High complication rates with pelvic allografts

Experience of 22 sarcoma resections

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We performed 22 reconstructions by allografts in patients with pelvic sarcoma: 14 Ewing's sarcomas, 7 chondrosarcomas, and 1 osteosarcoma. All patients with Ewing's sarcoma and osteosarcoma received chemotherapy. No patients with chondrosarcoma had adjuvant treatment. 12 reconstructions were iliosacral arthrodesis after resection of an ilium tumor, 1 was iliofemoral arthrodesis and 9 were pelvic reconstructions with total hip prosthesis after resection of an acetabulum tumor. In the surviving patients, the mean length of follow-up was 4 (2–6) years.

2 allografts fractured and 8 allografts developed an infection. The infection was commoner in patients who had chondrosarcomas, large tumors, and a long operation time. Neither chemotherapy nor radiotherapy increased the infection rate. All infected allografts had to be removed.

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After resection of pelvic tumors, autogenous bone grafts, allografts, or a prosthesis can be used for reconstruction (Enneking and Dunham 1978, O'Connor and Sim 1989, Mnaymneh et al. 1990b, Campanacci and Capanna 1991, Gradinger et al. 1991). Advantages with allografts include osteointegration (Mankin et al. 1982, Bloem 1989, Gross et al. 1993), revascularization, and partial replacement with host bone (Wang and Shih 1993). A disadvantage is the high infection rate (Langlais and Vielpeau 1989, Mnaymneh et al. 1990, Campanacci and Capanna 1991, Joyce and Makley 1991, Harrington 1992). We reviewed our experience with allografts following resection of pelvic tumors.

Patients and methods

Between 1989 and 1993, we performed allograft reconstructions in 22 patients with pelvic sarcomas (Table 1). The mean age at the time of the reconstruction was 27 (9–60) years. There were 14 Ewing's sarcomas, 7 chondrosarcomas, and 1 osteosarcoma. 12 lesions were located in the ilium and 10 in the acetabulum with or without involvement of the pubis or ischium. Tumor volume was evaluated according to Göbel et al. (1987). The mean tumor volume at surgery was 250 (70–1300) mL. The surgical stage and surgical margin were classified according to the system of the Musculoskeletal Tumor Society (Enneking et al. 1980). All tumors had an extraskeletal tumor component; there were 3 stage IB and 19 stage IIB tumors. Pelvic resections were classified into 3 types (Enneking and Dunham 1978). Type 1 involves the ilium, type 2 the periacetabulum, and type 3 the pubic rami or ischium. In case 7, part of the colon was included with the resection.

In 12 cases, allografts were used for iliosacral arthrodeses (type 1 procedure) (Figure 1). 1 case (case 20) underwent iliofemoral arthrodesis with allograft and 9 cases underwent allograft acetabular reconstructions and hip arthroplasties after type 2 with/without type 3 excision (Figure 2). The mean volume of the allograft was 295 (100–670) mL. The acetabular component was cemented and a cementless femoral stem was used. Host-graft junctions were stabilized, using a large cancellous screw. In case 20, 2 compression plates were also used for iliofemoral arthrodesis. Cement with gentamicin was used to fill the marrow cavity of 5 allografts (3 in type 1 and 2 in type 2 procedures) for the theoretical advantages of decreasing the infection and fracture rate. No patient underwent simultaneous autogeneic bone grafting at the allograft-host junctions, because we intended to keep bone stock in the event of pseudoarthrosis, which may develop during postoperative chemotherapy.

14 patients with Ewing's sarcoma received chemotherapy according to the CESS protocol (Jürgens et al. 1989). 1 patient with osteosarcoma received chemo-

