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RESEARCH ARTICLE

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Clinical utility of preoperative stress perfusion cardiac magnetic resonance for predicting cardiovascular events in patients undergoing major noncardiac surgery

Ngamsiree Sukprasert[a], Kasinee Wanitchung[a], Sumet Prechawuttidech[a], Sasima Tongsai[b] and Yodying Kaolawanich[a]

[a]Division of Cardiology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; [b]Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

ABSTRACT

Background: Although guidelines recommend preoperative stress testing for patients with risk factors, the appropriate indications for stress perfusion cardiac magnetic resonance (CMR) have not been clearly defined. This study aimed to investigate the value of preoperative stress perfusion CMR in predicting major adverse cardiovascular events (MACE) in patients undergoing major noncardiac surgery.

Methods: This study included 309 patients who underwent CMR within 180 days prior to major noncardiac surgery between 2010 and 2022. Patients were categorized based on the presence or absence of inducible myocardial ischemia. The primary outcome was MACE, defined as a composite of cardiovascular death, myocardial infarction, sustained ventricular arrhythmia, heart failure, or ischemic stroke occurring during the indexed hospitalization for surgery or within 30 days post-discharge.

Results: The mean patient age was 72 years (51% male), and 21% demonstrated inducible myocardial ischemia. Total MACE occurred in 4.5% of patients and was significantly higher in the inducible ischemia group compared to those without ischemia (16.9% vs. 1.3%, $p<0.001$). Cox regression analysis identified inducible ischemia as the strongest predictor of MACE (hazard ratio [HR] 10.72, 95% confidence interval [95% CI] 2.91–39.60, $p<0.001$). Other predictors included left ventricular ejection fraction (HR 0.94, 95% CI 0.92–0.97, $p<0.001$), the number of ischemic segments (HR 1.19, 95% CI 1.07–1.31, $p=0.001$), the presence of late gadolinium enhancement (LGE) (HR 6.28, 95% CI 1.93–20.44, $p=0.002$), and the number of LGE segments (HR 1.21, 95% CI 1.08–1.37, $p=0.002$). The predictive performance of the Revised Cardiac Risk Index score significantly improved after the addition of inducible ischemia (C-statistic 0.61 vs. 0.77; net reclassification improvement 0.58, $p<0.001$; integrative discrimination index 0.07, $p<0.001$).

Conclusions: In this retrospective cohort study, inducible myocardial ischemia detected by stress perfusion CMR in patients undergoing major noncardiac surgery was associated with MACE during hospitalization or within 30 days post-discharge. Larger prospective or multicenter studies are required to validate these findings and ensure generalizability.

Abbreviations: AUC: area under the curve; CAD: coronary artery disease; CCTA: coronary computed angiography; CI: confidence interval; CMR: cardiac magnetic resonance; ECG: electrocardiography; EDV: end-diastolic volume; EF: ejection fraction; ESV: end-systolic volume; eGFR: estimated glomerular filtration rate; FOV: field of view; HR: hazard ratio; IDI: integrated discrimination index; IQR: interquartile range; LGE: late gadolinium enhancement; LV: left ventricular; MACE: major adverse cardiovascular events; MET: metabolic equivalent; NRI: net reclassification improvement; RCRI: Revised Cardiac Risk Index; ROC: receiver operating characteristic; SSFP: steady-state free precession

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Major adverse cardiovascular events; noncardiac surgery; preoperative evaluation; prognosis; stress perfusion cardiac magnetic resonance

Introduction

Surgical procedures, including noncardiac procedures, can trigger major adverse cardiovascular events (MACE), including myocardial infarction (MI), heart failure, and cardiovascular death. Complex physiological responses to surgery, such as increased stress, inflammation, and coagulation factors, can contribute to MACE. Intraoperative factors such as tachycardia, hypotension, hypertension, and perioperative anemia

CONTACT Yodying Kaolawanich yodying.kao@gmail.com Division of Cardiology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand

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can also influence the occurrence of MACE [1,2]. Perioperative MI often goes undetected because of atypical symptoms, which can lead to an underestimation of MACE incidence [3,4]. Therefore, preoperative cardiac evaluation is essential in older-aged patients and in younger patients with associated risk factors.

The latest European Society of Cardiology (ESC) guidelines recommend using imaging stress testing in patients with cardiovascular risk factors scheduled to undergo major noncardiac surgery [5]. Despite extensive evidence supporting stress echocardiography [6,7], stress myocardial perfusion scintigraphy [8], and more recently, coronary computed tomography angiography (CCTA) [9,10] for preoperative assessment – including a systematic review and meta-analysis by Kalesan et al. that included 79 studies – no study using stress perfusion cardiac magnetic resonance (CMR) has been reported [11]. Additionally, the ESC guidelines do not list specific indications for the use of stress perfusion CMR [5].

Stress perfusion CMR is increasingly used in routine clinical practice for patients with known or suspected coronary artery disease (CAD), and its diagnostic accuracy is well established [12,13]. In addition to providing information about inducible myocardial ischemia, stress perfusion CMR yields data on cardiac function and details on the presence and extent of myocardial scarring using the late gadolinium enhancement (LGE) technique – all without radiation exposure. However, more information is needed to determine the clinical relevance of this preoperative diagnostic method for stratifying surgical risks. Accordingly, this study aimed to investigate the clinical utility of preoperative stress perfusion CMR in predicting MACE in patients scheduled for major noncardiac surgery.

Methods

Study design and setting

This retrospective cohort study included patients who underwent adenosine stress perfusion CMR as part of their preoperative evaluation for scheduled non-emergent major noncardiac surgery at the Division of Cardiology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University. Written informed consent from the patients was waived by the SIRB due to the retrospective nature and confidentiality-preserving design of the study.

Sample size and sampling procedure

Sample size estimation was performed based on a study by Hashimoto et al. [8] that assessed the prognostic value of stress myocardial perfusion scintigraphy in 481 patients undergoing noncardiac surgery. They found that 26% of patients had myocardial ischemia and 17% of these patients experienced adverse outcomes after surgery, while 5% of patients without ischemia experienced adverse outcomes. The estimated sample size for two proportions with independent samples, with a power of 80%, alpha of 0.05, and ratio of 4, revealed a required a sample size of at least 285, with 57 patients with ischemia and 228 patients without ischemia.

