

openheart Disability-free survival after coronary artery bypass grafting in women and men with heart failure

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ABSTRACT

Objective Heart failure (HF) impairs survival post coronary artery bypass grafting (CABG), but little is known about the postoperative quality of life (QoL) in patients with HF. We derived a patient-centred QoL surrogate and assessed the impact of different HF subtypes on this surrogate in the year post-CABG.

Methods We surveyed 3112 cardiovascular patients to derive a patient-centred disability outcome and studied this outcome in a population-based cohort. We defined preserved ejection fraction as $\geq 50\%$ and reduced ejection fraction as $< 50\%$. The primary outcome was disability, defined according to compiled patient-derived values. The secondary outcomes consisted of each individual component of disability, and death. The incidence of disability was calculated using cumulative incidence functions, with death as a competing risk. We identified predictors of disability using cause-specific hazard models.

Results Patient-derived disability outcome consisted of stroke, nursing home admission and recurrent hospitalisations. When applied to 40 083 CABG patients (20.6% women), the incidence of disability was 5.4% while the incidence of death was 3.7% in the year post-CABG. Female sex was associated with an adjusted HR of 1.25 (95% CI 1.13 to 1.37) for disability. Women with HF with preserved ejection fraction had an adjusted HR of 1.73 (95% CI 1.52 to 1.98) for disability.

Conclusions Disability was a more frequent complication than death in the year post-CABG. Women experienced higher burden of disability than men, and female sex and the presence of HF were important disability risk factors. Efforts should be dedicated to disability risk prediction to enable patient-centred operative decision-making and to developing sex-specific treatment strategies to improve outcomes.

INTRODUCTION

Heart failure (HF) is a sequela of severe coronary artery disease (CAD) and an important comorbidity in patients presenting for coronary artery bypass grafting (CABG). HF with reduced ejection fraction (HFrEF) is a widely regarded risk factor for morbidity and mortality following cardiac surgery,^{1–5} but HF with preserved ejection fraction (HFpEF)

Key questions

What is already known about this subject?

► Current revascularisation trials are sometimes termed ‘tombstone trials’ as they focus on mortality instead of outcomes that may be more important from a patient’s perspective.

What does this study add?

► We conducted a survey to derive a patient-centred disability outcome and assessed the impact of sex and heart failure on this outcome in the year post coronary artery bypass surgery.
► We found that disability was a more frequent complication than death, and women experienced higher rates of disability than men.

How might this impact on clinical practice?

► Our findings highlight the importance of sex-specific medical and surgical therapy to improve outcomes in patients with coronary artery disease.

remains poorly characterised in the cardiac surgery literature. Furthermore, revascularisation trials have largely focused on mortality and major adverse cardiac events (MACE),⁶ and few surgical studies have been dedicated to patient-centred outcomes such as quality of life (QoL) or have used patient-derived QoL instruments. There is no universal agreement on the definition of disability as a surrogate of QoL in cardiovascular research.⁷ In a survey of patients with stroke, patients prioritised ‘home time’ (time spent alive, outside of hospital and free from recurrent stroke).^{8,9} Stroke is an important complication of CABG, the second most common reason for hospitalisation in older adults and the most common cause of long-term disability.^{10,11} Building on these previously identified elements, we surveyed a large group of cardiovascular patient alumni to explore the relative importance of longevity versus proposed disability-defining events such as stroke (due to its association with disability and loss of ‘home time’), recurrent non-elective hospitalisations



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(loss of 'home time') and nursing home admission (loss of independence of living). We then investigated the impact of HF on disability in women and men in the year following CABG in a population-based cohort.

METHODS

Development of a relevant disability outcome

Following approval from the University of Ottawa Heart Institute (UOHI) Research Ethics Board, we partnered with the UOHI Patient Alumni Association to perform a survey of all current cardiovascular alumni members (N=3112). The UOHI Patient Alumni Association is a self-governing body that has been in place for over 40 years to provide support for patients and families living with cardiovascular diseases, as well as being a strategic partner with the UOHI in its delivery of patient-centred research and clinical care. The alumni communications officer first emailed the confidential survey link to all medical and surgical alumni members on 15 August 2017, followed by two reminders on 15 October 2017 and 1 January 2018. Survey results were collected anonymously using SurveyMonkey (San Mateo, California). The details of the survey are outlined in online supplementary appendix 1.

Population-based cohort study

We conducted a population-based, retrospective cohort study in Ontario, Canada, between 1 October 2008 and 31 March 2015 to evaluate the impact of sex and HF on the patient-derived disability outcome. Included were adult patients ≥ 40 years of age who underwent primary isolated CABG. We excluded patients who were non-Ontario residents, who had previous cardiac surgery, or who had missing information on age, sex and EF (online supplementary figure S1).

Data sources

We used the clinical registry data of CorHealth Ontario and population-level administrative healthcare databases with information on all Ontario residents available at the Institute for Clinical Evaluative Sciences. Individuals who underwent isolated CABG were identified from the CorHealth Ontario registry. CorHealth Ontario is a network of 20 hospitals that maintains a detailed prospective clinical registry of all patients who undergo invasive cardiac procedures in Ontario. It captures demographic, comorbidity and procedural-related information and has been validated through selected chart audits. In addition, CorHealth Ontario EF and angiographic data undergo core laboratory validation.¹²

Administrative databases were linked deterministically by using encrypted codes that preserved patient confidentiality. We first linked the CorHealth Ontario registry (date and type of cardiac procedures, left ventricular (LV) function data) with the Ontario Congestive Heart Failure (CHF) database to classify CABG patients by baseline EF and HF status. The CHF database was derived from physician billings based on either one documented HF

admission or two outpatient claims for HF within 1 year. This algorithm has been previously validated and shown to have 85% sensitivity and 97% specificity in identifying HF events.¹³ These data were then linked to the Canadian Institute for Health Information's Discharge Abstract Database (DAD; comorbidities and hospital admissions) and Same Day Surgery (SDS) database (comorbidities), Ontario Health Insurance Plan (OHIP) database (physician service claims), Registered Persons Database (RPDB; ascertainment of vital statistics), the Continuing Care Reporting System (CCRS; admissions to long-term care facilities) and Canadian census. These administrative databases have been validated for many outcomes, exposures and comorbidities.¹⁴⁻¹⁷

Classification of HF by LV function

Diagnosis of HFpEF is based on the presence of HF and LV ejection fraction (LVEF) of $\geq 50\%$.¹⁸ Preoperative EF was obtained from the CorHealth Ontario registry and classified as preserved (pEF) if $\geq 50\%$ and reduced (rEF) if EF was $< 50\%$.^{3, 18} The authors then categorised the patients into HFpEF, HFrfEF, pEF without HF and rEF without HF using previously described methods.^{3, 19}

