Predictors of Long-Term Mortality in Patients Undergoing Major or Minor Lower-Extremity Amputations

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Abstract

Purpose. Amputation as the initial treatment of choice remains prevalent despite advances in revascularization techniques and medical therapy. We evaluated the 7-year mortality of patients undergoing major and minor lower-extremity amputations and determined the impact of risk factors on long-term mortality. **Methods.** Patients undergoing non-traumatic lower-extremity amputations from 2011 to 2017 were retrospectively studied at a single-center community hospital. Patients were divided into cohorts based on major or minor amputation. Kaplan-Meier analysis was used to assess long-term survival out to 7 years. Univariate and multivariate analyses identified predictors of long-term mortality. We further analyzed the incremental impact of multiple atherosclerotic risk factors on long-term mortality. **Results.** A total of 698 patients were included, of which 309 patients (44%) underwent major amputations and 389 (56%) underwent minor amputations. Patients with major amputations had 1-, 5-, and 7-year mortality of 20%, 53%, and 65%, respectively and patients with minor amputations had 1-, 5-, and 7-year mortality of 12%, 40%, and 51%, respectively ($P<.001$). Multivariate analysis demonstrated that coronary artery disease (CAD) (odds Ratio [OR], 3.25; $P<.001$), chronic kidney disease (CKD) (OR, 2.3; $P<.001$), and major amputations (OR, 1.5; $P=.02$) were predictors of long-term mortality. Coexistence of >2 atherosclerotic risk factors (hyperlipidemia, diabetes mellitus, CAD, and CKD) was associated with significant increase in long-term mortality. **Conclusion.** Long-term (7-year) mortality remains high after major and minor amputations in this contemporary dataset. Major amputation, CAD, and CKD are independent risk factors for long-term mortality. Coexistence of multiple atherosclerotic risk factors is associated with significantly high mortality and poor 7-year prognosis.

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Key words: amputation, atherosclerosis, critical limb ischemia, diabetic foot ulcer, mortality

As of 2005, there were approximately 1.6 million people living with amputations in the United States, with these numbers expected to double by 2050.[1] Vascular disease, traumatic accidents, and cancer are the 3 major reasons for amputations, with vascular disease accounting for the majority of cases. With the overall increasing age of the population and more patients suffering from multiple risk factors, such as diabetes mellitus (DM) and coronary artery disease (CAD), the incidence of lower-extremity amputation continues to rise as primary amputation, without revascularization, has remained the first-line therapy for a majority of the population.[1-8]

Major amputations result in increased mortality, risk of subsequent amputations, and inflated healthcare costs.[9] Current studies are limited by data from previous decades and the maximum long-term mortality previously reported is only out to 5 years. Multiple studies demonstrate mortality rates after major amputation ranging from 8%-20% at 30 days, 40%-50% at 1 year, and 77%-85% at 5 years.[8,10-12] Over the past decade, there has been significant improvement in revascularization therapies, wound care, and reinforcement from major vascular societies promoting limb salvage and establishment of multidisciplinary care teams.[13-18] It would be anticipated that implementation of these strategies would improve mortality rates after amputation. Yet, there remains a discordance in the dissemination of comprehensive, guideline-based vascular care and we do not know the overall impact of these recent advancements on long-term mortality.

In this study, we evaluated the following: (1) contemporary 7-year mortality among patients who underwent non-traumatic major and minor amputations in a rural community hospital; (2) predictors of long-term mortality; and (3) aggregate impact of multiple atherosclerotic risk factors on long-term mortality.

Methods

Patients. This retrospective chart review was conducted at a rural community hospital and comprised patients who received a lower-extremity amputation in the contemporary era from 2011 to 2017. Patients were identified using the Internal Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and ICD-10 codes for lower-extremity amputations (**Appendix 1** and **Appendix 2**). All traumatic and cancer-related amputations were excluded. Patients undergoing amputations secondary to acute limb ischemia, critical limb ischemia (CLI), and diabetic foot ulcer were included in the study. Institutional review board approval was obtained from the Western Institutional Review Board and the requirement for informed consent was waived as no patients were contacted for this study.

Amputations. Patients were divided into cohorts based on the level of amputation (major or minor). *Major amputation* was defined as transection occurring proximal to the tarsometatarsal joint, which included transtibial, below-the-knee, and above-the-knee amputations. *Minor amputation* was defined as transection occurring distal to the tarsometatarsal joint, which included toe(s), transmetatarsal, Chopart, and Lisfranc amputations.

Any first major amputation (even if the patient received a prior minor amputation during the study) that occurred during the study period was included in the major amputation cohort. Any subsequent major or minor amputation(s) on the same patient were excluded from analysis. In patients who had only minor amputation(s), the first minor amputation was included in the minor amputation cohort. Any subsequent amputation(s) on the same patient were excluded. *Primary amputation* is defined as any amputation occurring without either surgical or endovascular revascularization intervention occurring within the year leading up to amputation.

