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Original Article

Predictive Value of Viable Myocardium of Papillary Muscle-Ventricular Wall Complex for Improvement in Moderate Ischemic Mitral Regurgitation

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ABSTRACT

Background: Performing a mitral valve procedure during coronary artery bypass grafting (CABG) in patients with coronary artery disease complicated by moderate ischemic mitral regurgitation (IMR) remains controversial. This study aimed to assess the benefit of isolated CABG and to develop a new index of viable myocardium within the papillary muscle-ventricular wall complex (VM-PM-VWC) to predict the improvement of IMR by CABG alone.

Methods: In total, 122 patients (age, 62.34 ± 8.53 years; 78.70% male) with moderate IMR who underwent CABG alone at Beijing Anzhen Hospital were retrospectively analyzed. All patients underwent ^{99m}Tc-sestamibi single-photon emission computed tomography (SPECT) and ^{18}-fluorine fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) to evaluate the VM-PM-VWC. Based on the postoperative echocardiography results at 1-year follow-up, patients were divided into IMR-unimproved (moderate or severe IMR, n = 38) and IMR-improved (no or mild IMR, n = 84) groups. Factors associated with improvement were analyzed by multivariate logistic regression.

Results: The VM-PM-VWC was an independent factor for moderate IMR improvement (odds ratio, 1.16; 95% confidence interval [CI], 1.09-1.24; $P < 0.001$). The cutoff value for moderate IMR improvement was 12.50%, with a sensitivity and specificity of 76.32% and 80.95%, respectively (area under the curve [AUC] 0.830; 95% CI, 0.741-0.919; $P < 0.001$). During a median follow-up of 3.71 (interquartile range: 2.17-5.10) years, major

RÉSUMÉ

Contexte : Une intervention à la valve mitrale pendant la réalisation d'un pontage aortocoronarien (PAC) chez les patients atteints d'une coronaropathie compliquée d'une insuffisance mitrale ischémique (IMI) demeure controversée. Cette étude visait à évaluer le bienfait d'un PAC isolé et à créer un nouvel indice de viabilité myocardique dans le complexe muscle papillaire-paroi ventriculaire pour prédire l'atténuation de l'IMI par le PAC seul.

Méthodologie : Au total, 122 patients (âgés de 62,34 ± 8,53 ans; 78,70 % d'hommes) qui étaient atteints d'une IMI modérée et qui ont subi un PAC seul à l'hôpital Beijing Anzhen ont fait l'objet d'une analyse rétrospective. Tous les patients ont été soumis à une tomographie d'émission monophotonique au ^{99m}Tc-sestamibi et à une tomographie par émission de positrons (TEP) au fluorodésoxyglucose ^{18}F afin d'évaluer la viabilité myocardique dans le complexe muscle papillaire-paroi ventriculaire. D'après les résultats d'échocardiographies postopératoires après un an de suivi, les patients ont été divisés en deux groupes : sans réduction de l'IMI (IMI modérée ou sévère, n = 38) et avec réduction de l'IMI (IMI absente ou légère, n = 84). Les facteurs associés à l'amélioration ont été analysés au moyen d'une régression logistique multivariée.

Résultats : La viabilité myocardique dans le complexe muscle papillaire-paroi ventriculaire était un facteur indépendant pour la réduction de l'IMI modérée (rapport des cotes, 1,16; intervalle de

The necessity of performing a mitral valve procedure during coronary artery bypass grafting (CABG) in patients with coronary heart disease (CAD) complicated with moderate ischemic mitral regurgitation (IMR) remains a topic of ongoing debate.[1] CABG combined with mitral valve annuloplasty has been reported to enhance functional capacity significantly in patients with moderate IMR compared with CABG alone.[2] Nevertheless, other studies have reported that adding a mitral valve procedure does not improve the clinical outcome or may even increase the risk of heart failure and neurologic complications.[3,4] Therefore, there is a pressing need for clear, evidence-based strategies to guide the surgical management of moderate IMR in patients undergoing CABG.

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cardiovascular and cerebrovascular event-free survival was higher in the improved group than in the unimproved group ($P < 0.001$).
Conclusions: Most patients with moderate IMR improved from isolated CABG. The VM-PM-VWC was an independent predictor of IMR improvement, which could help surgical decision making.
Clinical Trial Registration: ChiCTR2100042454.

confiance [IC] à 95 % : 1,09-1,24; $p < 0,001$). La valeur seuil de l'atténuation de l'IMI modérée était de 12,50 %, avec une sensibilité et une spécificité de 76,32 % et de 80,95 % respectivement (surface sous la courbe [SSC] 0,830; IC à 95 % : 0,741-0,919; $p < 0,001$). Pendant un suivi médian de 3,71 ans (écart interquartile : 2,17-5,10), la survie sans événements cardiovasculaires et cérébrovasculaires majeurs était plus élevée dans le groupe avec atténuation que dans le groupe sans atténuation ($p < 0,001$).
Conclusions : La plupart des patients atteints d'une IMI modérée ont vu leur état s'améliorer après un PAC seul. La viabilité myocardique dans le complexe muscle papillaire-paroi ventriculaire était un facteur prédictif indépendant de l'atténuation de l'IMI, ce qui pourrait faciliter la prise de décisions chirurgicales.
Numéro d'enregistrement de l'essai clinique : ChiCTR2100042454.

The mitral valve apparatus is composed of fibrous components (annulus, leaflets, and chordae tendineae) and muscular components (papillary muscle [PM] and the ventricular wall connected to the PM). IMR is primarily a consequence of left ventricle (LV) remodelling.[5] The muscular components of the mitral valve may play a critical role in the pathogenesis of IMR. Pioneer studies have demonstrated that viable myocardium (VM) in patients with CAD is an important factor affecting LV remodelling and serves as a predictor of postoperative outcome in patients with moderate IMR undergoing isolated CABG. In addition, the presence of more than 5 segments of VM has been associated with an improvement in regurgitation.[6,7] However, questions remain regarding the proportion of VM and which specific segment of the LV are most crucial for the improvement of moderate IMR.

