Patient and Surgical Risk Factors for Surgical Site Infection in Lower-Extremity Oncological Endoprosthetic Reconstruction

A Secondary Analysis of the PARITY Trial Data

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Background: The specific risk factors for surgical site infection (SSI) in orthopaedic oncology patients undergoing endoprosthetic reconstruction have not previously been evaluated in a large prospective cohort. In the current study, we aimed to define patient- and procedure-specific risk factors for SSI in patients who underwent surgical excision and endoprosthetic reconstruction for lower-extremity bone or soft-tissue tumors using the prospectively collected data of the Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) trial.

Methods: PARITY was a multicenter, blinded, randomized controlled trial with a parallel 2-arm design that aimed to determine the effect of a long duration (5 days) versus short duration (24 hours) of postoperative prophylactic antibiotics on the rate of SSI in patients undergoing surgical excision and endoprosthetic reconstruction of the femur or tibia. In this secondary analysis of the PARITY data, a multivariate Cox proportional hazards regression model was constructed to explore predictors of SSI within 1 year postoperatively.

Results: A total of 96 (15.9%) of the 604 patients experienced an SSI. Of the 23 variables analyzed in the univariate analysis, 4 variables achieved significance: preoperative diagnosis, operative time, volume of muscle excised, and hospital length of stay (LOS). However, only hospital LOS was found to be independently predictive of SSI in the multivariate regression analysis (hazard ratio per day = 1.03; 95% confidence interval = 1.01 to 1.05; $p < 0.001$). An omnibus test of model coefficients demonstrated that the model showed significant improvement over the null model ($\chi^2 = 78.04$; $p < 0.001$). No multicollinearity was found.

Conclusions: This secondary analysis of the PARITY study data found that the only independent risk factor for SSI on multivariate analysis was hospital LOS. It may therefore be reasonable for clinicians to consider streamlined discharge plans for orthopaedic oncology patients to potentially reduce the risk of SSI.

Level of Evidence: Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

Surgical site infections (SSIs) are potentially preventable postoperative complications that, when present, lead to increased patient morbidity and a 2- to 11-fold increase in the risk of mortality[1]. SSIs carry an estimated annual cost in the United States of $3.5 to $10 billion[2]. In orthopaedic surgery, the cost of treatment of a patient with an SSI is approximately double that of one without SSI[3,4].

SSI rates in orthopaedic surgery vary widely depending on subspecialty and patient-specific risk factors[5-7]. Surgical cases involving the use of metal implants, such as joint prosthetic devices or fixation plates, are at higher risk, as the foreign body serves as a nidus for bacterial adhesion and biofilm formation[8,9]. Patients undergoing orthopaedic surgery for musculoskeletal tumors, even those without metal implants, are often managed with associated chemotherapy and/or radiation and thus have higher rates of SSI when compared with patients treated in other subspecialties that do not use immunomodulating therapies[10-16]. The rate of SSI in

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orthopaedic oncology has been reported in the literature to be as high as 28%[14].

Numerous studies have examined risk factors that predispose patients to SSIs in general orthopaedic surgery, but few have done so specifically in the subspecialty field of orthopaedic oncology[10-12,15,16]. Furthermore, of the studies available, most report on retrospective data[10-12,15] and thus are inherently more susceptible to systematic bias than are prospective studies. To our knowledge, there is only 1 study that has sought to identify risk factors for SSI in lower-extremity oncological surgery using prospectively collected data; however, very few patients in that study required endoprosthetic reconstruction[16].

The specific risk factors that place orthopaedic oncology patients at high risk for SSI in endoprosthetic reconstruction have not, to our knowledge, been previously evaluated in a large prospective cohort. In the current study, we aimed to define patient- and procedure-specific risk factors for SSI among patients who underwent surgical excision and endoprosthetic reconstruction of the lower extremity for oncological indications using the prospectively collected data of the PARITY (Prophylactic Antibiotic Regimens in Tumor Surgery) trial.

