ORIGINAL RESEARCH

Prevalence and Predictors of Lower Limb Amputation in the Spinal Cord Injury Population

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Background: Despite limited data demonstrating altered hemodynamics in the lower extremities (LEs) among the population with spinal cord injury (SCI) and increased frequency of peripheral arterial disease (PAD), epidemiologic data are limited for amputations, a potential consequence. This study investigates the association of amputation due to vascular complications as a secondary outcome measure within the SCI population.

Methods: A retrospective cohort study was performed within a veteran population with SCI at a US Department of Veteran Affairs hospital to determine the prevalence of limb loss. We hypothesized that premorbid SCI increased the likelihood of LE amputation.

Results: Of 1055 charts reviewed, 91 (8.7%) patients had an amputation, 70 (76.1%) had a dysvascular etiology. Transfemoral amputations were the most common level (n = 53) of amputation. Our results showed a positive correlation between the completeness of injury and the prevalence of amputation.

Conclusion: There is an increased frequency of amputation among the veteran population with SCI compared with that of the general US population. Amputations frequently occur at more proximal levels with motor complete injuries. Studies using a larger population and multiple centers are needed to confirm this alarming trend.

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At the James A. Haley Veterans' Hospital (JAHVH) in Tampa, Florida, the prevalence of amputations among patients at the spinal cord injury (SCI) center seems high. Despite limited data demonstrating altered hemodynamics in the lower extremities (LEs) among the SCI population and increased frequency of peripheral arterial disease (PAD), amputations among patients with SCI have received little attention in research.[1-3]

In the United States, most amputations are caused by vascular disease related to peripheral arterial disease (PAD) and diabetes mellitus (DM).[4] PAD primarily affects the LEs and is caused by atherosclerotic obstruction leading to insufficient blood flow. PAD can present clinically as LE pain, nonhealing ulcers, nonpalpable distal pulses, shiny or cold skin, absence of hair on the LE, or distal extremity pallor when the affected extremity is elevated. However, PAD is often asymptomatic. The diagnosis of PAD is typically made with an ankle-brachial index (ABI) ≤ 0.9.[5] The prevalence of PAD is about 4.3% in Americans aged ≥ 40 years, increases with age, and is almost twice as common among Black Americans compared with that of White Americans.[6] Many studies in SCI populations have documented an increased prevalence of DM, dyslipidemia, obesity, hypertension (HTN), and cigarette smoking.[7-9] PAD shares these risk factors with coronary artery disease (CAD), but relative to CAD, tobacco smoking was a more substantial causative factor for PAD.[10] Given the preponderance of associated risk factors in this population, PAD is likely more prevalent among patients with SCI than in the population without disabilities. Beyond these known risk factors, researchers hypothesized that SCI contributes to vascular disease by altering arterial function. However, this is still a topic of debate.[11-13] Trauma also is a common cause of amputation, accounting for 45% of amputations in 2005.[4] Patients with SCI may experience traumatic amputations simultaneously as their SCI, but they may also be predisposed to traumatic amputations related to osteopenia and impaired sensation.

Since amputation is an invasive surgery, knowing the severity of this issue is important in the SCI population. This study quantifies the prevalence of amputations of the LEs among the patients at our SCI center. It then characterizes these amputations' etiology, their relationship with medical comorbidities, and certain SCI classifications.

METHODS

This retrospective cohort study used the US Department of Veterans Affairs (VA) Computerized Patient Record System. The cohort was defined as all patients who received an annual examination at our SCI center over 4 years from October 1, 2009 to September 30, 2013. Annual examination includes a physical examination, relevant

surveillance laboratory tests, and imaging, such as renal ultrasound for those with indwelling urinary catheters. One characteristic of the patient population in the VA system is that diagnoses, such as multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS), that involve spinal cord lesions causing symptoms are included in the registry, besides those with other traumatic or nontraumatic SCI. October 1 to September 30 was chosen based on the VA fiscal year (FY).

During this period, 1678 patients had an annual examination. Of those, 299 patients had an SCI etiology of ALS or MS, and 41 had nonfocal SCI etiology that could not be assessed using the American Spinal Injury Association Impairment Scale (AIS) and were excluded. Also excluded were 283 patients who did not have an annual examination during the specified time span. Some patients do not have an annual examination every year; for those with multiple annual examinations during that time frame, the most recent was used.

