Bovine Heterografts and Autogenous Veins as Canine Arterial Bypass Grafts

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Bovine arterial heterografts and autogenous veins were compared as femoral artery bypass grafts in 33 dogs observed from 1 to 39 weeks. The vein grafts had a patency rate of 97%. Glutaraldehyde and dialdehyde tanned bovine grafts had patency rates of 13% and 50%, respectively. The poor performance of the heterografts was associated with marked fibrous hyperplasia at the anastomoses. It was concluded that autogenous vein remains the material of choice for small vessel bypass procedures.

Bovine arterial grafts are collagen conduits prepared from bovine arteries by enzymatic digestion of their protein followed by aldehyde tanning. These heterografts are available for use as arterial bypasses, vascular patches, and as components in cardiac prostheses.†# Heterografts have usually been evaluated as replacements for either the canine or porcine thoracic or abdominal aorta.†# On the basis of these studies, some investigators have accepted the bovine heterograft as an alternative or even a preferable substitute for autogenous vein.†

Canine femoral bypass procedures have provided a more severe test for new materials than aortic replacement.† Comparative studies have shown better patency with autogenous vein bypasses of the canine femoral artery than with synthetic substitutes.†# These results have paralleled the clinical performance of these materials as small vessel bypasses and suggest that the canine femoral model can provide a meaningful comparative evaluation of new vascular prostheses. In this experimental study, both glutaraldehyde and dialdehyde tanned heterografts were evaluated and compared with autogenous veins as canine femoral artery bypass grafts.

MATERIALS AND METHODS

Under sterile precautions with pentobarbital sodium anesthesia, 66 femoral artery bypass grafts, 4 to 8 cm long, were performed on 33 mongrel dogs weighing 17 to 32 kg. Bovine heterografts with outside diameters of 4 to 10 mm were used in all 33 animals; 23 glutaraldehyde grafts and ten dialdehyde grafts were used. Autogenous jugular veins with outside diameters of 6 to 10 mm were used to bypass the contralateral femoral artery of 22 animals. The procedures were performed in rotation by two surgeons with little previous experience with arterial anastomoses. The graft material was alternated so that the surgeon was at the same level of experience when comparing heterografts and veins.

A longitudinal incision was made to expose the femoral artery from the inguinal ligament to beyond its first bifurcation. The outside diameters of the femoral arteries were 3 to 7 mm proximally and 2 to 5 mm distally. Heparin sodium, 1,500 units, was administered intravenously before occlusion and longitudinal arteriotomies 1½ times the graft diameter were made. End-to-side anastomoses were constructed using a single 6-0 polypropylene suture. In all ten dialdehyde grafts and 15 of the glutaraldehyde grafts, the suture was brought down each side of the anastomosis from its acute angle as a simple over-and-over evertting stitch. A continuous evertting horizontal mattress suture technique was used in the other eight glutaraldehyde grafts.

The bypassed segment of the femoral artery was ligated adjacent to the anastomoses. Protamine sulfate, 15 mg, was given intravenously on release of the occluding clamps. Penicillin G benzathine, 600,000 units, was given intramuscularly on the day of surgery and on the second and fourth postoperative days.

Patency was evaluated weekly by palpation. Nonpulsatile grafts were exploded and thrombosed grafts removed. Since the high patency rate for autogenous vein grafts had been previously established for this model, the animals were killed when the heterografts thrombosed.

RESULTS

Material Characteristics

The vein graft was much more elastic and pliable than either of the heterografts. The glutaraldehyde grafts were thicker (0.5 to 1.0 mm) and less pliable than the dialdehyde grafts. The inelasticity and rigidity of the heterografts facilitated the handling and shaping of the grafts, but suturing was prolonged because these features made evasion of the graft and simultaneous suturing through both the graft and the recipient artery more difficult. In
addition, the length of the heterograft had to be exact or cutting through by the suture was seen. This technical problem resulted in the failure to complete one procedure.

