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Original Article

Comparison of Preventive Cardiovascular Pharmacotherapy in Surgical vs Percutaneous Coronary Revascularization

Arden R. Barry, BSc, BSc(Pharm), PharmD, ACPR,^{a,b} Erica H.Z. Wang, BSc(Pharm), PharmD, ACPR, BCPS,^{a,c} Doson Chua, BSc(Pharm), PharmD, BCPS, BCCP, FCSHP,^c and Glen J. Pearson, BSc, BScPhm, PharmD, FCSHP, FCCS^d

^a Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, Canada
 ^b Chilliwack General Hospital, Lower Mainland Pharmacy Services, Chilliwack, British Columbia, Canada
 ^c St Paul's Hospital, Lower Mainland Pharmacy Services, Vancouver, British Columbia, Canada
 ^d Division of Cardiology, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada

ABSTRACT

Background: Data suggest that patients who undergo coronary artery bypass grafting (CABG) have a lower rate of secondary preventive cardiovascular pharmacotherapy use compared with patients who undergo percutaneous coronary intervention (PCI). This study sought to assess the rate of use of preventive pharmacotherapy at discharge in patients who underwent CABG vs PCI post—acute coronary syndrome (ACS).

Methods: A prospective cohort study was conducted at St Paul's Hospital in Vancouver, Canada. Patients aged \geq 18 years who presented with an ACS and underwent CABG or PCI between January and November 2018 were included. Data on preventive pharmacotherapy use and reasons for justified nonuse (eg, intolerance, contraindication) were collected.

RÉSUMÉ

Contexte : Les données semblent indiquer que le taux de recours à une pharmacothérapie cardiovasculaire en prévention secondaire est plus faible chez les patients qui subissent un pontage aortocoronarien (PAC) que chez ceux qui subissent une intervention coronarienne percutanée (ICP). Les auteurs ont tenté d'évaluer le taux de recours à une pharmacothérapie préventive à la sortie de l'hôpital après un syndrome coronarien aigu (SCA) chez les patients ayant subi un PAC et chez ceux ayant subi une ICP.

Méthode : Une étude de cohorte prospective a été menée à l'hôpital St. Paul de Vancouver, au Canada. Ont été inclus les patients âgés de 18 ans ou plus ayant présenté un SCA traité par un PAC ou par une ICP entre janvier et novembre 2018. Des données sur le recours à

Cardiovascular disease is the leading cause of death in North America and is responsible for approximately 31% of all deaths worldwide.¹ Approximately half of these deaths are estimated to be due to coronary artery disease. Encouragingly, the adjusted rate of fatal coronary artery disease or hospitalization for acute myocardial infarction (MI) has been declining steadily over the past 3 decades.² This is at least in part due to advancements in coronary

E-mail: arden.barry@ubc.ca

revascularization strategies, such as percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery, and secondary preventive medications, including acetylsalicylic acid (ASA), angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), β -blockers, and 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (ie, statins), all of which have been shown to reduce the risk of cardiovascular events and mortality in patients with established coronary artery disease.³⁻⁶

Secondary cardiovascular preventive pharmacotherapy is recommended regardless of revascularization strategy, yet multiple studies have demonstrated the rate of medication use in patients post-CABG surgery is low, both at discharge and at 1 year of follow-up.^{7–11} Low use of indicated medications after CABG surgery has been associated with adverse outcomes. A post hoc analysis of the **Pr**oject of **E**x-vivo **V**ein Graft **En**gineering via **T**ransfection (PREVENT) IV study

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Ethics Statement: The University of British Columbia and Providence Health Care Research Ethics Boards approved this study via a harmonized review.

Corresponding author: Dr Arden R. Barry, Faculty of Pharmaceutical Sciences, 2405 Wesbrook Mall, Vancouver, British Columbia V6T 1Z3 Canada. Tel.: +1-604-897-2439; fax: +1-604-822-3035.

See page 303 for disclosure information.

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²⁵⁸⁹⁻⁷⁹⁰X/© 2019 Canadian Cardiovascular Society. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http:// creativecommons.org/licenses/by-nc-nd/4.0/).

Results: A total of 275 patients were included. Mean age was 65 years, and 83% were male. Overall, 141 patients (51%) underwent CABG and 134 patients (49%) underwent PCI. All patients received acetylsalicylic acid, but more patients who underwent CABG received 325 mg (vs 80-81 mg) compared to PCI (25% vs 1%, P < 0.01). Use of P2Y12 inhibitors was higher in patients who underwent PCI (primarily ticagrelor) compared with patients who underwent CABG (primarily clopidogrel) (99% vs 26%, P < 0.01). All patients who underwent CABG received a β -blocker vs 96% of patients who underwent PCI (P = 0.017). Use of angiotensin-modulating agents was higher in patients who underwent PCI (98% vs 65%, P < 0.01). Statin use was similar between groups (99% vs 99%, P = 0.96), but more patients who underwent PCI received maximum-dose therapy (89% vs 64%, P < 0.01). Conclusions: Use of acetylsalicylic acid, β -blockers, and statins in patients post-ACS was high regardless of revascularization strategy, whereas P2Y12 inhibitors and angiotensin-modulating agents were underused in patients who underwent CABG even after adjusting for justified nonuse.