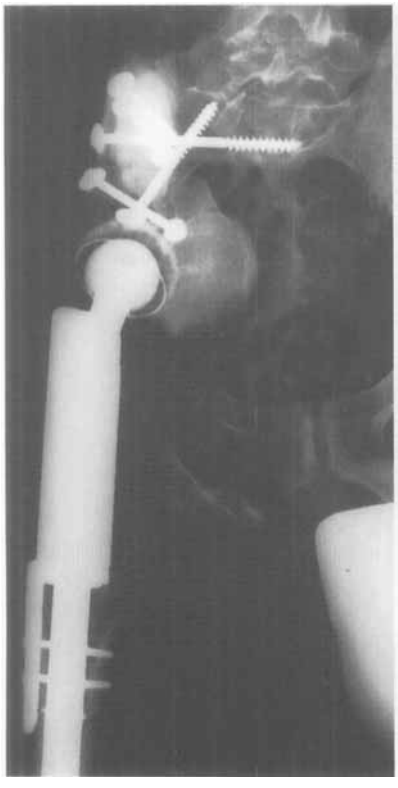
Table 1. Patient data

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z
1	31	M	E	2,3	260	2	W	300	–	2	9.0	6.4	1	1	55	1	(F)	N-R	–	15	1,2	1,2	1,3	–	C 37
2	18	M	E	2,3	100	2	W	670	+	2	8.3	12.5	1	2	44	–	F	U-U	–	–	–	–	–	–	C 48
3	15	M	E	1	100	2	M	240	–	1	5.7	9.0	1	1 3	55 15	1,2,3	(F)	R-R	–	4	3,4,5	1,2	–	–	C 30
4	20	M	E	1	70	2	W	330	–	1	5.2	3.7	1	1 3	55 10	1,4	G	U-U	17	–	–	–	–	M 23	A 39
5	24	F	E	1	80	2	IL	210	–	1	5.0	4.5	1*	1 3	55 10	1,3	G	N-N	–	–	–	–	–	M 10	D 25
6	30	F	E	1	120	2	IL	160	–	1	4.8	8.1	1	1 3	54 10	4	G	N-R	–	–	–	–	–	M 12	D 18
7	15	M	E	1	220	2	M	240	+	1	6.5	4.3	1	1	56	1,2,6	(F)	R-R	–	3	1	1,2	–	–	C 49
8	17	M	E	1	120	2	M	180	–	1	4.4	10.0	1	1 3	56 15	1	G	N-R	–	–	–	–	–	M 8	D 17
9	15	M	E	1	90	2	W	180	–	1	5.0	3.9	1	2	45	–	G	N-U	–	–	–	–	–	–	C 60
10	12	M	E	1	100	2	W	200	–	1	4.1	4.7	1	1	56	1,4	E	N-U	–	–	–	–	–	M 23	A 28
11	9	M	E	1	90	2	W	180	–	1	3.6	4.5	1	1	54	–	E	N-U	–	–	–	–	–	M 8	D 20
12	16	M	E	1	110	2	M	300	+	1	5.0	3.5	1	1	48	–	G	N-U	–	–	–	–	–	–	C 40
13	11	M	E	1	100	2	W	240	–	1	3.7	4.5	1	1	54	–	E	N-U	–	–	–	–	–	–	C 48
14	18	M	E	1	100	2	W	100	+	1	3.1	6.6	1	1	54	2	F	N-U	–	–	–	–	–	M 11	A 27
15	43	M	O	2	270	2	W	530	+	2	6.7	13.0	2	–	–	1	F	R-R	–	–	–	–	–	M 11	D 17
16	39	M	C	2	150	1	W	290	–	2	9.7	12.2	–	–	–	1	G	U-U	–	–	–	–	–	–	C 49
17	56	M	C	2	480	1	M	380	–	2	9.0	13.1	–	–	–	–	(P)	N-R	–	14	5	1,2	2	–	C 54
18	50	F	C	2	150	2	M	240	–	2	8.0	9.0	–	–	–	–	(P)	U-R	12	–	–	1	2	L 15	N 75
19	36	M	C	2	250	2	W	400	–	2	9.5	11.8	–	–	–	–	(F)	R-R	–	2	3,6	1,2	3	–	C 53
20	31	M	C	2,3	1300	2	W	430	–	3	13.0	13.1	–	–	–	5	(P)	R-R	–	4	1	1,2	–	–	C 34
21	29	M	C	2,3	750	1	M	340	–	2	16.4	21.2	–	–	–	1	(P)	R-R	–	0.5	4,5,7	1,2	2	–	C 53
22	60	F	C	2	500	2	W	370	–	2	5.7	4.8	–	–	–	2	(F)	R-R	–	2	2,8	1,2	3	–	C 61

