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Rates of diabetes-related lower-limb amputation in northwestern Ontario: an incidence study and introduction of a standardized diabetic foot ulcer management protocol

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Introduction: First Nations populations in Canada have higher incidence rates of type 2 diabetes mellitus than the general population and also incur more frequent complications, including lower-leg amputation. Patients with diabetes who present with a foot ulcer are at high risk for macrovascular events, with a 5-year mortality rate of up to 50%.
Methods: Using census and health administrative data, we reviewed the incidence of diabetes and rates of diabetes-related lower-limb amputation in 2010–2013 in the catchment area of the Sioux Lookout Meno Ya Win Health Centre in northwestern Ontario, which serves a largely First Nations population. We also describe a novel protocol for the management of diabetic foot ulcers.
Results: The rate of lower-limb amputation was 7 times the Ontario average and was 3 times higher than in other areas of the province. The Sioux Lookout Diabetic Foot Ulcer Protocol supports timely vascular assessment for concurrent peripheral vascular disease in patients with diabetic foot ulcers.
Conclusion: Patients with diabetes in the Sioux Lookout Meno Ya Win Health Centre catchment area appear to undergo below-knee amputation at a rate 3 times greater than in other Ontario regions. Patients with diabetic foot ulcers should be identified as being at high risk for other atherosclerotic events (e.g., myocardial infarction, cerebrovascular accident) and require aggressive risk-management strategies.

Introduction : Au Canada, les peuples des Premières Nations présentent des taux d'incidence de diabète de type 2 plus élevés que la population générale et ils en subissent également davantage les contrecoups, notamment les amputations des membres inférieurs. Les patients diabétiques qui souffrent d'ulcères pédieux sont exposés à un risque élevé de complications macrovasculaires, et à un taux de mortalité à 5 ans pouvant atteindre 50 %.
Méthodes : À partir des données du recensement et des données administratives sur la santé, nous avons établi l'incidence du diabète et les taux d'amputation des membres inférieurs liée au diabète de 2010 à 2013 dans la zone desservie par le Centre de santé Meno Ya Win de Sioux Lookout, dans le nord-ouest de l'Ontario, qui répond aux besoins d'une population en majeure partie autochtone. Nous décrivons aussi un nouveau protocole de prise en charge des ulcères pédieux diabétiques.
Résultats : Le taux d'amputation des membres inférieurs a été 7 fois plus élevé que la moyenne ontarienne et 3 fois plus élevée que dans d'autres régions de la province. Le protocole de Sioux Lookout pour l'ulcère pédieux diabétique permet une évaluation rapide de possibles maladies vasculaires périphériques concomitantes chez les patients présentant des ulcères pédieux diabétiques.

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Conclusion : Les patients diabétiques de la région desservie par le Centre de santé Meno Ya Win de Sioux Lookout semblent nécessiter une amputation sous le genou 3 fois plus souvent que les patients d'autres régions de l'Ontario. Les patients qui présentent des ulcères pédieux diabétiques devraient être reconnus comme exposés à un risque élevé à l'égard d'autres complications athéroscléreuses (p. ex., infarctus du myocarde, accident vasculaire cérébral) et ont besoin de stratégies dynamiques de gestion des risques.

INTRODUCTION

A diabetic foot ulcer may at first glance appear to be a limited foot issue, but it may herald a more serious vascular problem and identify patients with diabetes at higher risk for mortality.

The lifetime risk for development of a foot ulcer in patients with diabetes is estimated at 15%–25%.[1] Patients with diabetic foot ulcers constitute a high-risk atherosclerotic population with significant overall death rates, generally acknowledged to be around 50% at 5 years. The risk of mortality generally increases as the patient progresses through the need for amputation and hemodialysis (Table 1).[2–11] These patients often have underlying peripheral vascular disease, with a prevalence of 50%–70%.[12,13] Neuropathic changes further expose their lower limbs to risk of amputation[14] (Fig. 1).

First Nations populations in Canada are acknowledged to have an incidence of type 2 diabetes mellitus up to 5 times that of the general population.[16] What is less well documented is that First Nations populations also incur more frequent complications, including rates of lower-leg amputation up to 18 times those among the general population.[17]

We examined the incidence of type 2 diabetes and rates of lower limb amputation in the catchment area of the Sioux Lookout Meno Ya Win Health Centre (SLMHC) in northwestern Ontario, which serves a largely First Nations population. We also describe a novel diabetic foot ulcer protocol to encourage aggressive management and risk stratification of patients at risk for amputation and increased mortality.