demonstrated that patients post-CABG surgery taking $\leq 50\%$ of indicated medications at discharge, compared with those taking all indicated medications, had a higher rate of death or MI (8.0% vs 4.2%; adjusted hazard ratio, 1.69; 95% confidence interval [CI], 1.12-2.55) at 2 years.9 Further, many studies of medication use post-CABG surgery do not account for justified nonuse, such as patient intolerance or contraindication, which may have resulted in falsely low rates of use. The purpose of the present study was to prospectively evaluate use of secondary cardiovascular preventive pharmacotherapy in a contemporary cohort of patients who present with an acute coronary syndrome (ACS) and undergo coronary revascularization. Study objectives were to determine the rate of use at discharge of guideline-recommended secondary preventive medications (ASA, P2Y12 inhibitors, β-blockers, ACEI/ARBs, and statins), overall and after adjustment for justified nonuse, between patients who undergo revascularization with CABG surgery vs PCI.

Methods

Study design

This was a quantitative, prospective, longitudinal cohort study conducted at the Providence Health Care Heart Centre located at St Paul's Hospital, a quaternary cardiac referral centre in Vancouver, Canada. The University of British Columbia and Providence Health Care Research Ethics Boards approved this study via a harmonized review. une pharmacothérapie préventive et les raisons justifiant le nonrecours à une telle thérapie (p. ex. intolérance, contre-indication) ont été recueillies.

Résultats : Au total, 275 patients ont été retenus. Les sujets avaient en moyenne 65 ans, et 83 % d'entre eux étaient des hommes. Dans l'ensemble, 141 patients (51 %) ont subi un PAC et 134 (49 %), une ICP. Tous les patients ont recu de l'acide acétylsalicylique, mais les patients ayant subi un PAC ont été plus nombreux à recevoir une dose de 325 mg plutôt qu'une dose de 80-81 mg que chez les patients ayant subi une ICP (25 % vs 1 %, p < 0.01). L'emploi d'inhibiteurs du récepteur P2Y12 était plus fréquent chez les patients ayant subi une ICP (principalement le ticagrélor) que chez les patients ayant subi un PAC (principalement le clopidogrel) (99 % vs 26 %, p < 0.01). Tous les patients qui ont subi un PAC ont aussi reçu un bêtabloquant, comparativement à 96 % des patients qui ont subi une ICP (p < 0.017). L'emploi d'agents modulateurs de l'angiotensine était plus fréquent chez les patients ayant subi une ICP (98 % vs 65 %, p < 0,01). L'emploi de statines était comparable dans les deux groupes (99 % vs 99 %, p = 0.96), mais un plus grand nombre de patients ayant subi une ICP ont reçu un traitement à la dose maximale (89 % vs 64 %, *p* < 0,01).

Conclusions : Le recours à l'acide acétylsalicylique, aux bêtabloquants et aux statines chez les patients ayant subi un SCA était élevé quelle que soit la stratégie de revascularisation, tandis que les inhibiteurs du récepteur P2Y12 et les agents modulateurs de l'angiotensine étaient sous-utilisés chez les patients ayant subi un PAC, même lorsqu'on tenait compte des cas de non-utilisation justifiée.

Study population

Included were adult patients (aged \geq 18 years) who presented with an ACS, underwent CABG surgery or PCI during their index admission, and were discharged home. An ACS was defined as an ST-segment elevation MI (STEMI), non-STEMI, or unstable angina as per the accepted definitions.^{12,13} Patients who were diagnosed with a type 2 MI were excluded. Patients who were treated exclusively with medical management or died during their index hospitalization were excluded, as were patients who were transferred to another healthcare facility.

Data collection

Data on eligible patients were collected prospectively from the patient's inpatient medical record during their index hospitalization or retrospectively at the time of discharge. The following data were collected: age, sex, comorbid medical conditions, index event, revascularization strategy, type and details of revascularization procedure, vitals and laboratory values at discharge, secondary cardiovascular preventive pharmacotherapy (ASA, P2Y12 inhibitors, β-blockers, ACEI/ ARBs, statins), and other cardiovascular pharmacotherapy (oral anticoagulant therapy, non-statin lipid-lowering therapy, mineralocorticoid receptor antagonist therapy) at discharge, and documented reason(s) for nonuse of pharmacotherapy. Attempts were made to identify documentation of common reasons for nonuse of the aforementioned medications (eg, risk of bleeding, hypotension, bradycardia, renal dysfunction) through a proactive review of the patient's medical record. However, prescribers were not actively



Figure 1. Flow diagram of the index presentation of patients. ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; NSTEACS, non-ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

engaged to justify their reason(s) for nonuse. Data were collected from January to November 2018. Attempts were made to prospectively capture data for all eligible patients during the study period. Patient consent was not required because all data were collected in a de-identified manner. Data were captured using the Research Electronic Data Capture system, a secure web database application managed by the University of British Columbia.