Materials and Methods

Study Design and Setting

This study was a secondary analysis of the PARITY trial[17]. PARITY was a multicenter, blinded, randomized controlled trial (RCT) that used a parallel 2-arm design to investigate the effect of a long duration (5 days) versus short duration (24 hours) of postoperative prophylactic antibiotics on the rate of postoperative SSI among patients undergoing surgical excision and endoprosthetic reconstruction for lower-extremity bone or soft-tissue tumors. Patients, treatment providers, and outcome assessors were all blinded to treatment allocation[17,18]. The PARITY trial was registered at ClinicalTrials.gov (NCT01479283) and received ethics approval from the Hamilton Integrated Research Ethics Board (REB# 12-009) and relevant ethics boards at all participating sites. The PARITY trial included 48 actively enrolling sites in 12 countries across 6 continents. The trial completed enrollment in October 2019, meeting its recruitment target of 604 patients. We used prospectively collected data from the PARITY trial to determine risk factors for SSI in this patient population.

Participants

All patients who underwent lower-extremity endoprosthetic reconstruction as part of the PARITY trial were included in the secondary analysis in this study.

Identification of SSI

Patients were monitored for an SSI by their treating physician at 2 and 6 weeks; 3, 6, and 9 months; and 1 year postoperatively. A blinded central adjudication committee (CAC) of 3 orthopaedic surgeons and 1 infectious diseases specialist adjudicated all occurrences of SSI. The CAC used the Centers for Disease Control and Prevention (CDC) criteria[19] to define infection, which can be found in Appendix 1.

Data Sources and Patient-Related Variables

Patient demographics, tumor characteristics, surgical data, and infection rates were obtained from the PARITY database. Twenty-three variables were included (Tables I and II).

Statistical Analysis

Demographic data are reported using descriptive statistics, as the mean and standard deviation or median and interquartile range, as appropriate, depending on the data distribution. Univariate analysis was performed to explore differences between patients diagnosed with SSI and those with no SSI within the first year. Continuous outcomes were compared between groups using a Student t test, and dichotomous outcomes were compared between groups using a Pearson chisquare test. For continuous variables that were not normally distributed, the Mann-Whitney U test was used. The univariate analysis was adjusted for multiplicity.

A multivariate Cox proportional hazards regression model was constructed to explore predictors of SSI within 1 year of the index operation. The time from surgery to the date of SSI diagnosis was the primary outcome. The performance of the model was assessed using an omnibus test of model coefficients. To ensure no multicollinearity, a correlation matrix was constructed and an r value of >0.7 was used as a cutoff for exclusion. The results of the model are presented with hazard ratios (HRs) and 95% confidence intervals (CIs). Significance was set at $p < 0.05$ for all analyses. All analyses were performed using SPSS Statistics for Mac (version 26; IBM).

Source of Funding

The PARITY trial received funding through research grants from the Canadian Institutes of Health Research, the Canadian Cancer Society Research Institute, the Canadian Orthopaedic Foundation 2018 J. Édouard Samson Award, the Orthopaedic Research and Education Foundation in conjunction with the Musculoskeletal Tumor Society, and a Physicians' Services Incorporated Clinical Research Grant.

Results

Study Population Characteristics and Overall Rate of SSI

All 604 patients included in the PARITY trial were included in this secondary analysis. An SSI occurred in 44 patients (15.0%) allocated to the 5-day regimen and in 52 patients (16.7%) allocated to the 1-day regimen, for a total SSI rate of 15.9%. Of the 96 patients who had infections, 11 (11.5%) were diagnosed with an SSI within their index hospital stay. Patient demographics and patient-related variables are shown in Table I. The prospectively collected data set was complete and had no missing values.

Risk Factors for SSI: Univariate Analysis

Of the 23 variables analyzed in the univariate analysis, 4 variables achieved significance: preoperative diagnosis (soft-tissue sarcoma [STS] > bone sarcoma > benign aggressive bone tumor > metastatic bone disease [MBD]; $p = 0.021$), operative time (mean, 6.2 hours for SSI versus 4.9 hours for no SSI; $p < 0.001$), volume of muscle excised >50 cm^3 ($p = 0.001$), and hospital length of stay (LOS) (median, 8 days for

TABLE I Patient Demographics and Patient-Related Variables as Predictors of Surgical Site Infection (SSI)†

