Sounding the alarm on rising diabetes-related amputations

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KEY POINTS

- Lower-extremity amputation occurs predominantly in people with diabetes and represents a major cause of morbidity, mortality and health care cost.
- International and Ontario data had previously suggested a decline in amputation rates, but new data show a clear resurgence in the last decade in Ontario.
- The cause of the observed rise in rates of lower-extremity amputation is not known, but it is occurring despite effective vascular protective strategies associated with successful continued reductions in cardiovascular disease rates.
- Renewed efforts are needed for health services research and research programs into the component causes of amputation (vascular, neuropathic and foot care for prevention of trauma to skin), but clinicians must also renew their efforts in organizing clinical processes for identifying at-risk feet and applying preventive measures.
lower-limb amputations is fully explained by the increase in diabetes prevalence, or by other causes such as a failure of clinical prevention strategies or new risk factors for amputation in those with diabetes, or changes in practice patterns, such as surgeon preference for earlier minor amputation.

While an observed decline in cardiovascular disease, using similar data sources and analytical approaches, implies that vascular protective strategies can be effective enough to reduce overall cardiovascular events even if the prevalence of diabetes itself is increasing, it’s clear that such strategies are not enough to overcome the peripheral vascular disease component underlying amputation. Clinical vascular prevention strategies include healthy behaviour intervention (diet and exercise), smoking avoidance and cessation, management of glycemia, blood pressure and lipids, and use of medications including statins, renin–angiotensin–aldosterone system antagonists, sodium–glucose linked transporter (SGLT) inhibitors and glucagon-like peptide receptor agonists. Vascular protection alone may not overcome amputation risk because it addresses only 1 of the core component causes: the tissue ischemia from peripheral vascular disease, but not the loss of protective sensation from neuropathy, or the minor trauma to skin, induced by inadequacies in footwear and general foot care, which incites ulceration and infection.

Annual clinical foot examination for the component causes of amputation should be undertaken in patients with diabetes; this can be accomplished by way of very simple examinations for loss of protective sensation (testing pressure sensation with a monofilament, testing vibration sensation, or frankly the even simpler “touch the toes” approach adopted by Diabetes UK), for arterial patency (pedal pulses and skin changes), and foot inspection for presence of abnormalities such as callouses or deformity that indicate repetitive minor trauma. Depending on their number and severity, the presence of abnormalities should trigger several interventions, beginning with self-foot care education and professionally fitted therapeutic footwear, to referral for wound management and surgical consultation. Although no cause has been established for rising amputation rates in Ontario, clinicians should certainly renew their efforts in organizing clinical processes for identifying at-risk feet and facilitating preventive measures.

The paradoxical increase in amputation rate in the face of declining cardiovascular disease among people with diabetes might have been explained by the 2014 introduction to Canada of SGLT inhibitors. Although they are highly effective for glycemic control and reduction of cardiovascular (and renal) disease, controversy exists about the increased amputation risk. One large-scale, randomized, controlled cardiovascular outcome trial showed excess amputation risk that has not been reproduced in other trials, nor specifically in a similar large-scale trial design using the same agent in high-risk patients. Hussain and colleagues evaluated and excluded this possibility as a cause of the resurgence of lower-limb amputation in Ontario.

Research targeting the loss of protective sensation as a component cause of amputation risk has failed to identify neuroprotective strategies other than achieving target glycemic control. However, active research is currently investigating nutraceutical approaches, such as omega-3 supplementation, topical antimuscarinic therapy and erythropoietin analogues to prevent nerve injury and to restore sensation, and strategies to identify neuropathy at earlier stages, when interventions are more likely to be effective. In Canada, efforts aimed at preventing and managing the minor trauma to skin that constitutes the final component cause include evaluation of a chiropody-led clinical foot care program directed by Diabetes Action Canada, a national patient-oriented research strategy. The Ontario Ministry of Health and the World Economic Forum began planning a value-based medicine program focused on foot care, which lost funding after the Ontario general election in 2018. As we continue to advocate for these efforts, we thank our health services researchers for sounding the alarm, but we also encourage them to focus on the critical next steps. It is essential that our data systems gradually overcome current limitations, above those related to information bias that interfered with determining the cause of the resurgence in amputations in the current study. This would require steps such as facilitating medical record linkage, systems for pharmacovigilance, a digital health portal for patient-driven care and patient-reported outcomes research, and creation of algorithms to better identify diabetes and its type 1 and type 2 diabetes subtypes.

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