Statistical analysis

Descriptive statistics were used to report demographic data and medication use. Univariate comparisons were made with a Student's t test for continuous variables and chi-squared test for categorical variables using demographic data. Values were presented as percentages for categorical values and means with standard deviations for continuous variables. A stepwise multivariate logistic regression analysis was performed to identify determinants for use of secondary cardiovascular preventive pharmacotherapy. The multivariate analysis included age, sex, and any variable with a P value < 0.10 in the univariate analyses. All statistical analyses were performed with IBM SPSS Statistics (version 21, IBM Corporation, Armonk, NY). A P value of < 0.05 was considered to be statistically significant.

Results

A total of 294 patients were reviewed. Nineteen patients did not undergo revascularization and were excluded. Thus, the final cohort included 275 patients. A flow diagram of the index presentation of patients is included in Figure 1. Patient characteristics and details of revascularization procedures are included in Table 1. Mean age was 65 years and 83% were male. Of the 169 patients who presented with a non–ST-segment elevation ACS, 137 (81%) presented with a non-STEMI and 32 (19%) presented with unstable angina. Overall, 141 patients (51%) underwent CABG surgery and 134 patients (49%) underwent PCI. A total of 212 patients (77%) had an echocardiogram before discharge, mean left ventricular ejection fraction (LVEF) was 51% \pm 11%, and 43 patients (20%) had an LVEF of \leq 40%.

Unadjusted medication use at discharge is included in Figure 2, and medication use after adjustment for justified nonuse is included in Figure 3. Reasons for medication nonuse are included in Table 2. After the adjustment, 100% of patients in both groups received ASA. Patients who underwent CABG surgery were more likely to be discharged on ASA 325 mg daily (as opposed to 80-81 mg daily) than those who underwent PCI (25% vs 1%, P < 0.01). Use of P2Y12 inhibitors was significantly higher in patients who underwent PCI as opposed to CABG surgery (99% vs 26%, P < 0.01). The most common P2Y12 inhibitor was clopidogrel (31/36, 86%) among patients undergoing CABG surgery and ticagrelor (98/133, 74%) among patients undergoing PCI. Use of β-blockers was significantly higher in patients who underwent CABG surgery compared with PCI (100% vs 96%, P = 0.017). Use of ACEI/ARBs was significantly higher in patients who underwent PCI compared with CABG surgery (98% vs 65%, P < 0.01). Use of statin therapy was similar between groups (99% vs 99%, P = 0.96). Significantly more patients who underwent PCI received maximum-dose statin therapy (defined as atorvastatin 80 mg daily or rosuvastatin 40 mg daily) compared with CABG surgery (89% vs 64%, P < 0.01); however, there was no significant difference in use of high-intensity dose statin therapy (defined as atorvastatin 40-80 mg daily or rosuvastatin 20-40 mg daily) between the groups (97% vs 96%, P = 0.80).

Stepwise multivariate regression analysis of patients undergoing CABG surgery demonstrated that smoking status was an independent predictor of use of a P2Y12 inhibitor (odds ratio [OR], 3.56; 95% CI, 1.10-11.48; P = 0.034). Predictors for use of an ACEI/ARB included higher systolic blood pressure (OR, 1.06; 95% CI, 1.00-1.11; P = 0.038) and low-density lipoprotein cholesterol (OR, 1.98; 95% CI, 1.12-3.52; P = 0.02), whereas higher LVEF was less predictive of use of an ACEI/ARB (OR, 0.94; 95% CI, 0.87-0.99; P = 0.018). There were no independent predictors identified for use of ASA, β -blockers, or statins. A regression analysis of PCI patients was not performed because of the high rates of medication use.

Twenty-eight patients (10%) were discharged on oral anticoagulant therapy, of whom 18 (64%) were also discharged on a P2Y12 inhibitor. The most common oral anticoagulant was warfarin (16/19, 84%) among patients undergoing CABG surgery and rivaroxaban (4/9, 44%) or warfarin (4/9, 44%) among patients undergoing PCI. More patients who underwent CABG surgery were discharged on

