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Mortality and Morbidity Following Surgery for Primary Malignant Musculoskeletal Tumors in the Pelvis and Limbs: A Retrospective Analysis Using the Japanese Diagnosis Procedure Combination Database

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Abstract

Introduction: Resection of malignant pelvic tumors has long been considered to be associated with higher postoperative mortality and morbidity than resection of malignant limb tumors. We compared the postoperative adverse events of pelvic tumor surgery and limb tumor surgery using a national inpatient database. Methods: We identified patients who underwent surgery for primary musculoskeletal malignant tumors of the pelvis or limbs between July and December in 2007-2010 using the Japanese Diagnosis Procedure Combination inpatient database. We calculated the risk-adjusted odds ratio for the occurrence of postoperative complications following pelvic tumor surgery with reference to limb tumor surgery using a multivariable logistic regression analysis. Results: Of 3255 eligible patients, 3116 underwent limb tumor surgery and 139 underwent pelvic

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tumor surgery. In-hospital mortality was 0.6% and 0.7% and postoperative complication rates were 8.2% and 18.7%, respectively. The rate of blood transfusion and duration of anesthesia over 480 min were higher in the pelvic tumor group. Blood transfusion volume and duration of anesthesia were independently associated with worse outcomes, but there was no significant association between tumor location and occurrence of postoperative complications (odds ratio 1.18, 95% confidence interval 0.73 - 1.88, p = 0.502). Conclusions: Blood transfusion volume and duration of anesthesia were significant predictors of outcome. Our data demonstrate that the higher morbidity rate after pelvic tumor resection could result from the larger blood transfusion volume and longer anesthesia duration.

Keywords

Musculoskeletal Tumor Resection, Sarcoma, Pelvic Tumor, Postoperative Complication, Japanese Diagnosis Procedure Combination Database

1. Introduction

Resection of malignant pelvic tumors has long been considered to be associated with poorer outcomes and higher morbidity than resection of malignant limb tumors [1]-[7]. Although recent advances in perioperative management may have improved outcomes in pelvic tumor surgery, the availability of up-to-date data on mortality and morbidity is limited because these tumors are relatively rare. Data in previous studies were based on small sample sizes of fewer than 100 or obtained retrospectively over decades [2]-[8]. In the present study, we used a national inpatient database to compare in-hospital mortality and postoperative complications between primary malignant pelvic tumor surgery and primary malignant limb tumor surgery.

2. Patients and Methods

2.1. Data Source

In this study, we utilized the Japanese Diagnosis Procedure Combination (DPC) database. Details of the database have been described elsewhere [9]. Briefly, discharge abstract and administrative claims data are collected from participating hospitals between July 1 and December 31 each year. The numbers of inpatients in the DPC database were 2.99 million from 926 hospitals in 2007, 2.86 million from 855 hospitals in 2008, 2.57 million from 818 hospitals in 2009, and 3.19 million from 952 hospitals in 2010. The database includes the following data: patient age and sex; diagnoses, comorbidities at admission, and complications after admission recorded according to International Classification of Diseases, Tenth Revision (ICD-10) codes and text data in the Japanese language; procedures according to the original Japanese codes; drugs used; and in-hospital death.

2.2. Ethics

The anonymous nature of the data allowed the requirement for informed consent to be waived. This study was approved by the Institutional Review Board of The University of Tokyo.

2.3. Patient Background Characteristics

The following variables were abstracted from the DPC database: patient age and sex; tumor origin (bone and soft tissue); prosthetic joint replacement; free vascularized multi-tissue graft; distant metastasis (lung and brain); diabetes mellitus; use of hemodialysis; chemotherapy (cisplatin, doxorubicin hydrochloride, methotrexate, ifosfamide, dacarbazine, and etoposide); duration of anesthesia; volume of blood transfusion; and precise tumor site data.

Blood transfusion volume was categorized into 0, 1 - 999, 1000 - 2499, and ≥2500 ml. Duration of anesthesia was categorized into ≤119, 120 - 239, 240 - 359, 360 - 479, and ≥480 min. The DPC data do not include information on the duration of operation, but the duration of anesthesia generally reflects operative time [10].

2.4. Outcome Measurements

The primary outcomes were in-hospital mortality and postoperative complications. Postoperative complications included acute renal failure (N17), venous thromboembolism (I80.0-I80.3, A40-A41, and D65), pneumonia (J12-J18), and surgical site infection (T813 and T814).

