

Visceral Adhesions after Tension-Free Abdominal Wall Repair with Ultra-Lightweight Synthetic and Titanium-Containing Meshes

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Criteria of reliability and safety of abdominal wall prosthetic repair with the help of ultra-lightweight synthetic and titanium-containing materials are not clearly defined, and the results of their application are insufficiently studied.

The aim of the investigation was to study in the experiment the intensity of the abdominal adhesive process after tension-free repair with ultra-lightweight synthetic and titanium-containing meshes.

Materials and Methods. Ultra-lightweight synthetic and titanium-containing meshes were implanted to laboratory animals (n=128). Synthetic meshes (PP Light) were used in group 1, in group 2 titanium-containing meshes (TiMesh) were employed, and in group 3 meshes were from titanium filaments (Titan, Titanium silk).

In the first series of the investigation, intraperitoneal onlay mesh (IPOM) technique was used, in the second series sublay retromuscular (SRM) repair was performed. 30 and 60 days later, the zone of implantation was examined with photofixation of the results, viscera-parietal adhesions were evaluated using a modified Vanderbilt assessment scale. Differences were considered statistically significant at $p < 0.05$.

Results. The intensity of the adhesive process was significantly higher in the IPOM series (4.0 points) in comparison with the SRM series (0.44 points), $p = 0.000$. The intensity of this phenomenon in the PP Light, TiMesh, and Titan groups amounted on average to 2.73, 3.78, and 5.33 points, respectively. Differences of the results in the TiMesh group from the PP Light group were not statistically significant, $p = 0.07$, however, they were significant with the Titan group, $p = 0.03$. The intensity depended also on the postoperative period duration. In the PP Light group its value on day 30 and 60 was 3.16 and 2.20 points, respectively, $p = 0.22$; in the TiMesh group it was 3.64 and 4.0 points, respectively, $p = 0.81$; in the Titan group it was 6.60 and 4.42, $p = 0.004$.

Minimal formation of viscera-parietal adhesions was noted in the SRM series: in the groups PP Light, TiMesh, and Titan it was equal to 0.36, 0.44, and 0.50 points, respectively. In some cases the zone of repair was completely free of adhesions. Adhesive process in the IPOM series should be considered unacceptably intensive in all periods for all tested meshes. In the SRM series, opposite (the best) results have been obtained, which were comparable for all types of meshes used in the work. Safety of retromuscular repair using ultra-lightweight synthetic and titanium-containing meshes has been convincingly proved by the data of the experiment.

Conclusion. Retromuscular repair with ultra-lightweight synthetic and titanium-containing meshes should be used for the reconstruction of the abdominal wall. But application of titanium-containing meshes seem to be more preferable, as it is associated with formation of significantly more strong connective tissue in the implantation zone, and an inflammatory reaction induced by such a mesh is substantially less than by a synthetic one.

Key words: prosthetic repair; synthetic meshes; titanium-containing meshes; mesh; hernia.

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Abdominal wall repair using meshes represents the main variant of surgical intervention in patients with incisional hernia [1–4]. Patients with hernia made a considerable part of sick people in general surgery units, and this fact determines an interest to the questions of their operative treatment [4–6].

The technique of surgical intervention is elaborated in detail and is being constantly improved [1–5]. Among numerous methods of operative aid, reconstruction (augmentation) and correction (bridging repair) are usually distinguished. Modern investigators pay increasing attention to the first method, the aim of which is not only to close the abdominal wall defect with a mesh, but to restore the latter as fully as possible in a way close to its initial (intact) structure [2, 3]. Not only prosthetic repair but also a reconstruction of the natural anatomy is supposed to be an indispensable condition of further functional activity of the abdominal wall as well as an adequate rehabilitation of a patient, his full physical activity, and ability to work.

Biomechanical concept of hernia pathogenesis envisages the necessity of restoring medial points of muscle attachment for the following proper functioning of the abdominal wall as a single muscular aponeurotic complex [7] and prevention of recurrence. In a number of cases, presence of the synthetic material results in excessive collagen synthesis, which is evident in formation of a large amount of unnecessary dense connective tissue, which lacks compliance and resilience. Formation of such scars is the basis for a stiff-man syndrome, making natural processes of contracting and stretching of the operated abdominal wall impossible.