METHODS

Aggregate data for diabetes and lower limb amputations in patients with type 2 diabetes were retrospectively accessed for a 4-year period (2010–2013) for the catchment area of the SLMHC. Data were collected from the Decision Support Office at the Northwest Health Alliance, a shared health care data service organization. We used data from the

Table 1: Mortality rates for patients with diabetes with foot ulcers, amputation and hemodialysis

Investigator	Diabetes plus	No. of patients	Mortality rate, %
Moulik et al.,[2] 2003	Diabetic foot ulcer	30	44 (5 yr)
Iversen et al.,[3] 2009		155	37 (5 yr)
Søndergaard et al.,[4] 2015		43	36 (1 yr)
Wölfle et al.,[5] 2000	Diabetic foot ulcer, amputation	70	54 (3 yr)
Wölfle et al.,[6] 2001		312	27 (1 yr) 70 (5 yr)
Moulik et al.,[2] 2003		30	44 (5 yr)
Fortington et al.,[7] 2013		299	47 (1 yr) 77 (5 yr)
Wiessman et al.,[8] 2015		174*	33.1 (1 yr)
Wiessman et al.,[8] 2015		142†	45.1 (1 yr)
Hertzer et al.,[9] 2007		29	83 (4 yr)
Leers et al.,[10] 1998	Diabetic foot ulcer, amputation, hemodialysis	31	48 (2 yr)
Orimoto et al.,[11] 2013		234	44.8 (1 yr) 74.5 (3 yr) 76.6 (5 yr)

*Below-the-knee amputation.
†Above-the-knee amputation.

Statistics Canada population census, the Ontario Health Insurance Program diagnoses database and provincial hospital surgical codes to identify catchment population, numbers of adult patients with type 2 diabetes and incidence of below-knee amputation. Provincial statistics record all lower-limb amputations (both minor and major). Trauma- and cancer-related amputations were excluded.

We estimated the adult diabetic population from a 10-year analysis of province-wide physician billing for diabetes or related complications for the population of Sioux Lookout and the 31 northern First Nations communities served by the SLMHC.

Rates of diabetes and amputation were also calculated for 3 relevant provincial Local Health Integration Networks: Central Toronto, North West and North East.

We focused on patients with type 2 diabetes who had undergone below-knee amputation as they are the most common major amputation patient. It seemed more clinically relevant to focus on this major amputation than assessing the provincially tabulated rates of all lower-limb amputations, which include patients who might have repeated toe surgeries, eventually leading to a major amputation. We were able to access data for this single procedure for our catchment area and various Local Health Integration Networks in the province.

RESULTS

The population of the identified catchment area for the SLMHC from the 2013 census data was 22 776, 85% of which was First Nations.[18] The adult (age ≥ 18 yr) population with a diagnosis of diabetes was estimated to be 1585, 11% of the adult population.

The average rate of lower-limb amputation in the adult diabetic population in Ontario over the study period (2010–2013) was 146.5 per 100 000, compared to 1078.5 per 100 000 for the Sioux Lookout diabetic population.

The rate of diabetes-related below-knee amputation was 5.68 per 1000 adult patients, 3 times greater than the rates for other Local Health Integration Networks (Table 2).

The average age at below-knee amputation in the Sioux Lookout diabetic population was 50.2 (standard deviation [SD] 8.7) years, compared to 64.0 (SD 2.3) years in the Central Toronto, North West and North East Local Health Integration Networks.

The sex distribution was predominantly male (75.0%), as in other provincial regions.

