Single-Stage versus Two-Stage Intramedullary Nailing for Synchronous Impending or Pathologic Fractures of Bilateral Femur from Metastatic Disease and Multiple Myeloma

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INTRODUCTION: Modern advances in cancer diagnosis and treatment have increased survival rates, which has subsequently resulted in a higher incidence and prevalence of metastatic disease to the bone, including synchronous involvement of multiple long bones. The femur is the most common long bone involved. Although intramedullary nail (IMN) fixation is often utilized for surgical treatment of patients with metastatic bone disease of the femur, there is no consensus on the timing of IMN in patients who present with synchronous bilateral disease: single stage (SS) vs two stage (TS). Although SS bilateral IMN may confer additional theoretical benefits, including single anesthesia, expedited mobilization, early start of adjuvants, reduced length of stay and decreased overall cost, TS has been a favored approach historically due to an anecdotal decreased risk of cardiopulmonary complications and mortality. Some recent literature has supported noninferiority of SS in this regard, but the studies have lacked direct detailed comparison. As such, the optimal surgical timing (SS vs. TS) still remains unclear. Therefore, the objective of this study was to investigate the safety and efficacy of staging (SS vs. TS) of IMN as a treatment for synchronous bilateral femora impending or pathologic fractures secondary to metastatic disease and multiple myeloma.

METHODS: This study was a retrospective comparative analysis of a prospectively maintained Institutional Review Board approved single-surgeon database in an urban academic setting. Adult patients (≥18 years old) with synchronous bilateral femur disease secondary to multiple myeloma and/or metastasis undergoing bilateral femoral SS or TS IMN were included. Staging decisions were made by a multidisciplinary team, taking into consideration the patient's tumor burden, comorbidities and functional status, rehabilitation potential, timing of adjuvant therapeutic modalities, and personal or familial wishes. Patients who received additional plating, screws, arthroplasty, or endoprostheses were excluded. Those who received IMN of bilateral femora more than 12 weeks apart were also excluded from analysis. Extracted variables included patient demographics and details of the surgical procedure (e.g., age, sex, primary tumor, fracture type, laterality, cement augmentation, venting), measures of patient safety (complications, survivorship, mortality, blood loss and transfusion, implant failure), and measures of efficacy (postoperative length of stay [LOS], total time in operating room (OR=wheel in to wheel out)), time from surgery to initiation of rehabilitation and adjuvant therapy, patient costs estimated by 2022 US $3113.72 per day of total hospital LOS and 2022 US $46.04 per minute of OR time). Descriptive and statistical analyses, including 2-sided Fisher's exact and Student's t-tests to compare categorical and continuous variables, respectively, and Kaplan-Meier estimates of patient survivorship were performed in R Statistical Software using a p-value of <0.05 as threshold for statistical significance.

RESULTS SECTION: Between May 2011 and September 2023, 116 femoral IMNs were inserted in a total of 58 patients (27 [46.55%] males and 31 [53.45%] females) for synchronous impending or pathologic fractures of bilateral femora for metastatic disease (n=27) or multiple myeloma (n=31). 11 patients [18.97%] and 47 patients [81.03%] had bilateral femoral IMN in a SS and TS approach, respectively. There were no significant differences between the SS and TS cohorts in demographics and procedural variables (all, $p > 0.05$). Mean survivorship for available patients was 396.58 ± 452.29 days. There were no significant differences between the two cohorts (SS: 631.40 ± 599.33 days vs. TS: 351.42 ± 418.17 days; $p = 0.366$). Kaplan-Meier median survivorship was determined to be 233 days for the overall patient population with no significant difference between SS and TS (SS: 661 days vs. TS: 210 days; $p = 0.07$). There was no intraoperative mortality in both cohorts, but 3 patients in the TS cohort died during the same admission compared to none in the SS cohort ($p = 1.000$). There was a total of 37 complications (31.9%) in 116 surgeries, of which 36 were medical and 1 was surgical. These included 8 intraoperative complications (6.90%), all of which were medical and cardiopulmonary in nature, including hypotension requiring pressors, heart rate derangements, and hemodynamic instability requiring ICU admission. The rate of intraoperative complications was significantly higher in the SS cohort (4 [18.18%]) compared to patients in the TS group (4 [4.26%]) ($p=0.041$). There were 29 postoperative complications (25.00%), of which 28 (24.14%) and 1 (0.86%) were medical and surgical, respectively. This surgical complication was a painful distal screw on the right femur. Overall (27.27% vs 24.47%; $p=0.788$), medical (27.27% vs. 23.40%; $p=0.783$), and surgical (0.00% vs 1.06%; $p=1.000$) postoperative complication rates were similar between patients undergoing SS and TS bilateral femoral IMN. Rates of complication were similar following the first versus second TS procedure ($p=0.149$). No significant differences were detected between SS and TS IMN in intraoperative, 24-hour postoperative, and total admission blood transfusions, and estimated blood loss (all, $p > 0.05$). Postoperative LOS was significantly shorter following SS procedures (9.18 ± 5.51 days) compared to TS procedures (34.13 ± 36.68 days; $p < 0.001$). Mean OR time was significantly shorter in the SS cohort (325.56 ± 121.62 minutes) compared to combined procedure time in the TS cohort (495.35 ± 139.35 minutes) ($p = 0.003$). Mean total estimated patient cost was significantly less in the SS cohort (2022 US $58,580.69 ± 22,744.24) compared to the TS cohort (2022 US $177,233.27 ± 187,907.60) ($p<0.001$). There was no significant difference between the SS and TS cohorts regarding mean time from surgery to initiation of rehabilitation (cohorts (SS: 2.80 ± 1.88 days vs. TS: 2.48 ± 2.75 days; $p = 0.568$) or adjuvant therapy (SS: 28.17 ± 24.06 days and TS:48.08 ± 63.08 days; $p=0.066$).

DISCUSSION: This study supports a SS approach in select patients with synchronous complete and/or impending pathologic fractures of the bilateral femur. While there was a higher rate of intraoperative complications in the SS cohort compared to the TS cohort, other measures of patient safety (postoperative complications, survivorship and mortality, and blood loss and transfusion) were all comparable. In terms of efficacy, SS was associated with a shorter LOS and total OR time, which are associated with decreased costs. Furthermore, while time to rehabilitation and adjuvant therapy were comparable, time to adjuvant therapy approached statistical significance. This is the most comprehensive analysis of its kind that utilized homogeneity and continuity of variable collection to address those limitations of heterogeneity in the sparse existing literature on this topic. Nevertheless, higher-powered studies may further elucidate those proposed benefits of SS bilateral femoral IMN in these patients.

SIGNIFICANCE/CLINICAL RELEVANCE: The current study offers a novel contribution to the current debate on the optimal surgical timing for patients with synchronous impending or pathologic fractures of bilateral femora secondary to metastatic disease and multiple myeloma. It is the largest study of these unique patients to date, which addresses many limitations in the existing literature and supports the SS approach as non-inferior in safety and efficacy, with added benefits of shorter LOS and combined OR time, lower cost, and potentially faster initiation of adjuvant therapy compared to the TS approach.

IMAGES AND TABLES: