

The importance of the use of bovine pericardium for surgical reconstructions: a systematic review

A importância do uso de pericárdio bovino para reconstruções cirúrgicas: uma revisão sistemática

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ABSTRACT

Introduction: The use of bovine pericardium started in 1972 in cardiovascular surgeries. From the evolution of tissue engineering with care in the preparation of the material, minimizing the risk of rejection and facilitating the use for various types of surgeries, the bovine pericardium has become an important tool in reconstructive surgical procedures. **Purpose:** In this series, the present study proposes to evaluate the current scenario of the use of bovine pericardium in surgical procedures of different specialties, and the postoperative results found. **Methods:** Thus, a systematic literature review was carried out and the database consulted was MEDLINE, using the keywords “bovine pericardium”, listing studies published in the last five years in English and Portuguese and that did not use another type of patch. **Results:** 14 articles were selected, totaling 507 patients, who underwent surgery in several areas, such as cardiology, neurology, vascular, pediatrics, urology, and ophthalmology. **Conclusion:** It appears that the use of bovine pericardium as a surgical patch is safe, given that there are few cases of host rejection, in addition to being easy and quick to handle, with benefits compared to mechanical prostheses. It is relevant, therefore, to expand the number of studies on the subject, aiming at the great potential that this type of material has for regenerative medicine.

Keywords: Bioprosthesis; Reconstructive Surgical Procedures; Heterografts; Regenerative Medicine.

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RESUMO

Introdução: O uso de pericárdio bovino teve início em 1972 nas cirurgias cardiovasculares. A partir da evolução da engenharia de tecidos com os cuidados na preparação do material, minimizando os riscos de rejeição e facilitando a utilização para diversos tipos de cirurgias, o pericárdio bovino tornou-se ferramenta importante em procedimentos cirúrgicos reconstrutivos.

Objetivos: Nessa casuística, o presente estudo propõe avaliar o atual cenário da utilização do pericárdio bovino em procedimentos cirúrgicos de diversas especialidades e os resultados pós-operatórios encontrados. **Métodos:** Assim, foi realizada uma revisão sistemática da literatura e a base de dados consultada foi a MEDLINE, utilizando a palavra-chave “*bovine pericardium*”, elencando estudos publicados nos últimos cinco anos em inglês e português, e que não utilizavam outro tipo de “*patch*”. **Resultados:** Foram selecionados 14 artigos que totalizam 507 pacientes, submetidos a cirurgias em diversas áreas, tais quais, cardiologia, neurologia, vascular, pediatria, urologia e oftalmologia.

Conclusão: Depreende-se que o uso de pericárdio bovino como remendo cirúrgico é seguro, tendo em vista que existem poucos casos de rejeição do hospedeiro, além de fácil e rápido de ser manuseado, possuindo benefícios frente a próteses mecânicas. Faz-se relevante, portanto, ampliar o número de estudos sobre o tema, visando o grande potencial que esse tipo de material possui para a medicina regenerativa.

Palavras-chave: Bioprótese; Procedimentos Cirúrgicos Reconstrutivos; Xenoenxertos; Medicina Regenerativa.

INTRODUCTION

The use of biological tissues has evolved on a large scale to treat some diseases that are mainly related to cardiovascular surgery, for example, when an autologous vein was used to replace an artery¹. However, although it was essential for the treatment of many pathologies from different surgical areas, autologous or even synthetic grafts had to undergo an innovation, considering that rejection occurred in some patients.

In this context, in 1972, bovine pericardium (BP) started to be used, especially, as an adhesive for arterial closure during vascular and cardiac surgeries^{2,3}. Currently, despite the autologous graft being widely applied, it is important emphasize that bovine pericardium patches when opposed to autologous ones are associated with some benefits, for example, avoiding the need to remove a vein, which can lead to poor wound healing and pain⁴.

Concomitantly, it was found that BP requires preparation before being inserted into the patient, since collagen tissues presents fast degradation and need to be stabilized, in order to prolong the original mechanical structure and neutralize its antigenic properties to increase biocompatibility, then providing a heterologous tissue comparable to autologous tissue^{5,6}.

