Preventive Medicine Reports 23 (2021) 101505

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Opportunities for diabetes and peripheral artery disease-related lower limb amputation prevention in an Appalachian state: A longitudinal analysis

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A R T I C L E I N F O

Keywords:
Lower extremity amputation
Peripheral artery disease
Diabetes
Rural health
Risk factor modification
Disease management
Behavior change

A B S T R A C T

Lower extremity amputation due to peripheral artery disease (PAD) and diabetes (DM) is a life-altering event that identifies disparities in access to healthcare and management of disease. West Virginia (WV), a highly rural state, is an ideal location to study these disparities. The WVU longitudinal health system database was used to identify 1) risk factors for amputation, 2) how disease management affects the risk of amputation, and 3) whether the event of amputation is associated with a change in HbA1c and LDL levels.

Adults (≥18 years) with diagnoses of DM and/or PAD between 2011 and 2016 were analyzed. Multivariable logistic regression analyses were performed on patients with lab information for both HbA1c and LDL while adjusting for patient factors to examine associations with amputations. In patients who underwent amputation, we compared laboratory values before and after using Wilcoxon signed rank tests.

50,276 patients were evaluated, 369 (7.3/1000) underwent amputation. On multivariable analyses, Male sex and Self-pay insurance had higher odds for amputation. Compared to patients with DM alone, PAD patients had 12.3 times higher odds of amputation, while patients with DM and PAD had 51.8 times higher odds of amputation compared to DM alone. We found significant associations between odds of amputation and HbA1c (OR 1.31,CI = 1.15–1.48), but not LDL. Following amputation, we identified significant decreases in lab values for HbA1c and LDL.

These findings highlight the importance of medical optimization and patient education and suggest that an amputation event may provide an important opportunity for changes in disease management and patient behavior.

1. Introduction

Amputation is a devastating but preventable complication of diabetes (DM) and peripheral artery disease (PAD). The financial, physical and societal costs of amputation are high, with financial costs estimated at 8.7 billion dollars in 2013 alone (Limb Loss Task Force/Amputee Coalition of America, 2019). Amputation is also a marker for severe end-stage cardiovascular disease. Diabetic patients undergoing a PAD-related amputation have a 50–74% 5-year mortality primarily due to associated cardiac and cerebrovascular complications, (Limb Loss Task Force/Amputee Coalition of America, 2019) a prognosis worse than most forms of cancer.

DM and PAD-related amputations are largely preventable, a foot ulcer precedes 85% of diabetes-related amputations (Armstrong et al., 2017); (Pecoraro et al., 1990) , and high-quality primary care with timely podiatric and vascular intervention can substantially reduce the risk of amputation (Pecoraro et al., 1990; Rogers et al., 2010; Sloan et al., 2010; Blanchette et al., 2020; Armstrong et al., 2012; Sumpio et al., 2010; Musuuza et al., 2020; Feinglass et al., 2008; Tseng et al., 2007). As a result, amputations have become an increasingly important

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https://doi.org/10.1016/j.pmedr.2021.101505
Received 9 March 2021; Received in revised form 8 June 2021; Accepted 19 July 2021
Available online 23 July 2021

measure to study disparities in the quality of DM and cardiovascular disease care in the United States (U.S. Department of Health and Human Services, 2020; Chicago Department of Public Health, 2016). Previous studies have documented significant racial and economic disparities in amputation rates (Pecoraro et al., 1990; Tseng et al., 2007; U.S. Department of Health and Human Services, 2020; Chicago Department of Public Health, 2016; Nelson, 2002); however limited data exist focusing on rural disparities. This is of particular concern as rural populations tend to have multiple risk factors for amputation: they are older, economically depressed, with higher levels of chronic disease, riskier health behaviors and greater barriers to accessing health care than their non-rural counterparts (Harris et al., 2016). These issues are further amplified in Appalachia, a highly rural region with higher overall cardiovascular disease deaths, DM prevalence rates and tobacco use compared to the rest of the U.S. (Harris et al., 2016; Marshall et al., 2017; Center for Disease Control and Prevention, 2018a; Center for Disease Control and Prevention, 2014; Center for Disease Control and Prevention, 2018b).