Comorbidities

Comorbidities were identified from the CorHealth Ontario clinical registry and supplemented with data from DAD, SDS and OHIP using the International Classification of Diseases 10th Revision CA codes²⁰ within 5 years prior to CABG and using validated algorithms.^{14, 16, 21, 22} We estimated the socioeconomic status based on patients' neighbourhood median income in the Canadian census and determined their residence (rural vs urban) using Statistics Canada definitions.²³ Emergent procedural status was ascertained from the CorHealth Ontario registry and supplemented with OHIP claims data, where the anaesthesia provider identified the surgery as emergent under the American Society of Anesthesiologists physical status classification. Height, weight and body mass index (BMI) identified from the CorHealth Ontario registry were used to define morbid obesity (weight > 159 kg or BMI ≥ 40 kg/m²). Frailty status was identified using the Johns Hopkins Adjusted Clinical Groups frailty-defining diagnoses indicator, which is an instrument designed and validated for research of frailty-related outcomes and resource utilisation using administrative data.²⁴⁻²⁸

Outcomes

The primary outcome was disability, defined as patient-derived composite of stroke, nursing home admission and recurrent non-elective hospital admissions of ≥ 3 episodes occurring within 1 year of surgery. The secondary outcomes consisted of each individual component of the disability outcome, and death. Mortality was ascertained using the RPDB. Stroke was identified using a validated algorithm with 70% sensitivity and 99% specificity, based on either one stroke hospitalisation or two physician billings.²⁹ Non-elective hospital admissions were ascertained

using the DAD, and long-term care admissions were ascertained using the CCRS.

Statistical analysis

All analyses were performed in the overall cohort and then stratified by sex. Continuous variables were expressed as mean (SD) and categorical variables as number (proportions). Disability-free survival was defined as survival time from the date of index surgery until the date of a disability-defining event, death or last follow-up. For patients experiencing recurrent non-elective hospitalisations, disability was considered to occur on the date of the third admission. Patients were censored if they were ineligible for OHIP for >2 consecutive quarters (ie, have left Ontario).

We estimated the cumulative incidence of post-CABG disability over time using the cumulative incidence functions (CIFs) to account for death as a competing event. We plotted direct adjusted CIF curves for disability and each of its individual endpoints, stratified by sex and HF status. Direct adjustment was made for each of the covariates listed in [table 1](#), by adopting the Fine-Gray model as the underlying regression model to compute the adjusted CIFs.³⁰ We identified predictors of disability using multivariable cause-specific hazard models, with death as a competing risk. We then explored the modifying effect of sex using multiplicative interaction terms of sex with each of the covariates from the multivariable model, and identified sex-specific disability risk factors by stratifying the main regression analysis by sex.

We performed two sensitivity analyses. First, we used generalised estimating equations (GEE) to determine the adjusted association of patient-level characteristics with disability while accounting for clustering of patients within hospitals. Next, we added the completeness of revascularisation to this GEE model to evaluate the impact of incomplete revascularisation on disability. Incomplete revascularisation was defined as the presence of ≥ 1 ungrafted vessels with $\geq 70\%$ stenosis in the left anterior descending, circumflex or right coronary artery territories.

The measure of association was HR with 95% CI. Analyses were performed using SAS V.9.3, with statistical significance defined by a two-sided *p* value of <0.05.

RESULTS

Survey of patient-centred disability outcomes

A total of 1015 (32.6%) cardiovascular alumni responded to the survey (27.6% women, 68.5% over the age of 65). Of those who responded, 87.4% had a previous hospitalisation (33.0% for HF and 42.6% for myocardial infarction (MI)), 8.5% had stroke and 0.8% were nursing home residents. Due to the anonymous nature of the survey, demographic information was not available for the non-respondents. The majority of respondents (82.1%) indicated they would sacrifice longevity for treatments that would likely lead to improved QoL. Their specific preferences were to be free from stroke (81.0%);

hospital admissions, including those for HF (77.7%) and MI (78.8%); and nursing home admission (67.6%). Although many (55.5%) would be tolerant of a single hospital admission, 21.9% would be intolerant of 2, while the majority (60.7%) would be intolerant of ≥ 3 non-elective admissions per year. When asked to prioritise these outcomes, patients ranked freedom from stroke as most important, followed by staying alive for as long as possible, freedom from hospitalisation and nursing homes (online supplementary figure S2). We therefore defined disability as the composite of stroke, nursing home admission and recurrent non-elective hospital admissions of ≥ 3 episodes per year.

Prevalence and patient characteristics by HF subtype

A total of 40 083 CABG patients were included in the study (20.6% women). Overall, 22 231 (55.5%) had pEF without HF, 10 284 (25.7%) had rEF without HF, 2752 (6.9%) had HFpEF and 4816 (12.0%) had HFrEF. [Table 2](#) summarises the demographics and comorbidities of these patients by HF status.

[Table 3](#) summarises the baseline and operative characteristics of patients with HF, stratified by EF and sex. Of the patients with HFpEF, 873 (31.7%) were women. Women with HFpEF were more likely than men to be older, of lower socioeconomic status, to have emergent surgery, recent MI, hypertension, chronic lung disease, diabetes, hypothyroidism and anaemia, but less likely to have previous percutaneous coronary interventions, remote MI, atrial fibrillation, morbid obesity, chronic renal disease and dialysis. Of the patients with HFrEF, 1090 (22.6%) were women. Women with HFrEF were more likely than men to be older, to be of slightly lower income status, to have emergent surgery, recent MI, hypertension, chronic lung disease, diabetes, hypothyroidism and anaemia, but less likely to have remote MI, atrial fibrillation and morbid obesity.

Disability and HF status

[Table 4](#) summarises the rates of disability and individual disability-defining events by HF status. One year post-CABG, 2152 (5.4%) developed disability and 1466 (3.7%) died. In addition, 1215 (3.0%) developed stroke, 865 (2.2%) had recurrent non-elective hospitalisations and 254 (0.6%) were admitted to long-term care facilities.