Variable	Entire Cohort (N = 604)	SSI (N = 96)	No SSI (N = 508)	P Value
Age‡ *(yr)*	41.2 ± 22	41.7 ± 23.8	41.1 ± 22.0	0.794*
Sex				0.999**
Male	361 (59.8%)	57 (59.4%)	304 (59.8%)	
Female	243 (40.2%)	39 (40.6%)	204 (40.2%)	
Preoperative diagnosis				**0.021****
Bone sarcoma	438 (72.5%)	78 (81.3%)	360 (70.9%)	
Soft-tissue sarcoma	62 (10.3%)	12 (12.5%)	50 (9.8%)	
Metastatic bone disease	56 (9.3%)	3 (3.1%)	53 (10.4%)	
Benign aggressive bone tumor	48 (7.9%)	3 (3.1%)	45 (8.9%)	
Location of tumor				0.132**
Femur	498 (82.5%)	74 (77.1%)	424 (83.5%)	
Tibia	106 (17.5%)	22 (22.9%)	84 (16.5%)	
Associated soft-tissue mass	433 (71.7%)	75 (78.1%)	358 (70.5%)	0.140**
Diabetes	44 (7.3%)	4 (4.2%)	40 (7.9%)	0.283**
Smoking	60 (9.9%)	8 (8.3%)	52 (10.2%)	0.710**
Neoadjuvant chemotherapy	290 (48.0%)	46 (47.9%)	244 (48.0%)	0.999**
Neutropenic at time of surgery (<1,500 cells/μL)	96 (15.9%)	82 (85.4%)	14 (2.8%)	0.598**

†The values are given as the number, with the percentage in parentheses, except where otherwise noted. Independent t tests (*) were utilized to compare continuous outcomes between groups, and dichotomous variables were compared using a Pearson chi-square test (**). Bold indicates a significant value ($p < 0.05$). ‡The values are given as the mean and standard deviation. The mean difference (95% CI) for age was 0.63 (−4.1 to 5.4) years.

SSI versus 6 days for no SSI; $p < 0.001$). These findings are summarized in Tables I and II. The median hospital LOS for the 11 patients with SSI during their index hospitalization was 45 days, and the median hospital LOS for the 85 patients diagnosed with an SSI after their index hospitalization was 7 days, which remained significantly longer than the hospital LOS for those not diagnosed with an SSI during the 1-year follow-up period ($p < 0.001$).

Multivariate Cox Proportional Hazards Regression Analysis

For the multivariate Cox proportional hazards regression analysis, only 1 variable, hospital LOS (HR per day = 1.03; 95% CI = 1.01 to 1.05; $p < 0.001$), remained an independent predictor of SSI, and 2 approached significance: metastatic bone disease (HR = 0.28; 95% CI = 0.07 to 1.20; $p = 0.086$) and adjuvant chemotherapy (HR = 1.7; 95% CI = 0.92 to 3.11; $p = 0.090$). These findings are summarized in Table III. An omnibus test of model coefficients demonstrated that the model showed significant improvement over the null model ($\chi^2 = 78.04$; $p < 0.001$). No multicollinearity was found.

Discussion

We conducted this study to define patient- and procedure-specific risk factors for SSI in patients undergoing surgical excision and endoprosthetic reconstruction for bone or soft-tissue tumors of the lower extremity using the prospectively collected data of the PARITY trial. The specific risk factors that place orthopaedic oncology patients at high risk for SSI in endoprosthetic reconstruction have not, to our knowledge, been previously evaluated in a large prospective cohort. On univariate analysis, the diagnosis of STS invading bone, longer operative time, larger muscle volume excised, and longer hospital LOS were risk factors for SSI. However, the only independent risk factor for SSI on multivariate analysis was hospital LOS.

Findings in Relation to Previous Literature

Longer operative time has been found in retrospective orthopaedic oncological studies to be correlated with SSI[10,12,20]. One reason for this may be that longer procedures expose patients to potential contamination for a longer duration. However, this risk factor was not correlated with SSI in a prospective study of 110 consecutive patients who had had a major lower-extremity or pelvic orthopaedic oncological surgical procedure[16]. In that study, the length of the procedure was analyzed as a nominal variable (<4 hours, 4 to 8 hours, >8 hours) rather than as a continuous variable. In our study, the mean difference in operative time between the SSI and non-SSI groups was 1.3 hours. Therefore, the categorization of operative time by 4-hour intervals in the above-cited study may have reduced the precision of the statistical model and its ability to identify small differences in outcomes.

To our knowledge, the quantity of muscle excised has not previously been explored or reported as a risk factor for SSI in

TABLE II Operative and Perioperative Variables as Predictors of SSI†

Variable	Entire Cohort (N = 604)	SSI (N = 96)	No SSI (N = 508)	P Value
Operative time† *(hr)*	5.1 ± 2.4	6.2 ± 2.8	4.9 ± 2.2	**<0.001***
Intrawound vancomycin powder use	110 (18.2%)	14 (14.6%)	96 (18.9%)	0.315**
Betadine-coated prosthesis	111/601 (18.5%)	16/95 (16.8%)	95/506 (18.8%)	0.656**
Silver-coated prosthesis	32 (5.3%)	5 (5.2%)	27 (5.3%)	0.999**
Volume of muscle excised				**0.001****
≤50 cm^3	345	39	306	
>50 cm^3	247	54	193	
Intraoperative laminar air flow	234 (38.7%)	41 (42.7%)	193 (38.0%)	0.384**
Intraoperative arthroplasty helmet (space suit) use	243 (40.2%)	34 (35.4%)	209 (41.1%)	0.294**
Intraoperative tranexamic acid use	165 (27.3%)	23 (24.0%)	142 (28.0%)	0.421**
Postoperative suction drain	476 (78.8%)	78 (81.3%)	398 (78.3%)	0.545**
Postoperative negative pressure wound therapy (commenced at time of surgery)	83 (13.7%)	18 (18.8%)	65 (12.8%)	0.122**
Patient in private postoperative room	241 (39.9%)	35 (36.5%)	206 (40.6%)	0.496**
Hospital LOS§ *(d)*	6 [5, 8]	8 [5, 11]	6 [5, 8]	**<0.001#**
Adjuvant chemotherapy	337/597 (56.4%)	58/96 (60.4%)	279/501 (55.7%)	0.392**
Postoperative urinary catheter	552 (91.4%)	90 (93.8%)	462 (91.0%)	0.369**

†The values are given as the number, with the percentage in parentheses, except where otherwise noted. Independent t tests (*) were utilized to compare continuous outcomes between groups, and dichotomous variables were compared using a Pearson chi-square test (**). Bold indicates a significant value ($p < 0.05$). ‡The values are given as the mean and standard deviation. The mean difference (95% CI) for operative time was 1.3 (0.7 to 1.9) hours. §The values are given as the median, with the interquartile range in square brackets. #Mann-Whitney U test.

this patient population. Orthopaedic oncological procedures, in general, require substantial exposures and dissections across several vascular distributions. It is therefore reasonable to assume that a greater amount of muscle excised is correlated with a greater area of tissue subjected to devascularization, which in turn can lead to compromised wound healing and an increased likelihood of SSI. We found that patients treated for MBD, as opposed to STS invading bone or bone sarcoma, may be less likely to develop an SSI. This may be because of the fact that en bloc resection for MBD is generally indicated for patients with a good prognosis and an easily resectable tumor typically not requiring extensive soft-tissue resection, who are therefore likely to undergo faster and less complex operative procedures[21,22].

The main finding of our study is that the only independent predictor of SSI in endoprosthetic reconstruction of the lower extremity was a longer hospital LOS (HR = 1.03; 95% CI = 1.01 to 1.05; $p < 0.001$). In order to verify the validity of this result and to ensure that the result was not driven by the 11 (11.5%) of 96 patients diagnosed with an SSI within their index hospital stay, who likely had prolonged LOS due to the infection itself (median LOS, 45 days), we repeated the analysis without those 11 patients. Hospital LOS in the group of patients diagnosed later with an SSI remained significantly longer when compared with the noninfected cohort. Thus, our post hoc sensitivity analysis was able to exclude in-hospital postoperative infection as a likely confounding factor regarding our main study finding.