For the sampling procedure, we included all patients from our CMR database and medical records who had complete data within the study period, met the inclusion criteria, and did not meet any exclusion criteria, ensuring a representative dataset.

Study population

The inclusion criteria consisted of patients aged ≥65 years or ≥45 years with cardiovascular risk factors, as defined by the latest ESC guidelines (at least one of the following: hypertension, cigarette smoking, dyslipidemia, diabetes mellitus, or a family history of cardiovascular disease) [5], who underwent preoperative adenosine stress perfusion CMR between June 2010 and February 2022. Patients were excluded if they did not undergo noncardiac surgery within 180 days of the CMR or if follow-up data were unavailable.

Study variables

Data on patient demographics, clinical characteristics, preoperative comorbidities, surgical information, and postoperative outcomes were collected. The patients' functional status was determined based on their ability to perform a range of daily activities. Based on that information, the patient's functional status was categorized as either <4 metabolic equivalents (METs) or ≥4 METs. Patients with an unknown functional capacity were included in the <4 METs category. Surgery-specific risk was categorized as intermediate or high, according to the latest ESC guidelines [5]. The parameters

included in the modified Revised Cardiac Risk Index (RCRI) score included a history of CAD, high-risk surgery, congestive heart failure, diabetes mellitus requiring insulin therapy, serum creatinine level >2 mg/dL, and a history of cerebrovascular disease [14].

The primary outcome was MACE, defined as a composite of cardiovascular death, MI, sustained ventricular arrhythmia, heart failure, or ischemic stroke during the index hospitalization for surgery or within 30 days after discharge. To diagnose MI, we applied the criteria from the Fourth Universal Definition of Myocardial Infarction [15], which requires an elevated troponin concentration accompanied by one of the following: ischemic signs or symptoms, ischemic changes on the electrocardiogram, or new imaging abnormalities suggestive of MI. Heart failure was defined based on plain chest radiography findings in an appropriate clinical setting. Cardiovascular death was determined according to the standardized published definitions [16]. In cases where patients experienced multiple events, only the first event was considered for the survival analysis.

CMR

The CMR studies to evaluate cardiac function, myocardial perfusion, and LGE were performed on a 1.5 or 3.0 Tesla Philips Achieva XR scanner (Philips Medical Systems, Best, the Netherlands) [17,18]. Further details of the CMR protocol are provided in Supplemental Methods.

Quantitative measurements of standard left ventricular (LV) volume, mass, and left ventricular ejection fraction (LVEF) were derived from a series of short-axis steady-state free precession (SSFP) cine images. Stress perfusion and late gadolinium enhancement (LGE) images were visually analyzed, with a consensus reached among CMR-trained physicians who were blinded to the clinical and follow-up information. Stress perfusion images were reviewed segment by segment across the 16 visible segments (excluding segment 17 at the apex, which was not visible). LGE images were also visually evaluated and were considered present only when confirmed in both the short axis and at least one additional orthogonal plane [18]. The total number of LGE segments was calculated using the American Heart Association 17-segment model [19].

Statistical analysis

All statistical analyses were performed using SPSS Statistics for Windows (version 20.0; IBM Corp., Armonk, NY). The normality of the continuous variable distribution was assessed using the Kolmogorov–Smirnov test. Continuous variables with a normal distribution are presented as mean ± standard deviation, and continuous variables with a non-normal distribution are presented as median and interquartile range (IQR). Categorical variables are presented as absolute numbers and percentages. The comparison of normally distributed continuous variables between the two groups was performed using Student's unpaired *t*-test, while non-normally distributed variables were compared using the Mann–Whitney *U* test. Categorical data were compared using the chi-square test or Fisher's exact test, depending on the size of the samples being compared.

The primary outcome was estimated using Kaplan–Meier survival analysis, and comparisons between groups were performed using the log-rank test. Univariable Cox regression analysis was conducted to identify significant predictors of the primary outcome. The results of the univariable Cox analysis are presented as hazard ratios (HR) and 95% confidence intervals (95% CI). A p-value <0.05 was considered statistically significant for all tests.

The discriminative capacity of each model for predicting MACE was determined using Harrell's concordance (C)-statistic at baseline and after adding the CMR variables. The potentially enhanced predictive value of the RCRI score with the addition of CMR variables was evaluated using Harrell's C-statistic increment, the categorical net reclassification improvement (NRI) statistic, and the integrative discrimination index (IDI). The survC1 and survIDINRI packages of R software, version 4.3.2 (The R Project for Statistical Computing, Vienna, Austria), were used for these three calculations.

Results

Patient characteristics

A total of 392 patients who underwent adenosine stress perfusion CMR before major noncardiac surgery were screened for eligibility (Figure 1). Of these, 83 were excluded, and the remaining 309 patients were included in the final analysis. The median interval between CMR and surgery was 44 days (IQR 24–84). Patient baseline characteristics are listed in Table 1. The mean age was 72.0 ± 10.4 years, and 51.1% were male. Seventy-nine (25.6%) patients had a history of chronic CAD, and 56 (18.1%) had a history of prior MI. The median RCRI score for the entire cohort was 1 (IQR 1–2). A total of 20.4% underwent high-risk surgery,