Cumulative incidence of disability was higher in patients with HF compared with those without HF (Gray's test, $p < 0.001$). At 1 year, disability occurred in 11.4% of patients with HFpEF, 10.7% of HFrEF, 4.7% of rEF without HF and 3.8% of pEF without HF. The rates of individual disability-defining events were also higher in patients with HFpEF. One-year mortality rates were highest in the HFrEF group (11.1%), followed by HFpEF (8.3%), rEF without HF (2.9%) and pEF without HF (1.8%). Overall, patients with HFpEF experienced higher rates of disability, while patients with HFrEF experienced higher rates of death. After multivariable adjustment of all risk factors listed in [table 1](#), the cause-specific HRs for

Table 1 Multivariable predictors of disability at 1 year post-CABG in the pooled analysis

Variable	Main model	Cluster by site	Completeness of revascularisation added
	HR (95% CI)	HR (95% CI)	HR (95% CI)
HF group			
pEF, no HF	Reference	Reference	Reference
rEF, no HF	1.11 (0.99 to 1.25)	1.11 (1.00 to 1.24)	1.10 (0.98 to 1.24)
HFpEF	1.81 (1.57 to 2.08)	1.81 (1.61 to 2.04)	1.79 (1.55 to 2.06)
HFrEF	1.68 (1.49 to 1.90)	1.68 (1.46 to 1.93)	1.67 (1.48 to 1.89)
Age group			
40–64	Reference	Reference	Reference
65–74	1.14 (1.03 to 1.27)	1.14 (1.02 to 1.27)	1.13 (1.02 to 1.26)
75–84	1.57 (1.40 to 1.77)	1.57 (1.49 to 1.66)	1.57 (1.40 to 1.76)
≥85	1.91 (1.47 to 2.48)	1.91 (1.41 to 2.57)	1.87 (1.43 to 2.44)
Sex	1.25 (1.13 to 1.37)	1.25 (1.10 to 1.41)	1.25 (1.13 to 1.38)
Rural residence	0.97 (0.86 to 1.09)	0.97 (0.90 to 1.04)	0.97 (0.86 to 1.09)
Income quintile			
1 (lowest)	1.27 (1.11 to 1.45)	1.27 (1.12 to 1.43)	1.29 (1.12 to 1.47)
2	1.04 (0.91 to 1.20)	1.04 (0.90 to 1.21)	1.05 (0.91 to 1.21)
3	0.99 (0.86 to 1.14)	0.99 (0.88 to 1.12)	1.01 (0.88 to 1.17)
4	1.02 (0.89 to 1.18)	1.02 (0.94 to 1.12)	1.04 (0.90 to 1.20)
5 (highest)	Reference	Reference	Reference
Missing	1.81 (1.08 to 3.03)	1.81 (0.85 to 3.86)	1.83 (1.09 to 3.06)
Remote MI	1.05 (0.95 to 1.15)	1.05 (0.91 to 1.21)	1.04 (0.95 to 1.15)
Recent MI	1.32 (1.20 to 1.45)	1.32 (1.15 to 1.51)	1.31 (1.20 to 1.44)
Previous PCI	0.96 (0.86 to 1.09)	0.96 (0.85 to 1.09)	0.98 (0.87 to 1.10)
Hypertension	1.40 (1.16 to 1.68)	1.40 (1.14 to 1.71)	1.39 (1.15 to 1.68)
Atrial fibrillation	1.21 (1.06 to 1.38)	1.21 (1.08 to 1.35)	1.21 (1.05 to 1.38)
Cerebrovascular disease	2.16 (1.94 to 2.41)	2.16 (1.96 to 2.39)	2.18 (1.96 to 2.43)
Peripheral vascular disease	1.34 (1.20 to 1.49)	1.34 (1.22 to 1.46)	1.34 (1.20 to 1.49)
COPD/Asthma	1.33 (1.22 to 1.46)	1.33 (1.22 to 1.45)	1.34 (1.22 to 1.46)
Diabetes	1.40 (1.28 to 1.53)	1.40 (1.29 to 1.51)	1.39 (1.27 to 1.52)
Morbid obesity	1.02 (0.93 to 1.12)	1.02 (0.96 to 1.08)	1.03 (0.94 to 1.13)
Hypothyroidism	1.16 (0.87 to 1.55)	1.16 (0.83 to 1.62)	1.16 (0.86 to 1.55)
Anaemia	1.33 (1.14 to 1.55)	1.33 (1.18 to 1.50)	1.35 (1.16 to 1.57)
Chronic renal disease	1.56 (1.36 to 1.79)	1.56 (1.43 to 1.70)	1.56 (1.36 to 1.79)
Liver disease	1.79 (1.29 to 2.49)	1.79 (1.41 to 2.27)	1.81 (1.30 to 2.52)
Primary tumour	1.23 (1.04 to 1.45)	1.23 (1.05 to 1.44)	1.21 (1.02 to 1.43)
Metastatic tumour	1.28 (0.80 to 2.04)	1.28 (0.84 to 1.95)	1.32 (0.83 to 2.11)
Dementia	1.85 (1.25 to 2.74)	1.85 (1.36 to 2.51)	1.83 (1.23 to 2.72)
Emergent surgery	1.41 (1.22 to 1.63)	1.41 (1.23 to 1.60)	1.39 (1.20 to 1.61)
Incomplete revascularisation (yes)	–	–	1.09 (1.00 to 1.20)

CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; pEF, preserved ejection fraction; rEF, reduced ejection fraction.

disability were 1.11 (95% CI 0.99 to 1.25) for rEF without HF, 1.81 (95% CI 1.61 to 2.04) for HFpEF, and 1.68 (95% CI 1.46 to 1.93) for HFrEF.

Sex differences in disability

Female sex was associated with an increased risk of disability (adjusted HR 1.25 (95% CI 1.13 to 1.37)), and this