Baseline demographics. Charts were reviewed for age, gender, race/ethnicity, and the presence of risk factors, including hypertension, hyperlipidemia (HLD), DM, chronic kidney disease (CKD; defined as glomerular filtration rate ≤60 mL/min/1.73 m^2), CAD, peripheral artery disease, and obesity (body mass index >30 kg/m^2) documented in the history. Smoking was considered present if the patient was either a current or former smoker. History of prior amputation, presence of a wound, and clinical diagnosis of osteomyelitis or gangrene prior to amputation were also collected.

In-hospital outcomes. The in-hospital outcomes that were assessed included length of stay, discharge destination (either home or skilled nursing facility/rehabilitation facility), and in-hospital mortality.

Long-term mortality. Long-term mortality was collected from 2011 to 2017 and included the early release data from 2018 using the United States National Death Index. The National Death Index is a centralized database of death record information on file in the state vital statistics offices established by the National Center for Health Statistics.[19] Detailed records including patient's name, date of birth, social security number, age, gender, race, marital status, and state of residence were submitted, as available. Each patient who received matching records within the database was reviewed in detail to validate mortality based on the number of matching components within the records.

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Patient risk factors. The risk factors HLD, DM, CAD, and CKD were chosen to analyze for mortality since they have been identified as atherosclerotic risk factors for poor outcomes and mortality in patients with peripheral arterial disease. Hypertension was not analyzed since it was present in nearly 90% of this patient population and previous CLI studies/models have shown that other comorbidities better explain adverse events and mortality rates seen in patients with peripheral arterial disease and CLI. All patients were classified into 4 groups based on the cumulative number of the chosen risk factors present. To assess the long-term mortality, Kaplan-Meier survival curve analysis was performed based on the coexistence of 1, 2, 3, and 4 risk factors.

Statistical analysis. XLSTAT, version 2019.3.2 (XLSTAT-LifeScience Data Analysis and Statistical Solutions) was used for data collection and statistical analysis. Values presented are number (%) or mean ± standard deviation. Kaplan-Meier analysis (confidence interval [CI] determined via the Greenwood method and log-rank test statistic for comparison of survival functions/curves) was used to estimate freedom from death. For multiple comparisons, the adjusted *P*-values were generated via the Dunn-Sidak statistical method. In addition, logistic-regression multivariable analyses for predictors of death were conducted on all subjects. Briefly, a forward stepwise model selection was utilized with a likelihood ratio criterion and a probability for entry and removal in the multivariable model of 0.1 and 0.2, respectively. The overall classic logistic model was set to a tolerance of 0.001, CI of 95%, stop conditions of 100 iterations, a convergence of 0.000001, and a constraint of a 1=0. Variables included in a univariable model were age, race/ethnicity, obesity, smoking, CKD, DM, HLD, CAD, gangrene, prior amputation, and major amputation. Of the variables included in the univariable model, CAD, CKD, DM, age, prior amputation, and major amputation met the criterion (as described above) for inclusion in the multivariable model. To assess the trends in mortality between major and minor

TABLE 1. Baseline demographics and clinical characteristics.

Characteristics	Major Amputation (n = 309)	Minor Amputation (n = 389)	*P*-Value
Age (years)	62.7 ± 13.7	63.3 ± 14.2	.72
Male gender	209 (67.6%)	261 (67.1%)	.88
Race/ethnicity			.42
Caucasian	216 (69.9%)	275 (70.7%)	
Black	20 (6.5%)	16 (4.1%)	
Asian	2 (0.6%)	1 (0.3%)	
Hispanic	71 (23.0%)	97 (24.9%)	
Obese (body mass index >30 kg/m^2)	142 (46.0%)	168 (43.2%)	.46
Peripheral artery disease	141 (45.6%)	167 (42.9%)	.48
Smoker	155 (50.2%)	195 (50.1%)	.99
Chronic kidney disease	107 (34.6%)	116 (29.8%)	.18
Diabetes mellitus	215 (69.6%)	304 (78.1%)	.01
Hyperlipidemia	210 (68.0%)	252 (64.8%)	.38
Hypertension	270 (87.4%)	344 (88.4%)	.67
Coronary artery disease	139 (45.0%)	149 (38.3%)	.08
Gangrene	140 (45.3%)	179 (46.0%)	.93
History of prior amputation	76 (24.6%)	93 (23.9%)	.83
Wound	294 (95.1%)	366 (94.1%)	.54
Osteomyelitis	118 (38.2%)	142 (36.5%)	.80

Data presented as count (%) or mean ± standard deviation.
P-values for quantitative variables are from the Mann-Whitney U test. *P*-values for qualitative variables are from the Chi-square test or the Fisher's exact test (if theoretical frequencies were <5).

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amputations, Mann-Kendall test was performed. The threshold of statistical significance was $P<.05$.

Results

A total of 698 patients were identified as having undergone non-traumatic lower-extremity amputation(s) during the study period. Major amputations were performed in 309 patients (44%) and minor amputations were performed in 389 patients (56%).