West Virginia (WV) is an ideal location to study rural and Appalachian health disparities, as 97% of its land mass is regarded as rural (Census Bureau, 2012) and it is the only state considered to be 100% Appalachian (Marshall et al., 2017). WV also has significant state-wide disparities in the prevalence of cardiovascular disease, DM and other amputation risk factors (Center for Disease Control and Prevention, 2018a). In a recent study, we used state-level discharge data to identify significant geographic disparities in amputation risk across the state of WV (Minc et al., 2019), but this cross sectional analysis was not able to examine patient risk factors longitudinally. In order to gain a better understanding of this issue, and to identify opportunities for improvement of patient care, we examined the West Virginia Clinical and Translational Science Institute (WVCTSI) Integrated Data Repository (IDR) longitudinal patient database to identify 1) risk factors leading to amputation in this rural population, 2) how access to care/quality of care/patient management, represented by hemoglobin A1c (HbA1c) and low-density lipoproteins (LDL) affects the risk of amputation, and 3) whether the event of amputation is associated with a change in these levels.

2. Methods

We used a retrospective cohort study design, analyzing the WVCTSI IDR, a longitudinal database of over 2 million patients, containing electronic health record data for all inpatient and outpatient encounters at West Virginia University (WVU) and affiliated hospitals and clinics. Inclusion criteria were adult patients (≥18 years) with diagnoses of DM and/or PAD between 2011 and 2016. Diagnoses of DM/PAD were based on International Classification of Disease (ICD)-9-Clinical Modification (CM) and ICD-10-CM codes and major and minor lower limb amputations were identified using Current Procedural Terminology (CPT) codes. Major amputations were defined as those performed above the ankle (below-the-knee and above-the-knee) and minor amputations were defined as those below the ankle (foot and toes). Traumatic amputations were excluded. The study was approved by the WVU institutional review board (protocol #1704554319) and a waiver of consent was granted.

2.1. Statistical analyses

Patient characteristics were compared between those undergoing any amputation versus those without amputation. Categorical variables were compared using chi-square tests and Wilcoxon tests for continuous variables. We ran multivariable logistic regression models examining risk factors for the odds of any amputation. Models were adjusted for rurality, tobacco use, sex, insurance, age, coronary artery disease (CAD), PAD, DM, PAD with DM, congestive heart failure (CHF), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), hypercholesterolemia, obesity, and renal failure. Rurality was added as a covariate due to its' potential role as a barrier to healthcare access. Rurality was defined using rural–urban commuting area (RUCA) codes, a model that defines rurality based on population numbers, as well as access to tertiary medical care (see below for more information) (USDA, 2010).

We then ran models using a subset of our cohort that had laboratory information (25% of the total population) pertinent to amputation risk factors available. For patients undergoing amputation we used values only before their amputation. Laboratory values were trimmed at the 1st and 99th percentile upon examining their distributions. Prior to inclusion in our model laboratory variables were assessed for non-linearity and splines were created where necessary using a knot at the median value. We ran three iterations of models using the laboratory values; 1) including all 6 tests (cholesterol, HbA1c, HDL, LDL, non-HDL cholesterol, triglycerides, VLDL), 2) including only significant labs from univariate analysis, and 3) including only LDL and HbA1c. The decision to use only LDL and HbA1c was because these particular labs represent modifiable lab results that can be improved with access to quality care, appropriate medication and changes in behavior. The other lab values have a greater genetic influence and are not as representative of issues of access to care and patient behavior change. Model fit was evaluated using c-statistics for each iteration. Additionally, for the select amputation patients who had laboratory information present we compared their average values before and after their amputation using Wilcoxon's signed rank test. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

2.2. Definition of Rural and Urban

The Rural-Urban Commuting Area (RUCA) code system was used to classify patients as urban versus rural. RUCA is a validated classification system of 33 codes used by the United States (US) Federal Office of Rural Health Policy (Health Resources and Services Administration, 2021) as well as the US Department of Agriculture Economic Research Service to define rural and urban areas (USDA, 2010). RUCA uses measures of population density, levels of urbanization and journey-to-work commuting to characterize all US Census tracts with respect to their rural/urban status and commuting relationship to other tracts. RUCA codes reflect the reality that the terms "rural" and "urban" are multidimensional concepts that require different definitions based on the purpose of the code application. The University of Washington Rural Health Research Center RUCA zip code approximation system was used to translate patient zip codes into RUCA codes and the RUCA code aggregation model used for this study was "Categorization C" (Rural Health Research Center, 2018). This model aggregates the 33 codes into two groups, rural and urban, and was used to evaluate the dichotomous effect of rural/urban status on outcome.