2.5. Statistical Analysis

Univariable comparisons of the outcomes between the subgroups for individual patient characteristics were conducted using the chi-square test. A logistic regression analysis was performed to analyze the concurrent effects of various factors on the occurrence of postoperative complications, while adjusting for clustering of patients within hospitals using a generalized estimating equation [11]. The threshold for significance was set at $p < 0.05$. All statistical analyses were conducted using IBM SPSS version 19.0 (IBM SPSS, Armonk, NY, USA).

3. Results

The patient background characteristics are shown in **Table 1**. We identified 3255 eligible patients (1740 men and 1515 women; mean age (±standard deviation), 59.5 ± 18.8 years), consisting of 3116 patients with primary malignant limb tumor surgery and 139 patients with primary malignant pelvic tumor surgery. Sixty-three patients were excluded from the logistic regression analysis owing to lack of data about duration of anesthesia. Patients with pelvic tumors were more likely to receive blood transfusion (54.7%) than those with limb tumors (13.8%) ($p < 0.001$). More patients undergoing pelvic tumor surgery required longer duration of anesthesia (>480 min) than patients undergoing limb tumor surgery (34.5% vs 9.1%). The demographic patterns of the tumor sites and surgical procedures are shown in **Table 2**.

The in-hospital mortality and postoperative complications for each category are shown in **Table 3**. In-hospital mortality for pelvic tumor surgery was comparable to that for limb tumor surgery (0.6% vs 0.7%, $p = 0.830$). The incidence of postoperative complications following pelvic tumor surgery was two-fold higher than that following limb tumor surgery. Duration of anesthesia, use of blood transfusion, and volume of blood transfusion were associated with higher in-hospital mortality and postoperative complication rate. Of note, patients who required blood transfusion of more than 2500 ml were more likely to have postoperative complications than those who did not (44.6% vs 6.5%, $p < 0.001$). Similarly, patients with duration of anesthesia over 480 min were more likely to have postoperative complications than those who did not (25.0% vs 6.6%, $p < 0.001$).

Table 4 shows the results of logistic regression analyses for perioperative complications. Pelvic tumor surgery showed no significant differences for postoperative complications compared with primary limb tumor surgery (odds ratio, 0.96; 95% confidence interval, 0.60 - 1.55; $p = 0.869$). A higher complication rate was significantly associated with higher volume of blood transfusion, distant metastasis, and longer duration of anesthesia. In particular, patients with blood transfusion volumes greater than 2,500 ml and those with duration of anesthesia longer than 480 min showed high odds ratios for postoperative complications (≥2500 ml: 3.69; ≥480 min: 6.11).

4. Discussion

In this study, we used a Japanese nationwide inpatient database to compare the in-hospital mortality and postoperative complications of patients who underwent surgery for primary malignant musculoskeletal tumors of the pelvis and limbs. Our results indicate that increased risks in pelvic tumor surgery was largely attributable to major intraoperative bleeding requiring blood transfusion and long operation time requiring long duration of anesthesia.

The occurrence of postoperative complications following pelvic tumor surgery was twice as high as that following limb tumor surgery. Of note, patients who underwent pelvic tumor surgery were six-fold more likely to receive a blood transfusion volume greater than 2500 ml that those who underwent limb surgery. After adjusting for confounding variables, including the volume of blood transfusion, we found that the risk of perioperative complications did not differ between pelvic and limb tumor surgery. Our results indicate that the increased risk for pelvic tumor surgery was largely attributable to major intraoperative bleeding requiring blood transfusion. This finding is consistent with those in previous reports [3] [4], although the referred papers reported only external hemipelvectomy. Our data indicated similar tendency in postoperative complications both in external and

Table 1. Patient background characteristics.