A Patient number
B Age at diagnosis
C Sex
D Tumor
  E Ewing's sarcom
  O Osteosarcoma
  C Chondrosarcoma
E Tumor site and excision
  1 Ilium
  2 Acetabulum
  3 Pubis or ischium
F Tumor volume (mL)
G Surgical stage (Enneking et al. 1980)
H Surgical margin (Enneking et al. 1980)
  W Wide
  M Marginal
  IL Intralesional
I Allograft volume (mL)
J Cementation
K Reconstruction method
  1 Iliosacral arthrodesis
  2 Hip prosthesis
  3 Iliofemoral arthrodesis
L Duration of operation (h)
M Blood loss (thousands mL)
N Chemotherapy
  1 CESS (Jürgens et al. 1989)
  2 COSS (Winkler et al. 1990)
  * Bone marrow transplantation (Burdach et al. 1993)
O Radiation therapy
  1 Preoperative
  2 Postoperative
  3 Brachytherapy
P Radiation doses (Gy)
Q Postoperative problems
  1 Skin necrosis
  2 Superficial infection
  3 Hematoma
  4 Loosening of screw
  5 Thrombosis
  6 Sigmoid-skin fistula
R Function (without allograft)
  E Excellent
  G Good
  F Fair
  P Poor
S Union
  1–2 years
  U Union
  N Nonunion
  R Removal of allograft
T Fracture (months)
U Infection (months)
V Microbiology
  1 *Pseud. aeruginosa*
  2 Staph. aureus
  3 E. coli
  4 Enterococ. faecalis
  5 Staph. epidermidis
  6 *Peptococ. niger*
  7 Prot. mirabilis
  8 Klebsiella oxytoca
W Local treatment for failure
  1 Removal
  2 *Gentamicin beads*
X Second salvage surgery
  1 Allograft and prosthesis
  2 Hemipelvectomy
  3 Saddle prosthesis
Y Relapse (months)
  M Metastasis
  L Local recurrence
Z Outcome (follow-up months)
  CDF Continuous freedom from disease
  NED No evidence of disease
  AWD Alive with disease
  DOD Died of disease

therapy according to the COSS protocol (Winkler et al. 1990). 12 and 2 patients with Ewing's sarcoma received pre- and postoperative irradiation, respectively. In 6 patients who received intraoperative brachytherapy after tumor resection, the duration of brachytherapy was excluded from the operation time, because the operation field was completely closed and skin was aseptically covered by the surgical drape and clean clothes during the 2 hours of brachytherapy. Case 5 underwent bone marrow transplantation after development of metastases (Burdach et al. 1993). No patients with chondrosarcoma received adjuvant treatment.

All allografts were procured in a sterile operating room. Donors or cadavers from whom allografts were obtained met the selection criteria of the European



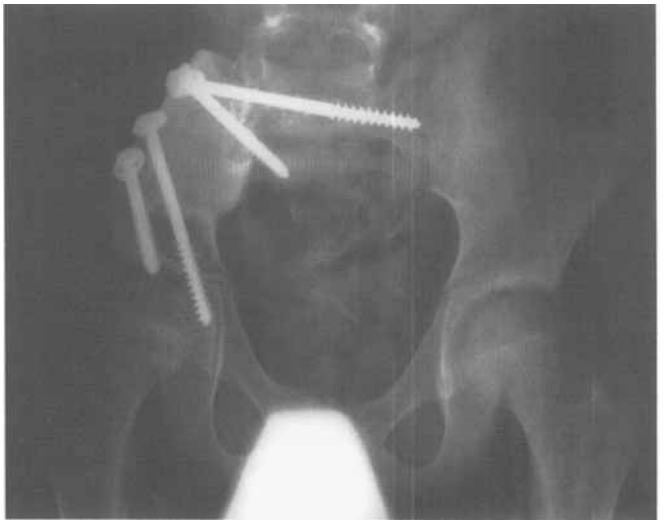


Figure 1. Case 11. Ewing's sarcoma, 18 months after surgery.

Figure 2. Case 15. Osteosarcoma, 9 months after surgery.

Association for Musculo-Skeletal Transplantation (EAMST 1993). All grafts were stored at –80 °C. The bone was sterilized using γ-radiation from radioactive cobalt in a dose of 26,000 Gy. All but 3 allografts (cases 14, 17, and 21) received irradiation for sterilization before implantation.

All patients received intravenous antibiotic therapy peroperatively and for 3 weeks after surgery. Oral antibiotic prophylaxis was given 3 months after surgery. Hemovac drains were removed at a mean of 10 days after surgery. Partial weight-bearing was started at 3 months after iliosacral arthrodesis and 6 months after hip plasty following acetabular resection. Total weight-bearing was begun at 6 months after iliosacral arthrodesis and 12 months after hip arthroplasty.

