Systematic review of preservation methods and clinical outcome of infrainguinal vascular allografts

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CRD summary
The authors could not draw firm conclusions about the most effective preservation technique for vascular allografts. However, they did suggest that glutaraldehyde-preserved human umbilical vein allografts may have greater benefits than other vascular allografts. The authors appear to have considered several limitations of the included studies, such as statistical and clinical variation between the studies, and their cautious conclusions seem reasonable.

Authors' objectives
To evaluate the evidence for the use of vascular allografts in the management of patients requiring an infrainguinal bypass operation, and to identify the most effective vascular preservation technique.

Searching
MEDLINE (January 1966 to January 2004), EMBASE (January 1988 to December 2003), the Cochrane Controlled Trials Register and the Cochrane Database of Systematic Reviews were searched for articles in any language; the search terms were reported. The authors also performed a manual cross-reference search of key articles.

Study selection
Studies of patients with acute or chronic infrainguinal arterial obstructive disease were eligible for inclusion. The included studies assessed patients with limb ischaemia, Fontaine stage two and critical limb ischaemia (Fontaine three to four), or anastomosis located crurally (tibial, peroneal and pedal arteries) or in the popliteal region (defined as above or below the knee).

Studies performing vascular allografts were eligible for inclusion. Donor vessels were required to be arterial (taken from the iliac or femoropopliteal arteries) or venous (taken from the saphenous vein or human umbilical vein, HUV), and studies were required to report methods of preservation of the allograft. Studies were not eligible for inclusion if they used composite conduits (with the exception of the Biograft – an HUV allograft externally reinforced by Dacron mesh) or xenografts, or included reconstructions for aneurysmal disease, access for haemodialysis, or vascular trauma. The included studies used the following vascular allograft preservation methods: cryopreservation performed in a dimethyl sulfoxide-containing solution and used for both arterial and venous allograft preservation; cold storage using a saline solution containing antibiotics (chloramphenicol and amphotericin) for venous preservation; and glutaraldehyde which used the HUV and 50% aqueous ethanol. Some included studies compared HUV allografts with prosthetic vascular grafts (polytetrafluoroethylene) and autologous vein grafts. Some studies also administered antiplatelet therapy (aspirin and/or clopidogrel) or anticoagulant therapy (warfarin). One study used immunosuppressive therapy with azathioprine or no immunosuppressive therapy.

Studies reporting patency rates as the primary outcome, measured using an accepted vascular imaging technique (e.g. duplex scanning, arteriography or magnetic resonance imaging), and reporting major complications, graft disintegration and major limb loss (defined as a below-knee or more proximal amputation) as the secondary outcomes, were eligible for inclusion. The included studies also reported 30-day mortality rates.

Clinical studies involving a series of at least 40 grafts were eligible for inclusion.

Two reviewers independently screened papers for relevance.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two reviewers independently extracted outcome data according to three published checklists, ultimately to calculate weighted means for primary and secondary patency data at 1 and 6 months, 1 year and 2 to 3 years.

**Methods of synthesis**
The data were presented as a narrative synthesis and in tabular format.

Statistical heterogeneity was assessed using the $I^2$ test. Linear regression was used to calculate the Pearson correlation coefficient for patients with Fontaine stage II.

**Results of the review**
Five prospective randomised controlled studies (RCTs), 2 prospective case series, 1 prospective cohort study and 15 retrospective case series were included in the review (3,263 patients; 3,837 allografts). The number of grafts performed ranged from 40 to 907. Follow-up ranged from 1 month to more than 5 years.

Cryopreserved allografts (5 studies): the weighted mean cumulative primary patency at 1 year’ follow-up was 41%; 49% for arterial allografts (1 study) and ranging from 13 to 79% for venous allografts (4 studies). The weighted mean cumulative primary patency at 2 to 3 years’ follow-up was reported as 31% (range: 18 to 79). It was reported that immunosuppression did not affect the patency of cryopreserved allografts, but no data were provided.

Cold-stored venous allografts (3 studies): the weighted mean cumulative primary patency was 71% at 1 year’ follow-up (range: 63 to 80), and 51% at 2 to 3 years’ follow-up (range: 38 to 62).

Glutaraldehyde-preserved venous allografts (15 studies): the weighted mean cumulative primary patency was 70% at 1 year’ follow-up (range: 40 to 91) and 56% at 2 to 3-year follow-up (range: 33 to 86).

There was significant heterogeneity between prospective RCTs and meta-analysis could not be undertaken. A significant positive correlation was reported between the percentage of patients with Fontaine stage two disease and the 2-year cumulative primary graft patency (Pearson correlation coefficient 0.58; p=0.01).

Thirty-day mortality was reported in 14 studies, with an overall mortality rate of 2.9%. The incidence of major complications (17 studies) ranged from 0 to 15% and major limb loss (17 studies) ranged from 0 to 69%. Graft disintegration (17 studies) occurred in 0 to 15% of grafts. Cumulative secondary patency rates were reported in the review.

**Authors’ conclusions**
The included studies did not directly compare different preservation methods of vascular allografts; firm conclusions could therefore not be drawn. However, evidence from graft performance suggests that glutaraldehyde-preserved human umbilical vein allografts may have greater benefits compared with other vascular allografts.

**CRD commentary**
The review question was clear and supported by appropriate inclusion criteria relating to the participants, interventions, outcomes and study designs. Attempts were made to identify the relevant literature by searching several electronic databases and other sources without any language restrictions. Although two papers were excluded because of problems with translation, and as unpublished material were apparently not sought, it is possible that relevant papers were missed. Attempts were made to minimise potential reviewer error and bias in the study selection and data extraction processes. The absence of a validity assessment, and the fact that the majority of studies were reported as having low level of evidence due to their study design, means that the reliability of the included studies and their subsequent synthesis is unclear. Appropriate methods were used to investigate statistical heterogeneity. However, given the significant statistical heterogeneity and the reported clinical heterogeneity for both methods and patient characteristics, use of the weighted mean to compare patency rates may not have been appropriate. The authors appear to have considered the limitations of the included studies and present cautious rather than firm conclusions, which seems reasonable.

**Implications of the review for practice and research**
Practice: The authors stated that, owing to recent advances in the preservation of vascular allografts and their expected
introduction for use in clinical vascular surgery, the results should be compared with the findings from their review.

Research: The authors did not state any implications for research.

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