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Minor vs. Major Leg Amputation in Diabetic Patients: Six-Month Readmissions, Reamputations, and Complications

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ABSTRACT

Objective

Management of diabetic foot ulcers is a complex issue, sometimes requiring amputation; the optimal level of amputation is debated. The objective of this study was to compare medium-term outcomes between comparable minor and major amputation subjects.

Research Design and Methods

We used data from the 2016 to 2017 National Readmissions Database to construct a representative cohort of 15,581 adults with diabetes who had lower extremity amputations. Patients were categorized based on the level of their index amputation (major or minor) and matched by propensity score to compare outcomes for patients who were candidates for either level of amputation. Outcomes, including readmission or reamputations, were assessed at 1, 3, and 6 months following the index amputation.

Results

In the 6 months following index amputation, large proportions of patients were readmitted (n = 7597, 48.8%) or had reamputations (n = 1990, 12.8%). Patients treated with minor amputations had greater odds of readmission (OR = 1.25; 95% CI 1.18–1.31), reamputation (OR = 3.71; 95% CI 3.34–4.12), and more proximal major reamputation (OR = 2.61; 95% 2.33–2.93) (all P <.001). During this same time period, minor amputation patients had higher odds of readmission for postoperative infection (OR = 4.45; 95% CI 3.27–6.05), and lower odds for readmission for sepsis (OR = 0.79; 95% CI 0.68–0.93).

Conclusion

Understandably, many patients desire to save as much limb as possible and should be counseled on the higher risk for reamputation, readmission, and infection with minor amputations during discussion of their care.

Management of lower extremity ulcerations in patients with diabetes is a complex, multifaceted issue, and sometimes requires amputation of the affected limb. Foot ulcers are a common problem in diabetes, afflicting 5% to 7% of patients at any given time and carrying a lifetime risk of 15% (1–3). It is estimated that foot ulcers have an annual incidence of 2% among patients with diabetes (3), although some estimates range as high as 6% (4). Definitive healing of these ulcers can prove challenging; 1 in 3 patients will have re-ulceration within 1 year, and 61% within 3 years (5,6). Care for foot ulcers comprises an estimated 25% of healthcare costs (7) and increased hospitals days, home health, emergency department visits, and outpatient visits for ulcer patients (8).

Lower extremity amputations (LEA) are also common in the diabetic population, in part due to the high prevalence and frequent recurrence of foot ulcers (9,10). An estimated 85% of amputations in diabetic patients are preceded by ulcers (10). The incidence of amputations is approximately 10 times higher in diabetic patients than in patients without diabetes (11,12), and epidemiological surveillance demonstrated a 2% prevalence of amputations among diabetic patients in the United States from 2006 to 2008 (13). National trends of diabetes-related amputations have shown an increase in the incidence of LEAs from 2009 to 2015, after a period of declining rates from 2000 to 2009 (14). This decline and rebound has primarily been driven by patients younger than age 65 and increasing rates of minor amputations (LEAs involving the foot or toes). The increase in the incidence of minor amputations relative to major amputations (LEAs occurring more proximally) has also been observed in European countries and other populations, perhaps reflecting a shift in clinical practice toward limb-preserving amputations (15,16).

While many providers and most patients may prefer minor amputations (17), the choice of optimal amputation level is difficult. Consideration of the effect of ulceration (18–20) and amputation (17,21) on a patient's well-being and quality of life requires balancing the desire to amputate as distally as possible with the hope that no more amputations will be needed, as multiple hospitalizations or surgeries can result in declines in health, functional status, and mental wellbeing (22,23). Some previous studies have shown rates of reamputation to vary by initial amputation level (24,25), while others have suggested that these differences may be due to baseline patient characteristics prior to amputation (26,27). A recent paper comparing short-term outcomes of minor and major amputations demonstrated that minor amputations were more likely to require follow-up irrigation and debridement. Our study expands on this work by examining both mid- and short-term outcomes in minor and major amputation in diabetic patients. Careful matching between amputation groups allows clinically meaningful comparisons between amputation types, both from a patient perspective, and in terms of resource utilization.

RESEARCH DESIGN AND METHODS

Data source

This study utilized the 2016 to 2017 Nationwide Readmissions Database (NRD). The NRD is part of the Healthcare Cost and Utilization Project, administered through the Agency for Healthcare Research and Quality (AHRQ), and is the only nationally representative readmissions database publicly available in the United States. The NRD captures roughly 50% of all hospitalizations and tracks patient readmissions across all hospitals within a state via deidentified patient linkage variables.

Cohort selection

We identified all elective hospital admission of adults 18 years or older with an International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) code indicating an associated diagnosis of diabetes. The presence of diabetes was defined using the Elixhauser comorbidity mapping software provided by the AHRQ (28). The first admission where a patient had both diabetes and a lower-extremity amputation, as defined by the ICD-10 codes listed in Supplemental Table S1, was considered to be their index admission. Patients with bilateral index amputations were excluded.

Only admissions from January to June of 2016 and 2017 were eligible for inclusion in this study, allowing each patient to have at least 6 months of follow-up. Patients admitted to out-of-state hospitals (i.e., a patient whose primary residence was not within the same state as the hospital) were not included because possible readmissions would not be included in the NRD.

