What Is the Effect of Advanced Age and Comorbidity on Postoperative Morbidity and Mortality After Musculoskeletal Tumor Surgery?

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Abstract

Background Although the elderly population is increasing rapidly, little information is available regarding how the risk of postoperative mortality and morbidity increases when combined with age and comorbidity burden in patients undergoing musculoskeletal tumor surgery.

Questions/purposes We evaluated the effect of age and comorbidity burden on the (1) postoperative complication rate and (2) in-hospital mortality rate after musculoskeletal tumor surgery.

Methods We identified 5716 patients undergoing musculoskeletal tumor surgery during 2007 to 2012 using a Japanese

national inpatient database. Logistic regression analyses were performed to examine the relationships of various factors with the rates of mortality and morbidity.

Results The postoperative complication rate (6.7%) was associated with male sex ($p = 0.033$), age 80 years or older ($p = 0.001$), tumor located in the lower extremity ($p = 0.001$) or trunk ($p = 0.019$), Charlson Comorbidity Index of 4 or greater ($p < 0.001$), blood transfusion ($p < 0.001$), and duration of anesthesia of 240 minutes or longer ($p < 0.001$). The in-hospital mortality (0.8%) was related to the Charlson Comorbidity Index of 4 or greater ($p < 0.001$), blood transfusion ($p < 0.001$), and high hospital volume ($p = 0.016$). The morbidity (21.6%; OR, 3.29; $p < 0.001$) and mortality (4.1%; OR, 5.95; $p < 0.001$) in patients 80 years or older with a Charlson Comorbidity Index of 4 or greater was increased three and six times, respectively, compared with patients 64 years or younger with no comorbidity.

Conclusions We found that age and comorbidity burden together greatly increased the risk of morbidity and mortality. Our study showed quantitative evidence that will assist physicians in assessing perioperative risk accurately and provide a more informative explanation to elderly patients undergoing musculoskeletal tumor surgery.

Level of Evidence Level IV, prognostic study. See the Instructions for Authors for a complete description of levels of evidence.

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Introduction

In patients with musculoskeletal sarcomas, complete resection with a negative surgical margin is a potentially curative treatment option. However, surgical treatment frequently demands an aggressive approach to achieve this objective. The proportion of the elderly population is rapidly increasing owing to demographic changes, and this trend is particularly evident in Japan where 23% of the population are 65 years or older [6, 9, 10, 12]. Consequently, the number of elderly patients with musculoskeletal sarcomas who are treated surgically also is increasing [9]. Surgeons and medical oncologists may be hesitant to treat elderly patients in a comparably intensive manner as that used for treatment of younger patients because the elderly usually have decreased performance status and several comorbidities and the natural history of disease may reduce enthusiasm for aggressive surgical intervention.

Studies of the surgical outcomes in elderly patients with various malignancies have been reported [2, 3, 11, 17, 18]. However, little information is available regarding the therapeutic outcomes in elderly patients with musculoskeletal sarcomas, and some studies have relatively small cohorts [1, 2, 4, 9, 15]. These studies mainly highlighted the long-term outcome with an endpoint of tumor-related death, local recurrence, or metastasis [1, 2, 4, 9, 15], and little information is available regarding the effect of advanced age or comorbidity on the short-term outcomes. Perioperative mortality and morbidity have not been well documented. Presumably, some musculoskeletal oncologists have had patients with several postoperative complications or patients who died after surgery and they may recognize the population at greater risk of these complications or death. However, to our knowledge, quantitative evidence to determine the effect of age and comorbidity burden on the risk of having postoperative complications or death after musculoskeletal tumor surgery has been lacking. More understanding of the effect of each factor would allow surgeons to better evaluate the perioperative risk for elderly patients with musculoskeletal sarcomas.

We therefore evaluated the effect of age and comorbidity burden on the (1) postoperative complication rate and (2) in-hospital mortality rate after musculoskeletal tumor surgery.

Patients and Methods

Data Source

The Diagnosis Procedure Combination database is a national administrative claims and discharge abstract data

on acute-care inpatients in Japan, the details of which have been described [6, 8, 13, 14]. Data were collected during 6 months (from July 1 to December 31) until 2010 and throughout the year from 2011. The numbers of admissions in the database were 2.7, 2.8, 2.8, 3.3, and 7.0 million in 2007, 2008, 2009, 2010, and 2011, respectively, representing approximately 50% of all inpatient admissions to secondary- and tertiary-care hospitals in Japan.

