Risk factors for postoperative deep infection in bone tumors

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RESEARCH ARTICLE

Risk factors for postoperative deep infection in bone tumors

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Abstract

Background

Postoperative deep infection after bone tumor surgery remains a serious complication. Although there are numerous reports about risk factors for postoperative deep infection in general surgery, there is only a small number of reports about those for bone tumor surgery. This retrospective study aimed to identify risk factors for postoperative deep infection after bone tumor resection.

Methods

We reviewed data of 681 patients (844 bone tumors) who underwent surgery. Associations between variables, including age, recurrent tumor, pathological fracture, surgical site (pelvis/other), chemotherapy, biological reconstruction, augmentation of artificial bone or bone cement, the use of an implant, intraoperative blood loss, operative time, additional surgery for complications, and postoperative deep infection were evaluated.

Results

The rate of postoperative deep infection was 3.2% (27/844 tumors). A pelvic tumor (odds ratio [OR]: 3.4, 95% confidence interval [CI]: 1.0–11.3) and use of an implant (OR: 9.3, 95% CI: 1.9–45.5) were associated with an increased risk of deep infection.

Conclusions

This retrospective study showed that pelvic tumor and use of an implant were independent risk factors for deep infection. This information will help surgeons prepare an adequate surgical plan for patients with bone tumors.

Introduction

Deep infection is one of the most serious complications after surgery. Postoperative deep infection usually requires additional surgery, the prolonged use of antibiotics, and delays in scheduled treatment such as chemotherapy. Among orthopaedic surgeries, 9–36% of patients had deep infection after bone tumor surgery [1–5]. McDonald et al. reported that 11.8% of patients who received limb salvage surgery experienced infection, and 22.2% of patients with postoperative infection underwent amputation [6]. To improve the outcome of bone tumor surgery, the risk of each surgery should be assessed and patients with high risk of deep infection should be treated with preventive measures such as nutritional optimization, perioperative antibiotics or MRSA nasal screening and decolonization. Although there are numerous reports describing risk factors for postoperative deep infection after orthopedic surgery, including arthroplasty and spine surgery, only a small number of studies have reported those after bone tumor surgery [5,7–11]. In the reports, African-American race, local infection at the limb sparing surgery, lower WBC, BMI, age, total number of procedures, preexisting implants, infection at another site, malignant disease, hip region affected, and duration of the procedure, were independent risk factor for deep infection after bone tumor surgery [5,7,9,11]. To choose adequate surgical treatment, it is important to assess the risk of postoperative deep infection in each patient preoperatively. In the present study, the frequency of postoperative deep infection and correlations of deep infection with various clinical parameters, including age, the tumor location, the use of an implant, chemotherapy, the use of artificial bone or cement, operative time, intraoperative blood loss, biological reconstruction, and additional surgery for complications, were investigated to identify risk factors for postoperative deep infection.

Methods

Patients

This was a single-center, retrospective case study. Overall, 681 patients with 844 bone tumors, who underwent surgery between January 1995 and December 2015, were enrolled in this study. Metastatic bone tumors were excluded from this study. The study patients comprised 390 men and 291 women whose ages ranged from 1 to 92 years (mean age, 28.0 years). The tumor diagnoses were confirmed through histopathological examinations (Table 1). Bone tumors located in the femur (n = 273), tibia (n = 176), humerus (n = 95), pelvis (n = 80), foot (n = 64), hand (n = 58), fibula (n = 33), rib (n = 17), scapula (n = 14), ulna (n = 14), radius (n = 14), clavicle (n = 4), sternum (n = 1), and patella (n = 1) were included in this study (Table 2). Patients with spine tumors and those who underwent surgery using implants with an antimicrobial coating were excluded from this study. The reconstructions after resection of bone tumors were classified into: no reconstruction, biological reconstruction, implant replacement, use of artificial bone or cement, or composite use of the materials. This retrospective study was approved by the ethics committee of Kanazawa University. All data were fully anonymized before access by the researchers, and the ethics committee waived the requirement for informed consent.

Outcome measure

In this study, the incidence of postoperative deep infection and its association with various factors were evaluated. The optimal cutoff levels for age, the operative time, and intraoperative blood loss were identified in receiver operator characteristic curve analysis. The patient-related parameters were as follows: age ($<$20 or $\geq$20 years), location of the tumor (pelvis or other), recurrent tumor (yes/no), pathological fracture (yes/no), and chemotherapy (yes/no). The

Table 1. Diagnoses of the lesions.