We proposed that the VM within the PM-ventricular wall complex (VM-PM-VWC) plays a critical role in improving IMR. Therefore, the purpose of this study was to evaluate the predictive value of VM-PM-VMC for the improvement of IMR in patients with CAD and moderate IMR undergoing isolated CABG, as well as its potential value in guiding surgical strategies for this patient population.

Materials and Methods

Ethical Approval

This single-centre, retrospective, observational cohort study was conducted in accordance with the Declaration of Helsinki and approved and monitored by the institutional review board of Beijing Anzhen Hospital, Capital Medical University, Beijing, China (Number 2021162X). This study was registered in the Chinese Clinical Trial Registry (ChiCTR2100042454).

Study population

Patients with moderate IMR measured via echocardiography and who underwent examination with ^{99m}Tc-sestamibi single-photon emission computed tomography (SPECT) and ^{18}-fluorine fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) were eligible for enrollment if they had been referred for CABG at Beijing Anzhen Hospital between March 2016 and September 2023. The exclusion criteria were as follows: structural abnormalities of the mitral valve, coexistence of other heart valve diseases, preoperative emergency surgery for cardiogenic shock, and recent myocardial infarction (< 1 week).

Study protocol

Preoperative clinical characteristics and echocardiography, ^{99m}Tc-sestamibi SPECT, and ^{18}F-FDG PET data were retrospectively collected from patients with moderate IMR. Patients were regularly followed up through telephone, WeChat, or outpatient visits and were categorized into 2 groups: the IMR-unimproved group (moderate or severe IMR) or IMR-improved group (no or mild IMR), based on the changes assessed via echocardiography 1 year postoperatively. Preoperative and follow-up data were compared between the 2 groups, and the predictors of IMR improvement after isolated CABG were explored. This work has been reported in line with the Strengthening the Reporting of Cohort, Cross-sectional, and Case-control studies in Surgery (STROCSS) criteria.[8]

Surgical procedure

All patients underwent conventional sternal median incision. The left internal mammary artery and saphenous veins were harvested and grafted onto the coronary arteries. Typically, transplantation involves grafting the left internal mammary artery to the left anterior descending branch, whereas saphenous veins are anastomosed with other coronary arteries.[9] Graft-to-coronary artery anastomoses were performed using 7-0 Prolene sutures (Ethicon Inc, Cornelia, GA), whereas other anastomoses were performed using 6-0 Prolene sutures. Off-pump or on-pump CABG was performed according to the patient's condition and surgeon's experience. The quality of the coronary artery graft anastomosis was evaluated using a transit-time flow meter. All patients underwent complete revascularization.

Echocardiography

Echocardiography was performed using a commercially available E9 ultrasound system (GE Healthcare, Piscataway, NJ). No regurgitation, mild MR (MR area of < 4 cm^2, effective regurgitation orifice area [EROA] of < 0.2 cm^2), moderate MR (MR area of 4-8 cm^2, EROA of 0.2-0.39 cm^2), and severe MR (MR area of > 8 cm^2, EROA of ≥ 0.4 cm^2) was quantified according to the guidelines of the European Cardiovascular Association.[10] Left ventricular end-diastolic volume (LVEDV), left ventricular end end-systolic volume (LVESV), and left ventricular ejection fraction (LVEF) were measured using the biplane Simpson method at rest within 1 week preoperatively and 1 year postoperatively. The LVESV index (LVESVI) was calculated using the formula LVESV/body surface area.

^{99m}Tc-sestamibi SPECT and ^{18}F-FDG PET examinations

A procedure identical to that previously outlined was employed for ^{99m}Tc-sestamibi SPECT myocardial perfusion imaging at rest.[11] Briefly, 740 to 925 MBq ^{99m}Tc-sestamib (China Atomic Hi-Tech Co, Ltd, Beijing, China) was injected intravenously, and imaging was performed 1.5 hours later. The electrocardiogram R-wave triggering gate circuit was collected synchronously for 15 minutes at an acquisition angle of 180°. The cardiac cycle was divided into 8 equal intervals. Cardiac-gated transaxial images were reconstructed using the flash 3-dimensional mode.

Myocardial metabolism was examined using a high spatial resolution full-ring PET scanner (Biograph mCT, Siemens Healthcare, Erlangen, Germany). After at least 12 hours of fasting, the blood glucose level was controlled through oral glucose loading and, if needed, supplemental intravenous insulin doses as recommended in the ASNC guidelines.[12] Subsequently, 296 to 370 MBq of ^{18}F-FDG (China Atomic Hi-Tech Co, Ltd) was injected, and data were acquired within 1 hour. The probe was rotated 360° for myocardial metabolic tomography imaging acquisition, and short-axis reconstruction of the original image was performed using True X and TOF Ultral HD iterative methods (Siemens Healthineers, Malvern, PA).[13]

After data acquisition, ^{99m}Tc-sestamibi SPECT and ^{18}F-FDG PET images were transferred to a Siemens e.Soft workstation and analyzed using the QGS/QPS software (version 3.1, Cedars Sinai Medical Center, Los Angeles, CA). In patients with large myocardial perfusion defects and insufficient endocardial and epicardial delineations, images were manually corrected. Both reorientation and data analysis were performed by an experienced nuclear medicine physician who was blinded to the patient data.

LV segmentation

The LV was divided into 17 segments according to the model proposed by the American Heart Association.[14] Myocardial perfusion and metabolism of each segment were double-blinded and analyzed by 2 experienced nuclear medicine physicians. As shown in Figure 1, according to the anatomic characteristics and functional myocardium of the mitral valve, PM-VWC was combined with 12 segments of the LV, including the basal anterior, mid-anterior, apical anterior, basal inferior, mid-inferior, apical inferior, basal inferolateral, mid-inferolateral, apical lateral, basal anterolateral, mid-anterolateral, and apex. Similar to our previous studies,[11,13,15] one segment accounts for 6% of the LV, and according to a mismatch score (perfusion score minus FDG score) less or more than 1.0, in a perfusion defect, infarcted myocardium (< 1.0) or VM (≥ 1.0) was identified. Total perfusion deficit was defined as a product of defect extent and defect severity.

