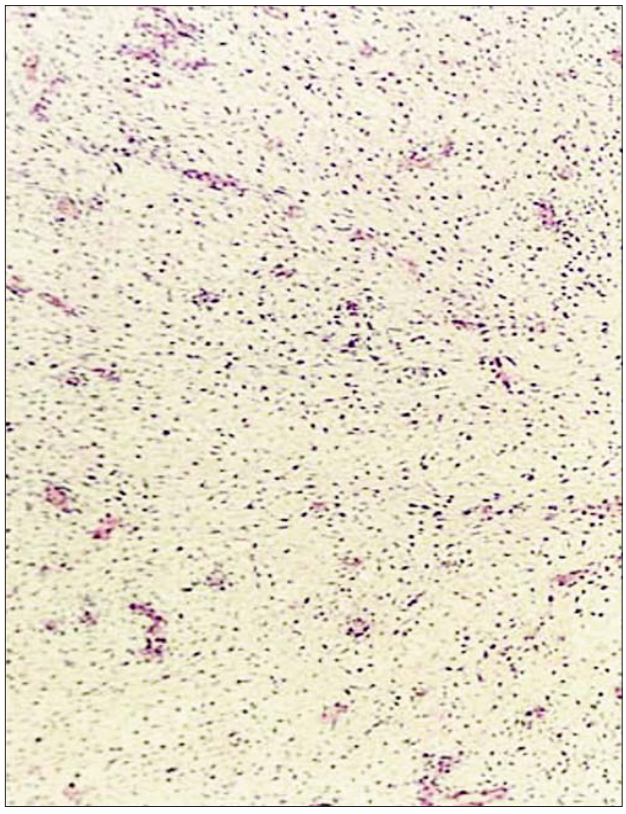

Figure 2. *Premuscular inlay mesh: fibroblasts, myofibroblasts*

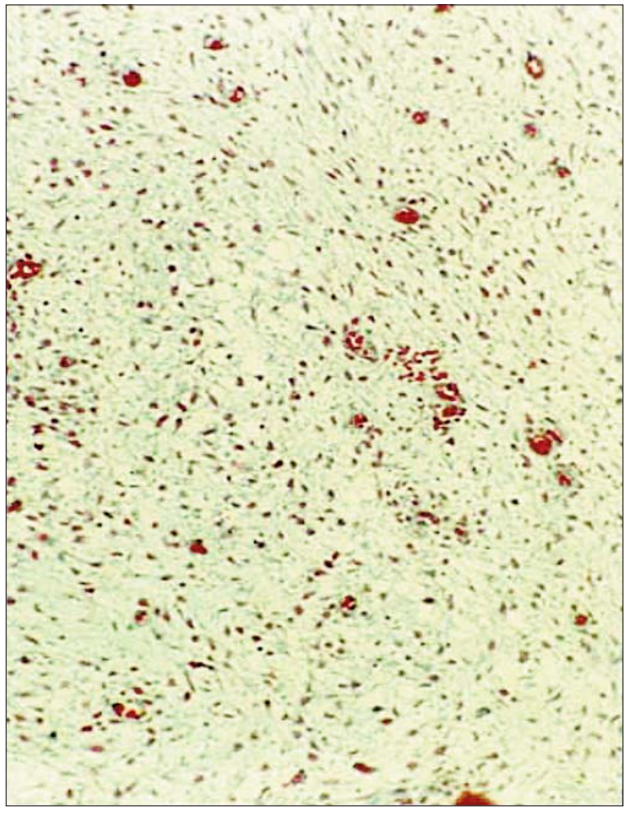

Figure 3. *Sublay, retromuscular mesh: thicker collagen fibres*

Recently, molecular biological investigations have proven the theory of vicious composition of the extracellular matrix in patients with hernia recurrence. In essence, there is a lower ratio between type I collagen and type III collagen. Type III collagen is an immature one, unstable, that has low elastic properties, and will be gradually replaced by type I collagen. In addition, fibroblasts were found to bear primary fault, independent of environment local conditions. Although scar formation is influenced by the amount of material, its quality is not improved. Accordingly, net fixation may prevent relapse in some cases. Although such data are not yet confirmed we can hypothesize that the prosthesis overlap width correlates with the delay in the occurrence of relapse. However, clinical experience with all techniques developed in recent years has consistently shown a tendency to use larger prostheses.

Conclusions

Use of prostheses has become essential for incisional hernia repair because recurrence rates are consistently lower when used. An ideal prosthesis should be strong, flexible, non-allergenic, inert, non-biodegradable, non-carcinogenic and should adequately stimulate fibroblast activity for optimal incorporation into tissues.

Prostheses used to repair incisional hernias can be non-absorbable composites (combinations of absorbable and non-absorbable fibres) or with a non-absorbable barrier. Surgeons should acquire sufficient knowledge regarding different types of prostheses for proper selection in any given case. Selecting the optimal size and its correct setting is obviously required. Complications can be avoided or reduced by an appropriate selection of the type of place in a particular case and by performing a meticulous technique.

Finally, the risk of relapse, despite treatment should be properly assumed by patients with incisional hernia. Therefore, this principle must be carefully analyzed in terms of technique and performance. Incisional hernias are at this moment considered a biological progressive phenomenon, not only a strictly technical one, a “simple hole of abdominal wall” that has to be firmly sutured.

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