Benign tumor		Malignant tumor	
Diagnosis	Number of lesions	Diagnosis	Number of lesions
Osteochondroma	195	Osteosarcoma	102
Bone cyst	126	Chondrosarcoma	55
GCT	83	MFH/UPS	20
Enchondroma	70	Ewing sarcoma	13
Fibrous dysplasia	27	Hemangiopericytoma	2
Chondroblastoma	20	Adamantinoma	2
NOF	20	Fibrosarcoma	1
ABC	18	Malignant GCT	1
Osteoid osteoma	14		
LCH	9		
OFD	9		
Ganglion	8		
Fibroma	5		
Chondroma	4		
BPOP	3		
Lipoma	3		
Hemangioma	2		
Others	32		

MFH, malignant fibrous histiocytoma; UPS, undifferentiated pleomorphic sarcoma; GCT, giant cell tumor; NOF, non-ossifying fibroma; ABC, aneurysmal bone cyst; OFD, osteofibrous dysplasia; LCH, Langerhans cell histiocytosis; BPOP, bizarre parosteal osteochondromatous proliferation

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surgery-related parameters were as follows: the use of an implant (yes/no), biological reconstruction (yes/no), use of artificial bone or bone cement for bone defect (yes/no), additional surgery for complications (yes/no), operative time (<5 or ≥ 5 hours), and intraoperative blood loss (<150 or ≥ 150 mL). Biological reconstruction was defined as the use of allograft, iliac bone, fibular bone, tibial bone, and tumor-bearing bone treated by freezing or autoclaving, for bone defect after bone tumor resection [12]. Artificial bone was defined as α-tricalcium

Table 2. Locations and incidence of postoperative deep infection.

Locations	Number of tumors	Infection (%)
Femur	273	5 (1.8%)
Tibia	176	13 (7.4%)
Humerus	95	1 (1.1%)
Pelvis	80	7 (8.8%)
Foot	64	1 (1.6%)
Hand	58	0 (0%)
Fibula	33	0 (0%)
Rib	17	0 (0%)
Scapula	14	0 (0%)
Ulna	14	0 (0%)
Radius	14	0 (0%)
Clavicle	4	0 (0%)
Sternum	1	0 (0%)
Patella	1	0 (0%)
Total	844	27 (3.2%)

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phosphate (TCP) or β-TCP. Bone cement was defined as polymethylmethacrylate. Additional surgeries for complications were defined as surgical treatment for delayed bone union, fracture, wound dehiscence, breakage of implants, hematoma, and intestinal perforation. Postoperative deep infections were defined using the US Centers for Disease Control classifications for surgical site infections [13].

Statistical analysis

To identify the risk factors for postoperative deep infection after bone tumor surgeries, univariate analysis was performed using the Fisher exact test. Multiple logistic regression analysis was used to identify the independent risk factors for postoperative deep infection. The parameters with univariate p values <0.1 were considered as candidates for the multiple logistic regression model. Statistical significance was defined as $p < 0.05$, and all analyses were performed using statistical software (EZR, Saitama Medical Center, Jichi Medical University).

Results

Risk factors for postoperative deep infection

Among the study patients, the incidence of postoperative deep infection was 3.2% (27/844 operations). Results of univariate analyses showed that a pelvic tumor, chemotherapy, the use of an implant, biological reconstruction, additional surgery for complications, operative time ≥5 hours, and intraoperative blood loss ≥150 mL were significantly associated with an increased risk of postoperative deep infection (Tables 3 and 4). The use of artificial bone or cement was significantly associated with a decreased risk of postoperative deep infection.

Multiple logistic regression analysis included the following 8 variables: pelvic tumor, chemotherapy, the use of an implant, biological reconstruction, augmentation of artificial bone or cement, additional surgery for complications, operative time ≥5 hours, and intraoperative blood loss ≥150 mL. Result of multivariate analysis showed that pelvic tumor and use of an implant were significantly associated with an increased risk of postoperative infection (Table 5).

Discussion

The treatment of bone tumors includes surgery, chemotherapy, radiation therapy, medications, and immunotherapy [14,15]. Surgical treatment for bone tumors comprises tumor

Table 3. Results of univariate analysis of the patient-related parameters.

Factor		Number (%) of tumors with deep infection	OR	95% CI	p value
Age	≥20 years	18/429 (4.2%)	2.23	0.91–5.99	0.072
	<20 years	8/415 (1.9%)			
Tumor location	Pelvis	7/80 (8.8%)	3.75	1.29–9.71	0.008
	Other	19/764 (2.5%)			
Recurrent tumor	Yes	2/95 (2.1%)	0.65	0.07–2.69	0.758
	No	24/749 (3.2%)			
Pathological fracture	Yes	0/37 (0%)	0.00	0.00–3.38	0.623
	No	26/807 (3.2%)			
Chemotherapy	Yes	16/108 (14.8%)	12.55	5.18–31.94	< 0.001
	No	10/736 (1.4%)			

OR, odds ratio; CI, confidence interval.

The p values were calculated with Fisher exact test.

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Table 4. Results of univariate analysis of the surgery-related parameters.

Factor		Number (%) of tumors with deep infection	OR	95% CI	p value
Use of an implant	Yes	22/130 (16.9%)	35.89	11.88–145.94	< 0.001
	No	4/714 (0.6%)			
Biological reconstruction	Yes	21/134 (15.7%)	26.02	9.31–90.21	< 0.001
	No	5/710 (0.7%)			
Artificial bone or cement	Yes	2/305 (0.7%)	0.14	0.02–0.58	0.001
	No	24/539 (4.5%)			
Additional surgery for complications	Yes	8/36 (22.2%)	12.43	4.30–33.32	< 0.001
	No	18/808 (2.2%)			
Operative time	≥5 h	18/84 (21.4%)	25.39	10.06–70.29	< 0.001
	<5 h	8/760 (1.1%)			
Intraoperative blood loss	≥150 mL	21/259 (8.1%)	10.20	3.69–35.06	< 0.001
	<150 mL	5/585 (0.9%)			

OR, odds ratio; CI, confidence interval.

The p values were calculated with Fisher exact test.

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resection and reconstruction for bone defects using an endoprosthesis, allograft, autograft, and artificial bone graft. The surgical outcomes of bone tumors such as limb function, recurrence, and complications can be influenced by several factors, including age, tumor histology (primary or metastatic tumor), chemotherapy, radiation therapy, and the surgical site. Among the complications, postoperative deep infection remains a common and severe complication after bone tumor surgery. The causes of the postoperative deep infection after tumor resection include immunocompromised patients with cancer, malnutrition, large bone and soft tissue defects, a long operative time, frequent red blood cell and platelet transfusions, neutropenia from postoperative chemotherapy, and frequent bacteremia from the use of indwelling central venous catheters [16]. The rate of postoperative deep infection after resection of bone tumor has been reported to range from 0.9% to 36% [3,4,17–20]. Postoperative deep infection requires additional treatment such as irrigation surgery, the use of antibiotics for a long period, and delays in the treatment course, which increases mortality. To improve the outcomes of patients with bone tumors, physicians need to recognize the risk factors for postoperative deep infection to determine the adequate surgical procedure.

Dietz et al. reported that 58% of orthopedic surgeries had bacterial contamination [21]. According to an intraoperative experiment, surgical wound, local bone harvested from surgical

Table 5. Risk factors for postoperative deep infection according to multivariate analysis.

Factor	OR	95% CI	p value
Pelvic tumor	3.42	1.04–11.30	0.044
Operative time ≥5 h	2.17	0.63–7.49	0.221
Use of an implant	9.28	1.89–45.50	0.006
Biological reconstruction	4.20	0.96–18.30	0.057
Chemotherapy	2.18	0.74–6.42	0.156
Additional surgery for complications	1.57	0.53–4.63	0.412
Artificial bone or cement	1.65	0.25–10.80	0.603
Intraoperative blood loss ≥ 150 mL	0.76	0.20–2.96	0.693

OR, odds ratio; CI, confidence interval.

Values were calculated by multiple logistic regression analysis.

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sites, surgeon's gloves, and implants were contaminated by the same bacteria that were cultured from the room air of the operating room, and the degree of contamination increased proportionally with the exposure time [22]. The National Nosocomial Infections Surveillance (NNIS) has identified an operative time of $\geq$4 hours as being predictive of deep infection after general surgery procedures [23].

The associations between postoperative deep infection and chemotherapy, and radiation therapy are controversial. Leukocytopenia and neutropenia due to chemotherapy and tissue damage caused by radiation therapy are thought to be associated with postoperative deep infection. However, a study about the risk factors of postoperative infection showed that adjuvant chemotherapy and radiotherapy were not significant risk factors for infection [11]. On the other hand, a study on spinal metastases showed that radiation therapy was an independent risk factor for postoperative infection [24].