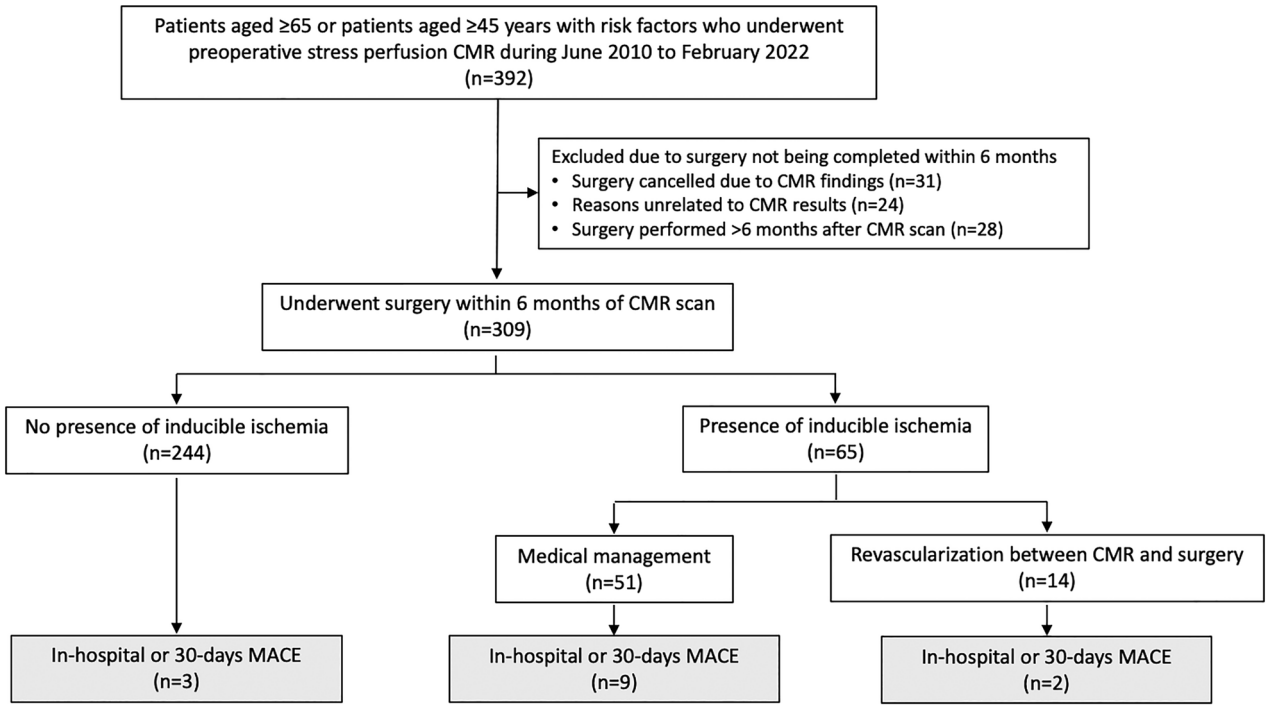

Figure 1. Study flow chart.

while the rest underwent intermediate-risk surgery. Sixty-five (21%) patients demonstrated inducible myocardial ischemia. Fourteen (4.5%) patients underwent coronary revascularization between CMR and surgery, all of whom had inducible myocardial ischemia on CMR.

Patient outcomes and the predictive value of CMR

All patients were followed up for at least 30 days after discharge from index hospitalization. MACE occurred in 14 patients (4.5%), including 3 cardiovascular deaths, 3 nonfatal MIs, 1 sustained ventricular arrhythmia, 8 heart failures, and 4 ischemic strokes. Table 1 presents a comparison of clinical and CMR characteristics between patients with and without MACE. Patients with MACE had significantly lower eGFR and more frequent insulin use ($p < 0.05$ for both). Regarding CMR variables, patients with MACE had significantly lower LVEF, a higher LV mass index, and a higher prevalence of both inducible ischemia and LGE ($p < 0.05$ for all). Additionally, patients with MACE had a greater number of ischemic segments and LGE segments, though these differences did not reach statistical significance ($p = 0.69$ and 0.89, respectively). Supplemental Table 1 presents a comparison of clinical and CMR characteristics between patients with and without inducible myocardial ischemia. Patients with inducible ischemia had a higher prevalence of cardiovascular risk factors, known CAD, and higher RCRI scores.

Table 2 shows the incidence of MACE for each surgical risk category, surgery type, and RCRI score. The incidence of MACE was higher among those who underwent high-risk surgery than among those who underwent intermediate-risk surgery (4 with MACE out of 63, 6.3% vs. 10 with MACE out of 246, 4.1%, respectively). MACE occurred most frequently among patients who underwent gynecologic surgery (7.1%) and vascular surgery (6.3%). However, only one patient who underwent gynecologic surgery experienced heart failure, whereas three cardiovascular deaths and three nonfatal MIs occurred exclusively among those who underwent vascular surgery. The rate of MACE increased with an increase in the RCRI score (RCRI 0 = 1.5%, RCRI 1 = 4.4%, and RCRI >1 = 6.3%).

Figure 2 demonstrates the risk of in-hospital or 30-day MACE compared between those with and without inducible ischemia relative to the surgical risk category (compared between intermediate- and high-risk surgery) and RCRI score (compared among RCRI scores of 0, 1, and >1). For both high- and intermediate-risk surgeries, patients with inducible ischemia had a significantly higher rate of MACE than those without inducible ischemia ($p < 0.001$ for both). Similarly, patients with inducible ischemia and an RCRI score of 1 or >1 had a significantly higher rate of MACE than those without inducible ischemia ($p < 0.001$ for both). Patients without inducible ischemia had a very low rate of MACE, even those who underwent high-risk surgery or had an RCRI score of >1.

Table 1. Clinical and CMR characteristics of all patients and compared between those with and without MACE.

