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Autoclaved tumor bone for reconstruction: an alternative in developing countries

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Autoclaved Tumor Bone for Reconstruction

An Alternative in Developing Countries

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The options for reconstruction after excision of skeletal tumors include reimplanting the autoclaved tumor-bearing bone. We asked whether such bone will survive and unite with normal bone and whether the local tumor recurrence rate increases after its use. We ascertained the functional outcome (Musculoskeletal Tumor Society score) and complications in 19 patients. After wide excision, the bony segment was autoclaved at 120° for 10 minutes and reimplanted at the original defect with intramedullary nails and compression plates. Twelve of our 19 patients were available for followup. The autoclaved segment united with the normal bone in 11 of the 12 patients. No patients had fracture or resorption of the autoclaved segment. Two patients had local tumor recurrence in nearby soft tissues, apparently unrelated to the autoclaved bone. The mean functional score was 70%. Complications included fatigue failure of the nail in one patient, superficial infection in three patients, and deep infection in two patients. Reconstruction with autoclaved tumor-bearing bone is a simple and effective tool in limb salvage. This technique is a cost-effective alternative for developing countries circumventing complications of prosthetic and allograft reconstruction.

Level of Evidence: Therapeutic study, Level IV (case series). See the Guidelines for Authors for a complete description of levels of evidence.

There has been an increasing trend toward limb-sparing approaches rather than amputation in musculoskeletal tumor surgery. Limb-sparing surgery is performed in 70% to 80% of patients, even patients with high-grade sarcomas.[6]

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Improvements in imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) and advances in neoadjuvant and adjuvant chemotherapy also have influenced the ratio of ablative and limb-salvage procedures.

Reconstruction of large skeletal defects after wide-margin excision of skeletal tumors is complicated and challenging. There are several limb-salvage options. Total joint replacement prostheses and modular tumor prostheses offer maintenance of motion and immediate functional restoration. However, prosthetic survival decreases with time, and prostheses are almost certain to fail in young patients.[12,27] Studies of large-tumor prostheses have reported failure rates of 33%,[19,39] 60%,[37] and 100%.[26] The failures occur from infection[24] and late complications such as implant breakage and aseptic loosening.[8,38] In developing countries such as Pakistan, prosthetic reconstruction is not practical because of the expense of primary prosthetic surgery for tumors.

Reconstruction with structural allografts is another alternative. Allograft reconstruction has a definite associated risk of disease transmission (eg, human immunodeficiency virus and hepatitis). Investigators have reported a 12% to 23% nonunion rate in allografts.[2,20] The rate of fracture and infection with structural allografts has been reported as 16%,[3,33] 67%,[17,34] and 12%.[35] Services providing allografts require standardization of donor selection, screening, procurement, storage, and retrieval. Importantly, a standardized bone bank needs a large budget, and in Pakistan, sociocultural reasons preclude wide use. Therefore, we have used autoclaved bone as an alternative in limb-salvage procedures.

We asked whether such autoclaved bone survives and unites with the host bone and whether there is risk of local tumor recurrence related to the reimplanted autoclaved tumor-bearing bone. We evaluated the functional outcome and complications associated with this technique of reconstruction.

MATERIALS AND METHODS

We retrospectively reviewed 19 consecutive patients with different malignant bone tumors. All patients with malignant bone

tumors requiring reconstruction for limb salvage and with preserved cortical structure of the involved bone were included. Three patients with aggressive lytic lesions or with tumors involving very long bony segments were excluded. One of these patients had telangiectatic osteosarcoma and two had Ewing's sarcoma. Ten of the 19 patients were males and nine were females. The mean age of the patients at the time of surgery was 21 years (range, 7–59 years). Twelve of our 19 patients were available for followup. Three patients died from systemic disease. Three patients were lost to followup in a 6-month to 8-month period, and one patient had an above-knee amputation.

The mean followup was 49 months (range, 18–80 months).