Table 2 Baseline characteristics by HF status

Variable	pEF, no HF (n=22 231)	rEF, no HF (n=10 284)	HFpEF (n=2752)	HFrEF (n=4816)	Total (n=40 083)	P values
Age (mean±SD)	65.3±9.7	65.0±10.0	69.5±9.3	68.0±9.9	65.8±9.9	<0.001
40–64	10 197 (45.9%)	4883 (47.5%)	815 (29.6%)	1730 (35.9%)	17 625 (44.0%)	<0.001
65–74	7838 (35.3%)	3436 (33.4%)	1015 (36.9%)	1680 (34.9%)	13 969 (34.9%)	
75–84	3937 (17.7%)	1829 (17.8%)	843 (30.6%)	1264 (26.2%)	7873 (19.6%)	
≥85	259 (1.2%)	136 (1.3%)	79 (2.9%)	142 (2.9%)	616 (1.5%)	
Female	4695 (21.1%)	1590 (15.5%)	873 (31.7%)	1090 (22.6%)	8248 (20.6%)	<0.001
Rural	3373 (15.2%)	1670 (16.2%)	403 (14.6%)	685 (14.2%)	6131 (15.3%)	0.036
Income quintile 1 (lowest)	4010 (18.0%)	1963 (19.1%)	584 (21.2%)	1061 (22.0%)	7618 (19.0%)	<0.001
2	4473 (20.1%)	2036 (19.8%)	614 (22.3%)	1054 (21.9%)	8177 (20.4%)	
3	4485 (20.2%)	2096 (20.4%)	552 (20.1%)	942 (19.6%)	8075 (20.1%)	
4	4579 (20.6%)	2179 (21.2%)	532 (19.3%)	877 (18.2%)	8167 (20.4%)	
5 (highest)	4578 (20.6%)	1947 (18.9%)	459 (16.7%)	848 (17.6%)	7832 (19.5%)	
Missing	106 (0.5%)	63 (0.6%)	11 (0.4%)	34 (0.7%)	214 (0.5%)	
Remote MI	3958 (17.8%)	3408 (33.1%)	917 (33.3%)	2072 (43.0%)	10 355 (25.8%)	<0.001
Recent MI	7509 (33.8%)	6033 (58.7%)	1418 (51.5%)	3255 (67.6%)	18 215 (45.4%)	<0.001
Previous PCI	3210 (14.4%)	1759 (17.1%)	542 (19.7%)	776 (16.1%)	6287 (15.7%)	<0.001
Hypertension	19 275 (86.7%)	8717 (84.8%)	2610 (94.8%)	4427 (91.9%)	35 029 (87.4%)	<0.001
Atrial fibrillation	968 (4.4%)	563 (5.5%)	433 (15.7%)	791 (16.4%)	2755 (6.9%)	<0.001
Cerebral vascular disease	1999 (9.0%)	965 (9.4%)	413 (15.0%)	675 (14.0%)	4052 (10.1%)	<0.001
Peripheral vascular disease	2306 (10.4%)	1197 (11.6%)	579 (21.0%)	1047 (21.7%)	5129 (12.8%)	<0.001
COPD/Asthma	5599 (25.2%)	2660 (25.9%)	1090 (39.6%)	1790 (37.2%)	11 139 (27.8%)	<0.001
Diabetes	9636 (43.3%)	4624 (45.0%)	1626 (59.1%)	3022 (62.7%)	18 908 (47.2%)	<0.001
Morbid obesity	6838 (30.8%)	2815 (27.4%)	954 (34.7%)	1538 (31.9%)	12 145 (30.3%)	<0.001
Hypothyroidism	201 (0.9%)	78 (0.8%)	70 (2.5%)	78 (1.6%)	427 (1.1%)	<0.001
Anaemia	555 (2.5%)	280 (2.7%)	318 (11.6%)	492 (10.2%)	1645 (4.1%)	<0.001
Dialysis	257 (1.2%)	141 (1.4%)	177 (6.4%)	268 (5.6%)	843 (2.1%)	<0.001
Chronic renal disease	620 (2.8%)	308 (3.0%)	348 (12.6%)	607 (12.6%)	1883 (4.7%)	<0.001
Liver disease	115 (0.5%)	65 (0.6%)	38 (1.4%)	70 (1.5%)	288 (0.7%)	<0.001
Primary tumour	939 (4.2%)	444 (4.3%)	184 (6.7%)	298 (6.2%)	1865 (4.7%)	<0.001
Metastatic tumour	88 (0.4%)	38 (0.4%)	16 (0.6%)	38 (0.8%)	180 (0.4%)	<0.001
Dementia	32 (0.1%)	22 (0.2%)	20 (0.7%)	37 (0.8%)	111 (0.3%)	<0.001
Frailty	4339 (19.5%)	2097 (20.4%)	898 (32.6%)	1469 (30.5%)	8803 (22.0%)	<0.001
Emergent surgery	873 (3.9%)	959 (9.3%)	169 (6.1%)	590 (12.3%)	2591 (6.5%)	<0.001

COPD, chronic obstructive pulmonary disease; HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; pEF, preserved ejection fraction; rEF, reserved ejection fraction.

association remained robust in sensitivity analyses that accounted for clustering of patients within hospitals and completeness of revascularisation (table 1).

The sex-specific rates of disability and disability-defining events are summarised in table 5 and figure 1. Women had higher rates of disability than men across most HF categories except HFrEF, and women with HFpEF constituted a high disability risk group. Sex modified the association between disability and HF, age, MI, cerebrovascular disease and chronic renal disease (table 6). Specifically, rEF and HFrEF were associated with disability in women

but not men, and HFpEF posed a greater risk of disability in women. Additionally, in patients aged 65–74 years, male sex alone was associated with an increased risk of disability, while in the ≥85 age group women had a higher risk of disability than men. Cerebrovascular and chronic renal diseases were also associated with higher disability risks in women.

The direct adjusted CIFs of stroke, recurrent non-elective hospitalisations and long-term care admissions were higher in women than men across most HF categories (figure 2). Women with HFpEF were at higher risk of

Table 3 Baseline characteristics of men and women with HFpEF and HFrEF

Variable	HFpEF		HFrEF		P values*
	Men (n=1879)	Women (n=873)	Men (n=3726)	Women (n=1090)	
Age (mean±SD)	68.57±9.50	71.41±8.65	67.54±10.01	69.58±9.43	<0.001
40–64	619 (32.9%)	196 (22.5%)	1406 (37.7%)	324 (29.7%)	<0.001
65–74	698 (37.1%)	317 (36.3%)	1291 (34.6%)	389 (35.7%)	
75–84	518 (27.6%)	325 (37.2%)	930 (25.0%)	334 (30.6%)	
≥85	44 (2.3%)	35 (4.0%)	99 (2.7%)	43 (3.9%)	
Rurality	282 (15.0%)	121 (13.9%)	532 (14.3%)	153 (14.0%)	0.64
Income quintile 1 (lowest)	346 (18.4%)	238 (27.3%)	800 (21.5%)	261 (23.9%)	<0.001
2	422 (22.5%)	192 (22.0%)	810 (21.7%)	244 (22.4%)	
3	387 (20.6%)	165 (18.9%)	738 (19.8%)	204 (18.7%)	
4	380 (20.2%)	152 (17.4%)	669 (18.0%)	208 (19.1%)	
5 (highest)	334 (17.8%)	125 (14.3%)	687 (18.4%)	161 (14.8%)	
Missing	10 (0.5%)	≤5 (0.1%)	22 (0.6%)	12 (1.1%)	
Remote MI	632 (33.6%)	285 (32.6%)	1618 (43.4%)	454 (41.7%)	<0.001
Recent MI	920 (49.0%)	498 (57.0%)	2444 (65.6%)	811 (74.4%)	<0.001
Previous PCI	387 (20.6%)	155 (17.8%)	599 (16.1%)	177 (16.2%)	<0.001
Hypertension	1766 (94.0%)	844 (96.7%)	3395 (91.1%)	1032 (94.7%)	<0.001
Atrial fibrillation	301 (16.0%)	132 (15.1%)	653 (17.5%)	138 (12.7%)	0.001
Cerebrovascular disease	283 (15.1%)	130 (14.9%)	514 (13.8%)	161 (14.8%)	0.56
Peripheral vascular disease	389 (20.7%)	190 (21.8%)	801 (21.5%)	246 (22.6%)	0.69
COPD/Asthma	717 (38.2%)	373 (42.7%)	1345 (36.1%)	445 (40.8%)	<0.001
Diabetes	1083 (57.6%)	543 (62.2%)	2261 (60.7%)	761 (69.8%)	<0.001
Morbid obesity	710 (37.8%)	244 (27.9%)	1235 (33.1%)	303 (27.8%)	<0.001
Hypothyroidism	29 (1.5%)	41 (4.7%)	47 (1.3%)	31 (2.8%)	<0.001
Anaemia	185 (9.8%)	133 (15.2%)	355 (9.5%)	137 (12.6%)	<0.001
Dialysis	128 (6.8%)	49 (5.6%)	205 (5.5%)	63 (5.8%)	0.26
Chronic renal disease	242 (12.9%)	106 (12.1%)	478 (12.8%)	129 (11.8%)	0.79
Liver disease	26 (1.4%)	12 (1.4%)	55 (1.5%)	15 (1.4%)	0.99
Primary tumour	133 (7.1%)	51 (5.8%)	231 (6.2%)	67 (6.1%)	0.52
Metastatic tumour	14 (0.7%)	≤5 (0.2%)	24 (0.6%)	14 (1.3%)	0.04
Dementia	14 (0.7%)	6 (0.7%)	13 (1.2%)	24 (0.6%)	0.326
Frailty	538 (28.6%)	360 (41.2%)	1022 (27.4%)	447 (41.0%)	<0.001
Emergent surgery	107 (5.7%)	62 (7.1%)	431 (11.6%)	159 (14.6%)	<0.001