Table 1. Patient characteristics

$\begin{array}{c c c c c c c c c c c c c c c c c c c $		All patients ($N = 275$)	CABG surgery $(n = 141)$	PCI (n = 134)	P value
	Mean age (y)	64.7 ± 10.6	65.2 ± 10.2	64.3 ± 11.1	0.48
Comobile medical conditions Hyperension 188 (68.4) 114 (80.9) 74 (55.2) < 0.01 Displexes mellinus 91 (33.1) 50 (35.5) 41 (30.6) 0.39 Smoker 75 (27.3) 34 (24.1) 41 (30.6) 0.23 Obseriv 65 (23.6) 40 (28.4) 25 (18.7) 0.06 Heart failure 37 (13.5) 24 (17.0) 13 (9.7) 0.08 Chronic kidney disease 36 (13.1) 24 (17.0) 12 (9.0) 0.047 Obstructive sleep apnea 27 (9.8) 14 (9.9) 31 (9.7) 0.95 Cerebrowascular disease 21 (7.6) 12 (8.5) 9 (6.7) 0.95 Cerebrowascular disease 21 (7.6) 12 (8.5) 9 (6.7) 0.98 Distructive sleep apnea 20 (7.3) 15 (10.6) 5 (3.7) 0.03 DLC ≥ 5 mmolL 6 (2.2) 2 (1.4) 4 (3.0) 0.37 Peripheral arrey disease 44 (1.5) 4 (2.8) 0 (0.0) 0.0050 Prior MI 48 (17.5) 24 (17.0) 24 (17.9) 0.85 Prior PC1 40 (14.5) 18 (12.8) 22 (16.4) 0.39 Prior CABG surgery 10 (3.6) 2 (1.4) 8 (6.0) 0.04 On discharge Systolic BP (mm Hg) 118.1 ± 16.0 119.5 ± 15.1 11.67 ± 16.9 0.16 Diasotic BP (mm Hg) 67.0 ± 9.2 66.3 ± 8.6 67.7 ± 9.7 0.20 Meatr rate (bestarmin) 70.8 ± 11.4 73.4 ± 10.8 67.9 ± 11.4 < 0.01 Serum creatinine ((tmolL)) 96.8 ± 65.5 97.5 ± 58.5 96.1 ± 72.3 0.86 Serum sodium (mmolL) 4.2 ± 1.0 4.2 ± 0.4 4.2 ± 0.4 On guant - 18.02.0 No. of garls	Male sex	227 (82.5)	123 (87.2)	104 (77.6)	0.04
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Comorbid medical conditions				
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Hypertension	196 (71.3)	118 (83.7)	78 (58.2)	< 0.01
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Dyslipidemia	188 (68.4)	114 (80.9)	74 (55.2)	< 0.01
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Diabetes mellitus	91 (33.1)	50 (35.5)	41 (30.6)	0.39
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Smoker	75 (27.3)	34 (24.1)	41 (30.6)	0.23
Hear failure 37 (13.5) 24 (17.0) 13 (9.7) 0.08 Chronic kidney disease 36 (13.1) 24 (17.0) 12 (9.0) 0.047 Obstructive sleep apnea 27 (9.8) 14 (9.9) 13 (9.7) 0.95 Cerebrovascular disease 21 (7.6) 12 (8.5) 9 (6.7) 0.03 LDL-C ≥ 5 mmol/L 6 (2.2) 2 (1.4) 4 (3.0) 0.37 Peripheral attery disease 4 (1.5) 4 (2.8) 0 (0.0) 0.050 Prior MI 48 (17.5) 24 (17.0) 24 (17.9) 0.85 Prior CABG surgery 10 (3.6) 2 (1.4) 8 (6.0) 0.04 On discharge 57.0 ± 9.2 66.3 ± 8.6 67.7 ± 9.7 0.20 Systolic BP (nm Hg) 118.1 ± 16.0 119.5 ± 15.1 116.7 ± 16.9 0.16 Discharge 57.5 ± 58.5 96.1 ± 72.3 0.86 Extinated CFR (mL/min) 76.4 ± 12.2 76.3 ± 32.6 76.6 ± 19.8 0.88 Serum sodium (rmsol/L) 138.2 ± 2.7 137.7 ± 3.0 138.6 ± 2.4 0.01 Serum sodium (rmsol/L) 2.5 ± 1.1 2.3 ± 1.1 2.7 ± 1.0	Obesity	65 (23.6)	40 (28.4)	25 (18.7)	0.06
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Heart failure	37 (13.5)	24 (17.0)	13 (9.7)	0.08
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Chronic kidney disease	36 (13.1)	24 (17.0)	12 (9.0)	0.047