Exposure and covariates

Patients were categorized into either minor or major index amputations based on the highest (i.e., most proximal) level of amputation that occurred during index admission. Specifically, if a patient had a staged amputation within the first hospitalization, that hospitalization was associated with the highest level of amputation which occurred. Amputations at the level of the foot or ankle (including transmetatarsal amputations) were considered to be minor, and any amputation above the ankle was considered to be major (Supplemental Table S1). Comorbidities present on index admission were adapted from the AHRQ's Elixhauser comorbidity mapping software (28) and the Quan/Charlson comorbidity mapping algorithms (29), with additional comorbidities added for smoking, neuropathy, and other comorbidities not provided by these mapping algorithms (Supplemental Table S2). Because ICD-10 codes specify laterality, limb-specific comorbid conditions (osteomyelitis, Charcot's foot, cellulitis, ulcers, open wounds, and stump complications) were counted as present on index admission if they occurred ipsilateral to the index amputation. Further, patients' baseline demographics were also assessed, including age, sex, and primary expected payer. Patients who died on index admission were excluded.

Outcomes

The primary outcomes were readmissions or reamputations within a readmission window of 30, 90, or 180 days of index discharge. Readmissions were defined as a second admission that occurred during the specified readmission period after discharge following the index procedure. Reamputations were defined as additional amputation(s), whether more proximal or not, occurring on the limb ipsilateral to the index amputation. Secondary outcomes included death, more proximal major ipsilateral reamputations, and cause-specific readmissions. Cause-specific readmissions were defined using diagnosis-related group (DRG) codes, which classifies admissions into groups of clinically similar reasons for hospitalization (Supplemental Table S3).

Statistical Analysis

Continuous variables are presented as mean and 95% confidence intervals, and categorical variables are presented as weighted frequencies and percentages. Bivariate calculations were conducted with *t* tests for continuous variables and chi-squared or Fisher's exact tests for categorical variables. Because the NRD uses a stratified sampling strategy, all analysis was conducted using weighted estimates and design-based standard errors to account for the complex design.

Patients with index major and minor amputations were matched by their propensity of receiving a minor amputation on index admission. The propensity score was calculated using the covariates/comorbidities listed in Table 1, incorporating the NRD's weights. Balance was assessed using balance plots and standardized mean differences. All covariates demonstrated balance after matching, with standardized differences ≤0.05. Each patient treated with a minor amputation was matched with up to 2 patients treated with a major amputation on index admission. Variables included in the propensity score were selected a priori based on the current literature, but 1 covariate (ophthalmic complications) was excluded owing to the frequency with which this comorbidity occurred in the data.

Conditional logistic regression models were used to assess risk factors for each outcome (for each readmission period) using the weighted data matched by propensity score. A 2-sided value of $P < 0.05$ was set for statistical significance. All analysis was conducted using the R Statistical Software (version 3.6.3) with the assistance of the *icd* and *MatchIt* packages.

RESULTS

Patients receiving major amputations were significantly more likely to die on index admission, with 1.8% (n = 193) of the 10,767 admissions for major amputations dying during their index admission, while only 0.9% (n = 46) of the 5,057 index admissions for minor amputations died ($P < 0.001$). After excluding patients who died on index admission, our final study population yielded 5,010 and 10,571 patients with minor and major amputations, respectively. When broken down by level of amputation, 4,340 (27.9%) had transmetatarsal amputations, 670 (4.3%) had other foot/ankle amputations, 6,134 (39.4%) had below the knee amputations, and 4,437 (28.5%) had amputations at or above the knee (Figure 1).

Prior to matching, patients with minor amputations were more likely to be male and slightly younger. They were also significantly more likely to have neuropathy, osteomyelitis, cellulitis, and ulcers. Major amputation patients were significantly more likely to have Medicare, cardiovascular comorbidities, be on dialysis, have Charcot foot, and have stump complications on index admission (Table 1).

Bivariate analysis before matching

Two thousand, seven hundred and twenty-one (54.3%) patients with minor amputations had at least 1 readmission during the 6 months they were followed, compared to 4,876 (46.1%) of the major amputation group ($P < 0.001$). Patients initially treated with minor amputations also had higher rates of reamputations, with 1,224 (24%) having ipsilateral reamputations during this time, compared to 766 (7%) of the major amputation group. Furthermore, 825 (16.5%) patients with minor amputations eventually received a major amputation during this time.

Patients with minor amputations were significantly more likely to be readmitted for wound/skin debridement, postoperative infection, and osteomyelitis, whereas major amputation patients were significantly more likely to be readmitted for sepsis (Table 2). Patients with major amputations were more likely to die during readmissions versus minor amputation patients (3.8% versus 3.0%), but this did not meet the threshold for significance ($P = 0.057$).

Propensity score matching

Owing to the underlying differences in baseline comorbidities, the 2 groups were matched by propensity score. Propensity-score matching achieved balance in all variables, as evidenced by standardized mean differences <0.05. Conditional logistic regression on the matched cohort demonstrated that in the 6 months following index discharge, minor amputations had 1.25 times (95% CI: 1.18–1.31) the odds of being readmitted, 3.7 times (95% CI: 3.34–4.12) the odds of having an ipsilateral reamputation, and 2.6 times (95% CI: 2.33–2.93) the odds of having a major ipsilateral reamputation (Table 3).

