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LOCAL INFLAMMATORY RESPONSE TO SUTURE MATERIAL IN SURGICAL PRACTICE: EXPERIMENTAL DATA

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Objective: to study the effect of various types of suture materials, potentially suitable for cardiovascular surgery, on experimental surgical outcomes. **Materials and methods.** Polypropylene sutures (Prolene 6/0), titanium nickelide (TiNi) sutures (6/0) and absorbable polydioxanone sutures (Monoplus 6/0) were used in the study. Male Wistar rats were used for *in vivo* studies. The effect of suture materials on abdominal adhesions was studied. *In vivo* calcification process was examined, and response of blood components in contact with suture materials was also assessed *in vitro*. **Results.** There is a negative inflammatory response to suture materials. The severity of this response depended on the type of material used. Polypropylene sutures demonstrated the most severe inflammatory response provoking massive adhesion formation. In addition, large calcium deposits were found both in the suture area and in the thickness of the biomaterial, stitched with prolene and implanted subcutaneously in the rats. Titanium nickelide sutures showed high hemocompatibility and biocompatibility. The Monoplus sutures caused minimal inflammatory response and provoked calcification of the biomaterial to a lesser degree. **Conclusion.** The suture material could have significant effects on surgical outcomes and could cause postoperative complications.

Keywords: suture material, cardiovascular surgery, adhesion, calcification, hemocompatibility.

INTRODUCTION

Among unsolved challenges for cardiovascular surgery, there are complications closely related to the quality of the used suture material [1–5]. Since the tissue reaction to suture material is similar to the response to implanted foreign body, it is natural that sutures of unsatisfactory quality can result in postoperative complications. After the suture material contacts surrounding tissues, a classic pathophysiological reaction to a foreign body develops, the essence of which is an inflammatory reaction [6, 7]. The intensity of this reaction and its consequences largely depend on the chemical composition and structure of the suture material [1, 3, 6]. When suture material is used in vascular surgery, a large amount of such blood proteins as albumin, γ-globulins, and fibrinogen, are entrapped at the "prosthesis – patient artery" interface within a few minutes after the anastomosis is applied [7–9]. This is followed by the coagulation system and the complement system activation which can gradually lead to thrombus formation and aseptic inflammation [7, 8].

In Russia, the number of reparative surgeries on various vascular basins is annually increasing; in particular, there is a significant increase in arterial reconstructions. In 2016, the total number of reoperations significantly exceeded those in previous years and amounted to 71,810, which is 20% more than in 2014, and 26% more than in 2012 [9, 10]. Thrombosis of the vascular graft is the most common complication after these operations. The reasons contributing to the thrombus formation in the anastomotic zone include damage to the vessel walls, especially the intima, as well as the presence of surgical suture material protruding into the vessel lumen, only aggravating the situation [11, 12]. In this regard, special requirements are imposed on suture materials directly contacting blood: they should not negatively affect blood and its components, i.e. should be maximally hemocompatible.

Cardiovascular surgery uses absorbable and non-absorbable sutures, but the most commonly applied suture material from the polyolefin group is polypropylene, which is considered to be highly inert and strong. At the same time, some researchers report that polypropylene sutures can cause a local aseptic inflammatory reaction which can turn into a chronic inflammatory process in the vascular anastomosis area and cause neointimal hyperplasia development [4, 5].

In addition to the development of neointimal hyperplasia, there are some life-threatening complications after the cardiovascular system surgery including such processes as calcification and adhesion, which also result from chronic inflammation in the surgery site [13]. When studying the long-term results of valved biological conduits, the signs of calcification along the line of bioprostheses fixation have been noted, indicating a conceivable effect of suture material upon the mineralization process [14]. In addition to all of the above, suture material can cause a pronounced adhesive process in the mediastinum which, in turn can lead to adhesions of the heart and large great vessels with the posterior surface of

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the sternum. In cardiovascular surgery, the complication significantly increases the risk of serious adverse events in case of reoperation [15, 16].

