Molecular Biology

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"Shape is the plastic image of function." Angelo Ruffini (1864-1929)

Keypoints Summary

- Collagen deficit: common findings between AAA and abdominal wall hernias
- Some evidence of metabolic etiopathogeny
- Mesh use strong recommendation or even imposition
- Complex hernia repair laparoscopic problems
- Robotic surgery solution portfolio

Introduction

For exactly three and a half decades, the association between smoking, abdominal aortic aneurysms (AAA), and inguinal hernias has attracted the attention of the international medical community. Under "Metastatic Emphysema" concept a new paradigm was broken revealing a systemic mechanism behind respiratory changes and the abdominal wall: blood flow proteases (elastases) arising from the current smoker's lungs [1]. In the early 1920s and based only on clinical observations, Keith and Harrison, independently, already foreshadowed this possibility, when they questioned dysmorphism as a single causative agent of inguinal hernias.

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R.Z. Abdalla, T.N. Costa (eds.), *Robotic Surgery for Abdominal Wall Hernia Repair*, DOI 10.1007/978-3-319-55527-0_12

Since then, several authors confirmed these and other connective tissue modifications in patients with hernia, inguinal or not [2]. It would then be seen as a systemic disease with localized manifestation (lower resistance sites), not mere isolated anatomical defects. The etiopathogenic substrate dipped in biochemical level, over the imbalance ratio of collagen type 1 (tougher) and type 3 (less resistant), at these patients' aponeuroses, making them weak and vulnerable to herniation of abdominal/peritoneal contents [3]. The fibroblast, directly responsible for the maintenance and renewal of connective tissue, also became the protagonist of these disorders [4].

Pros and Cons

Regarding the common etiophatogeny of both AAA as the abdominal wall defects, especially of incisional hernias (IH), there is strong evidence that both disease are related to changes of connective tissue, at the level of extracellular matrix, and its fibers (collagen and elastic) [5]. Patients undergoing reconstruction for AAA are three times as likely to develop IH, compared to patients with arterial occlusive disease, for example [6]. The basic metabolic shift in these conditions favors fibrillar rarefaction, because at the same time synthesis is inhibited, degradation is stimulated through overexpression of matrix metalloproteinases (MMPs), on one side, and a suppressing of their inhibitors (TIMP), on the other. Families with hernia patients are more likely to develop the disease, because the synthesis of those and any other protein express individual genetic patrimony.

This fact becomes quite evident in the Ehlers–Danlos and Marfan syndromes, for example. However, these collagenoses do not always have an evident clinical picture and the phenotype does not reflect the existence of the disease. Some patients are not diagnosed as having the syndrome, which will be perceived only on one or more episodes of hernia recurrence.

Some questions inevitably arise:

- Who and how many are they in general population?
- How can they be recognized on purely clinical grounds?
- What additional tests should be required to confirm the disease?
- Perhaps biopsy with histopathologic screening? From what part: of the skin, tendons, or aponeuroses?
- In these cases, do cutaneous superficial fibroblasts express the same collagen content and at the same proportions as the deep (aponeurotic) fibroblasts?
- If this is so, how do we explain the existence of hypertrophic or keloid scarring in the skin of patients who have concomitant underlying incisional hernia? One hypothesis refers to "metabolic paradox" of fibroblasts, wherein the same cell types have distinct gene expression on the same individual (Fig. 1).
- Should some form of adjuvant therapy or gene replacement be considered therefore?

Even if it becomes feasible, a possible side effect might result in undesirable adhesion formation, in the same local or distant to the site of hernia. If that occurs,

Fig. 1 Hypertrophic scarring/keloid in patients with underlying incisional hernia

it could lead to organ incarceration by serous thickening (pleura, pericardium, peritoneum), visceral obstruction, or hollow structures (intestines, vas deferens, fallopian tube, duodenal papilla, cardiac valves) caused by the induction of a "hyper scarring" systemic state.

Undeniably, many of these issues still need consistent response in the literature, but the biggest challenge, and certainly the only alternative is to try to recognize vulnerable groups or those at increased risk for hernia recurrence who are not typically syndromic. Until they could be identified, routinely, with noninvasive and inexpensive tests, the surgeon should guide any decision on the clinical suspicion at epidemiological basis. In other words, he or she has to recognize and validate elements for tracking patients with subclinical or asymptomatic collagenosis.