	All		Limb		Pelvis	
	n	(%)	*n*	(%)	*n*	(%)
Total	3255	(100)	3116	(95.7)	139	(4.3)
Sex						
Male	1740	(53.5)	1667	(53.5)	73	(52.5)
Female	1515	(46.5)	1449	(46.5)	66	(47.5)
Age (years)						
≤59	1400	(43.0)	1323	(42.5)	77	(55.4)
60 - 69	749	(23.0)	717	(23.0)	32	(23.0)
70 - 79	713	(21.9)	686	(22.0)	27	(19.4)
≥80	393	(12.1)	390	(12.5)	3	(2.2)
Bone tumor	330	(10.1)	235	(7.5)	95	(68.3)
Soft tissue tumor	2925	(89.9)	2881	(92.5)	44	(31.7)
Prosthetic joint replacement	104	(3.2)	97	(3.1)	7	(5.0)
Free vascularized multi-tissue graft	37	(1.1)	35	(1.1)	2	(1.4)
Preoperative vascular embolization	36	(1.1)	28	(0.9)	8	(0.2)
Distant metastasis	118	(3.6)	115	(3.7)	3	(2.2)
Blood transfusion (ml)						
0	2750	(84.5)	2687	(86.2)	63	(45.3)
1 - 999	312	(9.6)	287	(9.2)	25	(18.0)
1000 - 2499	137	(4.2)	104	(3.3)	33	(23.7)
≥2500	56	(1.7)	38	(1.2)	18	(12.9)
Hemodialysis	20	(0.6)	18	(0.6)	2	(1.4)
Diabetes	248	(7.6)	235	(7.5)	13	(9.4)
Chemotherapy	291	(8.9)	272	(8.7)	19	(13.7)
Duration of anesthesia (min)						
1 - 119	511	(15.7)	502	(15.4)	9	(6.5)
120 - 239	1420	(43.6)	1400	(43.0)	20	(14.4)
240 - 359	622	(19.1)	586	(18.0)	36	(25.9)
360 - 479	295	(9.1)	269	(8.3)	26	(18.7)
≥480	344	(10.6)	296	(9.1)	48	(34.5)
No record	63	(1.9)	63	(1.9)	0	(0.0)
In-hospital death	19	(0.6)	18	(0.6)	1	(0.7)
Postoperative complications	282	(8.7)	256	(8.2)	26	(18.7)
Acute renal failure	3	(1.1)	3	(1.2)	0	(0.0)
Venous thromboembolism	70	(24.8)	64	(25.0)	6	(23.1)
Pneumonia	6	(2.1)	6	(2.3)	0	(0.0)
Surgical site infection	218	(77.3)	197	(77.0)	21	(80.8)
Wound dehiscence	32	(1.0)	28	(0.9)	4	(2.9)

Table 2. Demographic patterns of tumor sites and surgical procedures.

	n	(%)
Total	3255	(100)
Tumor sites		
Soft tissue	2925	(89.9)
Shoulder	137	(4.7)
Upper arm	145	(5.0)
Elbow	30	(1.0)
Forearm	125	(4.3)
Hand	92	(3.1)
Thigh	1030	(35.2)
Knee	72	(2.5)
Inguinal region	62	(2.1)
Buttock	123	(4.2)
Lower leg	247	(8.4)
Foot	55	(1.9)
Other part	807	(28.9)
Bone	330	(10.1)
Pelvis	70	(2.2)
Humerus	58	(1.8)
Hand	11	(0.3)
Femur	136	(4.2)
Tibia	35	(1.1)
Foot	9	(0.3)
Other part	11	(28.9)
Type of surgery		
Amputation	161	(4.9)
Limb salvage surgery	3094	(95.1)
Resection only	2612	(80.2)
Resection + arthroplasty	104	(3.2)
Resection + biological reconstruction	378	(11.6)

internal hemipelvectomy.

Our results indicate that another increased risk in pelvic tumor surgery was largely attributable to long operation time requiring long duration of anesthesia. There are clear associations between longer duration of anesthesia or operation time and postoperative complications in various medical settings [12]-[15]. Shortening of the operation time was also important for musculoskeletal tumor resection. Therefore, to reduce complications after musculoskeletal malignant tumor resection, we should strive to decrease the operation time.