*P values were obtained using one-way analysis of variance test for means and χ^2 test for categorical variables.

COPD, chronic obstructive pulmonary disease; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

stroke and recurrent hospitalisations, while women with HFrEF were at higher risk of entering long-term care.

DISCUSSION

We derived a patient-centred disability outcome as a meaningful surrogate for postoperative QoL and demonstrated the feasibility of applying it in population-based data. We found that sex and HF were important risk factors for disability in the year following CABG. Specifically, disability was a more frequent complication than death. HFpEF

was associated with higher rates of disability, while HFrEF was associated with higher rates of death. In addition, disability rates were higher in women, especially women with HF. Our findings highlight the need for personalised disability risk prediction tools to empower shared surgical decision-making, and for future clinical trials to develop sex-specific medical and surgical strategies.

Need for patient-centred outcomes in cardiovascular research

Clinicians sometimes make decisions that are misaligned with patient preferences and values.³¹ The lack of

Table 4 Event rates within 1 year following coronary artery bypass grafting, by heart failure status

Event	pEF, no HF (n=22 231)	rEF, no HF (n=10 284)	HFpEF (n=2752)	HFrEF (n=4816)	Total (n=40 083)	P values*
Disability, n (%)	846 (3.8)	480 (4.7)	313 (11.4)	513 (10.7)	2152 (5.4)	<0.001
Death, n (%)	400 (1.8)	303 (2.9)	229 (8.3)	534 (11.1)	1466 (3.7)	<0.001
≥3 non-elective hospitalisations, n (%)	274 (1.2)	165 (1.6)	163 (5.9)	263 (5.5)	865 (2.2)	<0.001
Long-term care admission, n (%)	88 (0.4)	57 (0.6)	42 (1.5)	67 (1.4)	254 (0.6)	<0.001
Stroke, n (%)	533 (2.4)	299 (2.9)	147 (5.3)	236 (4.9)	1215 (3.0)	<0.001

*P values were obtained using one-way analysis of variance test for means and χ^2 test for categorical variables.

HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; pEF, preserved ejection fraction; rEF, reserved ejection fraction.

patient-oriented data from existing revascularisation trials, sometimes termed ‘tombstone trials’,³² plays a role. These trials focus primarily on mortality and MACE³³ as these endpoints are easier to measure and are perceived to be more objective than QoL.^{7 33–35} CABG is an advancing field where operative mortality has steadily declined over the years.³⁶ As CABG candidates (online supplementary appendix 1) advance in age and medical complexity, their expectations often shift towards how treatments would affect their personal freedom and mobility, rather than longevity alone.^{6 31–33 37}

The advent of population-based administrative databases and clinical registries offers efficient means for identifying disparities in healthcare systems. Long-term QoL outcomes are difficult to study prospectively and have so far been infeasible using administrative data due to lack of validated QoL elements in these repositories. We derived a working definition of ‘disability-free survival’ based on input of a large mixed cardiac medical and surgical cohort. This measure could be further developed through cardiovascular studies using administrative data.

Sex differences in post-CABG disability

Health-related QoL at 1 year post-CABG has been reported using the short form 36 (SF-36) in several smaller observational studies. In a single-centre study assessing the QoL of 112 patients from 2005 to 2008, patients reported higher than normative scores in the subscales of social functioning, role physical and role emotional, and lower scores in physical function, bodily pain, general health, vitality social function and mental health. Additionally, men reported higher postoperative physical function and role emotional scores compared with women.³⁸ In a study of 186 patients from 1995 to 1996, poor QoL at 1 year post-CABG was associated with poor preoperative health status, while high levels of social support were associated with improved postoperative QoL.³⁹ Using a patient-derived QoL surrogate, we were able to examine post-CABG outcomes at the population level. Our findings highlight the compounding risk of female sex, older age (≥85 years), cerebrovascular and chronic renal disease on disability and point to the importance of these factors in the perioperative risk stratification process.

Rates of short-term (30-day) readmissions have been reported in various population-based cohorts and range

Table 5 Event rates within 1 year following coronary artery bypass grafting, stratified by sex

Event	pEF, no HF		rEF, no HF		HFpEF		HFrEF		P values*
	Men (n=17 536)	Women (n=4695)	Men (n=8694)	Women (n=1590)	Men (n=1879)	Women (n=873)	Men (n=3726)	Women (n=1090)	
Disability, n (%)	601 (3.4)	245 (5.2)	357 (4.1)	123 (7.7)	189 (10.1)	124 (14.2)	395 (10.6)	118 (10.8)	<0.001
Death, n (%)	292 (1.7)	108 (2.3)	236 (2.7)	67 (4.2)	132 (7.0)	97 (11.1)	386 (10.4)	148 (13.6)	<0.001
Non-elective hospitalisations, mean±SD	0.2±0.6	0.3±0.8	0.3±0.7	0.4±0.8	0.5±1.0	0.7±1.1	0.6±1.1	0.6±1.0	<0.001
≥3 non-elective hospitalisations, n (%)	176 (1.0)	98 (2.1)	124 (1.4)	41 (2.6)	92 (4.9)	71 (8.1)	209 (5.6)	54 (5.0)	<0.001
Long-term care admission, n (%)	50 (0.3)	38 (0.8)	38 (0.4)	19 (1.2)	24 (1.3)	18 (2.1)	36 (1.0)	31 (2.8)	<0.001
Stroke, n (%)	403 (2.3)	130 (2.8)	225 (2.6)	74 (4.7)	95 (5.1)	52 (6.0)	180 (4.8)	56 (5.1)	<0.001

*P values were obtained using one-way analysis of variance test for means and χ^2 test for categorical variables.

HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; pEF, preserved ejection fraction; rEF; reduced ejection fraction.

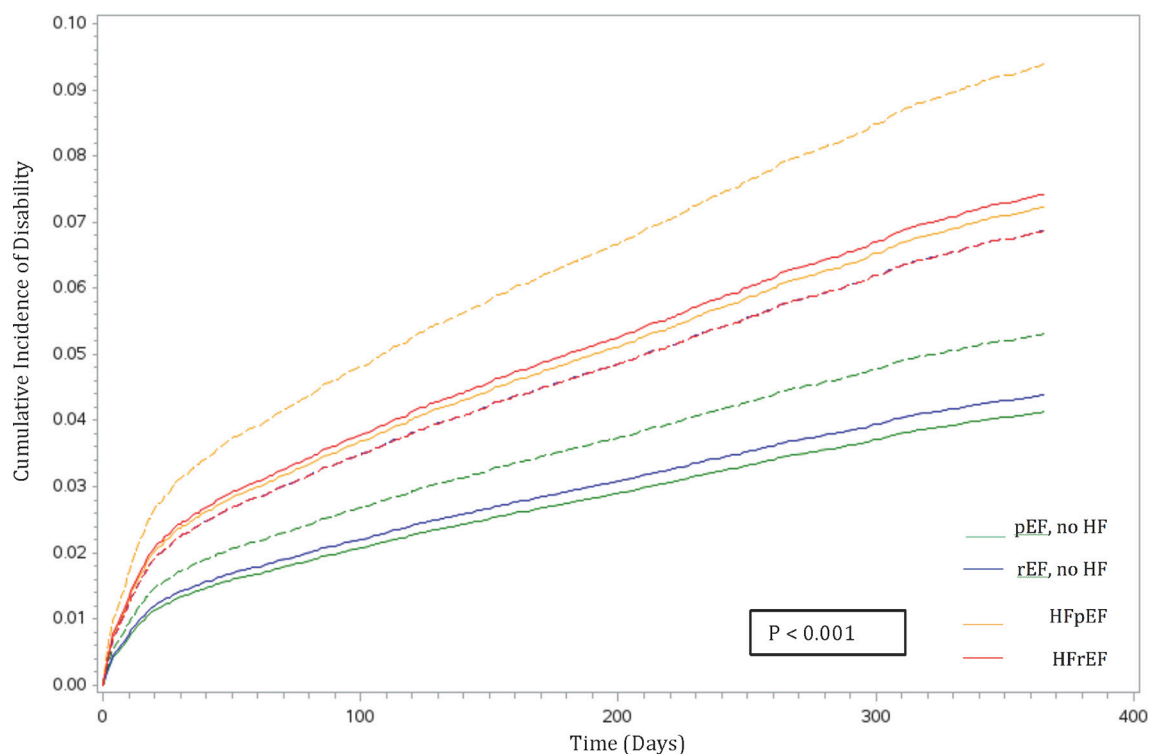


Figure 1 Adjusted cumulative disability incidence by sex and heart failure status. The solid lines represent adjusted cumulative incidence in men. The dotted lines represent adjusted cumulative incidence in women. HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; pEF, preserved ejection fraction; rEF, reduced ejection fraction.

from 0% to 27% following CABG.^{40–42} Long-term post-CABG readmissions have mostly been reported as part of composite outcomes such as in the case of the Surgical Treatment for Ischemic Heart Failure (STICH) trial.^{1 43} In STICH, 65% of patients were dead or hospitalised at 5 years of follow-up,⁴³ 89% at 10 years.¹ In a historical cohort

of 8910 patients who underwent primary isolated CABG between 1980 and 1993, 1-year survival without cardiac readmissions occurred in 93%.⁴⁴ Although lacking in detailed sex-specific analyses, these authors reported a higher rate of cardiac readmissions in women.⁴⁴ Our study reports on modern 1-year hospital readmission rates and

Table 6 Sex-specific disability risk factors post coronary artery bypass grafting

	Sex-specific HR (95% CI)		Interaction p values
	Men	Women	
HF group			
pEF, no HF	Reference	Reference	0.05
rEF, no HF	1.04 (0.85 to 1.27)	1.18 (1.04 to 1.33)	
HFpEF	1.24 (1.01 to 1.53)	1.73 (1.52 to 1.98)	
HFrEF	1.55 (0.99 to 2.41)	2.09 (1.52 to 2.88)	
Age group (years)			
40–64	Reference	Reference	0.003
65–74	1.30 (1.04 to 1.63)	1.06 (0.93 to 1.22)	
75–84	1.82 (1.46 to 2.28)	1.80 (1.51 to 2.14)	
≥85	1.30 (1.04 to 1.64)	1.84 (1.60 to 2.12)	
Remote myocardial infarction	1.21 (1.02 to 1.44)	0.99 (0.88 to 1.11)	0.04
Cerebrovascular disease	1.76 (1.45 to 2.15)	2.35 (2.08 to 2.66)	0.01
Chronic renal disease	1.26 (0.98 to 1.62)	1.68 (1.45 to 1.96)	0.05

HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; pEF, preserved ejection fraction; rEF, reduced ejection fraction.