Cause-specific readmissions at 6 months remained similar after matching, with minor amputation patients more likely to be readmitted for debridement, postoperative infections, and osteomyelitis, while major amputation patients were more likely to be readmitted for sepsis. However, the matched analysis additionally revealed that patients with major amputations were more likely to be admitted for procedures on the lower extremity bones/joints, which was not demonstrated on the unmatched analysis.

When these outcomes were assessed at 30 and 90 days (Table 3), the results followed a similar pattern in direction, but with some changes in magnitude. Readmissions for sepsis and procedures on the bones/joints of the lower extremity were more common in patients with major amputations, but this difference was most pronounced within the first 30 days. Readmissions for cellulitis was initially higher for patients with minor amputations at 30 days, but, with time, the difference decreased and was no longer significant, beginning at 90 days. Conversely, with osteomyelitis, there was no significant difference between 2 groups for readmissions at 30 days, but by 90 days patients with minor amputations became more likely to be readmitted for osteomyelitis. At later time points, the likelihood of patients with minor amputations to be readmitted for debridement, relative to those with major amputations, was greater.

CONCLUSIONS

Readmissions following lower extremity amputations are common, with reamputations and infections presenting substantial challenges to patients' recovery (26). We found markedly high rates of readmissions at 6 months for minor amputations (54.3% of patients). Among patients with minor amputations who were readmitted, nearly half had reamputations (24%) during their readmissions, two-thirds of which were major amputations. Conversely, 6-month readmission rates were also high (46.1% of major amputation patients), but less than a tenth of readmissions following a major amputation had reamputations (7.2%); this implies that patients initially treated with major amputations are requiring readmissions for reasons other than new amputation. As observed in an earlier study comparing major and minor complications and short-term outcomes, major amputations were more likely to be followed by greater blood loss; this systemic stress may have longer-term impacts as well (30). In any case, although a detailed examination of these causes is beyond the scope of this paper, they are a concern. First, they extend treatment for patients, and second, they place an increased burden on the healthcare system. Indeed, recent literature has demonstrated that costs of diabetes-related hospitalizations have been increasing nationally, at least in part due to long-term complications and LEA (31).

The relatively high rates of reamputations observed in the minor amputation group corroborate the existing literature and add clarity to the emerging picture of decreasing major and increasing minor amputation rates (14). For example, a study of 277 diabetic patients in the mid-1990s found minor amputations had a reamputation rate of around 20% at 1 year, as did a smaller study conducted in in the early 2000s (24,32). However, a recent study of 7,187 Veterans Affairs patients with diabetic foot ulcers found much higher rates of reamputations, with 40% of transmetatarsal amputations (TMA) requiring ipsilateral reamputation by 1 year (33). We found that 24.4% of minor amputations required ipsilateral reamputations at 6 months, and 24.0% of TMAs required ipsilateral reamputation (Supplemental Table S4). While our observed rate is slightly above what was observed in the earlier studies (perhaps due to changes in amputation trends) (14), it is well below the observation in the Veterans Affairs study. Further, our results substantiate the findings in a meta-analysis that found 28% of patients received reamputations following a TMA (27).

Several studies have suggested that receiving a minor amputation does not increase the risk of a subsequent major amputation (10,34), and those that do show such increased risk focused on toe, rather than TMA, amputations (25,32). The reasons for the high rates of major reamputation after minor amputation demonstrated in our study remain unclear, though it is known that loss of metatarsal heads changes gait and may lead to increased pressure and ulceration (35). Prior studies were conducted largely before the increase in the national incidence of minor LEAs observed in recent years (14–16), indicating that patients who would have received major amputations in years past are now being treated with minor amputations. This shift may reflect change in practice, change in acuity of patients, or improvements in techniques. While leading to earlier, more distal, amputations, this shift may not obviate the need for later, more proximal, amputations, which appear in this setting as reamputation, rather than the index amputation they might have been in earlier years. Thus, the appearance in the literature that rates of minor amputations are increasing relative to major may be slightly exaggerated; this may not be the best metric for judging success in limb salvage.

While it is possible that some of the reamputations in the minor group could be staged amputations (36), given our inclusion of staged amputation within first hospitalization as the most proximal amputation during that amputation, this not likely the case.

Cause-specific readmissions

In keeping with prior literature, readmission rates for infectious complications were high in this cohort, with a total of 14% of patients being admitted for an infectious reason (Table 2). Most of these admissions were either for debridement (4.2%) or sepsis (6.5%), with minor amputation patients readmitted more frequently for the former and major amputations more frequently for the latter.

More interesting were the increased rates of readmission for debridement in patients with minor amputations. Unlike the other outcomes assessed in this study, the difference between these groups in readmission rates for debridement increased with longer follow-up periods, suggesting that many of these admissions occurred months after the original amputation.

Limitations

Although this study uses nationally representative data, it has several limitations. First, despite accounting for many of numerous baseline comorbidities that are likely to influence a patient's index amputation level, there are additional clinical factors, such as tissue perfusion, HbA1c, and locations of infections that are not captured in the NRD. This could result in residual confounding or selection bias. Second, we categorized cause-specific readmission using DRG codes, which may not completely capture all reasons a patient was hospitalized. Since DRG codes only capture the main reason a patient was admitted, it is possible that lower-acuity DRG codes (e.g., wound debridement or cellulitis) may be masked if a higher-acuity reason for admission was also present (e.g., postoperative infection or osteomyelitis). Therefore, cause-specific readmissions should be interpreted cautiously, as they are likely underestimates of the true rates. Third, the time intervals we used were time from discharge after index amputation to readmission. Although we feel this is the most appropriate measure, it's possible the minor amputation patients are discharged from the hospital more quickly following their surgery, while major amputation patients are kept in the hospital for longer periods of postoperative care and observation. Finally, as with any study with secondary data, the quality of results depends on the quality of initial recording of data.