3. Results

3.1. Descriptive statistics

During the study period, we identified 50,276 patients with DM and/or PAD who visited a WVU health system clinic or was admitted to a WVU health system hospital. Overall, the median age of patients was 66, they were almost equally distributed by gender, 42.2% were on Medicare, 7.3% reported tobacco use, 76.6% were designated as urban by RUCA code, and 54.7% had DM alone (while 26.9% had PAD alone and 18.5% had both DM and PAD) (Table 1).

The total number of any amputation (major or minor) was 369, i.e.; the prevalence of amputation among patients with a diagnosis of DM and/or PAD was 7.3 per 1000 cases over the period of the study (or 1.2/1000 per year). Of these, 210 patients had major (4.2/1000) amputations, 128 had minor (2.5/1000) amputations and 31 patients had both (0.6/1000). Amputation patients were more likely to be males (69.4% vs

Table 1
Characteristics of study population.

Variable		Overall patients with DM and/or PAD (N = 50276)		Patients without amputation (N = 49907)		Patients with amputation (major and minor) (N = 369)		P-value
Age	Median	66.00		66.00		64.00		0.6330
		#	%	#	%	#	%	
Female	Yes	25,620	50.96	25,507	51.11	113	30.62	**<0.0001**
	No	24,656	49.04	24,400	48.89	256	69.38	
Payor type	Self-pay	2912	5.79	2875	5.76	37	10.03	**0.0006**
	Medicare	21,238	42.24	21,084	42.25	154	41.73	
	Medicaid	8603	17.11	8532	17.10	71	19.24	
	Private	15,422	30.67	15,332	30.72	90	24.39	
Tobacco Use	Yes	3658	7.28	3624	7.26	34	9.21	0.1502
	No	46,618	92.72	46,283	92.74	335	90.79	
Urban/Rural Location	Rural	11,711	23.29	11,626	23.30	85	23.04	0.9004
	Urban	38,530	76.64	38,246	76.63	284	76.96	
Diabetes / PAD	Diabetes and PAD	9285	18.47	9043	18.12	242	65.58	**<0.0001**
	PAD (alone, no DM)	13,510	26.87	13,413	26.88	97	26.29	
	Diabetes (alone, no PAD)	27,481	54.66	27,451	55.00	30	8.13	
Diabetes	Yes	36,766	73.13	36,494	73.12	272	73.71	0.7994
	No	13,510	26.87	13,413	26.88	97	26.29	
PAD	Yes	22,795	45.34	22,456	45.00	339	91.87	**<0.0001**
	No	27,481	54.66	27,451	55.00	30	8.13	
CAD	Yes	21,955	43.67	21,770	43.62	185	50.14	**0.0104**
	No	28,320	56.33	28,137	56.38	183	49.59	
CHF	Yes	9598	19.09	9483	19.00	115	31.17	**<0.0001**
	No	40,677	80.91	40,424	81.00	253	68.56	
CKD	Yes	8877	17.66	8750	17.53	127	34.42	**<0.0001**
	No	41,398	82.34	41,157	82.47	241	65.31	
COPD	Yes	11,559	22.99	11,451	22.94	108	29.27	**0.0036**
	No	38,716	77.01	38,456	77.06	260	70.46	
Hypercholesterolemia	Yes	25,663	51.04	25,455	51.00	208	56.37	**0.0349**
	No	24,612	48.95	24,452	49.00	160	43.36	
Obesity	Yes	13,426	26.70	13,309	26.67	117	31.71	**0.0268**
	No	36,849	73.29	36,598	73.33	251	68.02	
Renal Failure	Yes	2567	5.11	2519	5.05	48	13.01	**<0.0001**
	No	47,708	94.89	47,388	94.95	320	86.72	

a. Cumulative values do not reach 100% in all variables due to missing values in the dataset.
b. Abcbreviations: CAD: Coronary Artery Disease; CHF: Congestive Heart Failure; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; PAD: Peripheral Artery Disease **Boldface indicates statistical significance**

48.9%), have non-private insurance (71% vs 65.1%), have DM and PAD (65.6% vs 18.1%), CAD (50.1% vs 43.6%), CHF (31.2% vs 19%), CKD (34.4% vs 17.5%), COPD (29.3% vs 22.9%), hypercholesterolemia (56.4% vs 51.0%), obesity (31.7% vs 26.7%), and renal failure (13.0% vs 5.1%) (Table 1).