DISCUSSION

The rate of lower-limb amputation in the adult diabetic population in the SLMHC catchment area in

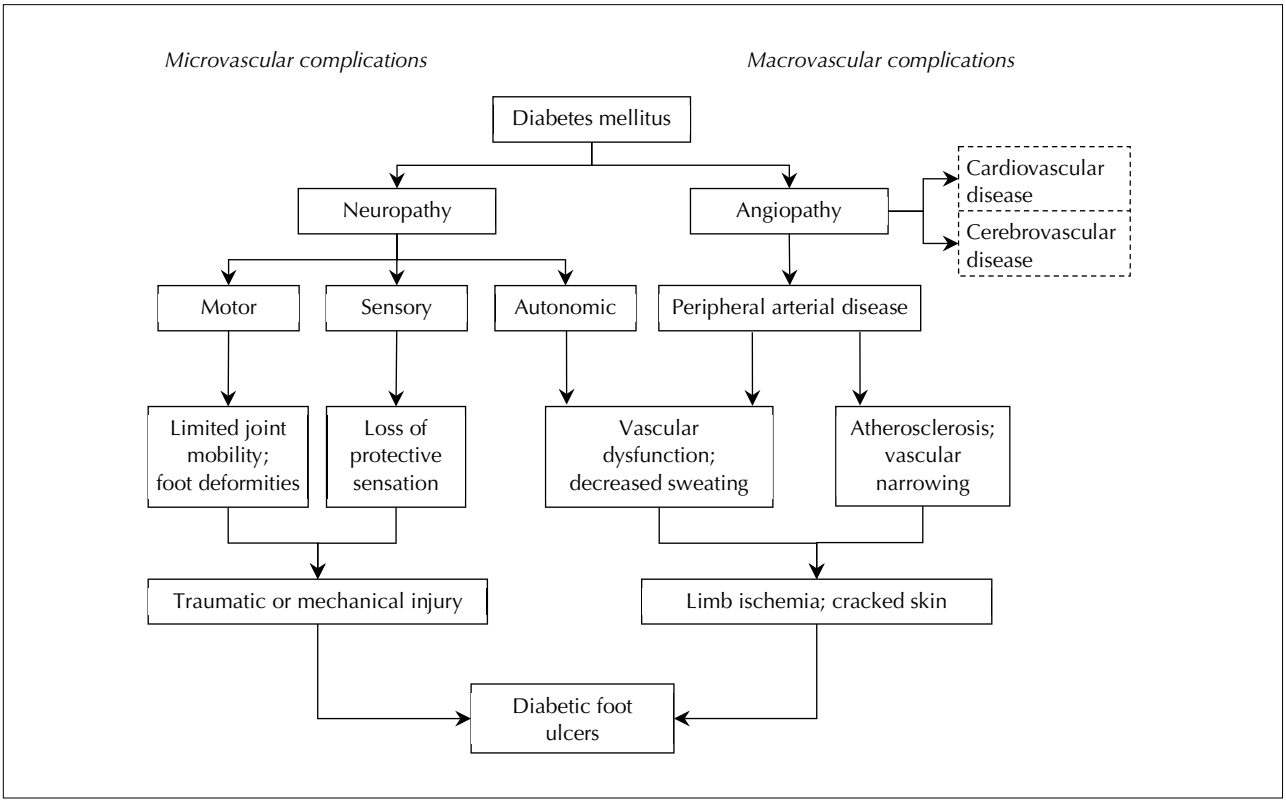


Fig. 1. Pathogenesis of diabetic foot ulcers (adapted from Alavi and colleagues[15]).

2010–2013 was 7 times the provincial rate and was 3 times that in other areas of the province.

This high rate does not appear to be an anomaly. A 2012 Institute for Clinical Evaluative Sciences study also showed that northwestern Ontario had the highest regional rate of diabetes-related total lower-limb amputations (major and minor) in the province between 2006 and 2010.[19]

Lower-limb amputation occurred at an earlier average age in our studied population than in the general Canadian population[20] (50.2 [SD 8.7] yr v. 67 [SD 13] yr). Multiple factors may be at play: potentially more aggressive disease (peripheral vascular disease, type 2 diabetes), late presentation of diabetic foot ulcer, limited access to foot care services including inadequate monitoring, and variable investigation and treatment plans owing to limited resources and/or lack of clear clinical guidelines. Host susceptibility (e.g., cardiovascular risk factors, including smoking, and nutritional status) and broader social determinants of health are all relevant, potentially contributing factors.

Interestingly, geography may be protective. In a 2007 study of Manitoba First Nations, Martens and colleagues[17] identified a rate of type 2 diabetes 4 times that among the general population. They described population-based amputation rates 18 times those of the rest of the province. They also found that the more remote First Nations communities fared better, with lower amputation rates and more medical referrals. Those authors postulated that the system of integrated community-based and visiting health care providers (i.e., J.A. Hildes Northern Medical Unit) lowered barriers to accessing care and improved care for patients with diabetes.

