Experience with the Modified Bovine Arterial Heterograft in Peripheral Vascular Reconstruction and Vascular Access for Hemodialysis

MOSHE HAIMOV, M.D., F.A.C.S.,* JULIUS H. JACOBSON II, M.D., F.A.C.S.†

The experience in the use of 37 Bovine heterografts for the treatment of arterial insufficiency and of 37 Bovine heterografts for construction of arterio-venous fistulas for hemodialysis is described. The Bovine heterograft was found unsuitable for use in the femoro-popliteal position, as contrasted to satisfactory follow-up in the aorto-iliac-femoral area. On the other hand, it was found to be an acceptable substitute to the autogenous saphenous vein in the construction of an arterio-venous fistula for chronic dialysis.

From the Department of Surgery, Division of Vascular Surgery, The Mount Sinai School of Medicine of the City University of New York, New York, New York

THE FIRST REPORT of the use of modified Bovine carotid arteries as vascular substitutes in the dog was published in 1956.[10] The first implantation in man was done six years later.[11] According to a recent editorial, over 3,000 grafts are currently in patients or in the hands of vascular surgeons.[12] With the exception of several favorable clinical reports,[2,9,13] the results from the use of all these grafts have not been reported. This report will deal with the experience with this prosthesis in a group of patients with peripheral vascular occlusive disease, and its use as a substitute for the autogenous saphenous vein in the construction of arterio-venous fistulas for hemodialysis in a second group of patients with terminal renal failure.

Materials and Methods

The Bovine arterial heterograft (Johnson and Johnson, Inc., New Brunswick, N. J.) is a tube prepared from the carotid artery of cows which has had the musculoelastic tissue removed by the enzyme ficin. The remaining tissue consists of at least 76% collagen and is tanned with dialydehyde starch. The grafts are up to 50 cm long and 7½–14 mm in diameter. Antigenicity of the graft has not been demonstrated.[3] Histologic studies of these grafts implanted in dogs and in man has demonstrated that there are non-living substitutes for arteries. The late histologic reaction observed was one of fibrous invasion, substitution and integration.[4]

During a three-year period, 1966–1969, 37 Bovine heterografts were inserted in 32 patients. The indication for surgery were severe incapacitating claudication, rest pain and impending or limited gangrene. Patient age varied between 42 and 80. They all exhibited various degrees of generalized arteriosclerosis affecting the coronary and cerebral vasculature. The indication for the use of the modified Bovine heterograft were the unavailability or unsuitability of the long saphenous vein which was usually the prosthesis of choice. In all, there were 32 femoro-popliteal bypasses; two ilio-femoral bypasses; one aorto-femoral; one femoro-femoral; and one popliteal artery substitution following excision of popliteal aneurysm.

Thirty-seven Bovine heterografts were used in 31 patients with terminal renal failure in the construction of subcutaneous arterio-venous fistula for hemodialysis. Four patients had a loop fistula in the forearm (Fig. 1); 19 grafts were put in a straight fashion between the radial or ulnar artery and the antecubital or deep vein in the forearm; 14 heterografts were implanted in the arm as an A–V fistula between the brachial artery and the axillary vein. Indication for the procedure were

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* Assistant Professor, Department of Surgery.

† Associate Professor, Department of Surgery and Chief, Division of Vascular Surgery.