$\begin{array}{cccc} Cerebrovascular disease 21 (7.6) 12 (8.5) 9 (6.7) 0.58 \\ Atrial fibrillation 20 (7.3) 15 (10.6) 5 (3.7) 0.03 \\ IDL-C \ge 5 mmol/L 6 (2.2) 2 (1.4) 4 (3.0) 0.37 \\ Peripheral artery disease 4 (1.5) 42 (2.8) 0 (0.0) 0.050 \\ Prior MI 48 (17.5) 24 (17.0) 24 (17.9) 0.85 \\ Prior PCI 40 (14.5) 18 (12.8) 22 (16.4) 0.39 \\ Prior CABG surgery 10 (3.6) 2 (1.4) 8 (6.0) 0.04 \\ On discharge \\ \\ Sysolic BP (mm Hg) 67.0 \pm 9.2 66.3 \pm 8.6 67.7 \pm 9.7 0.20 \\ Heart rate (beats/min) 70.8 \pm 11.4 73.4 \pm 10.8 67.9 \pm 11.4 < 0.01 \\ Serum creatinine (µmol/L) 96.8 \pm 65.5 97.5 \pm 85.5 96.1 \pm 72.3 0.86 \\ Estimated GFR (nL/min) 76.4 \pm 12.2 76.3 \pm 22.6 76.6 \pm 19.8 0.88 \\ Serum sodium (nmol/L) 138.2 \pm 2.7 137.7 \pm 3.0 138.6 \pm 2.4 0.01 \\ Serum potasium (nmol/L) 2.5 \pm 1.1 2.3 \pm 1.1 2.7 \pm 1.0 0.04 \\ CABG surgery details \\ On-pump - 128 (90.8) \\ 0.16 \\ On-gunp - 13 (9.2) \\ 0.17 \\ 0.16 \\ Cab Surgery details \\ 0.16 \\ Charge - \\ 1 \\ 0.17 \\ 1 \\ 0 \\ CH \\ CH \\ Charge - \\ 0 \\ (1.4) \\ CH \\ C$	Obstructive sleep apnea	27 (9.8)	14 (9.9)	13 (9.7)	0.95
Arrial fbrillation 20 (7,3) 15 (10.6) 5 (3,7) 0.03 LDL-C ≥ 5 mmol/L 6 (2.2) 2 (1.4) 4 (3.0) 0.37 Peripheral artery disease 4 (1.5) 4 (2.8) 0 (0.0) 0.050 Prior MI 48 (17.5) 24 (17.0) 24 (17.9) 0.85 Prior CABG surgery 10 (3.6) 2 (1.4) 8 (6.0) 0.04 On discharge	Cerebrovascular disease	21 (7.6)	12 (8.5)	9 (6.7)	0.58
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Atrial fibrillation	20 (7.3)	15 (10.6)	5 (3.7)	0.03
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	LDL-C > 5 mmol/L	6 (2.2)	2 (1.4)	4 (3.0)	0.37
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Peripheral artery disease	4 (1.5)	4 (2.8)	0 (0.0)	0.050
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Prior MI	48 (17.5)	24 (17.0)	24 (17.9)	0.85
Prior CABG surgery 10 (3.6) 2 (1.4) 8 (6.0) 0.04 On discharge	Prior PCI	40 (14.5)	18 (12.8)	22 (16.4)	0.39
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Prior CABG surgery	10 (3.6)	2 (1.4)	8 (6.0)	0.04
	On discharge				
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Systolic BP (mm Hg)	118.1 ± 16.0	119.5 ± 15.1	116.7 ± 16.9	0.16
Heart rate (beats/min) 70.8 \pm 11.4 73.4 \pm 10.8 67.9 \pm 11.4 < 0.01 Serum creatinine (tmol/L) 96.8 \pm 65.5 97.5 \pm 58.5 96.1 \pm 72.3 0.86 Estimated GFR (mL/min) 76.4 \pm 21.2 76.3 \pm 22.6 76.6 \pm 19.8 0.88 Serum sodium (mmol/L) 138.2 \pm 2.7 137.7 \pm 3.0 138.6 \pm 2.4 0.01 Serum potassium (mmol/L) 4.2 \pm 0.4 4.2 \pm 0.4 4.2 \pm 0.4 0.05 Serum potassium (mmol/L) 2.5 \pm 1.1 2.3 \pm 1.1 2.7 \pm 1.0 0.04 CABG surgery details 0 0 -	Diastolic BP (mm Hg)	67.0 ± 9.2	66.3 ± 8.6	67.7 ± 9.7	0.20
Serum creatinine (µmol/L) 96.8 ± 65.5 97.5 ± 58.5 96.1 ± 72.3 0.86 Estimated GFR (mL/min) 76.4 ± 21.2 76.3 ± 22.6 76.6 ± 19.8 0.88 Serum sodium (mmol/L) 138.2 ± 2.7 137.7 ± 3.0 138.6 ± 2.4 0.01 Serum potassium (mmol/L) 4.2 ± 0.4 4.2 ± 0.4 4.2 ± 0.4 0.05 Serum LDL-C (mmol/L) 2.5 ± 1.1 2.3 ± 1.1 2.7 ± 1.0 0.04 CABG surgery details - - - - On-pump - 13 (9.2) - - - Postoperative atrial fibrillation - 49 (34.8) - - - No. of grafts - - 11 (7.8) - - - 3 - 55 (39.0) - - - - 6 - <td>Heart rate (beats/min)</td> <td>70.8 ± 11.4</td> <td>73.4 ± 10.8</td> <td>67.9 ± 11.4</td> <td>< 0.01</td>	Heart rate (beats/min)	70.8 ± 11.4	73.4 ± 10.8	67.9 ± 11.4	< 0.01
