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Lower-Extremity Amputation Risk Following Charcot Arthropathy and Diabetic Foot Ulcer

Running Title: Amputation Risk of Charcot Arthropathy

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Objective: To compare risks of lower-extremity amputation between patients with Charcot arthropathy and those with diabetic foot ulcers.

Research Design and Methods: A retrospective cohort of patients with incident Charcot arthropathy or diabetic foot ulcers in 2003 was followed for five years for any major and minor amputations in the lower extremities.

Results: After a mean follow-up of 37±20 and 43±18 months, the Charcot and ulcer groups had 4.1 and 4.7 amputations per 100 person-years, respectively. Among patients < 65 years old at the end of follow-up, amputation risk relative to patients with Charcot alone was seven times higher for patients with ulcer alone and twelve times higher for patients with Charcot and ulcer.

Conclusions: Charcot arthropathy by itself does not pose a serious amputation risk, but ulcer complication multiplicatively increased the risk. Early surgical intervention for Charcot patients in the absence of deformity or ulceration may not be advisable.

Diabetic foot ulcers are serious threats to the foot (1-4). Amputation risks of Charcot arthropathy is less clear but previous studies suggest that it is a less serious but significant risk for lower-limb amputation (5). Our objective is to compare the amputation risk of Charcot arthropathy to that of diabetic foot ulcer using a nationwide diabetic population treated in the Department of Veterans Affairs (VA).

METHODS

From a national diabetic population treated in the VA in 2003 (6,7), we identified patients who were newly diagnosed with Charcot arthropathy (ICD-9-CM 713.5) and with a diabetic foot ulcer (707.1x or 707.9) but without Charcot arthropathy in years 2002 – 2007. In both groups, a condition was determined as newly diagnosed in 2003 if it was not found in any utilization records in 2002. We used 2002 as a full-year washout period (8).

Major and minor amputations were identified from the VA inpatient and outpatient records using ICD-9-CM and CPT-4 codes (foot, 84.10 – 84.12, 28800 – 28825; ankle or leg, 84.13 – 84.15, 27880 – 27889; knee or above, 8416 – 84.17, 27590 – 27598). Data for known risk factors of amputation including age, sex, race, marital status, diabetes duration and control, and all co-existing conditions in the Elixhauser co-morbidity method (9) were obtained from patient records for 2003.

We computed the time to event by following patients in either group from the date of the first diagnosis for up to five years to the first date of amputation and analyzed it using Cox proportional hazards regression.

Our initial analysis suggested that amputation risks were not significantly different between the two groups but that Charcot patients with foot ulceration had remarkably higher risks than those without. We thus stratified the study cohort into three groups (patients with Charcot alone, those with Charcot and foot ulcers, and those with foot ulcers alone) and compared amputation risks for patients in the three groups. For Medicare beneficiaries, some amputations might have been performed in non-VA hospitals and were not observable in the VA data. We therefore analyzed the data separately for patients who were less than 65 years old at the end of follow-up and those who were 65 or older.

This study was approved by our institutional review board.

RESULTS

From the VA cohort of diabetic patients in 2003, we identified 911 patients with incident Charcot arthropathy and 15,117 patients with incident diabetic foot ulcers after eliminating patients with previous history of lower-extremity amputations. Crude amputation rates were 14.7% for Charcot patients and 14.5% for foot ulcer patients. After a mean follow-up of 37±20 and 43±18 months for Charcot and ulcer groups, respectively, patients with Charcot arthropathy experienced 4.1 amputations per 100 person-years compared to 4.7 for patients with diabetic foot ulcers (Mantel-Haenszel rate ratio = 0.88; p = 0.15).

Among Charcot patients, 538 (59%) were treated for foot ulceration between 2002 and 2007; 66% (354 patients) were treated for foot ulceration immediately before or concurrently with Charcot arthropathy and 34% (184 patients) experienced it as a complication. Compared to patients with Charcot alone, those with ulcer alone had 7 times higher risk and those with both an ulcer and Charcot had 12 times higher risk of amputation among patients < 65 years (Table 1). Similarly, the two groups had 9 and 13

times higher risks compared to the reference for patients ≥ 65.

DISCUSSION

Our results show that amputation risk for Charcot arthropathy overall is not significantly different from that for diabetic foot ulcers. When Charcot patients were stratified by foot ulceration, Charcot alone was associated with low risk (<2%) and ulcerations were responsible for most amputations experienced by Charcot patients.

These results are consistent with the current practice guideline suggesting that prevention of ulceration is critical for Charcot limb salvage (10). They further call into question whether surgery is advisable early in the disease process. Feet affected by Charcot arthropathy are unlikely to ulcerate when they remain clinically plantigrade and the radiographic weight-bearing relationship between the hindfoot and forefoot is collinear (11,12). These suggest that amputation risk for Charcot arthropathy may be reduced by reserving corrective surgeries for patients with a high risk of Charcot-related ulceration.

Our results also suggest that patients with Charcot arthropathy in the community may have considerably higher risk of amputation than previously believed. The rate of 6.6% in a meta-analysis mentioned above represent half the rate observed for the VA Charcot patients (14.7%). This may be attributable to the secondary ulceration rate in this VA cohort (34% during a five-year follow-up), which is higher than others with corrective surgical intervention (12,13) and comparable to some series reported from specialty clinics (14,15).