Follow-up

Patients were followed up at 1, 3, 6, and 12 months postoperatively and every year thereafter. Echocardiographic data and incidence of major cardiovascular and cerebrovascular events (MACCEs) were collected during each review period. The MACCEs included all-cause mortality, acute myocardial infarction, heart failure, repeat revascularization, and cerebrovascular events. The primary endpoint was the improvement in IMR, and the secondary endpoint was the incidence of MACCEs.

Statistical analysis

The continuous data are presented as the median and interquartile range or the mean ± standard deviation. Categorical variables are presented as numbers and percentages. Intergroup comparisons of normally distributed numerical variables were performed using independent sample Student's *t*-tests. The Mann-Whitney U test was used for intergroup comparisons of non-normally distributed numerical variables. Categorical variables were compared using the χ^2 test. The cutoff value for VM-PM-VWC was determined by the area under the receiver operating characteristic (ROC) curve. The c-statistics of the VM-PM-VWC model vs the VM of LV model were compared using the Delong test to examine whether VM-PM-VWC could improve discrimination power for improved IMR. Multivariate logistic regression models were used to determine risk factors for lack of IMR improvement. Variables with a $P < 0.1$ in the univariate analysis and variables reported in previous studies, as well as those considered clinically closely related to the endpoint, were entered into the multivariate analysis. The Kaplan-Meier method was used to calculate the MACCEs-free survival curves of the 2 groups. The log-rank test was used to identify differences in survival curves between the 2 groups. All reported probability values were 2-tailed, and $P < 0.05$ was considered statistically significant. SPSS (version 26.0, IBM, Armonk, NY) and R 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) were used for statistical analyses and illustrations.

Results

A total of 1750 patients with CAD who underwent ^{99m}Tc-sestamibi SPECT and ^{18}F-FDG PET examinations for myocardial viability assessment using a 2-day protocol between March 2016 and September 2023 were included. Of these, 824 patients underwent cardiac surgery, and 258 had moderate IMR. Of the 258 patients, 76 underwent mitral valve plasty, 17 underwent mitral valve replacement, 8 underwent aortic valve replacement, 12 underwent other surgical procedures, and 145 patients with moderate IMR underwent isolated CABG. In addition, 15 without 1-year follow-up echocardiography results, 6 died of heart failure postoperatively, and 2 were lost to follow-up. Accordingly, a total of 122 patients with moderate IMR who underwent isolated CABG were enrolled in the current study (Fig. 2). The mean age of all patients was 62.34 ± 8.53 years, and 96 patients (78.7%) were male.

As presented in Table 1, 84 patients (68.9%) showed improvement in IMR, whereas 38 patients (31.1%) showed

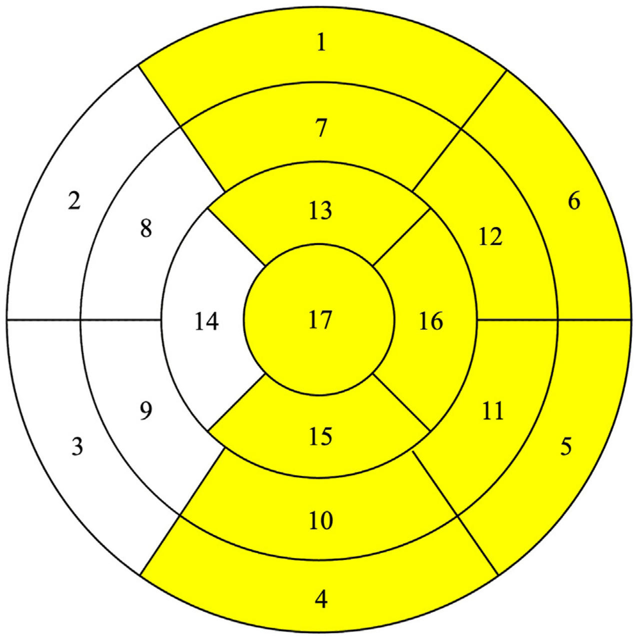

Figure 1. AHA 17-segments model. The **yellow segments** are the 12 segments that make up the PM-VWC. AHA, American Heart Association; PM-VWC, papillary muscle-ventricular wall complex.

no improvement at the 1-year follow-up after isolated CABG. Of the 38 patients with unimproved IMR, 37 had moderate IMR, and 1 had severe IMR. There were no significant differences in hypertension, diabetes mellitus, hyperlipidemia, renal insufficiency, cerebrovascular disease, previous myocardial infarction, history of percutaneous coronary intervention, body mass index, or body surface area between the IMR-unimproved and IMR-improved groups ($P > 0.05$). However, patients in the IMR-improved group were more likely to have hypertension than those in the IMR-unimproved group (58.3% vs 39.5%, $P = 0.053$).

There was no significant difference in the total perfusion deficit ($P = 0.152$) between patients with the IMR-improved and IMR-unimproved group. Nevertheless, regarding myocardial viability information, in comparison with the IMR-unimproved group, patients in the IMR-improved group had more VM-PM-VWC (22.31 ± 10.07% vs 10.47 ± 9.30%, $P < 0.001$), more VM of LV (28.06 ± 12.85% vs 15.55 ± 12.26%, $P < 0.001$), and less infarcted myocardium of LV (11.82 ± 12.29% vs 20.21 ± 13.06%, $P < 0.001$). All patients were safely discharged, and there was no significant statistic difference in mechanical ventilation time, intensive care unit stay, or hospital stay between the 2 groups ($P > 0.05$).