Our finding is consistent with that of a previous study that demonstrated that orthopaedic oncological surgery performed on an inpatient basis (i.e., with longer LOS), versus surgery on an outpatient basis, was an independent predictor of SSI[20]. In a high-quality observational cohort study that included 4,596 patients across general, orthopaedic trauma, and vascular surgery departments and in which data for all variables were collected in a strictly prospective manner as part of an RCT, postoperative LOS was an independent risk factor for SSI (odds ratio [OR] = 1.12; 95% CI = 1.10 to 1.14; $p < 0.001$)[23]. One possible reason for this finding is that a longer hospital stay is associated with an increased number of iatrogenic pathogen exposures. Therefore, efficient postoperative care and well-organized home care may reduce exposure to iatrogenic pathogens. In addition, longer hospital stays may increase the risk of exposure to medical errors and other hospital-associated complications (e.g., admission to the intensive care unit) potentially leading to infection[23].

Previous studies have found several risk factors to be independently correlated with SSI in orthopaedic oncology. These include diabetes[24], smoking[24], age[10], and malignant disease[10]. The current study results are not consistent with these previous findings. One explanation with regard to diabetes and smoking is the small number of patients in the PARITY study who presented with these potential risk factors; only 44 (7.3%) of the patients had diabetes and 60 (9.9%) were smokers at presentation in a total

TABLE III Multivariate Cox Proportional Hazards Regression Analysis†

Variable	HR	95% CI for HR		P Value
		Lower	Upper	
Age (per year)	1.00	0.99	1.01	0.568
Sex				
Female (ref.)				
Male	1.00	0.64	1.56	0.982
Location of tumor				
Femur (ref.)				
Tibia	1.24	0.70	2.20	0.457
Preoperative diagnosis				
Bone sarcoma (ref.)				
Soft-tissue sarcoma	0.95	0.47	1.91	0.886
Metastatic bone disease	0.28	0.07	1.20	0.086
Benign aggressive bone tumor	0.41	0.12	1.44	0.164
Neutropenic at time of surgery (<1,500 cells/μL)				
No (ref.)				
Yes	0.73	0.39	1.38	0.335
Diabetes				
No (ref.)				
Yes	0.55	0.16	1.83	0.327
Smoking				
No (ref.)				
Yes	0.77	0.35	1.67	0.499
Total operative time *(hr)*	1.06	0.96	1.20	0.269
Associated soft-tissue mass				
No (ref.)				
Yes	0.86	0.47	1.53	0.616
Volume of muscle excised				
<50 cm^3 (ref.)				
>50 cm^3	0.65	0.39	1.08	0.096
Intrawound vancomycin powder use				
No (ref.)				
Yes	0.94	0.46	1.92	0.856
Betadine-coated prosthesis				
No (ref.)				
Yes	0.76	0.39	1.47	0.414
Silver-coated prosthesis				
No (ref.)				
Yes	0.88	0.31	2.50	0.814
Intraoperative laminar air flow				
No (ref.)				
Yes	1.40	0.82	2.30	0.230
Intraoperative arthroplasty helmet (space suit) use				
No (ref.)				
Yes	0.76	0.50	1.30	0.295

continued

TABLE III (*continued*)

Variable	HR	95% CI for HR		P Value
		Lower	Upper	
Postoperative negative pressure wound therapy (commenced at time of surgery)				
No (ref.)				
Yes	1.20	0.62	2.03	0.696
Postoperative suction drain				
No (ref.)				
Yes	1.04	0.57	1.92	0.899
Postoperative urinary catheter				
No				
Yes (ref.)	1.05	0.40	2.74	0.927
Hospital LOS (per day)	1.03	1.01	1.05	**<0.001**
Neoadjuvant chemotherapy				
No (ref.)				
Yes	1.67	0.93	2.94	0.091
Adjuvant chemotherapy				
No (ref.)				
Yes	1.70	0.92	3.11	0.090
Intraoperative tranexamic acid use				
No (ref.)				
Yes	0.78	0.45	1.38	0.400
Patient in private postoperative room				
No (ref.)				
Yes	1.05	0.64	1.74	0.850

†HR = hazard ratio, and CI = confidence interval. Model fit showed significant improvement over the null model (χ^2 = 78.04; p < 0.001). No multicollinearity; r > 0.7. Bold indicates a significant value (p < 0.05).

cohort of 604 patients. The prevalence of smokers in our study was less than half of the worldwide prevalence of 22.3%[25]. Therefore, it is not surprising that the analysis did not achieve significance. Although the prevalence of diabetes in our cohort is closer to the worldwide prevalence of 9.3%, the small sample size of 44 patients may have nonetheless led to underpowered analyses[26].