Twelve patients had a pathologically confirmed diagnosis of osteogenic sarcoma, three patients had Ewing's sarcoma, two patients had chondrosarcomas, one patient had metastatic renal cell carcinoma, and one patient had nonHodgkin's lymphoma. All patients had preoperative pulmonary CT scans and bone scan to determine the stage of disease. We used preoperative MRI to define local staging according to the classifications described by Enneking et al.[16] Fourteen patients had Stage IIB disease, four patients had Stage IIIB disease, and one patient had Stage IIA disease (Table 1).

A wide surgical margin was achieved in all patients. Surgical margins were confirmed by frozen sections of bone marrow taken from the osteotomy site and soft tissues. The length of the resected bony specimens varied from 12 cm to 22 cm. After resection, the bone segment was denuded of all the attached soft tissue, and the intramedullary canal was reamed. The segment then was autoclaved at 120°C for 10 minutes. The specimen was washed with saline mixed with antibiotics (first-generation cephalosporin and aminoglycosides) and then fixed in the original defect by appropriate implants. Intramedullary Küntscher nails and dynamic compression plates were used across the osteotomy site for axial and rotational stability (Fig 1). Thirteen patients had concurrent knee arthrodeses. To promote union at the osteotomy site, fixation was supplemented by autogenous bone grafts in six patients, screened allografts in six patients, and free vascularized fibular grafts in three patients. Four patients did not have supplemental bone grafting. All patients with osteogenic sarcoma and Ewing's sarcoma received preoperative and postoperative chemotherapy.

Patients were followed up to observe the progress of union at the osteotomy site and to identify complications, including tumor recurrence or infection. We used the functional evaluation adopted by the Musculoskeletal Tumor Society (MSTS).[15,16] The clinical scoring was obtained on a point-by-point basis for every patient, including general and specific criteria of the extremity. Plain radiographs, CT scans, chest scans, and bone scans were done at 6-month intervals to observe any local or distant metastases. Criteria for radiographic union were trabecular continuity on at least three cortices at the graft-host bone (autoclave bone) junction (Fig 1). At least three of the authors (MJK, MU, HR, MU) reviewed the radiographic and clinical observations together in the outpatient clinic at the final followup. The senior surgeon (MU) was present on all occasions.

RESULTS

The survival of the autoclaved tumor-bearing bone was 100%. We observed no fractures and no resorption of the autoclaved segments. The autoclaved bony segment united with the normal bone in 11 of the 12 patients. The mean time for complete union was 24.2 months (range, 20–28 months). The patient without union had the nonunion at the distal osteotomy site. In that patient, the compression plating was revised with supplemental autogenous bone grafting at the distal osteotomy site.

Two patients with osteogenic sarcoma had local soft tissue recurrences not spatially related to the autoclaved bone. One of these patients was lost to followup after 3 months. The patient lived in a remote area and presented later with a local recurrence treated elsewhere. A plain radiograph showed the recurrence in the soft tissue near the distal osteotomy site. We recommended a course of evaluation and management but the patient did not follow up. The other patient did not receive postoperative chemotherapy and was lost to followup. After 3 years, the patient presented with local soft tissue recurrence and multiple metastases to the lung and died. The recurrence was near the proximal osteotomy site, but did not involve the bone on MRI. Three other patients died from multiple distant metastases with no evidence of local recurrence.

The average MSTS functional score was 21.08, representing 70% overall function (Table 1). Three patients had superficial wound infections. Each patient required two surgical débridements. Cultures from the tissues revealed no growth. These patients received intravenous first-generation cephalosporin and aminoglycosides for 2 weeks. Two patients had deep infections. One patient was treated successfully with multiple débridements, intravenous antibiotics, and a local rotational flap for skin coverage. One patient needed an above-knee amputation because the limb could not be salvaged. Fatigue failure of the intramedullary (IM) nail occurred in one patient, which was used without compression plates (Fig 2). We did an exchange nailing, and the osteotomy site eventually healed.

