Clinical Outcome Differences in the Treatment of Impending Versus Completed Pathological Long-Bone Fractures

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Background: The outcome differences following surgery for an impending versus a completed pathological fracture have not been clearly defined. The purpose of the present study was to assess differences in outcomes following the surgical treatment of impending versus completed pathological fractures in patients with long-bone metastases in terms of (1) 90-day and 1-year survival and (2) intraoperative blood loss, perioperative blood transfusion, anesthesia time, duration of hospitalization, 30-day postoperative systemic complications, and reoperations.

Methods: We retrospectively performed a matched cohort study utilizing a database of 1,064 patients who had undergone operative treatment for 462 impending and 602 completed metastatic long-bone fractures. After matching on 22 variables, including primary tumor, visceral metastases, and surgical treatment, 270 impending pathological fractures were matched to 270 completed pathological fractures. The primary outcome was assessed with the Cox proportional hazard model. The secondary outcomes were assessed with the McNemar test and the Wilcoxon signed-rank test.

Results: The 90-day survival rate did not differ between the groups (HR, 1.13 [95% CI, 0.81 to 1.56]; p = 0.48), but the 1-year survival rate was worse for completed pathological fractures (46% versus 38%) (HR, 1.28 [95% CI, 1.02 to 1.61]; p = 0.03). With regard to secondary outcomes, completed pathological fractures were associated with higher intraoperative estimated blood loss (p = 0.03), a higher rate of perioperative blood transfusions (p = 0.01), longer anesthesia time (p = 0.04), and more reoperations (OR, 2.50 [95% CI, 1.92 to 7.86]; p = 0.03); no differences were found in terms of the rate of 30-day postoperative complications or the duration of hospitalization.

Conclusions: Patients undergoing surgery for impending pathological fractures had lower 1-year mortality rates and better secondary outcomes as compared with patients undergoing surgery for completed pathological fractures when accounting for 22 covariates through propensity matching. Patients with an impending pathological fracture appear to benefit from prophylactic stabilization as stabilizing a completed pathological fracture seems to be associated with increased mortality, blood loss, rate of blood transfusions, duration of surgery, and reoperation risk.

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

Skeletal metastases compromise the structural integrity of involved bone, leading to an increased risk of pathological fracture[1]. Pathological fractures can result in substantial morbidity and loss of quality of life[2-4]. When a metastatic lesion is at risk for fracture, prophylactic stabilization is often advised to avert additional morbidity. Prophylactic surgery may be technically easier and allows for the consideration of multiple surgical options, including those that may not be feasible in cases of completed fractures. It also allows for optimal preoperative work-up and timing with respect to systemic therapy[3]. Finally, it avoids the potential "traumatic" morbidity of a completed fracture, for instance, hematoma formation after a fall.

Previous studies have suggested that prophylactic fixation of an impending pathological fracture is associated with lower levels of postoperative pain, a lower complication rate, faster rehabilitation, and improved survival[5-12]. However, most studies have been limited by small sample sizes or have been

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based on registry data, which often insufficiently control for potential confounders. Propensity score matching is a statistical technique that limits the inherent shortcomings of non-experimental study designs by generating comparable distributions of relevant variables to reduce confounding[13-15].

The purpose of the present study was to assess for differences between surgically treated impending and completed pathological fractures in patients with long-bone metastases with regard to (1) 90-day and 1-year survival rates and (2) intraoperative blood loss, perioperative blood transfusion, anesthesia time, duration of hospitalization, 30-day postoperative systemic complications, and reoperations.

Material and Methods

Study Design and Setting

Our institutional review board approved a waiver of informed consent for this retrospective propensity score matched cohort study. This study was performed at 2 urban tertiary care centers for orthopaedic oncology in the United States.

Study Subjects

We included all 1,064 consecutive adult patients (≥18 years of age) who had undergone surgery between 1999 and 2017 for the treatment of an impending or completed pathological fracture due to long-bone metastasis (Fig. 1)[16]. Exclusion criteria were (1) revision procedures, (2) metastases from sarcoma, (3) pathological fractures in multiple bones requiring simultaneous surgery, and (4) surgery other than intramedullary nailing, dynamic hip screw fixation, plate-screw fixation, endoprosthetic reconstruction, or a combination thereof. Sarcoma was excluded as we considered sarcoma metastasis treatment to be substantially different. Additionally, the large number of sarcomas treated at the included tertiary centers would have limited the generalizability of our findings. If patients required multiple surgical procedures during the study period, only the first procedure was included. Treatment choice was determined by mutual agreement between patient and surgeon. Generally, the Mirels score was used to estimate fracture risk, and prophylactic fixation was recommended for patients with a score of 8 or higher[17]. During the study period,

