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Bovine Heterografts for Hemodialysis

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Long-term results with 52 bovine, 53 saphenous vein and 78 radial-cephalic arteriovenous fistulas (AVF) were analyzed. Side-to-end radial-cephalic AVF provided the best patency data, and remain the preferred access system for hemodialysis. Bovine AVF were next in ranking with better patency rates than for the saphenous vein AVF studied. Corrected one-year patency rates were 71 percent for bovine, 45 percent for saphenous and 91 percent for radial-cephalic AVF. The incidence of nonthrombotic complications with bovine AVF was higher than with saphenous vein AVF. Distal ischemia due to "steal" and certain bleeding and wound complications were unique to bovine AVF. Excellent dialysis blood flow rates and easy accessibility were provided by bovine grafts. When a satisfactory radial-cephalic AVF cannot be created, bovine graft AVF is an acceptable alternative for hemodialysis access.

NUMEROUS METHODS for providing vascular access for hemodialysis have been described during the past decade. Subcutaneous arteriovenous fistulas (AVF) of Brescia-Cimino type are now generally preferred for long-term dialysis access systems.[1,2] However, in patients whose forearm blood vessels are unsuitable for direct radial-cephalic arteriovenous anastomosis, other forms of AVF with an interposed bridge between artery and vein may be employed. Bridged-AVF systems are applicable in patients with peripheral arterial occlusive disease and those with small or damaged forearm veins.

Autogenous saphenous veins have been employed as bridged grafts for AVF since 1969. Early experiences with saphenous arteriovenous fistulas were favorable,[3-6] but long-term results have been less satisfactory[7,8] in addition to which many patients do not have suitable saphenous veins. In 1972, modified bovine arterial heterografts were recommended by Chinitz and coworkers as self-sealing prostheses in hemodialysis

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ABBREVIATIONS USED IN TEXT

AVF = arteriovenous fistulas
BOV = bovine grafts
RCAV = radial-cephalic arteriovenous
SAV = saphenous arteriovenous

access systems.[9] Encouraging short-term success with bovine arteriovenous fistulas also has been reported by others.[8,10-14] However, published long-term follow-up data have not been sufficient to permit comparison with alternative forms of AVF. This report reviews our experience with bovine grafts (BOV) for dialysis access, and compares this experience with that for radial-cephalic arteriovenous (RCAV) and saphenous arteriovenous (SAV) fistulas.

Clinical Material and Methods

Fifty-two BOV fistulas were constructed between April 30, 1972 and July 1, 1974.* Twenty-eight of these were done before January 1974 and have been observed for more than a year. The longest follow-up is 32 months. The remaining 24 BOV fistulas were created between December 1973 and July 1974, and all have been followed at least six months. None were lost to follow-up.

For comparison with the BOV fistulas, 53 SAV and 78 RCAV fistulas which were constructed between August 1971 and December 1973 were studied. All patients in these latter groups were followed for at least a year. Pertinent information regarding the three groups of patients is shown in Table 1.

The three groups of BOV, SAV and RCAV fistulas comprised 151 patients. Eighty were men and 71 women. All had chronic renal failure requiring maintenance hemodialysis. Eleven patients were diabetic. Patient ages ranged from 22 to 77 years, with a mean age of 52 years. Thirty-three patients were 65 years or older, constituting 22 percent of the total group. Dialysis was provided by means of percutaneous puncture of the fistulas two or three times each week. Thirty-two patients died and four had successful renal transplants during the follow-up period.

Selection of the particular form of AVF was not random, but was based upon evaluation of each patient's blood vessels and clinical status. Nonbridged AVF has been the system of choice for dialysis access, and therefore side-to-end RCAV fistula was constructed first whenever possible. Fifty-nine patients had only an RCAV fistula. SAV or BOV fistulas were created in patients whose blood vessels were inadequate for RCAV or when failure of other forms of fistula occurred. Twenty-nine SAV and 28 BOV fistulas were constructed as the primary form of access. Thirty-five patients had more than one type fistula during the period studied, and thereby provided data for more than one category.

TABLE 1.—*Clinical Data for Three Groups of Patients with Different Types of Arteriovenous Fistulas*

	RCAV	SAV	BOV
No. of patients	72	44	46
Women	32	23	24
Diabetics	3	5	5
Mean age, years	51	50	55
No. of arteriovenous fistulas	78	53	52
Deaths in follow-up	16	13	13
Deaths with patent AVF	9	11	11

AVF = arteriovenous fistulas RCAV = radial-cephalic arteriovenous
BOV = bovine grafts SAV = saphenous arteriovenous

The techniques of the operations have been described previously.[6-14] All RCAV anastomoses were side-to-end. In bridged-AVF systems, the arterial anastomoses were done end-of-graft to side-of-artery. Venous anastomoses were end-of-graft to either side-of-vein or end-of-vein. When antecubital veins were inadequate or damaged, grafts originating in the forearm were carried across the elbow for anastomoses to brachial veins. The bovine heterografts which were used had internal diameters of 6 to 8 mm.