The specified problem is being actively investigated by the leading specialists in the field of herniology. Experimental studies in this direction play a special role [8–10]. Of great importance in the assessment of the reparative process are the key aspects of interaction of the mesh material and structure with the components of the abdominal wall at the tissue level. Aseptic inflammation in the implantation zone is established to last in some cases for a long time and may become chronic. Prolonged local inflammatory reaction with the participation of the components of the cellular immunity link localized on the periphery of the implanted mesh is accompanied by the changes of the mesh elements themselves and the connective tissue formed around them. The indicated processes lead to the remodeling of the latter, alterations of its strength properties, compliance and extensibility. In clinical conditions it is a morphological basis of forming an operated abdominal wall as functionally inadequate, of stiff and rigid structure.

A combination of macrophage reaction, associated with chronic inflammation, and false-persisting mechanisms of biodegradation become the cause of diastases occurrence in the zone of “mesh fiber–connective tissue” contact typical for late recurrences after prosthetic repair [11]. The described above

phenomena are pathogenically connected with a number of remote complications of the tension-free technique. And abdominal adhesive process is referred to them [12–15]. The pathogenesis of forming viscera-parietal and viscera-visceral adhesions is described in detail in the literature [16]. Clinically important disorders of intestinal content passage may result in the development of acute intestinal obstruction. In some cases, migration of meshes to the abdominal cavity is observed [17], mesh forms pressure sores on the walls of the hollow organs and enterocolonic fistulas [18]. Chronic accumulations of fluid (seromas) and development of chronic pain syndrome are typical situations for the persisting paraprosthesis inflammation. In case of forming paraprosthesis granulomas and mesh fistulas, bacterial contamination and biofilm process may play a role [19]. Mechanisms of seroma formation are considered in detail in the literature [20, 21]. The work on the problem of forming a fully functional connective tissue in the implantation zone and achieving complete integration of the mesh in the tissues of the abdominal wall implies solving a complex of interconnected tasks concerning improvements of the surgical technique, development of new meshes, optimization of the reparative process course, and prevention of infections in the area of operative intervention.

The advent of a new group of ultra-lightweight meshes as a means of abdominal wall reconstruction is connected with definite hopes of investigators to avoid a number of complications typical for heavy and standard meshes. For some authors [22], application of these meshes is associated with favorable clinical results, in other works [8] similar materials are not recommended for routine usage.

Apart from the well-known synthetic materials, titanium-containing meshes are actively implemented into herniological practice in recent years. This is a new group of implants possessing some advantages, and their fabrication is based on principally different technological processes [23, 24]. In some publications their capabilities have been appreciated as rather high, the authors report good experimental and clinical results [23–29].

Criteria of reliability and safety of abdominal wall prosthetic repair with the help of ultra-lightweight synthetic and titanium-containing materials are not clearly defined, and the results of their application including development of complications, the adhesive process in particular, are insufficiently studied.

The aim of the investigation was to study in the experiment the intensity of the abdominal adhesive process after tension-free repair with ultra-lightweight synthetic and titanium-containing meshes.

Materials and Methods. Meshes were implanted to the laboratory animals. Interventions were done with the permission of the Ethic Committee of the Central Clinical Hospital of the Russian Academy of Sciences in compliance with the legislation of the Russian Federation (Rules of humane treatment of laboratory

animals, Deontology of medico-biological experiment) and ethical principles established by European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (the Convention was passed in Strasburg, March 18, 1986, adopted in Strasbourg, June 15, 2006). The experiment was carried out in the M.M. Shemyakin and Yu.A. Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences (Moscow).

The study design, formation of groups, methodology of operations, anesthetic support, and management of the postoperative period fully corresponded to the postulates of the modern 3R concept (replacement, reduction, refinement) of Russell & Burch commonly accepted in the world and obligatory for observance in biology and experimental surgery [30].

