Research Paper

Quantitative preoperative patient assessments are related to survival and procedure outcome for osseous metastases

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Aims: Our objective was to determine if preoperative patient-reported assessments are associated with survival after surgery for stabilization of skeletal metastases.

Patients and Methods: All patients with metastatic cancer to bone and indications for skeletal stabilization surgery were approached to participate in a prospective cohort study at a tertiary care center from 2012 to 2017. Of the 208 patients who were eligible, 195 (94%) completed the 36-item Short Form Health Survey (SF-36) preoperatively and underwent surgical treatment of skeletal metastases with complete or impending fractures; the sample encompassed a range of cancer diagnoses and included cases of both internal fixation and endoprosthetic replacement. Cox proportional hazards models were used to identify associations between SF-36 scores and survival.

Results: In a model adjusted for clinical factors, patients’ mental and physical SF-36 component summary scores were significantly associated with survival, as was their SF-36 composite score (P = 0.004, P = 0.015, and P < 0.001, respectively). Scores in the general health, vitality, and mental health domains were each strongly associated with survival (P < 0.001).

Conclusions: Patients’ preoperative assessments of their health status are associated with their survival after surgery for skeletal metastases. Patient-reported assessments have the potential to contribute unique information to models that estimate patient survival, as part of efforts to provide optimal, individualized care and make informed decisions about the type and magnitude of surgery for metastatic bone disease that will last the patient’s lifetime.

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ABSTRACT

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1. Introduction

Accurate survival estimates are an important part of surgical decision making for patients with metastatic bone disease. These predictions allow surgeons to choose the most appropriate method of treatment [1–3]. In general, patients with shorter estimated survival may have the greatest net benefit from a less invasive procedure with faster postoperative recovery. However, those with longer estimated survival need a more durable bone reconstruction that would be worth the investment in a more invasive procedure with a longer rehabilitation period. The ability to predict patient survival objectively allows the surgeon to individualize the management of each patient and to avoid under- or overtreatment. This study evaluates the relationship between preoperative patient assessments of their health-related quality of life and their postoperative survival.

We have previously investigated the accuracy of a clinical decision support tool in estimating survival for patients with metastatic bone disease after surgical intervention [2,4–7]. The tool utilizes Bayesian clinical, pathological, and laboratory data to model survival after operative intervention for skeletal metastases. Model inputs include age, sex, oncologic diagnosis, presence of a completed pathologic fracture, Eastern Cooperative Oncology Group (ECOG) performance status,
hemoglobin concentration, absolute lymphocyte count, number of skeletal meatuses, presence of organ metastases, presence of lymph node metastases, and the physician’s estimate of survival. This model, available online (pathfx.org), has been validated both internally and externally in large international cohorts, and was recently updated and shown to have favorable accuracy and discriminatory ability. To keep this decision tool contemporary and accurate, we continuously seek to improve it.

Although they are not currently part of the decision tool, patient-reported outcomes (PROs) have been shown to be of prognostic value in estimating mortality in several oncologic diseases, including breast cancer, multiple myeloma, colorectal cancer, and lung cancer [8–11]. Notably, patient-reported health and quality-of-life (QOL) assessments have not yet been evaluated for associations with postoperative survival for patients with skeletal metastases [12–16].

Medical training emphasizes that physicians should listen to their patients [17]. In this light, we hypothesized that patients’ preoperative perceptions of their own health status—as assessed by the 36-item Short Form Health Survey (SF-36)—would be associated with postoperative survival and provide important insight into their condition. Such patient-reported assessments could supplement standard disease-related information, imaging characteristics, and laboratory data in clinical decision making for patients with metastatic bone disease.

