Trends in the incidence, treatment, and outcomes of acute lower extremity ischemia in the United States Medicare population

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Objective: **Acute lower extremity ischemia (ALI) is a common vascular surgery emergency associated with high rates of morbidity and mortality. The purpose of this study was to assess contemporary trends in the incidence of ALI, the methods of treatment, and the associated mortality and amputation rates in the U.S. Medicare population.**

Methods: **This was an observational study using Medicare claims data between 1998 and 2009. Outcomes examined included trends in the incidence of ALI; trends in interventions for ALI; and trends in amputation, mortality, and amputation-free survival rates.**

Results: **Between 1998 and 2009, the incidence of hospitalization for ALI decreased from 45.7 per 100,000 to 26.0 per 100,000 (*P* for trend < .001). The percentage of patients undergoing surgical intervention decreased from 57.1% to 51.6% (*P* for trend < .001), whereas the percentage of patients undergoing endovascular interventions increased from 15.0% to 33.1% (*P* for trend < .001). In-hospital mortality rates decreased from 12.0% to 9.0% (*P* for trend < .001), whereas 1-year mortality rates remained stable at 41.0% and 42.5% (*P* for trend not significant). In-hospital amputation rates remained stable at 8.1% and 6.4% (*P* for trend not significant), whereas 1-year amputation rates decreased from 14.8% to 11.0% (*P* for trend < .001). In-hospital amputation-free survival after hospitalization for ALI increased from 81.2% to 85.4% (*P* for trend < .001); however, 1-year amputation-free survival remained unchanged.**

Conclusions: **Between 1998 and 2009, the incidence of ALI among the U.S. Medicare population declined significantly, and the percentage of patients treated with endovascular techniques markedly increased. During this time, 1-year amputation rates declined. Furthermore, although in-hospital mortality rates declined after presentation with ALI, 1-year mortality rates remained unchanged. (J Vasc Surg 2014;60:669-77.)**

Acute lower extremity ischemia (ALI) resulting from arterial thrombosis, arterial embolus, or bypass graft thrombosis remains one of the most common vascular surgery emergencies. The postprocedure rates of mortality and limb loss have traditionally been reported to be as high as 20% to 40% and 12% to 50%, respectively.[1-8] However, the contemporary incidence of patients presenting with ALI and the outcomes after intervention in this patient population remain ill-defined. This is an especially relevant question in view of the substantial increase in the use of endovascular therapy during the past decade.

Conventional treatment of patients with ALI has been systemic anticoagulation and emergent open surgical intervention, specifically thromboembolectomy or bypass.

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Endovascular therapy and, more specifically, the use of catheter-directed thrombolytic therapy were initially described in several randomized controlled trials in the mid-1990s.[9-14] An endovascular therapeutic approach offers a less invasive alternative to conventional open surgical revascularization but often requires more time to restore arterial flow and can be associated with higher rates of hemorrhage. Despite these limitations, initial randomized trials reported that this less invasive approach for the treatment of ALI was associated with equivalent if not lower mortality and amputation rates compared with conventional surgery.[9-13] Since the time of these initial reports, however, no large studies have been performed to assess the diffusion of endovascular therapy for ALI or contemporary outcomes for endovascular and conventional surgical therapy for ALI. The primary objectives of this study were to examine trends in the incidence of ALI, to assess the relative use of open surgical vs endovascular therapy for ALI, and to document trends in the amputation and mortality rates for elderly Medicare beneficiaries presenting with ALI.

METHODS

Data sources. Data were obtained from the 1998-2009 Medicare Provider Analysis and Review (MedPAR) files, which contain hospital discharge abstracts for the acute care hospitalizations of all Medicare beneficiaries with Part A coverage. The data include admission and discharge dates, admission source, International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes, and discharge disposition. The MedPAR files were linked to Medicare denominator files, which include information on beneficiaries' date of birth, gender, race/ethnicity (categorized as black, white, or other), enrollment status, region of residence (Midwest, Northeast, South, or West), and vital status (including date of death).

Study sample. The initial patient population was defined by identifying Medicare fee-for-service beneficiaries 65 years or older. Patients residing outside the United States as well as patients enrolled in a Medicare health maintenance organization during the study period were excluded as MedPAR data may not capture complete health care claims data for these individuals.

Hospitalizations for ALI were identified on the basis of the presence of the following two criteria: (1) a principal discharge diagnosis of lower extremity embolism or thrombosis defined as ICD-9-CM codes 444.0 (abdominal aortic embolism and thrombosis), 444.22 (lower extremity embolism and thrombosis), and 444.81 (iliac artery embolism and thrombosis); and (2) admission type classified as either urgent or emergent in the MedPAR files.

To determine subsequent in-hospital interventions, the following ICD-9 procedural codes were used to capture surgical interventions: 38.06 (incision of vessel, abdominal arteries), 38.08 (incision of vessel, lower limb arteries), 38.16 (endarterectomy, abdominal arteries), 38.18 (endarterectomy, lower limb arteries), 38.46 (resection of abdominal vessels, replacement), 38.48 (resection of lower limb artery, replacement), 39.25 (aortoiliac-femoral bypass), 39.29 (other peripheral shunt/bypass), 39.49 (other revision of vascular procedure), 39.56 (repair of blood vessel with tissue graft patch), and 39.57 (repair of blood vessel with synthetic graft patch). We defined endovascular procedures by the following ICD-9 procedure codes: 99.10 (thrombolytic therapy), 39.50 (angioplasty or atherectomy of noncoronary vessel), 39.90 (insertion of noncoronary artery stent or stents), and 00.55 (insertion of drug-eluting stent of other peripheral vessels). Individuals who underwent both an endovascular and a surgical procedure for limb salvage during the same hospitalization were excluded. In addition, the ICD-9 procedure codes used to define major amputations were as follows: 84.13 (disarticulation of ankle), 84.14 (amputation of ankle through malleoli of tibia and fibula), 84.15 (other amputation below knee), 84.16 (disarticulation of knee), and 84.17 (amputation above knee). For individuals with more than one hospitalization for ALI, only the first hospitalization was included and was considered the index event.

