Deferring Amputation in Diabetic Foot Osteomyelitis: Doing More Harm Than Good?

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In a cohort of patients with diabetic foot osteomyelitis who were recommended to undergo below-knee amputation, those who deferred amputation and chose medical therapy were more likely to die during the follow-up time compared with those who proceeded with amputation.

Keywords. amputation; diabetic foot infection; osteomyelitis.

Diabetic foot osteomyelitis (DFO) is a serious complication of diabetic foot infection. Some patients can be managed with antibiotics alone or with conservative, limb-sparing surgery [1], but for those who fail medical management or fail to heal amputation sites from limited foot surgery [2], below-knee amputation (BKA) remains a definitive management strategy [3]. Unfortunately, outcomes following BKA are bleak. Among patients with diabetes who undergo BKA for any reason, overall mortality has been cited at 21.2% at 6 months after amputation [4], 38% at 1 year [5], and 40%–82% at 5 years [6].

Given these statistics, it is not surprising that some patients who fail medical management of DFO defer BKA. Patients with diabetic foot disease have ranked amputation as their most feared complication of diabetes, even more so than death [7]. Often these patients opt for continued local wound care and antibiotics for symptomatic relief without a realistic expectation of healing, in what is referred to as "wound palliation" [8]. Outcomes of patients who continue medical therapy after declining BKA have not been previously described. In this study, we compare the outcomes for patients who defer BKA with those of individuals who undergo amputation in that hope that the results can be used to better inform decision-making among patients and providers.

METHODS

Patients and Clinical Characteristics

From October 2015 to June 2019, adult patients with diabetes mellitus and a diagnosis of DFO at Michigan Medicine who were evaluated by podiatry and recommended to have BKA were included in the study. Patients were identified within a prospective database of podiatry patients. This study was approved by the University of Michigan Medical School Institutional Review Board.

Diagnosis of DFO was established by the clinicians at the time of BKA recommendation according to previously published guidelines [3, 9], based on criteria including signs and symptoms of clinical infection, laboratory values, and imaging studies. The first documented recommendation for BKA in the electronic medical record (EMR) by one of the surgical teams (podiatry, vascular surgery, or orthopedic surgery) was defined as the date of initial BKA recommendation. Patients who chose BKA following this recommendation were included in the BKA group. Patients who refused BKA at this time were included in the group that deferred amputation.

Study Variables

Demographics and comorbidities were obtained from the EMR. Microbiologic data, laboratory values, and imaging findings were abstracted at the time of BKA recommendation or, if not available at this time point, within the 2 weeks prior, at the time closest to BKA recommendation. Patients were followed through June 2020 for a minimum of 1 year or until death, whichever occurred first. The primary outcome was all-cause mortality following BKA recommendation. Secondary outcomes included complete healing of the affected limb during the follow-up time (defined as healing of the wound/surgical site with no further need for antibiotic therapy or local wound care) and total antibiotic days in the 6 months after BKA recommendation (including all therapeutically dosed intravenous antibiotics and highly bioavailable oral agents, ie, fluoroquinolones and linezolid).

Statistical Analysis

Bivariate analyses were conducted using the Student *t* test or Wilcoxon rank-sum test for continuous variables and the Fisher exact test or chi-square test for categorical variables. For the primary outcome, all-cause mortality was calculated for the BKA group and the group that deferred amputation at 1 year;

a Kaplan-Meier curve was constructed, and Cox proportional hazard modeling was performed to compare the hazard of death between the 2 groups in the total follow-up period. All *P* values were 2-sided. Statistical analysis was performed using SAS, version 9.4 (SAS Institute Inc, Cary, NC, USA).

RESULTS

A total of 44 patients with DFO were included (Supplementary Table 1). The mean age was 61; the majority were male (68.2%) and white (79.6%). The median Charlson Comorbidity Index (CCI) of the cohort (interquartile range [IQR]) was 6 (4–7). The mean hemoglobin a1c (standard deviation [SD]) was 8.55 (2.21), and the mean body mass index (SD) was 34 (9.5).

After BKA recommendation, 26 patients chose to defer amputation and 18 proceeded with BKA. Patients who deferred amputation had a significantly lower mean erythrocyte sedimentation rate (ESR) compared with the BKA group (71.5 vs 96.3, respectively; *P* = .005). In addition, when utilizing more stringent DFO criteria (ESR > 60 mm/h + CRP > 7.9 mg/dL + magnetic resonance image confirmation), fewer patients in the group that deferred amputation qualified for DFO as compared with the BKA group, though this did not reach statistical significance (34.6% vs 66.7%, respectively; *P* = .065) [10]. There were no other notable differences between the groups with regards to demographics or comorbid conditions (Supplementary Table 1).

Sixteen (61.5%) patients who initially deferred amputation eventually required major lower extremity amputation (mLEA); 14 (53.8%) had BKA, 1 of whom required subsequent AKA, and 2 patients proceeded directly to AKA. Amputations among those who deferred BKA occurred a median (IQR) of 76.5 (23–87) days after the initial BKA recommendation and most often occurred due to worsening ischemia or sepsis/gangrene. Two patients in the BKA group (11.11%) went on to have AKA.