Purpose: to perform a comparative analysis of the effect of biodegradable and non-biodegradable suture material on the development of postoperative complications in cardiovascular surgery.

MATERIALS AND METHODS

In the present study, Prolene 6/0 (Ethicon, USA) suture was used, most common in cardiovascular surgery. In comparison, the properties of absorbable suture material of Monoplus 6/0 (B. Braun, Germany) polydioxanone recommended for use in pediatric cardiovascular surgery were evaluated [2].

In vivo studies were made on Wistar subpopulation male rats, 10 animals in each group. All manipulations with laboratory animals were carried out under inhalation isoflurane (2.0%) anesthesia in a clean operating room in accordance with the Interstate Standard, Guidelines for the Care and Care of Laboratory Animals, in compliance with the Rules for the Maintenance and Care of Laboratory Rodents and Rabbits (Russian GOST 33216-2014) and the Rules for the equipment of premises and organization of procedures (Russian GOST 33215-2014).

Adhesion simulation

To study the role of suture material in the development of the adhesive process, 3–4 stitches of absorbable and non-absorbable suture materials were applied to the parietal side of animal peritoneum (200–250 g weight) under sterile conditions. The animals were taken out of the experiment after 7, 14 and 28 days. The removed "peritoneum – suture material – adhesions" complexes were examined by light microscopy with Axio Imager. A1 (Zeiss, Germany). The histological preparations were hematoxylin-eosin and Van Gieson stained.

Modeling accelerated calcification

Calcification was simulated using porcine aortic valve cusps preserved with ethylene glycol diglycidyl ether (EGDE) where several stitches of the test suture materials were applied. After that, biomaterial samples were implanted into the rat (55–65 g weight) subcutaneous pockets for 60 days. Ca amount in the removed samples was determined with Lambda-5100 (PerkinElmer, USA) atomic absorption spectrophotometer and calculated per 1 mg of dry tissue. The biomaterial structure after subcutaneous implantation was studied by light microscopy, and hematoxylin-eosin and Van Gieson staining of histological preparations.

Modeling systemic blood flow *in vitro*

The reaction of blood components upon contact with suture material was evaluated in *in vitro* test. For this, segments of the cattle internal thoracic artery preserved with EGDE were sutured with the polypropylene and polydioxanone-based material (forming a vascular anastomosis). Then, the anastomoses samples (L = 6 cm; d = 4 mm) were fixed on the pipe fittings of the 205CA multichannel peristaltic pump (Watson-Marlow, UK). The lines with fixed samples were filled with fresh citrated donor blood. The blood circulation rate was 0.04 L/min at 37 °C, with 30 min contact time. The microscopic assessment of the anastomosis area after contact with blood was studied by scanning electron microscopy (SEM) with S-3400N microscope (Hitachi, Japan). For this, a gold-palladium coating was applied to the studied sample surface by ion sputtering with the EmitechSC 7640 vacuum post (Quorum Technologies, UK).

The quantitative data were processed by conventional statistical methods with STATISTICA 6.0 data analysis and visualization program for processing medical and biological information (StatSoft Inc., USA). The nature of the distribution in the samples was assessed with Kolmogorov–Smirnov test. Distribution in the groups differed from normal ($p < 0.01$). Data are presented as mean and error of the mean. The statistical significance of the differences between two independent groups was assessed with Mann–Whitney U-test; the differences were considered significant at a significance level of $p < 0.05$.

RESULTS

Macroscopic description

7 days after surgery, adhesions were formed in the abdominal cavity of the animals, tightly clinging to the suture material. The adhesions corresponded to the phase of novice adhesions and had a loose structure. The most pronounced inflammatory reaction of the surrounding tissues was observed when polypropylene sutures were used, the adhesions had a denser structure and were separated only by sharp dissection (Fig. 1, a). A significantly less inflammatory reaction was observed with the biodegradable Monoplus suture (Fig. 1, b). The adhesion process with the polydioxanone suture was less expressed in the entire study group. The adhesions had a filmy, non-cohesive structure which could be separated by blunt dissection.