Risk factors. Information on the clinical comorbidities used in the Klabunde adaptation of the Charlson comorbidity index were obtained using a 2-year look-back window from the index admission date.[15,16] The comorbidities included chronic heart disease, congestive heart failure, peripheral vascular disease, cerebrovascular disease, atrial fibrillation or atrial flutter, dementia, chronic pulmonary disease, paralysis, ulcer disease, moderate or severe liver disease, chronic renal failure, chronic liver disease or cirrhosis, rheumatologic disease, diabetes mellitus, hypertension, hyperlipidemia, acquired immunodeficiency syndrome, and history of cancer.

Outcomes. Outcomes included the incidence of hospitalizations for ALI; rates of open vascular and endovascular procedures; and in-hospital, 30-day, and 1-year amputation, mortality, and amputation-free survival rates.

Statistical analysis. The annual incidence of hospitalization for ALI was calculated for each year from 1998 to 2009 and is reported as number of events per 100,000 Medicare beneficiaries. Rates were standardized to the age distribution of the year 2000 population. The demographic and clinical characteristics of individuals hospitalized for ALI are presented separately for each of three time windows: 1998-2001, 2002-2005, and 2006-2009. We used analysis of variance for comparisons of continuous variables and χ^2 tests for comparisons of categorical variables. We calculated in-hospital, 30-day, and 1-year amputation, mortality, and amputation-free survival rates. The 30-day and 1-year rates were calculated from the date of admission. Risk-adjusted rates were calculated by univariate analysis and multivariable logistic regression analysis controlling for age, gender, race, region, and medical comorbidities.

The significance of trends in ALI incidence and outcomes were assessed by including year as a continuous variable in regression models. Analyses were performed with the SAS 9.2 statistical package (SAS Institute, Cary, NC). P values $< .05$ were considered statistically significant with two-sided tests for all analyses.

RESULTS

Study population. We identified a total of 99,982 hospitalizations for ALI between 1998 and 2009. During the study period, the mean age was 80.6 years, 60.7% were female, and 8.6% were black (Table I). Over time, the portion of the population older than 80 years increased substantially, from 50.5% in 1998 to 58.9% in 2009 ($P < .001$ for trend). The gender and race distributions remained relatively stable over time.

Patients hospitalized for ALI had a high burden of known risk factors for ALI or peripheral vascular disease, the most prevalent being congestive heart failure, chronic heart disease, peripheral vascular disease, hypertension, diabetes, hyperlipidemia, chronic obstructive pulmonary disease, cerebrovascular disease, and atrial fibrillation. During the study period, there was a significant increase in the prevalence of multiple comorbidities, including diabetes, atrial fibrillation, hypertension, and hyperlipidemia.

Incidence of ALI. Hospitalizations for ALI decreased from 45.7 per 100,000 in 1998 to 26.0 per 100,000 in 2009 (P for trend $< .001$). In men, there was a decrease from 46.5 per 100,000 in 1998 to 23.8 per 100,000 in 2009; in women, there was a decrease from 45.2 per 100,000 in 1998 to 27.6 per 100,000 in 2009 (Fig 1).

Table I. Characteristics of U.S. Medicare patients with acute lower extremity ischemia (ALI) from 1998 to 2009

	1998-2001, No. (%)	*2002-2005, No. (%)*	*2006-2009, No. (%)*	P *value for trend*
Age, years				
65-69	3509 (8.9)	2792 (8.5)	2211 (8.0)	.001
70-74	7390 (18.6)	5464 (16.7)	4154 (15.1)	.000
75-79	8702 (21.9)	6676 (20.4)	4948 (18.0)	.000
80-84	8215 (20.7)	7063 (21.5)	5937 (21.6)	.007
≥85	11,839 (29.9)	10,800 (32.9)	10,282 (37.4)	.000
Gender				
Male	15,719 (39.6)	12,999 (39.6)	10,610 (38.5)	.006
Race				
White	34,874 (87.9)	28,585 (87.2)	24,258 (88.1)	.001
Black	3450 (8.7)	2933 (8.9)	2215 (8.0)	.000
Other	1331 (3.4)	1277 (3.9)	1059 (3.8)	.000
Region				
Midwest	10,184 (25.7)	8646 (26.4)	6972 (25.3)	.011
Northeast	9189 (23.2)	7319 (22.3)	6131 (22.3)	.005
South	15,393 (38.8)	12,342 (37.6)	10,327 (37.5)	.000
West	4889 (12.3)	4488 (13.7)	4102 (14.9)	.000
Comorbid conditions				
Chronic heart disease	14,464 (36.5)	12,313 (37.5)	9832 (35.7)	.000
Congestive heart failure	12,229 (30.8)	10,846 (33.1)	8725 (31.7)	.000
Peripheral vascular disease	13,547 (34.2)	11,395 (34.7)	8202 (29.8)	.000
Cerebrovascular disease	6200 (15.6)	4728 (14.4)	3695 (13.4)	.000
Chronic obstructive pulmonary disease	9089 (22.9)	8300 (25.3)	6470 (23.5)	.000
Dementia	1751 (4.4)	1274 (3.9)	957 (3.5)	.000
Paralysis	1243 (3.1)	723 (2.2)	599 (2.2)	.000
Diabetes	9508 (24.0)	8538 (26.0)	7228 (26.3)	.000
Chronic renal failure	2576 (6.5)	2469 (7.5)	4558 (16.6)	.000
Cirrhodites	194 (0.5)	199 (0.6)	179 (0.7)	.015
Liver disease	86 (0.2)	62 (0.2)	79 (0.3)	.036
Ulcer disease	1424 (3.6)	1062 (3.2)	651 (2.4)	.000
Rheumatologic disorder	1143 (2.9)	927 (2.8)	927 (3.4)	.000
AIDS	3 (0.0)	4 (0.0)	19 (0.1)	.000
Cancer	3478 (8.8)	3257 (9.9)	2730 (9.9)	.000
Atrial fibrillation	13,910 (35.1)	12,736 (38.8)	11,131 (40.4)	.000
Hypertension	20,658 (52.1)	19,851 (60.5)	17,213 (62.5)	.000
Hyperlipidemia	4781 (12.1)	7601 (23.2)	8837 (32.1)	.000

