



## Infective complications following tumour endoprosthesis surgery for bone and soft tissue tumours

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### Abstract

**Aims:** This study aims to describe the incidence of infective complications, including tumour endoprosthesis infection, in a cohort of patients undergoing tumour endoprosthesis surgery in Victoria, Australia.

**Methods:** This retrospective cohort study was performed over 15 years (January 1996–December 2010).

**Results:** 121 patients underwent tumour endoprosthesis surgery during the study period. Patients were followed for a median of 34 months (interquartile range [IQR] 17, 80). Overall, 34 patients (28%) experienced infective complications including: bacteraemia in 19 patients (16%) and tumour endoprosthesis infection in 17 (14%). The majority of patients with early and late acute infections (haematogenous) were managed with debridement and retention of the prosthesis in addition to biofilm-active antibiotics. Late chronic infections were predominantly managed by exchange of the prosthesis. The overall success rate of treatment was 71%. The success rate for debridement and retention was 75% compared with 67% for exchange procedures.

**Conclusions:** There is a significant rate of infective complications following tumour endoprosthesis surgery including 14% of patients experiencing infection involving the tumour endoprosthesis. This study is the first to report on outcomes from debridement and retention of the prosthesis; which had comparable success rates to other treatment modalities.

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**Keywords:** Tumour endoprosthesis surgery; Bone and soft tissue tumour; Tumour endoprosthesis infection; Infection; Epidemiology; Treatment; Outcome

### Introduction

Prior to the advent of tumour endoprosthetic surgery, the treatment of bone and soft tissue tumours, such as osteosarcoma, often entailed limb amputation. The development of sophisticated tumour endoprostheses led to significant improvement in patient mobility and quality of life.<sup>1</sup> Infection of the tumour endoprosthesis is a major complication of this surgery and the incidence reported in literature ranges from 2 to 19.5%.<sup>1–4</sup> There is however, a lag in knowledge about tumour endoprosthesis (TE) infections. The optimal management of these infections is not clear

and treatment approaches are often extrapolated from data regarding arthroplasty infection. Given the significant differences in these two patient cohorts this management approach may not be appropriate and further investigation is required.

This study aims to describe the overall infective complications following TE insertion and to assess risk factors for TE infection in a cohort of patients with primary bone and soft tissue tumours. In addition the study aims to document the management approaches and outcomes for TE infection.

### Patients and methods

#### Ethics

Ethics approval was obtained from the Human Research Ethics Committee at involved hospitals.

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### Study cohort

This retrospective cohort study was conducted over a 15-year period from January 1996 until December 2010. The study was conducted at SVHM and PMCC which are the major referral centres for bone and soft tissue tumours across Victoria and Tasmania, Australia. Tumour endoprosthesis surgery is performed at SVHM by 3 dedicated orthopaedic surgeons. Chemotherapy and radiotherapy is administered at PMCC.

At SVHM, there is an established protocol for management of arthroplasty and TE infections.<sup>5</sup> Patients with early and late acute (haematogenous) infections with stable implants are managed by debridement and retention of the prosthesis.<sup>6,7</sup> Patients with late chronic infections are managed with exchange of the prosthesis (either one- or two-stage depending on the surgeons preference), or where surgery is not possible, chronic antibiotic suppression may be used.<sup>7</sup>

Patients with primary bone and soft tissue tumours were identified for inclusion in this study from a review of the orthopaedic bone and soft tissue tumour database. This prospective database is managed by a dedicated team in the Department of Orthopaedics SVHM and collects information including type of tumour, patient demographics and surgical management of all patients with bone and soft tissue tumours (primary and metastatic) presenting to SVHM and PMCC. Patients were excluded from the current study if a tumour endoprosthesis was not inserted, or if they had metastatic tumours. Patients were followed from the date of diagnosis of bone and soft tissue tumour until discharge from clinical care or death.

A separate datasheet was developed to collect additional information including demographic characteristics, surgical treatment, chemotherapy and radiotherapy, complications and patient outcomes. A single dedicated researcher (TP) accessed the medical records of each patient and collected data based on predetermined definitions (Table 1).

### Microbiology

Anaerobic and aerobic blood cultures were obtained by venepuncture using aseptic techniques or through access of a central venous device, if present. Usually 2 sets of blood cultures were obtained and incubated in BacT/ALERT blood culture system (bioMérieux; Durham, NC, USA). All intra-operative specimens were handled according to a protocol. All were cultured on blood agar and chocolate agar incubated in 35 °C CO<sub>2</sub> and pre-reduced anaerobic agar at 35 °C anaerobically for 48 h. In addition, tissue specimens were incubated in Thioglycollate Broth for 7 days at 35 °C O<sub>2</sub>. Specimens from the Thioglycollate Broth were subcultured onto blood agar and incubated aerobically and anaerobically if the broth became cloudy. Terminal cultures were not performed on broth specimens.

Table 1  
Definitions.

Tumour endoprosthesis (TE) infection	TE infection was diagnosed if one or more of the following were present: <ol style="list-style-type: none"> <li>Presence of sinus tract in communication with the tumour endoprosthesis.</li> <li>Peri-prosthetic purulence observed intra-operatively.</li> <li>Isolation of the same micro-organism/s on <math>\geq 2</math> aseptically obtained specimens (intra-operative tissue specimens or aseptic joint aspiration).</li> <li>Histopathological features consistent with acute inflammation from peri-prosthetic tissue samples with <math>\geq 5</math> neutrophils per-high power field (<math>\times 500</math> magnification) in 5 different microscopic fields.<sup>16,22,23</sup></li> </ol>
Early infection	TE infection presenting within 90 days of implantation. <sup>7</sup>
Late chronic infection	TE infection presenting after 90 days of implantation with long duration ( $>21$ days) of symptoms. <sup>7</sup>
Late acute infection	TE infection presenting after 90 days of implantation with a short duration of symptoms ( $<21$ days). <sup>24</sup>
Treatment failure	Treatment failure was defined one or more of the following were present: <ol style="list-style-type: none"> <li>Reoccurrence of TE infection due to the same microorganism at a time subsequent to the original presentation.</li> <li>Occurrence of TE infection due to a different microorganism at a time subsequent to the original presentation.</li> <li>Development of a sinus tract subsequent to the original presentation.</li> <li>Presence of purulence surrounding the tumour endoprosthesis observed intra-operatively at a time subsequent to the original presentation.</li> <li>Death from TE infection as documented on the death certificate.<sup>22</sup></li> </ol>

### Statistical analysis

Descriptive statistics were based on percentages and frequencies for categorical variables and for continuous variables, means and standard deviation (SD) or medians and interquartile range (IQR) if the data were skewed. Univariate logistic regression was performed to identify factors associated with the development of infection. All reported  $p$ -values were two-tailed and for each analysis  $p < 0.05$  was considered statistically significant. The Hosmer–Lemeshow goodness-of-fit test was performed on the logistic regression model. Kaplan–Meier survival method was used to estimate 12-month survival rate free from treatment failure with 95% confidence intervals (95% CI). All analyses were performed using Stata 11.2 (StataCorp College Station, TX, 2009).

### Results

Following review of the database, 121 patients were included in the study. The demographic characteristics of the patients are outlined in Table 2. The median age of

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