Patients were followed routinely as outpatients at 3-monthly intervals. The mean follow-up for 17 survivors was 4 (2–6) years. Union of the graft to the host bone was said to have occurred if there was no visible osteotomy line at the junction sites or if greater than or equal to 75% of cortical thickness was fused on follow-up radiographs, according to the ISOLS radiological implants evaluation system (Glasser and Langlais 1991). The evaluation of union/nonunion at the junction was done at both 1 and 2 years. Functional evaluation (Enneking 1987) was performed at the most recent follow-up examination.

Infection which occurred within 4 months after implantation was defined as an early infection and that which occurred after 4 months was a late infection (Lord et al. 1988). If allograft infection was identified during the follow-up periods, administration of systemic antibiotics, in combination with effective drainage, was instituted before removal of the allograft. If inflammatory signs did not disappear or if the discharge persisted, the allograft was removed and the patients underwent debridement plus gentamicin-polymethyl methacrylate (PMMA) bead (Septopal®, Merck, Darmstadt, Germany) implantation. If infection was controlled following allograft removal, salvage surgery was planned.

Differences between proportions were evaluated by the chi-square test with Fisher's correction. The differences of the mean rank between 2 continuous variables were evaluated by the Mann-Whitney U test.

Results

1 patient with chondrosarcoma developed a local recurrence and was treated with hemipelvectomy. 7 of 14 patients with Ewing's sarcoma and the patient with

osteosarcoma developed metastases. At final follow-up, 4 of 14 patients with Ewing's sarcoma and 1 patient with osteosarcoma had died. All 7 patients with chondrosarcoma were alive and without disease.

Union

In 5 of 15 patients, union was noted at 1 year after implantation. In 9 of 10 patients, union was noted 2 years after implantation.

Complications

2 patients had large hematomas (cases 3 and 5) and 1 had a femoral artery thrombosis (case 20). 11 patients had skin necrosis or superficial infection around the operative wound and case 7 had colon-cutaneous fistula after an en-bloc resection of the iliac bone and the sigmoid colon. No nerve palsy was observed.

The screws in cases 4, 6, and 10 loosened between 9 and 11 months after implantation. In case 4, all screws were removed. In case 6, a meticulous radiographic follow-up was performed without further operation and this patient died of pulmonary metastasis 1.5 years after surgery. In case 10, the loosened screw was replaced by a longer screw.

Cases 4 and 18 sustained allograft fractures 17 and 12 months after implantation, respectively. Case 4 did not undergo additional surgery and had no further problems. The fracture did not heal. Case 18 had a local relapse 3 months after the fracture which was treated by hemipelvectomy.

6 patients had an early allograft infection and 2 patients had a late infection. Infection appeared as early as 2 weeks and as late as 15 months after implantation (mean 6 months). Case 1 had a late allograft infection after a urinary tract infection. Case 17 had a skin infection before a late allograft infection. 7 of 8 infections were caused by gram-negative or multiple organisms. Staphylococcus was identified in 5 infections, *Pseudomonas aeruginosa* in 3 infections, *Escherichia coli* in 2, *Enterococcus faecalis* in 2, *Proteus mirabilis* in 1, *Peptococcus niger* in 1, and *Klebsiella oxytoca* in 1.

Early infection was commoner in chondrosarcoma than in osteosarcoma or Ewing's sarcoma (p 0.05), in large tumors than in small tumors (p 0.02), after a long operation time than after a short one (p 0.03) (Table 2). The number of early infections did not increase after chemotherapy or preoperative irradiation.

The 8 infected allografts were treated with intravenous antibiotics, graft removal, and gentamicin bead implantation. In 6 cases (1, 3, 7, 19, 20, and 22), infectious and inflammatory signs disappeared and additional limb salvage surgery was performed in 3 of these cases (1, 19, and 22). Case 1 underwent further reconstruction with a new allograft and prosthesis, but a Pseudomonas aeruginosa infection occurred 1 year later. The allograft was removed and replaced by a saddle prosthesis. Cases 19 and 22 were treated with graft removal and insertion of saddle prostheses. Cases 3, 7, and 20 underwent no further reconstructive surgery. Cases 17 and 21 underwent hemipelvectomy to control infection.