Strengths

Our study uses nationally representative data, allowing us to better understand trends in rates of amputation and reamputations at various levels. The nature of the data ensure that minor and subsequent major amputations are counted within 1 patient, rather than being viewed as separate incidents, as could have been the case in other studies (14). In this regard, prior work has demonstrated that the incidence of hospitalizations for minor amputations has been increasing in recent years (14), and our results highlight that a change in the incidence of hospitalizations for amputations may not reflect the same increase in the number of individual patients receiving amputations. In fact, 12.8% of all patients with amputations required reamputations within 6 months. In other words, index amputations may be decreasing, while overall amputation rates are increasing. Our study has a slightly longer short-term follow-up period than other studies; this is important, since most reamputations occur within 6 months following index amputation, even in studies with many years of follow-up (24,27,32,33). Finally, the use of propensity-score matching allows us to compare situations where either major or minor amputations could have been used (37).

The choice between major and minor amputations remains a difficult one, for both patient and clinician. Both may prefer more distal amputations to preserve as much of the limb as possible, given that quality of life does not greatly differ (38). However, patients should be informed that minor amputations can be associated with increased rates of short-term complications. Major amputations may be more definitive if systemic/hemodynamic short-term stability can be achieved, but have increased risk of sepsis. The optimal level of amputation depends on a complex array of factors, and in addition to physiologic considerations (e.g., hemodynamic stability and vascular status of the extremity), the patient's preference plays an important role. A patient’s desire to preserve as much limb as possible must be balanced with their tolerance for potential readmissions, infections, and reamputations.

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REFERENCES

1. Reiber GE, McFarland L V. Epidemiology and Health Care Costs for Diabetic Foot Problems. In: The Diabetic Foot. Humana Press; 2007. p. 39–50.
2. Walters DP, Catling W, Mullee MA, Hill RD. The Distribution and Severity of Diabetic Foot Disease: a Community Study with Comparison to a Non-diabetic Group. Diabet Med. 1992;9(4):354–8.
3. Ramsey SD, Newton K, Blough D, McCulloch DK, Sandhu N, Reiber GE, et al. Incidence, outcomes, and cost of foot ulcers in patients with diabetes. Diabetes Care. 1999;22(3):382–7.
4. Margolis DJ, Malay DS, Hoffstad OJ, Leonard CE, MaCurdy T, de Nava KL, et al. Incidence of diabetic foot ulcer and lower extremity amputation among Medicare beneficiaries, 2006 to 2008: Data Points #2. Data Points Publication Series. Agency for Healthcare Research and Quality (US); 2011.
5. Apelqvist J, Larsson J, Agardh C. Long-term prognosis for diabetic patients with foot ulcers. J Intern Med. 1993;233(6):485–91.
6. Morbach S, Icks A, Rümenapf G, Armstrong DG. Comment on: Bernstein. Reducing foot wounds in diabetes. Diabetes care 2013;36:e48. Vol. 36, Diabetes Care. American Diabetes Association; 2013. p. e62.
7. Harrington C, Zagari MJ, Corea J, Klitenic J. A cost analysis of diabetic lower-extremity ulcers. Diabetes Care. 2000;23(9):1333–8.
8. Rice JB, Desai U, Cummings AKG, Birnbaum HG, Skornicki M, Parsons NB. Burden of diabetic foot ulcers for medicare and private insurers. Diabetes Care. 2014 Mar;37(3):651–8.
9. Apelqvist J, Bakker K, van Houtum WH, Schaper NC. Practical guidelines on the management and prevention of the diabetic foot. Diabetes Metab Res Rev. 2008 May;24(SUPPL. 1).
10. Larsson J, Agardh CD, Apelqvist J, Stenström A. Long-term prognosis after healed amputation in patients with diabetes. Clin Orthop Relat Res. 1998 May;(350):149–58.
11. Siitonen OI, Niskanen LK, Laakso M, Siitonen JT, Pyorala K. Lower-extremity amputations in diabetic and nondiabetic patients: A population-based study in eastern Finland. Diabetes Care. 1993;16(1):16–20.
12. Van Damme H, Limet R. Amputation in Diabetic Patients. Vol. 24, Clinics in Podiatric Medicine and Surgery. Elsevier; 2007. p. 569–82.
13. Margolis DJ, Malay DS, Hoffstad OJ, Leonard CE, MaCurdy T, López de Nava K, et al. Prevalence of diabetes, diabetic foot ulcer, and lower extremity amputation among Medicare beneficiaries, 2006 to 2008: Data Points #1. Rockville: Agency for Healthcare Research and Quality (US); 2011.
14. Geiss LS, Li Y, Hora I, Albright A, Rolka D, Gregg EW. Resurgence of diabetes-related nontraumatic lower-extremity amputation in the young and middle-aged adult U.S. Population. Diabetes Care. 2019 Jan 1;42(1):50–4.
15. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Vol. 62, Diabetologia. Springer Verlag; 2019. p. 3–16.
16. Harding JL, Pavkov ME, Gregg EW, Burrows NR. Trends of nontraumatic lower-extremity amputation in end-stage renal disease and diabetes: United States,