Echocardiographic data are summarized in Table 2. There was no significant statistical difference in the preoperative echocardiographic parameters between the 2 groups, including LVEDV, LVESV, LVESVI, and LVEF ($P > 0.05$). In comparison with that in the IMR-unimproved group, echocardiography in the IMR-improved group showed a significant improvement in LVEDV (137.05 ± 38.48 mL vs 153.77 ± 43.84 mL, $P = 0.035$), LVESV (69.00 ± 28.45 mL vs 85.24 ± 36.75 mL, $P = 0.009$), and LVESVI (37.48 ± 15.56 vs 46.79 ± 20.44, $P = 0.007$) at 1 year after isolated CABG. Besides, MR area and EROA were significantly reduced in the IMR-improved group ($P < 0.001$). Interestingly, echocardiographic variables including LVESV, LVESVI, and LVEF were significantly improved after CABG in both the IMR-improved and IMR-unimproved groups (Fig. 3), whereas a more significant improvement was observed in the IMR-improved group.

Univariate analysis showed that preoperative variables including hypertension (odds ratio [OR], 2.15; 95% confidence interval [CI], 0.98-4.69; $P = 0.055$), VM-PM-VWC (OR, 1.16; 95% CI, 1.09-1.24; $P < 0.001$), VM of LV (OR, 1.09; 95% CI, 1.05-1.14, $P < 0.001$), and infarcted myocardium of LV (OR, 0.95; 95% CI, 0.92-0.98; $P < 0.001$) were influencing factors for predicting IMR improvement after isolated CABG. Multivariate analysis showed that VM-PM-VWC was an independent influencing factor for predicting improvement in moderate IMR after isolated CABG, after adjustment for age and sex (Table 3).

ROC curve analysis was conducted to assess the ability of VM-PM-VWC to identify patients with an improvement in IMR after isolated CABG. The optimal cutoff value for VM-PM-VWC was 12.50%, with a sensitivity and specificity of 76.32% and 80.95%, respectively (area under the curve [AUC]: 0.830; 95% CI, 0.741-0.919; $P < 0.001$). Moreover, the VM-PM-VWC model, rather than the VM of LV model, could significantly increase the ability to predict the incidence of moderate IMR improvement in patients undergoing isolate CABG (AUC: 0.830; CI, 0.741-0.919 vs AUC: 0.785; CI, 0.690-0.879; $P = 0.037$) (Fig. 4). Patients were further divided into the low- and high-VM groups according to the cutoff point (details shown in Supplemental Table S1). Patients in the high-VM group (n = 45) had higher LVEF (48.04 ± 9.87% vs

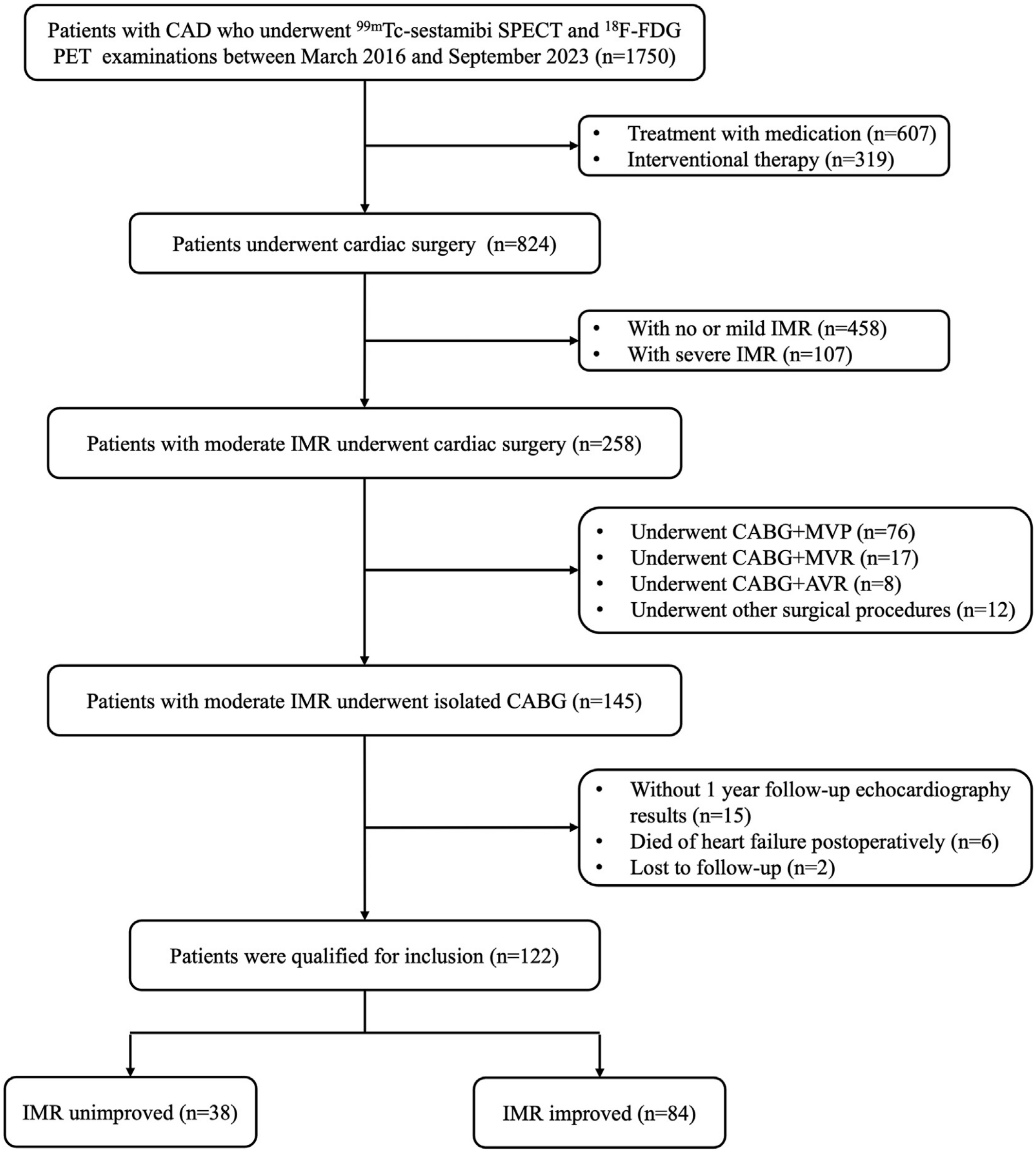

Figure 2. Flowchart of patient screening. AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CAD, coronary artery disease; IMR, ischemic mitral regurgitation; MVP, mitral valve plasty; MVR, mitral valve replacement.