Nevertheless, despite being widely used in cardiac and vascular surgeries, bovine pericardium is also currently

being used in other areas, for example, in abdominal, urological, renal and even plastic surgeries, demonstrating the importance of BP insertion in surgical medicine.

In this series, the present study proposes to evaluate the current scenario of the use of bovine pericardium in surgical procedures of different specialties, and the postoperative results found.

METHODS

This is a systematic review of the literature about the use of bovine pericardium as a patch in several areas of surgery and your benefits, evaluating the results found in the short and medium term. The research was carried out between January 6 and February 20, 2021 and the database consulted was a MEDLINE® (*Medical Literature Analysis and Retrieval System Online*), and the keywords used were: “bovine pericardium”, then, 1.703 results were found. And the filters used to delimit the results were articles in Portuguese and English, published in the last 5 years, that used only humans and which had an abstract available. 162 results were chosen and the studies were analyzed by the titles and excluded articles of systematic review, meta-analysis, in vitro studies and which one were not related to the proposed theme. As a result, 69 articles were selected and 93 articles were excluded.

The following exclusion criteria were adopted: articles that had repeated procedures and procedures that used other types of materials for graft, such as porcine patch. In addition, as inclusion criteria: articles describing the surgical technique using BP in different types of operations were selected, such as articles that analyzed the post-surgical results of patients operated with BP graft.

This article was not approved by the Research Ethics Committee (CEP), since it is a literature review article (Resolution No. 510 of April 2016 of the Local Committee).

At the end of the research, 22 articles were selected and were completely read, thus, 8 studies that, although addressing different pathologies that motivated the surgical intervention, were the same procedure of reconstruction in heart valves being excluded, leaving, therefore, 14 articles that were included in the review. The 14 selected studies were submitted to analysis and discussion of their results, as explained in Figure 1. The 14 selected studies were submitted to analysis and discussion of their results.

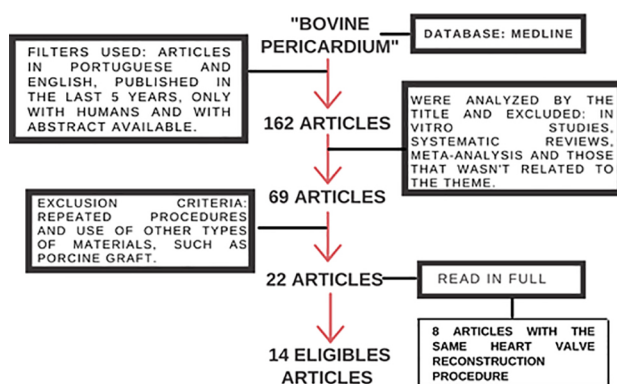


Figure 1. Flowchart with the methodology used.

RESULTS

In total, the sample consisted of 507 patients, who underwent surgery in several areas, such as cardiology, neurology, vascular, pediatrics, urology and ophthalmology (Table 1).

In general, it is clear that the use of BP has great practical applicability and a great predominance of findings involving cardiovascular surgery. In this review addressed studies that treated the reconstruction of heart valves, aorta and pericardium, finding good results in the short and medium term in regarding material stability, resistance to infections and normal cardiac function performance^{8,10,11,14}. In relation to vascular surgeries, this type of graft was used for vena cava reconstruction and repair of arteriovenous fistula (AVF), emphasizing the material's feasibility in terms of ease in handling, good permeability and dispensing with the use of anticoagulants^{12,15}.

With regard to gynecology and obstetrics, the patch was directed to breast repair in patients undergoing Conservative Mastectomy and repair of dehiscence of cesarean healing, obtaining good results aesthetics^{9,13}. About neurological intervention, the BP was used in peripheral nerve surgeries and as an artificial dura mater substitute in patients with

traumatic brain injury, without adverse reactions and with favorable clinical outcomes^{7,17}.