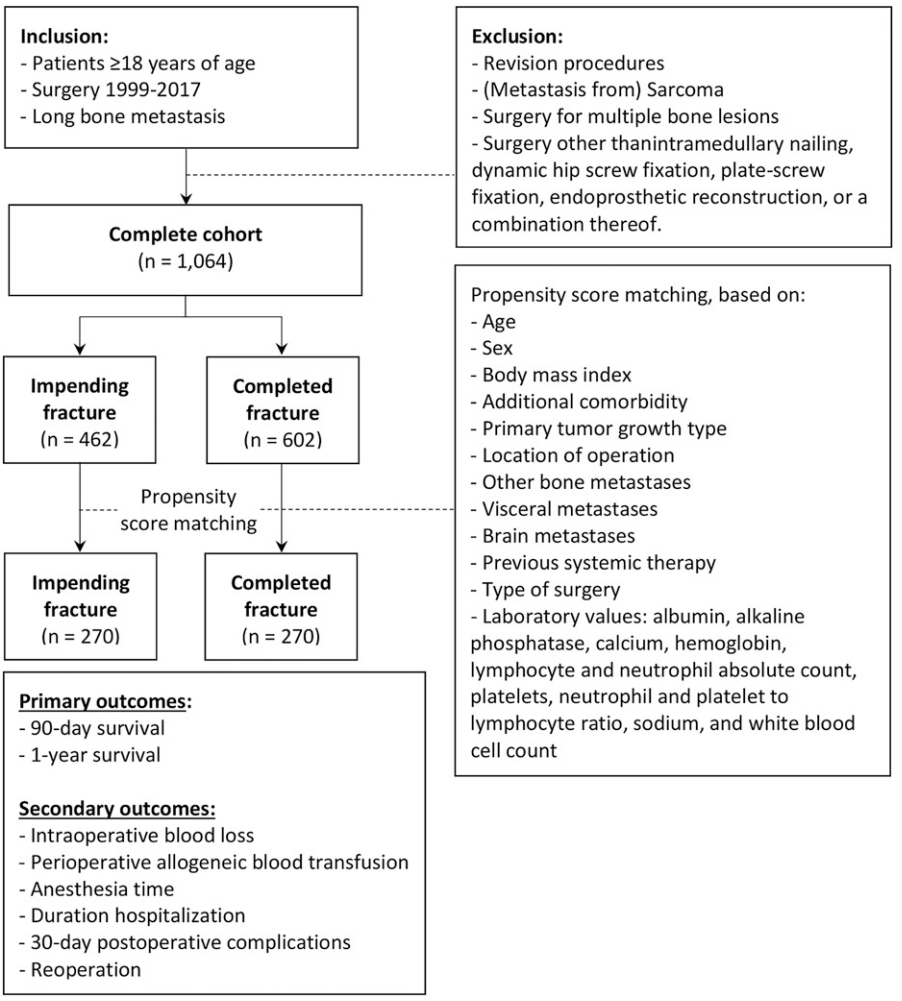

Fig. 1

Flow diagram illustrating the patient selection and matching process.

postoperative care and rehabilitation were tailored to disease severity.

Outcome Measures and Explanatory Variables

The primary outcome measures were 90-day and 1-year survival after surgery. The rate of loss to follow-up was 3% (33 of 1,064) at 90 days and 6% (60 of 1,064) at 1 year. The secondary outcome measures were (1) intraoperative blood loss (liters), (2) perioperative allogeneic blood transfusion (packed red blood cells within 7 days before and after surgery), (3) anesthesia time (hours), (4) duration of hospitalization (days), (5) 30-day systemic postoperative complications, and (6) local reoperation at the surgical site. We considered the following postoperative complications within 30 days: pneumonia, venous thromboembolism, sepsis, myocardial infarction, wound infection and/or dehiscence, and urinary tract infection[18-20].

Factors that are known or have been suggested to be associated with survival were included as explanatory variables[5-8,10-12,21-23]. Medical records were manually reviewed to obtain data on the following variables: age, sex, BMI (body mass index), Charlson comorbidity index, Eastern Cooperative Oncology Group (ECOG) performance score, primary tumor type according to the system of Katagiri et al.[24] (slow, moderate, or rapid growth), tumor location, additional bone metastases, visceral metastases (lung and/or liver), brain metastases, previous systemic therapy, surgical treatment, and 11 preoperative laboratory values (measured at a maximum of 7 days before surgery)[25]. Missing data are displayed in Table I and were imputed with use of single median imputation prior to propensity score matching. The ECOG score was not included in propensity score matching as missing categorical data cannot be imputed with use of median imputation.

Statistical Analysis

Nonparametric testing was used for continuous variables as some variables had skewed distributions. In bivariate analysis before matching, baseline characteristics were compared between patients with impending and completed fractures with use of the Mann-Whitney U test for continuous variables and the Fisher exact test for categorical variables.

