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Temporal Trends and Geographic Variation of Lower-Extremity Amputation in Patients With Peripheral Artery Disease

Results From U.S. Medicare 2000–2008

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Objectives This study sought to characterize temporal trends, patient-specific factors, and geographic variation associated with amputation in patients with lower-extremity peripheral artery disease (LE PAD) during the study period.

Background Amputation represents the end-stage failure for those with LE PAD, and little is known about the rates and geographic variation in the use of LE amputation.

Methods By using data from the Centers for Medicare & Medicaid Services (CMS) from January 1, 2000, to December 31, 2008, we examined national patterns of LE amputation among patients age 65 years or more with PAD. Multivariable logistic regression was used to adjust regional results for other patient demographic and clinical factors.

Results Among 2,730,742 older patients with identified PAD, the overall rate of LE amputation decreased from 7,258 per 100,000 patients with PAD to 5,790 per 100,000 ($p < 0.001$ for trend). Male sex, black race, diabetes mellitus, and renal disease were all independent predictors of LE amputation. The adjusted odds ratio of LE amputation per year between 2000 and 2008 was 0.95 (95% CI: 0.95–0.95, $p < 0.001$).

Conclusions From 2000 to 2008, LE amputation rates decreased significantly among patients with PAD. However, there remains significant patient and geographic variation in amputation rates across the United States. (J Am Coll Cardiol 2012;60:2230–6) © 2012 by the American College of Cardiology Foundation

Lower-extremity peripheral artery disease (LE PAD) is a prevalent disorder that affects approximately 8 million Americans (1). In its end stage, patients with severe PAD can require LE amputation (2). LE amputation is associated with significant morbidity, mortality, and healthcare costs (3,4). Over the past decade, treatment strategies for those with PAD have improved, including better early detection, more frequent referral for diagnostic imaging, and improved revascularization options. Combined, these may have significantly reduced the need for LE amputation, yet no national studies have summarized these changes. In addition, treatment of PAD often differs regionally (5–7), and it remains unclear whether geographic variation may further contribute to the risk of LE amputation. Consequently, we performed an analysis of the U.S. Medicare data to provide a more contemporary report of national temporal and geographic trends in amputation. Our specific aims were to: 1) characterize temporal trends in LE amputation during the study period; 2) examine patient factors that were associated with LE amputation; and 3) determine whether there was geographic variation in LE amputation across the United States.

Methods

Data sources. We obtained the 100% inpatient Medicare standard analytic files and corresponding denominator files from the Centers for Medicare & Medicaid Services (CMS) for January 1, 2000, to December 31, 2008. The inpatient files contain institutional claims for facility costs covered under Medicare Part A. The denominator files contain beneficiary demographic and clinical characteristic data. We

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restricted the study population to those patients with fee-for-service Medicare Parts A and B enrollment at the index admission and censored patients if they switched to managed care and/or dropped Medicare Part A or B.

Identification of patients. We identified beneficiaries for whom an International Classification of Diseases-Ninth Revision-Clinical Modification [ICD-9-CM] diagnosis code or procedure code for LE PAD was reported during the study period (Online Appendix 1). We also identified beneficiaries who underwent a first major LE amputation (as defined by above-knee or below-knee amputation, not including transmetatarsal or foot amputations) during the study period as those for whom an ICD-9-CM procedure code (84.13 to 84.18) for above-knee or below-knee amputation was reported. In subjects who underwent multiple LE amputations, those that occurred after the index major amputation were not included in the analysis.

Patient characteristics. Patient demographic characteristics included age, sex, race, state of residence, and ZIP code of residence. Medicare beneficiaries report race at the time of enrollment. We used previously validated methods to identify comorbid conditions using ICD-9-CM billing claims for up to 5 years before the index hospitalization (8). We used the patient's state of residence to group beneficiaries into 9 U.S. Census Bureau regions (Online Appendix 2) (6,7).