Our present study revealed that pelvic tumors significantly increased the risk of postoperative deep infection. Deep infection is one of the most frequent postoperative complications after pelvic surgery (range, 20–36%), and it requires surgical debridement and irrigation [1,3,17,20,25]. Bone tumors of the pelvis are often large, because they are diagnosed late. Furthermore, choosing an adequate surgical treatment is particularly difficult because of the size of the tumor, and its relationship to neurovascular structures and the urinary and intestinal tracts. Among the surgeries for bone tumors, pelvic reconstruction after the resection of bone sarcomas is challenging. Angelini et al. reported that pelvic reconstruction was an independent significant risk factor for infection, and 46% of patients with infection required removal of the reconstruction [1].

Our present study's results showed that use of implant was associated with an increased risk of postoperative deep infection. In general surgery, biomaterial has been considered to be a risk factor of postoperative deep infection [26]. Previous studies have reported that 9–28% of cases of deep infection occur after endoprosthetic reconstruction [2,4,16,17]. In contrast, reconstruction without an implant is associated with a low infection rate (0.9–1.2%) [19,27,28]. However, infection following biological reconstruction using allograft or autograft is common. Mankin reported that 13% of patients treated with allograft experienced infection [29]. Tsuchiya et al. reported that 11% of patients, who underwent reconstruction using autograft containing tumor treated by liquid nitrogen, had postoperative deep infection [30]. Our study's findings showed marginal significance for a correlation between biological reconstruction and postoperative deep infection. Thus, the presence of biological reconstruction may influence the incidence of infection.

To decrease postoperative deep infection, preventive care, including drainage and the administration of prophylactic antibiotics, is needed after bone tumor surgeries. Recently, several new techniques, including antibiotic-impregnated cement and an implant with silver coating or iodine coating, have been used to prevent deep infection after orthopaedic surgery [31–34]. More efforts should be made to decrease postoperative deep infection in patients with a high risk of infection.

In conclusion, our present study's findings showed that a pelvic tumor and the use of an implant are associated with an increased risk of postoperative deep infection. Surgeons will be able to use this information when deciding which operative procedure to use to treat patients with bone tumors.

Author Contributions

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References

1. Angelini A, Drago G, Trovarelli G, Calabro T, Ruggieri P. Infection after surgical resection for pelvic bone tumors: an analysis of 270 patients from one institution. *Clin Orthop Relat Res* 2014; 472: 349–359. https://doi.org/10.1007/s11999-013-3250-x PMID: 23975252
2. Capanna R, Scoccianti G, Frenos F, Vilardi A, Beltrami G, Campanacci DA. What was the survival of megaprostheses in lower limb reconstructions after tumor resections?. *Clin Orthop Relat Res* 2015; 473: 820–830. https://doi.org/10.1007/s11999-014-3736-1 PMID: 24964884
3. Ozaki T, Hillmann A, Bettin D, Wuisman P, Winkelmann W. High complication rates with pelvic allografts. Experience of 22 sarcoma resections. *Acta Orthop Scand* 1996; 67: 333–338. PMID: 8792734
4. Peel T, May D, Buising K, Thursky K, Slavin M, Choong P. Infective complications following tumour endoprosthesis surgery for bone and soft tissue tumours. *Eur J Surg Oncol* 2014; 40: 1087–1094. https://doi.org/10.1016/j.ejso.2014.02.241 PMID: 24655802
5. Gaur AH, Liu T, Knapp KM, Daw NC, Rao BN, Neel MD, Rodriguez-Galindo C, Brand D, Adderson EE. Infections in children and young adults with bone malignancies undergoing limb-sparing surgery. *Cancer* 2005; 104: 602–610. https://doi.org/10.1002/cncr.21212 PMID: 15952202
6. McDonald DJ, Capanna R, Gherlinzoni F, Bacci G, Ferruzzi A, Casadei R, Ferraro A, Cazzola A, Campanacci M. Influence of chemotherapy on perioperative complications in limb salvage surgery for bone tumors. *Cancer* 1990; 65: 1509–1516. PMID: 2155698
7. Lozano-Calderón SA, Swaim SO, Federico A, Anderson ME, Gebhardt MC. Predictors of soft-tissue complications and deep infection in allograft reconstruction of the proximal tibia. *J Surg Oncol* 2016; 113: 811–817. https://doi.org/10.1002/jso.24234 PMID: 27126893
8. Pugely AJ, Martin CT, Gao Y, Schweizer ML, Callaghan JJ. The Incidence of and Risk Factors for 30-Day Surgical Site Infections Following Primary and Revision Total Joint Arthroplasty. *J Arthroplasty* 2015; 30 (9 Suppl): 47–50. https://doi.org/10.1016/j.arth.2015.01.063 PMID: 26071247
9. Gradl G, de Witte PB, Evans BT, Hornicek F, Raskin K, Ring D. Surgical site infection in orthopaedic oncology. *J Bone Joint Surg Am* 2014; 96: 223–230. https://doi.org/10.2106/JBJS.L.01514 PMID: 24500584

