POSTOPERATIVE COMPLICATIONS ASSOCIATED WITH BIOMATERIALS USED IN HERNIOPLASTY

A. Mihăilescu¹, D. Mihăilescu², M.R. Diaconescu

“Gr.T. Popa” University of Medicine and Pharmacy, Iaşi
1) First Surgical Clinic, “St. Spiridon” Hospital, Iaşi
2) Clinic of Orthopedic Surgery, Rehabilitation Clinical Hospital, Iaşi

POSTOPERATIVE COMPLICATIONS ASSOCIATED WITH BIOMATERIALS USED IN HERNIOPLASTY (Abstract): Meshes of synthetic material are now being widely used to repair hernias (hernioplasty) but biomaterial-associated infections constitute a major clinical problem. The success of surgical repair of abdominal wall defects depends on the physico-chemical properties of biomaterials, their biocompatibility and design, preoperative handling and conditioning of implant, surgical technique and not least, the health status of the patient. The most common complications due to building materials are postoperative infection, seroma collection, bowel obstruction and enterocutaneous fistulas. The risk of such complications is minimized by using composite macro porous meshes (dual layer meshes, pore size < 1 mm) whose dimensions ensure adequate laxity without formation of folds.

KEY WORDS: BIOMATERIAL CHARACTERISTICS; MESH POROSITY; TISSUE INTEGRATION; POSTOPERATIVE COMPLICATIONS

SHORT TITLE: Biomaterials in hernioplasty


BACKGROUND

Ch.A.Th. Billroth, the famous surgeon whose name is linked to the first gastric resections with gastroduodenal/jejunal anastomosis, ever since the late 19th century intuited that by making and using an “artificial tissue with the density and resistance comparable to those of the muscle fascia, the secret of the radical healing of the hernia disease would have been discovered” [1].

The materialization of this desiderate started by introducing, in 1959, the first polymer nets, the polyethylene ones. After this year, the range of the biomaterials used to develop hernia meshes underwent important changes. In an attempt to find the best materials, new polymer fibers were used, the least suitable ones were given up at, multilayer composite materials start being used and devices with special shapes and sizes were designed. With special design and simple actions (sutures) or with the most complex shapes and characteristics (gastric banding, transtumoral stents, meshes and devices for parietal consolidation), the products made of biomaterials are used in surgical therapy for a high number of diseases: incisional hernias, hernias, neoplasm in advanced stages, morbid obesity [2-6].

GENERAL ASPECTS OF THE BIOMATERIAL/TISSUE INTERACTIONS

The success of the surgical healing of the defective abdominal wall depends on the physico-chemical properties of biomaterials,
and their biocompatibility and design, on the handling and conditioning of the implant in the pre-surgical phase, on the surgical technique itself, and last but not least, on the patient’s health condition. To all this we should add the capacity of the biomaterial to inhibit the development of adherences on the adjacent side of the abdominal organs and to answer in vivo similarly to the autologus tissues. These last features allow good tissue incorporation and fixation and a strong repair without the scar reaction and without the encapsulation problems noticed at the current prosthesis [7-12].

The response of the organism, due to the biomaterial / tissue interaction, is based on a series of complex processes and it is influenced by a range of factors. The area that best expresses the tolerance of the biomaterial is the tissue / implant interface. Figure 1 shows a diagram of the main phenomena that constitutes the body response to the presence of a biomaterial.

**Fig. 1** Scheme of the main phenomena of the biological response to biomaterial implants

An analysis of the organism / biomaterial relationship has in view that the latter one has to answer a great number of specific uses. Moreover, it has to take into consideration the fact that the live organism represents a complex in which proteins, enzymes, polysaccharides or other types of biopolymers are represented by “different individuals”. That is why the biomaterial must have the suitable features so that it does not disturb the natural features of the local or general biochemical processes.