Meshes (n=128) were implanted to rabbits under anesthesia using intramuscularly the following medications: Rometar (xylazine hydrochloride, 2 mg/kg) and Zoletil (tiletamine hydrochloride/zolazepam hydrochloride, 8 mg/kg). In group 1, synthetic meshes (PP Light, polypropylene fiber of 90 µm in diameter, 36 g/m² surface density, 39.6 cm³/m² index of the distributed volume) were used. According to Klinge and Klosterhalfen classification [31], this corresponds to the category of lightweight meshes [32] class 1a. In some papers (2014, 2015) the authors consider these meshes ultra-lightweight [8, 33]. Titanium-containing meshes were used in group 2 (TiMesh, polypropylene fiber of 65 µm in diameter with a titanium coating, 16 g/m² surface density, 17.58 cm³/m² index of the distributed volume). Such meshes are referred to 1c class [31] and ultra-lightweight meshes [8, 32, 33]. In group 3, meshes

from titanium fibers were implanted (Titan, Titanium silk, 65 µm filament, 45 g/m², 10.41 cm³/m² index of the distributed volume). These meshes are ultra-lightweight [8, 33]. All described meshes pertained by their structure to the meshes woven from monofilament fibers.

The operative technique was standard for experimental works [12, 34], the implantation procedure in the clinical environment was also typical. For adequate comparison of the results, intraperitoneal onlay mesh (IPOM) [5, 14] and sublay retromuscular (SRM) methods of plastic repair [1, 35] actively used in current herniology were chosen. For correct collation of the research data, standard dimensions of meshes (3×3 cm) were used, which were applied in our previous works and described by other authors [36–38]. The meshes were attached to the structures of the abdominal wall with an atraumatic synthetic thread 4/0 (polypropylene).

The distribution of operations by series and groups is presented in Table 1. By the time of intervention the rabbits weighed 3,495±345 g.

In the first series of the investigation, IPOM method was used (Figure 1). Midline laparotomy was performed.

Table 1

Performance of implantations in the groups of animals (abs. number)

Series	Groups			Total
	PP Light	TiMesh	Titan	
IPOM	22	18	24	64
SRM	22	18	24	64
Total	44	36	48	128

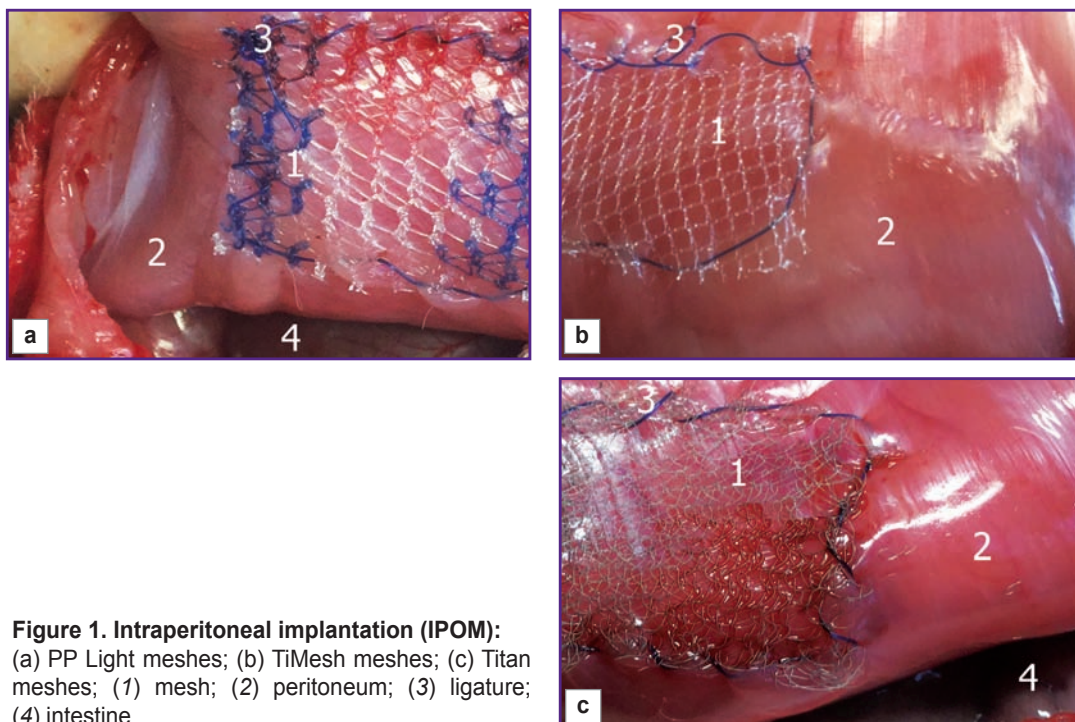


Figure 1. Intraoperative implantation (IPOM): (a) PP Light meshes; (b) TiMesh meshes; (c) Titan meshes; (1) mesh; (2) peritoneum; (3) ligature; (4) intestine