2. Patients and methods

2.1. Study design and participants

All patients indicated for operative fixation of skeletal metastases at a tertiary comprehensive cancer center from June 2012 to September 2017 were screened for entry into a prospective cohort study on improving survival estimates. Patients were eligible for the study if they were ≥18 years old, proficient in English, had a diagnosis of metastatic malignancy with either histologically proven skeletal metastasis in oligometastatic disease or clinical suspicion in widely metastatic disease, and were intending to undergo an operative orthopaedic intervention for skeletal metastases. Patients who experienced more than one skeletal event were enrolled for their first operatively treated fracture only. Approval was granted by the center’s institutional review board (IRB #11–121).

Of the 849 patients who were screened for eligibility, 649 did not meet the inclusion criteria or declined to participate in the study (often due to a desire not to know their estimated survival, which was shared with patients), leaving 208 patients who consented to participate. Thirteen were subsequently excluded because they did not complete the required questionnaires, yielding a final sample of 195 patients (Fig. 1). Enrolled patients were asked to complete licensed SF-36 questionnaires (version 2; RAND, Santa Monica, CA, USA) preoperatively within two weeks of their surgical procedure. The SF-36 is a validated patient-reported assessment, available in many languages, that measures health in eight domains, including physical functioning, body pain, vitality and social functioning. The domain scores can be combined into a physical component summary (PCS) score and a mental component summary (MCS) score. Additionally, we calculated a SF-36 composite score representing the arithmetic average of the eight domain scores [18].

Patients with a wide range of tumor locations and surgical procedures were enrolled to allow the results to be generalized to the spectrum of patients needing surgery for metastatic bone disease. Interventions included, but were not limited to, resection, curettage and cementation, internal fixation, arthroplasty, and decompression and instrumented fusion in the spine. Surgery was performed for both impending and completed fractures. All procedures were performed by fellowship-trained musculoskeletal oncologic surgeons, and were chosen at the surgeons’ discretion based on preoperative clinicopathologic data and clinical acumen and without knowledge of the patients’ SF-36 results.

Subjects were followed postoperatively for up to four years or until death. Deaths were tracked using a combination of automatic notifications from our hospital and calls to the patient’s home and/or next-of-kin in cases when a patient missed an expected postoperative visit. Data were collected prospectively during hospital stays and clinic visits using the patients’ electronic medical record and included information on age, sex, primary cancer diagnosis, ECOG score, pathologic fracture type (impending or completed), procedure type (endoprosthetic reconstruction, internal fixation, or resection alone), and postoperative survival.

2.2. Statistical analysis

We calculated descriptive statistics on patients’ demographic and clinical characteristics and SF-36 scores. Kaplan-Meier methods were used to estimate overall survival from surgery. The association between baseline SF-36 scores and overall survival was assessed using separate Cox proportional hazards models for each scale. In order to assess whether any association between baseline SF-36 scores and overall survival is independent of known potential confounding variables, the models were adjusted for primary cancer diagnosis (breast cancer, lung cancer, renal cancer, other), ECOG score (0–3), number of bone metastases (1, 2 +), presence of visceral metastases (yes/no), and hemoglobin level (g/dL), all of which are first-order predictors of survival in the PathFx system [2,4]. Model results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). A P value of 0.05 was considered statistically significant. All analyses were conducted in SAS v9.4 (Cary, NC, USA).

3. Results

Patients’ median age at baseline was 62 years (standard deviation = 12.4 years) (Table 1). Of the 195 patients, 117 (60 %) were female and 78 (40 %) were male. There were diverse primary cancer diagnoses, with the most prevalent being lung cancer (n = 46; 24 %) and breast cancer (n = 39; 20 %). Eighty patients (41 %) had completed fractures, while 115 (59 %) had impending fractures. Internal fixation was utilized in 40% of cases (n = 78), endoprosthetic replacement in 58 % (n = 113), and resection in only 2 % (n = 4). Anatomic locations treated included: femur (n = 110; 56 %), humerus (n = 39; 20 %), pelvis (n = 28; 14 %), tibia (n = 8; 4%), scapula (n = 4; 2 %), spine (n = 2; 1 %), calcaneus (n = 1; <1%), clavicle (n = 1; <1%), radius (n = 1; <1%), and ulna (n = 1; <1%). In cases of tumor involving more than one bone and treated with the same procedure, the more dominant lesion was recorded (e.g., pelvis for Harrington procedures, femur for proximal femoral replacement with total hip arthroplasty). The median duration of follow-up among patients who did not die was 10.6 months (interquartile range 2.5, 18.0). There were 131 deaths; median survival for the sample was 11.2 months (95% CI 7.8, 14.3) (Fig. 2). Mean SF-36 domain, MCS, PCS, and composite scores are shown in Table 2.