Propensity score matching was used to generate comparable cohorts with similar distribution of covariates by matching on variables known to be associated with survival in patients with long-bone metastases[13]. Propensity score matching was conducted with use of a 1-to-1 nearest-neighbor matching in a random order without replacement and with a caliper fixed at 0.005 (maximum allowable difference in propensity scores) based on a propensity score calculated through a logit model including all explanatory variables. Only patients matched with propensity scores were included in the analyses, in which 270 impending fractures were matched to 270 completed fractures. The adequacy of matching was demonstrated by (1) testing the standardized mean differences (SMDs), (2) comparing the matched variables with use of the Wilcoxon signed-rank test for continuous variables and the McNemar test for categorical variables, and (3) a kernel density plot[14]. After propensity score matching, the matched groups did not differ in terms of any of the explanatory variables ($p > 0.05$), and none of the differences were substantial (>0.25) as demonstrated by SMDs (Table I). Kernel density plots demonstrated adequate matching (Fig. 2).

The primary outcome survival was tested between the matched groups using 6 different methods to consolidate the strength of our findings. First, the log-rank test compared the equality of survival curves, stratified by propensity score matched pairs. Second, the McNemar test compared the matched pairs on a dichotomous predictor (impending versus completed fracture) and dichotomous outcome (deceased or not). Third, 4 different Cox proportional hazard models were used: (1) unadjusted, (2) stratified into 5 quintiles according to propensity scores followed by averaging of each quintile stratum, (3) using a robust variance estimator, and (4) weighted by the inverse probability of treatment with use of the propensity score[14,15].

The secondary outcomes were assessed with use of paired tests, specifically, the McNemar test for dichotomous outcomes and the Wilcoxon signed-rank test for continuous data. The level of significance was set at $p < 0.05$ (2-tailed). All statistical analyses were performed with use of Stata 15.0 (StataCorp).

Source of Funding

The authors have no sources of funding to disclose.

Results

Ninety-Day and 1-Year Survival

After propensity score matching, the 90-day survival rate did not differ between completed fractures and impending fractures, with a rate of 71% (193 of 270) for completed fractures and 73% (197 of 270) for impending fractures (hazard ratio [HR] = 1.13 [95% confidence interval (CI) = 0.81 to 1.56]; $p = 0.48$) (Table II). The 1-year survival rate was lower for completed fractures than for impending fractures, with rates of 38% (102 of 270) and 46% (123 of 270), respectively (HR = 1.28 [95% CI = 1.02 to 1.61]; $p = 0.03$) (Fig. 3). Unadjusted, stratified by quintiles, and robust variance estimator Cox hazard models yielded comparable results (see Appendix).

Secondary Outcomes

After propensity score matching, completed pathological fractures were associated with more intraoperative blood loss than impending fractures (median, 0.3 L [interquartile range (IQR) = 0.2 to 0.4] compared 0.2 L [IQR = 0.1 to 0.4]; $p = 0.03$) as well as with more blood transfusions (median, 1 transfusion [IQR = 0 to 2] compared to 0 transfusions [IQR = 0 to 2]; $p = 0.01$), longer anesthesia time (median, 3.1 hours [IQR = 2.5 to 3.6] compared with 2.8 hours [IQR = 2.1 to 3.5]; $p = 0.04$), and a higher rate of reoperations (6.7% [18 of 270] compared with 3.3% [9 of 270]; odds ratio [OR] = 2.50 [95% CI = 1.92 to 7.86]; $p = 0.03$). The groups did not differ in terms of the duration of hospitalization (median, 4 days [IQR = 3 to 7] in both groups; $p = 0.09$) or the 30-day rate of systemic complications 16% [42 of 270] for completed fractures compared with

TABLE I Comparison of Baseline Characteristics Between Impending and Completed Pathological Fracture Before and After Propensity Score Matching*