Trends in treatment modalities. The proportion of patients undergoing intervention for limb salvage during their ALI hospitalization increased from 66.6% in 1998 to 74.9% in 2009 (*P* < .001 for trend). There was a marked shift from open to endovascular limb salvage procedures during the study period (Fig 2). The proportion of patients undergoing open surgery declined from 57.1% in 1998 to 51.6% in 2009 (*P* for trend < .001). Concomitantly, the percentage of patients undergoing endovascular therapy increased from 15.0% in 1998 to 33.1% in 2009 (*P* for trend < .001).

Trends in amputation rates. In-hospital amputations rates did not change over time and were 8.1% in 1998 and 6.4% in 2009 (*P* for trend not significant) (Fig 3). Thirty-day amputation rates decreased from 10.4% in 1998 to 8.1% in 2009 (*P* for trend < .001). Predictors of 30-day amputation included black race, male gender, advanced age, diabetes, and a history of peripheral vascular disease. A history of atrial fibrillation and a history of hyperlipidemia were associated with a decreased risk of amputation (Table II and Supplementary Table I, online only).

In addition, 1-year amputation rates for ALI decreased over time from 14.8% in 1998 to 11.0% in 2008 (*P* for trend < .001). Predictors of 1-year amputation included black race, male gender, diabetes, and a history of peripheral vascular disease (Table III and Supplementary Table II, online only).

Trends in mortality. In-hospital mortality for patients with ALI decreased over time from 12.1% in 1998 to 9.0% in 2009 (*P* for trend < .001). The 30-day mortality for ALI remained unchanged over time at 18.3% in 1998 to 19.2% in 2008. Predictors of 30-day mortality included advanced age, chronic renal failure, dementia, cancer, and atrial fibrillation. Black race, male gender, and undergoing endovascular or surgical intervention were associated with lower 30-day mortality (Table IV and Supplementary Table III, online only).

The overall risk-adjusted 1-year mortality for ALI remained unchanged at 41.0% in 1998 to 42.0% in 2008 (Fig 4). Predictors of 1-year mortality for ALI included advanced age, congestive heart failure, dementia, chronic renal failure, and atrial fibrillation. As with 30-day mortality, black race, male gender, and undergoing endovascular

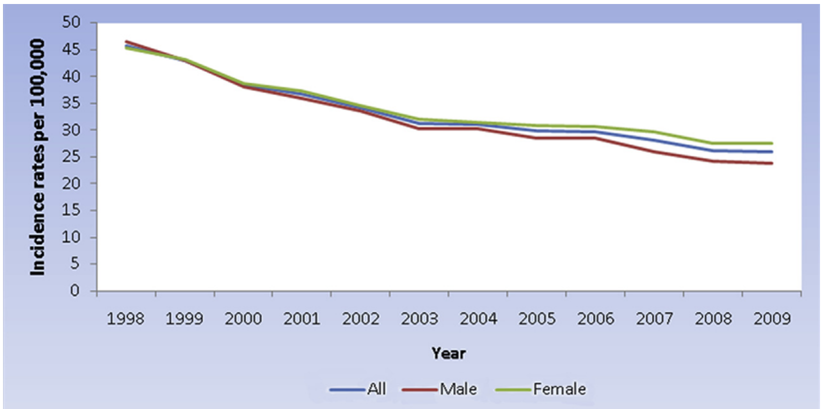

Fig 1. Age-adjusted incidence of acute lower extremity ischemia (ALI) in the U.S. Medicare population from 1998 to 2009.

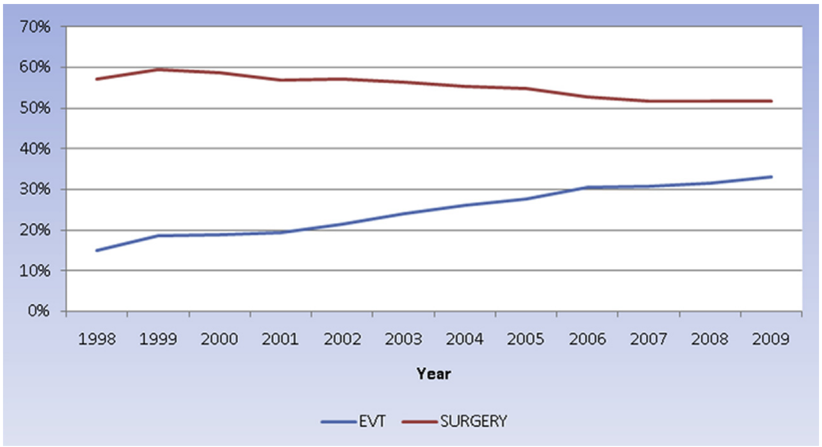

Fig 2. Trends in surgery and endovascular therapy (*EVT*) for the treatment of acute lower extremity ischemia (ALI) in the U.S. Medicare population from 1998 to 2009.

or surgical intervention were associated with lower 1-year mortality (Table V and Supplementary Table IV, online only).