In adjusted multivariable models, three of the eight SF-36 domains were associated with overall survival: general health (HR 0.64; CI 0.53–0.78; P < 0.001), vitality (HR 0.69; CI 0.56–0.85; P < 0.001), and mental health (HR 0.77; CI 0.65–0.90; P = 0.001) (Table 3). Moreover,
MCS and PCS scores were significantly associated with overall survival (HR 0.81; CI 0.69–0.93; P = 0.004 and HR 0.80; CI 0.66–0.96; P = 0.015, respectively), as was the overall SF-36 composite score (HR 0.63; CI 0.49–0.82; P < 0.001).

4. Discussion

This study demonstrates that patients’ preoperative assessment of their health status reflects their survival following surgery for skeletal metastases. We found that in adjusted multivariable models, a patient’s PCS score, MCS score, and composite SF-36 score were all associated with overall survival. Our data suggest that preoperative patient-reported assessments may prove to be a useful tool for surgeons when planning the most appropriate procedure for each patient.

In cases where both less and more invasive options exist, patient-reported assessments can guide the surgeon away from an extensive procedure with a long rehabilitation period if the patient is unlikely to experience additional benefit (compared to a less extensive option) because his or her projected long-term survival is poor. In this way, surgeons can avoid overtreatment for some patients. Conversely, when a patient is likely to have prolonged survival, surgeons can be guided toward a more durable procedure, even if it requires additional investment in recovery. In a cohort of patients with metastatic disease to long bones treated with intramedullary nails, Miller et al. demonstrated construct failures were most coincident with length of survival.[19] This work suggests that patients with longer estimated survival may need

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**Table 1**

Baseline characteristics of patients included in SF-36 score calculations.

| Characteristic                | N (%)         |
|------------------------------|---------------|
| Mean age in years (SD)       | 62 (12.4)     |
| Age (years)                  |               |
| <65                          | 104 (53.3)    |
| ≥65                          | 91 (46.7)     |
| Sex                          |               |
| Female                       | 117 (60.0)    |
| Male                         | 78 (40.0)     |
| Cancer diagnosis             |               |
| Bladder                      | 5 (2.6)       |
| Breast                       | 39 (20.0)     |
| Colorectal                   | 4 (2.1)       |
| Liver                        | 2 (1.0)       |
| Lung                         | 46 (23.6)     |
| Lymphoma                     | 1 (0.5)       |
| Melanoma                     | 7 (3.6)       |
| Myeloma                      | 7 (3.6)       |
| Nasopharyngeal               | 2 (1.0)       |
| Prostate                     | 12 (6.2)      |
| Renal                        | 38 (19.5)     |
| Thyroid                      | 8 (4.1)       |
| Other                        | 24 (12.3)     |
| ECOG grade                   |               |
| 0–2                          | 127 (65.1)    |
| 3–4                          | 68 (34.9)     |
| Nodal metastases             |               |
| No                           | 84 (43.1)     |
| Yes                          | 111 (56.9)    |
| Visceral metastases          |               |
| No                           | 65 (33.3)     |
| Yes                          | 130 (66.7)    |
| Number of bone metastases    |               |
| 1                            | 53 (27.2)     |
| ≥2                           | 142 (72.8)    |
| History of systemic chemotherapy |           |
| No                           | 79 (40.5)     |
| Yes                          | 116 (59.5)    |
| Pathologic fracture          |               |
| Completed                    | 80 (41.0)     |
| Impending                    | 115 (59.0)    |
| Procedure type               |               |
| Endoprosthesis               | 113 (57.9)    |
| ORIF                         | 78 (40.0)     |
| Resection only               | 4 (2.1)       |
| Median hemoglobin level in g/dL (range) | 10.7 (5.4, 17.0) |
| Vital status                 |               |
| Alive                        | 64 (32.8)     |
| Dead                         | 131 (67.2)    |