	Before Propensity Score Matching (N = 1,064)				After Propensity Score Matching (N = 540)			
	Impending (N = 462): Median (IQR)	Completed (N = 602): Median (IQR)	P Value	Std. Diff.	Impending (N = 270): Median (IQR)	Completed (N = 270): Median (IQR)	P Value	Std. Diff.
Age *(yr)*	61 (53-70)	64 (56-72)	**<0.01**	−0.17	63 (54-71)	63 (53-71)	0.95	0.03
Body mass index *(kg/m²)*	27 (23-30)	27 (23-30)	0.94	−0.01	27 (24-29)	27 (24-29)	0.81	0.02
Preoperative laboratory values								
Albumin *(g/dL)*	3.8 (3.3-4.2)	3.6 (3.2-4.0)	**<0.01**	0.26	4.1 (3.6-4.7)	4.0 (3.5-4.7)	0.75	0.04
Alkaline phosphatase *(IU/L)*	99 (73-131)	105 (75-156)	0.06	−0.19	101 (80-121)	101 (87-120)	0.30	−0.04
Calcium *(mg/dL)*	9.2 (8.8-9.7)	9.1 (8.7-9.6)	**0.01**	0.17	9.2 (8.9-9.6)	9.2 (8.9-9.6)	0.99	0.00
Hemoglobin *(g/dL)*	12 (10-13)	11 (10-12)	**<0.01**	0.24	11 (10-13)	11 (10-12)	0.39	0.02
Lymphocyte absolute count *($10^3/\mu L$)*	1.1 (0.7-1.6)	1.0 (0.6-1.5)	**0.02**	0.11	1.0 (0.8-1.3)	1.0 (0.8-1.2)	0.35	0.04
Neutrophil absolute count *($10^3/\mu L$)*	5.0 (3.5-7.3)	5.8 (3.9-8.2)	**<0.01**	−0.25	5.5 (4.1-6.6)	5.5 (4.5-6.9)	0.39	−0.04
Neutrophil to lymphocyte ratio	4.7 (3.0-7.4)	5.7 (3.2-9.8)	**<0.01**	−0.28	5.4 (3.8-6.2)	5.4 (4.2-6.7)	0.60	−0.04
Platelet count *($10^3/\mu L$)*	259 (199-343)	241 (174-322)	**<0.01**	0.20	251 (204-308)	251 (199-332)	0.46	−0.07
Platelet to lymphocyte ratio	230 (158-370)	239 (160-383)	0.31	−0.10	250 (179-320)	250 (186-344)	0.38	−0.05
Sodium *(mg/dL)*	138 (136-140)	138 (135-140)	**0.01**	0.20	138 (137-139)	138 (136-139)	0.26	0.08
White blood-cell count *($10^3/\mu L$)*	7.2 (5.1-9.5)	7.5 (5.2-10)	0.11	−0.11	7.3 (5.6-9.4)	7.3 (5.6-9.7)	0.76	−0.02
	No. of Patients	No. of Patients			No. of Patients	No. of Patients		
Female	262 (57%)	333 (55%)	0.66	−0.03	158 (59%)	161 (60%)	0.79	0.02
Additional comorbidity†	245 (53%)	331 (55%)	0.54	−0.04	149 (55%)	144 (53%)	0.67	0.04
ECOG performance score			0.55	0.05			0.93	−0.13
0-2	356 (89%)	454 (87%)			201 (86%)	209 (87%)		
3-4	45 (11%)	66 (13%)			32 (14%)	32 (13%)		
Primary tumor growth‡			**0.01**	0.18			0.24	−0.11
Slow	174 (38%)	280 (47%)			118 (44%)	107 (40%)		
Moderate	112 (24%)	134 (22%)			64 (24%)	60 (22%)		
Rapid	176 (38%)	188 (31%)			88 (33%)	103 (38%)		
Tumor location			**<0.01**	0.57			0.99	0.00
Upper extremity	49 (11%)	201 (33%)			47 (17%)	47 (17%)		
Lower extremity	413 (89%)	401 (67%)			223 (83%)	223 (83%)		
Other bone metastases§	355 (77%)	466 (77%)	0.83	−0.01	212 (79%)	216 (80%)	0.68	−0.04
Visceral metastases	217 (47%)	258 (43%)	0.19	0.08	120 (44%)	134 (50%)	0.25	−0.10
Brain metastases	89 (19%)	82 (14%)	**0.02**	0.15	48 (18%)	48 (18%)	1.00	0.00
Previous systemic therapy	289 (63%)	372 (62%)	0.85	0.02	175 (65%)	179 (66%)	0.72	−0.03
Type of surgery			**<0.01**	−0.38			0.99	0.24
Intramedullary nail	355 (77%)	269 (45%)			168 (62%)	169 (63%)		
Endoprosthetic reconstruction	37 (8.0%)	203 (34%)			36 (13%)	73 (27%)		
Plate and screw fixation	46 (10%)	107 (18%)			45 (17%)	23 (8.5%)		
Dynamic hip screw	10 (2.2%)	9 (1.5%)			9 (3.3%)	1 (0.4%)		
Multiple implants	14 (3.0%)	14 (2.3%)			12 (4.4%)	4 (1.5%)		