Statistical analysis. We present categoric variables as frequencies with percentages and continuous variables as means with standard deviations. To test for differences between groups, we used the Pearson chi-square test for categoric variables and the Wilcoxon ranksum test for continuous variables. We calculated the annual rates of lower-extremity amputation, the annual rates of hospitalization and amputation from 2000 to 2008, and the ratio of amputation in each state to the national rates and mapped these ratios. To determine whether geographic variation was associated with amputation, we performed multivariable logistic regression adjusting for clinical variables (age, sex, race, and comorbid conditions, including diabetes mellitus, renal disease, congestive heart failure, and cerebrovascular disease) and further adjusting for index year and geographic variation within the model. Odds ratios (ORs) and 95% confidence intervals (CIs) are presented for LE amputation.

The Duke University Institutional Review Board reviewed and approved this study design. We used SAS statistical software, version 9.2 (SAS Institute Inc., Cary, North Carolina) for all analyses.

Results

Patient characteristics. There were approximately 3 million Medicare beneficiaries hospitalized for PAD from 2000 to 2008. A total of 186,338 patients (6.8% of the overall hospitalized population with PAD) underwent LE amputation during the study period. Table 1 shows the demographic and clinical characteristics of all Medicare beneficiaries who were hospitalized for PAD and the characteristics of those with and without LE amputation during the study period.

Abbreviations and Acronyms

CI = confidence interval
CMS = Centers for Medicare & Medicaid Services
HRR = hospital referral region
ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification
LE PAD = lower-extremity peripheral artery disease
OR = odds ratio

Among beneficiaries who underwent major LE amputation, approximately 65% were >75 years old, approximately one-half were men, and one-quarter were black. Patients with PAD who underwent amputation were more likely to be black (28.1% vs. 9.5%, $p < 0.001$), to have diabetes mellitus (60.3% vs. 35.7%, $p < 0.001$), and to have renal disease (29.5% vs. 15.5%, $p < 0.001$) when compared with patients with PAD who did not undergo an amputation.

Table 2 shows the results of logistic regression models created to show the clinical predictors of LE amputation. Men, African Americans, and the presence of diabetes and renal disease were clinical and demographic variables independently associated with LE amputation, whereas coronary artery disease and cancer were associated with reduced risk of LE amputation.

Temporal trends in PAD treatment and LE amputation. From 2000 to 2008, the overall use of LE amputation decreased significantly during the study period (7,258 to 5,790 LE amputations per 100,000 Medicare beneficiaries with PAD, $p < 0.001$; Table 3). Table 3 also shows the temporal trends in LE amputation over the study period (total, above knee, below knee). The adjusted OR of LE amputation per year after 2000 was 0.95 (95% CI: 0.95 to 0.95, $p < 0.001$) (Table 2).

Geographic variation. There was significant geographic variation in the rate of lower-extremity amputation from 8,400 amputations per 100,000 patients with PAD in the East South Central region to 5,500 amputations per 100,000 patients with PAD in the Mountain region. Figure 2 shows the rate of amputation per the U.S. Census Bureau during the study period.

Geographic variation continued to be independently associated with LE amputation after adjusting for clinical variables and temporal trends in the multivariable model. Even after adjusting for clustering at the U.S. Census Bureau level, geographic variation in LE amputations remained. LE amputation was performed more often in the East South Central region (adjusted OR: 1.152, 95% CI: 1.131 to 1.174, $p < 0.001$) and West South Central region (adjusted OR: 1.115, 95% CI: 1.097 to 1.133, $p < 0.001$), and less often in the Middle Atlantic region (OR: 0.833, 95% CI: 0.820 to 0.847, $p < 0.001$) when compared with the South Atlantic region as reference (Table 2).