Trends in amputation-free survival. In-hospital amputation-free survival for all patients increased over time from 81.2% in 1998 to 85.4% in 2009 (P for trend < .001). However, 30-day amputation-free survival remained stable (73.5% in 1998 to 74.5% in 2008; trend not significant), as did 1-year amputation-free survival (51.8% in 1998 to 52.3% in 2009; trend not significant) (Fig 5).

DISCUSSION

The incidence of ALI in the U.S. Medicare population has decreased significantly in the past decade. During this time, the use of endovascular therapy for the treatment of ALI has increased significantly, whereas the use of conventional surgical therapy has decreased. Despite improvements in amputation rates, mortality after presentation with ALI remains significant and unchanged after hospital discharge. In addition, whereas there have been significant improvements in in-hospital amputation-free survival rates, there have been no concomitant improvements in amputation-free survival rates after hospital discharge.

Prior population-based studies evaluating the incidence of ALI during the past several decades have reported variable results. National data from Sweden in the 1980s reported an incidence of 9 per 100,000 for the entire population and 180 per 100,000 in patients older than 90 years.[4] Additional data from Sweden in the 1990s reported an incidence of 13 per 100,000,[8] whereas studies from the United Kingdom previously reported incidence rates of 3.7 per 100,000[17] and 14 per 100,000.[5] No prior studies have reported on the incidence of ALI in the U.S. Medicare population. Given that these prior studies focused on the overall incidence of ALI in general populations of all ages, the incidence of 26 per 100,000 reported herein appears reasonable for the Medicare population aged 65 years and older. Although there is no clear

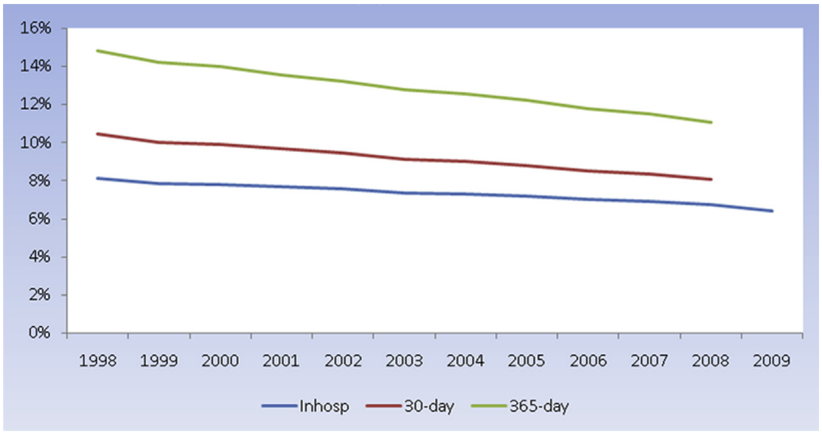

Fig 3. In-hospital, 30-day, and 1-year amputation rates for acute lower extremity ischemia (ALI) in the U.S. Medicare population from 1998 to 2009.

Table II. Independent predictors of 30-day amputation by multivariable analysis

	OR	*95% CI*	P *value*
Black race	2.01	1.89-2.15	.00
Peripheral vascular disease	1.90	1.81-2.00	.00
Dementia	1.63	1.49-1.79	.00
Rheumatologic disease	1.59	1.42-1.78	.00
Paralysis	1.40	1.23-1.58	.00
Male gender	1.32	1.26-1.39	.00
Age ≥85 years	1.30	1.19-1.42	.00
Other nonwhite race	1.27	1.14-1.42	.00
Diabetes	1.25	1.18-1.32	.00
South region	1.19	1.12-1.26	.00
Cerebrovascular disease	1.17	1.1-1.25	.00
Ulcer disease	1.15	1.03-1.29	.02
Age 80-84 years	1.14	1.04-1.25	.01
Chronic renal failure	1.09	1.01-1.18	.02
West region	1.09	1.01-1.18	.03
Cancer	1.08	1.01-1.17	.03
Congestive heart failure	1.06	1.01-1.13	.03
Atrial fibrillation	0.91	0.87-0.96	.00
Hypertension	0.91	0.87-0.96	.00
Chronic heart disease	0.87	0.82-0.92	.00
Hyperlipidemia	0.69	0.65-0.74	.00
Endovascular therapy at presentation	0.60	0.57-0.64	.00
Surgery at presentation	0.52	0.49-0.54	.00

CI, Confidence interval; *OR,* odds ratio.

Table III. Independent predictors of 1-year amputation by multivariable analysis

	OR	*95% CI*	P *value*
Black race	2.31	2.18-2.44	.00
Peripheral vascular disease	2.03	1.94-2.12	.00
Rheumatologic disease	1.57	1.42-1.73	.00
Dementia	1.51	1.38-1.64	.00
Diabetes	1.41	1.35-1.48	.00
Male gender	1.35	1.30-1.41	.00
Other nonwhite race	1.35	1.23-1.48	.00
Paralysis	1.31	1.17-1.47	.00
Ulcer disease	1.19	1.07-1.31	.00
Chronic renal failure	1.18	1.10-1.26	.00
Age ≥85 years	1.17	1.08-1.27	.00
Cerebrovascular disease	1.12	1.05-1.18	.00
South region	1.10	1.04-1.15	.00
Age 80-84 years	1.08	1.00-1.17	.06
Chronic heart disease	0.89	0.85-0.93	.00
Atrial fibrillation	0.86	0.82-0.90	.00
Hyperlipidemia	0.73	0.69-0.77	.00
Endovascular therapy at presentation	0.73	0.69-0.76	.00
Surgery at presentation	0.63	0.60-0.65	.00

CI, Confidence interval; *OR,* odds ratio.

explanation for the decrease in incidence observed over time, it may be due in part to an increased awareness and subsequent increase in the secondary prevention of different manifestations of cardiovascular disease during this period.[18-20] Furthermore, during this period, more patients with cardiac dysrhythmias, specifically atrial fibrillation, were diagnosed and treated with anticoagulation, reducing the rates of embolic events for a proportion of this patient population.[21,22] Also of note, the decrease in incidence was not as pronounced in the female population compared with the male population, perhaps in part because awareness of peripheral vascular disease in women has lagged behind that of men. In addition, it has been previously demonstrated that although women have fewer overall admissions for peripheral vascular disease and fewer interventions, they have higher rates of emergent admissions.[23] Although causality has not been demonstrated, this may be due to the fact that fewer elective procedures are done for women, placing them at higher risk for acute events.

Whereas the diffusion of endovascular therapy in the treatment of *acute* limb ischemia has not been well characterized, since its advent in the mid-1990s, the use of endovascular therapy for the treatment of *chronic* lower extremity peripheral arterial disease has increased markedly with a concomitant decrease in surgical interventions.[24-28] These practice pattern shifts, from open surgical to endovascular interventions, have been demonstrated in

Table IV. Independent predictors of 30-day mortality by multivariable analysis

	OR	*95% CI*	P *value*
Age ≥85 years	2.83	2.60-3.07	.00
Liver disease	1.91	1.38-2.64	.00
Dementia	1.79	1.66-1.92	.00
Cancer	1.78	1.68-1.87	.00
Age 80-84 years	1.74	1.59-1.89	.00
Chronic renal failure	1.55	1.46-1.64	.00
Age 75-79 years	1.41	1.29-1.54	.00
Paralysis	1.39	1.26-1.53	.00
Congestive heart failure	1.38	1.32-1.44	.00
Cerebrovascular disease	1.37	1.30-1.43	.00
Age 70-74 years	1.24	1.13-1.36	.00
Atrial fibrillation	1.21	1.16-1.25	.00
Chronic obstructive pulmonary disease	1.19	1.14-1.24	.00
West region	1.12	1.06-1.19	.00
Midwest region	1.08	1.03-1.14	.00
South region	1.06	1.01-1.11	.01
Chronic heart disease	1.05	1.01-1.09	.02
Diabetes	0.95	0.91-0.99	.01
Other nonwhite race	0.86	0.78-0.94	.00
Male gender	0.82	0.79-0.85	.00
Hypertension	0.80	0.76-0.83	.00
Black race	0.72	0.67-0.77	.00
Hyperlipidemia	0.65	0.62-0.69	.00
Endovascular therapy at presentation	0.64	0.62-0.66	.00
Surgery at presentation	0.61	0.58-0.64	.00

CI, Confidence interval; *OR,* odds ratio.

Medicare data,[24] the Nationwide Inpatient Sample (NIS),[25,26] and several state databases.[27,28] Among the general Medicare population, the rate of overall lower extremity vascular procedures nearly doubled between 1996 and 2006, with endovascular interventions increasing threefold and bypass surgeries decreasing by 42%; major amputations decreased by nearly 30% in that time. However, there is no clear causal link between these trends.[24] For patients specifically presenting with ALI, we found these trends to be similar although not as pronounced. In particular, although the percentage of ALI patients undergoing endovascular interventions doubled during the study period, the percentage of patients undergoing open surgical procedures decreased far less and remained greater than 50%. One possible explanation is that unlike in the chronic disease setting, the severity of ischemia in ALI often does not allow the time necessary for endovascular techniques to restore arterial flow to the lower extremity, resulting in a significant number of patients still requiring open surgical intervention for limb salvage.

An important finding of the current study was that despite the reduction in ALI incidence and the increase in the ratio of endovascular to surgical interventions for ALI, the impact on short-term and long-term outcomes was mixed. During the decade, in-hospital amputation rates remained stable, whereas amputation rates after discharge (at both 30 days and 1 year) declined significantly. At the same time, though, in-hospital mortality declined significantly, whereas 30-day and 1-year mortality rates did not show concomitant improvements. Amputation-free survival rates followed mortality trends, with significant short-term improvements but an absence of concomitant longer term improvements after hospital discharge. The reasons for these disparate trends are not entirely clear and are likely to be multifactorial.

Whereas short-term, in-hospital amputation rates did not decline, the significant reductions in 30-day and 1-year amputation rates are likely to be related to multiple factors. Increased use of endovascular interventions may have contributed to these improvements; however, as with prior reviews in the setting of chronic disease, no definitive causal relationship can be established. Given that the amputation rates declined after discharge, it is likely that better treatment of the comorbidities associated with ALI has contributed to these improved longer term outcomes. Specifically, increased treatment of hyperlipidemia, diabetes, and coronary heart disease along with smoking cessation efforts has been associated with improved outcomes after lower extremity interventions.[29,30] Despite these improvements, it is evident that a significant proportion of patients continue to be at risk of limb loss beyond the perioperative period.

Further, despite the declines in amputation rates demonstrated here and for patients with chronic lower extremity peripheral arterial disease, there remain significant differences in the patients undergoing amputations. Specifically, black race has previously been shown to be an independent predictor of amputation both among Medicare beneficiaries with chronic lower extremity ischemia[31] and for patients presenting with ALI from the NIS database.[32] Our analyses confirmed these earlier studies, which demonstrated that in-hospital amputation rates were higher among blacks, but also importantly extended these previous works by demonstrating that black race is the most significant independent predictor of amputation after presentation with ALI in the Medicare population at both 30 days and 1 year. Clearly, more work is needed to understand the drivers of these disparities.

Turning to survival after ALI, although in-hospital mortality rates fell during the study period, these rates now *exceed* the rates of amputation for ALI. The decline in in-hospital mortality has been previously demonstrated in a review of NIS data whereby these rates crossed in the late-1990s.[6] However, no previous study has reported on 30-day or 1-year mortality rates after presentation with ALI. Our study adds an important piece of information about the longer term prognosis after ALI: despite declines in in-hospital mortality, 30-day and 1-year mortality rates have not improved significantly and remain impressively high (19% and 42%, respectively). Despite the fact that more ALI patients are undergoing either open or endovascular revascularization procedures and more of these patients are being discharged alive from the hospital, we are not seeing concomitant longer term survival benefits. Certainly, there may be some degree of selection bias contributing to these findings in that more medically ill

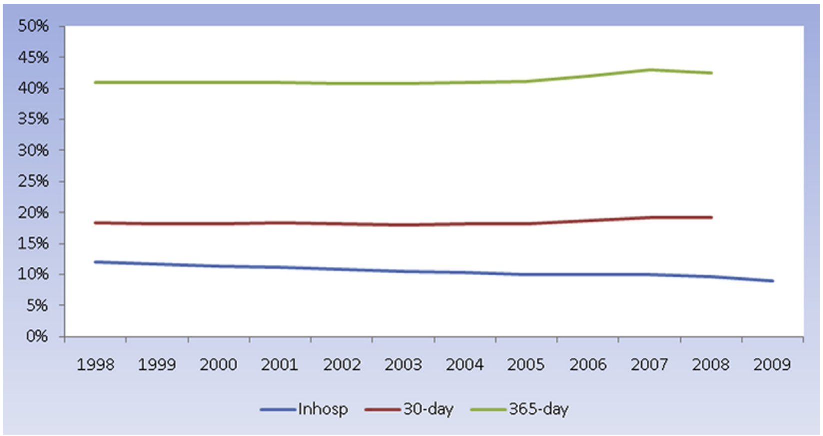

Fig 4. In-hospital, 30-day, and 1-year mortality rates for acute lower extremity ischemia (ALI) in the U.S. Medicare population from 1998 to 2009.

Table V. Independent predictors of 1-year mortality by multivariable analysis

	OR	*95% CI*	P *value*
Age ≥85 years	3.21	3.02-3.41	.00
Cancer	2.47	2.35-2.59	.00
Dementia	2.28	2.11-2.46	.00
Chronic renal failure	2.07	1.97-2.18	.00
Liver disease	1.99	1.46-2.73	.00
Age 80-84 years	1.82	1.72-1.94	.00
Congestive heart failure	1.70	1.64-1.76	.00
Paralysis	1.59	1.45-1.74	.00
Cirrhodites	1.42	1.17-1.72	.00
Age 75-79 years	1.38	1.30-1.46	.00
Cerebrovascular disease	1.33	1.27-1.39	.00
Chronic obstructive pulmonary disease	1.28	1.24-1.33	.00
Atrial fibrillation	1.28	1.24-1.32	.00
Rheumatologic disease	1.23	1.14-1.34	.00
Age 70-74 years	1.14	1.07-1.21	.00
Diabetes	1.11	1.07-1.15	.00
Ulcer disease	1.10	1.02-1.19	.02
Peripheral vascular disease	1.07	1.04-1.11	.00
Male gender	0.93	0.90-0.96	.00
Black race	0.92	0.87-0.96	.00
Hypertension	0.84	0.81-0.87	.00
Surgery at presentation	0.75	0.73-0.77	.00
Endovascular therapy at presentation	0.70	0.67-0.72	.00
Hyperlipidemia	0.63	0.61-0.65	.00

CI, Confidence interval; *OR,* odds ratio.

patients are now undergoing intervention, particularly with the increased use of less invasive endovascular techniques, allowing discharge. Regardless, it is evident that long-term mortality after ALI remains very poor, with more than 40% of patients expiring at 1 year. Combining the ALI end points of amputation and mortality, we found that amputation-free survival trends have mirrored mortality trends with significant improvements in in-hospital rates but no concomitant improvements in 30-day or 1-year rates. At 1 year, just more than 50% of patients were alive with an intact limb, demonstrating that despite technologic advances in treatment and the increased use of these treatments in practice, ALI remains a high-morbidity, high-mortality medical event.

The data presented here, specifically the striking 1-year mortality rates and the mortality-driven 1-year amputation-free survival rates, add to the contemporary knowledge of ALI as the only recent nationwide database review to examine outcomes beyond hospitalization. For patients presenting with ALI, management and decision-making remain challenging and have not been simplified with the addition of endovascular therapy and its increasing use. Although treatment will always need to be individualized, these data emphasize the need to examine the patient as a whole, particularly with regard to expected survival, given the overall poor survival rates at 1 year for patients presenting with ALI.

The primary limitation of this study relates to its reliance on administrative claims data. Our study relied on hospitalization principal discharge diagnosis codes to identify ALI events. Inherent to our study is reliance on accurate coding, and inaccurate coding is one of the major limitations of use of diagnosis codes to identify patients for study inclusion. Also, patients enrolled in a Medicare health maintenance organization during the study period were excluded as previously discussed on the basis of the concern that MedPAR data may not capture complete health care claims data for these individuals. Although these patients represent a small proportion of the total Medicare population, there is a possibility that some bias may have resulted from exclusion of these patients. In addition, for this study, only hospitalized patients were reviewed, and there is likely a very small percentage of patients with ALI who are being treated at outpatient facilities and subsequently are not included. However, despite increases in the spectrum of patients treated at such facilities, it is unlikely that a significant proportion of patients with true ALI are being cared for at these facilities on an outpatient basis. The extent to which there have been