The inflammatory reaction is exacerbated and chronically installed on these sites, as an additional hazard of metabolic deficiency, further distorting the tissue architecture even more, by the phagocytic activity (proteolytic) and the fibrosis that develops.

Mesh: The Necessary Evil

The use of prophylactic mesh is proposed to reinforce laparotomy wound closure, in susceptible IH patients, even in vascular and bariatric surgery or other abdominal procedures [7]. This strategy has its value but its effect is purely topical or local [8]. The results show the greater protection afforded to the scar, substantially reducing the incidence of IH, with no increase of local events, although some papers in the literature are controversial as to the number of cases of seroma and chronic pain associated with mesh use [9–12].

In spite of these advantages, there is always the possibility that these patients can develop fistulas and/or chronic surgical site infection and that the presence of a mesh, already incorporated in the wall tissues may create an obstacle to future laparotomies, as happens for trauma or cancer.

Unfortunately, we don't know the intimate mechanism by which the hernia is triggered, in a given location, from one or more metabolic alterations, on a systemic level, nor which of these events start and/or perpetuate other ones [6]. It must be considered, though, that hernia etiology is a multifactorial affection, where different causes are involved, metabolic factors (genetic), environmental/behavioral (smoking, obesity), anatomical (dysmorphism), and also of technical/iatrogenic origin (inadequate closure of abdominal wounds, surgical site infection). The contribution of these factors to a greater or lesser extent could explain the occurrence of these defects, which sometimes assume catastrophic proportions.

A New Look at the Abdominal Wall

It seems inevitable to consider the abdominal wall as a multisystem organ. Its contractile prerogative, thanks to the striated musculoaponeurotic contour, interspersed with periods of relaxation, promote changes in intra-abdominal pressure (IAP). This alternating pressure modifies both the form and content of viscera and peritoneal cavity structures, optimizing the performance of each organ that is located there, as well as the whole abdomen. Digestive, urogenital, cardiovascular, and respiratory systems gain efficiency, wherein the abdominal wall has a supporting role, but also the stability, splanchnic protection, and trunk movements, specific attributes of its locomotor interface. The latter, associated with cutaneous vitality, establishes and maintains body contouring, whose aesthetic consequences cannot be underestimated. Therefore, as in any organ, it is essential that the integrity of its neurovascular contingent is preserved, to perform all these functions completely.

Restoring or Rehabilitating

The surgeon will be required, depending on destruction degree and structural wall remaining, to not only do the simplest repair, but a complete restoration of the entire abdominal continent, in view of the complexity achieved by hernia disease. In this sense, all valuable reachable measures with the objective of re-establishing contents and continent must be done as a way to recover anatomical and physiological balance of the abdominal wall. Recovering its structure, partially or completely, is the only way to regain functional capacity to the wall.

Regardless of the success in getting the coveted parietal "dynamic support," the availability of prostheses of all kinds and sizes, is essential to meet the needs of each case. However, it is imperative that the surgeon always adhere to the "restorative principle," because any prostheses used for the repair of the abdominal wall seek only to restore the lack of continuity, offering a holding and fibrosis-inducing barrier, not new muscle fibers. There is no cell regeneration in these tissues, just scar. Even without this scaffold, the homeostatic forces of the body will try to do this (fibrosis) to fill the defect. The hernia sac, with its dense and mesothelial connective structure, is proof of this great effort, even though insufficient. Neither the mesh nor

the hernia sac provides active support to the wall. Only the musculoaponeurotic component well vascularized and innervated is capable of doing that.

Therefore, the most effective way to correct these lesions is to restore the continuity of this contractile belt surgically, often by combining techniques and prostheses [13]. On the degree of complexity achieved by hernia disease, in some circumstances, it must also subtract the herniated content (visceral and omentum resections). Working from the surface to the depth, the idea is to reconstitute all affected layers, considering relaxing incisions (discharge) and muscle advancing techniques. Even if it is possible to cover the parietal defect completely, reinforcement of the wall with the use of prostheses could be chosen, in a superficial position (onlay) or preferably deep (sublay or underlay) to decrease the chance of hernia recurrence [14].

Moreover, it is also important that the surgeon promote an acceptable cosmetic result, removing unsightly scars and associating dermolipectomy in patients with "fat apron abdomen". This procedure is, moreover, strategic and aims to create a suitable route of access to the musculoaponeurotic layer, so the anatomy can be contemplated in its full magnitude where the defect is even without primary aesthetic purpose. Similarly, resection of such large excesses of skin and subcutaneous fat will reduce the effect of the traction exerted on the suture lines and the mesh, when placed in a preaponeurotic position (onlay). In this regard, the collaboration of a plastic surgeon is extremely useful because the tactics and aesthetic prerogatives may be associated in the same surgical procedure and are shared by all.