Both straight and loop forms of SAV and BOV were constructed. Whenever possible, preference was given to straight configuration as originally described by Chinitz and co-workers. Locations included forearm, arm and anterior thigh. The distribution of the various bridged-AVF configurations which were constructed is shown in Table 2. Twenty-four BOV were in thigh locations, 26 in the forearm. All but one of the 53 SAV were placed in the forearm, 28 in straight and 24 in loop configuration.

Results

Patency Data. Nine spontaneous thromboses of BOV fistulas occurred. Of these, three fistulas were successfully maintained by thrombectomy and revision of anastomotic stenoses. Six could not be salvaged and required new dialysis access systems. Five BOV fistulas were surgically occluded

*The arterial graft (bovine) was obtained from Johnson & Johnson, New Brunswick, NJ.

TABLE 2.—*Distribution of Bridged Arteriovenous Fistula Locations and Configurations*

Configuration	*Location*	*Arterial Origin*	*Venous Insertion*	*No. SAV*	*No. BOV*
Straight	Forearm	Radial	Antecubital or brachial	23	17
	Arm	Brachial	Axillary	0	2
	Forearm	Brachial	Cephalic at wrist	5	2
	Thigh	Distal superficial femoral	Saphenous	0	16
Loop	Forearm	Brachial	Antecubital or brachial	24	7
	Thigh	Proximal femoral	Saphenous	1	8

BOV = bovine grafts SAV = saphenous arteriovenous

TABLE 3.—*One Year Patency Data for Radial-cephalic and Bridged Arteriovenous Fistulas*

	RCAV	*SAV*	*BOV*
Constructed at least one year before study	78	53	28
Patent on hemodialysis one year	62	19	17
Uncorrected patency rate	0.79	0.36	0.61
Excluded (patent at time of death or renal transplant)	10	11	4
At Risk one year	68	42	24
Corrected one-year patency, percent	91	45	71

BOV = bovine grafts RCAV = radial-cephalic arteriovenous SAV = saphenous arteriovenous

for treatment of complications of ischemia, bleeding and anastomotic disruption. Eight patients died with patent BOV. Thirty of the 52 BOV remain patent.

Mean survival time for all BOV fistulas was 13.7 months, with little variance for different locations or configurations.

Patency rates at one year are compared for the three forms of AVF in Table 3. Uncorrected one-year patency rates include as failures those patients with fistulas still functioning, who died or received successful renal transplants less than a year after the access procedure. More valid comparison is based upon a corrected one-year patency rate which includes only those fistulas which were actually at risk of occlusion for one year or more. Superiority of RCAV is clearly shown. Of the RCAV at risk, 91 percent remained patent at one year. Corrected one-year patency of BOV (71 percent) was definitely better than that of SAV fistulas (45 percent).

For SAV, little difference in patency was observed between straight and loop configurations. Thirty thrombotic occlusions of SAV fistulas occurred, three within one month and the rest within two years. Ten of 28 straight and 9 of 25 loop SAV were patent one year or longer. When only those SAV which were at risk one year are compared, the patency rate was 0.45 for each form. At two years, only 4 of 22 SAV fistulas remained patent. Mean survival time for all SAV fistulas was 11.2 months. Vein grafts which remained patent for long term were invariably 6 mm or greater in diameter. Mural hyperplasia with luminal stenosis caused most of the late SAV fistula failures, including some with veins of excellent caliber.

TABLE 4.—*Comparison of Patency of Saphenous (SAV) and Bovine (BOV) Arteriovenous Fistulas for Two Years After Construction*

	Months After Fistula Construction				
	3	6	12	18	24
Saphenous					
Patent/ At Risk ..	37/49	30/48	19/42	14/40	4/22
Patency, Percent ..	76	63	45	35	18
Bovine					
Patent/ At Risk ..	44/50	32/42	17/24	4/7	3/5
Patency, Percent ..	88	76	71	57	60

Table 4 compares corrected patency of all SAV and BOV at successive intervals of time. These data are shown graphically in Figure 1. The sharper initial decline of the SAV patency curve reflects the early failures of inadequate, small saphenous veins. After six months, the two curves assume somewhat more similar decline. Although only small numbers of BOV were at risk for 18 months (seven cases) and 24 months (five cases), patency remains above 50 percent.