Most of the Canadian literature on diabetic foot ulcers in Canadian Aboriginal populations comes from Manitoba.[21–23] Two retrospective reviews showed that Aboriginal Manitobans experienced higher rates of type 2 diabetes and a higher mean number of foot ulcers per patient and of diabetes-associated lower-extremity amputations than their non-Aboriginal counterparts.[21,23] A cross-sectional study of patients with diabetes from 1 First Nations community showed a disproportionately high rate of emergency department visits for complications of foot ulcers and relatively low availability of preventive foot and wound care services.[22]

Reid and colleagues'[22] 2006 study of 169 northern Manitoba Aboriginal patients showed an incidence of diabetic foot ulcers of 5% and the startling fact that 64% of the patients they studied were unable to perform their own foot surveillance. The patients received an average of 0.7 foot examinations annually over a 7-year period. In 2008, Rose and colleagues[21] concluded that the absence of home care services on reserve, inadequate footwear and limited access to foot care services contributed to foot ulcer development.

Similar trends are seen internationally. A 10-year retrospective study of diabetes-associated major amputations at a hospital in northern Queensland, Australia, showed disproportionately high amputation rates among Indigenous

Table 2: Population data, rate of amputation and characteristics of patients with type 2 diabetes mellitus in the Sioux Lookout Meno Ya Win Health Centre catchment area and in 3 Ontario Local Health Integration Networks (LHINs), 2010–2013

Variable	Sioux Lookout Meno Ya Win Health Centre catchment area	3 Ontario LHINs[19]
Population*	22 776	–
Population aged ≥18 yr, no. (%)	14 384 (63)	–
Population aged ≥18 yr with type 2 diabetes mellitus, no. (%)	1585 (11)	Central Toronto (7) North East (10) North West† (9)
Rate of below-the-knee amputation per 1000 adult patients with diabetes	5.68	Central Toronto 1.81 North East 1.45 North West 3.13
Age at below-the-knee amputation, mean ± SD, yr	50.2 ± 8.7	64.0 ± 2.3 for all 3 LHINs
Male/female ratio of patients who underwent below-the-knee amputation	75/25	74/26 for all 3 LHINs

*2013 population census.
†The population of the Sioux Lookout Meno Ya Win Health Centre catchment area is a subpopulation of the North West LHIN and contributes to the latter's rate.