Orthopaedic oncology patients frequently receive perioperative immunomodulating therapeutic modalities, which can interfere with wound healing and complicate the postoperative course[16]. In the current study, neoadjuvant and adjuvant chemotherapy were not found to be significant risk factors for SSI, although the HR and 95% CI indicate a possible significant effect (neoadjuvant chemotherapy, HR = 1.67; 95% CI = 0.93 to 2.94; p = 0.091; and adjuvant chemotherapy, HR = 1.7; 95% CI = 0.92 to 3.11; p = 0.090). Neoadjuvant chemotherapy as a risk factor for SSI remains a topic of debate not only in orthopaedic oncology but also in other fields of oncological surgery[11,20,24,27,28]. Lastly, in a recent review on the use of silver- and Betadine (povidone-iodine)-coated implants, it was concluded that both coatings demonstrated efficacy against early infections and were associated with lower risk of implant removal and eventual amputation[29]. However, the studies included in that review were retrospective observational studies in which the definition and diagnostic criteria for SSI varied across the studies. The fact that the PARITY study did not identify silver- and Betadine-coated implants as protective against SSI may therefore be related to the minimization of bias inherent in the study design. However, the PARITY study was not specifically designed to assess the impact of implant coating on infection, and therefore, no definitive conclusions on the protective role of silver- and Betadine-coated prostheses against SSI can be drawn from this secondary analysis of the PARITY database.

Implications

The findings of this secondary analysis of the PARITY study data suggest that hospital LOS is a key predictor of SSI following oncological endoprosthetic reconstruction of the lower extremity. What is not clear, however, is whether the LOS represents a surrogate for unknown variables that lead to increased LOS, or if the LOS itself leads to increased risk of infection. The latter could be due to increased exposure to pathogens, increased risk of medical errors leading to infection, or increased risk of other complications that occur in a hospital

inpatient setting. A recent study in the arthroplasty literature similarly found that increased LOS led to increased risk of postoperative readmission[30]. Although there are some cases in which LOS cannot be shortened, it may be reasonable for clinicians to consider taking steps to arrange home care earlier or engage in programs of remote monitoring at home in order to minimize the risk of postoperative complications overall[31].

Strengths and Limitations

The main strength of this study is that the PARITY database is the largest prospectively collected database to date pertaining to SSI in orthopaedic oncology. The database underwent 4 stages of data-quality validation throughout the course of the trial, and therefore, our findings are likely to be reliable. Another primary strength of this study is that the diagnosis of SSI was made by an independent adjudication committee on the basis of the CDC's definition of SSI, eliminating assessment bias that may result from between-site inconsistencies in definitions of SSI. A limitation of this study is that several factors that have been shown to be predictors of SSI specifically in orthopaedic oncology, such as estimated blood loss[11,12,20] and transfusion requirement[20], were not prospectively collected in the PARITY study. In addition, our study population underwent exclusively lower-extremity surgery, and thus, the results of this study may not be able to be extrapolated to upper-extremity oncological procedures[10,24]. Finally, we acknowledge that we are not establishing causality between LOS and SSI, and that increased LOS may be a proxy for other, unknown variables that may cause SSI.

Conclusions

In this secondary analysis of the PARITY study data, we found that, although a diagnosis of STS invading bone, longer operative time, larger muscle volume excised, and longer hospital stay were potential risk factors for SSI following endoprosthetic reconstruction of the lower extremity, the only independent factor on multivariate analysis was hospital LOS. As caring for the complex needs of a cancer patient is a patient-specific endeavor, it may be reasonable for clinicians to consider streamlined discharge plans when possible for orthopaedic oncology patients in order to reduce the risk of SSI.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/H560). ■

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References

1. Ban KA, Minei JP, Laronga C, Harbrecht BG, Jensen EH, Fry DE, Itani KM, Dellinger EP, Ko CY, Duane TM. American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. J Am Coll Surg. 2017 Jan;224(1):59-74.