	Total ($n=309$)	MACE ($n=14$)	No MACE ($n=295$)	p-value
Age (years)	72.0 ± 10.4	73.4 ± 12.8	71.9 ± 10.3	0.61
Male sex	158 (51.1%)	8 (57.1%)	150 (50.8%)	0.64
Body mass index (kg/m^2)	24.9 ± 5.1	23.2 ± 3.9	25.0 ± 5.1	0.18
Functional capacity				0.60
≥4 METs	108 (34.9%)	4 (28.6%)	104 (35.3%)	
<4 METs or unknown	201 (65.0%)	10 (71.4%)	191 (64.7%)	
RCRI score				0.31
0	64 (20.7%)	1 (7.1%)	63 (21.4%)	
1	134 (43.4%)	6 (42.9%)	128 (43.4%)	
2	82 (26.5%)	4 (28.6%)	78 (26.4%)	
≥3	29 (9.4%)	3 (21.4%)	26 (8.8%)	
Median RCRI score	1 (1, 2)	1.5 (1, 2)	1 (1, 2)	0.40
CAD risk factors				
Hypertension	259 (83.8%)	12 (85.7%)	247 (83.7%)	0.84
Diabetes mellitus	133 (43.0%)	5 (35.7%)	128 (43.4%)	0.57
Hyperlipidemia	248 (80.2%)	11 (78.5%)	237 (80.3%)	0.87
Smoking (current or past)	75 (24.2%)	4 (28.6%)	71 (24.1%)	0.70
CAD characteristics				
Chronic CAD	79 (25.6%)	4 (28.6%)	75 (25.4%)	0.79
Myocardial infarction	56 (18.1%)	2 (14.3%)	54 (18.3%)	0.70
Revascularization prior to CMR	53 (17.1%)	3 (21.4%)	50 (16.9%)	0.66
Invasive coronary angiography between CMR and surgery	24 (7.8%)	5 (35.7%)	19 (6.4%)	***<0.001***
Revascularization between CMR and surgery[a]	14 (4.5%)	2 (14.3%)	12 (4.1%)	0.07
Duration from CMR to revascularization (days)	34 (25, 89)	30.5 (N/A)	37 (20, 95)	0.73
Medical history				
Atrial fibrillation	26 (8.4%)	1 (7.1%)	25 (7.8%)	0.92
Heart failure	27 (8.7%)	2 (14.3%)	25 (7.8%)	0.38
Ischemic stroke	38 (12.3%)	1 (7.1%)	37 (12.5%)	0.55
Peripheral vascular disease	36 (11.6%)	3 (21.4%)	33 (11.2%)	0.24
Cancer	64 (20.7%)	5 (35.7%)	59 (20.0%)	0.15
Chronic lung disease	10 (3.2%)	0 (0.0%)	10 (3.4%)	0.48
Chronic kidney disease	69 (22.3%)	6 (42.9%)	63 (21.3%)	0.05
Medications				
ACEIs or ARBs	117 (37.8%)	5 (35.7%)	112 (38.0%)	0.86
Antiplatelets	151 (48.9%)	9 (64.3%)	142 (48.1%)	0.23
Anticoagulants	21 (6.8%)	1 (7.1%)	20 (6.8%)	0.97
Beta blockers	145 (46.9%)	7 (50.0%)	138 (46.8%)	0.81
Calcium channel blockers	123 (39.8%)	7 (50.0%)	116 (39.3%)	0.42
Statins	192 (62.1%)	8 (57.1%)	184 (62.3%)	0.69
Oral hypoglycemic agent	86 (27.8%)	2 (14.3%)	84 (28.5%)	0.24
Insulin	25 (8.1%)	5 (35.7%)	20 (6.8%)	***<0.001***
Q-wave on ECG	29 (9.4%)	2 (14.3%)	27 (9.1%)	0.51
eGFR (mL/min/1.73 m^2)	57.1 ± 29.1	38.9 ± 27.8	58.0 ± 28.9	***0.01***
Number of days from CMR to surgery	44 (24, 84)	60 (20, 84)	43 (24, 84)	0.73
Surgical risk category				0.43
Intermediate	246 (79.6%)	10 (71.4%)	236 (80.0%)	
High	63 (20.4%)	4 (28.6%)	59 (20.0%)	
Type of surgery				
Vascular	79 (25.6%)	5 (35.7%)	74 (25.1%)	0.37
Intrathoracic	17 (5.5%)	0 (0.0%)	17 (5.7%)	0.36
Intraperitoneal	100 (32.3%)	4 (28.6%)	96 (32.5%)	0.76
Orthopedic	75 (24.3%)	4 (28.6%)	71 (24.0%)	0.70
Head and neck/ear, nose and throat/neurosurgery	24 (7.8%)	0 (0.0%)	24 (8.1%)	0.26
Gynecologic	14 (4.5%)	1 (7.1%)	13 (4.4%)	0.63
Duration of index hospitalization (days)	6 (4, 10)	14 (10, 33)	6 (4, 10)	***0.006***
CMR				
LVEDV index (ml/m^2)	76.1 ± 23.7	96.1 ± 44.7	75.1 ± 21.9	0.10
LVESV index (ml/m^2)	26.5 ± 21.2	51.0 ± 46.8	25.3 ± 18.5	0.06
LVEF (%)	68.0 ± 13.2	53.4 ± 18.8	68.7 ± 12.5	***0.01***
LVEF <50%	25 (8.1%)	9 (13.8%)	16 (6.5%)	0.29
LV mass index (g/m^2)	50.4 ± 16.7	61.1 ± 22.7	49.9 ± 16.2	***0.01***
Presence of inducible ischemia	65 (21.0%)	11 (78.5%)	54 (18.3%)	***<0.001***
Number of ischemic segments[b]	5 (2, 9)	6 (2, 8)	4.5 (2, 9)	0.69
Presence of LGE	81 (26.2%)	10 (71.4%)	71 (24.0%)	***<0.001***
Number of LGE segments[c]	4 (2, 6)	5 (3, 6)	4 (2, 6)	0.89

Data presented as number and percentage, mean ± standard deviation, or median and interquartile range.
A p-value < 0.05 indicates statistical significance.
A p-value < 0.05 (bold-italic) indicates statistical significance.
[a]Revascularization procedures included percutaneous coronary intervention ($n=11$) and coronary artery bypass grafting ($n=3$).
[b]In patients with inducible ischemia.
[c]In patients with LGE.
ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; CAD: coronary artery disease; CMR: cardiac magnetic resonance; ECG: electrocardiogram; eGFR: estimated glomerular filtration rate; LGE: late gadolinium enhancement; LV: left ventricular; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; MACE: major adverse cardiovascular events; MET: metabolic equivalent; N/A: not available; RCRI: Revised Cardiac Risk Index.

Kaplan–Meier survival analysis revealed a significantly higher incidence of MACE among patients with inducible ischemia than among those without inducible ischemia (log-rank test: $p<0.001$) (Figure 3). Figure 4 shows the Kaplan–Meier survival analysis of the risk of in-hospital or 30-day MACE relative to RCRI scores of 0–1 and >1 (Figure 4(A,B)) as well as high- and intermediate-risk surgeries (Figure 4(C,D)), all of which were compared between patients with and without inducible ischemia. The results of the log-rank test showed a significant difference between the groups with and without inducible ischemia in all four analyses. Figure 5 shows the Kaplan–Meier survival analysis of the risk of in-hospital or 30-day MACE, comparing patients with and without inducible ischemia across various types of surgery (intraperitoneal Figure 5(A), oncologic Figure 5(B), orthopedic Figure 5(C), and vascular surgery Figure 5(D)). The results of the log-rank test showed a difference between the groups with and without inducible ischemia for all four types of surgery. However, this difference was not statistically significant for vascular surgery.