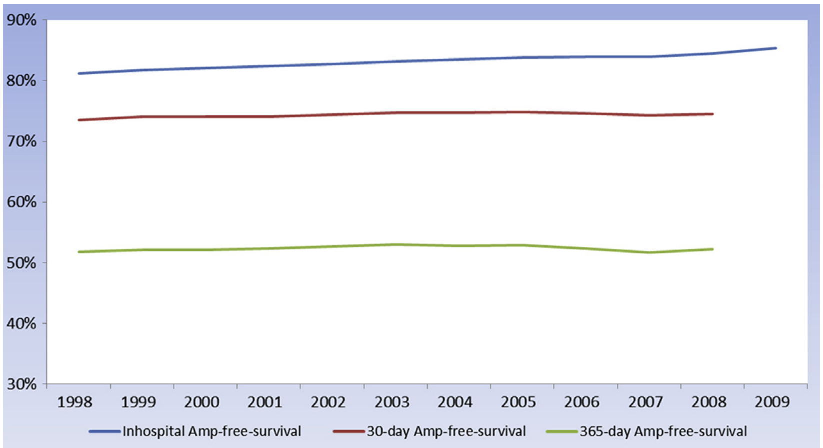

Fig 5. In-hospital, 30-day, and 1-year amputation-free survival rates for acute lower extremity ischemia (ALI) in the U.S. Medicare population from 1998 to 2009.

additions or changes to the ICD-9 codes for lower extremity arterial disease during the study period may have affected reported incidence rates. It is possible, therefore, that trends in the incidence of ALI hospitalizations may be decreasing to a lesser extent than reported here if a changing proportion of patients have been miscoded with ICD-9 codes conventionally used for *chronic* disease. Use of the "thrombosis and embolism" codes along with an admission status of "urgent" or "emergent" should but may not entirely have limited this misclassification to most clearly identify those Medicare beneficiaries who presented with an acutely ischemic limb. In addition, the use of these codes does not allow separate analyses of patients presenting with ischemia due to an embolism and of patients presenting with ischemia due to in situ thrombosis.

Furthermore, some components of patients' histories are not recorded in the Medicare claims data set, specifically previous surgical history and tobacco use, both of which may play a significant role in the outcomes after presentation with ALI. In addition, procedural data are limited within the data set specifically, and as such, patients who underwent both an open and endovascular procedure were excluded from review as the details including the timing of these procedures are not available from the Medicare database. These may have been performed sequentially, concomitantly, or days apart, and unfortunately, another limitation of using administrative claims data is determining these details. With regard to amputation as an end point, only major amputations above the ankle were included in this study. Although exclusion of minor amputations may represent a limitation of this study, such amputations have a markedly lesser impact on morbidity and mortality and are not conventionally included in defining limb salvage.

Another important limitation is that this study does not elucidate any causal relationships between the decline in ALI incidence, growth in endovascular therapy use, and subsequent trends in short- and long-term amputation and mortality rates. More research is needed to better elucidate these relationships. Despite these limitations, this analysis represents the only contemporary report on ALI trends among this patient population that specifically includes long-term outcomes after hospital discharge.

CONCLUSIONS

The incidence of ALI in the U.S. Medicare population has declined during the past decade. During this time, an increased proportion of patients have undergone an intervention for limb salvage, with a marked increase in the use of endovascular techniques. Although there have been improvements in overall amputation rates for these patients, mortality rates remain significant and have not improved after hospital discharge.

AUTHOR CONTRIBUTIONS

Conception and design: DB, AR
Analysis and interpretation: DB, KG, AR
Data collection: DB, KG, AR
Writing the article: DB, AR
Critical revision of the article: DB, KG, AR
Final approval of the article: DB, KG, AR
Statistical analysis: KG
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Overall responsibility: DB

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Supplementary Table I (online only). Predictors of 30-day amputation by univariate analysis

	OR	*95% CI*	P *value*
Atrial fibrillation	0.93	0.88-0.97	.00
Age 65-69 years	0.97	0.91-1.03	.30
Age 70-74 years	0.95	0.90-1.01	.11
Age 75-79 years	0.96	0.91-1.01	.15
Age 80-84 years	0.98	0.93-1.03	.43
Age ≥85 years	1.09	1.04-1.15	.00
AIDS	2.29	0.77-6.80	.14
Black race	2.25	2.11-2.39	.00
Cancer	1.12	1.04-1.20	.00
Cerebrovascular disease	1.38	1.31-1.47	.00
Chronic heart disease	1.06	1.02-1.11	.01
Congestive heart failure	1.19	1.14-1.25	.00
Chronic renal failure	1.34	1.25-1.43	.00
Cirrhodites	1.30	1.00-1.69	.05
Chronic obstructive pulmonary disease	1.20	1.14-1.26	.00
Dementia	2.06	1.89-2.25	.00
Diabetes	1.36	1.30-1.43	.00
Endovascular therapy on presentation	0.66	0.62-0.70	.00
Hyperlipidemia	0.73	0.69-0.78	.00
Hypertension	1.14	1.09-1.20	.00
Liver disease	1.45	0.97-2.16	.07
Male gender	1.29	1.24-1.35	.00
Midwest region	0.87	0.83-0.92	.00
Northeast region	0.90	0.86-0.95	.00
Paralysis	1.73	1.54-1.94	.00
Peripheral vascular disease	1.84	1.76-1.92	.00
Other nonwhite race	1.27	1.15-1.42	.00
Rheumatologic disease	1.54	1.38-1.72	.00
South region	1.23	1.17-1.28	.00
Surgery at presentation	0.58	0.55-0.61	.00
Ulcer disease	1.37	1.23-1.53	.00
West region	0.95	0.89-1.01	.10
White race	0.50	0.47-0.53	.00

CI, Confidence interval; *OR,* odds ratio.