The macroscopic examination of the removed valves preserved with EGDE and stitched with Prolene and Monoplus sutures showed the presence of calcium deposits in the biomaterial thickness. Calcification was observed in all test samples, but its size varied depending on the type of suture used. In the intact samples preserved with EGDE (control), Ca was absent indicating that it was the suture material that caused the calcification of the test samples.

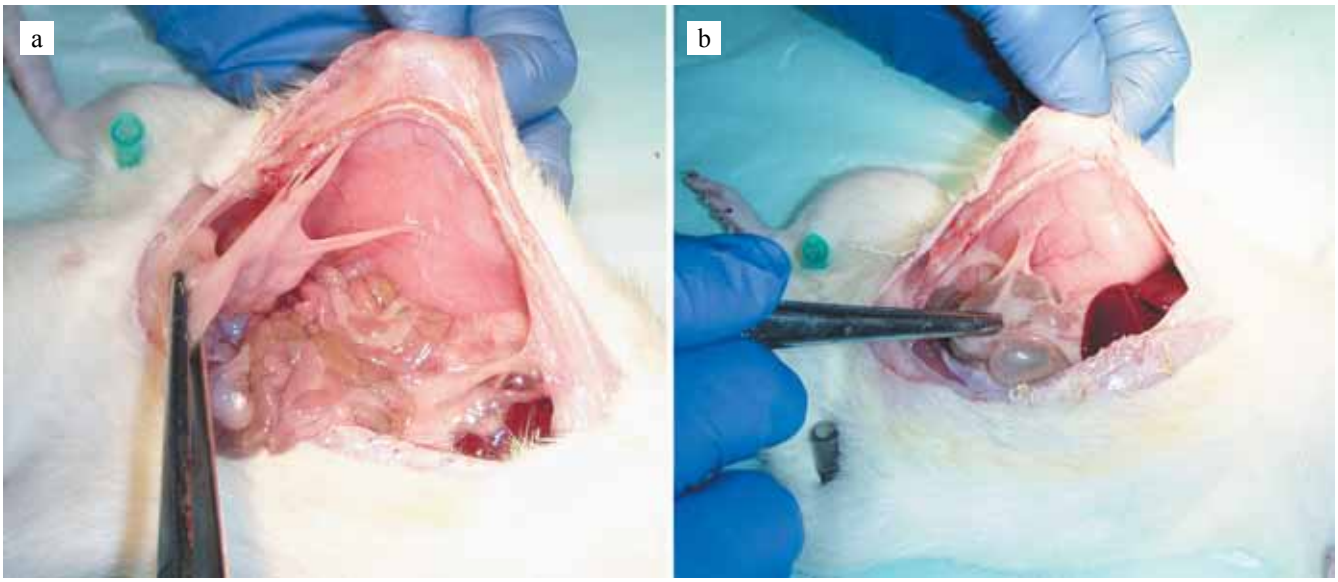

Fig. 1. The rate of adhesion formation after using a different suture material: a – Prolene; b – Monoplus