One-year mortality was greater in patients who deferred amputation compared with the BKA group (23.1% vs 0%, respectively; odds ratio [OR], 11.73; 95% CI, 0.62–222.87) (Supplementary Table 1). Considering the entire follow-up period for the cohort, the hazard ratio for death for the group that deferred amputation compared with the BKA group was 12.2 (95% CI, 1.58–94.8) (Figure 1).

Fewer patients who deferred amputation had complete healing of their wound/stump compared with the BKA group (46.2% vs 88.9%; OR, 9.33; 95% CI, 1.77–49.08). Nearly all patients from both groups received antibiotics aftert BKA recommendation (94.4% in BKA vs 92.3% in medical management), but the median days of antibiotics (IQR) were significantly greater among patients who deferred amputation (55 [42–78] vs 17 [10–37]; *P* = .0017).

DISCUSSION

Among patients with DFO who were recommended to undergo BKA, those who deferred amputation and chose medical therapy were more likely to die during the study period and had poorer healing of the affected limb and excess antibiotic exposure compared with the BKA group.

Similar to what has been reported, the mortality rate for the entire cohort was high (25% at 2 years). Notably, most
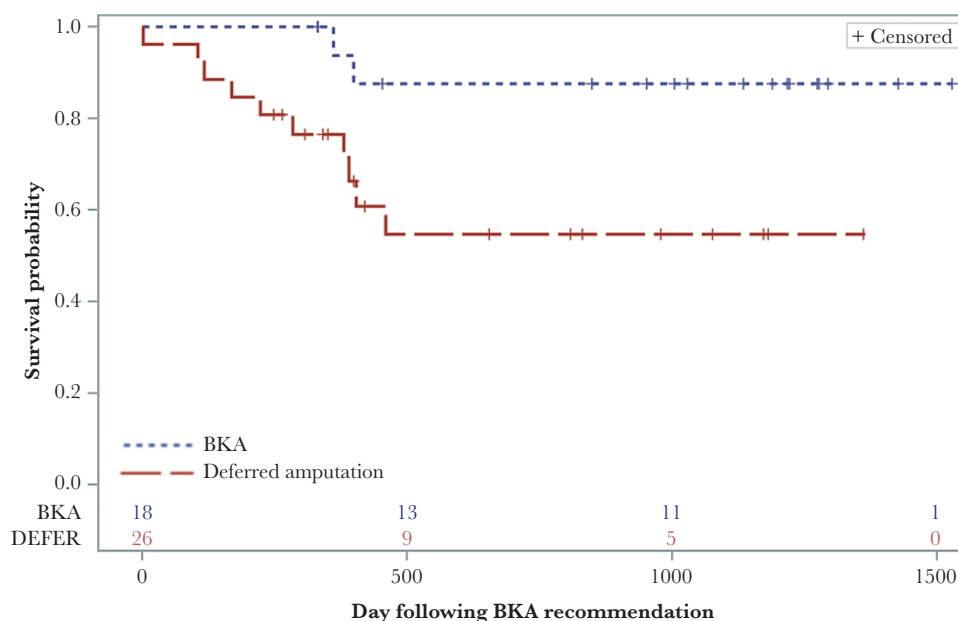

Figure 1. Kaplan-Meier survival analysis for mortality as a function of BKA vs deferring amputation following BKA recommendation. The hazard ratio for death for the group that deferred amputation compared with the BKA group was 12.2 (95% CI, 1.58–94.8). Abbreviation: BKA, below-knee amputation.

deaths occurred in patients who deferred amputation. This is striking as the 2 groups had similar baseline characteristics and comorbidities and all patients were deemed healthy enough to undergo surgery. In addition, patients who deferred amputation were treated with longer durations of antibiotics yet were less likely to achieve healing of the affected limb, demonstrating the futility in this cohort of "wound palliation."

This study suggests that when BKA is the preferred treatment option for DFO, palliation should be utilized only in patients for whom surgery would present an unacceptable risk. Providers must have a frank discussion with patients who decline BKA regarding the risks of deferring necessary surgery, as the delay may increase their risk of death, and amputation can lead to improved quality of life [11].

Our study was limited by its retrospective nature, which made it difficult to capture details regarding the decision-making process around amputation, including the strength of provider recommendations and specific reasons for deferring amputation by patients. More patients in the BKA group met the stringent criteria for DFO (Supplementary Table 1), and this may have led to a stronger recommendation for amputation from the clinicians. Despite efforts to control for differences between the 2 groups, which were limited by the small sample size, there may still be confounding variables related to patients with higher risk of death self-selecting for nonoperative management. The small sample size also resulted in wide confidence intervals, which limited our ability to meaningfully compare the 2 groups with regards to other outcomes, such as multidrug-resistant organism emergence and *Clostridioides difficile* infection.

This is the first study, to our knowledge, to evaluate the impact and outcomes of deferring BKA in patients with DFO and to quantify the risk to patients when amputation is deferred. Future prospective studies are needed to evaluate and provide insight regarding the decision-making process between physicians and patients at the time of BKA recommendation.

CONCLUSIONS

Among patients with DFO, deferring amputation in the setting of physician-recommended BKA was associated with increased mortality, poor healing of the affected limb, and excess antibiotic exposure. In clinical scenarios where BKA is recommended for treatment of DFO, the results from this study can be used to inform providers and patients regarding the risks and adverse effects of avoiding amputation and undertaking long-term medical management for this disease, which requires definitive surgical management.

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