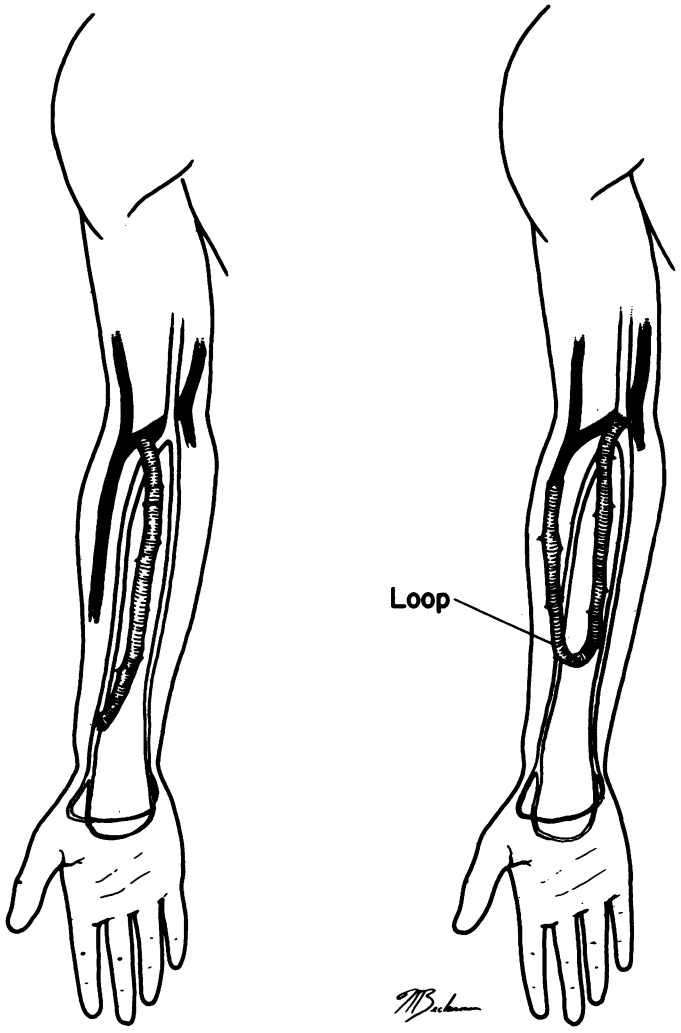

FIG. 1. Straight and loop heterograft A–V fistulas in the forearm.

TABLE 1. *Femoro-Popliteal Bypasses*
(32 Heterografts in 27 Patients)

Months Postop.	2	12	24–48
No. Open	20*	6	6
No. Closed	12	10†	10

* Includes 5 grafts which thrombosed postoperatively, but were successfully declotted.

† Three patients (4 grafts) died during the first year from unrelated causes.

unavailability of suitable artery or vein in the upper extremity for the construction of the standard subcutaneous arterio-venous fistula which is the vascular access of choice for hemodialysis. More than 50% of these patients were diabetic and many have had numerous vascular access procedures previously. No anticoagulants were used. All surgical procedures were done on an ambulatory basis using local infiltration anesthesia.

Results

Femora-Popliteal Bypasses (Table 1)

Of the 32 heterografts used in the femoro-popliteal location, 12 (38%) failed in the immediate postoperative period; 10 additional grafts failed during the first year of followup, six of them less than six months following surgery and six grafts (18% of the total or 38% if patient mortality is excluded) are patent for two to four years following implantation. Seventeen heterografts thrombosed in the immediate postoperative period and thrombectomy was done in 13 of them. In five, circulation was successfully restored, but the rest rethrombosed shortly thereafter. The clinical course and outcome of these 12

TABLE 2. *Femoro-Popliteal Bypasses Early Failures*

No.	Patient	No. of Grafts	Clinical Course and Outcome	No. of Operations
1	F. A.	1	Heterograft thrombosed postop. Thrombectomy unsuccessful. Peroneal artery injury with Fogarty catheter. Femoral endarterectomy performed. Groin infection .Expired.	3
2	F. B.	2	Graft degeneration with aneurysm formation, not at suture lines. New heterograft inserted which thrombosed postop. Thrombectomy attempted twice unsuccessfully. Limb viability preserved.	3
3	M. R.	1	Graft thrombosed in the early postop. course. False aneurysm developed with proteus sepsis. Graft removed.	3
4	C. S.	1	Early thrombosis postop. Circulation restored with thrombectomy. Aneurysmal degeneration of graft occurred necessitating graft ligation.	3
5	M. L.	1	Groin infection with massive bleeding. Expired.	2
6	T. M.	1	Massive bleeding from groin suture line .Expired.	1
7	J. R.	1	Early graft thrombosis. Thrombectomy. Acute myocardial infarction. Expired.	2
8	B. F.	1	Graft thrombosed. Thrombectomy unsuccessful. Arm vein graft also thrombosed. Above-knee amputation. Acute myocardial infarction. Expired.	4
9	C. G.	1	Graft thrombosed. Thrombectomy unsuccessful. A-K amputation.	3
10	B. I.	1	Graft thrombosed in one week. Limb remained viable.	1
11	W. R.	1	Graft thrombosed postop. Thrombectomy attempted twice without final success. A-K amputation.	4

TABLE 3. *Femoro-Popliteal Bypasses*
(2–48 Month Followup)

