The use of Valve Homografts and Autografts in Adult Cardiac Surgery

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Grafts derived from humans are called homografts. In the literature confusion exists with the use of terms: homografts, autografts, xenografts and allografts in cardiac surgery. Specifically, with the terms homograft and/or autograft many surgeons referred to the grafts coming from the patient himself (eg the transposition of the pulmonary valve to the aortic position – Ross procedure), while allograft was called the graft deriving from another person (cadaveric)[1]. Currently, the term homograft –aortic, mitral, pulmonary– indicates processed grafts coming from another person (cadaveric), while the term autograft is reserved only for grafts coming from the patient himself. The term allograft is nowadays rarely used, since it has the same literal meaning as the term homograft. Finally, the term xenograft refers to biological (tissue) prosthetic valves, originating from animals (porcine, bovine, etc).

In this article we review the utilisation of homografts (processed cadaveric valves) and autografts in adult cardiac surgery.

History

The utilisation of homografts in clinical practice began in 1956 by G. Murray, with the implantation of an aortic homograft in the descending aorta[2]. However, the first orthotopic (aortic) homograft implantation of was carried out in 1962 by D. Ross in England[3], after A. Gunning and C. Duran's experiments in Oxford[4]. The first successful applications were followed by a period during which every effort was made to perfect graft retrieval and preservation techniques and, consequently, the improvement of the clinical results. The sterilization of cadaveric homografts was initially performed with γ–radiation or with ethylene-oxide[5,6]. B. Barratt-Boyes from N. Zealand introduced the use of antibiotics in the sterilization process, in the early 70's[7], while cryopreservation as the graft preservation method, which is currently still in use, was introduced by the Australian M. O' Brien[8].

Protocols of homografts processing technique

Homograft retrieval should be performed within 48 hours from death. After harvesting, the grafts are placed in an antiseptic solution containing a combination of antibiotics (carbenicylin, polymixin, cefuroxime, canamycin, vancomycin and mycostatin), where they remain at 4^0C for 7 days. During this period the tissues are checked for contamination (aerobic, anaerobic, fungi, mycobacteria, etc) and examined for HIV, HbsAg, Anti-HCV, Q-fever, syphilis and treponima. After a detailed macroscopic check, suitable grafts are either kept in 0-4^0C for use within 6 weeks as "fresh", or are frozen at -150^0C in liquid nitrogen (cryopreservation) facilitating their preservation for

up to 10 years[9,10]. Other methods of preparation and sterilisation of homografts also exist, such as the use of radiation, propionolactone, chlorexidine, formaldehyde, etc[11].

Unsuitability of homografts results when the donor either has a history of AIDS, hepatitis B or C, syphilis or other contagious disease (of various pathology), or if the cause of his/her death was bacillar or virus septicemia, Marfan syndrome or myocardial tumor. Donor age is a relative contraindication for the utilisation of a graft and donors under the age of 60 (or 62) are generally preferred[9,10].

The histocompatibility (HLA) control– homograft crossmatching – to avoid graft degeneration (due to the activation of the recipient's immune system leading to antibody formation), although still performed in certain centres, appears to be unnecessary, as the valvular endothelium lacks expression of carbohydrate antigens[12]. Nevertheless, the effect of histocompatibility on the long-term results with the use of homografts is still being discussed[13].

Clinical applications of homografts

Indications for the use of homografts include: replacement of the aortic, pulmonary, mitral and tricuspid valve, replacement of the aortic root, as well as replacement or repair of cusps of the aortic, pulmonary, mitral and tricuspid valve and Ross procedure[14,15].

The advantages in their use are: no need for anticoagulation (absence of danger of thromboembolic events), absence of haemolysis, lack of ring/cuff of graft support (minimising the transvalvular gradient compared to the stented prosthetic valves) with, generally, very good haemodynamic performance (similar to that of stentless valves), higher resistance to endocarditis compared to all the other valves, etc. Particularly, the use of homografts as a complete aortic root replacement in cases of complex aortic valve endocarditis, allows the resection or isolation from the circulatory system of all the infected tissues with radical elimination of the infection.

Disadvantages include: more demanding implantation technique, not immediate reimplantation (transplantation) of the graft (with a possible need of immunosuppression) and, mainly, difficult access to a "Homograft Bank". The homografts' processing technique results in an acellular graft, which in time i degenerates and calcificies[16]. New methods which will preserve the cellular viability without activating the patient's immune system are believed to improve the result; Yacoub et al have already reported very good results with such a technique (homovital homografts)[17]. However, the problem of grafts' antigenic expression following such techniques exists[18], although the clinical importance of antibody production remains unknown. Finally, the considerable cost of homografts is an important disadvantage totalling roughly 1400 dollars a piece for the ad hoc preparation , while the open market cost averages 5000 dollars each[19].

Results from aortic homografts use

The homografts can be used for the replacement of the aortic valve in three ways: a) replacement of the valve with graft implantation under the coronary ostia (subcoronary implantation), b) "mini" replacement of the aortic root with intraluminar implantation of the graft (mini-root) and c) complete aortic root replacement with reimplantation of the coronary arteries[20].