For more, some procedures using BP in different specialties, for example, urology, neonatology and ophthalmology, there is still no concrete indication in the literature, however, favorable results were found for its use, such as, repair of a giant omphalocele in a newborn, and stretching of the tendon of the muscle medial rectum in patients with severe esotropia. In addition to surgical treatment of large tracheoesophageal fistulas with wall laceration tracheal membrane and tunic defect repair albuginea in patients with Peyronie's disease^{16,18-20}. In this context, there was no evidence of graft rejection and only four patients suffered adverse reactions, becoming a possibly safe option for such procedures.

DISCUSSION

About the preparation of the biomaterial, commercially available patches are processed to be acellular, preventing transplantation of bovine proteins or DNA into the host. Glutaraldehyde is a typical processing agent, crosslinking –NH₂ groups of lysine, hydroxylysine, or the N-terminus of amino acids, to form amine linkages with the elimination of water; these amine linkages form covalent bonds between adjacent proteins that are stable at physiological temperature and pH. The resultant cross linking process increases tissue strength to inhibit biodegradation, as well as reduces antigenicity to sterilize the tissue. The histological analysis showed a commercial grade BP prior to implantation, demonstrating its lack of cells or elastin; only collagen is easily detected in the patch. Elimination of residual glutaraldehyde, prior to patch implantation, is important to prevent late patch calcification *in vivo*²¹.

Consequently, Sheng et al. (2019)¹¹ related the replacement of the aortic valve in 36 patients with moderate to severe regurgitation, using the Ozaki technique, this cohort of patients was followed up for 6-47 months, and none of the patients until the moment had any fibrosis, contraction or calcification of the BP. The absence of embolic events in the absence of anticoagulation and the applicability to any type of aortic valve disease were probably the main advantages of this technique¹¹. At this juncture, Cua et al. (2020)⁸ reported the complete removal of the mitral valve in a 10-month-old patient diagnosed with Marfan syndrome, and the construction of a cylindrical valve from BP. Then, it becomes an initially safe option for valve replacement in pediatric's population, since bioprosthesis can undergo degeneration due to the host's response and mechanical values require the use of anticoagulation⁸.

Stephens et al. (2019)¹³, presented the case of a 30-year-old patient during the twentieth week of gestation who had a cesarean scar dehiscence, the BP was chosen because it is easy to suture and to stick to native tissue easily. As a result, interlaced fibers result in multidirectional strength and stability under tension, and these qualities are especially important in an increasingly distended uterus. Finally, the baby was born preterm at 35 weeks, however, healthy¹³. Concomitantly, in Castagnetti et al. (2020)⁹, all patients underwent conservative mastectomy with breast reconstruction based on immediate implantation using a BP matrix. And despite the costs, its use seems safe and

Table 1. Description of included studies.

Autores	Local do estudo	Tipo de estudo	Ano de publicação	Descrição do procedimento com PB	Conclusão
Carolus et al. ⁷	Germany	Case report (n=9)	2020	Use of processed bovine pericardium in peripheral nerve surgery.	All patients showed improvement in respect of function and of pain. There were no adverse reactions as a consequence of the material used.
Cua et al. ⁸	United States	Case report (n=1)	2020	Mitral valve construction using decellularized bovine pericardium in a neonatal patient with Marfan syndrome.	The use of BP at the MV construction had good early and midterm results 19 months after surgery with favorable impact on left ventricular function and both left ventricular and left atrial dimensions
Castagnetti et al. ⁹	Italy	Retrospective non-randomized observational study (n=123)	2020	Use of bovine pericardium for breast reconstruction in patients undergoing conservative mastectomy.	It's believed that procedures improved the aesthetic outcomes, optimizing the inframammary fold definition and allowing for more natural ptosis in patients who do not desire mastopexy in the contralateral safe breast.
Belkorissat et al. ¹⁰	France	Retrospective descriptive study (n=20)	2019	Tubular reconstruction with bovine pericardium xenografts to treat native aortic infections.	The results of one year show the resistance to infection of bovine pericardium tubes and their stability in the aortic position.
Sheng et al. ¹¹	China	Retrospective cohort (n=36)	2019	Aortic valve replacement using bovine pericardium in patients with aortic valve regurgitation.	The replacement of the aortic valve using bovine pericardium in the treatment of aortic insufficiency is feasible, and good initial and intermediate results are achieved.
Morris et al. ¹²	Australia	Retrospective cohort (n=15)	2019	Resection and reconstruction of the inferior vena cava using bovine pericardium for renal cell carcinoma.	Reconstruction of the inferior vena cava with bovine pericardial graft is safe in experienced centers. Bovine pericardium can be considered the material of choice, given its safety in the immediate postoperative period, ease of use and permeability, without routine long-term anticoagulation.
Stephens et al. ¹³	United States	Case report (n=1)	2019	Use of bovine pericardium to repair dehiscence of a caesarean scar during pregnancy.	Bovine pericardial graft is a viable graft as an option to correct cesarean scar dehiscence in the second trimester.
Fiedler et al. ¹⁴	United States	Case report (n=1)	2018	Use of fenestrated bovine pericardium to repair traumatic rupture of the pericardium with cardiac herniation.	The use of fenestrated BP allowed the heart to be returned to the normal anatomical location and, minimizing the postoperative collection of pericardial fluid.