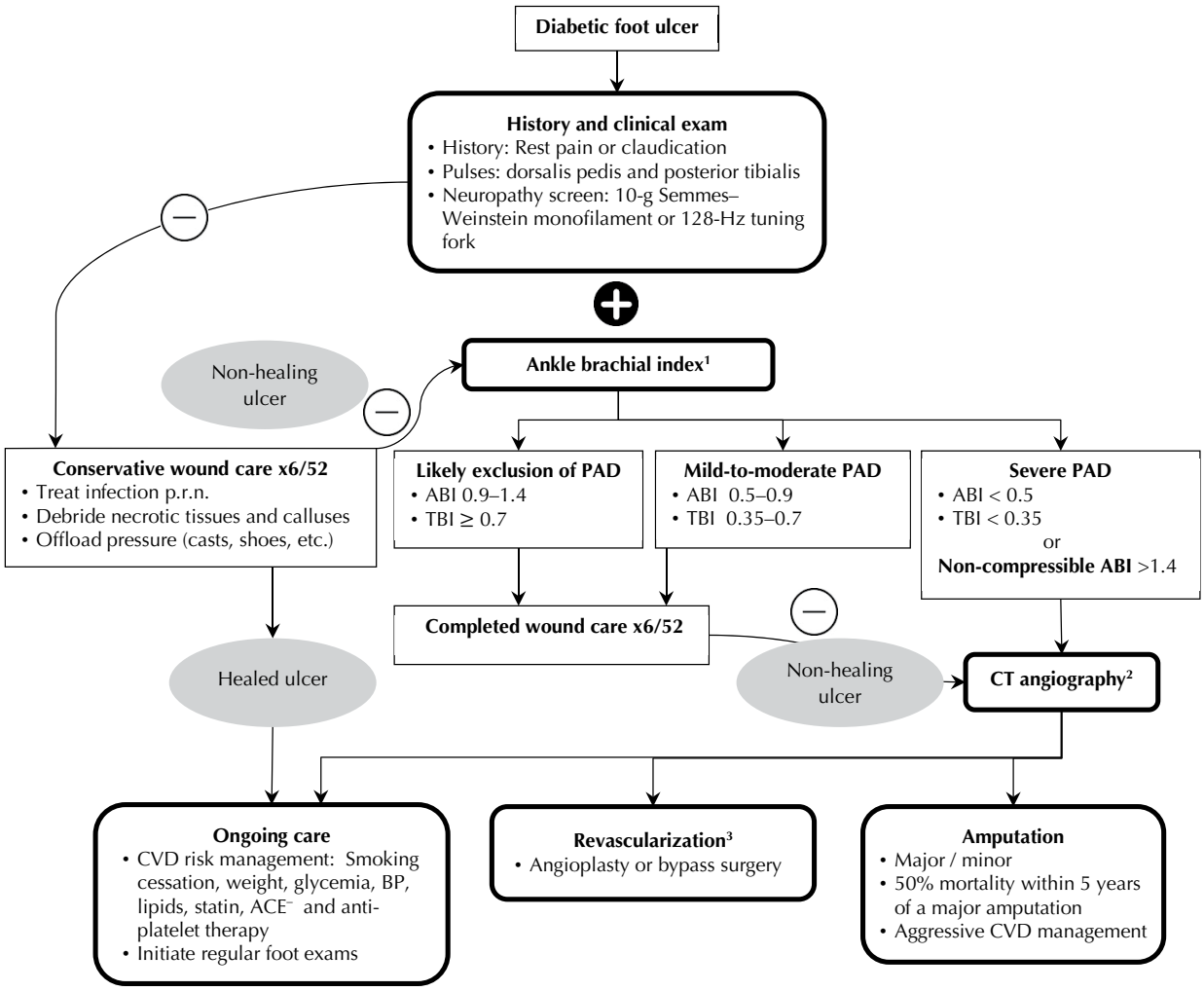
Australians.[24] Indigenous patients were, on average, 14 years younger than their non-Indigenous counterparts at the time of amputation. Our study reproduced this pattern, with below-knee amputation occurring 10–14 years earlier in our studied population. A US study of 1074 Aboriginal patients showed lower-limb amputation rates to be 3 times the national rate, with a hemoglobin A_{1c} level of 9.5% or higher.[25]

We found a male predominance (75%) in patients undergoing below-knee amputations. This is a common finding, for unknown reasons. A similar pattern exists in Canada-wide data, where males were more than twice as likely as females to undergo below-knee amputation.[20]

Sioux Lookout Diabetic Foot Ulcer Protocol

In response to such high amputation rates, we examined guidelines for management of diabetic foot ulcers, the common precursor to a diabetes-related lower-limb amputation. The International Working Group on the Diabetic Foot (http://iwgdf.org/guidelines/guidance-on-pad-2015/) guidelines were the most evidence-based and recommend early vascular assessment in patients with foot ulcers, especially patients whose ulcers fail to heal over 6 weeks.[13] Unfortunately, most of the working group's strong recommendations were supported by weak evidence.

We searched MEDLINE and Embase (January 2005–May 2016) for the MeSH search term "diabet-



ABI = ankle brachial index, ACE = angiotensin-converting enzyme, BP = blood pressure, CTA = computed tomographic angiography, CVD = cardiovascular disease, MR = magnetic resonance, PAD = peripheral artery disease.

1. Toe-brachial index (TBI), if ABI > 1.4 (incompressible, unreliable ABI result). If ABI results remain unclear, proceed to CTA. Many authors suggest ABIs for all diabetic foot ulcer patients; additional testing may include transcutaneous oxygen pressure (TcP02).
2. Vascular surgery consideration requires angiography: CTA (other tests include MR angiography, intra-arterial digital subtraction angiography, and duplex ultrasound.
3. Contraindications to revascularization: unsuitable lesions, unsalvageable limb, patient frailty/short life expectancy.