The latest results from the use of homografts in the aortic position are very good. Doty et al[21] report 10-year freedom from valve-related mortality - 93%, from thromboembolic events - 100%, from valve endocarditis - 98% and from reopearation - 92%. In another series with a 20-year follow-up, the results were respectively: a) 10-year survival - 78.5%, 15-year -65.7%, 20-year - 55.0%, b) freedom from reoperation in 10 years - 87.9%, in 15 years - 71.7%, in 20 years - 49.7% and c) freedom from valve endocarditis 98.4% in 10 years, 96.2% in 15 years, 95.1% in 20 years[22]. Finally, in the biggest series in the literature[23] 20-year survival was 19±7%, the reoperation rate over 20 years was 50% and freedom from endocarditis at 20 years was 89%, while over 15 years freedom from reoperation due to degeneration of the cryopreserved graft was dependent upon the patient's age: 47% in <20 year-old patients, 85% in 21-40 year-old patients, 81% in 41-60 year-old patients and 94% in >60 year-old patients.

Utilisation of homografts in aortic valve endocarditis has also given good results. In such a group of patients, Vogt et al report a 97% 5-year survival, with freedom from reoperation and endocarditis 69% and 85% respectively for the same period[24]. In another group of patients with aortic valve endocarditis the use of homograft or autograft had better results than the use of mechanical prosthetic valve.

Specifically, the 5-year survival was 69% in patients with homografts, 88% in patients with autografts and 29% in patients with mechanical valves, while recurrence of endocarditis was found in 3% in the first two groups and in 12.5% of the patients with mechanical valve[25].

Finally, the results from utilisation of homografts in aortic valve reoperations are also very good. In a 10-year follow-up of Albertucci et al's patients[26], freedom from valve related death and/or reoperation was 70%, while absence of recurrence of endocarditis was 88%. Moreover, the theory of accelerated degenerative process after reoperations does not appear to be correct, since it has a 93% 5-year and 82% 10-year survival, as well as freedom from reoperation 97% in 5 years and 82% in 10 years[27].

With regard to the haemodynamic performance of the homografts, transvalvular gradient is lower (3-5mmHg at rest[28]) and left ventricular mass index regression postoperatively is greater with homografts and stentless valves when compared to stented prostheses (mechanical or biological)[29]. Concomitantly, there is an earlier and, after all, greater regression of left ventricular hypertrophy, as well as better clinical result and improved quality of patients' life. However, valvular graft regurgitation may appear postoperatively in some patients. It seems that the main reason for the postoperative sufficiency or insufficiency of the valve is the operative technique. The intraluminar implantation of a graft in subcoronary position may lead to incomplete coaptation of the cusps of the graft and to distortion of the aortic root, resulting in the progressive insufficiency of the graft. On the contrary, the "mini" root, as well as the complete aortic root replacement, has excellent results, minimising the valvular insufficiency postoperatively[30]. Dearani et al recorded severe valvular insufficiency (stage III) after 7-year follow-up in 26% of their patients when the former technique was used and only in 12% following the latter procedures[31].

Regarding late morbidity with the use of homografts as opposed to mechanical prosthetic valves in a 4-year follow-up study, thromboembolic events and valve endocarditis were more frequent in patients with mechanical valves, while serious bleeding was noted only in these patients and not in those with homografts[32].

During the last decade clinical application of stentless valves appears to have results similar to those of homografts (in 5 years: survival 80% and 77%, freedom from endocarditis 99% and 91%, freedom from thromboembolic events 90% and 98%, freedom from reoperation 100% and 98%, respectively)[33]. Also, their haemodynamic performance is similar to that of homografts and better than that of mechanical prosthetic valves[34].

Results from pulmonary homografts use

Pulmonary homografts are used in paediatric cardiac surgery for correction of congenital anomalies, in Ross procedure for the pulmonary valve replacement and in the replacement of the aortic valve[35]. In the first two options the results are very good, while in the aortic position it seems that they are inferior to aortic homografts[36], because their use constitutes an independent prognostic factor of valvular insufficiency[37]. The forces that develop in the aortic root can dilate a pulmonary homograft roughly about 30% more than an aortic[38], thus causing insufficiency of the valve in up to 1/3 of the patients[39].

After the first aortic valve replacement with a pulmonary autograft by D. Ross[40] and the initial enthusiasm, the Ross procedure was widely questioned; however, after the publication of good results in the early '90s[41] and the establishment of an International Registry in 1993, it reappeared in the "foreground".