One thousand fifty-five patients were included in the statistical analysis. Date of birth, sex, race, ethnicity, date of death, smoking status, DM diagnosis, HTN diagnosis, use of an antiplatelet, antihypertensive, or lipid-lowering agent, blood pressure, hemoglobin A_{1c}, and lipid panel were collected. The amputation level and etiology were noted. The levels of amputation were classified as toe/partial foot, transtibial amputation (TTA), or transfemoral amputation (TFA). Hip and knee disarticulations were classified at a TFA level. The etiology was classified as dysvascular, traumatic, other, or unknown. Dysvascular included a range of clinical etiologies, including DM, PAD, infection, and poor wound healing. These etiologies were grouped because patients tended to have an overlap of etiologies in the medical record. This collective dysvascular category is consistently used in amputation research, even though the difficulty of

TABLE 1 Population Health Risk Factors and Amputation History

Variables	Amputation (n = 91)	No Amputation (n = 964)	*P* value
Race and ethnicity, No. (%)			.10
White	72 (80)	735 (76)	
Black	11 (12)	155(16)	
Hawaiian/Pacific Islander	3 (3)	9 (1)	
Hispanic White	2 (2)	43 (4)	
Asian	0 (0)	2 (< 1)	
Combination	1 (1)	15 (2)	
Age, y			
Median (IQR)	62.0 (55.0-67.0)	59.0 (49.0-66.0)	.006
Mean (SD)	61.2 (9.9)	57.1 (13.3)	< .001
Cholesterol, median (IQR)			
High-density lipoprotein	34.0 (29.0-41.0)	39.0 (33.0-47.0)	< .001
Low-density lipoprotein	87.0 (66.0-105.0)	93.0 (74.0-115.0)	.03
Total	149.5 (126.0-175.0)	161.0 (137.0-183.0)	.02
Triglycerides	137.0 (97.0-192.0)	114.0 (78.0-162.0)	.006
Hemoglobin A_{1c}, median (IQR)	5.7 (5.6-6.2)	5.7 (5.3-6.1)	.02
Body mass index, median (IQR)	25.1 (22.7-29.6)	26.8 (23.1-30.4)	.15
Smoking status, No. (%)			.03
Never smoked	17 (18.7)	281 (29.2)	
Current smoker	34 (37.4)	249 (25.8)	
Former smoker	40 (44.0)	434 (45.0)	
Diabetes mellitus, No. (%)			< .001
Yes	33 (36.3)	202 (21.0)	
No	58 (63.7)	762 (79.1)	
Hypertension, No. (%)[a]			.004
Yes	59 (64.8)	473 (49.1)	
No	32 (35.2)	491 (50.9)	
Peripheral artery disease, No. (%)			< .001
Yes	38 (41.9)	65 (6.7)	
No	53 (58.2)	899 (93.3)	

[a]Hypertension was defined as systolic blood pressure > 130 mmHg or diastolic blood pressure > 80 mmHg.

identifying this group of etiology can be challenging.[4,14] In the setting of peripheral vascular disease, there may be decreased oxygen delivery, nutrients, or antibiotics that could impair wound healing, leading to infection. Additionally, infection causes microthrombi formation that could lead to worsening ischemia, necrosis, and gangrene.[15] The traumatic classification was applied if the amputation was related to a traumatic event or fracture, including those who failed conservative management of a fracture. The other classification included amputations for cancer.

Statistical Analysis
Descriptive data were summarized as the median and IQR for continuous variables or the number and percentage for categorical variables. The χ^2 test was used to analyze the association between categorical variables and

amputation status. A nonparametric Wilcoxon test was used to investigate the distribution of continuous variables across patients with amputation and patients without amputation. Binary logistic regression analysis was used to investigate amputation risk factors. We report goodness of fit using the Hosmer and Lemeshow test and the area under the curve (AUC) for the multivariate model. Statistical significance was prespecified at a 2-sided $P < .05$. SAS version 9.4 was used for all statistical analyses.

RESULTS

Mean age was approximately 61 years for the 91 patients at the time of the most recent amputation (Table 1). Among those with amputation, 63% were paraplegic and 37% were tetraplegic.

Of 1055 patients with SCI, 91 (8.6%) patients had an amputation. Of those, 70 (76.1%) were from nontraumatic causes (dysvascular), 17 (18.5%) were traumatic, 4 (4.3%) were from other causes (ie, cancer), and only 1 (1.1%) was of unknown cause.