*IQR = interquartile range, Std. Diff. = standardized difference, ECOG = Eastern Cooperative Oncology Group. Bold indicates significance ($p < 0.05$). Patient data were available for the impending and completed pathological fracture groups, respectively, as follows: BMI, 375 (81%) and 458 (76%); albumin, 313 (68%) and 441 (73%); alkaline phosphatase, 317 (69%) and 439 (73%); calcium, 370 (80%) and 498 (83%); hemoglobin, 392 (85%) and 529 (88%); lymphocyte absolute count, 318 (69%) and 428 (71%); neutrophil absolute count, 322 (70%) and 428 (71%); neutrophil to lymphocyte ratio, 318 (69%) and 428 (71%); platelet count, 393 (85%) and 528 (88%); platelet to lymphocyte ratio, 318 (69%) and 427 (71%); sodium, 365 (79%) and 504 (84%); white blood-cell count, 392 (85%) and 529 (88%); and ECOG, 401 (87%) and 520 (86%). ECOG was available after propensity matching in 233 (86%) patients with impending fractures and 241 (89%) patients with completed pathological fractures. †These values were based on any additional comorbidity on top of the metastatic disease score according to the modified Charlson comorbidity index. ‡Based on histology groupings; slow growth includes hormone-dependent breast cancer, hormone-dependent prostate cancer, malignant lymphoma, malignant myeloma, and thyroid cancer; moderate growth includes non-small-cell lung cancer with molecularly targeted therapy, hormone-independent breast cancer, hormone-independent prostate cancer, renal cell carcinoma, sarcoma, other gynecological cancer, and others; and rapid growth includes other lung cancer, colon and rectal cancer, gastric cancer, hepatocellular carcinoma, pancreatic cancer, head and neck cancer, other urological cancer, esophageal cancer, malignant melanoma, gallbladder cancer, cervical cancer, and unknown origin. When testing primary tumor type distribution after propensity score matching, we found no difference between groups ($p = 0.59$). §Any bone metastasis outside of the lesion treated.

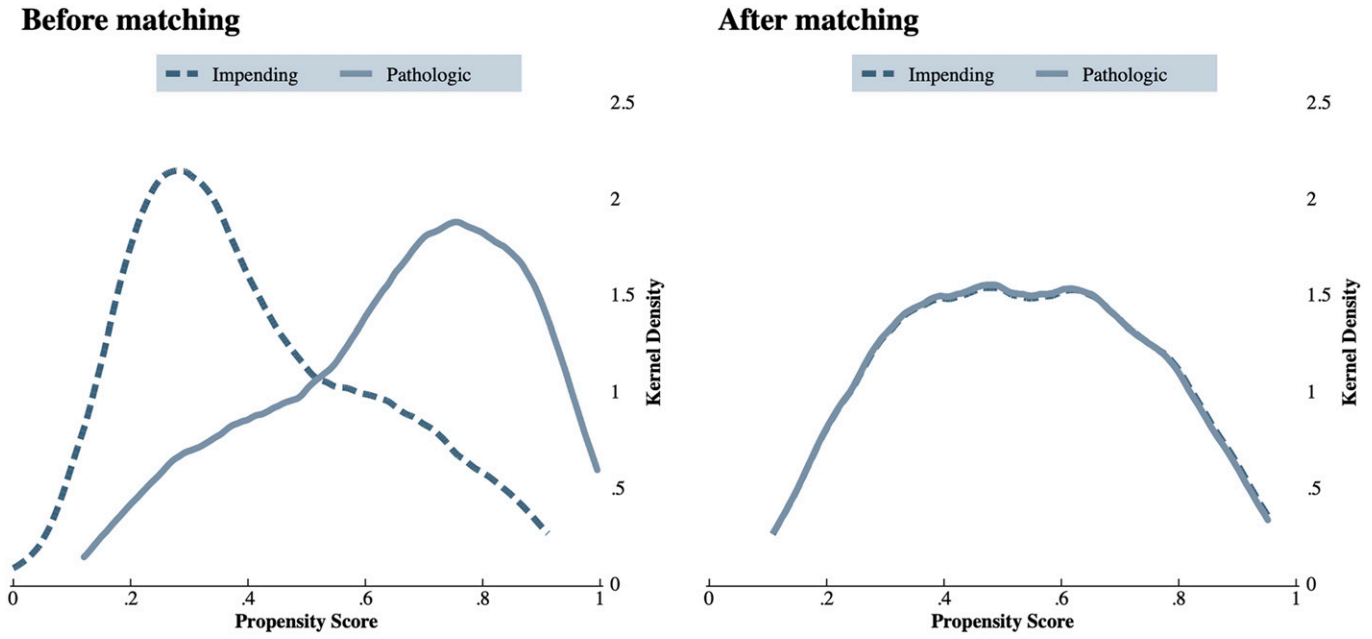

Fig. 2

Kernel density plots showing the distribution of the propensity score before and after matching, demonstrating the adequateness of propensity score matching.

TABLE II Comparison of Primary and Secondary Outcomes in Patients with Impending and Completed Pathological Fractures Before and After Propensity Score Matching*