2. Scott RD. The direct medical costs of healthcare-associated infections in U.S. hospitals and the benefits of prevention. 2009. Accessed 2022 Jan 3. https://stacks.cdc.gov/view/cdc/11550

3. Poultsides LA, Ma Y, Della Valle AG, Chiu YL, Sculco TP, Memtsoudis SG. In-hospital surgical site infections after primary hip and knee arthroplasty—incidence and risk factors. J Arthroplasty. 2013 Mar;28(3):385-9.

4. Thakore RV, Greenberg SE, Shi H, Foxx AM, Francois EL, Prablek MA, Nwosu SK, Archer KR, Ehrenfeld JM, Obremskey WT, Sethi MK. Surgical site infection in orthopedic trauma: A case-control study evaluating risk factors and cost. J Clin Orthop Trauma. 2015 Dec;6(4):220-6.

5. Lee J, Singletary R, Schmader K, Anderson DJ, Bolognesi M, Kaye KS. Surgical site infection in the elderly following orthopaedic surgery. Risk factors and outcomes. J Bone Joint Surg Am. 2006 Aug;88(8):1705-12.

6. Greene LR. Guide to the elimination of orthopedic surgery surgical site infections: an executive summary of the Association for Professionals in Infection Control and Epidemiology elimination guide. Am J Infect Control. 2012 May;40(4):384-6.

7. Ee WWG, Lau WLJ, Yeo W, Von Bing Y, Yue WM. Does minimally invasive surgery have a lower risk of surgical site infections compared with open spinal surgery? Clin Orthop Relat Res. 2014 Jun;472(6):1718-24.

8. Peel TN. Studying biofilm and clinical issues in orthopedics. Front Microbiol. 2019 Feb 26;10(FEB):359.

9. Scheuermann-Poley C, Wagner C, Hoffmann J, Moter A, Willy C. [The significance of biofilm for the treatment of infections in orthopedic surgery: 2017 Update]. Unfallchirurg. 2017 Jun;120(6):461-71.

10. 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 Feb 5;96(3):223-30.

11. Morii T, Mochizuki K, Tajima T, Ichimura S, Satomi K. Surgical site infection in malignant soft tissue tumors. J Orthop Sci. 2012 Jan;17(1):51-7.

12. Nagano S, Yokouchi M, Setoguchi T, Sasaki H, Shimada H, Kawamura I, Ishidou Y, Kamizono J, Yamamoto T, Kawamura H, Komiya S. Analysis of surgical site infection after musculoskeletal tumor surgery: risk assessment using a new scoring system. Sarcoma. 2014;2014:645496.

13. Li X, Moretti VM, Ashana AO, Lackman RD. Perioperative infection rate in patients with osteosarcomas treated with resection and prosthetic reconstruction. Clin Orthop Relat Res. 2011 Oct;469(10):2889-94.

14. 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 Sep;40(9):1087-94.

15. Jeys LM, Grimer RJ, Carter SR, Tillman RM. Periprosthetic infection in patients treated for an orthopaedic oncological condition. J Bone Joint Surg Am. 2005 Apr;87(4):842-9.

16. 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 Aug;10(7):778-82.

17. Ghert M, Schneider P, Guyatt G, Thabane L, Vélez R, O'Shea T, Randall RL, Turcotte R, Wilson D, Wunder JS, Baptista AM, Cheng EY, Doung YC, Ferguson PC, Giglio V, Hayden J, Heels-Ansdell D, Khan SA, Sampath Kumar V, McKay P, Miller B, van de Sande M, Zumárraga JP, Bhandari M; Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) Investigators. Comparison of Prophylactic Intravenous Antibiotic Regimens After Endoprosthetic Reconstruction for Lower Extremity Bone Tumors: A Randomized Clinical Trial. JAMA Oncol. 2022 Mar 1;8(3):345-53.