Of the 91 patients with amputation, 64 (69.6%) had at least 1 TFA—33 were unilateral and 31 were bilateral. Two patients had a TFA on one side and a TTA on the other. Partial foot/toe and TTA were less common amputation levels with 14 (15.4%) and 13 (14.3%), respectively. Most amputations (86.8%) occurred over 6 months from the day of initial SCI, and were most commonly dysvascular (Table 2). Traumatic amputation occurred more evenly at various stages, pre-SCI, during acute SCI, subacute SCI, and chronic SCI.

Injury by Impairment Scale Level

Forty-nine (11.5%) of 426 patients with AIS level A SCI had undergone amputation. In order of prevalence, 23 (46.9%) were unilateral TFA, 17 (34.6%) were bilateral TFA, 10.2% were partial foot/toe, 4.1% were unilateral TTA, and 4.1% were a TTA/TFA combination. Both hip and knee disarticulations were classified in the TFA category.

Sixteen (13.0%) of 123 patients with AIS level B SCI had undergone amputation; 5 (31.3%) of those amputations were unilateral TFA, 6 (37.5%) were bilateral TFA, 3 (18.8%) were partial toe or foot, and 1 (6.3%) was for unilateral and bilateral TTA each.

Twelve (8.4%) of 143 patients with AIS level C SCI had undergone amputation: 6 (50.0%) were bilateral TFA; 3 (25.0%) were unilateral TFA; and 3 (25.0%) were unilateral TTA.

Fourteen (3.9%) of 356 patients with AIS level D SCI had undergone amputation. Of those 6 (42.9%) underwent a partial foot/toe amputation; 5 (35.7%) had undergone a unilateral TTA, and 1 (7.1%) underwent amputation in each of the following categories: bilateral TTA, unilateral TFA, and bilateral TFA each.

None of the 7 individuals with AIS E level SCI had undergone amputation.

Health Risk Factors

Of the 91 patients with amputation, the majority (81.3%) were either former or current smokers. Thirty-six percent of those who had undergone amputation had a diagnosis of DM, while only 21% of those who had not undergone amputation had a diagnosis of DM.

At the time of their annual examination 532 patients had a diagnosis of HTN while 523 patients did not. Among patients with amputations, 59 (64.8%) had HTN, while 32 (35.2%) did not. Of the 964 patients without amputation, the prevalence of HTN was 50.9%.

Of 1055 patients with SCI, only 103 (9.8%) had a PAD diagnosis, including 38 (41.9%) patients with amputation. Just 65 (6.7%) patients with SCI without amputation had PAD ($P < .001$). PAD is highly correlated with dysvascular causes of amputation. Among those with amputations due to dysvascular etiology, 50.0% (35/70) had PAD, but for the 21 amputations due to nondysvascular etiology, only 3 (14.3%) had PAD ($P = .004$).

Amputation Predictive Model

A multivariate logistic regression analysis was used to build a predictive model for amputation among patients with SCI while controlling for covariates. In our multivariate analysis, high-density lipoprotein cholesterol (HDL-C), tetraplegia, and PAD were predictive factors for amputation. Patients with SCI who had PAD were 8.6 times more likely to undergo amputation compared to those without PAD (odds ratio [OR], 9.8; $P < .001$; 95% CI, 5.9-16.3). Every unit of HDL-C decreased the odds

of amputation by 5% (OR, 0.95; *P* < .001; 95% CI, 0.93-0.98).

Having tetraplegia decreased the odds of amputation by 43%, compared with those with paraplegia (OR, 0.57; *P* = .02; 95% CI, 0.36 - 0.92). AUC was 0.76, and the Hosmer and Lemeshow goodness of model fit test *P* value was .66, indicating the good predictive power of the model (Table 3).

DISCUSSION

In the US, 54 to 82% of amputations occur secondary to chronic vascular disease. Our study showed similar results: 76.1% of amputations were dysvascular.[4,16] Even in a 2019 systematic review, the most recent prevalence of amputation data was in 2005.[17] The study concluded that among the general population in the US, prevalence of amputation was estimated to be 1 in 190 people, or about 0.5% of the population.[4] We found that the prevalence of amputation among the SCI population in this study was 8.7%. This result is consistent with our initial hypothesis that the prevalence of amputation would be higher among the people with SCI. Using a different case acquisition method, Svircev and colleagues reported that about a 4% prevalence of LE amputation among veterans with chronic SCI (over 1 year from the initial SCI), with an emphasis that it was not a study of amputation incidence.[18] In comparison, we calculated a 7.5% prevalence of amputation during the chronic SCI stage, which showed institutional variation and a consistent observation that LE amputations occurred more frequently in the SCI population.