Table 2. Incidence of MACE for each surgical risk category, surgery type, and RCRI score.

	Total	MACE
	($n=309$)	($n=14$)
Surgical risk category		
Intermediate	246	10 (4.1%)
High	63	4 (6.3%)
Type of surgery		
Vascular	79	5 (6.3%)
Nonvascular	230	9 (3.9%)
Intrathoracic	17	0 (0.0%)
Intraperitoneal	100	4 (4.0%)
Orthopedic	75	2 (5.6%)
Head and neck/ear, nose and throat/neurosurgery	24	0 (0.0%)
Gynecologic	14	1 (7.1%)
RCRI score		
0	64	1 (1.5%)
1	134	6 (4.4%)
>1	111	7 (6.3%)

Data were presented as numbers and percentages. The percentage of patients with MACE is calculated based on the number of patients in the first column.
MACE: major adverse cardiovascular events; RCRI: Revised Cardiac Risk Index.

Cox regression analysis for predictors of MACE

Table 3 shows univariable Cox regression analysis to identify significant predictors of in-hospital or 30-day MACE. Univariable analysis identified inducible myocardial ischemia as the strongest predictor of MACE (hazard ratio [HR] 10.72, 95% confidence interval [CI] 2.91–39.60, $p<0.001$). Other predictors included left ventricular ejection fraction (HR 0.94, 95% CI 0.92–0.97, $p<0.001$), LV mass index (HR 1.03, 95% CI 1.002–1.05, $p=0.003$), the number of ischemic segments (HR 1.19, 95% CI 1.07–1.31, $p=0.001$), the presence of LGE (HR 6.28, 95% CI 1.93–20.44, $p=0.002$), and the number of LGE segments (HR 1.21, 95% CI 1.08–1.37, $p=0.002$). Multivariable analysis was not performed due to the limited number of MACE; however, an adjusted HR analysis was conducted instead, accounting for conventional risk factors and factors known to be associated with MACE (age, sex, functional capacity, RCRI score, atrial fibrillation, and peripheral arterial disease). All aforementioned variables remained significantly associated with MACE: inducible myocardial ischemia (HR 10.75, 95% CI 2.71–42.62, $p=0.001$), left ventricular ejection fraction (HR 0.95, 95% CI 0.92–0.98, $p<0.001$), LV mass index (HR 1.02, 95% CI 1.001–1.05,

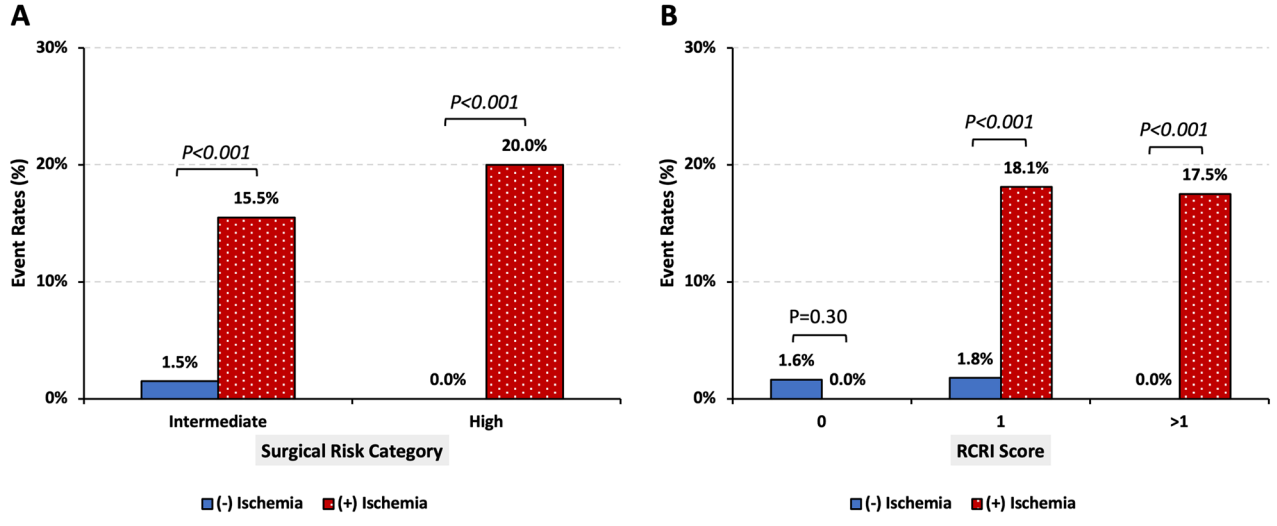

Figure 2. The risk of in-hospital or 30-day MACE compared between those with and without inducible ischemia relative to the surgical risk category (compared between intermediate- and high-risk surgery) and RCRI score (compared among RCRI scores of 0, 1, and >1). Abbreviations: MACE: major adverse cardiovascular events; RCRI: Revised Cardiac Risk Index.

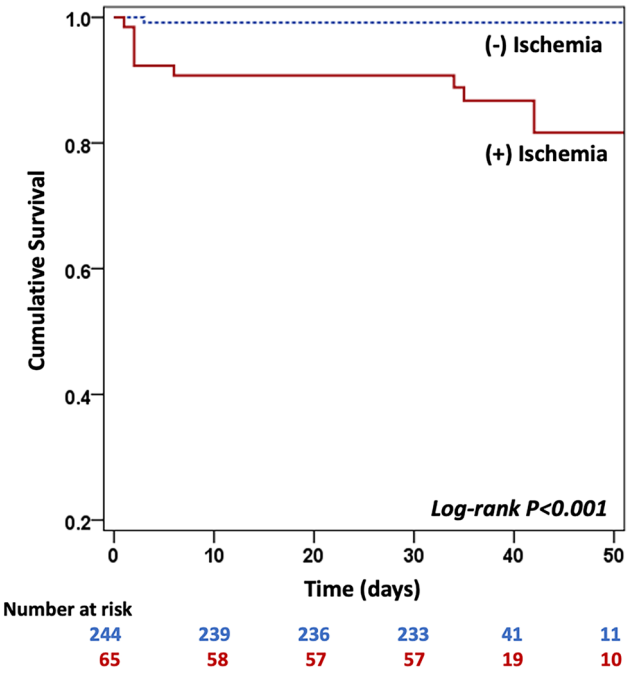

Figure 3. Kaplan–Meier Survival analysis showing the cumulative incidence of an in-hospital or 30-days MACE compared between patients with and without inducible ischemia. Abbreviations: MACE: major adverse cardiovascular events.