Estimated GFR (mL/min) 76.4 ± 21.2 76.3 ± 22.6 76.6 ± 19.8 0.88 Serum sodium (mmol/L) 138.2 ± 2.7 137.7 ± 3.0 138.6 ± 2.4 0.01 Serum potassium (mmol/L) 4.2 ± 0.4 4.2 ± 0.4 4.2 ± 0.4 0.25 ± 0.4 0.27 ± 0.4 0.01 Serum LDL-C (mmol/L) 2.5 ± 1.1 2.3 ± 1.1 2.7 ± 1.0 0.04 CABG surgery details 0.01 0.25 ± 1.1 2.3 ± 1.1 2.7 ± 1.0 0.04 CABG surgery details 0.98 $ -$ <	Serum creatinine (µmol/L)	96.8 ± 65.5	97.5 ± 58.5	96.1 ± 72.3	0.86
Serum sodium (mmol/L) 138.2 \pm 2.7 137.7 \pm 3.0 138.6 \pm 2.4 0.01 Serum potassium (mmol/L) 4.2 \pm 0.4 4.2 \pm 0.4 4.2 \pm 0.4 0.55 Serum LDL-C* (mmol/L) 2.5 \pm 1.1 2.3 \pm 1.1 2.7 \pm 1.0 0.04 CABG surgery details 0n-pump -	Estimated GFR (mL/min)	76.4 ± 21.2	76.3 ± 22.6	76.6 ± 19.8	0.88
Serum potassium (mmol/L) 4.2 ± 0.4 4.2 ± 0.4 4.2 ± 0.4 4.2 ± 0.4 0.55 Serum LDL-C* (mmol/L) 2.5 ± 1.1 2.3 ± 1.1 2.7 ± 1.0 0.04 CABG surgery details $0n$ -pump $ 128 (90.8)$ $ -$ Off-pump $ 13 (9.2)$ $ -$ Postoperative atrial fibrillation $ 49 (34.8)$ $ -$ No. of grafts $ 1 (0.7)$ $ -$ 1 $ 1 (0.7)$ $ -$ 2 $ 5 (39.0)$ $ -$ 3 $ 20 (14.2)$ $ -$ 6 $ 2 (1.4)$ $ -$ PCI details $ 25 (18.7)$ $ 0$ $ 25 (18.7)$ $ 2$ $ 2 (15)$ $-$	Serum sodium (mmol/L)	138.2 ± 2.7	137.7 ± 3.0	138.6 ± 2.4	0.01
Serun LDL-C* (mmol/L) 2.5 ± 1.1 2.3 ± 1.1 2.7 ± 1.0 0.04 CABG surgery details On-pump - 128 (90.8) -<	Serum potassium (mmol/L)	4.2 ± 0.4	4.2 ± 0.4	4.2 ± 0.4	0.55
CABG surgery details - 10 <td< td=""><td>Serum LDL-C* (mmol/L)</td><td>2.5 ± 1.1</td><td>2.3 ± 1.1</td><td>2.7 ± 1.0</td><td>0.04</td></td<>	Serum LDL-C* (mmol/L)	2.5 ± 1.1	2.3 ± 1.1	2.7 ± 1.0	0.04
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	CABG surgery details				
Off-pump - 13 (9.2) -	On-pump	_	128 (90.8)	_	_
Description - 40 (34.8) - -	Off-pump	_	13 (9.2)	_	_
No. of grafts - 1 (0.7) - - - 1 - 11 (7.8) - <t< td=""><td>Postoperative atrial fibrillation</td><td>_</td><td>49 (34.8)</td><td>_</td><td>_</td></t<>	Postoperative atrial fibrillation	_	49 (34.8)	_	_
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	No. of grafts		-5 (8 -10)		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1	_	1 (0 7)	_	_
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2	_	11 (7.8)	_	_
4 $ 52 (36.9)$ $ 5$ $ 20 (14.2)$ $ 6$ $ 2 (1.4)$ $ -$ PCI details $ 2 (1.4)$ $ 0$ $ 4 (3.0)$ $ 1$ $ 94 (70.1)$ $ 2$ $ 25 (18.7)$ $ 3$ $ 9 (6.7)$ $ 4$ $ 2 (15)$ $-$	3	_	55 (39.0)	_	_
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4	_	52 (36.9)	_	_
6 $ 2$ (1.4) $ -$ PCI details 0 $ 2$ (1.4) $ 0$ $ 4$ (3.0) $ 1$ $ 94$ (70.1) $ 2$ $ 25$ (18.7) $ 3$ $ 9$ (6.7) $ 4$ $ 2$ (15) $-$	5	_	20(14.2)	_	_
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	2	_	_	9 (67)	_
	4	_	_	2(15)	_