Our results are consistent with a previous study of amputation risks of diabetic foot ulcer. Moulik et al. (4) followed diabetic foot ulcer patients for a median of 28 months and reported a 5-year rate of 19%. The VA cohort consisting of foot ulcer patients, who were overall older than the Moulik et al., sample had a 5-year rate of 20%.

One limitation of this study is that it relied on patient data recorded for administrative purposes. Regarding the accuracy of data, our chart reviews suggest that diabetic foot ulcers can be identified from administrative data with 93% sensitivity and 91% specificity. We also confirmed the presence of Charcot arthropathy for 12 of 13 patients (92%) through medical records. Importantly, however, we could not link the affected limb at study entry with the limb amputated during follow-up due to the lack of information in ICD-9-CM codes. Secondly, we did not have access to data for Medicare utilization by elderly VA users and some amputations performed in the non-VA hospitals could not be observed. For this reason, the findings for patients aged 65 years older need to be interpreted carefully.

In summary, diabetic foot ulcers pose a significant risk for amputation, while Charcot arthropathy does not unless it is complicated by an ulcer. Further research is needed to evaluate comparative effectiveness of corrective surgery versus accommodative treatments in preventing amputations for Charcot patients (10,13).

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Table 1: Adjusted Hazard Ratios from the Full Cox Proportional Hazards Regression Models On All Patients with Incident Charcot Arthropathy or Foot Ulcer Stratified by Age at the End of Follow-Up*

	Persons < 65 Years Old (N = 5,392)			Persons 65 Years or Older (N = 10,636)		
Variables	HR (95% CI)		P-Value	HR (95% CI)		P-Value
Comparison Groups [Charcot Alone] †						
DFU Alone	11.161	(4.070 - 30.605)	< 0.001	12.983	(4.061 - 41.511)	< 0.001
DFU and Charcot	7.297	(2.729 - 19.513)	< 0.001	8.846	(2.847 - 27.484)	< 0.001
Age						
55 or older [< 55]	0.912	(0.801 - 1.038)	0.163			
75 - 84 years [65 - 74]				0.864	(0.733 - 1.019)	0.083
85 or older [65 - 74]				0.728	(0.612 - 0.867)	< 0.001
Race/ethnicity [NH White]						
NH Black	1.053	(0.890 - 1.246)	0.544	1.276	(1.105 - 1.474)	0.001
Hispanic	0.875	(0.634 - 1.206)	0.415	1.180	(0.871 - 1.597)	0.285
Other/Unknown	0.988	(0.833 - 1.172)	0.890	1.198	(0.924 - 1.555)	0.173
Male [Female]	1.870	(1.078 - 3.244)	0.026	1.354	(0.764 - 2.399)	0.299
Married [Not Married]	0.723	(0.635 - 0.824)	< 0.001	0.870	(0.779 - 0.971)	0.013
Diabetes Duration ≥ 6 years	1.120	(0.978 - 1.284)	0.102	1.303	(1.166 - 1.456)	< 0.001
A1c > 9%	1.539	(1.342 - 1.766)	< 0.001	1.340	(1.138 - 1.579)	< 0.001
Body Mass Index [< 25 kg/m2]						
25 - 30	0.798	(0.637 - 0.999)	0.049	0.691	(0.582 - 0.819)	< 0.001
30 - 35	0.548	(0.438 - 0.686)	< 0.001	0.479	(0.400 - 0.575)	< 0.001
35 or higher	0.299	(0.212 - 0.422)	< 0.001	0.212	(0.139 - 0.325)	< 0.001
Unmeasured	0.577	(0.471 - 0.707)	< 0.001	0.650	(0.556 - 0.759)	< 0.001
Comorbidities‡						
Peripheral Vascular Disease	1.880	(1.636 - 2.161)	< 0.001	2.324	(2.083 - 2.592)	< 0.001
Congestive Heart Failure	1.263	(1.023 - 1.558)	0.030	1.319	(1.145 - 1.520)	< 0.001

Paralysis	0.919	(0.643 -	1.314)	0.643	1.307	(1.018 -	1.679)	0.036
Renal Failure	1.549	(1.257 -	1.909)	< 0.001	1.272	(1.080 -	1.498)	0.004
Liver Disease	0.868	(0.637 -	1.182)	0.368	0.755	(0.449 -	1.270)	0.289
Coagulopathy	0.699	(0.417 -	1.172)	0.174	0.673	(0.454 -	0.998)	0.049
Weight Loss	1.368	(0.935 -	2.002)	0.107	1.423	(1.041 -	1.943)	0.027
Fluid & Electrolyte Disorder	1.349	(1.097 -	1.659)	0.005	1.246	(1.038 -	1.496)	0.018
Blood Loss	2.649	(1.272 -	5.519)	0.009	1.260	(0.703 -	2.259)	0.438
Deficiency Anemias	1.053	(0.849 -	1.306)	0.640	1.169	(1.004 -	1.360)	0.044
Alcohol Abuse	1.042	(0.815 -	1.333)	0.744	1.398	(1.008 -	1.939)	0.045
Depression	0.950	(0.791 -	1.141)	0.584	0.776	(0.630 -	0.955)	0.017

[*] HR indicates hazard ratios; CI, confidence interval; DFU, diabetic foot ulcer; NH, non-Hispanic.
[†] Reference categories are in brackets.
[‡] All co-morbidities in the Elixhauser method were included except conditions common to all patients in the cohort (diabetes with or without chronic complications) were included in the models. Only conditions that were statistically significant at $\alpha < 0.05$ in either model are shown.