Historical Overview of Vascular Allograft Transplantation

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Abstract

There is a mix of therapeutic options for revascularisation in vascular surgery. The authors performed a literature review on the evolution of vascular allograft transplantation and its use and acceptance by vascular surgeons. This review exposed three stages: the first stage involved preliminary experimentation; the second stage was a decline in use due to long-term complications, and the third stage is its current use in special indications subject to a thorough analysis. There are few indications for the use of vascular allografts in clinical guidelines. However, there are publications of long series of case studies with variable results reflecting international use of the procedure. There is a current trend that favours its use with limited and individualised indications.

Keywords

Vascular allografts, vascular transplant, grafts

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The donation and transplantation of organs, tissues and cells is now an attractive and widely proven therapeutic option, which involves practices, that are accepted as commonplace, such as kidney and liver donation; but it also involves less striking practices such as tissue transplantation. A literature review was conducted to know the history of this practice. Three different stages were stablished according to the authors' perspective. Eligible English- and Spanish-language articles published were identified through searches of PubMed (no time limits).

With more and more indications, the transplantation of vascular tissue is an emergent practice, which began in the early 20th century and has gone through several stages. Since the publication of preliminary experiences, its use was abandoned due to possible long-term complications and it has been taken up at the end of the 20th century for special indications and has been subject to in-depth analysis.[1,2]

Stage 1

Although Hopfner described the possibility of performing the technique in 1903, the history of vascular tissue transplantation began in the hands of Alexis Carrel. This French biologist, physician and researcher is considered a pioneer in vascular surgery. Carrel described surgical techniques used on animals by 1905. These techniques involved transplant of venous segments in arterial territories in mice and he described the process of arterialisation and exposition of the conservation of blood vessels for transplant with the intention of avoiding the need to find possible donors.[2–5]

In 1906, there was an important publication describing the first two successful human cases of bypass using autonomous vessels.[6] The first described a femoro-popliteal shunt with a femoral vein and the second was a resection of a popliteal syphilitic aneurysm and its subsequent replacement by a popliteal vein.[6]

A year later, Lexer described the transplantation of an 8-cm vein segment after resection of a left subclavian artery aneurysm caused by dislocation of the humerus. These initial steps saw the beginnings of vascular tissue transplantation with autologous grafts.[7]

Other isolated publications included the case described by Pirovano in 1910 of the first transplant of vascular allografts, which was not successful, and a case series reported by Moure in 1914, who described 17 transplants of venous allografts with good results.[2,6]

In 1908, Carrel made a significant breakthrough by creating the first experimental blood vessel bank, leading to the Nobel Prize for Medicine in 1912 in recognition of his work on vasculature and the transplantation of blood vessels and organs.[2] In the same year, he also published an article in which he demonstrated that an artery portion can be preserved and kept 'alive' in a chamber for several days or even weeks before transplantation. He found that blood vessels from dogs kept in a cold room can be transplanted successfully into cats and concluded that these methods could be applied to humans and there should be no delay to exploring this, but it was not until 1951 that Fontaine and Leriche founded the first bank of blood vessels for clinical use.[2,6]

Stage 2

The second stage of vascular tissue transplantation is characterised by a significant decline in its use due to unsatisfactory long-term

results. The poor results were possibly related to deficient preparation and preservation techniques. In this stage, there were cases of degenerative alterations with subsequent aneurysmal dilatation related to immunological responses. This led to an exploration of the use of synthetic prostheses.[6]

In 1952, Voorhees et al. performed animal studies that demonstrated the patency of synthetic derivatives in vascular territory and translated its application into clinical practice.[7] This technique had a rapid evolution. Among the materials used were Ivalon, Orlon, nylon, Teflon and Dacron. In 1969, prostheses that are still in use today were developed by Gore, which developed the Teflon graft.[6,8]

Prostheses were developed with the ideal aim being described in 1953 as: "biologically inert, with stable physicochemical properties, guaranteed sterilisation, easy handling, non-carcinogenic and non-thrombogenic surface". These criteria were later modified by Moneta and Porter in 1995 when they described the ideal prosthesis as "strong, inexpensive and possible to be used throughout the patient's life, with easy and permanent insertion, biocompatible with the host, resistant to infection, with appropriate gauges, that remains permeable due to the visco-elastic properties resembling a natural artery without allowing blood or serum to escape, that does not degenerate or elicit an abnormal proliferative response of the vessel or tissue, non-thrombogenic or emboligenic, the one that does not occlude by flexing and does not damage the components of the blood".[9] These criteria revealed large defects in the vascular allografts; however, no synthetic arterial substitute has ever been able to comply with all these conditions.