$p=0.03$), the number of ischemic segments (HR 1.17, 95% CI 1.05–1.31, $p=0.006$), the presence of LGE (HR 7.28, 95% CI 1.97–26.83, $p=0.003$), and the number of LGE segments (HR 1.22, 95% CI 1.07–1.40, $p=0.004$).

The receiver operating characteristic curve analysis showed an ischemic burden of ≥1 segment to be the best cutoff for predicting MACE with a sensitivity and specificity of 79% and 82%, respectively (area under the curve [AUC] 0.80, 95%CI 0.68–0.93, $p<0.001$).

Additive value of CMR on the predictive value of RCRI score

Table 4 presents reclassification analyses showing that adding CMR variables to the RCRI score – specifically LVEF, the presence of inducible ischemia, and the presence of LGE – significantly improved RCRI score performance in predicting perioperative MACE. The combination of the RCRI score and the presence of inducible ischemia resulted in the highest C-statistic (C-statistic of RCRI score alone = 0.61 vs. RCRI score + presence of inducible ischemia = 0.77; NRI = 0.58, $p<0.001$; and IDI = 0.07, $p<0.001$).

Discussion

In this study of patients who underwent preoperative stress perfusion CMR for major noncardiac surgery, there were three main findings: 1) Patients with inducible myocardial ischemia on CMR had a significantly higher MACE rate compared to those without ischemia, and inducible myocardial ischemia was the strongest predictor of MACE; 2) Inducible myocardial ischemia, LVEF, and LGE provided incremental prognostic value in addition to the RCRI score for predicting MACE; and 3) Patients without inducible ischemia exhibited very low MACE rates, regardless of their surgical risk category or RCRI score. These results underscore the value of stress perfusion CMR in patients undergoing major noncardiac surgery.

Preoperative evaluation before major noncardiac surgery is important. A recent large prospective study by Lurati Buse et al. on clinical evaluation before noncardiac surgery, which included 15,406 patients, examined whether self-reported effort tolerance improves the prediction of in-hospital MACE after noncardiac surgery [20]. They found that self-reported functional capacity was independently associated with MACE but did not improve prognostic accuracy compared to clinical risk factors. They also stated that caution is needed in the use of functional capacity to guide clinical decisions based on risk assessment in patients undergoing noncardiac surgery. These findings suggest that there may be room for further investigation into complementary evaluations alongside clinical assessments.

Stress perfusion CMR provides a comprehensive assessment of cardiac function, inducible ischemia, and tissue characterization, but its clinical utility has not yet been studied in patients undergoing noncardiac surgery. In our study, approximately 20% of the patients demonstrated inducible ischemia on CMR. Patients with inducible ischemia had a higher prevalence of cardiovascular risk factors, known CAD, and higher RCRI scores. These findings are consistent with those of previous studies using stress echocardiography and myocardial perfusion scintigraphy [6–8,11].

The CMR results may have influenced clinical decisions that could have affected surgical risk assessment and patient treatment plans. The information obtained from stress perfusion CMR could have led clinicians to alter management strategies for patients, potentially postponing surgery, implementing preoperative optimization, selecting less invasive procedures, or deciding on revascularization procedures for patients with ischemia on CMR to mitigate the risk. In our study, surgery was canceled in 31 patients because of CMR findings, such as high-risk CMR features and a large ischemic burden, which led to a joint decision between surgeons and patients to cancel surgery. By identifying patients with inducible myocardial ischemia, CMR may prompt more aggressive medical management or closer