Rossetti et al. ¹⁵	Italy	Case report (n=1)	2018	Repair of arteriovenous fistula (AVF) with bovine pericardium in drug abuse patients.	Surgical repair of AVF in drug users by interposition of biological adhesive is a challenging technique, but viable and effective, with encouraging results in the medium term in terms of permeability and resistance to infections.
Vargas-Mancilla et al. ¹⁶	Mexico	Case report (n=1)	2018	Repair of a giant omphalocele with bovine pericardium in a newborn patient.	The repair of a giant omphalocele with a BP implant resulted in a short stay in the hospital, early integration into the patient's family environment, as well as early oral administration without restrictions on food or special care.
Sun et al. ¹⁷	China	Retrospective observational study (n=195)	2018	Bovine pericardium as a substitute for artificial dura mater in patients with traumatic brain injury undergoing decompressive craniectomy.	The bovine pericardium membrane is a successful substitute for decompressive craniectomy and the patients achieved better results than the control group.
Oeverhaus et al. ¹⁸	Germany	Retrospective observational study (n=60)	2018	Stretching of the tendon of the medial rectus muscle with bovine pericardium in patients with severe esotropia after Decompression in Graves' Orbitopathy.	Stretching the tendon with bovine pericardium is a safe surgical method to correct severe esotropia after decompression, which cannot be corrected with simple recessions of the medial rectum.
Suciu et al. ¹⁹	Romania	Case report (n=1)	2018	The use of heterologous bovine pericardium in the surgical treatment of large tracheoesophageal fistulas and laceration of the membranous wall of the trachea.	In addition to the use of a heterologous patch of bovine pericardium in the reconstruction of the membranous wall of the trachea, BP was also used to protect the esophageal suture.
Otero et al. ²⁰	Spain	Retrospective cohort (n=43)	2017	Use of bovine pericardium graft to repair tunical defects in patients with Peyronie's disease.	There is no evidence of rejection or infection, and only four patients experienced an adverse event.

facilitates less invasive procedures and with less capsular contracture in the long-term⁹.

Carolus et al. (2020) used a BP patch in nine patients who underwent peripheral nerve surgery, surrounding the injured nerve or as a fixed extension. In 5 cases, patients suffered from motor and sensory loss in the ulnar or median nerves that had occurred after trauma surgery and that did not involve complete nerve separation. 3 patients had recurrent nerve compression syndrome, and 1 patient had a nerve trauma with a complete nerve cut. With regard to the criteria of sensitivity to touch, sensitivity to temperature, sensation of "burning" and sensation of "electric pain" all patients showed improvements⁷. In this perspective, Sun et al. (2018)¹⁷ analyzed

192 patients who were treated with standard decompressive craniectomy without dura mater repair (Control Group), and 195 patients were treated with decompressive craniectomy followed by repair of defective areas of the dura mater with BP (ADM group). The results showed that the control group had a higher rate of complications, such as subcutaneous hematoma, intracranial infection, spontaneous cerebrospinal fluid leak and seizures¹⁷.