There were important achievements in this second stage, such as that of Gross in 1948, who replaced a segment of homologous aorta in a case of coarctation, establishing the technique as the first choice until the development of the prostheses. Similarly, Oudot in 1950 was the first to replace the aortic bifurcation and Dubost in 1951 the first to use a homograft after resection of an abdominal aneurysm.[6,8]

During this stage, some groups, including the one led by DeBakey, published series of cases that have not been possible to match.[6,8]

At present, thanks to advances in techniques of collection, processing and storage of the grafts, now called vascular allografts, and the progress in organ donation and transplantation, cryobiology, immunobiology, histocompatibility determinations and immunosuppressive therapy, these grafts are being reconsidered for use in a greater number of indications, thus starting the third stage of vascular tissue transplantation. All this is in the context of the development of commercial prostheses as the first indication in almost all cases of vascular segment replacement.[6]

Stage 3

Vascular transplantation began being used again with prudence and with limited indications. Among these indications was the replacement of complex arterial segments, complex vascular lesions, replacement of infected arterial prostheses and, although it is little studied, the use in vascular access for patients on haemodialysis. Mestres summarised the use of these grafts in three indications and confirmed long-term results. He described some benefits regarding the reduction of hospital mortality, a high patency rate and a minimal rate of reinfection and rupture up to 10 years' post-intervention.[2,6,10,11]

In this third stage, immunology was the objective of research. In 1989, Koene described the role of adaptation in the acceptance of allografts. He concluded that the long-term survival of the allograft depends on these immune responses.[12] Previously Prendergast et al. observed immunological sensitivity and concluded that allografts generated immunological responses.[13]

More recently, the role that innate immunity and antibodies play in the rejection of grafts has been explored. So-called 'allograft vasculopathy' has been linked to a chronic inflammatory response mediated by natural killer cells, but carried out directly by donor-specific antibodies. Donor antibodies ultimately induce intracellular cascades that facilitate recruitment of monocytes and neutrophils, damaging the transplanted tissue. This area is still being researched.[14]

This gave rise to the experimental application of tissue transplantation and to the development of animal models. In 1983, Chow et al. performed the replacement of femoral arteries with cryopreserved tissues and compared the results with the replacement of autologous tissues, concluding that both techniques were similar.[15]

In 1997, Neves et al. published their findings on mechanisms of degeneration of cryopreserved grafts, analysing them in sheep. They concluded that there is partial loss of the endothelium and lymphocytic invasion in the entire graft, despite which the grafts maintain their integrity and cellular viability after transplantation. They showed evidence of re-epithelialisation of the graft and after a short period of neural degeneration, a reinnervation occurred. No statistically significant differences were found between transplants of fresh vascular tissue versus those that were cryopreserved.[16]

Among the alternative studies in the translational field is the model on venous grafts treated with glutharaldehyde performed by Moura in 2009. He performed experiments in rabbits whose grafts were assessed macroscopically and microscopically at 24 hours, 14 and 28 days. In his conclusions, he suggested the need to expand studies in the field of autologous tissue transplantation, since he showed that there were no clear differences in the technique he proposed. He also explained that this technique could provide an important tool for human use.[17]

Perhaps the three most recent translational works are those published by Sun et al. in 2010, Hwang et al. in 2011 and Olmos-Zúñiga et al. in 2016.[18–20] Sun et al. explained an improved technique for performing aortic transplants in a murine model and demonstrates pathognomonic changes of chronic rejection but with longer-term tissue survival rather than usual techniques.[18] Hwang et al. designed an experimental platform for the development of biocompatible microvasculature in rats and he showed that its model is potentially translatable and effective for future tissue engineering studies of small vessels.[19]

Olmos-Zuñiga et al. published the haemodynamic, gasometric and imaging results, as well as macroscopic and microscopic findings of the reconstruction of pulmonary arteries of dogs with lyophilised grafts (those not treated with glutaraldehyde) and cryopreserved arterial grafts. They suggested that the lyophilisation techniques may play in favour of less antigenicity, as well as preventing thrombosis and calcification of the grafts. Finally, they concluded that the lyophilisation without treatment with glutaraldehyde represents a feasible alternative with promising clinical results.[20]