Baseline characteristics. Baseline characteristics of the 2 cohorts are described in **Table 1**. The average age was 62.7 ± 13.7 years in the major amputation group and 63.3 ± 14.2 years in the minor amputation group (P=.72). There was no statistical difference between any of the baseline characteristics, except patients who underwent minor amputations had a higher prevalence of DM (78%) compared with patients who underwent major amputations (70%; P=.01). There was no statistically significant difference in clinical presentation between major and minor amputations: wound (95% vs 94%, respectively; P=.54), gangrene (45% vs 46%, respectively; P=.93), and clinical osteomyelitis (38% vs 36%, respectively; P= .80).

In-hospital outcomes. The length of stay was significantly higher in patients who underwent major amputations (12.1 days) compared with minor amputations (10.1 days; $P<.001$) (**Table 2**). A majority of the major amputation patients were discharged to a skilled nursing facility (61%) and 37% of the patients were discharged to home ($P<.001$). A majority of the minor amputation patients were discharged home (72%), with 28% discharged to a skilled nursing/rehabilitation facility ($P<.001$). There was a numerically higher trend for in-hospital mortality among patients who underwent major amputations, although it did not reach statistical significance (P=.05).

Long-term mortality. The 7-year mortality rates for patients undergoing major or minor amputations are demonstrated in the bar graph and Kaplan-Meier analysis (**Figure 1** and **Figure 2**). The mean survival time was significantly higher for patients undergoing minor amputations (5.4 years) vs major amputations

TABLE 2. In-hospital outcomes.

	Major Amputation (n = 309)	Minor Amputation (n = 389)	*P*-Value
Length of Stay (days)	12.1 ± 8.8	10.1 ± 8.9	<.001
Discharge destination			<.001
Home	115 (37.2%)	280 (72.0%)	<.001
Skilled nurse facility/ rehabilitation	189 (61.2%)	108 (27.8%)	<.001
In-hospital mortality	5 (1.6%)	1 (0.3%)	.05

Data presented as count (%) or mean ± standard deviation.
P-values for quantitative variables are from the Mann-Whitney U test. *P*-values for qualitative variables are from the Chi-square test or the Fisher's exact test (if theoretical frequencies were <5).

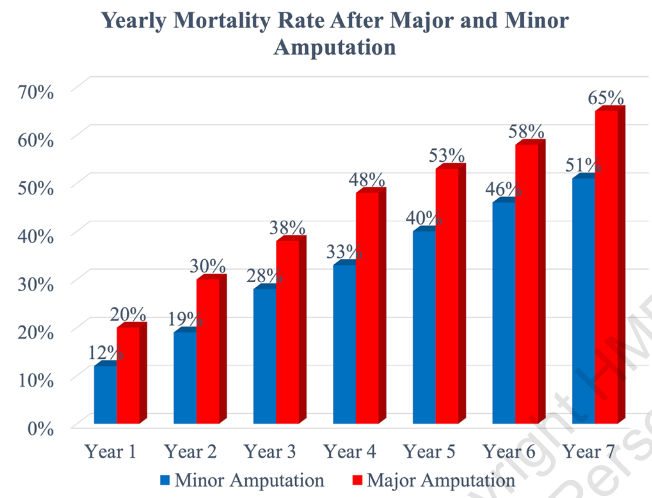
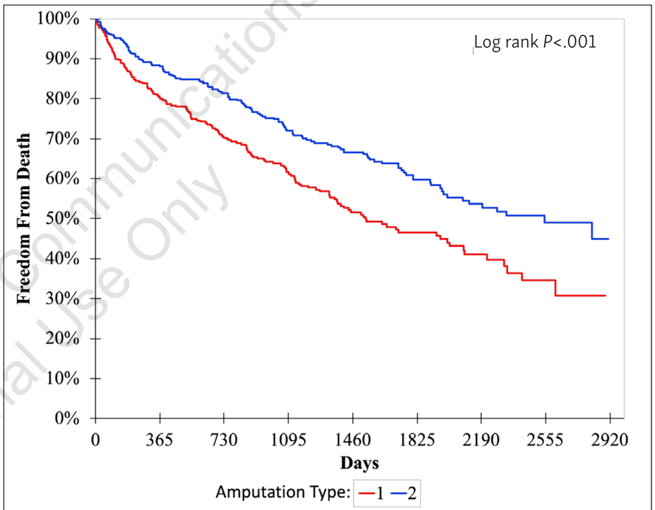


FIGURE 1. Bar graph demonstrating the yearly mortality rates of patients with major and minor amputations for 7 years.