44.18 ± 10.05%, $P = 0.041$) and a greater proportion of IMR improvement (88.3% vs 35.6%, $P < 0.001$) at 1 year after isolated CABG compared with that in the low-VM group.

During a median follow-up of 3.71 (interquartile range: 2.17-5.10) years, 7 patients developed MACCEs. Of them, 1 patient event in the improved group had a cerebrovascular event. In the unimproved group, 2 patients died, 2 had heart failure requiring rehospitalization, and 2 had cerebrovascular events. Kaplan-Meier survival analysis revealed that the MACCEs-free survival in the unimproved group was significantly lower than that in the improved group ($P < 0.001$), whereas the MACCEs-free survival in the low-VM group ($P < 0.05$) was significantly lower than that in the high-VM group (Fig. 5).

Discussion

The major findings in our current study are as follows: first, 68.9% of patients experienced improvement in moderate IMR following isolated CABG. Second, VM-PM-VWC could predict moderate IMR improvement postisolated CABG, with more than 12.5% VM-PM-VWC indicative of such improvement according to the ROC analysis. Third, at 1-year follow-up, patients with IMR improvement were significantly associated with better outcomes than those without improvement. The gradual advancement in surgical techniques has significantly improved the postoperative survival of patients with IMR.

A key issue is accurately tailoring personalized valve management strategies based on specific clinical data and imaging findings for each patient. These strategies aim to maximize the

Table 1. Perioperative clinical variables of patients

Variables	Whole cohort (n = 122)	IMR unimproved (n = 38)	IMR improved (n = 84)	P value
Preoperative data				
Age (years)	62.34 ± 8.53	63.26 ± 8.04	61.93 ± 8.76	0.426
Male (%)	96 (78.7)	27 (71.1)	69 (82.1)	0.166
Hypertension (%)	64 (52.5)	15 (39.5)	49 (58.3)	0.053
Diabetes mellitus (%)	54 (44.3)	13 (34.2)	41 (48.8)	0.133
Hyperlipidemia (%)	36 (29.5)	11 (28.9)	25 (29.8)	0.927
Renal insufficiency (%)	3 (2.5)	0 (0.0)	3 (3.6)	0.583
Cerebrovascular disease (%)	8 (6.6)	1 (2.6)	7 (8.3)	0.433
Previous myocardial infarction (%)	37 (30.3)	12 (31.6)	25 (29.8)	0.840
History of PCI (%)	18 (14.8)	5 (13.2)	13 (15.5)	0.738
Coronary lesion				0.777
One lesion (%)	2 (1.6)	1 (2.6)	1 (1.2)	
Two lesions (%)	29 (23.8)	8 (21.1)	21 (25.0)	
Triple lesions (%)	91 (74.6)	29 (76.3)	62 (73.8)	
Body mass index (kg/m^2)	25.06 ± 3.80	24.54 ± 5.02	25.29 ± 3.11	0.316
Body surface area (m^2)	1.84 ± 0.16	1.83 ± 0.14	1.85 ± 0.17	0.503
^{99m}Tc-sestamibi SPECT and ^{18}F-FDG PET				
VM-PM-VWC (%)	18.62 ± 11.24	10.47 ± 9.30	22.31 ± 10.07	< 0.001
Total perfusion deficit (%)	38.60 ± 14.68	35.76 ± 13.59	39.88 ± 15.05	0.152
VM of LV (%)	24.16±13.90	15.55±12.26	28.06±12.85	< 0.001
Infarcted myocardium of LV (%)	14.43±13.08	20.21±13.06	11.82±12.29	< 0.001
Intraoperative data				
Number of grafts	3.40 ± 0.82	3.45 ± 1.03	3.38 ± 0.71	0.680
LIMA + SVG	102 (83.6)	32 (84.2)	70 (83.6)	0.904
Off-pump	97 (79.5)	30 (78.9)	67 (79.8)	0.918
Operation time (hours)	4.25 ± 0.98	4.32 ± 0.93	4.23 ± 0.99	0.632
Postoperative data				
Mechanical ventilation time (hours)	23.50 (18.00-47.12)	25.00 (20.38-55.00)	22.50 (16.63-46.75)	0.102
ICU stay (hours)	27.50 (20.38-69.13)	42.25 (20.75-74.25)	26.50 (20.25-68.50)	0.200
Hospital stay (days)	19.00 (15.00-25.25)	20.00 (15.00-27.75)	18.50 (15.00-23.88)	0.248

ICU, intensive care unit; IMR, ischemic mitral regurgitation; LIMA, left internal mammary artery; LV, left ventricle; PCI, percutaneous coronary intervention; PM-VWC, papillary muscle-ventricular wall complex; SVG, saphenous vein graft; VM, viable myocardium.

Table 2. Echocardiographic variables of patients and follow-up results

Variables	Whole cohort (n = 122)	IMR unimproved (n = 38)	IMR improved (n = 84)	P value
Preoperative data				
LVEDV (mL)	168.74 ± 54.00	168.06 ± 52.54	169.05 ± 54.96	0.926
LVESV (mL)	100.36 ± 49.57	98.76 ± 48.94	101.08 ± 50.14	0.812
LVEF (%)	39.28 ± 12.13	40.16 ± 10.95	38.88 ± 12.68	0.592
LVESVI (mL/m^2)	54.42 ± 26.16	53.96 ± 25.97	54.62 ± 26.39	0.897
MR area (cm^2)	5.57 ± 1.12	5.63 ± 1.20	5.54 ± 1.10	0.682
EROA (cm^2)	0.31±0.05	0.32±0.05	0.31±0.05	0.259
Follow-up data				
LVEDV (mL)	142.26 ± 40.79	153.77 ± 43.84	137.05 ± 38.48	0.035
LVESV (mL)	74.06 ± 32.02	85.24 ± 36.75	69.00 ± 28.45	0.009
LVEF (%)	46.61 ± 10.07	44.97 ± 10.73	47.36 ± 9.73	0.228
LVESVI (mL/m^2)	40.38 ± 17.68	46.79 ± 20.44	37.48 ± 15.56	0.007
MR area (cm^2)	2.95 ± 2.27	6.08 ± 1.35	1.54 ± 0.52	< 0.001
EROA (cm^2)	0.17 ± 0.11	0.31 ± 0.05	0.11 ± 0.05	< 0.001
MACCEs	7 (5.7)	1 (1.2)	6 (15.8)	0.005

EROA, effective regurgitation orifice area; IMR, ischemic mitral regurgitation; LVEDV, left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end systolic volume; LVESVI, left ventricular end-systolic volume index.