For the solving of this desiderate, a tight collaboration is necessary between chemists, biochemists, doctors, biologists and pharmacists. They should work together to develop biomaterials compatible with live tissues, as well as to discover the mechanisms of the biocompatibility and biodegradability and to elaborate some efficient methods for the shaping of the implant/tissue systems, with the purpose of reproducing the balance and the native morphological and functional performance. Anyway, all complications caused by the consolidation material can be prevented if their causes are known. Therefore, the prevention of postoperative complications caused by the insertion of a biomaterial implies the thorough knowledge of the physical properties of the implanted biomaterial, among which the surface characteristics (dimensions and distributions of pores, watering capacity, permeability to fluids) are the most important.

**MATERIAL CHARACTERISTICS THAT FAVORISE POSTOPERATIVE COMPLICATIONS**

The success or the failure of a hernioplasty depends, to a certain important extent, on the material characteristics of the used implant. If, by their chemical nature, all synthetic polymers are perfectly biocompatible materials, the differences between their physical and morphological properties could explain some of the complications associated to the prosthetic materials.

Statistics show that, in the United States, among all the implanted devices, 1-6% are infected pre- or post-surgery, and it is considered that most of the infections are nosocomial (40%). It is also considered that the possibility of infection is higher in the open techniques (7-18%) compared to the laparoscopic ones (0-2%) [13-15].

For the design of an advanced material it is also necessary the exact understanding
of the phenomena taking place at the tissue-implant contact. Thus, from the first post-implant moments, between the cells of the host tissue and bacteria there is a “competition for the conquest” of the prosthesis surface. If this race is won by the host cells, then they will attach or they will integrate into the surface of the implant, protecting it. The fixing capacity of the bacteria is influenced by the reactive surface of the implant, a characteristic which is determined not only by the size of the pores or of the mesh eyelets, but also by their shape and distribution.

Data on the reaction of a foreign body induced by the “parietal consolidation materials” show that the response of the organism appears on the surface of the yarns that the mesh is made of. A comparative analysis of the reaction caused by polypropylene meshes, with different surface characteristics (size, shape and distribution of pores) shows that the more reduced the reaction of a foreign body is, the smaller the reactive mesh surface. Thus, the DynaMesh will be better tolerated than the materials with a reduced porosity that are characterized by higher values of the total surface of the yarns (Fig. 2). It is seen that meshes with reduced FS value minimize the reaction of a foreign body, favors the formation of the scar tissues and gives a higher comfort to the patient [16].

The classification of the prosthetics materials according to the size of the pores, made by Armid in 1997, allowed the identification of 4 wide ranges of meshes used presently in the surgical treatment of hernias:

- Type 1 – completely macroporous prosthetics (Atrium C-QUR® and Trelex®); the diameter of the pores is higher than 75μ, a dimension that allows the entry at the level of the prosthetic pores of the macrophages, fibroblasts, collagen fibres and neoangiogenesis vessels;
- Type 2 – completely microporous prosthetics: (ePTFE, Gore-Tex®); they contain pores with less than 10μ diameter in at least one of the 3 dimensions;
- Type 3 – macroporous prosthetics with multi-filaments or macroporous elements like the PTFE (Teflon) mesh, Dacron® and Mersilene® woven mesh, the mesh from woven polypropylene filaments (SurgiproTM) or the preshaped patches made of PTFE (Mycro-Mesh®);
- Type 4 – biomaterials with sub-micronic size pores, such as: Cellgard® polypropylene meshes and Preclude® pericardial membrane. These types of prosthetics are not suitable for the repair of the hernia defects, but combined with type 1 biomaterials they form composite materials whose main characteristic are to decrease the risk of viscero-prosthetic adherences [17,18].

The size of the pores influences the mechanisms for the integration of the implant. It has been seen that, for the polypropylene prosthetics whose eyelets have at least 1 mm, the monofilaments of the mesh are surrounded by granules of foreign bodies, generating thus a normal granulation tissue.