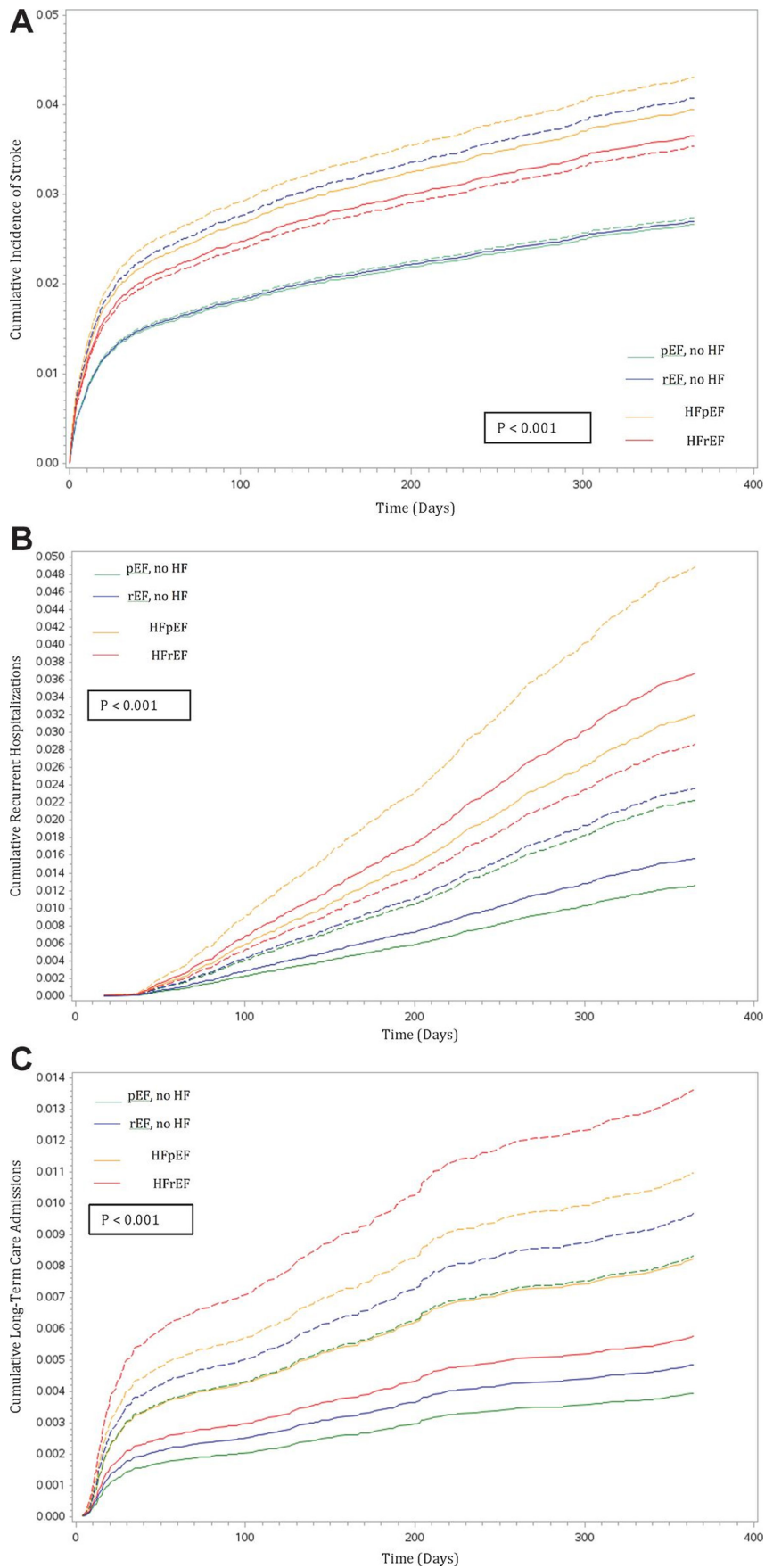


Figure 2 Adjusted cumulative incidence of stroke, by sex and heart failure status. The solid lines represent cumulative incidence in men. The dotted lines represent cumulative incidence in women. HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; pEF, preserved ejection fraction; rEF, reduced ejection fraction.

adds to the literature that female sex and HF (especially HFpEF) are important risk factors for recurrent non-elective hospitalisations. Our findings suggest that extended postoperative follow-up should be tailored to women with signs and symptoms with HF and not based on EF alone.³

Our reported rates of stroke are consistent with the literature.^{45–47} In addition, our finding of higher rates of stroke in women and those with HFpEF expanded our knowledge of this complication. Consistent with previous reports,^{19 48 49} we found a higher prevalence of HFpEF in women presenting for CABG surgery. This is likely due to HFpEF being a disease of older women and those with chronic arterial hypertension, whose rightward cerebral autoregulation shift predisposes them to cerebral ischaemia when exposed to even mild degrees of intraoperative hypotension.⁵⁰ Women and those with HFpEF may therefore benefit from individualised perioperative haemodynamic management to mitigate the risk of perioperative stroke.⁵⁰

In summary, our findings highlight an important care gap in that current delivery of medical and surgical therapies for CAD are insufficiently specific to women. Women are under-represented in clinical trials, and much of the practice guidelines are based on extrapolated trial data from male patients. Future trials could focus on evaluating the specific effect of pharmacological and surgical techniques (such as multiple arterial grafting and off-pump CABG) in women as well as in men. Furthermore, our findings point to women with HF as a specific group that is likely to benefit from targeted medical and social interventions.

Limitations and strengths

This study has several limitations. First, our disability measure needs to be prospectively validated against established QoL instruments. However, our study is a first step towards describing the burden of disability post-CABG at the population level. Second, data pertaining to stroke severity are unavailable in the databases used. As some patients with stroke experience full functional recovery, our findings may have overestimated the burden of stroke-related disability. Third, the lack of natriuretic peptides measurements precluded the use of this biomarker as a third diagnostic criterion for HFpEF.¹⁸ However, brain natriuretic peptide (BNP) measurements are not a routine practice in Ontario, and whether BNP would further improve risk stratification in patients with HF, above and beyond physician-diagnosed HF, remains to be determined. Finally, cohort studies are by nature subjected to residual confounding.

CONCLUSIONS

We used a patient-derived disability measure to identify gaps in health outcomes in a large cohort of patients who underwent isolated CABG. We found disability to be a more frequent complication than death in the year postsurgery, and in addition we identified female

sex and the presence of HF as important disability risk factors. Future research should be dedicated to personalised disability risk prediction to guide patient-centred operative decision-making, and to sex-specific medical and surgical strategies to improve outcomes in patients with CAD.

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Patient consent Not required.

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Data sharing statement The data and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