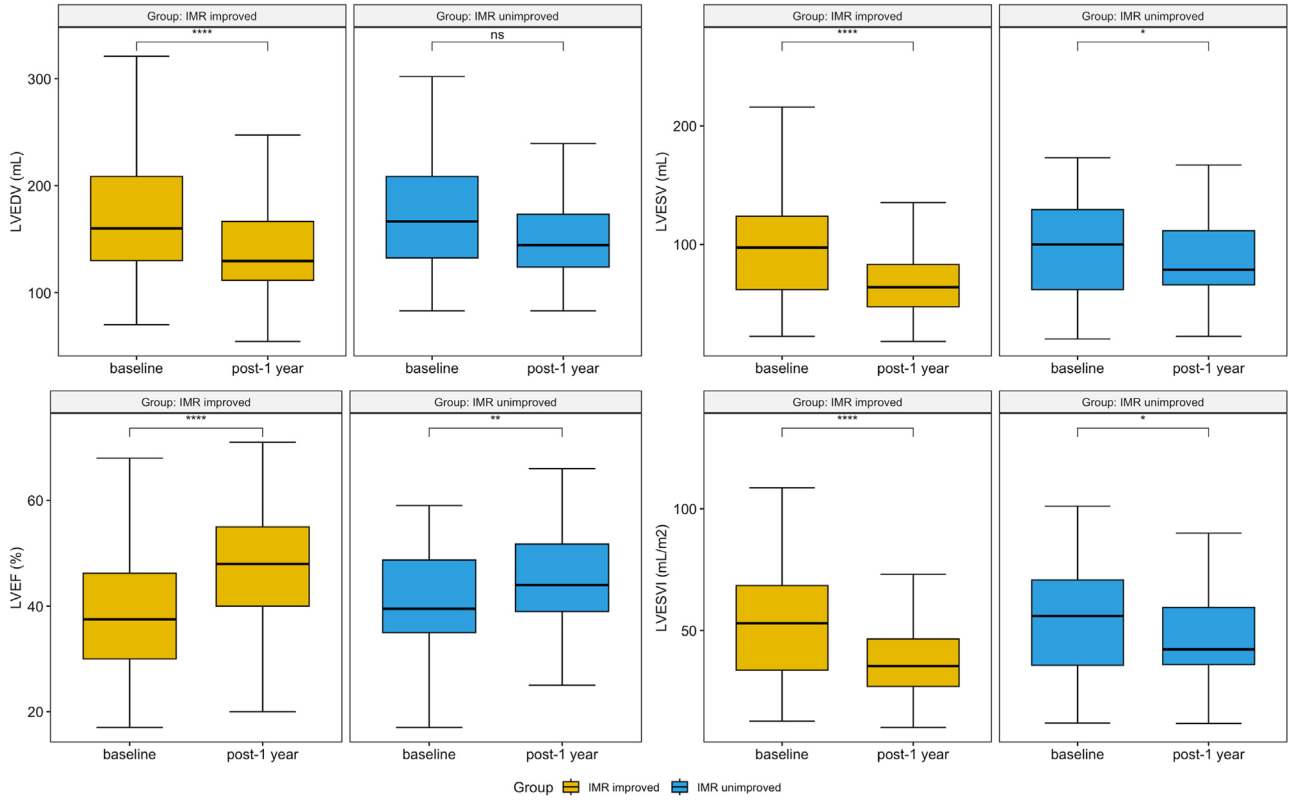

Figure 3. Changes in echocardiographic variables at baseline and 1 year after CABG in the IMR-improved and IMR-unimproved groups (*****P* < 0.0001, ****P* < 0.001, ***P* < 0.01, **P* < 0.05, $^{ns}P > 0.05$). CABG, coronary artery bypass grafting; IMR, ischemic mitral regurgitation; LVEDV, left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end systolic volume; LVESVI, left ventricular end-systolic volume index.

improvement of left ventricular function through surgery while ensuring the durability of surgical outcomes and reducing the recurrence rate of MR. Thus, the new index of VM-PM-VWC in this study offers a more accurate predictive value for balancing the benefits and risks of surgery, as well as the clinical outcomes. This index will aid clinicians in making more precise decisions regarding surgical approaches in patients with moderate IMR.

Most patients with CAD and varying degrees of IMR are referred for cardiac surgery. Clinical guidelines recommend mitral valve surgery for patients with severe IMR undergoing CABG[1]; however, the necessity of mitral valve surgery for moderate IMR remains a subject of debate. The **P**latelet-**O**riented **I**nhibition in **N**ew **T**IA and Minor Ischemic Stroke (POINT) study, the first randomized controlled trial to address this issue, revealed that mitral valve surgery in conjunction with CABG could improve heart failure symptoms and cardiac functional status.[16] Nonetheless, subsequent studies have produced conflicting results, preventing a consensus from being reached. Recently, a systematic review and meta-analysis of existing randomized controlled trials concluded that adding mitral valve surgery to CABG does not significantly improve the clinical outcomes compared with those with isolated CABG in patients with moderate IMR.[17]

Given these findings, it is crucial to determine which patients are most likely to benefit from CABG alone vs CABG

Table 3. Logistic analysis for predictors of ischemic mitral valve regurgitation improved

	Univariate analysis			Multivariate analysis		
Characteristics	OR	95% CI	*P* value	OR	95% CI	*P* value
Age	0.98	0.94-1.03	0.423			
Male	1.87	0.77-4.59	0.170			
Hypertension	2.15	0.98-4.69	0.055			
VM-PM-VWC	1.16	1.09-1.24	< 0.001	1.16	1.09-1.24	< 0.001
VM of LV	1.09	1.05-1.14	< 0.001			
Infarcted myocardium	0.95	0.92-0.98	0.002			

Age, male sex, hypertension, VM of LV, infarcted myocardium, and VM-PM-VWC were included in the multivariate logistic regression analysis.