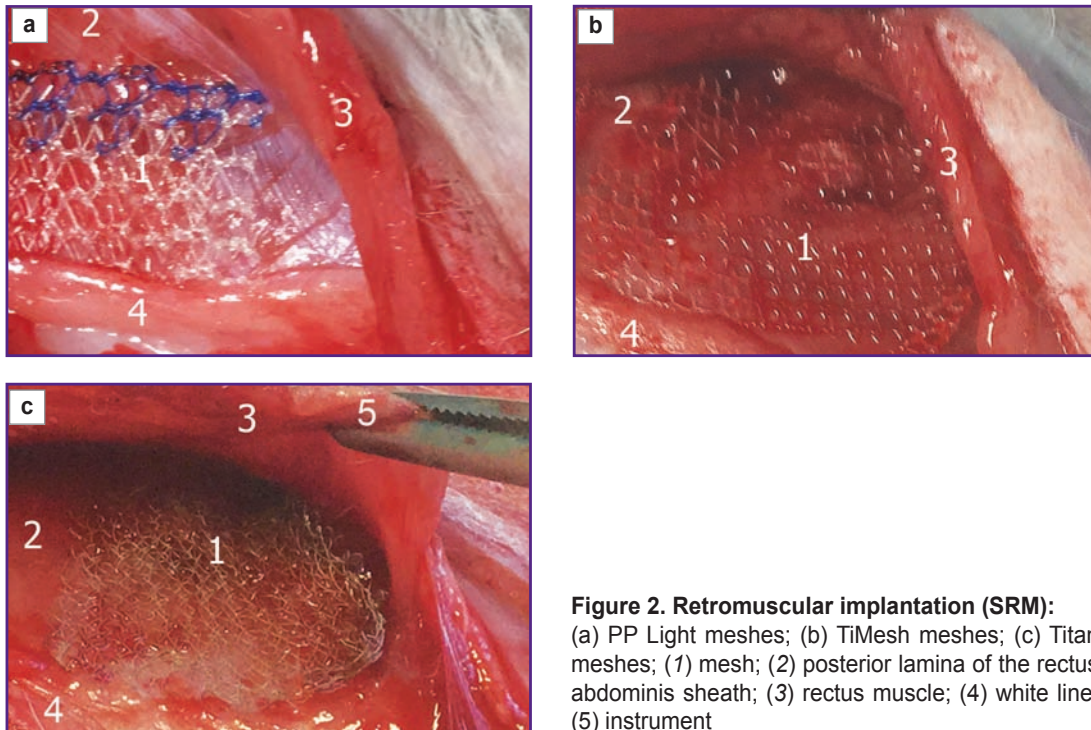


Figure 2. Retromuscular implantation (SRM):
 (a) PP Light meshes; (b) TiMesh meshes; (c) Titan meshes; (1) mesh; (2) posterior lamina of the rectus abdominis sheath; (3) rectus muscle; (4) white line; (5) instrument

Table 2
The scale of adhesive process assessment in the zone of plastic repair (according to Yegiyev and Lyadov, 2010)

Adhesive process area (0–4 points)	No adhesions — 0
	Up to 25% of the mesh area — 1 point
	From 25 to 50% of the mesh area — 2 points
	From 50 to 75% of the mesh area — 3 points
	More than 75% of the mesh area — 4 points
Adhesion strength (0–3 points)	No adhesions — 0
	Easily separated — 1 points
	Separated by the instrument — 2 points
	May be separated only by sharp dissection — 3 points

Note. Points are summed up amounting from 1 to 7.

Mesh was fixed to the parietal peritoneum from the side of the abdominal cavity, then the abdominal cavity and the wound were closed with a continuous suture using an atraumatic synthetic thread.

In the second series of interventions, SRM method was employed (Figure 2). Midline laparotomy was performed. Anterior laminae of the rectus abdominis sheaths were medially dissected, retromuscular space was bilaterally prepared. The abdominal cavity was closed by a continuous suture using an atraumatic synthetic thread, posterior laminae of the rectus abdominis sheaths were joined. A mesh was placed in the retromuscular space, fixed to the posterior laminae of the sheath with an atraumatic synthetic thread 4/0 without tension. Anterior laminae of the rectus abdominis sheaths were joined by

a continuous suture using an atraumatic synthetic thread, thereafter the wound was closed.