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REFERENCES

- Velazquez EJ, Lee KL, Jones RH, et al. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. *N Engl J Med* 2016;374:1511–20.
- Velazquez EJ, Williams JB, Yow E, et al. Long-term survival of patients with ischemic cardiomyopathy treated by coronary artery bypass grafting versus medical therapy. *Ann Thorac Surg* 2012;93:523–30.
- Sun LY, Tu JV, Bader Eddeen A, et al. Prevalence and long-term survival after coronary artery bypass grafting in women and men with heart failure and preserved versus reduced ejection fraction. *J Am Heart Assoc* 2018;7:e008902.
- Wrobel K, Stevens SR, Jones RH, et al. Influence of baseline characteristics, operative conduct, and postoperative course on 30-day outcomes of coronary artery bypass grafting among patients with left ventricular dysfunction: results from the Surgical Treatment for Ischemic Heart Failure (STICH) Trial. *Circulation* 2015;132:720–30.
- Hillis GS. Outcome of patients with low ejection fraction undergoing coronary artery bypass grafting: renal function and mortality after 3.8 years. *Circulation* 2006;114:l-414–419.
- Rahimi K, Malhotra A, Banning AP, et al. Outcome selection and role of patient reported outcomes in contemporary cardiovascular trials: systematic review. *BMJ* 2010;341:c5707.
- Wenger NK, Froelicher ES, Smith LK, et al. Cardiac rehabilitation as secondary prevention. Agency for health care policy and research and national heart, lung, and blood institute. *Clin Pract Guidel Quick Ref Guide Clin* 1995;17:1–23.
- Hannah D, Lindholm B, Maisch L. Certain uncertainty: life after stroke from the patient's perspective. *Circ Cardiovasc Qual Outcomes* 2014;7:968–9.
- O'Brien EC, Xian Y, Fonarow GC, et al. Clinical commentary on "Certain uncertainty: life after stroke from the patient's perspective". *Circ Cardiovasc Qual Outcomes* 2014;7:970.
- Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics-2014 update: a report from the American Heart Association. *Circulation* 2014;129:e28–292.
- Xian Y, O'Brien EC, Fonarow GC. Patient-centered research into outcomes stroke patients prefer and effectiveness research Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research: implementing Implementing the patient-driven research paradigm to aid decision making in stroke care. *Am Heart J* 2015;170:36–45.
- Tu JV, Ko DT, Guo H, et al. Determinants of variations in coronary revascularization practices. *CMAJ* 2012;184:179–86.
- Schultz SE, Rothwell DM, Chen Z, et al. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can* 2013;33:160–6.
- Tu K, Campbell NR, Chen ZL, et al. Accuracy of administrative databases in identifying patients with hypertension. *Open Med* 2007;1:e18–26.
- Juurink D, Preya C, Croxford R. *Canadian institute for health information discharge abstract database: a validation study. ICES Investigative Report*. Toronto, ON: Institute for Clinical Evaluative Sciences, 2006.
- Hux JE, Ivis F, Flintoft V, et al. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care* 2002;25:512–6.
- Austin PC, Daly PA, Tu JV. A multicenter study of the coding accuracy of hospital discharge administrative data for patients admitted to cardiac care units in Ontario. *Am Heart J* 2002;144:290–6.
- Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;37:2129–200.
- Dalén M, Lund LH, Ivert T, et al. Survival after coronary artery bypass grafting in patients with preoperative heart failure and preserved vs reduced ejection fraction. *JAMA Cardiol* 2016;1:530–8.
- Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130–9.
- Gershon AS, Wang C, Guan J, et al. Identifying patients with physician-diagnosed asthma in health administrative databases. *Can Respir J* 2009;16:183–8.
- Gershon AS, Wang C, Guan J, et al. Identifying individuals with physician diagnosed COPD in health administrative databases. *COPD* 2009;6:388–94.
- Plessis du V, Beshiri R, Bollman RD. *Definitions of "rural". Agriculture and rural working paper series, No. 61*. Ottawa, ON: Statistics Canada, 2002.
- Lieberman RAC, Weiner J. *Development and evaluation of the Johns Hopkins university risk adjustment models for medicare+ choice plan payment*. MD Baltimore, 2003.
- Sternberg SA, Bentur N, Abrams C, et al. Identifying frail older people using predictive modeling. *Am J Manag Care* 2012;18:e392–7.
- The Johns Hopkins adjusted clinical groups technical reference guide, version 9.0*. Baltimore, MD: Johns Hopkins University, 2009.
- Bronskill SCM, Costa A. *Aging in Ontario: an ICES chartbook of health services use by older adults - a technical report*. Ontario, Canada: Institute for Clinical Evaluative Sciences, 2010.
- Bronskill SCX, Gruneir A, Ho M. *Health system use by frail Ontario seniors: an in-depth examination of four vulnerable cohorts*. Ontario, Canada: Institute for Clinical Evaluative Sciences, 2011.
- Tu K, Wang M, Young J, et al. Validity of administrative data for identifying patients who have had a stroke or transient ischemic attack using EMERALD as a reference standard. *Can J Cardiol* 2013;29:1388–94.
- Zhang X, Zhang MJ. SAS macros for estimation of direct adjusted cumulative incidence curves under proportional subdistribution hazards models. *Comput Methods Programs Biomed* 2011;101:87–93.
- Mulley AG. Inconvenient truths about supplier induced demand and unwarranted variation in medical practice. *BMJ* 2009;339:b4073.
- Chalmers I, Clarke M. Outcomes that matter to patients in tombstone trials. *Lancet* 2001;358:1649.
- Myles PS. Meaningful outcome measures in cardiac surgery. *J Extra Corpor Technol* 2014;46:23–7.
- Caine N, Harrison SC, Sharples LD, et al. Prospective study of quality of life before and after coronary artery bypass grafting. *BMJ* 1991;302:511–6.
- Chocron S, Etievent JP, Viel JF, et al. Prospective study of quality of life before and after open heart operations. *Ann Thorac Surg* 1996;61:153–7.
- Ferguson TB, Hammill BG, Peterson ED, et al. A decade of change-risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990–1999: a report from the STS national database committee and the duke clinical research institute. Society of thoracic surgeons. *Ann Thorac Surg* 2002;73:480–9.
- Selby JV, Beal AC, Frank L. The Patient-Centered Outcomes Research Institute (PCORI) national priorities for research and initial research agenda. *JAMA* 2012;307:1583–4.
- Taghipour HR, Naseri MH, Safarian R, et al. Quality of life one year after coronary artery bypass graft surgery. *Iran Red Crescent Med J* 2011;13:171–7.
- Lindsay GM, Hanlon P, Smith LN, et al. Assessment of changes in general health status using the short-form 36 questionnaire 1 year following coronary artery bypass grafting. *Eur J Cardiothorac Surg* 2000;18:557–64.
- Hannan EL, Zhong Y, Lahey SJ, et al. 30-day readmissions after coronary artery bypass graft surgery in New York State. *JACC Cardiovasc Interv* 2011;4:569–76.
- Li Z, Armstrong EJ, Armstrong EJ, et al. Hospital variation in readmission after coronary artery bypass surgery in California. *Circ Cardiovasc Qual Outcomes* 2012;5:729–37.
- Price JD, Romeiser JL, Gnerre JM, et al. Risk analysis for readmission after coronary artery bypass surgery: developing a strategy to reduce readmissions. *J Am Coll Surg* 2013;216:412–9.
- Velazquez EJ, Lee KL, Deja MA, et al. Coronary-artery bypass surgery in patients with left ventricular dysfunction. *N Engl J Med* 2011;364:1607–16.
- Bradshaw PJ, Jamrozik K, Le M, et al. Mortality and recurrent cardiac events after coronary artery bypass graft: long term outcomes in a population study. *Heart* 2002;88:488–94.
- Stone GW, Sabik JF, Serruys PW, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. *N Engl J Med* 2016;375:2223–35.
- Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med* 2012;367:2375–84.
- Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360:961–72.
- Steinberg BA, Zhao X, Heidenreich PA, et al. Trends in patients hospitalized with heart failure and preserved left ventricular ejection fraction: prevalence, therapies, and outcomes. *Circulation* 2012;126:65–75.



49. Bhatia RS, Tu JV, Lee DS, *et al.* Outcome of heart failure with preserved ejection fraction in a population-based study. *N Engl J Med* 2006;355:260–9.
50. Sun LY, Chung AM, Farkouh ME, *et al.* Defining an intraoperative hypotension threshold in association with stroke in cardiac surgery. *Anesthesiology* 2018;129:440–7.