The database includes the following data for each patient: location of hospital; age and sex; diagnoses and comorbidities at admission and complications after admission recorded with text data in the Japanese language and the ICD-10 codes; procedures coded with Japanese original codes; drugs and devices used; length of hospital stay; and discharge status. Complications that occur after admission are clearly differentiated from comorbidities present at admission.

Because of the anonymous nature of the data, informed consent for this study was waived. Study approval was obtained from the Institutional Review Board of The University of Tokyo.

Data Extraction

Two authors (KO and HY) retrospectively identified the records of all patients in the Diagnosis Procedure Combination database who underwent musculoskeletal tumor surgery (bone tumor resection [Japanese procedure code, K053]; soft tissue tumor resection [K031]; and amputation [K084]) for a primary malignant musculoskeletal tumor (malignant bone tumor [ICD-10 codes, C40.x, C41.x]; and primary malignant soft tissue tumor [C47.x, C48.0, C49.x]) during 2007 to 2012. Of the approximately 20 million inpatients whose data were collected in the database during this period, we identified 5716 eligible patients at 409 hospitals who underwent musculoskeletal tumor surgery (Table 1). For each patient, we extracted the following data: sex, age, main diagnosis, tumor location, type of surgery, presence or absence of blood transfusion, duration of anesthesia, postoperative length of stay, and the following comorbidities (ICD-10 codes) that may affect the rates of postoperative complications or in-hospital mortality: diabetes mellitus (E10.x-E14.x), chronic lung disease (I27.8, I27.9, J40.x-J47.x, J60.x-J67.x, J68.4, J70.1, J70.3), cardiac disease (I25.2, I09.9, I11.0, I13.0, I13.2, I20.x, I21.x, I22.x, I25.5, I42.0, I42.5-I42.9, I43.x, I50.x, P29.0), cerebrovascular disease (G45.x, G46.x, H34.0, I60.x-I69.x), chronic renal failure (N18.x), and liver disease (I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7). Based on the protocol of Quan et al. [16], each ICD-10 code of a comorbidity was converted to

Table 1. Characteristics of the study population according to surgical procedures

Variable	Overall (n = 5716)	Soft tissue tumor resection (n = 4534)	Bone tumor resection (n = 896)	Amputation (n = 286)	p value
Age (years)*	58 (20)	61 (18)	46 (23)	56 (24)	
Age group (number of patients)					< 0.001
≤ 64 years	3183 (56%)	2373 (52%)	643 (72%)	167 (58%)	
65–79 years	1845 (32%)	1551 (34%)	218 (24%)	76 (27%)	
≥ 80 years	688 (12%)	610 (14%)	35 (4%)	43 (15%)	
Sex (number of patients)					0.222
Male	3129 (55%)	2463 (54%)	496 (55%)	170 (59%)	
Female	2587 (45%)	2071 (46%)	400 (45%)	116 (41%)	
Tumor site (number of patients)					< 0.001
Upper extremity	839 (15%)	712 (16%)	65 (7%)	62 (22%)	
Lower extremity	2692 (47%)	2256 (50%)	292 (33%)	144 (50%)	
Trunk	1715 (30%)	1141 (25%)	519 (58%)	55 (19%)	
Unknown	470 (8%)	425 (9%)	20 (2%)	25 (9%)	
Charlson Comorbidity Index (number of patients)					< 0.001
2	4206 (74%)	3345 (74%)	676 (75%)	185 (65%)	
3	863 (15%)	710 (16%)	113 (13%)	40 (14%)	
≥ 4	647 (11%)	479 (10%)	107 (12%)	61 (21%)	
Hospital volume (number of patients)					< 0.001
≤ 13 cases	1741 (31%)	1476 (33%)	186 (21%)	79 (28%)	
14–28 cases	2062 (36%)	1596 (35%)	350 (39%)	116 (40%)	
≥ 29 cases	1913 (33%)	1462 (32%)	360 (40%)	91 (32%)	
Blood transfusion (number of patients)					< 0.001
No	4702 (82%)	4058 (89%)	438 (49%)	206 (72%)	
Yes	1014 (18%)	476 (11%)	458 (51%)	80 (28%)	
Anesthesia time (minutes) [†]	216 (142–345)	195 (135–307)	379 (251–567)	204 (157–278)	< 0.001
Anesthesia time group (number of patients)					< 0.001
≤ 120 minutes	932 (17%)	862 (19%)	44 (5%)	26 (9%)	
121–240 minutes	2261 (40%)	1951 (44%)	159 (18%)	151 (54%)	
> 240 minutes	2417 (43%)	1646 (37%)	666 (77%)	105 (37%)	
Postoperative length of stay (days) [†]	19 (11–35)	17 (11–29)	35 (19–66)	29 (17–56)	< 0.001