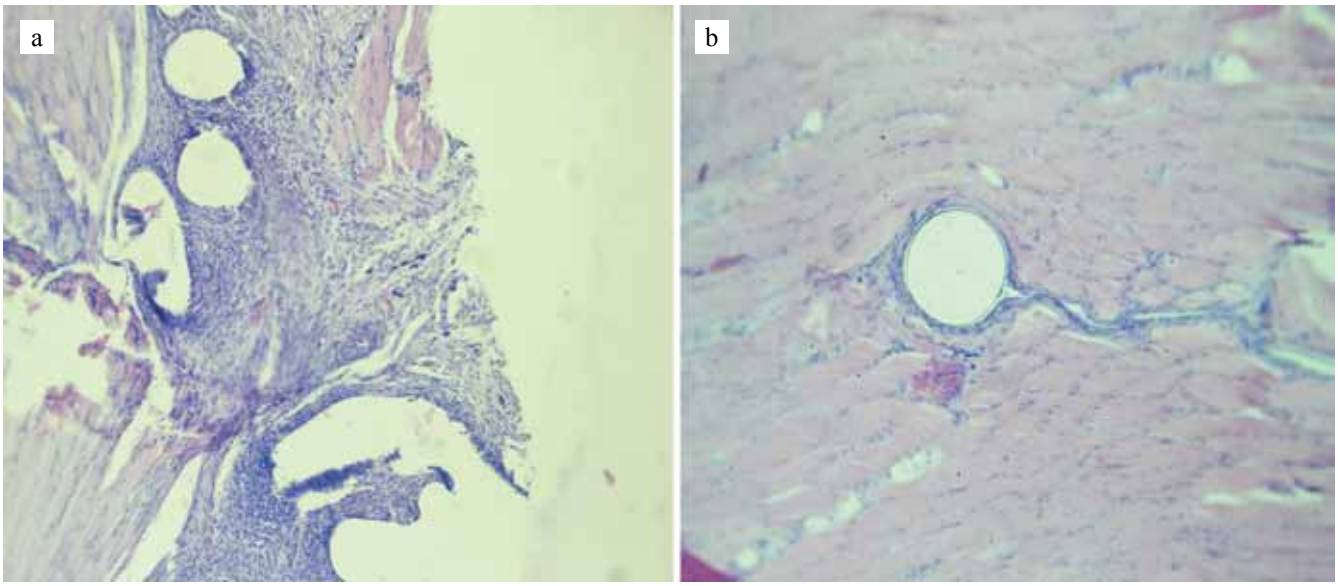

Fig. 2. Histological sections of the adhesion-peritoneum following the use of different suture material: a – Prolene; b – Monoplus. Stained with hematoxylin-eosin, ×200

Histology

Histological examination of the removed fragments showed granulation tissue formed in large amount around the sutures and massive lymphocytic infiltration with the formation of blood vessels. Smooth muscle cells were found in histological sections. This pattern is especially characteristic for Prolene sutures (Fig. 2, a). Collagen fibers were fragmented, had a loose fibrous capsule with a large number of capillaries indicating a pronounced inflammatory process around the suture material. The use of polydioxanone biodegradable sutures made it possible to minimize the destruction of collagen fibers and reduce the number of inflammatory cells in the peri-suturing area (Fig. 2, b).

Microscopic examination of the cusp tissue revealed large and small granular calcium deposits, mainly in the peri-suturing zone. Hematoxylin-eosin staining of the samples confirmed the presence of calcium phosphate. In the samples with Monoplus sutures, fine-grained calcium deposits were revealed, mainly around the suture material and in the spongy layer (Fig. 3, b). Outside the calcifications, collagen fibers retained crimp and compact arrangement. When using the Prolene suture, large calcium deposits were detected both in the suture material and in the thickness of the biomaterial (Fig. 3, a). With large calcium deposits, collagen fibers acquired a loose arrangement, fragmented in places.