Our results showed a positive correlation between the completeness of injury and the prevalence of amputation. Those individuals with a motor complete injury, AIS A (40.3%) or AIS B (11.7%) account for approximately half of all amputations in our population with SCI. Another finding was that proximal amputations were more frequent with more neurologically complete SCIs. Of those with an injury classified as AIS A and an amputation, 42 of 49 subjects underwent at least 1 TFA (23 were unilateral TFA, 17 were bilateral TFA, 2 were a TFA/TTA combination). Of those with an AIS B injury and an amputation, 11 of 16

TABLE 2 Amputation Level and Timing

Amputation Measures	Dysvascular	Traumatic	Others
Level, No. (%)			
Partial foot/toe	11 (78.6)	2 (14.3)	1 (7.1)
Unilateral TTA	6 (54.6)	4 (36.4)	1 (9.1)
Bilateral TTA	0 (0)	1 (50.0)	1 (50.0)
TTA/TFA combination	2 (100)	0 (0)	0 (0.0)
Unilateral TFA	24 (75.0)	8 (25.0)	0 (0.0)
Bilateral TFA	27 (90.0)	2 (6.7)	1 (3.3)
Timing of spinal cord injury, No.			
Before injury	2	3	0
Acute (within 1 mo of injury)	1	4	0
Subacute (within 2-6 mo of injury)	1	1	0
Chronic (> 6 mo)	66	9	4

Abbreviations: TFA, transfemoral amputation; TTA, transtibial amputation.

subjects (68.8%) had at least 1 TFA (5 unilateral TFA and 6 bilateral TFA). Among patients with AIS C injury and amputation, 75% had a TFA. At the same time, only 13.3% of all amputations were at the transfemoral level in those with an AIS D injury. None of the participants with an injury classified as AIS E had undergone an amputation.

Given a paucity of literature available regarding amputation levels in patients with SCI, a discussion with a JAHVH vascular surgeon helped explain the rationale behind different levels of amputation among the SCI population—TFA was performed in 64 of 91 cases (70%). Institutionally, TFAs were performed more often because this level had the greatest chance of healing, avoiding infection, and eliminating knee contracture issues, which may affect quality of life. This was believed to be the best option in those individuals who were already nonambulatory. Although this study did not collect data on ambulatory status, this helps explain why those with an SCI classification of AIS D were more likely to have had a more distal amputation to preserve current or a future chance of ambulation, provided that whether the limb is salvageable is the priority of surgical decision.

The prevalence of PAD among veterans is generally higher than it is in the nonveteran population. Studies show that the prevalence of PAD risk factors in the veteran population exceeds national estimates. Nearly two-thirds of veterans have HTN, 1 in 4 has DM, and 1 in 4 is a current smoker, placing veterans at a significantly increased

Table 3 Amputation Predictors[a]

Variables	Univariate Odds Ratio (95% CI)	Univariate P value	Multivariate Odds Ratio (95% CI)	Multivariate P value
Peripheral artery disease	9.92 (6.10-16.13)	< .001	9.82 (5.93-16.27)	< .001
High-density lipoprotein cholesterol	0.95 (0.93-0.97)	< .001	0.95 (0.93-0.98)	< .001
Tetraplegia	0.53 (0.34-0.83)	.005	0.57 (0.36-0.92)	.02

[a]Hosmer and Lemeshow goodness of model fit test, P = .66.

risk of PAD and, therefore, amputation.[19,20] These rates were about the same or greater in our SCI population: 50.4% had HTN, 22.3% had a diagnosis of DM, and 71.8% smoked previously or currently smoked. In 3 large studies, HTN was second only to current smoking as the most attributable risk factor for PAD.[21]

Ongoing research by JAHVH vascular surgeons suggests that patients with SCI were younger and less likely to have HTN, PAD, and/or CAD compared with patients undergoing TFA without SCI. Additionally, patients with SCI had better postoperative outcomes in terms of 30-day mortality, 3-year mortality, and had no increased rate of surgical revisions, strokes, or wound-healing complications. This supports the previous thought that the AIS classification plays a large role in determining amputation levels.