Years	0	1	2	3	4	5	6	7	8
Days	0	365	730	1095	1460	1825	2190	2555	2920
(1) Major AMP									
At risk	309	248	193	146	95	62	43	12	1
Events	0	61	90	112	133	141	146	151	152
FF Death ± SE (%)	100 ± 0.0	80.2 ± 2.3	70.3 ± 2.6	61.6 ± 2.9	51.6 ± 3.2	46.6 ± 3.3	42.1 ± 3.6	34.5 ± 4.3	30.7 ± 5.3
Mean survival time	1617 days (4.4 years)								
(2) Minor AMP									
At risk	389	342	273	198	156	97	61	28	1
Events	0	46	71	99	113	126	134	138	139
FF Death ± SE (%)	100 ± 0.00	88.1 ± 1.6	81.3 ± 2.0	72.0 ± 2.4	66.5 ± 2.7	59.7 ± 3.0	53.6 ± 3.4	49.0 ± 3.8	44.9 ± 5.3
Mean survival time	1972 days (5.4 years)								

FIGURE 2. Kaplan-Meier survival analysis over 7 years from the date of first major or minor amputation.

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(4.4 years). The mortality rates for patients at 1, 5, and 7 years were 20%, 53%, and 65% for major amputations and 12%, 40%, and 51%, respectively, for minor amputations (log rank *P*<.001).

When the mortality trends were analyzed, there was significant difference in mortality trends from year 0 to year 7 (*P*=.046). There was significant difference in mortality between major and minor amputations in year 0-year 1 (*P*<.01). When the analysis was performed excluding the first year, ie, year 1 to year 7, the trend analysis did not reach clinical significance (*P*=.17).

Predictors of long-term mortality. A multivariate analysis was conducted to identify independent variables associated with increased mortality. Variables that reached statistical significance are summarized in **Table 3**. This demonstrated that patients with a history of CAD had 3.3 times higher odds (*P*<.001), history of CKD had 2.3 times higher odds (*P*<.001), and patients undergoing major amputations had 1.5 times higher odds of long-term mortality (*P*=.02). Patients with history of DM were found to have protective impact on long-term mortality (odds ratio, 0.64; *P*=.02).

Long-term mortality with individual risk factors. Four major atherosclerotic risk factors (HLD, DM, CAD, and CKD) were analyzed individually for long-term survival in all patients (**Figure 3**). Patients with a single risk factor of HLD, CAD, or CKD demonstrated increased mortality after any amputation. DM did not have any impact on mortality after amputation.

TABLE 3. Multivariate analysis of predictors of long-term mortality for all patients.

	All Amputation Patients (n = 698)	
	Odds Ratio (95% CI)	*P*-Value
Coronary artery disease	3.255 (2.221-4.772)	<.001
Chronic kidney disease	2.327 (1.640-3.303)	<.001
Major lower-extremity amputation	1.511 (1.083-2.109)	.02

Significant predictors shown. CI = confidence interval.

Long-term mortality for cumulative risk factors. There was not a significant difference between the presence of 1 risk factor vs 2 (*P*=.68) (**Figure 4**). Patients with 3 or 4 aggregate risk factors demonstrated increased mortality at 1, 5, and 7 years (3 risk factors: 17%, 53%, and 74%; 4 risk factors : 31%, 74%, and 83%, respectively).

Discussion

The main results of this study were: (1) patients undergoing major amputations had longer length of stay and were more frequently discharged to a skilled nursing facility or rehabilitation as opposed to discharged to home; (2) major amputation is associated with higher 7-year mortality compared with minor amputation, and this appears driven by differences in the first year; (3) in order of hazard, CAD, CKD, and major amputation were independent predictors of mortality for patients undergoing amputations; and (4)coexistence of >2 atherosclerotic risk factors was associated with a substantial increase in 7-year mortality.

CLI and subsequent major amputations carry a 5-year mortality rate of 60% in previous studies.[20] These mortality rates are higher than 5-year mortality rates of ovarian cancer (53%), myeloma (50%), leukemia (39%), colorectal cancer (35%), and breast cancer (10%), prompting recent interest in multidisciplinary care, early revascularization, and high adherence to guideline-directed medical treatment.[21] Our study evaluated the 7-year mortality of patients undergoing major and minor amputations in a contemporary dataset. It is promising that in our population, the 5-year mortality was 40% for minor amputations and 53% for major amputations. Even though the mortality rate is lower than previous reports, direct comparison is difficult considering the heterogeneity of the population and the inclusion of both major and minor amputations. In our study, we report a 7-year mortality of 65% for patients undergoing major amputations and 51% for patients undergoing minor amputations, indicating a continual increase in mortality up to 7 years.

Minor amputations have a lower in-hospital mortality and improved outcomes compared with patients undergoing major amputations.[22] However, there are limited data on whether the short-term mortality benefits of minor amputations persist on long-term follow-up. This study demonstrated the mortality advantage for patients undergoing minor amputations persisted out to 7 years, although this remains driven by differences in the first year. We also found that major amputation was an independent predictor of mortality in this study. In landmark analysis after one year, there was no difference in trends for mortality between major and minor amputations. It is likely that the higher surgical risk of a major amputation on the cardiovascular system, impaired mobility, longer length of stay, and more frequent discharge to long-term care facilities contributed to early mortality.