* Values are expressed as mean, with SD in parentheses; [†]values are expressed as median, with interquartile range in parentheses.

a score, and the sum of the scores was used to calculate the patient's Charlson Comorbidity Index [5]. The Charlson Comorbidity Index assigns points for different types of comorbidities; for example, 1 point each for diabetes and heart disease, 2 points for a malignant tumor, 3 points for liver disease, and 6 points for metastatic malignancy. A Charlson Comorbidity Index of 2 in this study indicates a patient has no preoperative comorbidities except for musculoskeletal tumor.

Diagnoses (ICD-10 codes) were categorized in two groups: primary malignant bone tumor (C40.x, C41.x) or primary malignant soft tissue tumor (C47.x, C48.0, C49.x), and tumor location was categorized in three subgroups: upper extremity, lower extremity, or trunk. The type of surgery was categorized in three subgroups: bone tumor

resection, soft tissue tumor resection, or amputation. The Diagnosis Procedure Combination data do not include information regarding duration of surgery, but the period of anesthesia generally reflects this. The duration of anesthesia was categorized as less than 120 minutes, 120 to 240 minutes, or more than 240 minutes. The hospital volumes for all musculoskeletal surgery were determined using the unique identifier for each hospital and categorized by patient tertiles into low (< 13 cases/year), medium (14–28 cases/year), or high volume (> 28 cases/year). Patients were divided in tertiles according to hospital volume (number of musculoskeletal surgeries per year) so that the number of patients in each group was almost equal: low, 13 or fewer/year; medium, 14 to 28/year; or high, 29 or more/year.

Endpoints

The primary endpoints were (1) in-hospital mortality rate and (2) postoperative rate of complications (ICD-10 codes), including surgical site infection (T813), sepsis (A40.x, A41.x), pulmonary embolism (I26.x), cardiac events (I20.x, I21.x, I50.x), respiratory complications (J10.x–J18.x, J95.2, J96.0), cerebrovascular events (I60.x–I64.x), and acute renal failure (N17.x).

Statistical Analyses

We performed univariate comparisons of proportions using the chi-square test and comparisons of means using ANOVA. Logistic regression analyses were performed to examine the relationships of each factor with the rates of postoperative complications and in-hospital mortality. Differences were considered statistically significant with *p* values less than 0.1 in univariate analyses and less than 0.05 in multivariate analyses.

Results

The overall rate of postoperative complications was 6.7% (381 of 5716): 6.3% in the group 64 years or younger, 6.1% in the group 65 to 79 years old, and 9.9% in the group 80 years or older (Table 2). Univariate analyses showed higher postoperative complication rates for males than for females (*p* = 0.009); for patients 80 years or older (*p* = 0.001); for patients with tumor location in the lower extremity (*p* < 0.001) or trunk (*p* = 0.001) rather than in the upper extremity; patients with a Charlson Comorbidity Index of 3 (*p* < 0.001) or with a Charlson Comorbidity Index of 4 or greater (*p* < 0.001); patients who underwent bone tumor resection than for patients who underwent soft tissue tumor resection (*p* = 0.049), patients who received blood transfusion (*p* < 0.001); patients with duration of anesthesia of 120 to 240 minutes (*p* = 0.077) or greater than 240 minutes (*p* < 0.001) rather than less than 120 minutes; and for patients treated in medium-volume hospitals rather than low-volume hospitals (*p* = 0.048) (Table 3). Multivariate analyses showed associations between postoperative complication rates and female sex (odds ratio [OR], 0.79; 95% CI, 0.63–0.98; *p* = 0.033), age of 80 years or older (OR, 1.68; 95% CI, 1.23–2.30; *p* = 0.001), tumor location in the lower extremity (OR, 1.96; 95% CI, 1.33–2.91; *p* = 0.001) or trunk (OR, 1.65; 95% CI, 1.08–2.50; *p* = 0.019), Charlson Comorbidity Index of 3 (OR, 1.93; 95% CI, 1.47–2.55; *p* < 0.001), or Charlson Comorbidity Index of 4 or more (OR, 2.85; 95% CI, 2.17–3.74; *p* < 0.001), blood transfusion (OR, 1.79;