If the distance between monofilaments is less than 1 mm, the incorporation of the mesh in the neo-formation tissue is followed by its confluence and by the formation of scar tissues that considerably reduce the patient’s comfort [16].
The use of materials with suitable mechanical characteristics reduces the probability of complications due to mesh deterioration or tearing. The prosthesis should resist to pressures of at least 16 N/cm² and, after implanting, it should keep unaltered its mechanical properties for long periods. Data about the use of polypropylene meshes with mechanical properties (Marlex®, Prolene® and Atrium) showed that if tearing occurs, it usually occurred at the muscle fascia – prosthetics junction [18]. The tearing of the mesh on its margin is the result of the decreased resistance of the structure compared to that of the mesh. The rate of the complications generated by these processes can be diminished by using suture materials similar to the material of which the mesh is made of.

A feature that can influence the success of a hernioplasty is the anisotropy of the prosthetics material.

The mechanical properties of the mesh (resistance to tearing, resistance to cutting, elongation), generated by the mono-axial tension on two perpendicular directions, showed that they can have different values on the two directions on which the tension is applied. This behaviour will reflect into a non-homogenous deformation of the implant, a change of the biomechanics of the abdominal wall and the rise of the risk of late post-surgery complications [19].

Notwithstanding many processes registered in the field of the biomaterials applied in the abdominal wall repairs, the number of post-surgery complications is rather high, many of these (~ 20% cases) being attributed to the characteristics of the material used for the implant.

POSTOPERATIVE COMPLICATIONS

The most frequent post-surgery complications that can be caused by the characteristics of the bio-materials are: infection, seroma, intervisceral adhesion (postsurgical adherential syndrome), intestinal obstruction, wearing of the prosthesis due to the erosion of the cavity viscera wall, failure of the repair caused by the contraction of the prosthesis [20].

1) Infection

The postsurgical infection, which can be linked to the implantation of biomaterials (e.g. stitches and/or meshes), is caused by bacteria infiltration and proliferation in eyelets, interstitial spaces and pores that characterize the implant.

Right after implantation, the surface of the prosthesis is “disputed” between the host cells in charge with the regeneration (neoformation) and the bacteria in the material. If the “competition” is gained by the bacteria, they will form on the implant a biofilm that will be removed/eradicated, most often, only by taking the prosthesis out [21].

The biofilm or the bacterial plaque, that most of the time has many species of bacteria included in a self-excreting viscous substance, adhere on the surface of the implant and assures the protection of bacteria for their proliferation. It is considered that the eradication of the infections, which involve microbial microfilms, needs therapies with high doses of antibiotics - up to 1000 higher compared to the planktonic etiology infections caused by planktonic bacteria [22-24].

The pathogenicity of the implant infections records:
- infiltration of bacteria at the moment of implanting or in the immediate postoperative period (patient’s skin flora, pre-existing infection in the proximity of the area of intervention, hospital environment, supporting therapy).
- adhesion and colonization of bacteria on the implant; they produce a self-protective biofilm and they escape the conventional therapy with antibiotics and the immune response of the patient [16].

The results of the investigations regarding the influence of the surface characteristics of hernia meshes on their bio-inertia in front of the microorganims’ attack
shows that the pathology of the implant infections is different according to the size of the implanted mesh eyelets.

Thus, in the case of the type 1 meshes (large eyelets - Ø > 75 µ) their macroporous structure allows the rapid admission of the macrophages that destroy the bacteria, and a quick process of fibroplasia and angiogenesis that, being fast, does not allow anymore the access of bacteria in interstitial spaces.

Sometimes the postoperative infection that appears after the use of type 1 meshes for the repair of hernia defects is caused by the use of the multifilament stitches for fixing the prosthesis. These post-procedural infections are wrongly attributed to type 1 meshes.

Type 2 and 3 prostheses are similar to the multifilament stitches and may generate post-operative infections due to their microporous structure.