Table 1 Demographic and Clinical Characteristics

	Overall (N = 2,730,742)	PAD Without LE Amputation (N = 2,544,404)	PAD With LE Amputation (N = 186,338)	p Value
Age, yrs	77.4 ± 7.6	77.3 ± 7.5	78.5 ± 8.2	<0.001
Age, yrs				
65–69	490,087 (17.9)	459,538 (18.1)	30,549 (16.4)	<0.001
70–74	559,312 (20.5)	524,965 (20.6)	34,347 (18.4)	<0.001
75–79	627,886 (23.0)	589,502 (23.2)	38,384 (20.6)	<0.001
≥80	1,053,457 (38.6)	970,399 (38.1)	83,058 (44.6)	<0.001
Male	1,352,662 (49.5)	1,263,035 (49.6)	89,627 (48.1)	0.001
Race				
White	2,342,742 (85.8)	2,217,917 (87.2)	124,825 (67.0)	<0.001
Black	293,285 (10.7)	240,874 (9.5)	52,411 (28.1)	<0.001
Asian	17,483 (0.6)	16,417 (0.6)	1,066 (0.6)	<0.001
Other	77,232 (2.8)	69,196 (2.7)	8,036 (4.3)	<0.001
U.S. geographic region				
New England	132,094 (4.8)	124,789 (4.9)	7,305 (3.9)	<0.001
Middle Atlantic	406,576 (14.9)	381,189 (15.0)	25,387 (13.6)	<0.001
South Atlantic	595,493 (21.8)	550,437 (21.6)	45,056 (24.2)	<0.001
East North Central	525,337 (19.2)	494,627 (19.4)	30,710 (16.5)	<0.001
East South Central	217,045 (7.9)	198,798 (7.8)	18,247 (9.8)	<0.001
West North Central	195,749 (7.2)	184,858 (7.3)	10,891 (5.8)	<0.001
West South Central	333,659 (12.2)	306,032 (12.0)	27,627 (14.8)	<0.001
Mountain	104,083 (3.8)	98,350 (3.9)	5,733 (3.1)	<0.001
Pacific	220,706 (8.1)	205,324 (8.1)	15,382 (8.3)	0.005
Comorbidities				
Cancer	236,135 (8.6)	223,021 (8.8)	13,114 (7.0)	<0.0001
Cerebrovascular disease	436,161 (16.0)	388,865 (15.3)	47,296 (25.4)	<0.001
Congestive heart failure	987,779 (36.2)	895,135 (35.2)	92,644 (49.7)	<0.001
Chronic obstructive pulmonary disease	973,553 (35.7)	907,824 (35.7)	65,729 (35.3)	<0.001
Coronary artery disease	1,674,727 (61.3)	1,571,028 (61.7)	103,699 (55.7)	<0.001
Dementia	97,360 (3.6)	79,930 (3.1)	17,430 (9.4)	<0.001
Diabetes mellitus	1,021,469 (37.4)	909,131 (35.7)	112,338 (60.3)	<0.001
Hypertension	2,107,597 (77.2)	1,958,113 (77.0)	149,484 (80.2)	<0.001
Renal disease	448,747 (16.4)	393,778 (15.5)	54,969 (29.5)	<0.001

Values are mean ± SD or n (%).

Discussion

The primary findings from this cohort study of elderly Medicare beneficiaries with PAD are that there has been a marked reduction in LE amputations within the United States. Between 2000 and 2008, the overall annual rates of LE amputation significantly decreased from 7,258 to 5,790 per 100,000 patients with PAD. Second, there remains significant geographic variation. Rates of LE amputation were generally higher in the East South Central, West South Central, and South Atlantic regions, whereas the Mountain, New England, and West North Central regions had lower rates (Fig. 1). Of note, geographic variation remained statistically associated with LE amputation after adjustment for clinical factors.

