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ORIGINAL ARTICLE

Efficiency and safety of coronary CT angiography compared to standard care in the evaluation of patients with acute chest pain: a Canadian study

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Abstract The optimal assessment of patients with chest pain and possible acute coronary syndrome (ACS) remains a diagnostic dilemma for emergency physicians. Cardiac computed tomographic angiography (CCTA) may identify patients who can be safely discharged home from the emergency department (ED). The objective of the study was to compare the efficiency and safety of CCTA to standard care in patients presenting to the ED with low- to intermediate-risk chest pain. This was a single-center before-after study enrolling ED patients with chest pain and low to intermediate risk of ACS, before and after implementing a cardiac CT-based management protocol. The primary outcome was efficiency (time to diagnosis). Secondary outcomes included safety (30-day incidence of major adverse cardiovascular events (MACE)) and length of stay in the ED. We enrolled 258 patients: 130 in the standard care group and 128 in the cardiac CT-based management group. The cardiac CT group had a shorter time to diagnosis of 7.1 h (IQR 5.8–14.0) compared to 532.9 h (IQR 312.8–960.5) for the standard care group ($p<0.0001$) but had a longer length of stay in the ED of 7.9 h (IQR 6.5–10.8) versus 5.5 h (IQR 3.9–7.7) ($p<0.0001$). The MACE rate was 1.6 % in the standard care group and 0 % in the cardiac CT group. In conclusion, a cardiac CT-based management strategy to rule out ACS in ED patients with low- to intermediate-risk chest pain was safe and led to a shorter time to diagnosis but increased length of stay in the ED.

Keywords Cardiac care · Acute coronary syndrome · Cardiac care · Diagnosis · Efficiency · Imaging · CT/MRI · Safety

Introduction

An estimated 300,000 to 500,000 patients with chest pain present to Canadian emergency departments (EDs) every year and approximately 62,000 are admitted to hospital with acute myocardial infarction (MI) [1]. In the USA, chest pain units (CPUs) have been established in which patients presenting to the ED with low-risk chest pain are observed with serial enzyme testing, exercise stress testing, and/or imaging with or without stress [2], with a goal to reduce the missed acute coronary syndrome (ACS) rate to <1 %. However, this strategy is expensive and may result in a high cost to the health care system. In Canada, CPUs do not exist and although several risk stratification tools have been developed, none optimally assist physicians in identifying which patients can be safely discharged without extensive investigation [1].

ECG-gated coronary computed tomographic angiography (CCTA) has emerged as an attractive alternative to standard investigation in patients at low to intermediate risk of ACS [3]. Previous studies have reported close to 100 % negative predictive value for exclusion of significant coronary artery stenosis [4–9]. In our tertiary care center, patients who present to the ED with chest pain, a normal or nondiagnostic electrocardiogram (ECG)

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and no elevation in cardiac enzymes are generally discharged home with a referral to an Acute Cardiac Referral Clinic (ACRC). Diagnostic tests are then performed on an outpatient basis after which a final diagnosis is rendered by the consulting cardiologist. As in most centers across Canada, CCTA in the ED has not been incorporated into patient management algorithms.

The objective of this study was to compare the efficacy and safety of a cardiac CT-based strategy to standard care in the assessment of low- to intermediate-risk patients who present to the ED with chest pain. The primary hypothesis stipulated that the cardiac CT-based management would significantly decrease the time to diagnosis, although the total time in the ED might be increased and that there would be a decrease in the incidence of major adverse events at 30 days.

Methods

Study design and participants

Study approval was obtained from the institutional research ethics board. Individual informed consent was waived from patients participating in the study as the work reflected a change in standard practice, and no patients were randomized. Clinical information abstracted from the charts was only obtained from patients who had consented to have their charts reviewed for research purposes.

This before-after study compared the role of CCTA to standard care in patients presenting to the ED with low- to intermediate-risk chest pain syndromes to rule out ACS. The primary outcome was efficiency, defined as time to diagnosis and measured as the time from registration in the ED until either the first test that diagnosed coronary artery disease (CAD) or the final test that ruled out CAD as a cause of the chest pain. Secondary outcomes included (a) safety as defined by 30-day major adverse cardiovascular events (MACE - recurrent ischemic chest pain resulting in MI, coronary revascularization, or cardiac death) and (b) length of stay (LOS), measured from the time of registration to the time of the ED discharge order in the patient's chart.