The rate of post-procedural infections associated to the use of type 2 and 3 meshes is currently at a reasonable level (Smith 1971 reports the highest rate of 50% from all the interventions where the same type of meshes had been used, and DeBord and Wyffels report in 1999, only 6%) [cit 17]. As for the surgeries where type 1 meshes were used, the reported values for the post-operative infections are a lot smaller [17].

If we refer to (postsurgical) postoperative infections due to other causes, when this complication appears after a surgery where type 1 materials were used, the most important thing is that it is not necessary to remove the mesh. The exigent drainage of the infected area, accompanied by a strict monitoring of the wound was enough to heal the complication. Unlike the behavior of type 1 meshes, in the case of the same complication (post-operative infection) after procedures where type 2 and 3 meshes were used, it is necessary: (i) to completely remove the mesh (type 2 mesh), (ii) partial removal (type 3 mesh).

When the eyelets or the interstitial spaces of the material have sizes under 10 µ in each of the 3 structure sizes (Type 4 meshes), the bacteria of almost 1 µ cannot be destroyed by large macrophages or neutrophile granulocytes that cannot enter this undersized pores. As a result, the multifilament stitches and the prosthetic materials with eyelets, interstitial spaces and pores of under 10 µ are an excellent location for the bacterial proliferation and for the development of local infections. The complications are explained through the possibility of quartering the small bacteria and the impossibility of the macrophages to enter these interstitial spaces [17].

According to the post-operative period when the sepsis is developed, two types of infections may appear:

- early infections – they appear during the first 10 days from surgery;
- late infections – the complication appears several years after surgery.

Both types of infections, early and late, can be attributed to the formation of microbial biofilms. In the first case, the implant is colonized by bacteria and the treatment is not effective due to the biofilms’ resilience. On a long term, the bacteria may create a biofilm on the prosthesis material, remaining inactive during long periods (even years) until when a stimulus causes their reactivation [25,26].

The clinical impact of the implant infections is linked to the pain increase, a higher discomfort for the patient, a longer time for healing and recovery, a higher morbidity and mortality rate and a longer hospitalization at higher costs. Moreover, the implant infections can cause the failure of the hernia repair and they impose an additional surgery for the removal of the altered material [27].

The antimicrobial technology, applied for the realization of the DualMeshPlus meshes, materialised in a decrease of implant infections thanks to the inhibition of the bacterial colonization processes and to the fact that it prevents the formation of the initial biofilm, for at least 14 days from the implant.

The prevention capacity of the post-operative contamination was tested on that
particular area of the implant which benefited of microbial inhibition treatment. Biotests proved that the biomaterial can achieve a substantial high activity against both clinical and laboratory strains, isolated from the following gram-positive and gram-negative microorganisms: methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus faecalis* resistant to vancomicine (VRE), *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Staphylococcus epidermidis*, *Candida albicans*, and *Acinetobacter baumannii* [28].

The special behaviour of *DualMesh Plus* meshes is explained by the synergy of the two anti-microbial agents: silver carbonate and chlorhexidine. Silver’s capacity of linking and destroying proteins of the bacterial cells, causing the loss of their biological function, is combined with the activity of the chlorhexidine that penetrates and disaggregates the bacterial cell wall thus causing the elimination of the bacterial cell’s content [14].

The antimicrobial therapy of *DualMesh Plus* prostheses has an inhibitory effect for the early and late infections. DeBord JR et al. monitored the short-term evolution of 37 randomly selected patients and they observed that *Dual-Mesh Plus*® hernioplasties do not seem to produce any kind of systemic or clinical adverse reactions [cit 25]. The same authors show, based on a great number of cases (over 150,000 implants) monitored for a long period (almost 10 years) that the information regarding the hypersensitivity of the subjects of this study to the implanted materials was not confirmed [25].

Analyzing the data regarding the link between the characteristics of the material and the development of the implant related infections we reach to following statements: 1) macroporous materials (with pores bigger than 10 µ) lead to the decrease of the postoperative infections; 2) the use of meshes treated with antimicrobial products eliminate highly both the risk of early and late infections. [28,29].