There are multiple potential explanations for the dramatic decrease in the number of LE amputations observed in the current study. First, the importance of prevention of LE amputation and emphasis on early screening and detection of vascular disease in patients at risk for LE amputation may be contributing to the decline in amputation rates (9,10). Second, studies of revascularization procedures in patients with PAD have consistently shown that the use of endovascular revascularization has increased significantly after 2000 and when combined with improved screening and detection methods may contribute to the decline in amputation rates (11). In the current study, we used the Part A Medicare dataset that captured inpatient billing claims, and because of this, we were unable to fully explore the use of screening tests and revascularization procedures, some of which may be performed more frequently on an outpatient basis. The national shift to outpatient care and procedures in cardiovascular medicine is unlikely to affect the measurement of major LE amputations, such as above-knee and below-knee amputations, but it may be possible for ray amputations.

When studying the effect of geographic variation, prior work from Medicare beneficiaries with diabetic foot ulcers has proposed that the risk of LE amputation is more an

Table 2 Factors Associated With Lower-Extremity Amputation

	Unadjusted					Adjusted				
Effect	OR: Estimate	Lower 95% Confidence Limit for OR	Upper 95% Confidence Limit for OR	Chi-Square	p Value	OR: Estimate	Lower 95% Confidence Limit for OR	Upper 95% Confidence Limit for OR	Chi-Square	p Value
Geographic and temporal factors										
East North Central	0.76	0.75	0.77	1,303.5	<0.001	0.83	0.82	0.84	546.7	<0.001
East South Central	1.12	1.10	1.14	157.0	<0.001	1.15	1.13	1.17	220.3	<0.001
Middle Atlantic	0.81	0.80	0.83	644.3	<0.001	0.83	0.82	0.85	467.4	<0.001
Mountain	0.71	0.69	0.73	552.0	<0.001	0.96	0.94	0.99	6.5	0.011
New England	0.72	0.70	0.73	664.8	<0.001	0.89	0.86	0.91	82.9	<0.001
Pacific	0.92	0.90	0.93	83.6	<0.001	1.02	1.00	1.04	3.7	0.056
West North Central	0.72	0.70	0.74	891.2	<0.001	0.92	0.90	0.94	61.4	<0.001
West South Central	1.10	1.09	1.12	151.5	<0.001	1.12	1.10	1.13	171.3	<0.001
South Atlantic (Reference)	1.00	1.00	1.00			1.00	1.00	1.00		
Year (per 1-yr increase)	0.97	0.96	0.97	1,325.4	<0.001	0.95	0.95	0.95	2,565.9	<0.001
Clinical factors										
Race: black vs. white						2.90	2.83	2.90	29,606.2	<0.001
Diabetes mellitus						2.40	2.38	2.43	27,639.2	<0.001
Renal disease						1.63	1.61	1.65	6,614.3	<0.001
Dementia						2.09	2.05	2.13	5,958.5	<0.001
Coronary artery disease						0.67	0.66	0.68	5,724.8	<0.001
Age (per 5-yr increase)						1.13	1.13	1.14	5,659.2	<0.001
Congestive heart failure						1.47	1.46	1.49	4,963.9	<0.001
Cerebrovascular disease						1.49	1.47	1.50	4,315.7	<0.001
Race: other vs. white						1.52	1.49	1.56	1,102.3	<0.001
Male						1.14	1.13	1.15	655.1	<0.001
Cancer						0.82	0.80	0.83	438.5	<0.001
Hypertension						0.92	0.91	0.93	156.4	<0.001
COPD						1.03	1.02	1.04	30.9	<0.001
Race: Asian vs. white						0.89	0.83	0.95	13.1	<0.001

COPD = chronic obstructive pulmonary disease; OR = odds ratio.