To prevent infections in the area of surgical intervention a single injection of beta-lactam antibiotic was made, the dosage was calculated depending on the animal body mass. Food, water, and movement regimens were not limited. Non-narcotic analgesics were routinely used. Animals were followed up for 2 months. They were withdrawn from the experiment under anesthesia using the above-mentioned drugs in the same dosage by means of air embolism (7 ml/kg). The implantation zone was inspected with photofixation of the results with special attention to the assessment of visceroparietal adhesions.

The score (from 0 to 7 points, Table 2) was counted according to the modified scale of Vanderbilt University [34]. Distribution of the population data was evaluated by Shapiro–Wilk and Lilliefors (Origin Pro 8) tests. The analysis of nonparametric sequences was done using Mann–Whitney and Kolmogorov–Smirnov methods (Origin Pro 8). Data arrays with normal distribution were studied using Student’s t-test (Excel 2016). Differences were considered significant at $p < 0.05$.

Results. The postoperative period was uneventful in all animals, the wounds healed by primary intention. Animal body mass at the beginning of the experiment was $3,495 \pm 345$ g, 30 days later it became $3,420 \pm 477$ g (i.e. less than the initial mass, $p = 0.03$), 60 days later it reached $3,808 \pm 470$ g (i.e. greater than the initial value, $p = 0.014$).

The intensity of the adhesive process was statistically higher in the IPOM series (4.0 points) compared to the SRM series (0.44 points), $p = 0.000$ (Table 3).

Table 3
Intensity of the adhesive process (points)

Series	Group			Mean*
	PP Light	TiMesh	Titan	
IPOM	2.73	3.78	5.33	4.00
SRM	0.36	0.44	0.50	0.44
Mean	1.55	2.11	2.92	2.22

* Arithmetic mean.

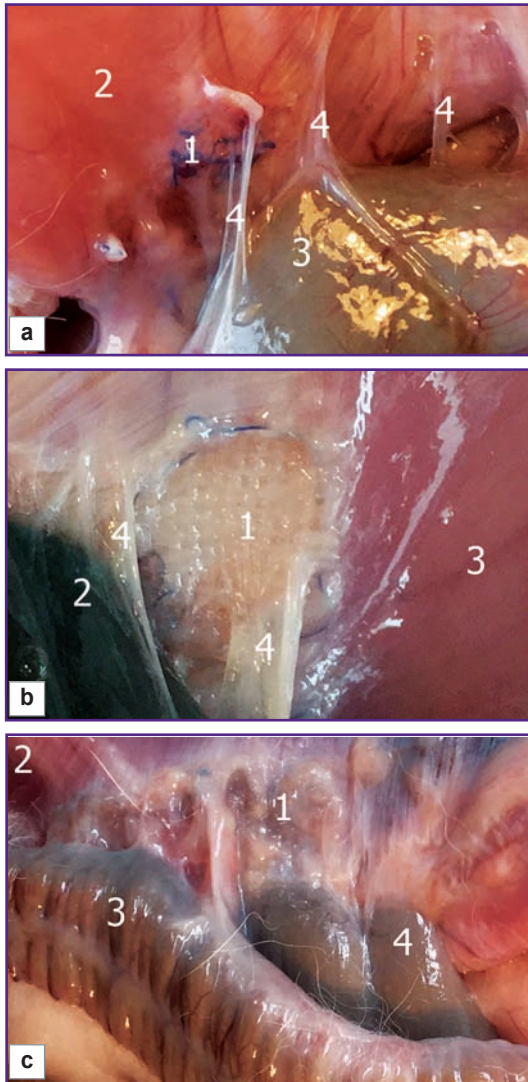


Figure 3. The result of intraperitoneal implantation (IPOM): (a) PP Light meshes; (b) TiMesh meshes; (c) Titan meshes; (1) mesh; (2) peritoneum; (3) intestine; (4) adhesions. Adhesive process

Formation of visceroparietal adhesions is shown on Figure 3. The extent of this phenomenon in the PP Light, TiMesh, and Titan groups corresponded on average to 2.73, 3.78, and 5.33 points. A definite tendency was found when a more comprehensive comparison was performed within the IPOM series: the intensity of the

adhesive process depended on the kind of a mesh in case of intraperitoneal repair. In particular, when the PP Light and TiMesh groups were compared, differences were not statistically significant, $p=0.07$. However, they were significant, $p=0.03$, when the TiMesh and Titan groups were collated.