Regards to vascular surgery, Belkorissat et al. (2019)¹⁰ carried out a retrospective descriptive study including all patients with extensive aortic mycotic aneurysms and the arterial reconstruction was performed with a tube made with BP. In this study, no death was directly related to the

graft, and no early or late complications were observed, with a higher permeability rate than with allografts, which are associated with reported occlusion rates between 5% and 9%¹⁰. Otherwise, Morris et al. (2019)¹² performed an analysis on patients undergoing reconstruction of the inferior vena cava as part of oncological resections for renal cell carcinoma with BP, either as a patch repair or tubular interposition graft. There were two thrombotic complications associated with the long-term graft, which required only temporary anticoagulation; however, there were no short or long-term infectious complications. In addition, improved overall survival for stage 4 patients¹². Finally, Rossetti et al. (2018)¹⁵ reported the repair of a femoro-femoral AVF by interposing a bovine pericardium patch in a 36-year-old patient with a history of heroin and cocaine abuse. At 18-month follow-up, a doppler scan confirmed the permeability of femoral arteries and veins, the absence of AVF or deep vein thrombosis, or signs of infection in the right groin¹⁵.

Fiedler et al. (2018)¹⁴ presented a case of a 15-year-old patient who cursed with chest and abdominal trauma secondary to the collision of a motor vehicle, with a late diagnosis of traumatic pericardial rupture with cardiac herniation. Three fenestrated BP patches were used to correct the problem and the heart was returned to its anatomical position¹⁴. Therefore, Suciu et al. (2018)¹⁹ exemplified the case of a 32-year-old patient, victim of multiple trauma due to traffic accident, because of this, gastroscopy and bronchoscopy exams revealed a large 7x3cm tracheoesophageal fistula, with tearing of the tracheal membranous wall. The reconstruction of the membranous wall of the trachea was performed with a heterologous patch of BP, as well as the restoration of the esophageal wall. Bronchoscopy performed 20 days after surgery revealed the complete integration of the patch with the absence of any signs of esophagotracheal fistula or rejection¹⁹.

Same way, Vargas-Mancilla et al. (2018)¹⁶ narrated a case of a newborn male patient of 2 days of extrauterine life with giant omphalocele. Soon, the patient was stabilized, and the abdominal wall defect was closed with the BP implant. After the sixth month, in a medical-surgical session, it was decided to remove the implant and continue with the secondary reconstruction of the abdominal wall. The histological results showed an implant in the process of muscle remodeling, characterized by bundles of well-formed muscle fibers, with abundant vascular neoformation and total absence of inflammatory cells, in favor of an adequate muscle remodeling¹⁶. In addition, Otero et al. (2017)²⁰ they analyzed a total of 43 patients with disabling penile curvature that interfered in sexual intercourse due to Peyronie's Disease. In the present series, a BP patch was used for grafting. The results achieved were highly satisfactory, with 75% of treated patients not needing any additional treatment, whether pharmacological or surgical, to achieve a successful sexual relationship and complete penile straightening was achieved in 80% of patients²⁰.

Like this, Oeverhaus et al. (2018)¹⁸ described the stretching technique of the tendon with BP in patients with severe esotropia after decompression in Grave's orbitopathy. The posterior end of the implant was sutured with the muscle, just behind the insertion, the muscle was then detached and the proximal end of the implant sutured to the sclera, 4mm behind the insertion to avoid

visibility through the conjunctiva. With regard to bilateral tendon stretching, both MR muscles were moved back by 4mm and stretched with bovine pericardium. Although this cohort of patients contained the most severely affected class of patients with decompression, the final success rate is satisfactory. About 83% of all patients had stereopsis at 1-year follow-up¹⁸.

CONCLUSION

Therefore, it is found that the use of bovine pericardium is safe and effective in several types of surgical procedures, because of the few cases evident in the literature about host rejection, since its preparation inactivates the donor cells. In addition, it has low cost and high malleability, being easy to use and not requiring a long time of operation. Furthermore, it works well as an adhesive in different types of structures, such as vessels, nerves and skin, proving to be useful for many medical specialties. It also does not require anticoagulant therapy, as opposed to mechanical prostheses. Nevertheless, long-term studies are needed to better evaluate the results of these implants in different samples.

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