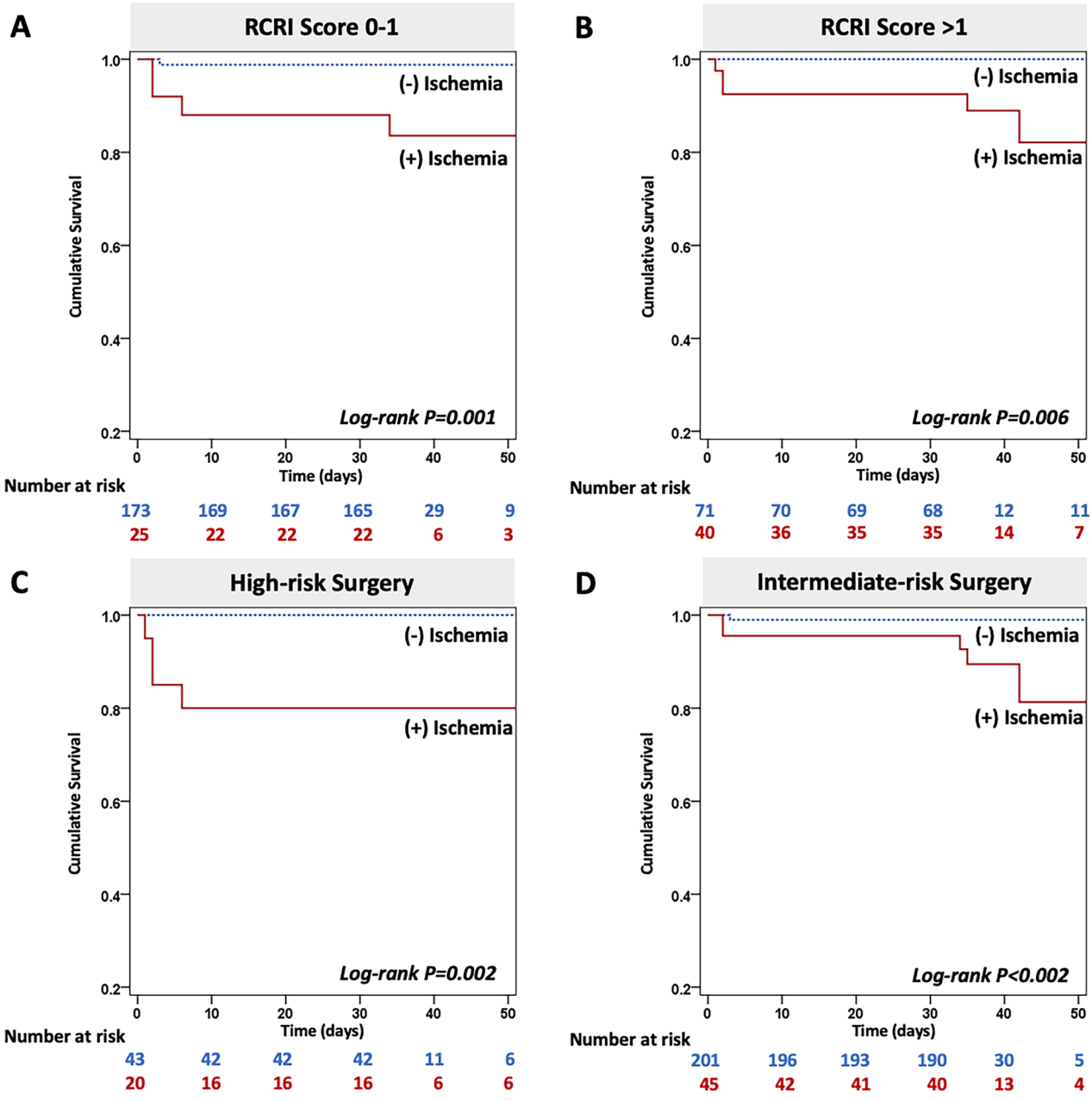

Figure 4. Kaplan–Meier survival analysis of the risk of in-hospital or 30-day MACE relative to RCRI scores of 0-1 and >1 (A, B) as well as high- and intermediate-risk surgeries (C, D), all of which were compared between patients with and without inducible ischemia. Abbreviations: MACE: major adverse cardiovascular events; RCRI: Revised Cardiac Risk Index.

postoperative monitoring, thereby affecting the overall outcome and skewing the perceived prognostic value.

Our study revealed an overall MACE rate of 4.5%. The prevalence of MACE has varied in previous studies owing to differences in the definition of outcomes and study populations. Cullen et al. using dobutamine stress echocardiography, reported a 30-day postoperative cardiac event rate comprising MI, cardiac arrest, and all-cause mortality of 2.3% [6]. Hwang et al. used CCTA and found a 30-day perioperative MACE (defined as cardiac death, MI, or pulmonary edema) rate of 3% [9]. A plausible explanation for the higher rate of MACE in our study may be that we enrolled a higher-risk population that included patients with a history of chronic CAD, prior MI, and CKD, which differs from the study by Hwang et al. which did not include patients with known CAD [9].

Myocardial ischemia is an important predictor of perioperative MACE on stress echocardiography and myocardial perfusion scintigraphy [6–8,11]. Despite the lack of randomized controlled trials that investigated the outcomes of surgery, other large prospective studies reported a link between stress test findings and perioperative cardiac complications [6–8,11]. Our study

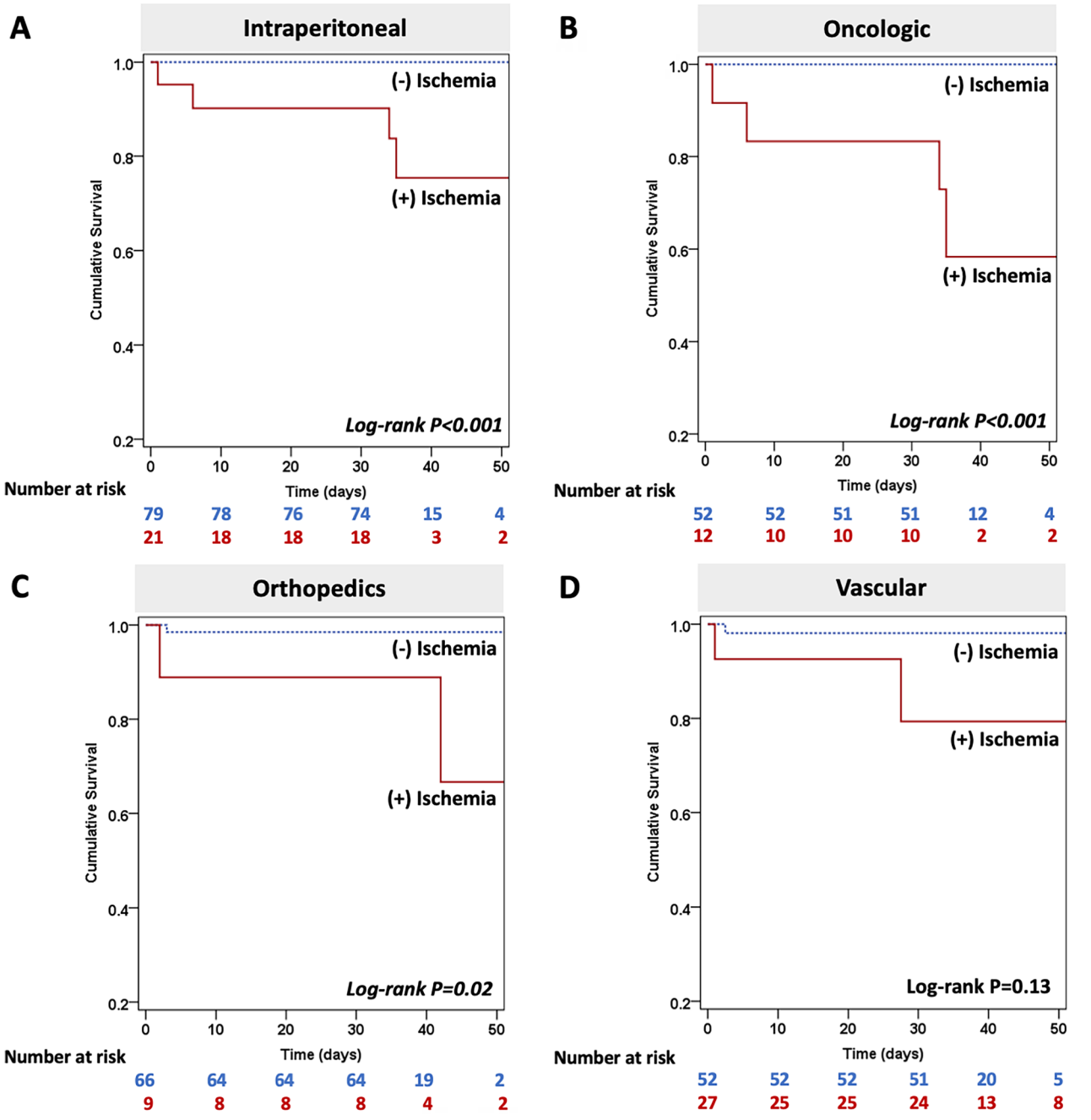

Figure 5. Kaplan–Meier survival analysis of the risk of in-hospital or 30-day MACE, comparing patients with and without inducible ischemia across various types of surgery (intraperitoneal [A], oncologic [B], orthopedic [C], and vascular surgery [D]). Abbreviations: MACE: major adverse cardiovascular events.