The intensity of the adhesive process depended also on the postoperative terms. In the PP Light group it was 3.16 and 2.20 points on day 30 and 60, respectively, $p=0.22$; in the TiMesh group it was 3.64 and 4.0 points on day 30 and 60, respectively, $p=0.81$; and in the Titan group in later terms of the postoperative period the intensity of the adhesive process appeared to be statistically significantly less: 6.60 and 4.42 points, respectively, $p=0.004$.

Minimal formations of viscera-parietal adhesions were noted in the SRM series (Figure 4). The measured index

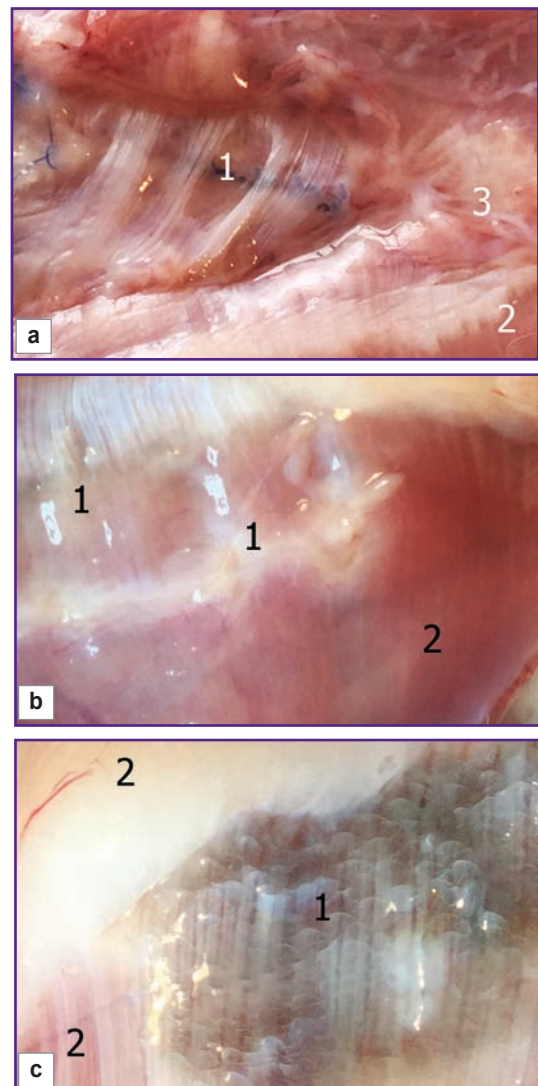


Figure 4. Results of retromuscular implantation: (a) PP Light meshes; (b) TiMesh meshes; (c) Titan meshes; (1) mesh; (2) peritoneum; (3) zone of abdominal wall suture. Absence of the adhesive process

in the PP Light, TiMesh, and Titan groups was 0.36, 0.44 and 0.50 points, respectively, $p=0.76$ (See Table 3). In some cases the zone of repair was completely free of adhesions. Application of the mesh from titanium filaments for the retromuscular repair, the usage of which in the IPOM series was associated with the highest value according to the scale of adhesion process, did not also show a marked formation of adhesions. On Figure 4 (c), it is well seen how the titanium mesh literally shines through very thin structures of the posterior layers of the rabbit abdominal wall. Nevertheless, the significant visceroparietal adhesive process is not observed.

The result of the conducted study allows us to assert that formation of visceroparietal adhesions associated with implantation of ultra-lightweight synthetic and titanium-containing meshes significantly depends on the chosen method of the abdominal wall endoprosthesis repair. It is true for all tested implants and periods of follow up. In the IPOM series, statistically significant reduction of the adhesive process intensity was found in the late terms of the postoperative period for Titan implants. In the same series, statistically significant differences of visceroparietal adhesion formation between the examined groups were revealed. Nevertheless, the adhesive process in the IPOM series should be considered to be unacceptably intensive in all periods for all tested meshes. In the SRM series the opposite (the best) results were obtained, which were comparable for all types of meshes used in the work. Safety of retromuscular repair by the ultra-lightweight synthetic and titanium-containing meshes has been convincingly proved by the experimental data.