95% CI, 1.37–2.34; *p* < 0.001), and duration of anesthesia greater than 240 minutes (OR, 2.66; 95% CI, 1.78–3.98; *p* < 0.001) (Table 3).

The overall in-hospital mortality rate was 0.8% (45 of 5716): 0.7% in the group 64 years or younger, 0.6% in the group 65 to 79 years, and 1.6% in the group 80 years or older. Univariate analyses showed higher in-hospital mortality rates in patients 80 years or older (*p* = 0.030), patients with a Charlson Comorbidity Index of 3 (*p* = 0.038) or with a Charlson Comorbidity Index of 4 or higher (*p* < 0.001), patients who underwent amputation than patients who underwent soft tissue tumor resection (*p* = 0.010), patients who received blood transfusion (*p* < 0.001), and patients treated in high-volume hospitals than low-volume hospitals (*p* = 0.009) (Table 4). Multivariate analyses showed associations between in-hospital mortality rates and Charlson Comorbidity Index of 4 or greater (OR, 4.06; 95% CI, 2.05–8.03; *p* < 0.001), blood transfusion (OR, 10.95; 95% CI, 5.59–21.44; *p* < 0.001), and high-volume hospital (OR, 0.34; 95% CI, 0.14–0.82; *p* = 0.016) (Table 4). Because elderly patients frequently have several coexisting comorbidities, preoperative risk should be evaluated with consideration of age and comorbidity, and therefore, we performed additional analyses of postoperative complications (Fig. 1A) and in-hospital mortality (Fig. 1B) focusing on age and Charlson Comorbidity Index. The morbidity and mortality in patients 80 years or older with a Charlson Comorbidity Index of 4 was approximately three (OR, 3.29; 95% CI, 2.53–4.27; *p* < 0.001) and six times (OR, 5.95; 95% CI, 3.07–11.05; *p* < 0.001), respectively, as frequent as for patients 64 years or younger with no preoperative comorbidity.

Discussion

Although nearly 50% of patients with soft tissue sarcoma are older than 65 years, it was reported that elderly patients with musculoskeletal sarcoma did not receive definitive treatment until the 1990s [7]. Farshadpour et al. [7] analyzed 40 patients with soft tissue sarcomas who received no definitive treatment and reported that 23% of these patients who were 65 years or older had treatment withheld for patient-related reasons, such as patient refusal, comorbidity, or poor general condition. With demographic changes and the rapid increase in the number of elderly patients with musculoskeletal sarcomas, more elderly patients are likely to require surgical intervention. However, it usually is difficult to treat elderly patients in an intensive manner comparable to that for younger patients because of their decreased performance status and comorbidities. Musculoskeletal tumor surgery is challenging and potentially is associated with high complication rates. In addition, little

Table 2. Postoperative complications and in-hospital mortality for each surgical procedure