One result in this study is that paraplegia is one of the predictors of future amputation compared with tetraplegia. To our knowledge, there is no literature that supports or explains this finding. A hypothetical factor that could explain this observation is the difference in duration of survival—those with paraplegia who live longer are more likely to experience end-stage consequence of vascular diseases. Another proposed factor is that those with paraplegia are generally more active and have a higher likelihood of sustaining a traumatic cause of amputation, even though this etiology of amputation is minor.

An unexpected finding in our study was that of 1055 patients with SCI, only 9.8% had a PAD diagnosis. In contrast, 41.3% of those with amputation had a PAD diagnosis. JAHVH does not screen for PAD, so this likely represents only the symptomatic cases.

Diagnosing PAD in patients with SCI is challenging as they may lack classic clinical symptoms, such as pain with ambulation and impotence, secondary to their neurologic injury. Instead, the health care practitioner must rely on physical signs, such as necrosis.[22] Of note given the undetermined utility of diagnosing PAD in patients with SCI, early endovascular interventions are not typically performed. We could not find literature regarding when intervention for PAD in patients with SCI should be performed or how frequently those with SCI should be assessed for PAD. One study showed impaired ambulation prior to limb salvage procedures was associated with poor functional outcomes in terms of survival, independent living, and ambulatory status.[23] This could help explain why endovascular procedures are done relatively infrequently in this population. With the lack of studies regarding PAD in the SCI population, outcomes analysis of these patients, including the rate of initial interventions, reintervention for re-amputation (possibly at a higher level), or vascular inflow procedures, are needed.

It would be beneficial for future studies to examine whether inflammatory markers, such as C-reactive protein (CRP), were more elevated in patients with SCI who underwent amputation compared with those who did not. Chronic underlying inflammation has been shown to be a risk factor for PAD. One study showed that, independently of other risk factors, elevated CRP levels roughly tripled the risk of developing PAD.[24] This study suggested that there is an increased risk of dysvascular amputation among the SCI population at this center. This information is significant because it can help influence JAHVH clinical practice for veterans with SCI and vascular diseases.

Limitations
As a single-center study carried out at an SCI specialized center of a VA hospital, this

study's finding may not be generalizable. Incomplete documentation in the health record may have led to underreporting of amputations and other information. The practice of the vascular surgeons at JAHVH may not represent the approach of vascular surgeons nationwide. Another limitation of this study is that the duration of SCI was not considered when looking at health risk factors associated with amputation in the SCI population (ie, total cholesterol, hemoglobin A_{1c}, etc). Finally, the medication regimens were not reviewed to determine whether they meet the standard of care in relation to eventual diagnosis of PAD.

A prospective study comparing the prevalence of amputation between veterans with SCI vs veterans without SCI could better investigate the difference in amputation risks. This study only compared our veterans with SCI in reference to the general population. Veterans are more likely to be smokers than the general population, contributing to PAD.[17] In addition, data regarding patients' functional status in regard to transferring and ambulation before and after amputation were not collected, which would have contributed to an understanding of how amputation affects functional status in this population.

CONCLUSIONS

There is an increased prevalence of amputation among veterans with SCI compared with that of the nationwide population and a plurality were TFAs. This data suggest that those with a motor complete SCI are more likely to undergo a more proximal amputation. This is likely secondary to a lower likelihood of ambulation with more neurologically complete injuries along with a greater chance of healing with a more proximal amputation. It is challenging to correlate any variables specific to SCI (ie, immobility, time since injury, level of injury, etc) with an increased risk of amputation as the known comorbidities associated with PAD are highly prevalent in this population. Having PAD, low HDL-C (< 40 mg/dL), and paraplegia instead of tetraplegia were independent predictors of amputation.

Health care professionals need to be aware of the high prevalence of amputation in the SCI population. Comorbidities should be aggressively treated as PAD, in addition to being associated with amputation, has been linked with increased mortality.[25] Studies using a larger population and multiple centers are needed to confirm such a concerning finding.

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Ethics and consent
All authors adhere to the ethical principles for medical research. The study was initially approved on 12/10/2018 by the University of South Florida/James A. Haley Veterans' Hospital Institutional Review Board, and it is up-to-date with the continuing review. The submission for publication was approved by the local research office.

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