3.2. Laboratory values and changes after amputation

When examining lab values comparing amputation patients to non-amputation patients, amputation patients had statistically significant lower average lab values for cholesterol (median 158 vs. 167, $p = 0.0064$) HDL (median 35 vs. 39.8, $p = 0.0001$) and LDL (median 83.4 vs. 93, $p = 0.0095$), and higher values for HbA1c (median 7.3 vs. 6.5, $p < 0.0001$) (Table 2). Additionally, we further compared these lab values before and after amputation for patients who had labs available for both time points. We found statistically significant differences for HbA1c, and LDL. Specifically, prior to amputation the average HbA1c value for amputation patients had a median of 7.7, which was reduced to 7.0 after amputation ($p < 0.0001$), and amputation LDL levels decreased from a median of 100.3 to 84 ($p = 0.045$) (Table 3). When examining the number of days before and after amputation and laboratory results, we found that the median number of days between a patient's last lab and their amputation was 14.5 days (IQR: 3–69) and the median number of days between a patients amputation and their first follow-up lab was 58 days (IQR: 4.5–157.5).

3.3. Multivariable logistic regression

Our multivariable logistic regression model (Table 4) found the following factors associated with increased odds of amputation: self-pay had 69% higher odds of amputation than private insurance. Patients with PAD alone vs DM alone had 12.3 times higher odds of amputation,

Table 2
Laboratory values overall.

Laboratory test	**Overall (N = 50276)**		**No amputation (N = 49907)**		**Any amputation (N = 369)**		**P-value**
	#	Median	#	Median	#	Median	
CHOL	**17,876**	**166.80**	**17,751**	**167.00**	**125**	**158.13**	**0.0064**
HbA1c	**21,689**	**6.50**	**21,469**	**6.50**	**220**	**7.30**	**<0.0001**
HDL	**17,857**	**39.67**	**17,736**	**39.75**	**121**	**35.00**	**0.0001**
LDL	**17,255**	**93.00**	**17,133**	**93.00**	**122**	**83.38**	**0.0095**
Non-HDL	16,899	124.00	16,776	124.00	123	121.00	0.0640
TRIG	17,886	137.00	17,759	137.00	127	143.00	0.2920
VLDL	17,546	27.00	17,421	27.00	125	28.00	0.3189

a. Abbreviations: CHOL: Cholesterol; HbA1c: Hemoglobin A1c; HDL: High-density lipoproteins; LDL: Low-density lipoproteins; TRIG: Triglycerides; VLDL: Very-low density lipoproteins; **Boldface indicates statistical significance**

Table 3
Laboratory values before and after amputation.

Laboratory test	Patients median value before (IQR)	Patients median value after (IQR)	Wilcoxon signed rank test
CHOL	171.5 (146.9–199.3)	153.8 (127.5–201.8)	0.1121
HbA1c	**7.7 (6.4–10.0)**	**7.0 (5.8–8.6)**	**<0.0001**
HDL	35.7 (32.5–45.0)	35.3 (27.9–43.5)	0.0760
LDL	**100.3 (69.5–118.0)**	**84.0 (58.7–113.0)**	**0.0450**
Non-HDL	133.8 (107.0–161.5)	121.0 (94.0–152.5)	0.1317
TRIG	168.3 (133.0–258.0)	158.5 (117.9–245.9)	0.5010
VLDL	33.3 (26.3–47.0)	30.8 (23.5–48.3)	0.7351

a. Abbreviations: CHOL: Cholesteroal; HbA1c: Hemoglobin A1c; HDL: High-density lipoproteins; LDL: Low-density lipoproteins; TRIG: Triglycerides; VLDL: Very-low density lipoproteins **Boldface indicates statistical significance**