ASA, acetylsalicylic acid; BP, blood pressure; CABG, coronary artery bypass grafting; GFR, glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCI, percutaneous coronary intervention.

* Based on 162 values (113 were missing).

[†]No patient received a bare metal stent.

oral anticoagulant therapy than PCI, but the difference was not statistically significant (14% vs 7%, P = 0.064). Use of non-statin lipid-lowering therapy was not significantly different between groups (3% for CABG surgery group vs 3% for PCI group, P = 0.94), as was the use of mineralocorticoid receptor antagonist therapy (10% vs 9%, P = 0.78).

Discussion

This prospective study of patients who underwent coronary revascularization demonstrated variability in the use of guideline-recommended secondary preventive medications in those who underwent CABG surgery vs PCI. Because this included a nonrandomized cohort, there were significant differences in the baseline patient characteristics between the groups; specifically, more patients in the post-CABG surgery group were male with a higher incidence of hypertension, dyslipidemia, and chronic kidney disease (CKD). These cardiovascular disease risk factors may have biased the post-CABG surgery group in favour of a higher use of secondary preventive pharmacotherapy; however, this was not observed.

Use of antiplatelet therapy was high in both groups with the exception of P2Y12 inhibitors in patients who underwent CABG surgery. Although these patients did not receive coronary stenting, all presented with an ACS and thus had a guideline-recommended indication for dual antiplatelet therapy. Contemporary Canadian Cardiovascular Society guidelines recommend dual antiplatelet therapy for 12 months in patients post-ACS after CABG surgery.¹⁴ A survey of Canadian cardiac surgeons published in 2015 revealed that 47%



Figure 2. Unadjusted secondary preventive cardiovascular medication use at discharge. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

stated they would reinitiate dual antiplatelet therapy postoperatively in patients with ACS who had undergone routine/ uncomplicated CABG surgery, which is higher than the 26% identified in the present study, although only 9% of survey respondents were from British Columbia.¹⁵ A recent review also highlighted evidence demonstrating the underuse of dual antiplatelet therapy in patients post-CABG surgery who pre-sent with an ACS.¹⁶ There were no documented reasons for not using a P2Y12 inhibitor in patients post-CABG surgery (eg, due to postoperative bleeding risk). Further, the low use of P2Y12 inhibitor therapy was not explained by concurrent oral anticoagulant therapy because only 14% of patients post-CABG surgery were prescribed an oral anticoagulant at discharge. However, despite guideline recommendations, there are currently no prospective randomized controlled trials showing a statistically significant benefit with ASA and a P2Y12 inhibitor vs ASA alone in patients with ACS post-CABG surgery.¹⁷ A post hoc analysis of the Future Revascularization Evaluation in Patients With Diabetes Mellitus: **O**ptimal Management of **M**ultivessel Disease (FREEDOM) trial showed that dual antiplatelet therapy was not superior to ASA alone at reducing death and cardiovascular events in patients with diabetes and an ACS who underwent CABG surgery; however, this was a small, nonrandomized population.¹⁸ To the contrary, in the CABG surgery subgroup of the Platelet Inhibition and Patient Outcomes (PLATO) trial, dual antiplatelet therapy with ASA and ticagrelor vs ASA and clopidogrel did not show a statistically significant difference in the primary composite end point of cardiovascular death, MI, and stroke, but did show a reduction in total and cardiovascular mortality.¹⁹ The only independent predictor of P2Y12 inhibitor use in patients post-CABG surgery was smoking. Thus, these patients may have been perceived to be at higher risk of future cardiovascular events and therefore warranted more aggressive therapy.

Use of β -blockers was significantly higher in patients who underwent CABG surgery, but overall use was high in both groups. β -Blockers are also indicated for the prevention of postoperative atrial fibrillation after CABG surgery, which may have explained the higher use.⁶ Further, lower use of β-blockers among patients who undergo PCI may have been due to the lack of contemporary randomized controlled trial data and recent observational studies that have not demonstrated a benefit with long-term β -blocker therapy post-MI.²⁰ As well, patients with inferior STEMI may be more prone to sinus bradycardia, which also may have contributed to the low rate of β-blocker use in patients undergoing PCI. Although this is also true of patients who presented with an inferior STEMI and underwent CABG surgery, the bradycardia may have resolved by the time of discharge. Additionally, a greater proportion of patients with STEMI underwent PCI vs CABG surgery. Recent American College of Cardiology Foundation/ American Heart Association guidelines recommend that β -blockers be held for patients with inferior STEMI until the bradycardia resolves.⁴

Overall, the use of ACEI/ARBs in patients post-CABG surgery was low at 48%, which increased to only 65% after adjustment for patients with a documented intolerance or contraindication. This is despite most patients having an additional indication for therapy, such as diabetes mellitus, heart failure/reduced LVEF, CKD, or hypertension. This was supported by the logistic regression analysis, which showed that patients with a higher systolic blood pressure or lower LVEF were more likely to be discharged on an ACEI/ARB. The low use of ACEI/ARBs may have been influenced by the results of the Ischemia Management With Accupril Post-Bypass Graft via Inhibition of the Converting Enzyme (IMAGINE) trial, which demonstrated that early ACEI therapy after CABG surgery did not reduce cardiovascular events.²¹ However, this trial was conducted in a highly selected group of patients. All patients had an LVEF of \geq 40%, whereas only 47% had hypertension, 39% had an MI, and 10% had diabetes mellitus. Low use of ACEI/ARBs may have also been affected by the preferential use of β-blockers to prevent postoperative atrial fibrillation.⁶



Figure 3. Secondary preventive cardiovascular medication use after adjustment for justified nonuse. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

Despite the low ACEI/ARB use at discharge, patients undergoing CABG surgery may have been initiated/reinitiated on ACEI/ARB therapy by their primary care provider or cardiologist postdischarge, based on recent ACS guideline recommendations.^{3,4,6} A previous study by Barry and colleagues¹¹ noted that the use of ACEI/ARBs increased from 43% at discharge to 65% at 1 year postsurgery in a cohort of patients who underwent CABG surgery.