Table 3 Rate of Lower-Extremity Amputations per U.S. Census Bureau During Study Period

	2000	2001	2002	2003	2004	2005	2006	2007	2008
Total no. of LE amputations per 100,000 patients with PAD	7,258	7,525	7,359	7,091	6,919	6,580	6,072	6,000	5,790
No. of LE amputations above knee per 100,000 patients with PAD	4,155	4,286	4,216	4,034	3,977	3,800	3,540	3,484	3,312
No. of LE amputations below knee per 100,000 patients with PAD	3,104	3,239	3,142	3,057	2,942	2,780	2,532	2,517	2,478
East North Central	6,511	6,608	6,276	5,949	5,791	5,570	5,141	4,893	5,043
East South Central	8,268	9,202	9,261	8,753	8,797	8,146	7,359	7,565	7,591
Middle Atlantic	6,295	6,906	6,659	6,631	6,456	5,992	5,550	5,781	5,269
Mountain	6,134	6,394	6,275	5,663	5,182	5,188	4,616	4,575	5,052
New England	6,484	6,529	5,525	5,668	5,267	5,094	4,745	4,658	5,006
Pacific	7,270	7,368	7,692	7,185	7,289	6,801	6,767	6,189	5,655
South Atlantic	7,959	7,995	8,102	7,973	7,779	7,468	6,884	6,789	6,198
West North Central	5,934	6,230	5,996	5,530	5,606	5,511	4,792	5,035	4,804
West South Central	9,237	9,339	8,919	8,636	8,256	7,853	7,251	7,085	6,874

All values are reported as number of LE amputations per 100,000 patients with PAD.
LE = lower extremity; PAD = peripheral artery disease.

effect of the location of a hospital referral region (HRR) rather than the HRR itself (12). This report found that spatial clustering was present, in other words, that higher LE amputation rates in HRRs were more likely in the presence of nearby HRRs with high LE amputation rates rather than in nearby HRRs with lower LE amputation rates. Given the clustering of regions with a higher risk of LE amputation in the current study, this suggests that similar, unmeasured effects of socioeconomic status, access to care, and application of care may contribute to the risk of LE amputation in patients with PAD. In addition, the timing of patient presentation for evaluation of patients with rest leg pain or ischemic ulceration may vary, and underscores the importance of patient education and awareness in those at highest risk for LE amputation. Finally, the threshold to perform LE amputation differs among providers, and therefore further exploration of the presence of vascular specialists per region and the presence of integrated vascular care specialty centers may help explain some of the variation in our study. Regardless of these factors, this variation highlights the importance of programs to educate patients and providers in the areas with the highest use of LE amputation.

The study findings provide focus for areas of further research. Analyses are needed to determine whether hospital and provider characteristics contributed to the observed

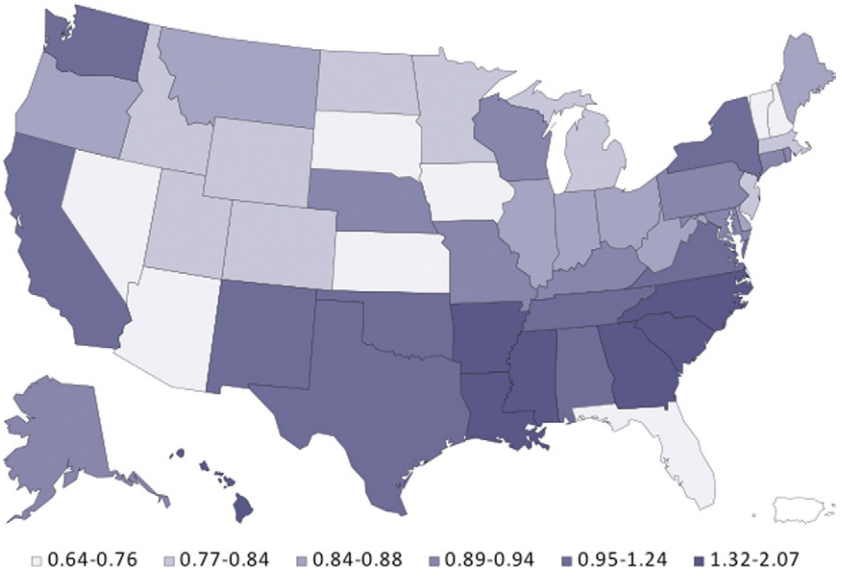

Figure 1 Geographic Variation in Use of Lower-Extremity Amputation

Geospatial map showing the ratio of rates of LE amputation per state compared with the national average. LE = lower extremity.