SD, standard deviation; ECOG, Eastern Cooperative Oncology Group; ORIF, open reduction with internal fixation.

**Table 2**

Mean baseline SF-36 domain, summary, and composite scores.

| SF-36 Outcome   | Mean (SD) |
|-----------------|-----------|
| **Domains**     |           |
| Physical function | 27.1 (12.12) |
| Role-physical   | 27.8 (10.00) |
| Body pain       | 32.5 (9.77)  |
| General health  | 37.9 (9.41)  |
| Vitality        | 42.5 (9.99)  |
| Social functioning | 35.0 (12.68) |
| Role-emotional  | 36.6 (16.33) |
| Mental health   | 43.5 (11.11) |
| **Summary/composite measures** | | |
| PCS             | 25.9 (10.99) |
| MCS             | 45.1 (12.77) |
| Composite       | 35.4 (8.19)  |

SD, standard deviation; PCS, physical component summary; MCS, mental component summary.

**Table 3**

Adjusted hazard ratios from models assessing associations of baseline SF-36 domain scores, summary scores, and composite score with survival. General health, vitality, and mental health scores, PCS and MCS scores, and the overall composite score were all associated with survival.

| SF-36 outcome | Adjusted hazard ratio (95 % CI)* | P value |
|---------------|----------------------------------|---------|
| **Domains**   |                                  |         |
| Physical function | 0.88 (0.75, 1.03) | 0.102   |
| Role-physical | 0.84 (0.69, 1.02)      | 0.073   |
| Body pain     | 0.90 (0.74, 1.08)      | 0.249   |
| General health | 0.64 (0.53, 0.78)      | <0.001  |
| Vitality      | 0.69 (0.56, 0.85)      | <0.001  |
| Social functioning | 0.88 (0.76, 1.02) | 0.098   |
| Role-emotional | 0.90 (0.80, 1.01) | 0.065   |
| Mental health | 0.77 (0.65, 0.90)      | 0.001   |
| **Summary measures** |               |         |
| PCS           | 0.80 (0.66, 0.96)      | 0.015   |
| MCS           | 0.81 (0.69, 0.93)      | 0.004   |
| Composite     | 0.63 (0.49, 0.82)      | <0.001  |

SD, standard deviation; PCS, physical component summary; MCS, mental component summary.

MCS and PCS scores were significantly associated with overall survival (HR 0.81; CI 0.69–0.93; P = 0.004 and HR 0.80; CI 0.66–0.96; P = 0.015, respectively), as was the overall SF-36 composite score (HR 0.63; CI 0.49–0.82; P < 0.001).

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![Fig. 2. Kaplan-Meier plot of survival among enrolled patients. Median survival was 11.2 months (95 % confidence interval, 7.8 to 14.3 months).](image-url)
more aggressive intervention. The authors also point out that survival is difficult to predict. Given our finding that postoperative survival is associated with preoperative patient reported assessments, we feel that using these preoperative assessments can help steer the surgeon to the most appropriate, individualized treatment.

Among the specific domains of the SF-36, general health, vitality, and mental health were strongly associated with survival and were the main determinants of the component score and composite score findings. Therefore, patients’ perceptions of their own health in these specific domains are important to include in the surgeon’s preoperative evaluation; they can give insight into the likely survival of each patient, allowing the surgeon to individualize interventions.