Bleeding from the anastomosis was subjectively greater with the autogenous vein grafts than with the bovine grafts when using the simple suture technique, but he¬mostasia was not a problem with either graft material. Bleeding was greater when the horizontal mattress suture was used with glutaraldehyde grafts. Exsanguination occurred in two instances. Dragging of adventitia into the anastomosis by the polypropylene suture did not occur, even with the shaggy adventitia of the dialdehyde grafts.

**Patency**

**Autogenous Vein Grafts.**—Early thrombosis at two weeks occurred in one of 32 autogenous vein grafts, resulting in an overall 97% patency rate 1 to 39 weeks following operation (Fig 1). This thrombosed graft was redundant, and kinking probably contributed to this failure. There was one infection in the presence of a patent vein graft resulting in the early killing of the animal.

**Bovine Grafts: Simple Suture Technique.**—Twelve of 15 glutaraldehyde grafts thrombosed within three weeks and one thrombosed at nine weeks (Fig 2). Two grafts were functional at the time of killing at 35 and 39 weeks, giving an overall patency rate of 13%. The patent grafts were 8 and 10 mm in diameter. All five glutaraldehyde grafts of 4 to 6.5 mm in diameter failed. Infection occurred in the wound of one thrombosed graft.

Four of ten dialdehyde grafts failed within nine weeks (Fig 2). One graft was pulsatile but not patent at the time of killing at 26 weeks. Five, or 50%, of the grafts were patent at the time of killing at 25 to 31 weeks. All grafts showed marked stenosis at one or both anastomoses.

**Bovine Grafts: Horizontal Mattress Suture Technique.**—There was a 25% patency rate for the eight glutaraldehyde grafts using the horizontal mattress technique (Fig 3). However, no graft functioned longer than two weeks. In two instances, the suture eroded through the recipient artery, resulting in exsanguination. Thrombosis occurred in the remaining six animals.

**Pathologic Findings**

Early graft failure was associated with recent thrombus adherent to one or both suture lines, and in late failures recent thrombus was found adherent to the fibrous tissue covering the anastomoses. The lumen of the grafts contained recent nonadherent thrombus. Except at the site of the anastomoses, the lumen was smooth and the color of the original graft tissue. Grossly, the fibrous tissue covering the suture lines narrowed the lumen of both heterografts and vein grafts, but the narrowing was more pronounced in the heterografts (Fig 4). The suture line pannus was smooth, except where thrombus was adherent. Neither embolization of intimal material nor elevation of intimal flaps was observed.

Microscopically, fibrous invasion of the suture line and intimal and medial fibrous hyperplasia in the recipient artery were observed when either heterograft or vein was used. The fibrosis was more proliferative and less uniform in the heterografts (Fig 5) than in vein grafts (Fig 6). No difference was observed between the glutaraldehyde and dialdehyde heterografts.

Intimalization was remarkably more uniform in the vein grafts where a thin, homogeneous intimal layer was seen as well as vascular invasion of the vein graft that appeared thickened by collagen material (Fig 7). In contrast, the heterografts remained acellular without vascular invasion and had an irregular intimal lining (Fig 8).

**COMMENT**

The present study was conducted in the same manner as previous experimental evaluations of graft materials in our laboratories. Each surgeon performed both a heterograft and an autogenous vein bypass procedure at the same level of experience so that differences in results cannot be attributed to the technical capabilities of the operator. The results were similar to those of others who have
compared various materials as bypass grafts or replacements of the canine femoral artery. Phillips et al. reported 45% to 65% patency for crimped Teflon and Dacron grafts as compared to 100% patency for vein grafts. In other series, the synthetic materials were even less satisfactory: Cate reported 40% satisfactory results with Dacron and nylon grafts; Dale and Niguidula obtained 30% overall satisfactory results with synthetic grafts; and Shirkey et al. reported 36% patency with Dacron grafts, in contrast with 95%, 86%, and 93% satisfactory results with vein grafts in these series. The 50% patency for the dialdehyde heterografts in the present series surpassed the results of others who reported a high failure rate in femoral bypasses and cross-femoral bypasses with similar dialdehyde grafts.