18. Ghert M, Deheshi B, Holt G, Randall RL, Ferguson P, Wunder J, Turcotte R, Werier J, Clarkson P, Damron T, Benevenia J, Anderson M, Gebhardt M, Isler M, Mottard S, Healey J, Evaniew N, Racano A, Sprague S, Swinton M, Bryant D, Thabane L, Guyatt G, Bhandari M; PARITY Investigators. Prophylactic antibiotic regimens in tumour surgery (PARITY): protocol for a multicentre randomised controlled study. BMJ Open. 2012 Nov 28;2(6):e002197.

19. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: A modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol. 1992 Oct;13(10):606-8.

20. Anatone AJ, Danford NC, Jang ES, Smartt A, Konigsberg M, Tyler WK. Risk Factors for Surgical Site Infection in Orthopaedic Oncology. J Am Acad Orthop Surg. 2020 Oct 15;28(20):e923-8.

21. Mavrogenis AF, Pala E, Romagnoli C, Romantini M, Calabro T, Ruggieri P. Survival analysis of patients with femoral metastases. J Surg Oncol. 2012 Feb;105(2):135-41.

22. Potter BK, Chow VE, Adams SC, Letson GD, Temple HT. Endoprosthetic proximal femur replacement: metastatic versus primary tumors. Surg Oncol. 2009 Dec;18(4):343-9.

23. Mujagic E, Marti WR, Coslovsky M, Soysal SD, Mechera R, von Strauss M, Zeindler J, Saxer F, Mueller A, Fux CA, Kindler C, Gurke L, Weber WP. Associations of Hospital Length of Stay with Surgical Site Infections. World J Surg. 2018 Dec;42(12):3888-96.

24. Moore J, Isler M, Barry J, Mottard S. Major wound complication risk factors following soft tissue sarcoma resection. Eur J Surg Oncol. 2014 Dec;40(12): 1671-6.

25. World Health Organization. Tobacco. 2022 May 24. Accessed 2022 June 10. https://www.who.int/news-room/fact-sheets/detail/tobacco

26. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R; IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019 Nov;157: 107843.

27. Holubar SD, Brickman RK, Greaves SW, Ivatury SJ. Neoadjuvant Radiotherapy: A Risk Factor for Short-Term Wound Complications after Radical Resection for Rectal Cancer? J Am Coll Surg. 2016 Aug;223(2):291-8.

28. Decker MR, Greenblatt DY, Havlena J, Wilke LG, Greenberg CC, Neuman HB. Impact of neoadjuvant chemotherapy on wound complications after breast surgery. Surgery. 2012 Sep;152(3):382-8.

29. Trovarelli G, Angelini A, Pala E, Cappellari A, Breda A, Ruggieri P. Infection in orthopaedic oncology: crucial problem in modern reconstructive techniques. Eur Rev Med Pharmacol Sci. 2019 Apr;23(2):271-8.

30. Benito J, Stafford J, Judd H, Ng M, Corces A, Roche MW. Length of Stay Increases 90-day Readmission Rates in Patients Undergoing Primary Total Joint Arthroplasty. J Am Acad Orthop Surg Glob Res Rev. 2022 Mar 16;6(3):e21.00271.

31. McGillion MH, Parlow J, Borges FK, Marcucci M, Jacka M, Adili A, Lalu MM, Ouellette C, Bird M, Ofori S, Roshanov PS, Patel A, Yang H, O'Leary S, Tandon V, Hamilton GM, Mrkobrada M, Conen D, Harvey V, Lounsbury J, Mian R, Bangdiwala SI, Arellano R, Scott T, Guyatt GH, Gao P, Graham M, Nenshi R, Forster AJ, Nagappa M, Levesque K, Marosi K, Chaudhry S, Haider S, Deuchar L, LeBlanc B, McCartney CJL, Schemitsch EH, Vincent J, Pettit SM, DuMerton D, Paulin AD, Simunovic M, Williams DC, Halman S, Harlock J, Meyer RM, Taylor DA, Shanthanna H, Schlachta CM, Parry N, Pichora DR, Yousuf H, Peter E, Lamy A, Petch J, Moloo H, Sehmbi H, Waggott M, Shelley J, Belley-Cote EP, Devereaux PJ; PVC-RAM-1 Investigators. Post-discharge after surgery Virtual Care with Remote Automated Monitoring-1 (PVC-RAM-1) technology versus standard care: randomised controlled trial. BMJ. 2021 Sep 30;374: n2209.