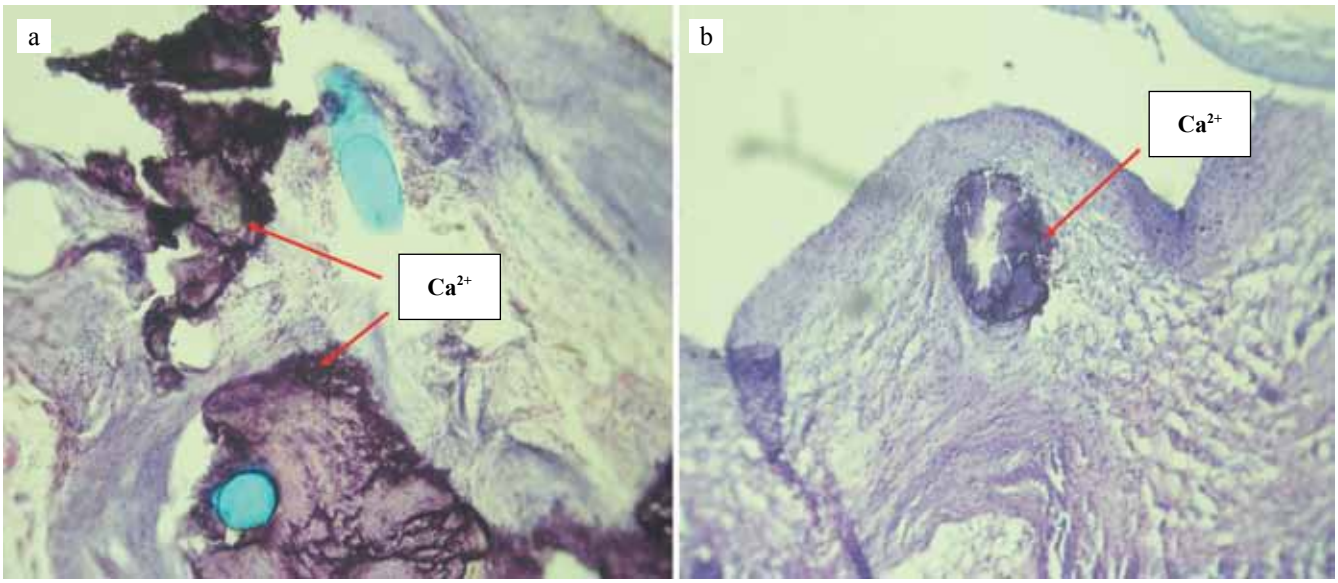

Fig. 3. Formation of calcification around retained suture material: a – Prolene; b – Monoplus. Stained with hematoxylin-eosin, ×200

Quantifying calcium level in explanted samples

2 months after implantation, the quantitative determination of the Ca level in the test samples confirmed that the use of polypropylene sutures largely provokes Ca accumulation in the biomaterial. In samples with Prolene sutures, Ca level was 151.2 ± 4.8 mg/g, while in the control samples of cusps preserved with EGDE without suture material, Ca level slightly exceeded metabolic and amounted to 2.4 ± 0.35 mg/g ($p < 0.05$). With Monoplus suture material, Ca level in the biomaterial was significantly lower than with Prolene, of up to 36.0 ± 3.1 mg/g ($p < 0.05$).

SEM

When examining by scanning electron microscopy, after their contact with blood, the anastomoses areas performed with two types of suture materials, a noticeable difference in the structure of protein deposits was found. The data obtained after 30 min of contact of the samples with blood showed that deposits of proteins with blood corpuscles appear in the anastomoses area. When using Prolene suture, the protein deposits were the most massive, with a loose and coarse structure (Fig. 4, a). Anastomosis with the polydioxanone suture had less loose protein deposits (Fig. 4, b).