	Before Propensity Score Matching (N = 1,064)					After Propensity Score Matching (N = 540)				
	Impending (N = 462)	Completed (N = 602)	HR (95% CI) for Completed Fractures	Standard Error	P Value	Impending (N = 270)	Completed (N = 270)	HR (95% CI)† for Completed Fractures	Standard Error	P Value
	No. of Patients					No. of Patients				
Survival†										
90 days	341 (74%)	424 (70%)	1.17 (0.93-1.48)	0.139	0.17	197 (73%)	193 (71%)	1.13 (0.81-1.56)	0.188	0.48
1 year	202 (44%)	236 (39%)	1.16 (0.99-1.36)	0.094	0.07	123 (46%)	102 (38%)	1.28 (1.02-1.61)	0.148	**0.03**
	Median (IQR) or No. of Patients		OR (95% CI)			Median (IQR) or No. of Patients		OR (95% CI)		
Intraoperative blood loss† *(L)*	0.2 (0.1-0.3)	0.3 (0.2-0.5)	—	—	**<0.01**	0.2 (0.1-0.4)	0.3 (0.2-0.4)	—	—	**0.03**
Perioperative allogeneic blood transfusion	0 (0-2)	1 (0-3)	—	—	**<0.01**	0 (0-2)	1 (0-2)	—	—	**0.01**
Anesthesia time† *(hr)*	2.8 (2.2-3.5)	3.1 (2.5-3.8)	—	—	**<0.01**	2.8 (2.1-3.5)	3.1 (2.5-3.6)	—	—	**0.04**
Duration of hospitalization† *(day)*	4 (3-6)	5 (3-7)	—	—	**<0.01**	4 (3-7)	4 (3-7)	—	—	0.09
Systemic postoperative complications within 30 days	66 (14%)	83 (14%)	0.96 (0.68-1.36)	0.171	0.82	38 (14%)	42 (16%)	1.12 (0.69-1.83)	—	0.64
Reoperations	16 (3.5%)	44 (7.3%)	2.20 (1.22-3.95)	0.657	**0.01**	9 (3.3%)	18 (6.7%)	2.50 (1.92-7.86)	—	**0.03**

*IQR = interquartile range, Std. Diff. = standardized difference, CI = confidence interval, HR = hazard ratio, OR = odds ratio. Bold indicates significance ($p < 0.05$). †The presented hazard ratios after matching are based on the Cox proportional hazard model weighted by inverse probability of treatment weighting (IPT) using the propensity score. Additional survival analyses can be found in the Appendix. ‡Patient data before propensity score matching were available for the impending and completed fracture groups, respectively, as follows: 90-day survival, 447 (97%) and 584 (97%); 1-year survival, 436 (94%) and 568 (94%); intraoperative blood loss, 408 (88%) and 517 (86%); anesthesia time, 365 (79%) and 493 (82%); and hospitalization, 456 (99%) and 585 (97%). Patient data after propensity score matching were available for the impending and completed fracture groups, respectively, as follows: 90-day survival, 262 (97%) and 262 (97%); 1-year survival, 256 (95%) and 253 (94%); intraoperative blood loss, 233 (86%) and 238 (88%); anesthesia time, 210 (78%) and 222 (82%); and hospitalization, 267 (99%) and 261 (97%). Both outcomes in matched pairs were available for the following: estimated blood loss, 203 (75%); anesthesia time, 175 (65%); and hospitalization, 258 (96%).