Fig. 2. Sioux Lookout Diabetic Foot Ulcer Protocol.

ic foot" combined with "arterial occlusive diseases" or "peripheral vascular disease"). We found 63 citations but none that described evidence that aggressive management of foot ulcers prevented amputation or conclusive evidence that any specific diabetic foot ulcer protocol improved outcomes. On discussion with clinicians, we were struck by the variety of approaches taken with patients with foot ulcers. Even in focused tertiary care centre "diabetic foot clinics," clinicians had different thresholds for ordering imaging investigations for concomitant peripheral arterial disease. We felt that describing a reasonable approach that organized investigations for concomitant peripheral vascular disease and coronary artery disease would at least standardize management of diabetic foot ulcers.

The purpose of the Sioux Lookout Diabetic Foot Ulcer Protocol (Fig. 2) is 2-fold. The first is to identify a time frame for conservative wound management (6 wk), after which vascular assessment is suggested. The second is to identify the patient with a foot ulcer as being at high risk for other, extensive arterial disease. Patients who have comorbid peripheral, coronary or cerebral arterial disease would likely benefit from a risk-management approach. The protocol includes clinical history-taking, physical examination and risk-management components as well as vascular imaging, treatment of peripheral vascular disease and referral suggestions.

A history of claudication or pain at rest may indicate vascular compromise, whereas an easily palpable pedal pulse likely excludes serious arterial disease.[15] Many authors, however, recommend that all patients with diabetic foot ulcers receive an ankle–brachial index test at presentation.[26] This easy bedside Doppler examination uses the ratio of arm and leg pressures measured with a blood pressure cuff (Fig. 3); a small cuff can also be attached to a toe to perform a toe–brachial index test, which can correct for a false-negative result of an ankle–brachial index text (e.g., an ankle–brachial index > 1.4 suggests incompressible ankle arteries).[27] Any ankle–brachial index outside the normal range (0.9–1.4) necessitates further assessment (toe–brachial index test and/or computed tomography angiography). A low ankle–brachial index identifies vascular compromise, and a value above the normal range denotes a calcified and incompressible vessel; both necessitate further vascular assessment.

Patients with abnormal clinical findings or ankle–brachial index, or delayed foot ulcer healing require anatomic imaging. Computed tomography angiography may be the most readily available in some rural Canadian locations. Other angiographic imaging includes digital subtraction angiography or magnetic resonance angiography, both of which require contrast medium and may be nephrotoxic.[12] The sooner poor vascularization is identified, the better, as nutrient-deprived ulcers heal poorly (Fig. 4).

Macrovascular risk management is also suggested for all patients with diabetic foot ulcers. In a recent Ontario study, 791 patients with peripheral



Fig. 3. Bedside Doppler examination uses ratio of arm and leg pressures measured with blood pressure cuff.

vascular disease (25% of whom were diabetic) were followed for 7 years.[28] The authors focused on 8 management categories: use of statins, angiotensin-converting-enzyme inhibitors and antiplatelet medications, and attention to smoking, weight, blood pressure, and lipid and glycemic control. They showed a 40% relative reduction in death, myocardial infarction and cerebrovascular accidents (adjusted hazard ratio 0.63, 95% confidence interval 0.13–0.54) and a 53% relative reduction for major amputations (adjusted hazard ratio 0.47, 95% confidence interval 0.29–0.77).

Wound management at our facility consists of measurement of the ulcer and débridement of both callus and devitalized tissue. Since there is such an array of wound care products, we have standardized ulcer management to the use of medical honey (Medihoney, Derma Sciences) under a dressing.[29] The Society for Vascular Surgery recommends expected healing as a 50% reduction in ulcer size after 4 weeks of conservative management.[30] Offloading with full-contact casts or boot/inserts may further benefit healing of plantar foot ulcers.[30]

This protocol may help standardize vascular assessment in patients with diabetic foot ulcers and, it is hoped, serve as a reminder that acetylsalicylic acid, statins and blood pressure control would benefit these patients even if they are not applied directly to the foot!