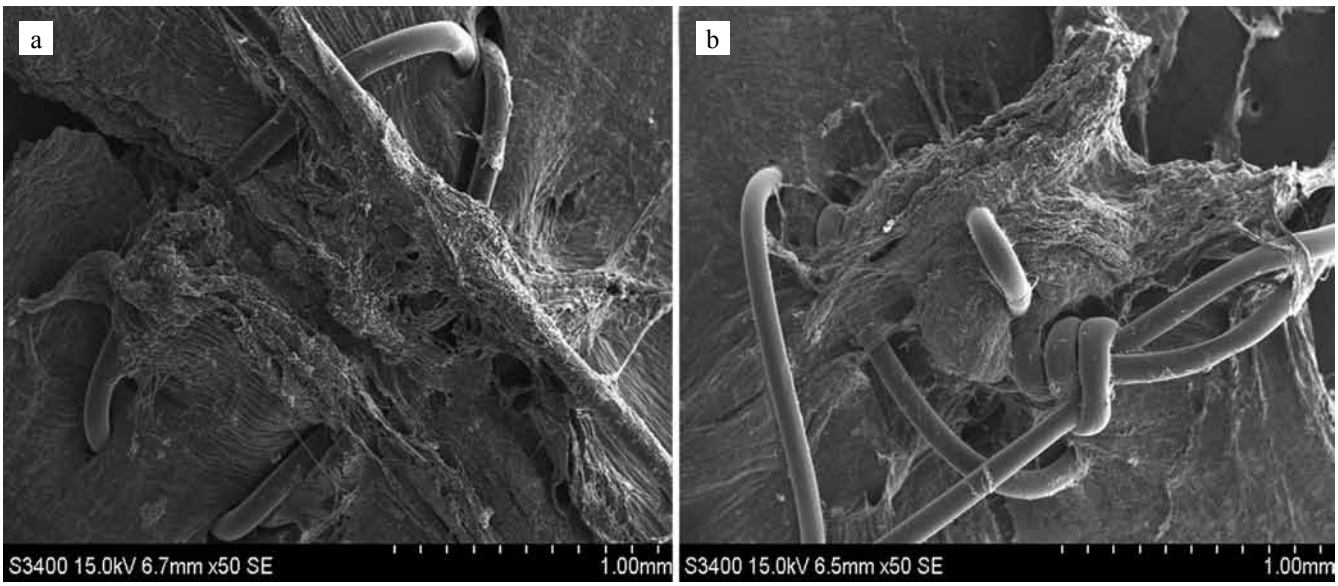

Fig. 4. Scanning electron microscopy of anastomotic sutures: a – Prolene; b – Monoplus, ×50

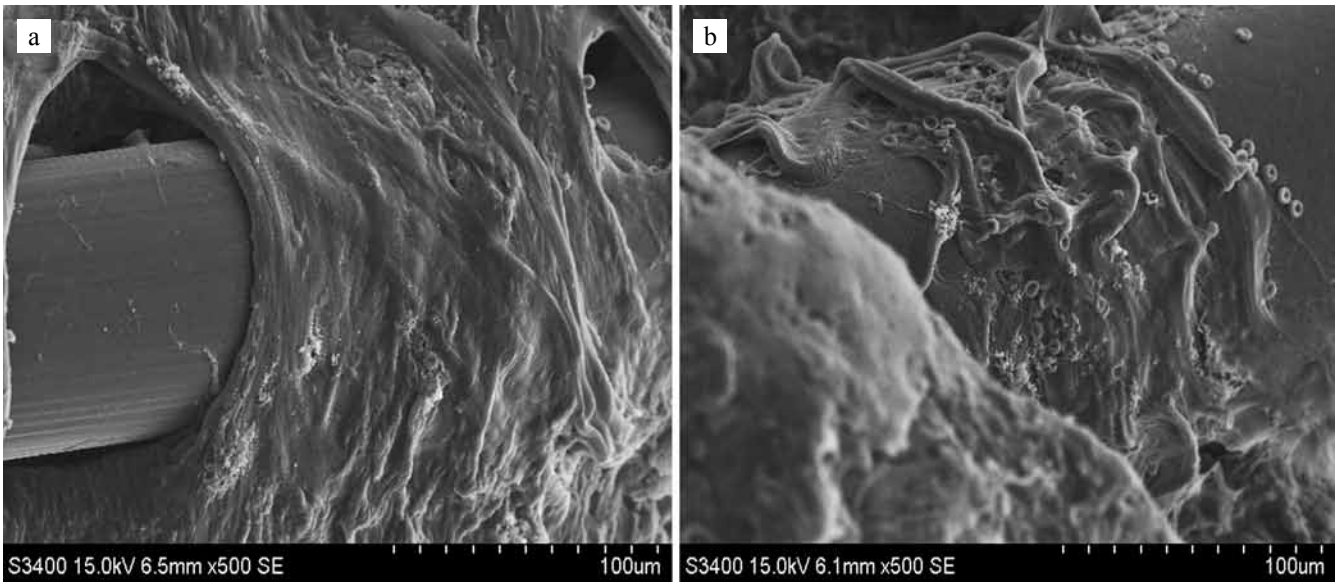

Fig. 5. Scanning electron microscopy of anastomotic sutures: a – Prolene; b – Monoplus, ×500