and patients with PAD and DM vs DM alone had 51.8 times higher odds of amputation. Lastly, we found that CKD was associated with a 75% increase in the odds of amputation. With regards to protective factors, CAD was associated with a 74% reduction in the odds of amputation. Our results were similar when running our model amongst the subset of patients that had lab information available (n = 12,409, i.e.: 26% of our population), however the effect size for PAD vs DM as well as PAD and DM vs DM alone were substantially increased when laboratory values were included in the model. Specifically, the adjusted odds ratios (AOR) were 28.6 and 69.9 respectively. HbA1c was the only laboratory value found to be a statistically significant risk factor in the model, with a 32% higher odds of amputation for each 1-unit increase in A1c. While HDL was the only value found to be protective for amputation, with a 16% reduction of amputation odds with each 5 unit increase in HDL up to a value of 50 mg/dL, and an 18% reduction for each 5 unit increase greater than or equal to a value of 50 mg/dL. When we further restricted the model to just labs that had significant univariate results (cholesterol, HDL, HbA1c and LDL, see appendix Table 1), we found similar patterns to our model adjusted only for patient risk factors. This was also the case when we ran our model including only HbA1c and LDL along with patient risk factors.

4. Discussion

In this retrospective cohort study of a longitudinal system-wide database from 2011 to 2016, we found that the prevalence of amputation in patients with DM and/or PAD in WV was 7.3/1000 over 5 years, or 1.2/1000 on average annually. Our multivariable analysis found that patients with PAD alone had significantly higher odds of amputation compared to patients with DM alone, and that patients with PAD and DM had a remarkable 51.8 times higher odds for amputation than patients with DM alone. In addition, we found significant increases in the odds of amputation in patients with increased HbA1c and decreased odds for patients with increased HDL. Finally, we found that patients that underwent amputation had significant decreases in HbA1c and LDL on post-operative visits.

Our finding of a 7.3/1000 (1.2/1000 per year) prevalence of amputation in patients with DM and/or PAD from 2011 to 2016 is lower than data previously published by our group, where we used the West Virginia Health Care Authority Healthcare Cost and Utilization Project (HCUP) dataset (2011–2016) to find an amputation rate of 12.4/1000 in patients with DM and/or PAD (Minc et al., 2019). While our prior study used a cross-sectional state-wide database to show that the prevalence of amputation was high in WV, the use of a longitudinal database in this

Table 4
Multivariable Logistic Regression.

Variable	Any amputation (without controlling for lab values) N = 48,142 OR (95% CI)	Any amputation (controlling for all variables + all lab values) N = 12,409 OR (95% CI)	Any amputation (controlling for all variables + statistically significant lab values)$_a$N = 12,712 OR (95% CI)	Any amputation (controlling for all variables + LDL and HbA1c) N = 12,930 OR (95% CI)
Rural	0.98 (0.77–1.27)	1.13 (0.66–1.93)	1.1 (0.65–1.86)	1.03 (0.61–1.74)
Tobacco user	0.9 (0.62–1.31)	0.86 (0.39–1.86)	0.82 (0.38–1.78)	0.78 (0.36–1.68)
Male vs Female	**2.43 (1.93–3.07)**	**2.26 (1.38–3.69)**	**2.23 (1.38–3.6)**	**2.44 (1.54–3.86)**
Medicaid vs Private	1.35 (0.98–1.87)	0.93 (0.48–1.78)	0.9 (0.47–1.73)	0.92 (0.49–1.71)
Medicare vs Private	1.12 (0.83–1.52)	0.76 (0.42–1.37)	0.84 (0.47–1.5)	0.79 (0.45–1.38)
Self-pay vs Private	**1.69 (1.13–2.52)**	1.66 (0.81–3.41)	1.71 (0.83–3.49)	1.52 (0.75–3.08)
Age	**0.99 (0.98–1)**	0.99 (0.97–1.01)	0.99 (0.97–1.01)	0.99 (0.97–1.01)
CAD	**0.26 (0.2–0.33)**	**0.13 (0.08–0.22)**	**0.14 (0.09–0.23)**	**0.15 (0.09–0.24)**
PAD vs Diabetes	**12.29 (7.93–19.07)**	**28.59 (8.49–96.28)**	**23.9 (7.84–72.86)**	**25.38 (8.44–76.33)**
PAD and Diabetes vs Diabetes	**51.81 (33.85–79.3)**	**69.87 (24.4–200.07)**	**55.25 (21.25–143.64)**	**57.76 (22.27–149.79)**
CHF	1.24 (0.95–1.62)	1.43 (0.85–2.39)	1.38 (0.83–2.29)	1.42 (0.87–2.32)
CKD	**1.75 (1.34–2.27)**	**1.86 (1.11–3.13)**	**1.8 (1.07–3)**	**1.75 (1.06–2.89)**
COPD	1 (0.78–1.29)	0.68 (0.41–1.13)	0.68 (0.41–1.11)	0.72 (0.45–1.17)
Hypercholesterolemia	0.89 (0.71–1.13)	1.18 (0.66–2.13)	1.11 (0.63–1.95)	0.99 (0.58–1.7)
Obesity	0.93 (0.73–1.19)	0.8 (0.5–1.27)	0.83 (0.53–1.32)	0.93 (0.6–1.44)
Renal Failure	1.24 (0.87–1.77)	1.69 (0.9–3.16)	1.69 (0.9–3.15)	1.69 (0.92–3.1)
HDL (per 5 unit increase < 50)		**0.84 (0.72–0.99)**	**0.85 (0.73–0.99)**	–
HDL (per 5 unit increase >= 50)		**0.82 (0.68–0.99)**	**0.83 (0.69–1)**	–
HbA1c (per 1 unit increase)		**1.32 (1.15–1.51)**	**1.3 (1.14–1.48)**	**1.31 (1.15–1.48)**
LDL (per 5 unit increase)		1.13 (0.92–1.39)	0.99 (0.96–1.03)	0.98 (0.95–1.01)
Non-HDL (per 5 unit increase)		0.88 (0.71–1.08)	–	–
TRIG (per 5 unit increase)		1.01 (0.98–1.05)	–	–
VLDL (per 5 unit increase)		1.06 (0.88–1.29)	–	–
C statistic	0.848	0.878	0.864	0.859