Our initial bovine implants were straight femoral-saphenous grafts, and these fistulas have provided excellent long-term patency. However, despite our preference for the straight configura-

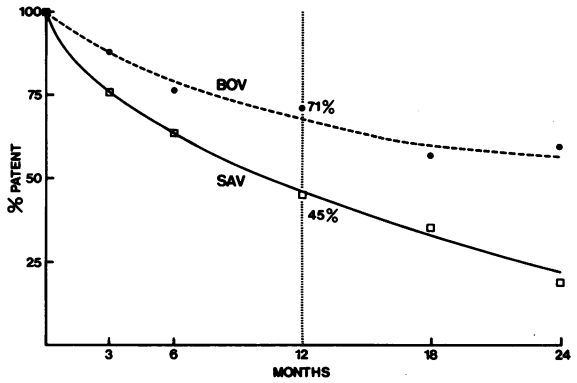

Figure 1.—Diagram comparing decrease in patency with time for bovine graft (BOV) and saphenous arteriovenous (SAV) fistulas.

tion, our data show that loop forms provided better patency at one year. All of the seven BOV loops at risk for one year have remained patent, regardless of location in arm or leg. Ten of 16 straight BOV (62 percent) were patent at one year.

Complications. Complications of BOV and SAV fistulas are listed in Table 5. Twenty-nine nonthrombotic BOV complications occurred. Eight of these, however, led directly to graft occlusion, either spontaneously or by surgical ligation.

Three patients had severe inflammatory reaction along the bovine graft tunnel, one of which persisted for several months and resembled a foreign body rejection phenomenon. This may have been due to insufficient washout of the preservative solution from the graft before implantation.

Bleeding complications occurred on three occasions when BOV puncture was performed earlier than seven days. In each instance, blood which extravasated from the needle puncture site dissected along the graft tunnel, producing tunnel hematomas and graft occlusion. In one patient, brisk external bleeding occurred through the six-day-old incision.

Ischemic complications due to fistula "steal" phenomena occurred with four of the 52 BOV fistulas. In one patient with severe peripheral arteriosclerosis, there was ischemic rest pain and loss of pedal pulses after a straight femoral-saphenous bovine fistula was constructed. Surgical ligation of the fistula produced relief of symptoms and return of distal pulses. Banding constriction of a forearm loop relieved hand ischemia in one patient, and spontaneous thrombotic occlusion accomplished the same result in another. The fourth patient has had no worsening of mild hand coolness and claudication noted immediately after creation of the fistula. We have not observed ischemic complications with any other form of dialysis access.

Early postoperative deaths include one patient who died 24 hours following construction of a BOV fistula in the thigh. Death occurred suddenly during hemodialysis carried out by means of a pre-existing Scribner shunt, and was due to ventricular arrhythmia. Another patient died one month after BOV fistula construction. She had extensive arteriosclerotic occlusive disease and a thrombotic propensity which precluded establishment of satisfactory vascular access for hemodialysis.

Late complications of BOV include one case of staphylococcal septicemia. Although no overt graft infection was apparent, the BOV fistula was a possible source of this sepsis, which resulted in death. No other deaths were related to the BOV fistula operations.

Late anastomotic disruption occurred in two patients, resulting in large false aneurysms with overlying skin necrosis. In one patient with a brachial artery to brachial vein BOV loop constructed in the forearm, two reoperations were done within 48 hours for correction of hand ischemia due to "steal." The venous anastomosis disrupted seven weeks later. The other patient had a profunda femoris artery-to-saphenous-vein BOV loop in the thigh. An abscess developed below the groin incision after 3½ months and responded to incision and drainage. Cultures repeatedly grew no organisms. Two months later (5½ months after construction of the BOV fistula), the arterial anastomosis disrupted, producing a rapidly expanding false aneurysm. Cultures

TABLE 5.—*Nonthrombotic Complications of Bridged Arteriovenous Fistulas*

	SAV	*BOV*
Early (within one month)		
Wound complication	0	3
Bleeding	0	3
Ischemia due to "steal"	0	4
Death	4	2
Late (after one month)		
Septicemia	3	1
Anastomotic disruption with false aneurysm and skin necrosis	0	2
Mid-graft false aneurysm	2	1
Graft infection	2	3
High output heart failure	0	1
Anastomotic stenosis	5	2

BOV = bovine grafts SAV = saphenous arteriovenous

taken at operation again showed no growth of microorganisms.

False aneurysms of mid-graft puncture sites were observed in one patient. This graft was not initially punctured until three weeks after surgical operation. Numerous pseudoaneurysms developed at puncture areas within one year.

Three infections involving bovine grafts occurred several months after operation, eventually resulting in occlusion of all three fistulas. Incision, drainage and removal of graft segments were required for eradication of these graft infections.

Only one instance of high output heart failure has been noted in our entire dialysis access experience. This was relieved by banding the patient's straight femoral-saphenous bovine graft. The fistula has continued to function satisfactorily for 21 months.

Impaired fistula blood flow due to anastomotic stenosis was corrected by surgical revision in two patients.