The clinical relevance of this finding is that the avoidance of major amputation itself may impact the 1-year and hence long-term mortality of CLI patients. Regardless of revascularization strategy, whether endovascular or surgical, it is likely that a subset of major amputations may be converted to minor amputation or delayed amputation, potentially improving early and long-term mortality.[23-25] Conservative management of lower-extremity non-healing wounds would not increase mortality in selected patients and has been reported previously.[26] We also found that major amputation patients had higher likelihood of being discharged to a skilled nursing/rehabilitation facility rather than being discharged home, which causes an increased burden upon the healthcare system and potential for nosocomial infection.[9,27] From these observations in the literature, it is reasonable to assume that prompt and complete revascularization with the intention of conversion of major amputation to a minor amputation (or deferred amputation) improves mobility and independence, allows patients to return home, and may improve quality of life, healthcare costs, length of stay, and long-term mortality, although further data in this space would be required.

The long-term mortality for patients undergoing any amputation gradually increased beyond 1 year. This could be due to associated risk factors. In a multivariate analysis, we confirmed that the atherosclerotic risk factors of CAD and CKD are independent predictors for long-term mortality, which has been validated in multiple studies.[28-30] The coexistence of 1 or 2 atherosclerotic risk factors did not significantly increase mortality; however, coexistence of 3 and 4 risk factors reduced the survival by an average of 1.2 years. Interestingly, the presence of DM tracked with lower mortality. However, as the prevalence of DM was higher among patients with minor amputations, it is possible that this association confounded the potential impact of this known risk factor. Clinically, this information may help with risk stratification for patients with multiple atherosclerotic risk factors when discussing long-term prognosis. Optimal treatment of atherosclerotic risk factors, aggressive medical therapy, smoking cessation, and exercise are likely as important as performing timely revascularization in determining long-term mortality. Multiple studies have also shown that statin therapy can reduce mortality in patients

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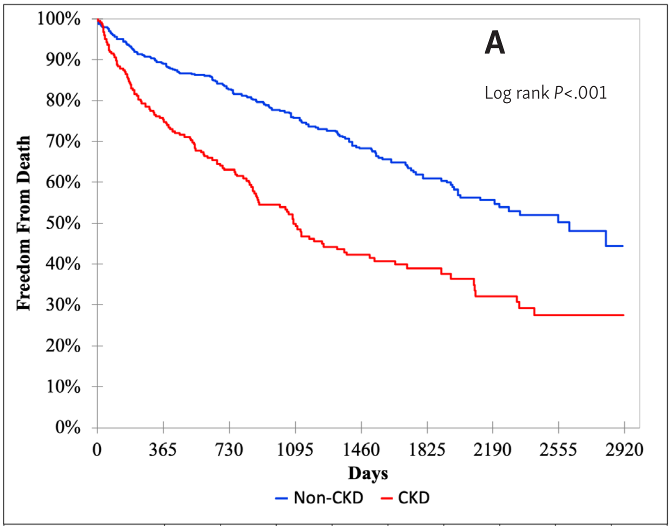
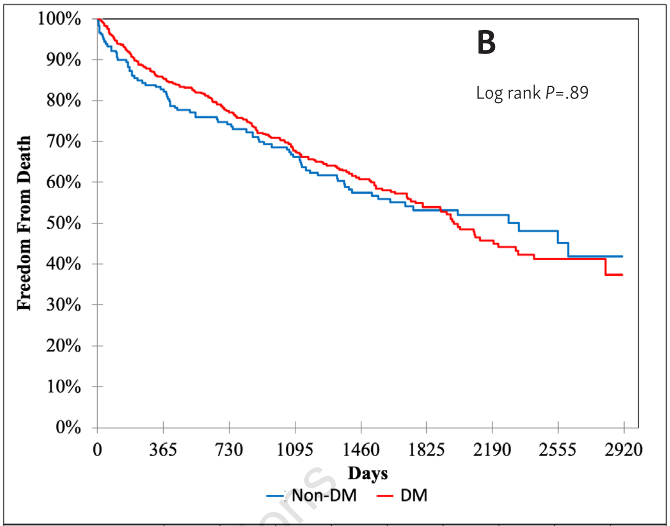
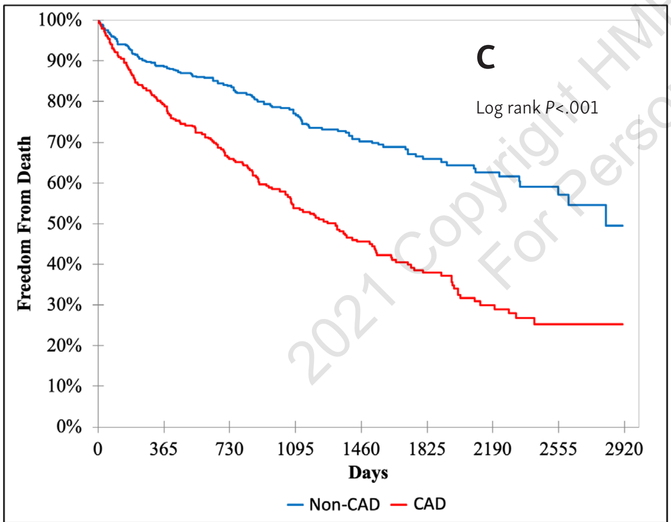