The highest patency rate was seen with the extremely pliable and elastic autogenous veins and the lowest rate with the rigid glutaraldehyde grafts. These results would suggest that pliability might be a factor in determining patency. Heterografts cannot be made elastic. As described by Rosenberg, it is necessary to sacrifice the elastic component of the bovine vessel in order to preserve the collagen matrix. The tanning agent can alter the pliability, but, with present techniques, no bovine heterografts can be elastic. Elasticity may facilitate compensation for mechanical distortion of the grafts, but the importance of conformity at the anastomosis was disputed by Phillips et al.; who angiographically observed the greatest turbulence at the anastomoses of vein grafts.

The results might also suggest that the size of the graft influences the patency. Dale and Lewis used dialdehyde grafts at the femoral level with failure in 19 grafts of 10- to 11-mm diameter and patency of two of 11 grafts that were 5 to 6 mm in diameter. In the present series, glutaraldehyde grafts of smaller diameters, 4 to 6.5 mm, all
failed; better patency was observed in the larger diameter grafts. These findings support the hypothesis of Phillips et al\(^9\) that turbulence is not an important determinant of patency and conflict with the suggestions of Dale and Lewis\(^4\) and Rosenberg et al\(^6\) that oversized grafts should be avoided.

Failure of the heterografts was primarily related to occlusion from thrombosis in association with fibrous infiltration and narrowing of the anastomoses. Phillips et al\(^5\) reported similar findings in the failure of 6-mm diameter synthetic grafts. However, in the aortic model, Rosenberg et al\(^6\) reported that fibrosis of the suture lines of heterografts was only occasionally prominent after seven years. Clinically, significant stenoses of heterografts due to anastomotic thickening have been reported in femoral-popliteal bypasses.\(^1,2\) It was postulated that this excessive pannus might be related to the presence of a foreign body suture. However, the use of a horizontal mattress stitch, which has less internal suture exposed, did not decrease the thrombosis rate but only increased the failure rate from bleeding.

In the seven-year aortic model, Rosenberg et al\(^6\) re-
ported that heterografts appeared encased in host fibrous tissue with variable preservation of the graft fibers and no cellular reaction or infiltration. They also reported almost complete intimal coverage. Dale and Lewis found after one year that the inner surface of the graft was unchanged except for adherent fibrous material, and no intima extended only from the suture lines with intimalization being complete only in short grafts. Similarly, heterografts in the present series showed a lack of intimal development as well as lack of vascular invasion. These findings were in contrast to the vascular invasion of vein grafts where a uniform inner layer was observed. The poor performance of the heterografts and the microscopic observations supported the concept that arteriogenesis as described by Wesolowski et al is important in an ideal graft material. It appeared that bovine heterografts acted as collagen barriers, preventing vascular and fibroblastic invasion. Without transmural vascular support, the proliferating fibrous lining depended on its pedicle, a pedicle based at the suture line. It is suggested that further proliferation of the fibrous lining from its base resulted in thickening of the pannus at the anastomosis, which finally resulted in critical stenosis and thrombosis. The observed differences in arteriogenesis between canine autogenous vein grafts and bovine heterografts correlated with the superior performance of vein grafts as small vessel bypasses.

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References


Editorial Comment

The authors have presented their results from a carefully designed study that has compared the fate of bovine heterografts versus autogenous veins, when used to replace the femoral arteries in dogs. The inferiority of the heterografts is clear in this model, and there can be no quarrel with the results. However, the authors have concluded "... that autogenous vein remains the material of choice for small vessel bypass procedures," and, while many (myself included) will agree with this view for other reasons, the conclusion is not supported by the evidence presented. There are no data available in this work to validate the assumption that results of peripheral vessel replacement in dogs may be compared so strictly with human experience. Some surgeons have reported on the successful use of bovine heterografts in peripheral vascular procedures in humans and at least two groups have shown good results with the material in the construction of arteriovenous fistulas for use in chronic dialysis patients. Therefore, a somewhat dissident view may appreciate the data derived from these careful studies, while maintaining an open mind concerning its applicability to clinical vascular surgery.

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