Our study has several limitations inherent to all administrative database studies. First, the DPC database does not provide important clinical data, such as pathological data of each case, tumor volume, individual chemotherapy

Table 3. In-hospital mortality and postoperative complications.

		n	In-hospital mortality, *n* (%)		p	Postoperative complications, *n* (%)		p
All		3255	19	(0.6)		282	(8.7)	
Tumor localization	Limb	3116	18	(0.6)	0.830	256	(8.2)	<0.001
	Pelvis	139	1	(0.7)		26	(18.7)	
Age (years)	≤59	1400	6	(0.4)	0.071	124	(8.9)	0.462
	60 - 69	749	3	(0.4)		62	(8.3)	
	70 - 79	713	4	(0.6)		55	(7.7)	
	≥80	393	6	(1.5)		41	(10.4)	
Sex	Male	1740	13	(0.7)	0.190	156	(9.0)	0.512
	Female	1515	6	(0.4)		126	(8.3)	
Tumor origin	Bone	330	6	(1.8)	0.009	61	(18.5)	<0.001
	Soft tissue	2925	13	(0.4)		221	(7.6)	
Prosthetic joint replacement	No	3151	18	(0.6)	0.461	257	(8.2)	<0.001
	Yes	104	1	(2.8)		25	(24.0)	
Free vascularized multi-tissue graft	No	3218	19	(0.6)	1.000	274	(8.5)	0.012
	Yes	37	0	(0.0)		8	(21.6)	
Preoperative vascular embolization	No	3219	18	(0.6)	0.191	271	(8.4)	<0.001
	Yes	36	1	(2.8)		11	(30.6)	
Distant metastasis	No	3137	16	(0.5)	0.004	261	(8.3)	<0.001
	Yes	118	3	(2.5)		21	(17.8)	
Blood transfusion (ml)	0	2750	7	(0.3)	<0.001	178	(6.5)	<0.001
	1 - 999	128	5	(1.6)		51	(16.3)	
	1000 - 2499	184	3	(2.2)		28	(20.4)	
	≥2500	76	4	(7.1)		25	(44.6)	
Hemodialysis	No	3235	16	(0.5)	<0.001	278	(8.6)	0.071
	Yes	20	3	(15.0)		4	(20.0)	
Diabetes mellitus	No	3007	16	(0.5)	0.178	250	(8.3)	0.014
	Yes	248	3	(1.2)		32	(12.9)	
Chemotherapy	No	2964	16	(0.5)	0.294	229	(7.7)	<0.001
	Yes	291	3	(1.0)		53	(18.2)	
Duration of anesthesia (min)	1 - 119	511	2	(0.4)	0.294	17	(3.3)	<0.001
	120 - 239	1420	4	(0.3)		62	(4.4)	

regimens and dosage of each agent, and details of surgical procedures such as type of pelvic resection or instrumentation used for limb salvage. Second, the DPC database is restricted to information on in-hospital and major complications only and does not provide any information pertaining to those before admission and after discharge. Third, the DPC database provides epidemiological and broad data. Thus, precise and extensive analysis

Table 4. Logistic regression analyses for postoperative complications.

		Postoperative complications		
		OR	95% CI	p
Tumor localization	Limb	Reference		
	Pelvis	0.96	0.60 - 1.55	0.869
Tumor origin	Bone	Reference		
	Soft tissue	1.55	0.55 - 1.15	0.214
Prosthetic joint replacement	No	Reference		
	Yes	1.06	0.58 - 1.943	0.847
Diabetes	No	Reference		
	Yes	1.23	0.79 - 1.91	0.357
Distant metastasis	No	Reference		
	Yes	1.79	1.13 - 2.84	0.013
Blood transfusion (ml)	0	Reference		
	1 - 999	1.57	0.98 - 2.53	0.062
	1000 - 2499	1.54	0.90 - 2.62	0.113
	≥2500	3.69	1.68 - 8.12	0.001
Duration of anesthesia (min)	1 - 119	Reference		
	120 - 239	1.27	0.72 - 2.24	0.415
	240 - 359	2.79	1.55 - 5.00	<0.001
	360 - 479	4.24	2.28 - 7.88	<0.001
	≥480	6.11	3.23 - 11.56	<0.001

is difficult for the DPC database study.

5. Conclusion

Our data demonstrated that a larger blood transfusion volume and longer operative time were significantly associated with worse outcomes. The higher morbidity rate after pelvic tumor resection could result from the larger blood transfusion volume and longer anesthesia duration. We need to decide carefully whether to carry out surgical treatment with consideration of the risk and benefit of each candidate treatment plan, in cases with expectations of larger volume of blood transfusion and longer operative time.

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Competing Interests

The authors declare that they have no competing interests.

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Abbreviation

DPC: Diagnosis Procedure Combination.