2000-2015. Diabetes Care. 2019 Aug 1;42(8):1430–5.
17. Wukich DK, Raspovic KM, Suder NC. Patients With Diabetic Foot Disease Fear Major Lower-Extremity Amputation More Than Death. Foot Ankle Spec. 2018 Feb 1;11(1):17–21.
18. Carrington AL, Mawdsley SKV, Morley M, Kincey J, Boulton AJM. Psychological status of diabetic people with or without lower limb disability. Diabetes Res Clin Pract. 1996 Apr 1;32(1–2):19–25.
19. García-Morales E, Lázaro-Martínez JL, Martínez-Hernández D, Aragón-Sánchez J, Beneit-Montesinos J V., González-Jurado MA. Impact of diabetic foot related complications on the health related quality of Life (HRQol) of patients - A regional study in Spain. Int J Low Extrem Wounds. 2011;10(1):6–11.
20. Peters EJG, Childs MR, Wunderlich RP, Harkless LB, Armstrong DG, Lavery LA. Functional status of persons with diabetes-related lower-extremity amputations. Diabetes Care. 2001;24(10):1799–804.
21. Ragnarson Tennvall G, Apelqvist J. Health-related quality of life in patients with diabetes mellitus and foot ulcers. J Diabetes Complications. 2000;14(5):235–41.
22. Sager MA, Rudberg MA, Jalaluddin M, Franke T, Inouye SK, Seth Landefeld C, et al. Hospital Admission Risk Profile (HARP): Identifying older patients at risk for functional decline following acute medical illness and hospitalization. J Am Geriatr Soc. 1996 Mar 1;44(3):251–7.
23. Hoogerduijn JG, Schuurmans MJ, Duijnstee MSH, De Rooij SE, Grypdonck MFH. A systematic review of predictors and screening instruments to identify older hospitalized patients at risk for functional decline. Vol. 16, Journal of Clinical Nursing. John Wiley & Sons, Ltd; 2007. p. 46–57.
24. Izumi Y, Satterfield K, Lee S, Harkless LB. Risk of reamputation in diabetic patients stratified by limb and level of amputation: A 10-year observation. Diabetes Care. 2006 Mar 1;29(3):566–70.
25. Borkosky SL, Roukis TS. Incidence of re-amputation following partial first ray amputation associated with diabetes mellitus and peripheral sensory neuropathy: a systematic review. Diabet Foot Ankle. 2012 Jan 20;3(1):12169.
26. Curran T, Zhang JQ, Lo RC, Fokkema M, McCallum JC, Buck DB, et al. Risk factors and indications for readmission after lower extremity amputation in the american college of surgeons national surgical quality improvement program. J Vasc Surg. 2014 Nov 1;60(5):1315–24.
27. Thorud JC, Jupiter DC, Lorenzana J, Nguyen TT, Shibuya N. Reoperation and Reamputation After Transmetatarsal Amputation: A Systematic Review and Meta-Analysis. Vol. 55, Journal of Foot and Ankle Surgery. Academic Press Inc.; 2016. p. 1007–12.
28. Healthcare Cost and Utilization Project. Elixhauser Comorbidity Software for ICD-10-CM (beta version) [Internet]. 2018 [cited 2020 Oct 5]. Available from: https://www.hcup-us.ahrq.gov/toolssoftware/comorbidityicd10/comorbidity_icd10.jsp
29. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005 Nov;43(11):1130–9.
30. Jupiter DC, Beaino M El, LaFontaine J, Barshes N, Wukich DK, Shibuya N.

Transmetatarsal and Minor Amputation Versus Major Leg Amputation: 30-Day Readmissions, Reamputations, and Complications. J Foot Ankle Surg. 2020 May 1;59(3):484–90.
31. Shrestha SS, Zhang P, Hora I, Geiss LS, Luman ET, Gregg EW. Factors contributing to increases in diabetes-related preventable hospitalization costs among U.S. Adults during 2001–2014. Diabetes Care. 2019 Jan 1;42(1):77–84.
32. Skoutas D, Papanas N, Georgiadis GS, Zervas V, Manes C, Maltezos E, et al. Risk factors for ipsilateral reamputation in patients with diabetic foot lesions. Int J Low Extrem Wounds. 2009 Jun;8(2):69–74.
33. Norvell DC, Czerniecki JM. Risks and Risk Factors for Ipsilateral Re-Amputation in the First Year Following First Major Unilateral Dysvascular Amputation. Eur J Vasc Endovasc Surg. 2020 Oct 1;60(4):614–21.
34. Morbach S, Furchert H, Gröblinghoff U, Hoffmeier H, Kersten K, Klauke GT, et al. Long-term prognosis of diabetic foot patients and their limbs: Amputation and death over the course of a decade. Diabetes Care. 2012 Oct;35(10):2021–7.
35. Dillon MP, Barker TM. Preservation of residual foot length in partial foot amputation: A biomechanical analysis. Foot Ankle Int. 2006;27(2):110–6.
36. Cheun TJ, Jayakumar L, Sideman MJ, Ferrer L, Mitromaras C, Miserlis D, et al. Short-term contemporary outcomes for staged versus primary lower limb amputation in diabetic foot disease. In: Journal of Vascular Surgery. Mosby Inc.; 2020. p. 658-666.e2.
37. Jupiter DC. Propensity Score Matching: Retrospective Randomization? J Foot Ankle Surg. 2017 Mar 1;56(2):417–20.
38. Quigley M, Dillon MP, Duke EJ. Comparison of quality of life in people with partial foot and transtibial amputation: A pilot study. Prosthet Orthot Int. 2016 Aug 25;40(4):467–74.