Patients greater than 25 years of age presenting to the ED with a primary complaint of chest pain possibly secondary to acute coronary syndrome, with negative cardiac enzyme (Troponin I [TnI] < 0.045 μg/L) and normal or nondiagnostic ECG, were included. Exclusion criteria included hypotension (systolic blood pressure <80 mmHg), allergy to iodinated contrast media, known anatomic coronary disease (previous CCTA or cardiac catheterization), renal insufficiency (creatinine clearance < 30 mL/min), arrhythmias, history of erectile dysfunction medications in the last 48 h, recent cocaine use, calcium score >800, and pregnancy. A second TnI was drawn 8 h after the documented onset of chest pain, which if positive, also excluded the patient.

The study took place in the emergency department of a tertiary care hospital with 75,000 annual patient visits and staffed by certified emergency physicians and residents. Prior to initiation of the cardiac CT protocol, all patients fulfilling inclusion and exclusion criteria were referred as outpatients to an Acute Cardiology Referral Clinic (ACRC) at our hospital. These were defined as standard care (SC group) patients and were identified through a retrospective chart review between August 2006 and February 2008. Between June 2008 and May 2015, the cardiac CT pathway was initiated and patients fulfilling the inclusion criteria were prospectively enrolled and underwent CCTA (CardCT group). Recruitment into the cardiac CT pathway was left up to the discretion of the individual ED physician. The service was offered Monday to Friday between 0800 and 1700 hours. Twenty-four-hour coverage was not available due to a shortage of CCTA-trained imaging physicians. A positive CCTA for obstructive coronary artery disease was defined as the presence of at least one coronary artery with a ≥50 % stenosis. Patients with a completely normal CCTA were discharged home with instructions to follow-up with their family physician. Patients with stenosis 1–30 % were followed up in a dedicated Heart Disease Prevention Clinic. Those with 30–49 % stenosis were followed in the ACRC as an outpatient. Patients with 50–69 and ≥70 % stenosis were referred back to the ED for immediate physician reassessment. Patients included in the CardCT group had a structured telephone interview at 30 days to assess compliance and safety outcomes (Online Resource 1). Patients presenting outside the CCTA service window received standard care.

CCTA procedure

The examination was performed on a 64-detector CT scanner (General Electric, LightSpeed VCT, GE Healthcare, Waukesha, Wisconsin) in the ED. Prior to the CCTA examination, patients received dose-adjusted metoprolol or diltiazem, to a target heart rate less than or equal to 60 beats per minute to maximize image quality. All patients with a systolic blood pressure of >90 mmHg received 0.8 mg nitroglycerin spray before image acquisition. Patients underwent an unenhanced prospectively triggered cardiac CT for calcium scoring, and the study was cancelled if the calcium score was >800. Retrospective ECG-gated images were then obtained at 120 kVp, 400–800 mA, 0.35-s rotation time, and 0.625-mm slice thickness using dose modulation. As of July 14, 2010, iterative reconstruction (ASIR 4) was instituted to reduce radiation dose and was used in 63 consecutive patients. A triphasic injection protocol with 60–100 ml of contrast (Omnipaque 350 mg/ml GE Healthcare, Waukesha, Wisconsin) at 5–8 cc/s was used. Further, 2.5-mm-thick reconstructions were made on mediastinal and lung windows, with a larger field of view to evaluate the noncardiac portion

of the CT. All images were evaluated on a workstation (Advantage Workstation 4.3, GE Medical Systems). An experienced cardiothoracic radiologist (level III equivalent) assessed the 17 segments of the coronary arteries according to AHA guidelines [10].

Structured data collection was performed for both groups, including demographics, cardiac risk factors, medications, number of noninvasive tests, and the rate of cardiac intervention. Other safety outcomes were recorded and included periprocedural complications (stroke, bleeding, anaphylaxis, and renal failure) and the cumulative radiation exposure from the time of presentation to the time of diagnosis (including CCTA, nuclear perfusion imaging, positron emission tomography computed tomography (PET/CT), and invasive coronary angiography as calculated by standard methods) [11].