These findings are consistent with those of nonsurgical studies in patients with various cancers. A systematic review demonstrated that in most instances, health-related QOL was a strong predictor of survival duration. This finding held true for multiple cancer diagnoses, of which lung, breast, gastroesophageal, colorectal, head and neck, and melanoma were the most studied. Findings also suggested that QOL data had prognostic value for patients with advanced disease and solid tumors, but not those with early-stage disease [20]. In another systematic review, Gotay et al. found that in 36 of the 39 included studies, at least one PRO was associated with survival [21]. The authors assert that PROs provide information beyond that of standard clinical outcome measures in cancer trials and are better predictors than performance status. Further, they highlight the impressive level of agreement among a heterogeneous group of studies that a link exists between PROs and survival. Finally, a meta-analysis on the topic from Quinten et al. pooled 31 studies with 11 different cancer diagnoses and demonstrated again that health-related QOL scales provide predictive information beyond that of more traditional clinical and socioeconomic measures [22]. Thus, the consensus in the literature is that there is a strong link between patient-reported assessments and survival in patients with various cancer diagnoses; our work suggests that such a link exists also for specific manifestations of cancer, such as osseous metastases requiring surgical intervention.

This study has several limitations. The analysis includes only surgical patients with bone metastases, and thus the results may not be generalizable to patients treated nonoperatively who may have been directed to surveillance or radiation therapy. Similarly, many patients who were eligible to participate declined to do so, which reduces the generalizability of the findings if there were differences between patients who consented to participate and those who did not. In our study, the SF-36 was administered within two weeks of surgery. For patients with an acute, completed fracture, this would have included the immediate period of cause worsening. Therefore, patients’ SF-36 assessments may have been influenced by their immediate trauma, and scores may have been artificially worse than they would have otherwise. Still, the SF-36 would have addressed the patients’ perceptions of their own health, and as the questionnaire includes a substantial portion of questions that reflect on the past four weeks, we feel that responses would indeed account for the whole period in question and not just the acute change. Additionally, the diverse anatomic locations of skeletal metastases treated in this study can be seen as confounding; while we recognize this limitation, we also feel this maintains the generalizability of our findings. It is possible that other patient-derived assessment tools, such as the Patient-Reported Outcomes Measurement Information System (PROMIS), may supplant the SF-36. However, those instruments address different aspects of the patient experience. Therefore, the SF-36 remains relevant in oncology, in orthopaedics, and in spine, trauma, foot, sports, and upper extremity surgery, and it has the additional advantage of having been internationally validated [23–31]. Finally, as with all observational studies, it is possible that we are not accounting for an unobserved confounder. However, given the strength of the association observed, we do not believe that the inclusion of additional variables would change the conclusions presented.

We demonstrate that preoperative patient-reported assessments are associated with postoperative survival after surgical stabilization of skeletal metastases in patients with a wide range of metastatic disease. This study emphasizes the role of patient-reported assessments in obtaining insight into a patient’s condition. Therefore, we recommend patient self-assessment instruments to be considered, along with other clinical factors that may help to predict survival, by surgeons as part of their preoperative assessment in order to provide individualized interventions to each patient and to avoid undertreatment and overtreatment of disease. Patients with poor preoperative self-reported assessments may be considered for less invasive interventions when possible, as this may reflect shorter postoperative survival, and therefore decreased risk of less invasive construct failure. Meanwhile, those with more favorable assessments may be considered for relatively invasive procedures requiring more extensive recovery and rehabilitation in order to maximize long term QOL and minimize failure risk that could require further intervention.

Given the promising relationship between preoperative SF-36 scores and postoperative survival, our next steps will involve assessing how to best incorporate patient-reported outcomes in our clinical decision support tool, PathFx. We hypothesize that inclusion of SF-36 scores or other widely available patient-reported measures will improve the global accuracy of the current model.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data statement

Deidentified participant data will be made available to others for review and for collaboration upon written request to the corresponding author (MKB), pending approval of a proposal and signed data access agreement.

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