DISCUSSION

Reconstruction after wide excision in skeletal tumors is challenging. Prosthetic reconstruction is attractive, but long-term results have not been successful in younger patients.[14,21,28,40] Also, the expenses involved with prosthetic reconstruction preclude its use in many areas. Allograft reconstruction is another alternative, but establishing a standard bone bank requires financing not available in Pakistan and many other countries. Socioreligious reasons

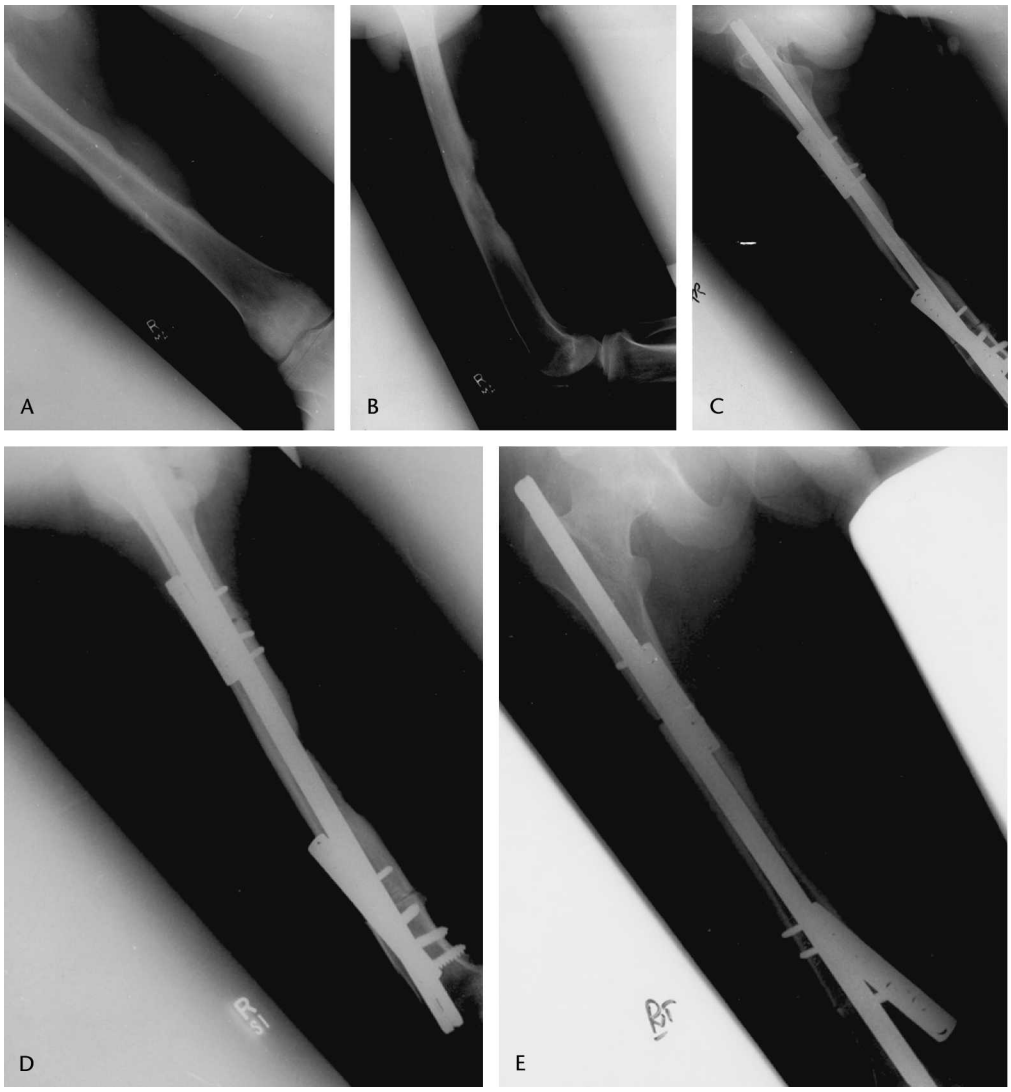

Fig 1A–E. (A) An AP radiograph shows diaphyseal osteogenic sarcoma of the femur in a 21-year-old man. (B) A lateral radiograph of the same patient shows posterior cortical erosion. (C) A postoperative radiograph taken immediately after wide-margin excision is shown. The autoclaved segment was 12 cm long and was stabilized by an IM nail and compression plates. (D) Oblique and (E) AP radiographs taken 1 year postoperatively show how the distal osteotomy site healed with progressive union at the proximal osteotomy site. The proximal osteotomy site also healed after 8 months.

preclude use of allograft in many of our patients. Therefore, we have used autoclaved bone for reconstruction. This is a well-recognized reconstructive technique.[1,4,10,18,24,48,49] In contrast to allografts, autoclaved autografts conform to the defect and use the patients' tissue for reconstruction. This eliminates the need for bone banking and the risk of disease transmission associated with allografts.