Statistical analysis

The minimal sample size was estimated to be 128 patients in both the preimplementation and postimplementation phase, on the basis of a type I error of 0.05, a type II error of 0.10, a baseline time to diagnosis of 14 days, and a minimum clinically important difference of 5 days. This difference was based on consensus among Canadian radiologists and emergency physicians that a decrease in time to diagnosis of one work week would be the smallest increment considered to be clinically meaningful. Continuous data are expressed as means ± SD or medians (interquartile range (IQR)). Differences between phases for other data were analyzed with the Wilcoxon sign rank-sum test, the chi-squared test, the Fisher's exact test, or Student's *t* test, as appropriate. Time to discharge and time to diagnosis were presented using Kaplan-Meier methods, and the differences between groups were assessed using log rank testing.

Results

During the period of June 1, 2006, and May 1, 2015, we enrolled 258 patients. There were 130 patients in the SC group and 128 consecutive patients in the cardiac CT group. Table 1 summarizes the baseline characteristics for both groups. There was no difference in age, gender, or baseline risk factors between the two groups; however, patients in the SC group were more likely to have a history of systemic hypertension ($p = 0.003$) and congestive heart failure ($p = 0.045$) whereas CardCT patients were more likely to have a family history of CAD ($p = 0.023$). Fourteen patients in the CardCT group were excluded either due to a high calcium score, an elevated second TnI or protocol violation. Details of patient enrollment are outlined in Fig. 1. Complete follow-up at 30 days was achieved in 128 (98.5 %) patients in the SC group and in all CardCT patients.

Diagnostic testing and treatment

Of the 130 patients in the SC group, 98 (75.4 %) patients underwent outpatient diagnostic testing after their index visit to the ED. Seventy-five (57.7 %) patients had a radionuclide stress test, 14 (10.7 %) had both a radionuclide stress test and CCTA, 4 (3 %) had CCTA alone, and 4 (3 %) had exercise stress testing while 8 (6.1 %) had either echocardiography, stress echocardiography or PET/CT. Twenty (15.4 %) patients had invasive coronary angiography (ICA) of which 17 (85 %) patients had ≥50 % coronary artery stenosis and 14 of the 17 had a minimum of one artery with a stenosis ≥70 % (70 %). Fifteen (11.5 %) patients underwent revascularization (13 percutaneous coronary intervention (PCI), 1 coronary artery bypass grafting (CABG), 1 fibrinolytics).

Of the 128 subjects who were enrolled in the CardCT group, 114 (89.1 %) underwent CCTA. The most common reason for not undergoing the examination was a high calcium score (9 (10.9 %) patients). Three other patients were excluded due to an elevated TnI and 2 for protocol violation. The distribution of patients with at least one vessel with a maximal stenosis in each category is listed in Table 2. Twenty-two patients (19.3 %) underwent ICA of which 15 (68.2 %) had ≥50 % stenosis and 14 (12.3 %) underwent revascularization (14 PCI). After the index visit to the ED, 21 (18.4 %) patients in the CardCT group had additional noninvasive testing. Eight (6.2 %) patients underwent stress myoview, 4 (3.1 %) had an echocardiogram, 3 (2.3 %) had a stress echocardiogram, 3 (2.3 %) had PET/CT, and 3 (2.3 %) had exercise stress testing. Details of patient diagnostic testing, treatment and outcomes are outlined in Fig. 1. There was no difference in the rate of ICA or intervention between groups.

Efficiency

Time to diagnosis was significantly shorter for the CardCT group compared to the SC group ($p < 0.001$) (Fig. 2), although LOS in the ED was longer for the CardCT group (7.9 h (IQR 6.5–10.8) vs. 5.5 h (IQR 3.8–7.7) ($p < 0.001$)) (Fig. 3).

Safety

There were 2 MACE (1.6 %) in the SC group and 0 MACE in the CardCT group at 30 days ($p = 0.279$). Two patients in the SC group returned to the ED with MI (12 and 4 days after the index visit, respectively) and were successfully treated with PCI. There were no deaths in either group.