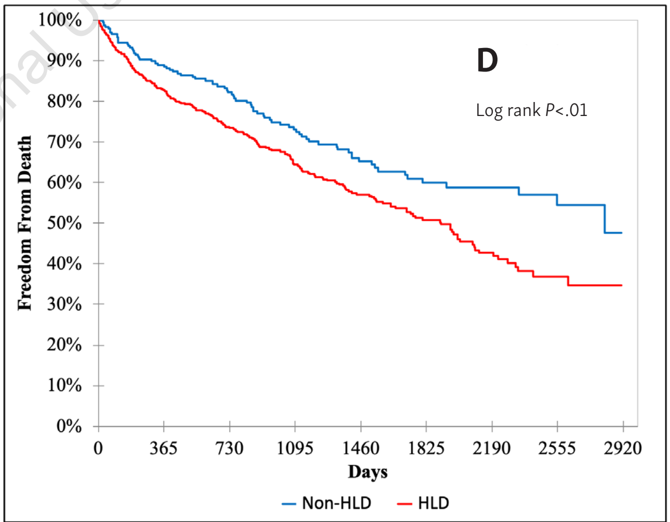
Years	0	1	2	3	4	5	6	7	8
Days	0	365	730	1095	1460	1825	2190	2555	2920
CKD									
At risk	223	167	129	83	58	38	24	11	1
Events	0	55	81	105	117	121	126	129	129
FF Death ± SE (%)	100 ± 0.0	75.3 ± 2.9	63.0 ± 3.3	49.8 ± 3.5	42.2 ± 3.6	38.9 ± 3.7	32.1 ± 4.1	27.4 ± 4.3	27.4 ± 4.3
Mean survival time	1414 days (3.9 years)								
Non-CKD									
At risk	475	423	338	260	193	121	69	29	1
Events	0	52	80	106	129	146	155	160	162
FF Death ± SE (%)	100 ± 0.00	89.0 ± 1.4	82.7 ± 1.8	75.7 ± 2.1	68.3 ± 2.4	61.0 ± 2.7	55.6 ± 3.0	50.3 ± 3.6	44.4 ± 5.2
Mean survival time	2013 days (5.5 years)								



Years	0	1	2	3	4	5	6	7	8
Days	0	365	730	1095	1460	1825	2190	2555	2920
DM									
At risk	519	442	344	236	171	105	60	24	1
Events	0	75	115	152	174	190	203	208	209
FF Death ± SE (%)	100 ± 0.0	85.5 ± 1.5	77.2 ± 1.9	67.7 ± 2.2	60.7 ± 2.4	53.9 ± 2.7	45.8 ± 3.1	41.2 ± 3.4	37.5 ± 4.7
Mean survival time	1814 days (5.0 years)								
Non-DM									
At risk	179	148	123	107	80	54	33	16	1
Events	0	32	46	59	72	77	78	81	82
FF Death ± SE (%)	100 ± 0.00	82.1 ± 2.9	74.1 ± 3.3	66.1 ± 3.6	57.5 ± 3.9	53.2 ± 4.0	52.0 ± 4.1	45.2 ± 5.2	42.0 ± 5.7
Mean survival time	1802 days (4.9 years)								



Years	0	1	2	3	4	5	6	7	8
Days	0	365	730	1095	1460	1825	2190	2555	2920
CAD									
At risk	288	227	171	117	87	56	31	13	1
Events	0	60	96	124	141	154	164	168	168
FF Death ± SE (%)	100 ± 0.0	79.1 ± 2.4	66.0 ± 2.8	53.8 ± 3.1	45.5 ± 3.2	37.9 ± 3.3	30.0 ± 3.4	25.3 ± 3.6	25.3 ± 3.6
Mean survival time	1445 days (4.0 years)								
Non-CAD									
At risk	410	363	295	226	164	103	62	27	1
Events	0	47	65	87	105	113	117	121	123
FF Death ± SE (%)	100 ± 0.00	88.5 ± 1.6	83.8 ± 1.8	77.0 ± 2.2	70.3 ± 2.5	65.9 ± 2.8	62.6 ± 3.1	57.1 ± 3.9	49.6 ± 6.3
Mean survival time	2104 days (5.8 years)								