Our study has some limitations. We have no histologic evidence of union, and strong fibrous tissue interposition between the bony segments can eliminate pain and simulate bony union. We also have no histologic evidence of graft revascularization and long-term graft survival. Long-term studies with advanced imaging techniques are required to answer these questions.

Union occurred in 11 of our 12 patients who were followed up, a rate comparable to those in other series.[4,9,42] The time for union was 24.2 months (range, 20–28 months). This long period delays rehabilitation and functional restoration, which is much faster after prosthetic reconstruction. The extended duration for healing of the graft has been its greatest criticism. The inductive capacity and the mechanical strength of bone are largely destroyed after autoclaving.[41,43,44] For the same reason, temperatures

TABLE 1. Patient Demographics, Complications, and Results

Patient Number	Age (years) Gender	Diagnosis	Stage	Surgery	Length of Augoclaved Segment	Results (Musculoskeletal Tumor Society score)
1	11/F	Osteogenic sarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	18 cm	23/30
2	21/M	Osteogenic sarcoma (femur)	IIB	Wide-margin excision	12 cm	22/30
3	7/M	Ewing's sarcoma (femur)	IIB	Wide-margin excision	15 cm	20/30
4	59/M	NonHodgkin's lymphoma (femur)	III	Wide-margin excision	12 cm	21/30
5	15/F	Osteogenic sarcoma (femur)	III	Wide-margin excision, knee arthrodesis	18 cm	Died from systemic disease
6	15/F	Osteogenic sarcoma (tibia)	IIB	Wide-margin excision, knee arthrodesis	15 cm	Died from systemic disease
7	23/M	Osteogenic sarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	20 cm	20/30
8	45/M	Chondrosarcoma (femur)	IIA	Wide-margin excision	15 cm	Deep infection leading to amputation
9	15/M	Osteogenic sarcoma (humerus)	IIB	Wide-margin excision	14 cm	Lost to followup, had local recurrence, died from systemic disease
10	44/M	Metastatic renal carcinoma (femur)	III	Wide-margin excision	16 cm	Lost to followup
11	11/F	Osteogenic sarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	20 cm	23/30
12	17/F	Osteogenic sarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	18 cm	20/30
13	21/M	Ewing's sarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	14 cm	20/30
14	17/M	Chondrosarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	31 cm	21/30
15	10/F	Osteosarcoma (humerus)	IIB	Wide-margin excision	13 cm	22/30
16	17/M	Osteosarcoma (tibia)	IIB	Wide-margin excision, knee arthrodesis	22 cm	22/30
17	18/F	Osteosarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	12 cm	Loss to followup (local recurrence)
18	15/F	Osteosarcoma (tibia)	IIB	Wide-margin excision, knee arthrodesis	21 cm	Died from systemic disease
19	15/F	Ewing's sarcoma (femur)	IIB	Wide-margin excision, knee arthrodesis	14 cm	19/30

Disease staged according to classification system described by Enneking et al.[16]

and heating times are different between studies[7] (Table 2).

Healing of autoclaved bone segments seems to be a function of mechanically optimized osteosynthesis and supplementation by bone grafts. Harding[22] suggested an autoclaved bone segment acts as a foreign body. Histologic observation 3 years after the procedure showed the grafts were covered by fibrous tissue.[22] In contrast, Wangerin et al[46] reported histologic incorporation with no inflammatory reaction and early bony remodeling of the avascular autoclaved bone. We presumed the absence of surrounding fibrous tissue to indicate the bone was not considered a foreign body. Fibrous tissue also may form in reaction to construct instability.