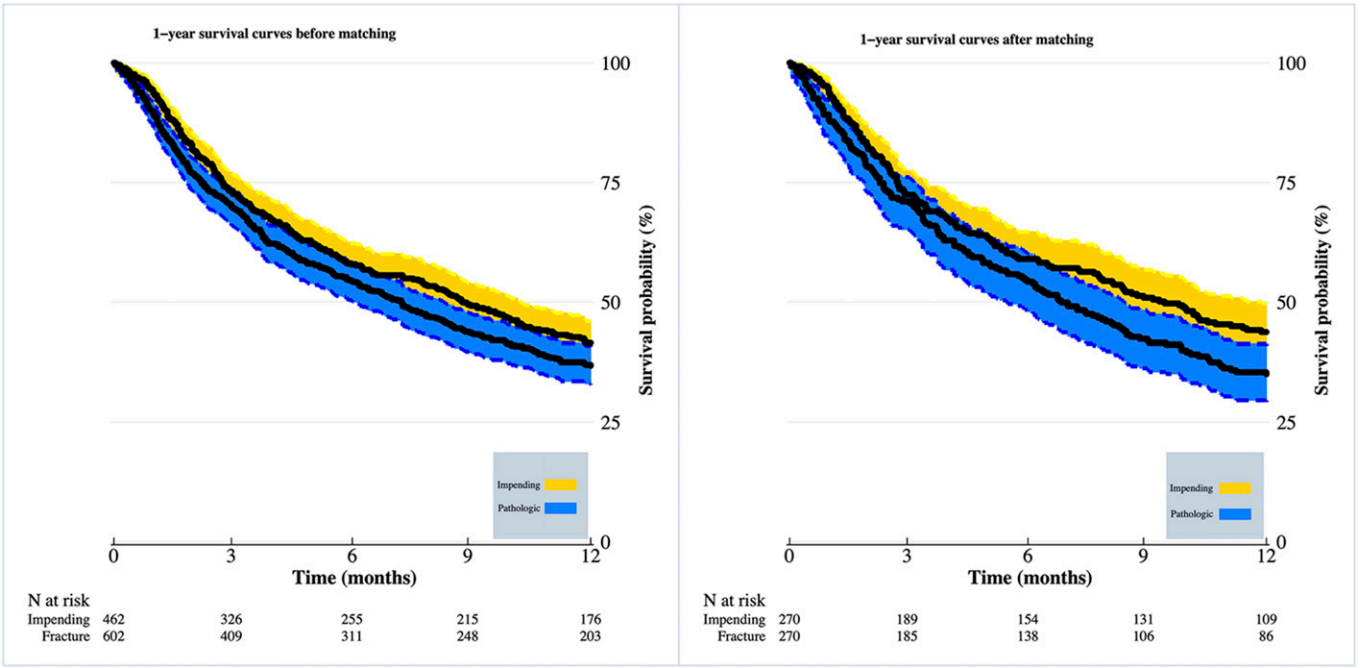

Fig. 3

Kaplan-Meier survival curves with 95% CIs for patients with impending and completed pathological fracture before and after propensity score matching.

(14% [38 of 270] for impending fractures; OR = 1.12 [95% CI = 0.69 to 1.83]; p = 0.64).

Discussion

Metastatic bone disease can lead to pain, disability, and risk of development of a pathological fracture, which is associated with further deterioration in quality of life and possibly a worse prognosis. Several studies have suggested improved outcome after prophylactic fixation of an impending fracture as compared with an acute pathological fracture; however, those studies were limited by small sample sizes or were based on registry data with insufficient controlling for confounding[5-12]. Our relatively large study, in which propensity score matching was used to create comparable cohorts across 22 explanatory variables, showed that patients who underwent surgery for an impending pathological fracture had better 1-year survival, less intraoperative blood loss, fewer perioperative blood transfusions, shorter anesthesia time, and fewer reoperations in comparison with patients who underwent surgery for a completed pathological fracture. No differences between the 2 groups were found in terms of 90-day survival, 30-day systemic postoperative complications, or the length of hospitalization.

Primary Outcome

The 90-day survival rate did not differ between the impending and completed fracture groups in the present study. Two previous studies—both of which used the same U.S.-based registry (National Surgical Quality Improvement Program [NSQIP]) during the same time period—also showed no difference in terms of 30-day survival among 1,317 patients with long bone metastases (OR = 2.38 [95% CI = 0.88 to 6.25]; p = 0.09) or 620 patients with femoral metastases (OR = 1.71 [95% CI = 0.95 to 3.09]; p = 0.07) (see Appendix)[7,8].

In the present study, long-term (1-year) survival was 8% better for patients who underwent prophylactic stabilization compared with those who underwent acute stabilization of a pathological fracture. Ward et al. found a similar difference in a single-institution cohort of 182 patients (1-year survival rate, 35% for impending fractures compared with 25% for completed fractures, p = 0.02) but did not control for confounding factors[12]. In addition, 3 other registry-based studies demonstrated improved long-term survival for impending femoral fractures as compared with completed femoral fractures[6,10,11].

Overall, long-term survival is generally poor for patients who undergo surgery for the treatment of metastatic bone disease, regardless of whether the surgery is prophylactic or for an acute pathological fracture. However, our results, supported by those of previous studies, suggested that there is no difference in survival in the short term but that patients with a completed fracture have worse survival over the long term. This finding might be related to the perioperative time frame, which may be pivotal in determining long-term cancer outcomes, or to the functional disabilities and the period of immobilization following a completed fracture[1,26].

Secondary Outcomes

Our finding that prophylactic fixation was associated with lower rates of perioperative blood loss and less blood transfusions is in

line with all 3 previous studies related to this topic. Both McLynn et al. and Aneja et al., in registry-based studies of 620 and 5,579 patients with femoral metastases, reported a similarly decreased risk of blood transfusion among patients with impending fractures (OR = 0.62 [95% CI = 0.38 to 0.89]; p = 0.01] and OR = 0.74 [95% CI = 0.65 to 0.84]; p < 0.01])[5,7]. Ward et al. investigated intraoperative blood loss in a study of 182 patients and reported less average blood loss among those who underwent prophylactic surgery in comparison with those who sustained a completed fracture (438 vs. 636 cc; p = 0.01)[12]. Increased transfusions have been reported to have an immunosuppressive effect, which in turn might lead to worse survival[18]. This immunosuppressive effect offers another possible explanation as to why patients who were treated for a completed fracture had decreased 1-year survival compared with patients treated for an impending fracture[26].

Anesthesia time was shorter for patients with impending fractures. Arvinius et al. reported similar results, although they included only 65 patients and did not account for confounding factors (23 minutes [impending] vs. 48 minutes [completed]; p = 0.003)[10]. However, McLynn et al., in a registry-based study of 620 femoral metastases, did not report a difference in surgery time (OR = 1.31 [95% CI = 0.90 to 1.90]; p = 0.16)[7].