Years	0	1	2	3	4	5	6	7	8
Days	0	365	730	1095	1460	1825	2190	2555	2920
HLD									
At risk	462	380	298	217	163	100	55	20	1
Events	0	80	120	153	176	191	204	210	211
FF Death ± SE (%)	100 ± 0.0	82.6 ± 1.8	73.5 ± 2.1	64.4 ± 2.4	57.1 ± 2.5	50.8 ± 2.7	42.7 ± 3.1	36.9 ± 3.5	34.6 ± 4.0
Mean survival time	1711 days (4.7 years)								
Non-HLD									
At risk	236	210	168	126	88	59	38	20	1
Events	0	27	41	58	70	76	77	79	80
FF Death ± SE (%)	100 ± 0.00	88.6 ± 2.1	82.2 ± 2.5	73.1 ± 3.1	65.2 ± 3.5	59.9 ± 3.8	58.7 ± 3.9	54.5 ± 4.7	47.7 ± 7.6
Mean survival time	2022 days (5.5 years)								

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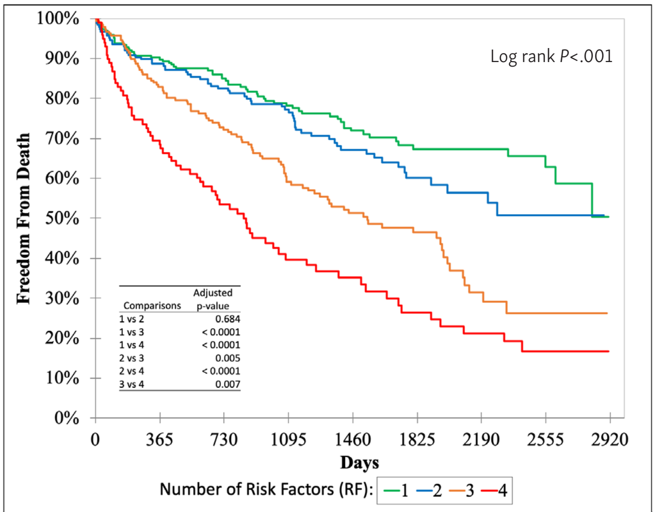
FIGURE 3. Kaplan-Meier survival analysis for the presence of different risk factors: (A) chronic kidney disease (CKD); (B) diabetes mellitus (DM); (C) coronary artery disease (CAD); and (D) hyperlipidemia (HLD). FF = freedom from; SE = standard error.



Years	0	1	2	3	4	5	6	7	8
Days	0	365	730	1095	1460	1825	2190	2555	2920
RF1									
At risk	225	203	163	128	95	67	44	21	1
Events	0	23	33	45	54	59	59	61	63
FF Death ± SE (%)	100 ± 0.0	89.8 ± 2.0	85.0 ± 2.4	78.2 ± 2.9	71.9 ± 3.4	67.4 ± 3.7	67.4 ± 3.7	62.8 ± 4.7	50.4 ± 9.2
Mean survival time	2169 days (5.9 years)								
RF2									
At risk	187	166	135	107	75	41	23	10	1
Events	0	21	32	40	53	59	61	63	63
FF Death ± SE (%)	100 ± 0.00	88.7 ± 2.3	82.5 ± 2.8	77.2 ± 3.2	67.2 ± 3.8	60.1 ± 4.4	56.4 ± 4.8	50.8 ± 5.8	50.8 ± 5.8
Mean survival time	1990 days (5.5 years)								
RF3									
At risk	187	156	121	82	62	37	15	6	1
Events	0	32	51	70	80	85	94	96	96
FF Death ± SE (%)	100 ± 0.00	82.9 ± 2.8	72.2 ± 3.3	59.1 ± 3.9	51.3 ± 4.1	46.5 ± 4.2	31.4 ± 5.1	26.2 ± 5.4	26.2 ± 5.4
Mean survival time	1572 days (4.3 years)								
RF4									
At risk	99	67	49	28	21	16	13	5	1
Events	0	31	45	56	59	64	67	69	69
FF Death ± SE (%)	100 ± 0.00	68.5 ± 4.7	53.5 ± 5.1	39.7 ± 5.2	35.2 ± 5.3	26.4 ± 5.2	21.1 ± 5.0	16.8 ± 4.8	16.8 ± 4.8
Mean survival time	1140 days (3.1 years)								

FIGURE 4. Kaplan-Meier survival analysis over 7 years following first major or minor amputation for cumulative risk factors. FF = freedom from; RF = risk factor; SE = standard error.

with peripheral arterial disease and those undergoing amputations.[31,32] As far as we know, this is the first study demonstrating the incremental effect of multiple atherosclerotic risk factors on long-term mortality for patients undergoing amputations, validating the current drive toward CLI teams with aggressive, multi-disciplinary care. In addition, the more than 3-fold increased odds of mortality among patients with CAD suggests aggressive surveillance and management of this risk factor in particular is paramount.