Postoperative chemotherapy also can contribute to delayed healing of the reimplanted segment. The effect of chemotherapy on osseointegration is well documented. Studies have indicated chemotherapeutic agents including doxorubicin, cisplatin, and ifosfamide substantially affect new bone formation.[45,50]

Experiments suggest supplementation with vascularized fibular grafts, allogeneic bone matrix, and bone marrow increases the rate of incorporation and strength.[5] We also have used different supplementary bone grafts in most of our patients.

Two of our patients had local recurrence unrelated to autoclaved bone. We think the results are acceptable and comparable to those in previously published reports (Table 3).

Fig 2A–F. (A) An AP radiograph of an 11-year-old girl shows osteogenic sarcoma of the left distal femur. (B) A lateral radiograph shows the patient's knee. The bony structure of the femur is nicely preserved, and can be used for reconstruction after autoclaving. (C) A postoperative radiograph shows the autoclaved reimplanted segment after bone grafting and knee arthrodesis using custom-made intramedullary K nails. (D) Anteroposterior and lateral radiographs of the knee and tibia show how three-point fixation was achieved using long custom Kuntscher nails. (E) Anteroposterior and (F) lateral radiographs show the patient 2 years postoperatively. Exchange nailing was done after 6 months because of fatigue failure. The radiographs show a healed and consolidated autoclaved tumor-bearing bone at the proximal and distal osteotomy sites.

TABLE 2. Comparison of Temperature and Time Used to Autoclave Tumor-bearing Bone Segments

Authors	Temperature/Time	Local Recurrence
Smith and Simon[41]	135°C/12–15 minutes	1/8 patients
Harrington[23]	135°C/7–10 minutes	2/48 patients
Lauritzen et al[29]	120°C/20 minutes	0/13 patients
Harrington et al[24]	135°C/10 minutes	0/4 patients
Suk et al[42]	65°C/30 minutes	0/12 patients

The high infection rate in our patients was a concern, but it could not be attributed solely to the reconstruction technique. Bone tumor excision necessitates extensive soft tissue resection to obtain tumor-free margins. Local clearance of the tumor cannot be compromised. This affects the blood supply of the surgically treated area, which makes it vulnerable to infection. The amputation rates associated with periprosthetic infection are even greater (40–87%).[25,47] Our infection rate was comparable with those of other methods of reconstruction, including autografts and allografts.[11,13,30] We think careful surgical planning, meticulous dissection, strict aseptic technique, and perioperative antibiotic coverage can help reduce infection. In addition, if plastic and microvascular surgeons are involved in the surgical planning, it could help to avoid ischemic local skin flaps and dead space, minimizing the risk of infection.

Unlike prosthetic reconstruction, this technique has not always provided a mobile joint: 13 of our patients had knee arthrodeses. However, the overall function of our patients was 70%, which is acceptable and comparable to function provided by other modes of reconstruction.[12,14,20] Although arthrodesis is not a desirable result, stiff and pain-free weightbearing limbs can serve most functions. Our technique produced good results. Our patients are now disease free with durable biologic reconstructions and acceptable functional outcomes.

We think reimplantation of tumor-bearing autoclaved bone segments is a simple, cost-effective, and practical reconstruction method in limb-salvage surgery. The autoclaved segments take longer to heal but result in biologic replacement of the resected segment, minimizing the chances of revision surgery. Local tumor recurrence, complication rate, and functional outcome of the technique are acceptable. Using autoclaved bone segments is worth considering in developing countries where the resources for tumor prostheses and bone banks are limited.[31,32,36] All established reconstruction methods are associated with high complication rates, and new surgical options should be explored.

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TABLE 3. Comparison with Previous Studies

Authors	Number of Patients	Temperature and Time of Heat Treatment	Union Rate	Time to Union	Local Recurrence	Infection	Nonunion
Current study	19	120°C/10 minutes	91.7%	24.2 months (range, 20–28 months)	2/19 patients	5 cases (three superficial, two deep)	1
Suk et al[42]	12	65°C/35 minutes	91.7%	4.6 months (range, 3–7 months)	0	0	1
Chang et al[9]	14	N/A	78.5%	N/A	2/14	1	3
Bohm et al[4]	9	120°C/20 minutes	100%	13 months	0	1	0

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