Discussion. The data given within the scope of the current investigation are subject to a detailed comparison with the findings of other studies and thorough critical analysis. Upon the whole, the obtained indices of the visceroparietal adhesive process intensity agree in many ways with other similar measurements [12, 34, 36–38], though there are some differences. However, data about implantation of the titanium meshes are published for the first time in the present work.

In the series of intraperitoneal repair with ultra-lightweight meshes, the intensity of the adhesive process was lower than the analogous indices for standard meshes presented previously by the Russian leading scientists [12, 34]. The same authors prefer using lightweight meshes in the clinical environment, placing them extraperitoneally [22]. Other investigators use these meshes intraperitoneally [5]. In the existing situation, one can only suppose that probably there are some advantages of using the light and ultra-lightweight implants, but not assert that they must be placed intraperitoneally, as investigations on this topic have not been found.

The obtained indices of the adhesive process intensity for the PP Light implanted according to IPOM technique agree with the previous investigations [37], in which close values of 3.77 points (M is mean) and 4 points (Me

is median) were shown. It is substantially better than the similar indices for standard polypropylene: 4.64 points (M) and 5 points (Me), obtained in the same investigation [37]; 5.81 points (M) in another one [36], about 5 points in the third [34, 39], and 6–7 points in the fourth research [12]. It is because of serious intraabdominal complications that the standard polypropylene mesh is not recommended to be used by IPOM technique [18]. In recent years, more advanced materials with different chemical composition are being actively studied, such for example, as polyvinylidene fluoride, whose index of the adhesive process intensity after IPOM was found to be from 2 to 3.15 points without antiadhesive coatings, and from 1.39 to 2 points with their application [12, 37].

Notably, that the danger of intraperitoneal implantation of a standard polypropylene mesh widely known in the herniological sphere is not adequately grounded in terms of evidence-based medicine, which is convincingly set forth in detail in the work of Ramakrishna [14].

Nevertheless, retromuscular repair remains a standard of safety in relation to the development of adhesive process, which is proved within the frames of the given and earlier investigations [38] for ultra-lightweight synthetic and titanium-containing meshes. This statement is also true for the lightweight and standard synthetic meshes, which was substantiated by us in previous studies [40].

The feasibility of intraabdominal implantation of titanium-containing mesh meshes has already attracted attention abroad [29, 41]. It has been shown that the results of intraperitoneal repair using meshes from polypropylene with a titanium coating (TiMesh) are not inferior to the meshes from the stretched polytetrafluoroethylene (ePTFE) after their intraperitoneal placement [41], the material which has been considered for a long time to be a standard of implant for IPOM [34, 39]. However, according to the data of the conducted experimental work and the analysis of the latest publications it may be supposed that an optimal mesh for IPOM has not yet been proposed. It is unlikely that this problem will be overcome in the nearest time. It is mainly connected with the specificity of the methodology rather than with only constructive or technical drawbacks of any given implant.

All the above said determines the necessity of investigating the possibility of using ultra-lightweight synthetic and titanium-containing meshes for the reconstruction of the abdominal wall by means of retromuscular repair. And the application of the titanium-containing meshes seems to be more preferable as they are associated with the formation of reliably stronger connective tissue in the zone of implantation [42], and the inflammatory reaction induced by a titanium-containing mesh is substantially less than by a synthetic mesh [43].

The point of view presented in this work about the necessity of a wide usage of lightweight and ultra-lightweight meshes has been sufficiently substantiated

by clinical and experimental data, but does not coincide with the position of some researchers in Russia and abroad [8, 35]. It should be clearly understood that preference of using lightweight and ultra-lightweight materials should be given only in case of performing adequate reconstruction of the abdominal wall by retromuscular plastic method, and in difficult situations by the technique of component separation. It is also necessary to take into consideration the known risk factors of hernia recurrence.

Conclusion. Retromuscular repair with the help of ultra-lightweight synthetic and titanium-containing meshes should be used for the reconstruction of the abdominal wall. This approach is an experimentally grounded, reliable and safe solution associated with minimal formation of visceroparietal adhesions in the zone of implantation.

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Conflicts of Interest. The authors have no conflicts of interest to declare.

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