There were no peri-procedural complications in either group. The cumulative radiation dose in the entire SC cohort was less than in the CardCT group (9 mSv (IQR 0–9) vs. 9 mSv (IQR 9–16)) ($p < 0.001$), but of the 90 patients who received radiation-based diagnostic testing in the SC group,

Table 1 Baseline patient characteristics

Characteristic	SC	CardCT	p
Male, *n* (%)	80 (61.5)	81 (63.3)	0.773
Age (years)	57.1 ± 14.3	56.7 ± 11.7	0.792
Heart rate (beats per minute ± SD)	57 ± 14	57 ± 12	0.793
Systolic blood pressure (mmHg ± SD)	149 ± 25	148 ± 23	0.723
Diastolic blood pressure (mmHg ± SD)	84 ± 13	82 ± 14	0.484
TIMI score (IQR)	1 (1,3)	1.5 (1,2)	0.831
Hypertension, *n* (%)	51 (39.2)	26 (21.7)	*0.003
Diabetes, *n* (%)	12 (9.2)	4 (3.3)	0.057
Hypercholesterolemia, *n* (%)	37 (28.5)	31 (25.8)	0.641
Congestive heart failure, *n* (%)	4 (3.1)	0 (0)	*0.045
Stroke, *n* (%)	1 (0.8)	1 (0.8)	0.991
Peripheral vascular disease, *n* (%)	1 (0.8)	0 (0)	0.320
Valvulopathy, *n* (%)	6 (4.6)	1 (0.8)	0.058
No prior cardiac history, *n* (%)	121 (93.1)	125 (97.7)	0.081
Smoking history, *n* (%)	38 (29.5)	39 (32.5)	0.604
Family history, *n* (%)	24 (18.5)	37 (30.8)	*0.023
Medications			
No medication, *n* (%)	69 (53.5)	63 (52.5)	0.876
Beta-blockers, *n* (%)	18 (13.9)	18 (14.1)	0.960
Calcium channel blockers, *n* (%)	5 (3.9)	9 (7.0)	0.259
Nitroglycerin/Nitrates, *n* (%)	6 (4.6)	13 (10.2)	0.088
Cholesterol lowering, *n* (%)	18 (13.9)	17 (13.3)	0.895
Acetylsalicylic acid, *n* (%)	33 (25.4)	32 (25.4)	0.943
Clopidogrel, *n* (%)	1 (0.8)	3 (2.3)	0.306
Other anticoagulants, *n* (%)	6 (4.6)	1 (0.8)	0.058

SC standard care, *CardCT* cardiac CT group, *mmHg* millimeters of mercury, *TIMI* thrombolysis in myocardial infarction, *CAD* coronary artery disease

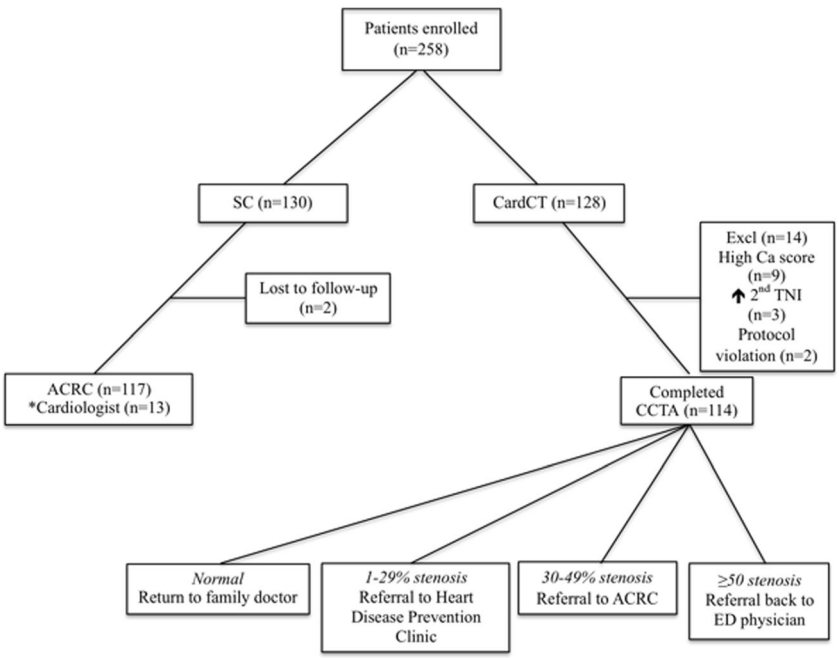

Fig. 1 Patient enrollment, diagnostic testing, and referral flowchart. *Cardiologist—referral to individual cardiologist. *SC* standard care, *CardCT* cardiac computed tomography group, *Ca score* calcium score, *TnI* troponin I, *CCTA* coronary computed tomographic angiography, *ACRC* Acute Cardiac Referral Clinic

Table 2 CCTA results in CardCT group ($n = 114$)

% Coronary artery stenosis	*N* (%)
0	34 (29.8)
1–29	35 (30.7)
30–49	18 (15.8)
50–69	8 (7.0)
≥70	19 (16.7)

Right column represents number (%) in whom the maximal stenosis in at least one vessel is in this category

CCTA coronary computed tomographic angiography

radiation dose was equivalent to the CardCT group (9 mSv (IQR 9–14) vs. 9 mSv (IQR 9–16)) ($p = 0.308$).