Supplementary Table II (online only). Predictors of 1-year amputation by univariate analysis

	OR	*95% CI*	P *value*
Atrial fibrillation	0.86	0.82-0.89	.00
Age 65-69 years	1.08	1.03-1.14	.00
Age 70-74 years	1.07	1.02-1.12	.01
Age 75-79 years	1.04	0.99-1.09	.13
Age 80-84 years	0.96	0.92-1.01	.10
Age ≥85 years	0.94	0.90-0.98	.00
AIDS	2.08	0.76-5.69	.15
Black race	2.60	2.46-2.75	.00
Cancer	1.04	0.98-1.11	.22
Cerebrovascular disease	1.31	1.25-1.38	.00
Chronic heart disease	1.12	1.08-1.17	.00
Congestive heart failure	1.16	1.12-1.21	.00
Chronic renal failure	1.50	1.41-1.59	.00
Cirrhodites	1.15	0.91-1.46	.25
Chronic obstructive pulmonary disease	1.20	1.15-1.26	.00
Dementia	1.77	1.64-1.92	.00
Diabetes	1.59	1.53-1.66	.00
Endovascular therapy on presentation	0.76	0.73-0.80	.00
Hyperlipidemia	0.82	0.78-0.86	.00
Hypertension	1.22	1.17-1.27	.00
Liver disease	1.25	0.86-1.80	.24
Male gender	1.37	1.32-1.42	.00
Midwest region	0.87	0.84-0.91	.00
Northeast region	0.96	0.92-1.01	.10
Paralysis	1.56	1.40-1.73	.00
Peripheral vascular disease	2.07	1.99-2.15	.00
Other nonwhite race	1.36	1.24-1.49	.00
Rheumatologic disease	1.52	1.38-1.67	.00
South region	1.20	1.15-1.24	.00
Surgery at presentation	0.68	0.66-0.71	.00
Ulcer disease	1.42	1.29-1.56	.00
West region	0.91	0.86-0.96	.00
White race	0.44	0.42-0.46	.00

CI, Confidence interval; *OR,* odds ratio.

Supplementary Table III (online only). Predictors of 30-day mortality by univariate analysis

	OR	*95% CI*	P *value*
Atrial fibrillation	1.70	1.64-1.76	.00
Age 65-69 years	0.46	0.44-0.49	.00
Age 70-74 years	0.54	0.52-0.57	.00
Age 75-79 years	0.67	0.64-0.70	.00
Age 80-84 years	0.93	0.90-0.97	.00
Age ≥85 years	2.34	2.27-2.42	.00
AIDS	0.47	0.11-2.01	.31
Black race	0.66	0.62-0.71	.00
Cancer	1.57	1.50-1.66	.00
Cerebrovascular disease	1.62	1.55-1.69	.00
Chronic heart disease	1.21	1.17-1.25	.00
Congestive heart failure	1.80	1.74-1.86	.00
Chronic renal failure	1.56	1.48-1.64	.00
Cirrhodites	1.44	1.19-1.76	.00
Chronic obstructive pulmonary disease	1.22	1.18-1.27	.00
Dementia	2.74	2.56-2.94	.00
Diabetes	0.95	0.91-0.98	.01
Endovascular therapy on presentation	0.61	0.58-0.64	.00
Hyperlipidemia	0.64	0.61-0.67	.00
Hypertension	1.07	1.03-1.10	.00
Liver disease	2.09	1.57-2.79	.00
Male gender	0.70	0.67-0.72	.00
Midwest region	1.04	1.01-1.08	.03
Northeast region	1.01	0.97-1.05	.65
Paralysis	1.92	1.76-2.10	.00
Peripheral vascular disease	0.94	0.91-0.97	.00
Other nonwhite race	0.85	0.77-0.93	.00
Rheumatologic disease	1.11	1.01-1.22	.04
South region	0.93	0.89-0.96	.00
Surgery at presentation	0.71	0.69-0.74	.00
Ulcer disease	1.18	1.08-1.29	.00
West region	1.07	1.02-1.12	.00
White race	1.42	1.34-1.50	.00

CI, Confidence interval; *OR,* odds ratio.

Supplementary Table IV (online only). Predictors of 1-year mortality by univariate analysis

	OR	*95% CI*	P *value*
Atrial fibrillation	2.01	1.96-2.07	.00
Age 65-69 years	0.46	0.45-0.48	.00
Age 70-74 years	0.52	0.50-0.54	.00
Age 75-79 years	0.68	0.66-0.70	.00
Age 80-84 years	1.01	0.98-1.05	.45
Age ≥85 years	2.50	2.43-2.57	.00
AIDS	1.29	0.55-3.05	.56
Black race	0.84	0.80-0.88	.00
Cancer	2.09	2.00-2.19	.00
Cerebrovascular disease	1.73	1.66-1.79	.00
Chronic heart disease	1.40	1.36-1.44	.00
Congestive heart failure	2.41	2.34-2.47	.00
Chronic renal failure	2.28	2.18-2.38	.00
Cirrhodites	1.85	1.56-2.19	.00
Chronic obstructive pulmonary disease	1.44	1.40-1.49	.00
Dementia	3.65	3.40-3.92	.00
Diabetes	1.21	1.17-1.24	.00
Endovascular therapy on presentation	0.66	0.64-0.69	.00
Hyperlipidemia	0.70	0.68-0.72	.00
Hypertension	1.30	1.26-1.33	.00
Liver disease	2.57	1.95-3.40	.00
Male gender	0.77	0.75-0.79	.00
Midwest region	0.99	0.96-1.02	.57
Northeast region	1.11	1.07-1.14	.00
Paralysis	2.23	2.05-2.42	.00
Peripheral vascular disease	1.14	1.11-1.18	.00
Other nonwhite race	0.92	0.86-0.99	.02
Rheumatologic disease	1.29	1.20-1.39	.00
South region	0.92	0.90-0.95	.00
Surgery at presentation	0.82	0.80-0.84	.00
Ulcer disease	1.46	1.36-1.57	.00
West region	1.02	0.98-1.06	.28
White race	1.17	1.12-1.21	.00

CI, Confidence interval; *OR,* odds ratio.