Table 1. Covariate balance before matching

	Overall (N = 15,581)	Major (n = 10,571)	Minor (n = 5,010)	*P* value
Age on index admission (SD)	63.93 (12.58)	64.37 (12.52)	63 (12.68)	<0.001
Female (%)	4,777 (30.7%)	3,467 (32.8%)	1,310 (26.2%)	<0.001
Primary payer (%)				<0.001
Medicare	10,511 (67.5%)	7,318 (69.2%)	3,193 (63.7%)	
Private insurance	2,738 (17.6%)	1,737 (16.4%)	1,001 (20%)	
Medicaid	1,775 (11.4%)	1,170 (11.1%)	605 (12.1%)	
Other Gov / Work Compensation	332 (2.1%)	219 (2.1%)	113 (2.3%)	
Self-pay	182 (1.2%)	99 (0.9%)	83 (1.7%)	
Other	43 (0.3%)	28 (0.3%)	15 (0.3%)	
Smoker (%)	2,620 (16.8%)	1,797 (17.0%)	823 (16.4%)	0.559
Obesity (%)	3,652 (23.4%)	2,510 (23.7%)	1,142 (22.8%)	0.383
CKD/ESRD (%)	6,727 (43.2%)	4,576 (43.3%)	2,151 (42.9%)	0.787
Dialysis (%)	2,270 (14.6%)	1,620 (15.3%)	650 (13.0%)	0.016
Hypertension (%)	13,389 (85.9%)	9,158 (86.6%)	4,231 (84.5%)	0.024
Peripheral vascular disease (%)	7,654 (49.1%)	5,518 (52.2%)	2,136 (42.6%)	<0.001
Neuropathy (%)	6,294 (40.4%)	3,929 (37.2%)	2,365 (47.2%)	<0.001
Cerebrovascular disease (%)	1,071 (6.9%)	844 (8.0%)	227 (4.5%)	<0.001
Congestive heart failure (%)	4,188 (26.9%)	2,990 (28.3%)	1,198 (23.9%)	<0.001
Myocardial infarction (%)	2,180 (14.0%)	1,584 (15.0%)	596 (11.9%)	0.001
Other heart disease (%)	7,664 (49.2%)	5,373 (50.8%)	2,291 (45.7%)	<0.001
Charcot foot (%)	153 (1.0%)	136 (1.3%)	17 (0.3%)	<0.001
Open wounds (%)	127 (0.8%)	80 (0.8%)	47 (0.9%)	0.415
Osteomyelitis (%)	3,253 (20.9%)	1,744 (16.5%)	1,509 (30.1%)	<0.001
Cellulitis (%)	2,555 (16.4%)	1,178 (11.1%)	1,377 (27.5%)	<0.001
Stump complications (%)	2,517 (16.2%)	2,018 (19.1%)	499 (10.0%)	<0.001
Ulcers (%)	6,901 (44.3%)	3,871 (36.6%)	3,030 (60.5%)	<0.001

Abbreviations: SD = standard deviation, Other Gov = other government programs, CKD/ESRD = chronic kidney disease/end-stage renal disease

Table 2. Primary and secondary outcomes at 6 months before matching

	Overall (N = 15,581)	Major (n = 10,571)	Minor (n = 5,010)	*P* value
Readmitted (%)	7,597 (48.8%)	4,876 (46.1%)	2,721 (54.3%)	<0.001
Reamputation (%)	1,990 (12.8%)	766 (7.2%)	1,224 (24.4%)	<0.001
Major reamputation (%)	1,591 (10.2%)	766 (7.2%)	825 (16.5%)	<0.001
Died (%)	550 (3.5%)	402 (3.8%)	148 (3.0%)	0.057
Wound/skin debridement (%)	658 (4.2%)	404 (3.8%)	254 (5.1%)	0.014
Soft-tissue procedure (%)	344 (2.2%)	256 (2.4%)	88 (1.8%)	0.098
Procedures on bones/joints of lower extremity (%)	132 (0.8%)	106 (1%)	26 (0.5%)	0.066
Osteomyelitis (%)	67 (0.4%)	26 (0.2%)	41 (0.8%)	0.001
Cellulitis (%)	185 (1.2%)	111 (1.0%)	74 (1.5%)	0.178
Postoperative infection (%)	268 (1.7%)	94 (0.9%)	174 (3.5%)	<0.001
Sepsis (%)	1,013 (6.5%)	747 (7.1%)	266 (5.3%)	0.003