10. Kabirian N, Akbarnia BA, Pawelek JB, Alam M, Mundis GM Jr, Acacio R, Thompson GH, Marks DS, Gardner A, Sponseller PD, Skaggs DL; Growing Spine Study Group. Deep Surgical Site Infection Following 2344 Growing-Rod Procedures for Early-Onset Scoliosis: Risk Factors and Clinical Consequences. *J Bone Joint Surg Am* 2014; 96: e128. https://doi.org/10.2106/JBJS.M.00618 PMID: 25100781

11. Morris CD, Sepkowitz K, Fonshell C, Margetson N, Eagan J, Miransky J, Boland PJ, Healey J. Prospective identification of risk factors for wound infection after lower extremity oncologic surgery. *Ann Surg Oncol* 2003; 10: 778–782. PMID: 12900369

12. Tsuchiya H, Abdel-Wanis ME, Tomita K. Biological reconstruction after excision of juxta-articular osteosarcoma around the knee: a new classification system. *Anticancer Res* 2006; 26: 447–454. PMID: 16739304

13. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for disease control and prevention (CDC) hospital infection control practices advisory committee. *Am J Infect Control* 1999; 27: 97–132. PMID: 10196487

14. Rutkowski P, Ferrari S, Grimer RJ, Stalley PD, Dijkstra SP, Pienkowski A, Vaz G, Wunder JS, Seeger LL, Feng A, Roberts ZJ, Bach BA. Surgical downstaging in an open-label phase II trial of denosumab in patients with giant cell tumor of bone. *Ann Surg Oncol* 2015; 22: 2860–8. https://doi.org/10.1245/s10434-015-4634-9 PMID: 26033180

15. Hoffman RM, Singh AS, Eilber FC. Potential of immunotherapy for sarcoma. *Cancer* Feb 27. https://doi.org/10.1002/cncr.30603 [Epub ahead of print] PMID: 28241102

16. Healey JH. CORR Insights™: High infection rate outcomes in long-bone tumor surgery with endoprosthetic reconstruction in adults: a systematic review. Clin *Orthop Relat Res* 2013; 471: 2028–2029. https://doi.org/10.1007/s11999-013-2893-y PMID: 23479231

17. Bus MP, Szafranski A, Sellevold S, Goryn T, Jutte PC, Bramer JA, Fiocco M, Streitbürger A, Kotrych D, van de Sande MA, Dijkstra PD. LUMiC® endoprosthetic reconstruction after periacetabular tumor resection: short-term results. *Clin Orthop Relat Res* 2017; 475: 686–95. https://doi.org/10.1007/s11999-016-4805-4 PMID: 27020434

18. Aponte-Tinao LA, Ayerza MA, Muscolo DL, Farfalli GL. What Are the Risk Factors and Management Options for Infection After Reconstruction With Massive Bone Allografts?. *Clin Orthop Relat Res* 2016; 474: 669–673. https://doi.org/10.1007/s11999-015-4353-3 PMID: 25991435

19. Dierselhuis EF, Gerbers JG, Ploegmakers JJ, Stevens M, Suurmeijer AJ, Jutte PC. Local Treatment with Adjuvant Therapy for Central Atypical Cartilaginous Tumors in the Long Bones: Analysis of Outcome and Complications in One Hundred and Eight Patients with a Minimum Follow-up of Two Years. *J Bone Joint Surg Am* 2016; 98: 303–313. https://doi.org/10.2106/JBJS.O.00472 PMID: 26888678

20. Farfalli GL, Albergo JI, Ritacco LE, Ayerza MA, Muscolo DL, Aponte-Tinao LA. Oncologic and clinical outcomes in pelvic primary bone sarcomas treated with limb salvage surgery. *Musculoskelet Surg* 2015; 99: 237–242. https://doi.org/10.1007/s12306-015-0379-7 PMID: 26238978

21. Dietz FR, Koontz FP, Found EM, Marsh JL. The importance of positive bacterial cultures of specimens obtained during clean orthopaedic operations. *J Bone Joint Surg Am* 1991; 73: 1200–1207. PMID: 1890121

22. Ahn DK, Park HS, Kim TW, Yang JH, Boo KH, Kim IJ, Lee HJ. The degree of bacterial contamination while performing spine surgery. *Asian Spine J* 2013; 7: 8–13. https://doi.org/10.4184/asj.2013.7.1.8 PMID: 23508998

23. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004; 32: 470–485. https://doi.org/10.1016/S0196655304005425 PMID: 15573054

24. Demura S, Kawahara N, Murakami H, Nambu K, Kato S, Yoshioka K, Okayama T, Tomita K. Surgical site infection in spinal metastasis: risk factors and countermeasures. *Spine* 2009; 34: 635–639. https://doi.org/10.1097/BRS.0b013e31819712ca PMID: 19282745

25. Hillmann A, Hoffmann C, Gosheger G, Rödl R, Winkelmann W, Ozaki T. Tumors of the pelvis: complications after reconstruction. *Arch Orthop Trauma Surg* 2003; 123: 340–344. https://doi.org/10.1007/s00402-003-0543-7 PMID: 12838435

26. Busscher HJ, van der Mei HC, Subbiahdoss G, Jutte PC, van den Dungen JJ, Zaat SA, Schultz MJ, Grainger DW. Biomaterial-associated infection: locating the finish line in the race for the surface. *Sci Transl Med* 2012; 4: 153rv10. https://doi.org/10.1126/scitranslmed.3004528 PMID: 23019658

27. Verdegaal SH, Brouwers HF, van Zwet EW, Hogendoorn PC, Taminiau AH.Low-grade chondrosarcoma of long bones treated with intralesional curettage followed by application of phenol, ethanol, and bone-grafting. *J Bone Joint Surg Am* 2012; 94: 1201–1207. https://doi.org/10.2106/JBJS.J.01498 PMID: 22760388

28. Zhen W, Yaotian H, Songjian L, Ge L, Qingliang W.Giant-cell tumour of bone. The long-term results of treatment by curettage and bone graft. *J Bone Joint Surg Br* 2004; 86: 212–216. PMID: 15046435

29. Mankin HJ, Doppelt SH, Sullivan TR, Tomford WW. Osteoarticular and intercalary allograft transplantation in the management of malignant tumors of bone. *Cancer* 1982; 168: 252–257.

30. Tsuchiya H, Wang SL, Sakayama K, Yamamoto N, Nishida H, Tomita K. Reconstruction using an autograft containing tumour treated by liquid nitrogen. *J Bone Joint Surg [Br]* 2005: 87B: 218–225.

31. Sprowson AP, Jensen C, Chambers S, Parsons NR, Aradhyula NM, Carluke I, Inman D, Reed MR. The use of high-dose dual-impregnated antibiotic-laden cement with hemiarthroplasty for the treatment of a fracture of the hip. *Bone Joint J* 2016; 98-B:1534–1541. https://doi.org/10.1302/0301-620X.98B11.34693 PMID: 27803231

32. Hardes J, von Eiff C, Streitbuerger A, Balke M, Budny T, Henrichs MP, Hauschild G, Ahrens H. Reduction of periprosthetic infection with silver-coated megaprostheses in patients with bone sarcoma. *J Surg Oncol* 2010; 101: 389–395. https://doi.org/10.1002/jso.21498 PMID: 20119985

33. Tsuchiya H, Shirai T, Nishida H, Murakami H, Kabata T, Yamamoto N, Watanabe K, Nakase J. Innovative antimicrobial coating of titanium implants with iodine. *J Orthop Sci* 2012; 17: 595–604. https://doi.org/10.1007/s00776-012-0247-3 PMID: 22806173

34. Shirai T, Shimizu T, Ohtani K, Zen Y, Takaya M, Tsuchiya H. Antibacterial iodine-supported titanium implants. *Acta Biomater* 2011; 7: 1928–1933. https://doi.org/10.1016/j.actbio.2010.11.036 PMID: 21115142