No.	Patient	No. of Grafts	Clinical Course and Outcome	No. of Operations
1	I. S.	2	Bilateral femoro-popliteal bypass (not simultaneous). One graft thrombosed postop., but was sucessfully declotted. Died after 12 months from myocardial infarction.	3
2	D. J.	1	Graft thrombosis postop. but was sucessfully declotted. Died after 6 months from mesenteric thrombosis.	2
3	M. M.	1	Graft thrombosed postop.—declotted. thrombosed again in 3 months. Above-knee amputation.	3
4	S. J.	2	Bilateral femoro-popliteal bypass. One graft thrombosed in 5 months. Two attempts of thrombectomy failed and A-K amputation was done. Second graft remained open for 9 months. Patient died from cerebrovascular accident.	5
5	R. J.	2	Graft removed because of false aneurysm formation after 3 months. Second heterograft failed (2 thrombectomies). A-K amputation.	4
6	H. L.	1	Graft thrombosed postop. Thrombectomy sucessful in restoring circulation. Graft thrombosed after 5 months.	2
7	R. K.	1	Graft thrombosed in 3 months.	1
8	F. B.	2	Bilateral femoro-popliteal bypass. Both grafts thrombosed within 6 months.	2
9	F. R.	1	Graft thrombosed in 5 months.	1
10	M. P.	1	Graft thrombosed postop. Thrombectomy successful. Thrombosed again in 8 months, this time thrombectomy failed.	3
11	S. I.	1	Graft remained open for 3 years, when patient died from myocardial infarction.	1
12	E. M.	1	Open for 2 years. Patient died following acute myocardial infarction.	1
13	B. S.	1	Graft open for 4 years.	1
14	B. M.	1	Graft open for 2 years.	1
15	W. V.	1	Graft open for 4 years.	1
16	M.G.	1	Graft open for 2 years.	1

failed heterografts in 11 patients are summarized in Table 2.

Ten grafts in 10 patients thrombosed luring the first year of followup (thrombectomy was attempted and was unsuccessful in seven of these patients). Two patients expired, six and nine months following graft implantation with open grafts for unrelated reasons. One patient died from mesenteric thrombosis and a second one following a cerebro-vascular accident. Three patients underwent major amputations following failures of the grafts and in five patients the viability of the extremity was preserved despite the graft failure. Clinical course and outcome of these patients is summarized in Table 3. In six patients the grafts have remained open for two to four years.

Six heterografts were implanted in other than the femoropopliteal location (Table 4). Only one of these grafts has failed (that was an ilio-femoral bypass in a young patient with severe large and small vessel disease which closed three months following implantation). The rest have all remained open for 24 to 36 months.

Mortality and Morbidity

Both mortality and morbidity were high. A total of 61 operations were performed in this group of 27 patients undergoing femoro-popliteal bypasses. Sixteen patients out of 27 (60%) had more than one operation. The morbidity and mortality are summarized in Table 5. Five patients died in the immediate postoperative period (15%). The causes of death were graft infection and sepsis in one patient; false aneurysms with massive bleeding in two patients; acute myocardial infarction in two other patients. There were four instances of graft infections (13%), two of these patients expired; two patients recovered and in one of the graft had to be removed with limb survival, while in the fourth patient the infection was superficial and he recovered with the graft intact. Graft degeneration or true aneurysms of the

TABLE 4. *Heterografts in Other Locations*

No.	Patient	No. of Grafts	Clinical Course and Outcome	No. of Operations
1	G. V.	1	Ileo-femoral bypass. Patent at 24 months.	1
2	S. S.	1	Femoro-femoral bypass. Patent at 36 months.	1
3	M. P.	1	Aorto-femoral bypass. Patent at 36 months.	
4	W. A.	1	Popliteal artery replacement after aneurysm resection. Patent 36 months.	1
5	P. A.	1	Ileo-femoral closed in 3 months (young patient with severe large and small vessel disease).	1

TABLE 5. *Morbidity and Mortality*

Type	No.	
Mortality	5	Graft infection and sepsis—1 patient
	(15%)	False aneurysms, massive bleeding—2 patients
		Acute myocardial infarction—2 patients
Infection	4	2 Patients died.
	(13%)	2 Patients recovered, on one the graft had to be removed with limb survival.
Graft Degeneration	2	1 Graft was ligated.
(True aneurysm)	(7%)	1 Graft replaced with second heterograft which also failed.
False Aneurysm	4	2 Patients died from hemorrhage.
	(13%)	1 Graft removed, replaced with heterograft which also failed, followed by A-K amputation.
		1 Graft ligated with limb survival.

heterografts occurred in two patients (7%), one graft was ligated, the second graft was replaced with another heterograft which also failed. Viability of the limb was preserved in both patients. False aneurysms formed in four patients (13%); two patients died from hemorrhage, one graft was removed and replaced with a second heterograft which also failed, and eventually an above-knee amputation was required. One graft was ligated with survival of the limb.