Table 3. Conditional logistic regression for outcomes at 1, 3, and 6 months

	Rate: Major	Rate: Minor	OR	95% CI	*P* value
Readmitted					
1 month	189.7	240.7	1.33	(1.23 - 1.45)	<.001
3 months	343	433.6	1.30	(1.23 - 1.38)	<.001
6 months	451.5	547.9	1.25	(1.18 - 1.31)	<.001
Reamputation					
1 month	27.7	94.1	3.57	(3.01 - 4.23)	<.001
3 months	60.6	197.7	3.49	(3.11 - 3.92)	<.001
6 months	71.7	251	3.71	(3.34 - 4.12)	<.001
Reamputation: Major only					
1 month	27.7	65.1	2.44	(2.04 - 2.93)	<.001
3 months	60.4	141.1	2.52	(2.22 - 2.85)	<.001
6 months	71.3	171	2.61	(2.33 - 2.93)	<.001
Died					
1 month	8.3	6.8	0.86	(0.56 - 1.33)	0.501
3 months	21.1	18.4	0.93	(0.71 - 1.22)	0.614
6 months	35.8	30.4	0.89	(0.72 - 1.10)	0.273
DRG: Wound skin debridement					
1 month	13.1	14.7	1.18	(0.86 - 1.63)	0.311
3 months	30.4	35.9	1.31	(1.06 - 1.61)	0.012
6 months	37.1	52.2	1.52	(1.27 - 1.82)	<.001
DRG: Soft-tissue procedure					
1 month	9.1	7.9	0.99	(0.65 - 1.50)	0.964
3 months	17.9	15.4	0.93	(0.69 - 1.25)	0.616
6 months	22.4	18.5	0.91	(0.70 - 1.19)	0.506
DRG: Procedure on bones/joints of the lower extremity					
1 month	1.9	0.4	0.20	(0.04 - 0.98)	0.047
3 months	5.7	3.2	0.53	(0.29 - 0.98)	0.043
6 months	8.3	5.5	0.55	(0.34 - 0.89)	0.015
DRG: Osteomyelitis					
1 month	0	1.3	4×10^9	(0.00 - Inf)	0.999
3 months	1.6	7	3.15	(1.58 - 6.26)	0.001
6 months	2.3	8.1	2.67	(1.48 - 4.83)	0.001
DRG: Cellulitis					
1 month	0.6	4.7	5.25	(1.86 - 14.83)	0.002
3 months	5.1	9	1.56	(0.99 - 2.48)	0.058
6 months	10.9	14.1	1.34	(0.96 - 1.89)	0.088
DRG: Postoperative infection					
1 month	2.8	16.7	6.09	(3.71 - 9.98)	<.001
3 months	6.2	29.9	4.56	(3.23 - 6.43)	<.001
6 months	7.9	36.3	4.45	(3.27 - 6.05)	<.001
DRG: Sepsis					
1 month	22.6	12.8	0.66	(0.49 - 0.89)	0.007
3 months	45.5	31.6	0.72	(0.59 - 0.88)	0.001
6 months	68.4	52.6	0.79	(0.68 - 0.93)	0.004

Odds ratios (OR) and 95% confidence intervals (CI) are presented for the minor amputation group, as compared to the major amputation group. Rate: Major and Rate: Minor are the rates per 1,000 patients that each outcome occurred, stratified by index amputation group, in the matched cohort. DRG (diagnosis-related group) indicates the outcome is cause-specific readmission, as assessed by DRG codes.