Study limitations. There are inherent limitations given the retrospective nature of this study. However, a randomized controlled trial is unlikely as revascularization therapies are proven to be beneficial compared with primary amputation, and the decision to perform major vs minor amputation is clinically driven. The medical therapy and revascularization strategies were not reported in this study, and therefore we cannot account for differences in pharmacologic or endovascular treatment leading up to or in the years following amputation. Mortality information was obtained from the National Death Index. Although administrative databases are prone to errors, patient-level data collected from our institution and multiple patient identifiers submitted could decrease potential bias. Other confounding variables, such as (but not limited to) congestive heart failure, dementia/delirium, and ambulatory status, which were not reported in this study, could have impact on the long-term mortality. The quality of life after amputations as long-term health outcome was not reported in this study.

Conclusion

This is the first study demonstrating long-term, 7-year mortality in a contemporary population undergoing major and minor amputations in the United States. Mortality is highest in the first year, with a trend of higher mortality in patients undergoing major amputation, and continues to increase over time. Logistic multivariable analysis indicated that CAD, CKD, and major amputation are predictors of long-term mortality in this patient population. The coexistence of 3 or more atherosclerotic risk factors is associated with a significant incremental increase on long-term mortality. Further studies are needed to see whether multidisciplinary teams prioritizing early complete revascularization will improve outcomes in this complex patient population.

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Supplemental Materials

APPENDIX 1. ICD-9 procedural coding to identify patients with lower-extremity amputations between 2011-2017.

ICD-9 Procedural Codes	Description
84.17	Above the knee -Amputation of leg through femur -Amputation of thigh -Conversion of below-knee amputation to above-knee amputation -Supracondylar above-knee amputation
84.15	Below the knee -Amputation of leg through tibia and fibula
84.16	Disarticulation of knee -Batch, Spitler, and McFadden amputation -Mazet amputation -S.P. Rogers amputation
84.12	Amputation through foot -Amputation of forefoot -Amputation through middle of foot -Chopart's amputation -Midtarsal amputation -Transmetatarsal amputation
84.11	Amputation of toe -Amputation through metatarsophalangeal joint -Disarticulation of toe -Metatarsal head amputation -Ray amputation of foot

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APPENDIX 2. ICD-10 procedural coding to identify patients with lower-extremity amputations between 2011-2017.

ICD-10 Procedural Codes	Description
Above the knee	
0Y6D0Z1	Detachment at left upper leg, high, open approach
0Y6C0Z1	Detachment at right upper leg, high, open approach
0Y6D0Z2	Detachment at left upper leg, mid, open approach
0Y6C0Z2	Detachment at right upper leg, mid, open approach
0Y6D0Z3	Detachment at left upper leg, low, open approach
0Y6C0Z3	Detachment at right upper leg, low, open approach
Below the knee	
0Y6J0Z1	Detachment at left lower leg, high, open approach
0Y6H0Z1	Detachment at right lower leg, high, open approach
0Y6J0Z2	Detachment at left lower leg, mid, open approach
0Y6H0Z2	Detachment at right lower leg, mid, open approach
0Y6J0Z3	Detachment at left lower leg, low, open approach
0Y6H0Z3	Detachment at right lower leg, low, open approach
Foot (complete) (Chopart, Lisfranc, disarticulation through the ankle, transmetatarsal)	
0Y6N0Z0	Detachment at left foot, complete, open approach
0Y6M0Z0	Detachment at right foot, complete, open approach
Foot (partial) (metatarsal shaft, transmetatarsal, metatarsal level)	
0Y6N0Z9	Detachment at left foot, partial 1st ray, open ppproach
0Y6N0ZB	Detachment at left foot, partial 2nd ray, open ppproach
0Y6N0ZC	Detachment at left foot, partial 3rd ray, open ppproach
0Y6N0ZD	Detachment at left foot, partial 4th ray, open ppproach
0Y6N0ZF	Detachment at left foot, partial 5th ray, open ppproach
0Y6M0Z9	Detachment at right foot, partial 1st ray, open ppproach
0Y6M0ZB	Detachment at right foot, partial 2nd ray, open ppproach
0Y6M0ZC	Detachment at right foot, partial 3rd ray, open ppproach
0Y6M0ZD	Detachment at right foot, partial 4th ray, open ppproach
0Y6M0ZF	Detachment at right foot, partial 5th ray, open ppproach
Toes	
0Y6N0Z4	Detachment at left foot, partial 1st ray, open ppproach
0Y6M0Z4	Detachment at left foot, partial 2nd ray, open ppproach
0Y6N0Z5	Detachment at left foot, partial 3rd ray, open ppproach
0Y6M0Z5	Detachment at left foot, partial 4th ray, open ppproach
0Y6N0Z6	Detachment at left foot, partial 5th ray, open ppproach
0Y6M0Z6	Detachment at right foot, partial 1st ray, open ppproach
0Y6N0Z7	Detachment at right foot, partial 2nd ray, open ppproach
0Y6M0Z7	Detachment at right foot, partial 3rd ray, open ppproach
0Y6N0Z8	Detachment at right foot, partial 4th ray, open ppproach
0Y6M0Z8	Detachment at right foot, partial 5th ray, open ppproach

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