a. Based on univariate analysis of lab values, see supplemental table I for details
b. Abbreviations: CAD: Coronary Artery Disease; CHF: Congestive Heart Failure; CHOL: Cholesterol; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; HbA1c: Hemoglobin A1c; HDL: High-density lipoproteins; LDL: Low-density lipoproteins
PAD Peripheral Artery Disease; TRIG: Triglycerides; VLDL: Very-low density lipoproteins

study allowed us to follow individual patients through multiple hospitalizations and clinic visits and is therefore more likely to reflect the true amputation prevalence in our patient population. In addition, the HCUP dataset provides discharge data for all patients hospitalized for DM and/or PAD across the state, while the IDR dataset only covers the WVU system (both outpatient and inpatient visits) which is a quaternary health care system with access to vascular surgeons and limb preservation specialists, which may also account for the difference. Currently, it is difficult to compare data on amputation rates in the U.S. because of inconsistent methodology between sources. However, our data is most consistent with the Dartmouth Atlas data, which looked at major amputation in Medicare enrollees and found the U.S. average to be 0.572/1000 in 2015, with WV having the highest rate at 0.9/1000 (Dartmouth Institute for Health Policy and Clinical Practice, 2021). Our study's finding of a higher rate in WV is likely related to our database including patients $\geq$ 18 years of age and our inclusion of major and minor amputation in this rate.

Another important finding of this study includes the impact of PAD on risk for amputation compared to that of DM alone. On multivariable analysis, patients with PAD alone had 12 times higher odds of amputation than patients with DM, and patients with DM and PAD had a 52 times higher odds of amputation than patients with DM alone. This emphasizes the importance of identifying and modifying PAD risk factors as part of public health efforts to decrease atraumatic amputation. PAD is not a significant priority in current public health quality improvement efforts for atraumatic amputation, which focus on diabetic foot exam and foot care education for DM patients, but do not account for PAD patients or PAD risk factor modification (Collaborative and Core, 2019). Medical optimization for PAD such as statins, antiplatelet therapy and smoking cessation will likely improve amputation outcomes for PAD and PAD/DM patients. Further evidence for this concept is noted in the finding that CAD is protective for amputation in our study (a phenomenon that has been documented in other studies) (Durazzo et al., 2013; Eslami et al., 2007), and may be due to patients carrying the diagnosis of CAD already undergoing medical optimization with statins and anti-platelets that would also be beneficial for underlying PAD. This study therefore, provides a potential area of public health focus for secondary amputation prevention by suggesting that patients with PAD risk factors should receive the same level of medical optimization as CAD patients and the same level of foot surveillance as DM patients.