FIGURE LEGENDS

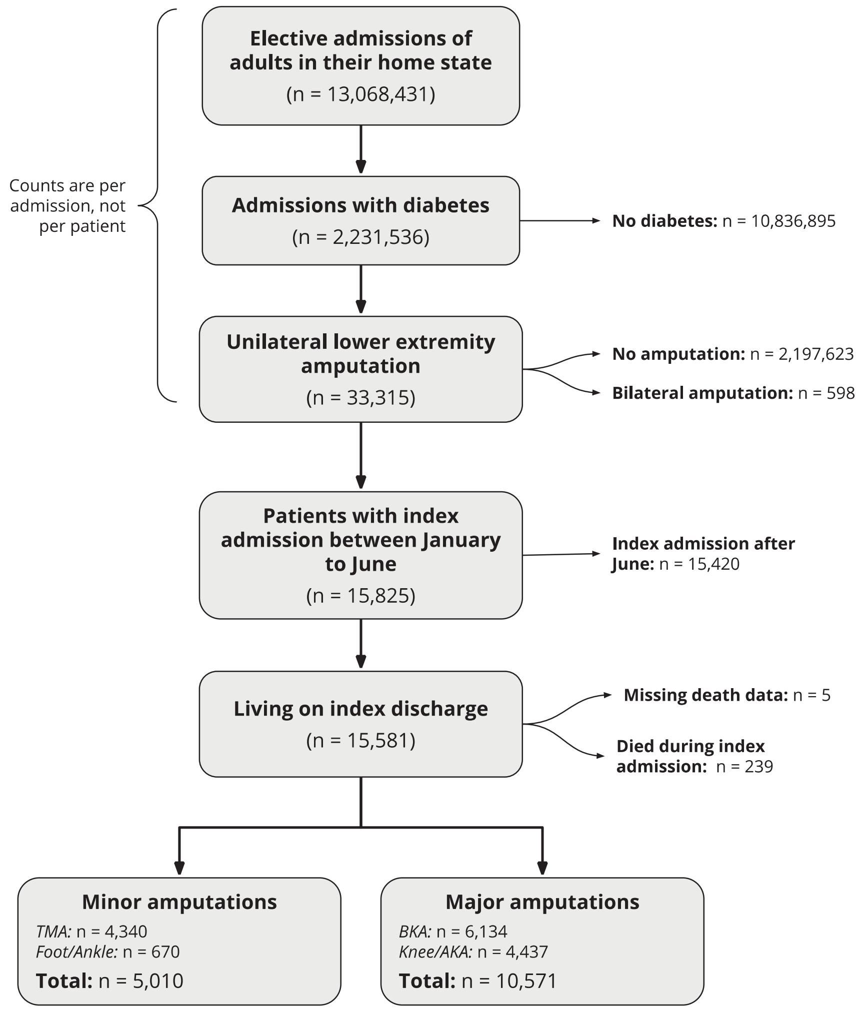

Figure 1. Study flow diagram. The counts for the first 3 boxes are numbers of admissions (indicated by the bracket to the left), while the numbers in the lower four boxes are numbers of patients. Abbreviations: TMA = transmetatarsal amputation, BKA = below the knee amputation, AKA = above the knee amputation.

Supplemental Table S 1: ICD-10 codes used to identify levels of lower extremity amputations

TMA (minor LEA)	0Y6N0Z9, 0Y6M0ZB, 0Y6M0ZC, 0Y6M0ZD, 0Y6M0ZF, 0Y6N0ZB, 0Y6N0ZC, 0Y6N0ZD, 0Y6N0ZF, 0Y6M0Z9
Foot/ankle (minor LEA)	0Y6M0Z0, 0Y6N0Z0, 0Y6N0Z4, 0Y6M0Z5, 0Y6M0Z6, 0Y6M0Z7, 0Y6M0Z8, 0Y6N0Z5, 0Y6N0Z6, 0Y6N0Z7, 0Y6N0Z8, 0Y6M0Z4
BKA (major LEA)	0Y6H0Z1, 0Y6H0Z2, 0Y6H0Z3, 0Y6J0Z1, 0Y6J0Z2, 0Y6J0Z3
Knee/AKA (major LEA)	0Y6F0ZZ, 0Y6G0ZZ, 0Y670ZZ, 0Y680ZZ, 0Y6C0Z1, 0Y6C0Z2, 0Y6C0Z3, 0Y6D0Z1, 0Y6D0Z2, 0Y6D0Z3, 0Y620ZZ, 0Y630ZZ

TMA = transmetatarsal amputation, LEA = Lower extremity amputation, BKA = below the knee amputation, AKA = above the knee amputation

Supplemental Table S2: ICD-10 codes used to identify comorbidities

Comorbidity	**ICD-10 codes**
Smoking	F17.2x
Obesity	AHRQ: Obesity
CKD/ESRD	AHRQ: Renal Failure
	E13.2x
Dialysis	N25.0x, Z49.x, Z99.2x
Hypertension	AHRQ: Hypertension (both uncomplicated and complicated
Peripheral vascular disease	AHRQ: Peripheral vascular disorders
	Z95.9, E13.51, E13.59
Neuropathy	G90.09, G90.8, G90.9, G99.0, G90.01, I95.1, K31.84, N31.9, E11.4x, G57.x, M14.6x
Cerebrovascular disease	Charlson: Cerebrovascular disease
Congestive heart failure	Charlson: Congestive heart failure
Myocardial infarction	Charlson: Myocardial infarction
Other heart disease	I20.x, I25.x, I47.x, I48.x, I49.x
Osteomyelitis*	M86.16x, M86.17x, M86.26x, M86.27x, M86.66x, M86.67x
Charcot's foot*	M14.67x, M14.69
Cellulitis*	L03.03x, L03.115, L03.116, L03.04x, L03.125, L03.126
Ulcers*	E11.621, L97.3x, L97.4x, L97.5x
Open wounds*	S91.x
Stump complications*	T87.3x, T87.4x, T87.5x, T87.8x

*Denotes patients who were matched only if comorbidity was present ipsilateral to the index amputation. AHRQ = Agency for Healthcare Research and Quality, CKD/ESRD = chronic kidney disease/end-stage renal disease. AHRQ: ICD-10 codes from the Elixhauser comorbidity mapping software provided by AHRQ (29). Charlson: ICD-10 codes from Quan adaptation of Charlson comorbidities (30).

Supplemental Table S3: DRG codes used for cause-specific readmissions

Cause for readmission	DRG codes
Cellulitis	602, 603
Osteomyelitis	539 – 541
Postoperative infection	862, 863, 856 – 858
Procedure on bones/joint of lower extremity	492 – 494
Sepsis	870 – 872
Soft-tissue procedures	477 – 479, 500 – 502
Wound/skin debridement	570 – 572, 622 – 624, 463 – 465

DRG = diagnosis-related group

Supplementary Table S4: Primary outcomes, stratified by level of index amputation

	TMA (n = 4,340)	Foot (n = 670)	BKA (n = 6,134)	Knee/AKA (n = 4,437)	*P* value
Readmitted (%)	2,360 (54.4%)	361 (54.0%)	2,756 (44.9%)	2,120 (47.8%)	<0.001
Reamputation (%)	1,042 (24.0%)	182 (27.2%)	567 (9.2%)	199 (4.5%)	<0.001
Major reamputation (%)	674 (15.5%)	151 (22.5%)	567 (9.2%)	199 (4.5%)	<0.001

TMA = transmetatarsal amputation, BKA = below the knee amputation, AKA = above the knee amputation