The differences in the reaction of the blood cell elements to the suture material are most clear at 500x (Fig. 5). The surface and surroundings of the polypropylene suture, significant fibrin and erythrocytes accumulations were seen, partially transformed into spherocytes and echinocytes (Fig. 5, a). The change of the disc-shaped form of erythrocytes into spherocytes or echinocytes is due to a negative effect, i.e. the erythrocytes reaction to a foreign body, while the transformed membrane of the altered erythrocyte tends to hemolysis [19].

The surface of the polydioxanone suture had a thin fibrin fibers network on which erythrocytes, partially transformed into echinocytes and spherocytes, were adhered (Fig. 5, b).

DISCUSSION

The comparative analysis of two types of surgical suture material showed the advantage of a biodegradable suture over polypropylene. The obtained results are consistent with the data of other studies which showed that polypropylene suture caused a more intense inflammatory response compared to biodegradable suture material [2, 13, 18]. A pronounced adhesion process, calcification, transformation of erythrocytes into echinocytes provoked by suture material based on polypropylene indicate a negative effect of the suture. The transformation of erythrocytes into echinocytes indicates low hemocompatible properties of the polypropylene suture, since such changes in erythrocytes are observed mainly during extensive surgical interventions [19] and can lead to violations of the aggregation characteristics of blood, increasing its viscosity, and as a consequence, increased risk of thrombosis of the vascular anastomosis area.

The use of a biodegradable polydioxanone suture material led to a lesser inflammatory reaction, and as a consequence, less calcification of tissues in the perisuture area. The adhesion process based on tissue injury as well as a reaction to the suture material showed a significant advantage of the biodegradable suture material over polypropylene suture. The evaluation of the effect of Monoplus suture on protein sorption in the vascular anastomosis area did not show significant advantages over polypropylene suture; nevertheless, the absence of transformed blood cells indicates higher hemocompatible properties of polydioxanone sutures.

CONCLUSION

The results of the present study show the negative reaction to the suture material and the degree of its severity depending on the type of material used. The most striking inflammatory response was demonstrated by polypropylene-based suture material, while it is polypropylene suture that is widely used in cardiovascular surgery. The polypropylene suture also significantly enhances the inflammatory response, adhesion, and calcification of the surrounding tissues. The biodegradable polydioxanone-based suture material has demonstrated significant advantages over polypropylene sutures. Monoplus suture causes less inflammation, calcification, and adhesion.

The authors declare no conflict of interest.

REFERENCES

1. *Holzheimer RG.* Adverse events of sutures: possible interactions of biomaterials? Eur *J Med Res*. 2005; 10 (12): 521–526.
2. *Gasbarro V, Traina L, Mascoli F, Coscia V, Buffone G, Grande R et al.* Absorbable suture material in carotid sur-