2) Seroma

The formation of post-implant seroma in a prosthetic biomaterial has as etiology the inflammatory reaction of the host body (for the latest biomaterials this reaction is neglectable), and the presence of the “dead” spaces between the prosthesis and the surrounding tissue.

Admitting the importance of the “dead” spaces in the formation of seromas, K. Amid shows that, in the case of the macroporous prosthesis (type 1 and 3), the size of the pores of these materials allows a rapid accumulation and fixation of the proteins in the interstitial spaces [17]. Thus the “dead” spaces between the prosthesis and the host tissue are eliminated, and the risk for developing a post-implant seroma is minimal [17].

A high molecular permeability will cause a rapid and efficient incorporation of prosthetic material in the host tissue and thereby “filling” the pores which makes impossible the local quartering and the bacterial proliferation, thereby decreasing the risk of post-implant infection and the formation of seroma. The risk of postoperative seroma can be reduced to zero by placing the prosthesis in a subaponeurotic or retromuscular position thus avoiding the direct contact of the biomaterial with the subcutaneous adipose tissue. In addition, a useful way to avoid seromas is using postoperative drainage, especially useful in the case when the surgeon used a large prosthetic material.

Due to the inadequate size of the pores, the type 2 biomaterials/meshes lack the optimum permeability to accumulate in the interstices protein material and fibrin, which results in a slow and incomplete disappearance of the “dead” spaces between the prosthesis and the host tissue where seromas can form subsequently. When using type 2 meshes percentages between 9.6% (for hernia surgery) and 14.6% (for incisional hernia surgery) were reported in terms of post-procedural seroma formation.
When correctly using the type 1 or 3 meshes, such complications are not reported.

In most cases, seromas are solved within 30 days without the need for additional therapeutic gestures. Aspiration is indicated in cases where the collection persists for more than 6 weeks, volume of the seroma increases over time, clinical symptoms appear or it is suspected of being infected [20].

3) Adherential syndrome
The most important properties / characteristics of the ideal prostheses for hernia surgery are the macroporosity and the surface texture. These characteristics favor the infiltration of the prosthesis in the host tissue, a process which is vital for a lasting repair. On the other hand, an adverse side effect of macroporosity is an increased adhesion of the macroporous mesh to the intestinal serous membrane when the two surfaces come into direct contact. Currently, all existing prosthesis (absorbable or non-absorbable) determine viscero-prosthetic adhesions, this process being more important when non-absorbable meshes are used. For this reason, it is recommended that the prosthesis not be implanted in contact with hollow viscera [30].

A limitation of the formation of adhesions to the prosthesis is found with bioabsorbable and PTFE materials. However, neither the complete covering of the visceral surface of the mesh with a layer of absorbent material such as Vicryl®, nor the application of expanded PTFE patches, does not lead to a complete resolution of post-operative adherential syndrome. Recent experimental studies have shown that composite biomaterials made of types 1 and 4 meshes could prevent adhesions and they are useful in preventing other post-implant complications, secondary to adhesions, namely intestinal obstruction or the development of intestinal fistulas [17,30].

4) Intestinal erosion and fistulas
One of the complications attributed to the material characteristics of the prosthesis is the erosion of the adjacent tissues. Prosthetic macroporous materials can cause erosion of the tissue in direct contact with them and so it may begin the migration of the prosthetic material within the gastrointestinal tract when the mesh is in contact with the intestines. This complication is more common when the prosthesis is in contact with segments of the gastrointestinal tract unprotected by the peritoneal serous membrane: distal esophagus, rectum, bladder and any segment of the intestinal tract that does not have a serous membrane. However even the direct contact between the prosthesis and intestines that are covered by an intact serous membrane can lead to fistula formation.

Experimental and clinical observations up to date have shown that covering the mesh with a layer of bioabsorbable material which will come in contact with the intra-abdominal organs - visceral side of the mesh will be covered - is not an effective method in preventing intestinal erosion or the migration of the prosthesis from the initial point of placement [17].