Variable	Number of patients				p value
	Overall (n = 5716)	Soft tissue tumor resection (n = 4534)	Bone tumor resection (n = 896)	Amputation (n = 286)	
In-hospital death	45 (0.8%)	30 (0.7%)	9 (1.0%)	6 (2.1%)	0.021
≤ 64 years	23 (0.7%)	12 (0.5%)	6 (0.9%)	5 (3.0%)	0.001
65–79 years	11 (0.6%)	8 (0.5%)	3 (1.4%)	0 (0.0%)	
≥ 80 years	11 (1.6%)	10 (1.6%)	0 (0.0%)	1 (2.3%)	
Postoperative complications					
Surgical site infection	242 (4.2%)	195 (4.3%)	39 (4.4%)	8 (2.8%)	0.464
Cardiac events	61 (1.1%)	45 (1.0%)	12 (1.3%)	4 (1.4%)	0.558
Respiratory complications	36 (0.6%)	26 (0.6%)	7 (0.8%)	3 (1.0%)	0.506
Sepsis	26 (0.5%)	13 (0.3%)	9 (1.0%)	4 (1.4%)	0.001
Pulmonary embolism	17 (0.3%)	11 (0.2%)	5 (0.6%)	1 (0.3%)	0.281
Acute renal failure	7 (0.1%)	4 (0.1%)	2 (0.2%)	1 (0.3%)	0.303
Cerebrovascular events	5 (0.1%)	5 (0.1%)	0 (0.0%)	0 (0.0%)	0.521
At least one complication	381 (6.7%)	288 (6.4%)	73 (8.1%)	20 (7.0%)	0.140
≤ 64 years	201 (6.3%)	130 (5.5%)	56 (8.7%)	15 (9.0%)	0.004
65–79 years	112 (6.1%)	95 (6.1%)	14 (6.4%)	3 (3.8%)	
≥ 80 years	68 (9.9%)	63 (10.3%)	3 (8.6%)	2 (4.7%)	

information regarding the effect of advanced age or comorbidity burden on rates of mortality and postoperative complications make it difficult to judge whether surgical intervention should be performed in such populations. We therefore evaluated the effect of age and comorbidity burden on the (1) postoperative complication rate and (2) in-hospital mortality rate after musculoskeletal tumor surgery. Our study showed that advanced age and comorbidity burden together greatly increased the risk of morbidity and mortality.

Our study has several limitations. First, the use of an administrative claims database could have led to underestimation or overestimation of comorbidities or postoperative complications because of incomplete reporting. Second, the participation rate of small hospitals in the Diagnosis Procedure Combination database was relatively low, which may have resulted in a sample selection bias. However, there are few patients with musculoskeletal sarcomas treated in small non-Diagnosis Procedure Combination hospitals because patients with sarcomas in Japan usually are treated in academic hospitals or cancer treatment centers that participate in the Diagnosis Procedure Combination system. Third, we were unable to determine complications and deaths after discharge or transfer to another hospital, which may have resulted in underestimation of these outcomes. However, most patients with postoperative complications or in-hospital death would be included in our analysis, as the median postoperative hospital stay was 19 days, and the majority of

such early postoperative events occur during that period. Fourth, we were not able to identify several important clinical parameters that may have affected the rates of postoperative complications and mortality, including histologic diagnosis, clinical stage of the tumor, severity of preoperative comorbidities, adjuvant chemotherapy and radiotherapy, and details of the surgery. Fifth, we were not able to determine the decision process for treatment because we extracted only the data of patients with musculoskeletal sarcoma treated surgically. Therefore, the indication for surgery in elderly patients with numerous comorbidities may have been different among hospitals, which may have resulted in selection bias. Finally, it is possible that individual patients may have been counted more than once in the database if they initially received inappropriate surgical treatment at a local hospital and then underwent surgery in a specialized hospital. However, such cases are rare in Japan because there are a limited number of hospitals specializing in musculoskeletal oncology, and patients usually are referred to a specialized hospital if a musculoskeletal sarcoma is suspected.

Despite these limitations, we believe that our results are epidemiologically important, as they show the incidence of postoperative complications and in-hospital death after musculoskeletal tumor surgery in the Japanese population. The population from the Diagnosis Procedure Combination database is representative of the population in Japan and includes the majority of patients undergoing musculoskeletal tumor

Table 3. Univariate and multivariate logistic regression analyses for postoperative complications