Using ICA as the gold standard, for patients who had both ICA and CCTA, the sensitivity of CCTA with a cutoff of 70 % stenosis was 94.7 % (95 % CI [74.0, 99.9]) with a specificity of 62.5 % (95 % CI [54.4, 96.0]). The receiver operating curve (ROC) area was 0.786 (95 % CI [0.600, 0.973]). The positive predictive value of this cutoff was 85.7 % (95 % CI [63.7, 97]) and the negative predictive value was 83.3 % (95 % CI [35.9, 99.6]). Utilizing a cutoff of at least 50 % stenosis increased sensitivity (100 %, 95 % CI [85.2, 100]) with a specificity of 75 % (95 % CI [19.4, 99.4]) and an ROC area of 0.875 (95 % CI [0.630, 1.000]). The positive predictive value of this cutoff was 95.8 % (95 % CI [78.9, 99.9]), and the negative predictive value was 100 % (95 % CI [29.2, 100]).

Discussion

In this single-center before-after study, incorporating a CCTA-based management strategy led to a significant decrease in the time to diagnosis, although LOS in the emergency increased compared to standard care. Although there were less MACE

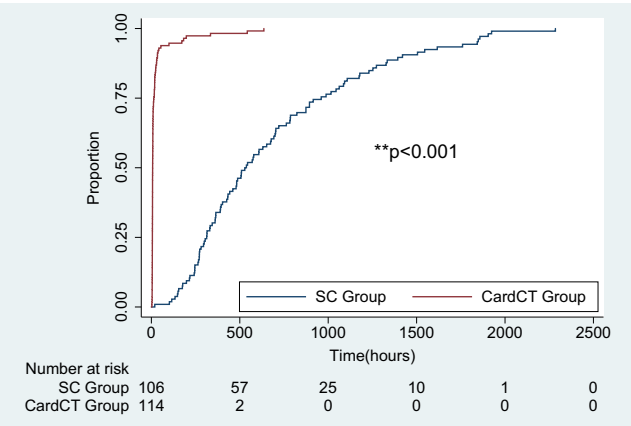

Fig. 2 Time to diagnosis between the two groups. *SC* standard care, *CardCT* cardiac CT group

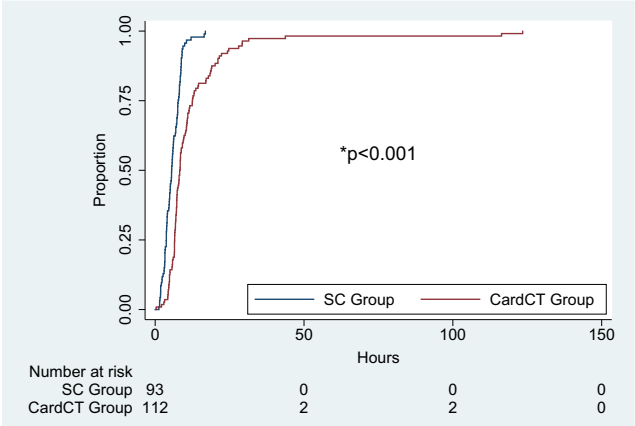

Fig. 3 Time to discharge from ED between the two groups. *SC* standard care, *CardCT* cardiac CT group

in the CardCT group, this did not reach statistical significance. Thus, the implementation of this strategy proved to have a similar safety profile at 30 days compared to standard care. In those patients who had invasive coronary angiography correlation, CCTA demonstrated high sensitivity (100 %) and negative predictive value (100 %) for a cutoff value of 50 % stenosis in line with previous studies [6–8, 12], confirming the ability of CCTA to detect and rule out obstructive coronary artery disease in the emergency setting.