Table 2. Analysis of the early infection

Value		Infection	No infection	P-value
Diagnosis				
Ewing's sarcoma or osteosarcoma		2	13	
Chondrosarcoma		4	3	0.05
Site: ilium		2	10	
acetabulum		4	6	0.3
Mean tumor volume (mL)		483	118	0.002
Mean operation time (h)		9	6	0.03
Blood loss (L)		11	8	0.2
Reconstruction type	1	2	10	
	2	4	6	0.3
Gentamicin cement	+	1	4	
	–	5	12	0.9
Skin problems	+	5	7	
	–	3	10	0.7
Chemotherapy	+	2	13	
	–	4	3	0.05
Radiation	+	2	12	
	–	4	4	0.1

Mean operation time for type 1 procedures 5 h, type 2 10 h.

Function

At the final examination, the allograft remained in 13 patients. After type 1 procedure, the outcome was excellent in 3 patients, good in 6, and fair in 1. After type 2 procedure, the outcome was good in 1 and fair in 2 patients. 2 and 7 patients were without allograft following type 1 and 2 procedures, respectively. 2 patients with no reconstructions after type 1 procedures had fair function. Following type 2 procedures, 3 were poor after hemipelvectomy, 3 were fair after saddle prosthesis insertion, and 1 was poor after no reconstruction.

Discussion

Local control of disease did not appear to be compromised by local resection of pelvic sarcomas. The local relapse rate (1/22) was satisfactory because 19 of 22 patients had high-grade tumors. However, the follow-up time is short, especially patients with chondrosarcoma may have late local recurrences.

Nonunion is a major complication of this procedure and some have attributed this to systemic chemother-

apy and local irradiation (Friedlaender et al. 1984). Our early experience (unpublished data) with extremity sarcomas corroborates this. In this study, 9 of 10 patients had union at 2 years' follow-up although we used no complementary autografts. Perhaps, the large contact area between allograft and host bone in the pelvis may have contributed to this.

Allograft fracture is another complication, but is seldom reported after pelvic reconstructions. 2 of our 22 patients had fatigue fractures, and this compares favorably with Harrington's series (1992) who had 2 of 10.

Infection of the allograft is a serious complication. High infection rates (15, 25, and 50%) have been reported (Loty et al. 1990, Mnaymneh et al. 1990a, Joyce and Makley 1991). In our series, one third of the patients were infected. Other types of extensive surgery using allografts do not have such a high rate of infection in our hospital. The possible causes of infection are long operation time, large blood loss, foreign body reaction, skin complications, radiation therapy, chemotherapy, and infection of another organ (e.g., urinary tract). Of 8 infections in this series, 6 appeared within 4 months after implantation. However, 2 infections occurred 14 and 15 months after implantation. The causes of delayed infection were infections of the urinary tract and skin. Disorders which may become causes of the delayed infection must be treated promptly and adequately.

The majority of complications and unsatisfactory results with allografts have been reported in patients receiving chemotherapy, radiation therapy, and high doses of steroids (Mankin et al. 1983, Friedlaender et al. 1984). To this, we add operation time. The average tumor volume of chondrosarcomas was significantly larger than that of Ewing's sarcomas or osteosarcomas. Reducing the tumor volume before surgery by adjuvant treatment leads shortens the operation times, and this may reduce the infection rate of the allograft. Moreover, Ewing's sarcomas mainly affected the ilium, as compared to chondrosarcomas which involved the acetabulum. The difficulty in performing acetabular resection and reconstruction, as compared to iliac resection, leads to a longer operative time and thus an increased risk of infection. Temple et al. (1995) reported a significant relationship between infection and intraoperative blood loss. However, the influence of the blood loss on the infection may be explained by the duration of the surgery.

Lord et al. (1988) were able to eradicate 6 of 33 single gram-positive bacterial infections with antibiotics, debridement, and graft preservation. Conservation of the allograft was difficult in all our cases of infection. If an infection is identified, we suggest that the allograft should be removed using a gentamicin-impregnated polymethylmethacrylate spacer, and the wound should be closed over drains. If the discharge persists, inflammatory signs remain positive, or organisms continue to be identified, antibiotic treatment should not be given for a long period and the only solution may be hemipelvectomy.

In conclusion, the infection rate of the pelvic reconstruction by using allograft after resection of the tumor was high and more frequent in acetabular tumors than in ilium tumors. Allograft reconstruction of the pelvis, especially for the acetabular tumors, has an unacceptable complication rate.

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