Variable	Number of patients	Number of patients with complications (%)	Univariate analysis		Multivariate analysis	
			Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Total	5716	381 (6.7%)				
Sex						
Male	3129 (55%)	233 (7.4%)	Reference		Reference	
Female	2587 (45%)	148 (5.7%)	0.75 (0.61–0.93)	0.009	0.79 (0.63–0.98)	0.033
Age						
≤ 64 years	3183 (56%)	201 (6.3%)	Reference		Reference	
65–79 years	1845 (32%)	112 (6.1%)	0.96 (0.76–1.22)	0.730	0.91 (0.71–1.17)	0.482
≥ 80 years	688 (12%)	68 (9.9%)	1.63 (0.22–2.17)	0.001	1.68 (1.23–2.30)	0.001
Tumor location						
Upper extremity	846 (15%)	32 (3.8%)	Reference		Reference	
Lower extremity	2698 (47%)	207 (7.7%)	2.11 (1.45–3.09)	< 0.001	1.96 (1.33–2.91)	0.001
Trunk	1718 (30%)	124 (7.2%)	1.98 (1.33–2.95)	0.001	1.65 (1.08–2.50)	0.019
Data not provided	454 (8%)	18 (4.0%)	1.05 (0.58–1.89)	0.871	0.85 (0.45–1.59)	0.611
Charlson Comorbidity Index						
2	4206 (74%)	202 (4.8%)	Reference		Reference	
3	863 (15%)	87 (10.1%)	2.22 (1.71–2.89)	< 0.001	1.93 (1.47–2.55)	< 0.001
≥ 4	647 (11%)	92 (14.2%)	3.29 (2.53–4.27)	< 0.001	2.85 (2.17–3.74)	< 0.001
Type of surgery						
Soft tissue tumor resection	4534 (79%)	288 (6.4%)	Reference		Reference	
Bone tumor resection	896 (16%)	73 (8.1%)	1.31 (1.00–1.71)	0.049	0.80 (0.58–1.11)	0.180
Amputation	286 (5%)	20 (7.0%)	1.11 (0.69–1.77)	0.667	0.91 (0.56–1.48)	0.696
Blood transfusion						
Yes	1014 (18%)	126 (12.4%)	2.47 (1.98–3.10)	< 0.001	1.79 (1.37–2.34)	< 0.001
Anesthesia time						
< 120 minutes	932 (17%)	31 (3.3%)	Reference		Reference	
120–240 minutes	2261 (40%)	107 (4.7%)	1.44 (0.96–2.17)	0.077	1.40 (0.93–2.12)	0.107
> 240 minutes	2417 (43%)	234 (9.7%)	3.12 (2.13–4.57)	< 0.001	2.66 (1.78–3.98)	< 0.001
Hospital volume						
Low	1741 (31%)	131 (7.5%)	Reference		Reference	
Medium	2062 (36%)	122 (5.9%)	0.773 (0.60–0.99)	0.048	0.71 (0.54–0.93)	0.108
High	1913 (33%)	128 (6.7%)	0.88 (0.68–1.14)	0.327	0.89 (0.68–1.16)	0.391

surgery in Japan. The data included approximately 50% of all the hospital admissions in Japan during 2011. According to data from the nationwide bone and soft tissue tumor registry in Japan, more than 80% of patients with primary musculoskeletal tumors underwent surgery at university hospitals or cancer treatment centers contributing to the Diagnosis Procedure Combination system because of the rarity of the disease and the specialized surgical procedures required.

Several investigators have reported the clinical outcomes of elderly patients with musculoskeletal sarcomas along with the demographic changes (aging) and the development of perioperative management [1, 2, 4, 9, 15]. However, these reports mainly highlighted the long-term outcome such as metastasis, local recurrence, or tumor-

related death, and little information is available regarding short-term surgical outcomes such as morbidity and mortality [2, 4, 9]. The perioperative mortality and morbidity was 0.9% to 2.2% and 31% to 38%, respectively [2, 4, 9]. The mortality rate for our study patients was comparable to rates reported previously and the morbidity in our study patients was less than reported for patients in the previous studies. However, direct comparison with existing data is difficult since these were based on small cohorts of patients with different definitions of aged. Although there have been no previous reports regarding how advanced age and comorbidity burden increase the risk of postoperative complications and in-hospital mortality, our results showed that the comorbidity burden as

Table 4. Univariate and multivariate logistic regression analyses for in-hospital mortality