Among the described clinical cases is the correction of coarctation of the thoraco-abdominal aorta with autologous cryopreserved arterial graft performed in a 7-year-old boy with a correct postoperative ultrasound, doppler ultrasonography with no significant changes with respect to a healthy subject, correct clinical values and good quality of life after the procedure.[21]

In 1998, an extensive study was published by Chiesa et al. that assessed differences between cryopreserved and fresh vascular tissues and concluded that there were no statistically significant differences between them.[22] They described a 12-month tissue survival of 73% and reported the possibility of assessing ABO blood group compatibility among donors. This possible incompatibility has been dismissed in 2015 by Della Schiava et al., who considered that the immunological response may be related mainly to incompatibility of the major histocompatibility system. In this way, the clinical variables associated with the donor and recipient allografts become important.[23]

The use classically associated with this type of graft is the replacement of infected prosthetic segments. This was described in 2004, where the replacement of infected grafts in the infrarenal aorta by vascular allografts was presented in a series conducted over 14 years.[24] Kieffer et al. concluded that vascular allografts, in the short as well as long-term are at least similar in behaviour to other replacement techniques in terms of the management of infra-renal prosthesis infections. They also found that most of the complications associated with this type of grafts are avoidable with an adequate cryopreservation process. Previously in 2001, Leseche et al. had commented on the usefulness of the use of vascular allografts in prosthetic infections, and in 1996, Koskas et al. documented 6 years of experience replacing infected prostheses from 83 cases with several postoperative complications, but with a limb survival rate of 100%.[25,26]

In 2009, Brown et al. published their mid-term results for arterial reconstruction with cryopreserved vascular tissue in cases of prosthesis infections.[27] They presented a series of 52 patients followed up over 10 years that showed that the replacement of infected vascular prostheses by vascular allografts was a viable alternative. They stated that with adequate cryopreservation, allografts are resistant to reinfection, thrombosis and aneurysmal dilatation and recommended a long-term study to evaluate whether this technique is the most successful, effective and safe.

More recently, in Greece, Locati et al. published a short series of 18 patients where 25 infected prostheses were replaced in different areas such as femoro-popliteal, aorto-iliac, and subclavian, concluding that these techniques are very useful in this indication since these grafts seem to have a greater resistance to infection.[28]

In 2010, a German team published an 8-year follow-up of patients treated with cryopreserved arterial homografts using exposure to C-reactive protein and leukocytes as analytical parameters to monitor during the immediate postoperative period.[29] They also proposed that platelets and body temperature were important clinical parameters in the postoperative period. The team reported an 81% survival of transplanted tissue and free of re-interventions at 3 years. In the remaining 19% of patients, there were occlusions, stenosis, aneurysmal degenerations and graft-duodenal fistulas. It was concluded that the vascular allografts were a useful alternative.

A more unusual use as pulmonary artery augmentation in a lung transplant has been described by Pablo Rueda et al. in 2005.[30] They performed enlargement of the pulmonary artery in a case of inadequate organ extraction using an aortic artery allograft and concluded that the technique was useful to avoid the loss of the organ.

The use of a graft in vascular access construction for hemodialysis was described in 2016 by Ha et al. as an alternative for immediate dialysis and with a survival rate comparable with other types of grafts.[31] However, not all published results are so positive. In Italy in 2011, Ravenni et al. reported a case of total calcification of a homologous vascular graft used in the replacement of the aortic root in a 66-year-old man.[32] Similarly, Minga Lowampa et al. published a series of 103 patients with replacement of prostheses infected by allografts whose short-term results were unfavourable with a high rate (29%) of postoperative complications, such as graft thrombosis, anastomotic pseudoaneurysm, aneurysmal degeneration and graft rupture.[33] However, the authors comment on methods that could improve these results.

Conclusion

There are limited data on the long-term evolution of vascular allografts. The research continues with a focus on advances in cryopreservation, immunology and alternative tissue preparation. At present, only one indication of vascular allografts have been established in clinical guidelines (replacement of infected grafts). Despite the wide use around the world, each case, indication, patient and territory should be assessed individually, with more data and studies needed to clarify the most appropriate indications. ■

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