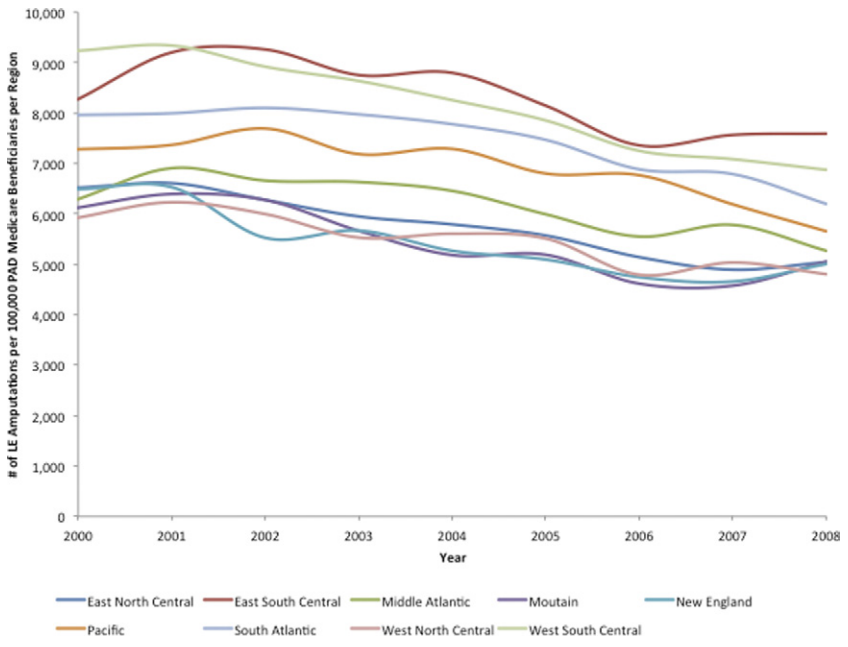

Figure 2 **Temporal Trends in Lower-Extremity Amputation by U.S. Census Bureau**

Graph showing the temporal patterns of performance of LE amputation by U.S. Census Bureau. LE = lower extremity.

geographic variation. Further research also is needed in understanding "best practices" and features associated with low amputation regions and areas with significant reductions in amputations over the study period. In fact, a recent analysis from Medicare Part B data reported a significant variation in the intensity of diagnostic angiography, endovascular revascularization, and surgical revascularization in the year preceding LE amputation, potentially providing some early insights into practice patterns (5).

Study limitations. The current study has multiple limitations. First, Medicare claims data do not include information regarding PAD duration or progression of symptoms, severity and burden of disease, and patients and physician treatment preferences that may affect the decision to perform amputation and the rates of amputation. Second, patients without a definitive diagnosis of PAD who underwent amputation may have been excluded from our analysis. Third, Medicare Part A data only capture inpatient hospital claims and procedures. Although it is unlikely that major LE amputations are performed on an outpatient basis, the association of revascularization procedures before amputation could not be assessed because of a shift from inpatient vascular care to outpatient care. Finally, this analysis included only those patients enrolled in fee-for-service Medicare, and the generalizability to all U.S. patients, including non–fee-for-service Medicare beneficiaries, those with private insurance, and younger patients, is unclear. However, it should be noted that PAD is a disease of the elderly, a population most represented in Medicare.

Conclusions

LE amputation rates have decreased significantly since 2000 in the United States. Significant geographic variation exists in the performance of LE amputation in Medicare beneficiaries with PAD. Future studies should aim to determine the factors associated with the observed reduction in amputations and geographic variation. Finally, the current study demonstrates the critical need for education programs for clinicians and patients that will focus on best practices for the prevention and treatment of PAD in patients at risk for LE amputation nationwide.

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Key Words: critical limb ischemia ■ geographic variation ■ lower-extremity amputation ■ peripheral artery disease.

APPENDIX

For supplementary material, please see the online version of this article.