gery. *Vasa*. 2015; 44 (6): 451–457. doi: 10.1024/0301-1526/a000468.
3. *Lock AM, Gao R, Naot D, Coleman B, Cornish J, Musson DS.* Induction of immune gene expression and inflammatory mediator release by commonly used surgical suture materials: an experimental *in vitro* study. *Patient Saf Surg*. 2017; 11: 16. doi: 10.1186/s13037-017-0132-2.
4. *Beloyarcev DF, Talybly OL, Volkov SK.* Sostoyanie bifurkacii sonnoj arterii posle operacii s primeneniem rassasyvayushchegosya shovnogo materiala. *Angiologiya i sosudistaya hirurgiya*. 2015; 21 (4): 192–197.
5. *Bae S, DiBalsi MJ, Meilinger N, Zhang C, Beal E, Korneva G. et al.* Heparin-eluting Electrospun Nanofiber Yarns for Antithrombotic Vascular Sutures. *ACS Applied Materials a Interfaces*. 2018; 10 (10): 8426–8435. doi: 10.1021/acsami.7b14888.
6. *Selvi F, Cakarer S, Can T, Kirli Topcu Sİ, Palancioglu A, Keskin B et al.* Effects of different suture materials on tissue healing. *J Istanb Univ Fac Dent*. 2016; 50 (1): 35–42. doi: 10.17096/jiufd.79438.
7. *Anderson JM, Rodriguez A, Chang DT.* Foreign body reaction to biomaterials. *Semin Immunol*. 2008; 20 (2): 86–100. doi: 10.1016/j.smim.2007.11.004.
8. *Moore LB, Kyriakides TR.* Molecular Characterization of Macrophage-Biomaterial Interactions. *Adv Exp Med Biol*. 2015; 865: 109–122. doi: 10.1007/978-3-319-18603-0_7.
9. *Kudryavceva YuA, Zinchenko SS, Zhuravleva IYu, Ivanov SV, Barbarash LS.* Sorbcionnye i kontaktno-aktivacionnye svojstva zony anastomoza “bioprotez–arteriya”: vliyanie shovnogo materiala (soobshchenie II). *Angiologiya i sosudistaya hirurgiya*. 2008; 14 (1): 113–117.
10. *Pokrovskij AV, Ivandaev AS.* Sostoyanie sosudistoj hirurgii v Rossii v 2016 godu. *Rossijskoe obshchestvo angiologov i sosudistyh hirurgov*. 2017: 5.
11. *Thevenot P, Hu W, Tang L.* Surface chemistry influences implant biocompatibility. *Curr Top Med Chem*. 2008; 8 (4): 270–280. doi: 10.2174/156802608783790901.
12. *Kur’yanov PS, Razuvaev AS, Vavilov VN.* Giperplaziya intimy v zone sosudistogo anastomoza. *Angiologiya i sosudistaya hirurgiya*. 2008; 14 (4): 146–151.
13. *Kastellorizios M, Tipnis N, Burgess DJ.* Foreign Body Reaction to Subcutaneous Implants. *Adv Exp Med Biol*. 2015; 865: 93–108. doi: 10.1007/978-3-319-18603-0_6.
14. *Latypov AK.* Kliniko-funkcional’naya ocenka biologicheskih klapanosoderzhashchih konduitov v posleoperacionnom periode u detej. [Dissertation]. Novosibirsk, 2005, 23.
15. *Krane M, Bauernschmitt R, Hiebinger A, Wottke M, Voss B, Badiu CC et al.* Cardiac reoperation in patients aged 80 years and older. *Ann Thorac Surg*. 2009; 87 (5): 1379–1385. doi: 10.1016/j.athoracsur.2009.01.045.
16. *Svobodov AA, Zelenikin MA.* Sposob bezopasnoj resternotomii. *Grudnaya i serdechno-sosudistaya hirurgiya*. 2008; 1: 66–67.
17. *Gyunter VEh, Hodorenko VN, Chekalkin TL, Olesova VN, Dambaev GC, Sysolyatin PG i dr.* Medicinskie materialy s pamyat’yu formy. Medicinskie materialy i implantaty s pamyat’yu formy. T. 1. Tomsk, 2011, 534.
18. *Ye X, Wang Z, Zhang X, Zhou M, Cai L.* Hemocompatibility research on the micro-structure surface of a bionic heart valve. *Biomed Mater Eng*. 2014; 24 (6): 2361–2369. doi: 10.3233/BME-141049.
19. *Shen X, Su F, Dong J, Fan Z, Duan Y, Li S. In vitro* biocompatibility evaluation of bioresorbable copolymers prepared from L-lactide, 1, 3-trimethylene carbonate, and glycolide for cardiovascular applications. *J Biomater Sci Polym Ed*. 2015; 26 (8): 497–514. doi: 10.1080/09205063.2015.1030992.

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