Discussion

From October 1964 to October 1974, the authors provided surgical access for hemodialysis in 611 patients at Cedars-Sinai Medical Center. A total of 1,411 Scribner shunt cannulations and 320 internal AVF of all types were constructed.[13] During the past four years, a side-to-end RCAV fistula has been our preference for dialysis access whenever feasible. Our initial enthusiasm for SAV fistulas as a suitable alternative was diminished by their high incidence of late occlusion. In 1972, we began constructing BOV fistulas for patients with failures of RCAV or SAV fistulas. Favorable experiences led to employment of bovine access systems for new patients whose blood vessels were inadequate for RCAV.

The present study documents the long-term superiority in patency of BOV over SAV fistulas. The 71 percent one-year patency rates obtained with BOV are quite acceptable, and are clearly better than with SAV. The blood flow rates provided for dialysis by BOV fistulas are excellent. Graft puncture for access to the circulation has been accomplished with relative ease in all patients. Operative morbidity for BOV procedures is definitely less than for SAV fistulas, since the tedious and not atraumatic vein removal is avoided. For forearm fistulas, the operation can be done entirely under local anesthetic.

We are in agreement with Payne and coworkers[8] regarding preference for placement of the graft in the thigh in a straight alignment, with arterial origin from the distal superficial femoral artery. However, our data suggest that loop forms in either leg or arm locations may provide higher patency rates.

The groin area has been long recognized as highly susceptible to postsurgical infection. Other locations for hemodialysis access should therefore be given careful consideration before selecting the groin, particularly for implantation of foreign body material such as bovine arterial grafts.

Despite our general satisfaction with BOV fistulas, a significant qualification is necessary. The incidence of complications was greater with BOV than with SAV, and certain complications were severe and difficult to manage. Of the 52 BOV fistulas studied, 10 early and 10 late nonthrombotic complications occurred. Six were serious: one bleeding problem, three cases of ischemia and two late anastomotic disruptions. Each of these posed a definite threat to the patient's life or limb, and five required urgent surgical occlusion of the BOV fistula.

Infections of BOV fistulas were usually more difficult than those seen with RCAV or SAV. Puncture site infections of RCAV and SAV generally responded well to systemic antibiotics, hot compresses and limited incision and drainage. Similar infections of BOV grafts were not eradicated as easily. Three graft infections led directly to thrombotic occlusion. Moreover, persisting infection of the occluded grafts required subsequent surgical drainage or graft removal, similar to experiences with synthetic prosthetic implants.

The development of multiple pseudoaneurysms in one bovine graft raises the possibility that this graft was defective. In addition, the three inflammatory wound complications associated with graft necrosis and the two instances of late anastomotic disruption may have been due to degenerative changes in the bovine grafts.

The ischemic complications seen with BOV fistulas can be prevented by appropriate measures during operation. It is essential that peripheral pulses be evaluated before surgery. Ischemia results from the high blood flow rates and the shunting of large volumes of blood through the BOV fistulas. Restriction of the size of the arterial orifice is the critical factor for controlling the volume shunted. After completion of the anastomoses but before releasing blood flow through the fistula, a known distal pulse is observed. The

quality of this pulse is then noted as the fistula is opened. If the pulse disappears, it is advisable to constrict the arterial end of the graft with a prosthetic band before wound closure. With this technique, we have avoided limb ischemia since our initial experiences with this complication.

The complication data reflect the presence of a few problem patients who had strong thrombotic tendencies or extremely poor vasculature for fistula construction. Four such patients in this study accounted for eight SAV and nine BOV complications, and all four eventually died. These deaths were related to our inability to provide satisfactory permanent vascular access for dialysis. No allowance has been made for the adverse influence of these patients upon the complication data.

The high death rate in this report (32 of 151 patients) reflects the relatively old age of our patient population and the high mortality associated with long-term hemodialysis.[15] Thirteen deaths occurred in both the BOV and SAV groups. Four deaths in the SAV group were attributed to SAV complications. Only two of the deaths in the BOV group were directly related to the fistulas. The death due to cardiac arrhythmia during dialysis 24 hours after operation must be regarded as a postoperative mortality. The death due to septicemia seven months after operation represents a late lethal complication.

A need remains for the reporting of larger numbers of one-year and two-year results with BOV fistulas. We hesitate to endorse BOV without qualification: the serious nature of certain complications which were encountered with BOV in this study requires a note of caution. We believe that the potential for serious or lethal complications is greater with bovine heterografts than with autogenous grafts. We still prefer an RCAV fistula for dialysis access in all patients when feasible. When an adequate RCAV cannot be established, consideration is given to an SAV fistula, provided the saphenous vein appears optimal. When these options do not exist, we prefer BOV fistula as an acceptable alternative for hemodialysis access.

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