In Kouchoukos et al's Ross procedure patients[41], after a mean follow-up of 21 months, no mortality and no endocarditis were observed and there was no reoperation of the aortic valve, whereas reoperation for replacement of the stenotic pulmonary homograft was required in 3%. Elkins[42] reported 89% survival, 94% freedom from autograft replacement in aortic position and 90% freedom from homograft replacement in pulmonary position after 8 years of follow-up. The results of the 1394 (decade 1987-1998) out of 2523 patients (in total, from 1967 to 1998) of the International Registry[43], from 122 cardiac centres (166 surgeons) worldwide, are the following: operative mortality 2.5%, late mortality 1.7%, reoperation 5.4% (1.9% autograft replacement, 2.2% autograft repair, 1.3% reoperation for degeneration of the homograft in the pulmonary position), freedom from severe insufficiency of the valve 86%. Finally, in the group of patients of Moidl et al[44] morbidity after the Ross procedure was: bleeding or thromboembolic events - 0%, endocarditis - 0.7% and valvular insufficiency - 0.7% per patient per year.

A relatively important advantage in the use of pulmonary autograft in the aortic position is the

continuation of valve's growth, since it is a living tissue of the same patient (hence, we have a case of "autotransplantation"). On the contrary, homografts are processed and fixed tissues, which, of course, cannot keep growing. The transformation of a single valve (aortic) to double valve (aortic and pulmonary) disease is considered a disadvantage. Although, as shown in the results of the International Registry, the problem of graft degeneration in the pulmonary position is not that large, there are series of patients where severe stenosis of the graft (> 20 mmHg transvalvular gradient) was found in up to 1/3 of patients after 3 years[45]. Various factors could be blamed for these unsatisfactory results, such as the youth of the donor' and a short period of graft' cryopreservation that could lead to increased cellular viability and likely activation of the immune system[45]. Moreover, it seems that the intraluminar implantation of the autograft decreases its ability to grow and can lead to its calcification[46].

Application of the Ross procedure in active endocarditis is questioned, as it may also lead to infection of the homograft in the pulmonary position. However, good preliminary results from this practice have recently been reported[47]. It should be pointed out that use of pulmonary homograft in young individuals with active rheumatic fever is not recommended, because it can lead to graft infection. Furthermore, the pulmonary valve of individuals with Marfan syndrome is not a graft of choice, as in these cases medial necrosis of the pulmonary artery and myxomatous degeneration of the valve are noted[45].

Comparison of autografts with homografts in the aortic position shows similar results for their haemodynamic performance[48], as well as in 10-year follow-up with regards to survival (77% vs. 67%) and freedom from reoperation (88% vs. 72%), degeneration of the graft (97% vs. 79%) and graft-related complications (73% vs. 64%)[49]. In any case, while degeneration of both grafts during the first 8 years is limited, it then begins to increase particularly in homografts[49].

Pulmonary homografts for mitral valve replacement were first used by D. Ross in the '60s[40]. However, even though good results have been reported[50], difficult operative technique, prolonged operation and several relative contraindications (pulmonary hypertension, chronic atrial fibrillation, other coexisting cardiac diseases that require concomitant repair, small left atrium, etc.), limit its usefulness and popularity.

Results from mitral homografts use

Early results from utilisation of mitral homografts in the mitral position are not particularly satisfactory. Kumar et al reported severe insufficiency of the graft in 85% of their patients over a 3-year period[51]. However, good results (60% of patients with trivial insufficiency in 2 years[52] and 79% freedom from valve-related events in 3 years[53]) have been published. In a selected group of patients (endocarditis of mitral valve) partial or complete replacement of the valve with homograft, particularly in young patients and in cases where there is contraindication for mechanical valve use, it constitutes an effective alternative[54].

Difficulty in the choice of the suitable size of a graft, technically demanding implantation and early dehiscence of the suture-line with the papillary muscles, are certain reasons for the not always successful use of the mitral homografts in the mitral position[55].

Finally, the use of mitral homografts for partial replacement (posterior leaflet and subvalvular apparatus) of the mitral valve has been applied with good early results[56].

Mitral homografts have been limitedly used also in tricuspid position, with very good early results[57,58]. Homograft use particularly in cases of endocarditis of the tricuspid valve appears to have an advantage against sole valve resection or use of a prosthetic valve[59]. Mitral homograft for partial replacement of tricuspid valve has also been used with promising early results[14,60].

Conclusions

Advantages of homograft use for cardiac valve replacement include low risk of thromboembolism, freedom from anticoagulation, low transvalvular gradient (particularly in small size valves) and resistance to infection[61], while disadvantages include a more demanding surgical technique (and particularly significant operative difficulty in case of reoperation), progressive degeneration of the graft and limited access to the existing "Homograft Banks"[62]. Moreover, due to the superiority of aortic homografts compared to pulmonary ones and, hence, their almost exclusive utilisation, the problem of their availability becomes significantly larger. The new technology of "tissue-engineered" valves could be an alternative solution to the problem and may possibly improve the long-term results of biological valves[63].

Despite the pros and cons for the use of homografts, it seems that the overall result is in favour of

the patient. Particularly, in cases of endocarditis of the mechanical prosthetic valve in the aortic position with coexisting abscesses of the ascending aorta, the implantation of a homograft constitutes a life-saving solution. Generally, logical use of homografts in adult cardiac surgery when indicated with the proper surgical technique ensures a very good postoperative result and an excellent quality of life for the patient.

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