Table 2.	Reasons	for nonuse	of secondary	preventive	cardiovascular
medicati	ons				

	n (%)
ASA (N = 4)	
Concurrent oral anticoagulant	3 (75)
therapy	
Recent gastrointestinal bleed	1 (25)
No identifiable reason	0 (0)
P2Y12 inhibitors (N $=$ 106)	
No identifiable reason	106 (100)
β -Blocker (N = 16)	
Asthma	3 (19)
Bradycardia	2 (13)
Hypotension	2 (13)
Cocaine use	2 (13)
Concurrent non-dihydropyridine	2 (13)
calcium channel blocker	
No identifiable reason	5 (31)
ACEI/ARBs (N = 89)	
Acute kidney injury	24 (27)
Hypotension	24 (27)
Hyperkalemia	1 (1)
Renal artery stenosis	1 (1)
No identifiable reason	39 (44)
Statins $(N = 8)$	
Intolerance	4 (50)
No identifiable reason	4 (50)

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid. Most patients in both groups received statin therapy. However, patients post-PCI generally received more aggressive therapy in the form of the maximum recommended dose of atorvastatin or rosuvastatin. Patients in the PCI group had a slightly higher serum low-density lipoprotein cholesterol level at discharge (2.7 vs 2.3 mmol/L, P = 0.04), which may have prompted the use of higher-intensity statin therapy in those patients with the goal of achieving a low-density lipoprotein cholesterol level of < 2.0 mmol/L in accordance with recent Canadian Cardiovascular Society dyslipidemia guidelines.²²

A retrospective study using registry data in the United States from 1998 to 1999 investigated the use of secondary cardiovascular preventive pharmacotherapy at discharge in more than 37,000 patients aged ≥ 65 years after an acute MI.⁷ Patients who underwent CABG surgery, as opposed to those who did not, had a higher rate of ASA use (88% vs 83%). However, patients who underwent CABG surgery had lower use of β -blockers (62% vs 72%), ACEIs (56% vs 72%), and lipid-lowering therapy (35% vs 56%), which remained significant after adjustment for clinical variables. The rates of use of secondary preventive medications were lower than the present study except for the use of ACEIs, which was similar between studies. This likely represents a shift toward improved medication use in contemporary practice, which could be attributed to variety of factors, including multidisciplinary teams, improved clinician education, and standardized order sets.

A more contemporary study evaluated the use of secondary preventive therapy at discharge in 1031 patients who underwent CABG surgery using a retrospective database analysis in Alberta, Canada.¹¹ Approximately half of the patients had an ACS as their index presentation. Use of ASA (96%), β -blockers (94%), and statins (95%) was relatively high in this study, whereas use of ACEI/ARBs was low at 42%. However, this study did not account for justified nonuse. Notwithstanding, 92% of patients had a guideline-recommended indication for an ACEI/ARB, specifically hypertension, diabetes mellitus, CKD, or an LVEF of < 40%. In the present study, use of ACEI/ARBs was comparable at 48%, but increased to only 65% when adjusted for appropriate nonuse.

The present study was strengthened by the prospective collection of data on justified nonuse of secondary preventive therapy. In addition, because all data were collected from patients' medical records, consent was not required, thereby removing the risk of responder bias. However, this study has limitations that warrant discussion. This was a single-centre study that may not be representative of other practice settings and only included patients who presented with an ACS and were discharged home. The high turnover of individuals undergoing PCI prevented the collection of data for all patients. The Providence Health Care Heart Centre is the cardiac referral centre for British Columbia. Therefore, many patients are repatriated back to their referring healthcare centre or discharged before being seen by the multidisciplinary team. As well, many patients undergo elective PCI, who were excluded from this study. However, the PCI group in this study is a reasonable representative sample that is comparable to the number of patients who underwent CABG surgery over the same time period. Finally, this study relied on the accuracy and completeness of the medical record and did not undergo external validation. For example, the reason for not using a given therapy would have been captured only if the reason was explicitly documented.

Conclusions

This prospective cohort study demonstrated that use of guideline-recommended secondary cardiovascular preventive pharmacotherapy among patients with ACS was generally high regardless of revascularization strategy. However, opportunities exist to optimize use of P2Y12 inhibitors and ACEI/ARBs among patients with ACS who undergo CABG surgery.

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Disclosures

The authors have no potential conflicts of interest.

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