CI, confidence interval; LV, left ventricle; LVEDV, left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end systolic volume; LVESVI, left ventricular end-systolic volume index; OR, odds ratio; PCI, percutaneous coronary intervention; PM-VWC, papillary muscle-ventricular wall complex; VM, viable myocardium.

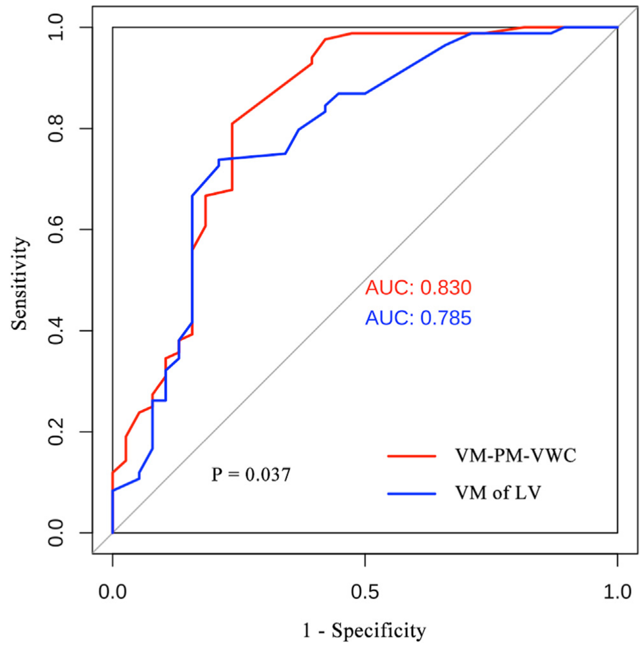

Figure 4. ROC curve analysis of the VM-PM-VWC model (**red**) and the VM of LV model (**blue**). AUC, area under the curve; LV, left ventricle; PM-VWC, papillary muscle-ventricular wall complex; ROC, receiver operator characteristic curve; VM, viable myocardium.

combined with mitral valve surgery. Our study found that approximately 31% of patients with moderate IMR did not achieve optimal outcomes with CABG alone and were more likely to develop MACCEs compared with those who showed improvement in IMR. Ongoing LV remodelling caused by persistent MR may be the primary cause of these adverse outcomes.[2] Identifying patients with moderate IMR who could benefit from isolated CABG is crucial for guiding further optimal treatment strategies.

Notably, IMR is usually secondary to LV remodelling and PM dysfunction resulting from myocardial ischemia.[18] Different studies have reported different perspectives as a primary contributor to IMR, mainly focusing on the viable myocardium, regarding the global LV myocardium or in the different specific regions, or myocardial infarction in the inferior and posterior septal wall.[6,19] Our findings revealed that patients with moderate IMR and a greater extent of VM did experience benefits from CABG alone. It is well established that an increase in VM is associated with improved myocardial function postrevascularization.[20] However, a critical question remains: Which LV segment and proportion of VM are crucial for the improvement of moderate IMR? The PM plays a pivotal role in maintaining normal mitral valve function, and its infarction has been linked with moderate-to-severe IMR.[21] Previous research indicated that a reduced number of myocardial infarction segments connected to the PM was correlated with better IMR outcomes following isolated CABG.[22] However, that study did not determine the optimal percentage of VM in segments associated with the PM for sustaining mitral valve function. Moreover, it overlooked the role of the entire anterior LV and basal segments of LV.

In the current study, we introduced a new index of PM-VMC and quantified the VM using ^{18}F-FDG PET combined with ^{99m}Tc-sestamibi SPECT to identify which patients with moderate IMR might benefit from CABG. Our study demonstrated that both VM in the entire LV and VM-PM-VMC was linked with the improved moderate IMR postisolated CABG. Multivariate logistic regression analysis revealed that, after adjusting for age, male sex, hypertension, and infarcted myocardium, VM-PM-VMC, rather than VM of the entire LV, was the key determinant for the improvement in moderate IMR following isolated CABG. Patients with VM-PM-VMC exceeding 12.5% were more likely to show improvement in moderate IMR, and its discrimination ability was significantly higher than VM of LV. For patients with moderate IMR who underwent isolate CABG, more attention should be paid to improve or recover myocardial blood flow of the PM-VWC by complete revascularization, maximal solving its ischemia to achieve better results.

Hypertension has been identified as a clinical determinant of MR in the general population.[23] Increased afterload may contribute to more grade of MR. But we find an interesting result that hypertension might be one of the predictors of less MR after CABG in our cohort ($P = 0.053$). The possible reason might be that patients with hypertension in our study may be treated unsystematic therapy before CABG. Poorly controlled blood pressure may affect the severity of MR. After revascularization, these individuals received more effective treatment for hypertension, which might have resulted in reduced MR. In addition, after adjusting for multiple analyses, the effect of hypertension on lower MR was not significant.