This study does identify a potential area for intervention to improve patient outcomes in the WV patient population. We found that only 26% of patients with DM/PAD treated at WVU hospitals and clinics during the study period had a recent laboratory blood test. This rate is significantly lower than rates documented by other states across the country. For example, according to the Texas Department of Health and Human Services data, 85.6% of adults living in Texas with DM has had one or more HbA1c test conducted within the year, and the national rate of HbA1c testing has been reported by the national Behavioral Risk Factor Surveillance System (BRFSS) to be 89% per year (Nelson et al., 2001). We speculate that a combination of lack of access to healthcare, poor health literacy and low socio-economic status are the most likely contributors to our low testing rates. While our study did not explore barriers to patient care specifically, as a state, it is imperative that we clearly identify these barriers and develop practical solutions.

One encouraging finding in our study is a significant decrease in both HbA1c and LDL levels in patients following an amputation of the lower extremity. This may represent a turning point in patient behavior or an improvement in intensity and access to care because of surgery. This turning point, has been described in the literature and has been termed the "Sentinel Event Effect" and built into a conceptual model by Boudreaux et al. (2012). In their model, Boudreaux et al. use variables such as event severity, event-related fear, and event-related causal attribution, to predict whether a health event will lead to behavior change. Further in the literature, health behavior change has been described in women who have had a first-degree relative diagnosed with breast cancer (Lemon et al., 2004), and in smoking cessation following a major cardiac event (Riley et al., 2019). For vascular surgery patients, it is particularly important to note that for health behaviors such as smoking cessation, the Sentinel Event Effect is significantly leveraged if it is combined with intervention during the same hospitalization period (i.e.: in-hospital smoking cessation education and referral). For example, a randomized controlled trial found that in patients who have had a cardiac event, the long-term smoking cessation rate is significantly higher in patients who have had an in-hospital smoking cessation intervention, compared to those who did not (Dornelas et al., 2000). Similar strategies should be adopted for PAD and foot complication patients during their hospitalizations.

While this study is significantly strengthened by its' longitudinal nature and overall study size, it does have limitations. First, as a database study, there are inherent limitations such as the potential for type 1 error due to the large sample size. Second, our findings are constrained to the predetermined variables created at the time of the dataset creation, which limits our ability to understand certain nuances in patient history and care. This includes variables such socioeconomic status, which we are only able to assess by using insurance status as a proxy, as well as race/ethnicity, which, although very important to consider in amputation research, is not well documented in the WVU Hospital System, and would not be appropriate to use in analysis. Third, certain data elements, such as tobacco use, are dependent on patient history and veracity, which may not be accurate. For example, the prevalence of tobacco use in WV is known to be 25% (Center for Disease Control and Prevention, 2018b), however, only 7% of our patient population admitted to using tobacco which is unlikely to be accurate. Another limitation is that this study only includes patients within the WVU health system, and despite the large sample size, does not fully represent the state of West Virginia. Finally, in our definition of "rurality", we used the RUCA coding system, which is based on commuting patterns to understand rural patient access to tertiary care centers. As a result, our rural numbers are likely to be artificially low, as all patients in the study were able to access the WVU health system. A state-based dataset would improve the latter issues but would come at the cost of access to longitudinal data, which was critical for our research question.

5. Conclusions

In this study, we found evidence to support several levels of public health level interventions to improve amputation efforts in our state, as well as in PAD/DM patients in general. We found that laboratory testing for cholesterol and HbA1c levels in patients with DM and/PAD is significantly lacking in our patient population and efforts should be made to improve this issue system-wide. We also found that the event of amputation likely represents a Sentinel Event that can be leveraged to change patient behavior to improve future outcomes. Finally, our results emphasize that public health efforts for amputation prevention should include identifying patients at risk for PAD, so they might benefit from the same cardiovascular risk factor modifications that CAD patients receive, as well as the same attention to foot care and education that is present in high quality DM care.

Funding

This work was supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number 5U54GM104942. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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