Clinically it is considered that the erosion of a hollow viscera and a fistula formation is, most of the times, a severe late complication with a difficult evolution and a high mortality rate notwithstanding the intervention [30].

5) Prosthesis contraction
The characteristics of the implant material influence the rate and the speed of the adhesions formation. Once formed, the adherential tissue reduces mesh flexibility and its ability to simulate the physiological movements of the abdominal wall. Because of the “immobilization” of the consolidating material in the network of adhesions, hernia mesh size changes and local tensions appear, that may lead to recurrence of the hernia defect or to the appearance of a new one [31].

The post-implant dimensional changes can reach high proportions depending not only on the nature of the material, but also on the design of the consolidation system. Thus, for the “plug”-type prostheses, depending on the nature of the biomaterial,
the size may decrease even by 75% compared to the initial values, the process leading to the failure of the surgical repair.

A “too loose” or “too soft” prosthetic plug can be outlined intraoperatively by using the test of “pinching” between two fingers. The prosthetic plug loses its size during wound healing. The mechanism by which the reconstructive surgical technique is compromised is the following: during the healing process the prosthetic plug tightens as a result of the adhesions between it and adjacent tissues, and this process puts pressure on the stitches connecting the implanted mesh with the hernia edges. They open and cause relapse.

In the case of the “patch” systems, the mesh fibres contraction decreases the overall mesh. Radiographic measurements of the distances between the metal clips used to fix the mesh in preperitoneal position in hernia surgery showed a decrease by approximately 20% of the prosthetic material a few months after surgery [17]. Moreover, the comparison made between a mesh removed from a patient (cleaned by using a solution of sodium salicylate in methanol) and the control mesh (unused), showed a reduction of approximately 20% of the eyelet size of the removed mesh. The contraction of the prosthesis evolves over time and reaches high levels after relatively long periods - 10 months after implantation. This observation is important for surgeons, who must ensure a degree of laxity to the prosthesis to avoid postoperative pain and mesh desinsertion [17,30]. Due to the processes involved in the postoperative contraction, the implants, even the soft ones, have a consistency similar to the cartilage and may erode even the bladder walls. These type of complications are felt by the patient as clinical dysuria or miotional difficulty and may appear even after several years from the implantation of the prosthesis. [31,32].

CONCLUSIONS

Clinical data regarding the complications caused by parietal consolidation materials show that:

- the risk of infection is minimized by using pore/large eyelet meshes;
- the formation of postoperative seromas can be virtually eliminated by the implantation of the macroporous prostheses in retromuscular or subaponeurotic position; when the implanted biomesh is large, the post-operative drainage is recommended;
- the erosion of the intestinal serous membrane, intestinal obstructions and development of postoperative fistulas can be eliminated by avoiding the direct contact between the mesh and the gastrointestinal tract, by avoiding folds or mesh plugs or by using composite biomaterials that does not cause post-operative adhesions;
- the contraction-related complications can be avoided by using a generously sized bio-prosthesis so that the edges of the biomaterial exceed the limits of the hernia defect and by keeping an adequate laxity of the mesh after its attachment to the abdominal wall.

The use of synthetic biomaterials in abdominal wall hernia surgery increased significantly in recent years. It should be noted however, that some of the features of the bioprosthesis can lead to unwanted side effects including postoperative infection, seromas formation, intestinal obstruction, development of intestinal fistulas.

When all the mechanisms causing postoperative complications mentioned above will be fully understood and the precautions for their prevention will be properly taken, then the consolidating materials for the abdominal wall will not cause postoperative complications anymore.

ACKNOWLEDGEMENTS

The first author is Ph.D. student at “Gr.T. Popa“ University of Medicine and Pharmacy, First Surgical Clinic, “St. Spiridon” Universitary Hospital, Iași. This paper is the result of the documentation undertaken during the doctoral internship.

CONFLICT OF INTERESTS

None to declare
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