The LVESVI is typically used as an indicator to evaluate LV remodelling and the prognosis of ischemic myocardial disease.[24] In our study, a significantly reduced LVESVI (31% vs 13%, $P = 0.007$) was observed in the IMR-improved group compared with that in the IMR-unimproved group. Furthermore, a better clinical outcome was observed in the

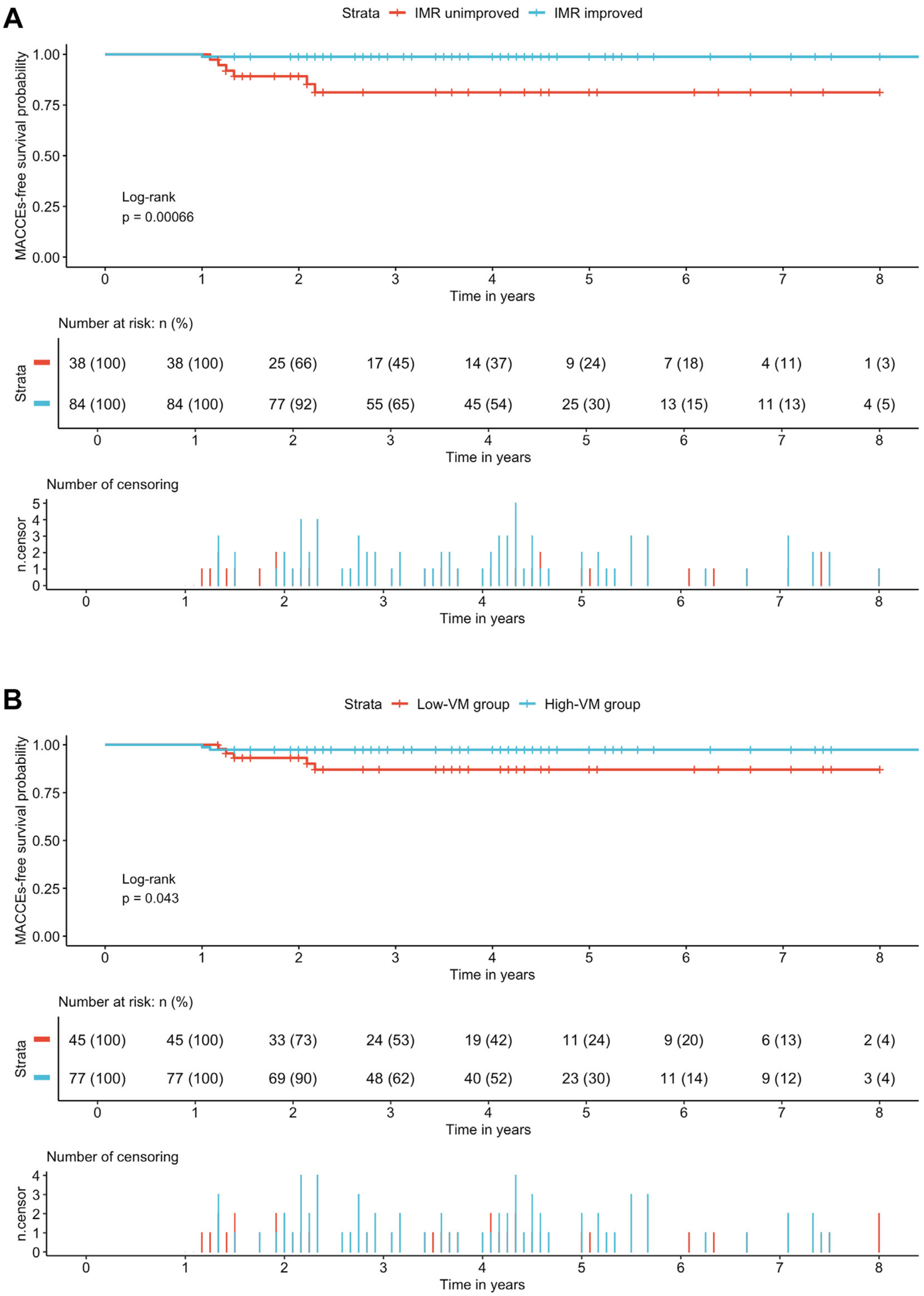

Figure 5. MACCEs-free survival curve plotted using the Kaplan-Meier method. (**A**) In the IMR-unimproved group and IMR-improved group. (**B**) In the low-VM group and high-VM group. IMR, ischemic mitral regurgitation; MACCEs, major adverse cardiovascular and cerebrovascular events; VM, viable myocardium.

IMR-improved group at 1-year follow-up. However, there were no obvious differences in LVEF between IMR-improved and IMR-unimproved groups. It could be explained that the LVEF was overestimated in the IMR-unimproved group because of the regurgitant volume into the left atrium. LVEF represents the cumulative effects of the extent of myocardial infarction and VM, both of which are pivotal to the prognosis of IMR.[6] Upon further subdividing patients based on the optimal cutoff point for VM-PM-VWC, we observed that those with a high VM-PM-VWC demonstrated an increased LVEF after undergoing CABG at the 1-year follow-up. This suggests that CABG can mitigate myocardial ischemia and recover VM function both in the PV-VMC and in the entire LV, thus improving LVEF and reducing LVESVI. VM-PM-VWC is crucial in the amelioration of moderate IMR following CABG alone. These findings indicated that VM-PM-VWC is an independent predictor of improvement in moderate IMR after isolated CABG. Furthermore, the VM-PM-VWC can effectively guide surgical strategies, reduce the incidence of MACCEs, and improve the prognosis of patients with moderate IMR undergoing CABG.

Limitations

First, this was a single-centre, retrospective, observational cohort study with a small sample size. To address this, our team has planned a multicentre, prospective study with a larger sample size for further validation. Second, the study did not include postoperative VM data, which limited our ability to compare preoperative and postoperative VM findings. Future studies that include both pre- and postoperative VM data may provide more reliable insights into the improvement of IMR. Finally, the follow-up period was relatively short. A longer follow-up period in the future study is warranted.

Conclusions

Most patients with moderate IMR could benefit from isolated CABG. The new index of VM-PM-VWC independently predicted the improvement in patients with moderate IMR undergoing isolated CABG. Patients exhibiting moderate IMR, if more than 12.5% VM-PM-VWC measured by PET imaging, could be recommended as isolated CABG without mitral valve surgery, and associated with the optimal outcomes.

Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki and approved and monitored by the institutional review board of Beijing Anzhen Hospital, Capital Medical University, Beijing, China (Number 2021162X).

Patient Consent

This is a retrospective case report using deidentified data; therefore, the institutional review board (IRB) did not require consent from the patient.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca and at https://doi.org/10.1016/j.cjco.2024.11.021.