Previous observational and randomized-controlled trials have demonstrated the practicality of utilizing CCTA in the ED in low- to intermediate-risk chest pain patients [5, 8, 9, 13–15] and have led to the widespread incorporation of this strategy in many US practices. In contrast to our results, CCTA has been established to decrease LOS in the emergency by 6–12 h in the American system [13, 16–18].

On the other hand, the reported LOS in American ED at 20 h [15, 17] is on average much longer as compared to 7.9 h for our CardCT group in a Canadian tertiary care hospital. This longer LOS in the ED in the USA as compared to Canada is due to the fact that in the USA, patients with low- to intermediate-risk profiles are observed and receive testing in dedicated chest pain units. This is not the case in Canada where similar risk profile patients are generally discharged home and worked up as outpatients. Hence, Canadian standard care results in much shorter LOS in the ED (5.5 h in our study) overall as compared to US centers. By incorporating CCTA in the ED in our study rather than doing most imaging tests as an outpatient, this resulted in a longer LOS in the CardCT group compared to SC. The additional time required to achieve heart rate control prior to CCTA imaging may explain the lack of enthusiasm for the widespread use of CCTA in the ED in many Canadian institutions. On the other hand, this could be expected to improve over time as the workflow becomes more common and familiar. As CT technology also improves, high-quality studies can be expected with less need for patient heart rate control.

A recent study by Scheuermeyer et al. explored the safety and efficiency of outpatient versus ED-based CCTA for the evaluation of patients with suspected ACS in 521 patients [19]. One hundred seventy-one patients had CCTA during their ED visit while 350 patients were discharged home from ED and had outpatient CCTA within 72 h of discharge. Median LOS in the ED was similar for both groups (6.6 vs. 7.0 h) and was similar to LOS in our study, and there was no MACE prior to CCTA in either group. The authors concluded that outpatient CCTA may be a safe strategy in patients with a low risk of ACS.

There are several limitations to our study. This was a single-center before-after trial, and the use of historical controls in clinical trials has been recognized to overestimate the benefit of new treatments; thus, the improvement in the time to diagnosis after the introduction of CCTA may have been overestimated. However, significant reductions in time to diagnosis with CCTA have been shown in all randomized controlled trials to date [14, 15, 17]. In addition, even though groups were similar in most baseline variables, unmeasured confounders or physician preference may have played a role in referral patterns although both groups appeared to have similar rates of nonobstructive and obstructive coronary artery lesions and the median age and risk-factor profile as well as the prevalence of CAD are comparable to those of other studies of low- to intermediate-risk patients with chest pain [20–22]. Selection bias was introduced as the CCTA procedure was only available weekdays between 0800–1700 hours, and patients were enrolled into the CT arm at the discretion of the ED physician. Those at slightly higher risk in the ED physician's opinion may have been recruited while others continued to receive standard care even after implementation of the CCTA pathway. The latter patients were not followed. We also encountered difficulty with patient recruitment since the ED physicians were responsible for achieving heart rate control prior to the CT, thus adding to their busy workload. In addition, the gold standard of cardiac catheterization was only obtained in a minority of patients in both groups. Other limitations to our CCTA procedure include the use of retrospective gating with dose modulation leading to a higher radiation exposure than the recently reported dose levels of 1 to 4 mSv [23–25], using prospectively triggered or high-pitch helical image acquisition. With the advent of recent technological advances, radiation exposure from CCTA [26] is now less than from nuclear myocardial perfusion imaging [11].

In conclusion, a cardiac CT-based strategy to rule out ACS in patients presenting to the ED with low-intermediate-risk chest pain in a Canadian center was safe and lead to a shorter time to diagnosis compared to outpatient testing but it did increase LOS in the ED. This increase in LOS was the result of incorporating an imaging test into the ED visit rather than following standard care which involves performing imaging testing on an outpatient basis following ED discharge. The increased LOS may be a barrier to the incorporation of this technology in Canadian emergency departments. Further prospective research is warranted to determine the economic and quality of life implications of these findings in the Canadian system.

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Compliance with ethical standards Study approval was obtained from the institutional research ethics board. Individual informed consent was waived from patients participating in the study as the work reflected a change in standard practice, and no patients were randomized. Clinical information abstracted from the charts was only obtained from patients who had consented to have their charts reviewed for research purposes.

Conflict of interest The authors declare that they have no conflict of interest.

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