Limitations

Census data are not always accurate, particularly when enumerating numerous remote communities. Although other estimates of the population exist, we used census data in this study as it allowed us to make reliable comparisons to other regions of Ontario. We believe the population estimate may be underreported, owing to occasional community nonparticipation in census activity and remoteness. This would overestimate amputation rates to some degree but would not alter the underlying message

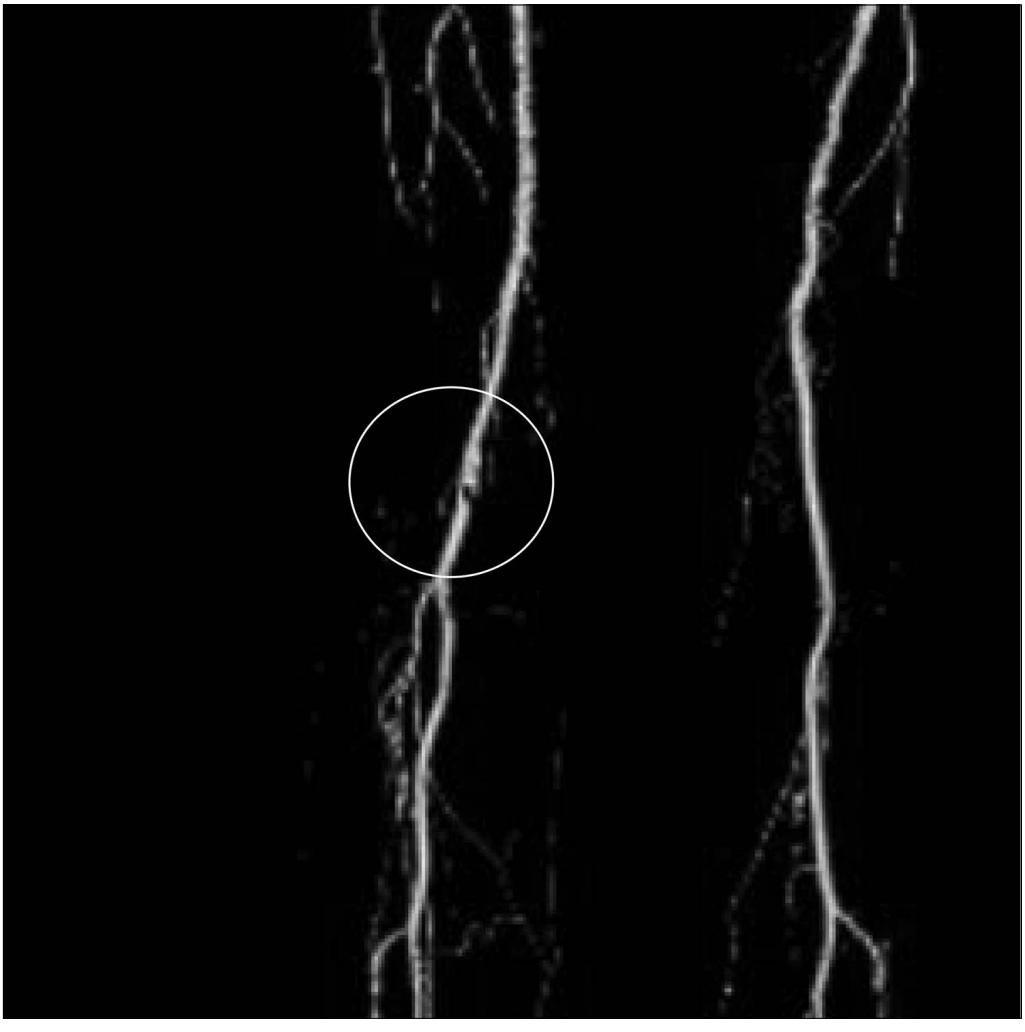


Fig. 4. Computed tomography scan showing 90% narrowing of right superficial femoral artery proximal to knee.

that the rate of major amputation is very high in adult patients with diabetes in our catchment area.

CONCLUSION

Patients with diabetes in the SLMHC catchment area appear to undergo major below-knee amputation at a rate 3 times greater than in other Ontario regions. Patients with diabetic foot ulcers are at high risk for arterial disease in the affected limb as well as for cardiac and cerebral events and death.

Poorly healing diabetic foot ulcers may be the first indication that a patient needs vascular assessment and aggressive management of cardiovascular disease risk.

We have developed a protocol that we hope will increase early detection of vascular compromise and assist in healing of diabetic foot ulcers and limit amputation. A prospective study to evaluate the application and outcomes of the protocol is planned.

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