Variable	Number of patients	Number of patients with in-hospital death (%)	Univariate analysis		Multivariate analysis	
			Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Total	5716	45 (0.8%)				
Sex						
Male	3129 (55%)	27 (0.9%)	Reference		Reference	
Female	2587 (45%)	18 (0.7%)	0.81 (0.44–1.47)	0.478	0.74 (0.40–1.37)	0.335
Age						
≤ 64 years	3183 (56%)	23 (0.7%)	Reference		Reference	
65–79 years	1845 (32%)	11 (0.6%)	0.82 (0.40–1.63)	0.599	0.72 (0.34–1.50)	0.376
≥ 80 years	688 (12%)	11 (1.6%)	2.23 (1.08–4.60)	0.030	1.71 (0.78–3.73)	0.178
Tumor location						
Upper extremity	846 (15%)	4 (0.5%)	Reference			
Lower extremity	2698 (47%)	19 (0.7%)	1.49 (0.51–4.40)	0.467		
Trunk	1718 (30%)	19 (1.1%)	2.35 (0.80–6.94)	0.121		
Data not provided	454 (8%)	3 (0.7%)	1.40 (0.31–6.28)	0.660		
Charlson Comorbidity Index						
2	4206 (74%)	19 (0.5%)	Reference		Reference	
3	863 (15%)	9 (1.0%)	2.32 (1.05–5.15)	0.038	1.86 (0.82–4.23)	0.137
≥ 4	647 (11%)	17 (2.6%)	5.95 (3.07–11.50)	< 0.001	4.06 (2.05–8.03)	< 0.001
Type of surgery						
Soft tissue tumor resection	4534 (79%)	30 (0.7%)	Reference		Reference	
Bone tumor resection	896 (16%)	9 (1.0%)	2.52 (0.72–3.22)	0.270	0.65 (0.28–1.47)	0.295
Amputation	286 (5%)	6 (2.1%)	3.22 (1.33–7.79)	0.010	1.57 (0.62–3.97)	0.343
Blood transfusion						
Yes	1014 (18%)	31 (3.1%)	10.56 (5.60–19.92)	< 0.001	10.95 (5.59–21.44)	< 0.001
Anesthesia time						
< 120 minutes	932 (17%)	6 (0.6%)	Reference			
120–240 minutes	2261 (40%)	12 (0.5%)	0.82 (0.31–2.20)	0.699		
> 240 minutes	2417 (43%)	24 (1.0%)	1.55 (0.63–3.80)	0.340		
Hospital volume						
Low	1741 (31%)	20 (1.1%)	Reference		Reference	
Medium	2062 (36%)	18 (0.9%)	0.76 (0.40–1.44)	0.396	0.74 (0.38–1.45)	0.384
High	1913 (33%)	7 (0.4%)	0.32 (0.13–0.75)	0.009	0.34 (0.14–0.82)	0.016

measured by the Charlson Comorbidity Index was strongly associated with postoperative complications and in-hospital mortality. Advanced age (80 years or older) was associated with an approximately twofold increase in the risk of postoperative complications, whereas no association was noted with in-hospital mortality. The morbidity and mortality in patients 80 years or older with a Charlson Comorbidity Index of 4 was approximately three and six times, respectively, as frequent as in patients 64 years or younger with no preoperative comorbidity (Fig. 1). Quantitative data regarding the effect of age and comorbidity burden on postoperative morbidity and mortality after musculoskeletal tumor surgery have been

lacking, and our results will enable physicians to assess perioperative risk more accurately and inform their patients of their overall risk for surgery. In addition, because the Charlson Comorbidity Index can predict 1-year mortality from preexisting comorbidity, a comparison between predicted tumor mortality and death from preexisting comorbidity also may be beneficial for treatment decision-making.

We believe that our findings provide critical information regarding the factors associated with poorer outcomes in patients undergoing surgical treatment for musculoskeletal sarcoma. The study indicated that age and comorbidity burden together greatly increased the risk of morbidity and

Age (years)	CCI = 2	CCI = 3	CCI ≥ 4
≤ 64	169 (5.9%) Reference	191 (6.9%) OR, 2.22; p < 0.001	21 (21.6%) OR, 3.29; p < 0.001
65–79			
≥ 80			

A

Age (years)	CCI = 2	CCI = 3	CCI ≥ 4
≤ 64	20 (0.7%) Reference	21 (0.8%) OR, 2.32; p = 0.038	4 (4.1%) OR, 5.95; p < 0.001
65–79			
≥ 80			

B

Fig. 1A–B The (A) postoperative complications and (B) in-hospital mortality stratified by age and Charlson Comorbidity Index are shown. CCI = Charlson Comorbidity Index.

mortality. A greater understanding of each factor's contribution to postoperative outcomes would allow surgeons to better evaluate perioperative risk.

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