We found no difference between the groups in terms of the duration of hospitalization. Multiple studies have investigated the duration of hospitalization, with the majority suggesting a shorter hospital stay in association with impending factures[7,8,10-12]. For example, El Abiad et al., in a registry-based study of 1,317 patients, found that those with impending fractures had a shorter hospital stay than those with completed fractures (mean, 6.9 vs. 8.2 days; p = 0.01)[8]. Earlier mobilization after prophylactic stabilization and greater likelihood of being discharged to home may explain the shorter hospital stay in association with impending fractures.

In the present study, the rate of systemic complications within 30 days postoperatively did not differ between the groups. Prior studies have shown mixed findings; however, the majority have suggested a higher complication rate after prophylactic surgery[5,7,8,10,11]. For instance, El Abiad et al. found that prophylactic fixation was associated with a lower risk of major medical complications within 30 days after controlling for age, BMI, and disseminated cancer (OR = 0.64 [95% CI = 0.45 to 0.93]; p = 0.02)[8]. However, the studies that suggested a difference in complication rates involved the use of mostly registry-based databases and are subject to coding bias because complications are frequently miscoded by physicians[27].

Last, we found a lower rate of reoperation among patients who were treated for an impending fracture. Only El Abiad et al. reported on reoperation rates within 30 days after surgery. Although those authors used registry data and controlled only for age, BMI, and disseminated cancer, their results trended toward a similar difference (OR = 0.65 [95% CI = 0.42 to 1.01]; p = 0.06)[8]. These findings may suggest that prophylactic surgical constructs are more stable (and less prone to fail) because of the presence of relatively healthier local bone in comparison with those in patients with completed fractures. Additionally, the operative treatment of a completed fracture is considered to be more complex because of the need for fracture reduction and reconstruction and the possibility of more soft-tissue damage, which contribute to impaired surgical constructs compared with prophylactic surgery.

Implications for Practice

Correct and timely identification of metastatic bone lesions that are at risk for the development of a completed pathological fracture, and substantial morbidity, is essential for physicians who provide oncological care, including radiation oncologists, orthopaedic oncologists, and medical oncologists. Accurate identification creates opportunity for prophylactic surgical stabilization, which seems to result in improved clinical outcomes. Additionally, the limited survival of patients with metastatic bone disease must be considered when contemplating surgical stabilization in order to allow physicians and patients to make informed treatment decisions in line with their goals and expectations. Therefore, it is fundamental to correctly identify which lesions are causing disability and are at risk for fracture in order to prevent unnecessary surgical intervention. Currently available predictive models for fractures are limited by their inaccuracies and difficulty in use. The Mirels score has been shown to lack sufficient sensitivity and specificity and to have moderate interobserver agreement[17,28]. Computed tomography-based predictive algorithms have shown promising results, but clinical application might be limited because of selection bias and difficulty in use[29,30]. Future research should aim to develop an accessible, practical, and accurate prediction tool that identifies patients who are at risk for developing a completed fracture and could benefit from prophylactic surgery.

Limitations

The present study had a number of limitations. First, this was a retrospective study from medical centers affiliated with 1 healthcare entity, causing the inevitable risk of selection and confounding bias. To correct for such bias, propensity-matching analysis was used. An experimental study design—such as a randomized controlled trial—is not possible and is considered to be unethical for the clinical question being investigated. Second, quality-of-life outcomes were not recorded during standard case visits; such information would have been a valuable addition to this study of a frail patient population. Third, estimated blood loss was based on surgeon and anesthesia reports, whereas measuring hemoglobin balance is a more accurate method. However, complete data to calculate hemoglobin-based blood loss (height, weight, and preoperative and postoperative hemoglobin) were available for only 31% of the cohort (325 of 1,064). When analyzing these data, we found a similar significant difference in terms of increased blood loss for completed pathological fractures compared with impending fractures (before and after propensity score matching; data not shown). Fourth, we were unable to account for patients who initially abstained

from prophylactic surgery due to compelling factors as this information was not documented uniformly. Fifth, propensity matching on specific systemic therapy data and postoperative strategies is limited by diverse regimens and their change over time. Sixth, a recent study demonstrated an association between higher C-reactive protein and lower 1-year survival, indicating a potentially important confounder[31]. Unfortunately, we were unable to include this covariate in our propensity score matching model because of insufficient data. Last, we were unable to account for the ECOG score in propensity score matching as median imputation is not possible with categorical variables. However, we compared the ECOG score in both the unmatched and matched groups, and there were no differences.

Conclusions

This retrospective propensity score matched study of patients with a metastatic long bone lesion showed that those who were treated for an impending pathological fracture had better 1-year survival, less intraoperative blood loss, fewer perioperative blood transfusions, shorter anesthesia time, and fewer reoperations than those who were treated for a completed pathological fracture. Choosing the optimal candidate for prophylactic surgery remains paramount to avoid overtreatment. The advancement of clinical oncological care will benefit from an accurate, validated, and practical prediction tool which identifies patients with a metastatic bone lesion at risk for developing a completed pathological fracture.

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/G817). ■

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