Heterografts for Arterio-Venous Fistulas (Table 6)

Of the four heterografts implanted in a loop fashion in the forearm, all four eventually failed. Three of them thrombosed shortly postoperatively. Thrombectomy was attempted but was unsuccessful. The fourth one developed infection following trauma over the skin overlying the subcutaneously placed graft. The infected heterograft was removed. Three of the straight forearm heterografts failed in the first three months on dialysis. All failures were due to low flow either because of advanced arteriosclerosis or because of high venous resistance due to an inadequate-size vein. None of the failures seems related to the graft itself. One patient had acute thrombosis of the graft four months following implantation during a period of hypotension. This graft was successfully declotted and has remained open now for an additional six months. Fifteen heterografts have been used for dialysis for a period of three to 14 months. Three of the 14 arm heterografts have failed, two because of infection with false aneurysm formation and one due to axillary vein phlebitis. Three of these patients also developed severe vascular insufficiency with numbness and coldness of the fingers. In two of these patients, this insufficiency progressed to gangrene of the fingers requiring amputation. In one patient the graft outflow was narrowed with a Dacron cuff, decreasing the flow from 1200 cc/min to 400 cc/min with disappearance of the vascular insufficiency symptoms.

The final results are summarized in Table 7. Ten grafts failed in the first three months, giving a patency rate of 72% (this would be 81% if the four loop fistulas are excluded); one graft has failed in the 3–6 month period with a patency rate of 93% and no failures have occurred in the grafts that have been used for more than nine months. A more detailed account of the use of heterografts for A-V fistulas for dialysis will be given in a separate publication.[8]

Discussion

There is always the natural tendency both for authors to report and for journals to accept positive results. In the field of vascular prosthesis, however, knowledge of failure is just as crucial. From the paucity of clinical reports about the 3,000 grafts mentioned previously, one would have to presume that our unfortunate experience is not unique. This suspicion is reinforced by the fact that in spite of the urgent need for a satisfactory substitute for the long saphenous vein and the easy availability of the Bovine heterograft, the latter has not gained wide-spread acceptance in more than 12 years of clinical use. All patients in the first group of this report were private patients, operated upon by an experienced senior vascular surgeon (JJ) which excludes the possibility of technical factors accounting for the high incidence of failures. The high incidence of re-operation will attest to the fact that failures could not be attributed to

TABLE 6. *Heterografts Used for Arterio-Venous Fistulas for Hemodialysis*
(37 Grafts in 30 Patients)

Type	No.	Failed*	Patent
Loop Foreman Grafts	4	4	—
Straight Forearm Grafts	19	4	15
Straight Arm Grafts	14	3	11

* Immediately postop or during the first two months on dialysis.

TABLE 7. *Heterograft A-V Fistula Followup*

Months in Use	3	6	9	12
No. of Fistulas	27	14	6	3
Patency Rate	72%*	93%	100%	100%

* This would be 81% if the four loop fistulas are excluded.

lack of aggressiveness on the part of the surgeon involved. The high morbidity, mortality, early and late failure rate encountered renders the modified Bovine heterograft an unacceptable substitute for the saphenous vein in the femoro-popliteal position.

The number of multiple operations in this group (60%) has a direct relationship to the incidence of infection, aneurysm formation, bleeding and mortality. In a contrast to this, all of the six patients with patent grafts for more than 24 months were operated only once. The small group of patients with grafts in the aorto-femoral, ilio-femoral and femoro-femoral positions did well, which parallels the experience reported in the literature and is similar to that of the cloth prosthesis in these locations. The failure rate of the heterograft in the femoro-popliteal location corresponds to the experience reported by other authors using cloth grafts in that position.[5,14]

On the other hand, the modified Bovine heterograft did prove to be an acceptable substitute for the saphenous vein when used in the construction of an arterio-venous fistula for dialysis purposes. This can be concluded in spite of the relatively short follow-up because the criteria of evaluating success in these patients is different. In all these patients a standard subcutaneous arteriovenous fistula[1,7] could not be performed, therefore, the alternative was the use of a silastic cannula shunt which has a mean patency rate of six to eight months.[6] Any method which has the advantages of the arterio-venous fistula over the shunt and functions for a similar or longer period of time would be acceptable. The hemodynamic situation in this use of the heterograft is obviously entirely different. In the arterio-venous fistula one is dealing with a high-flow, low-resistance system in which a tendency to thrombosis is markedly decreased. Also, the known platelet function deficiency of the uremic patient decreases the tendency to thrombosis. True aneurysms or graft degeneration did not occur in these heterografts for the period of observation. The "loop" fistula was unsuccessful in four patients. This type of fistula has failed also when an autogenous vein has been used, and is therefore probably hemodynamically wrong.[6,8] It seems, therefore, that the modified Bovine heterograft is an acceptable substitute for the saphenous vein in the construction of an arterio-venous fistula for hemodialysis.

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