From Laparoscopic Platform to Robotic Jump

When all the goals of treatment seem to be well defined and achievable by conventional or open surgery, the videolaparoscopic approach became available just to cover or line up those parietal defects. Applying extensive prostheses in the intraperitoneal position, without promoting any kind of muscular approximation was shown to be possible and feasible to repair both IH and primary ventral hernias. But what *should be* done must be always balanced with what *can be* done to achieve a goal.

Patients with midline incisional hernia treated with reconstruction of the linea alba have a isokinetic contraction strength of trunk muscles greater than patients who have undergone only mesh defect covering. Moreover, the presence of any intraperitoneal foreign body, the adhesions that promote on the wall (incorporation) and also in the abdominal contents can create difficulties for *de novo* interventions that could be time consuming to access the cavity and/or also present a higher risk of accidental lesions or inadvertent visceral injury.

The technical difficulty imposed by wider rings (>10 cm), where there is no room to overlay adjacent tissues beyond the defect borders in sufficient extension to support and fix the mesh, surely helped discourage most surgeons in laparoscopic repair of large abdominal wall hernias.

However, to be able to perform the full range of necessary procedures to make a complete abdominal wall repair (anatomical and physiological), using mini-invasive surgery, has become the major challenge for laparoscopic surgeons. They saw themselves limited, not for personal reasons such as a lack of ability or nonacceptance of the method, even with the equipment and materials (videocameras, monitors, blowers, special energy sources and forceps, coated fabrics, staplers etc.), but because of the imperfect ergonomics and restricted hand movement provided by laparoscopic surgical instruments. This forced the surgeons to expend much effort in intracavitary maneuvers and even more in the parietal layers because they were forced to work with rigid and straight tools in the same axis they use to approach the cavity. The only aim they had was to modify the operative table degree and switch a variety of instruments between trocars, several times in each procedure, taking as much advantage as possible of the natural abdominal shape. Laparoscopy favored a complete and global understanding, as a diagnostic tool, of the parietal defects, especially in hernia with multiple rings, but it was frustrating from the therapeutic point of view, because of method limits.

The statement "treat illness being minimally aggressive to the patient" has always been a doctor's corollary, moreover. The advance represented by minimally invasive videosurgery to solve cavity problems preserving abdominal wall healthy, abbreviating convalescence, was notorious for the surgeon and patient. Adapting it also to approach and repair defects of abdominal continent was missing.

Robotic surgery filled this gap, making feasible the complete treatment of the most severe and extensive parietal injuries through a minimally invasive approach, inherited from laparoscopic surgery. It represents a whole set of possibilities, mediated by the surgeon, enabling similar maneuvers in performance even more precise than human hands inside the abdominal cavity (because of greater range and degree of freedom in robotic arm articulation) in a safer, ergonomic, and comfortable way. Those procedures are made in both continent (wall) or contents (viscera) of the abdomen. In addition, it rescued the experience of the three-dimensional view.

Laparoscopic surgery is considered a great step forward when compared to the conventional approach (open), but the distance represented by robotics, regarding laparoscopy, is exponentially larger. This progress has been so extensive that the robotic arms allow the surgeon to do even better, almost everything one could do with bare hands, but without extra-damage, thanks to the minimally invasive approach. When these two modalities are close in fact, they summarize their advantages and subtract their disadvantages from each other at the same time.

Neither robotic nor laparoscopic surgery corrects skin lesions and subcutaneous tissue, unfortunately (unsightly scars, ulcers, entero-atmospheric fistulas, fat apron abdomen), a common finding in most patients with complex hernias. This is for obvious reasons and even in the conventional open approach they are not routinely treated at the same surgical time. Its correction will continue to be performed in the classic open way, either by general surgeons or, preferably, by a plastic surgeon.

Concluding Remarks

- Several authors confirmed connective tissue modifications in patients with hernia.
- Although it can cause various complications, mesh is an advisable tool in some or many hernia repairs.
- The abdominal wall is a multisystem organ.
- The surgeon has to restore the abdominal wall, often by combining techniques and prostheses.
- Robotic surgery can make feasible the complete treatment of the most severe and extensive parietal injuries through a minimally invasive approach.

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