is the first to demonstrate the predictive value of stress perfusion CMR, showing that both the presence and extent of inducible ischemia are associated with an increased risk of MACE, with patients with inducible ischemia having more than 10 times the risk of MACE compared to those without ischemia. Moreover, combining inducible ischemia with the RCRI score provided additional prognostic value. This is consistent with previous studies on stress echocardiography and myocardial perfusion scintigraphy [6–8].

Studies and meta-analyses have demonstrated similar prognostic values of stress echocardiography and myocardial perfusion scintigraphy for perioperative risk assessment, with a slightly higher negative predictive value of stress echocardiography [21]. Concerning CMR, recent studies and meta-analyses have shown that CMR has a higher sensitivity for detecting obstructive CAD compared to stress echocardiography and myocardial perfusion imaging, without a difference in specificity [22,23]. Other benefits of stress perfusion

CMR include higher spatial resolution without the limitations of the echocardiographic window and no harmful ionizing radiation. However, since CMR may not be widely available in all regions, and its prognostic value is similar to that of myocardial perfusion scintigraphy, as well as stress echocardiography – which is a lower-cost alternative – the selection of these modalities should be guided by local guidelines, disease prevalence, and cost-effectiveness analyses. Future research on the cost-benefit comparison between CMR and other modalities would be valuable.

Table 3. Univariable cox regression analysis to identify predictors of in-hospital or 30-day MACE.

	HR (95% CI)	*p*-value
Age	1.009 (0.96–1.06)	0.73
Male sex	1.17 (0.39–3.49)	0.77
Body Mass Index	0.96 (0.86–1.08)	0.52
Poor functional capacity[a]	1.09 (0.33–3.55)	0.88
RCRI score	1.60 (0.97–2.64)	0.06
Hypertension	0.97 (0.21–4.37)	0.96
Diabetes mellitus	0.76 (0.25–2.32)	0.62
Hyperlipidemia	0.78 (0.22–2.84)	0.71
Smoking	1.38 (0.42–4.46)	0.60
History of chronic CAD	1.27 (0.39–4.11)	0.69
Prior myocardial infarction	0.80 (0.18–3.59)	0.77
Revascularization prior to CMR	1.34 (0.37–4.87)	0.65
Revascularization between CMR and surgery	3.55 (0.78–16.02)	0.10
Atrial fibrillation	1.02 (0.13–7.83)	0.98
History of heart failure	1.69 (0.37–7.70)	0.49
Ischemic stroke	0.82 (0.10–6.42)	0.85
Peripheral vascular disease	1.26 (0.31–5.15)	0.74
Cancer	2.30 (0.75–7.05)	0.14
Chronic kidney disease	2.96 (0.99–8.80)	0.05
Q-wave on ECG	1.67 (0.37–7.54)	0.50
eGFR	0.98 (0.96–1.001)	0.06
High-risk surgery	1.21 (0.35–4.18)	0.75
LVEDV index	1.02 (1.009–1.03)	***0.001***
LVESV index	1.02 (1.01–1.04)	***<0.001***
LVEF	0.94 (0.92–0.97)	***<0.001***
LV mass index	1.03 (1.002–1.05)	***0.03***
Presence of inducible ischemia	10.72 (2.91–39.60)	***<0.001***
Number of ischemic segments	1.19 (1.07–1.31)	***0.001***
Presence of LGE	6.28 (1.93–20.44)	***0.002***
Number of LGE segments	1.21 (1.08–1.37)	***0.002***

A *p*-value < 0.05 indicates statistical significance.
A *p*-value < 0.05 (bold-italic) indicates statistical significance.
[a]<4 METs or unknown.
95% CI: 95% confidence interval; CAD: coronary artery disease; CMR: cardiac magnetic resonance; ECG: electrocardiogram; eGFR: estimated glomerular filtration rate; HR: hazard ratio; LGE: late gadolinium enhancement; LV: left ventricular; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; MACE: major adverse cardiovascular events; MET: metabolic equivalent; RCRI: Revised Cardiac Risk Index.

The ESC guidelines state that, when using myocardial perfusion scintigraphy, reversible perfusion defects, compared to fixed defects, are associated with a higher risk of perioperative cardiac death or non-fatal MI [5]. Similarly, the latest American College of Cardiology/American Heart Association Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery indicates that fixed defects do not suggest additional risk for postoperative cardiac events. However, as an indicator of CAD, fixed defects have prognostic and therapeutic implications for longer-term cardiac and mortality outcomes [24]. However, no studies have examined the prognostic value of preexisting MI, as detected by LGE-CMR, for predicting perioperative MACE. In our study, 26% of patients demonstrated LGE, and LGE was significantly associated with MACE in univariable Cox regression analysis. Given that LGE-CMR has high spatial resolution and greater accuracy in detecting prior MI, especially small MIs, LGE may be a potential predictor of MACE in this patient group. This issue warrants further investigation in larger studies.

Coronary revascularization before noncardiac surgery remains an important topic of discussion and research. A landmark study by McFalls et al. involving 5,859 patients who underwent elective vascular surgery found that revascularization did not significantly alter long-term outcomes, including mortality [25]. In our study, 37% of patients with inducible ischemia underwent invasive coronary angiography, and 21% of those patients underwent coronary revascularization, which is a relatively low rate. One explanation may be that approximately one-fifth of the patients underwent time-sensitive cancer surgery. In our study, patients who underwent coronary revascularization before surgery and those who did not had relatively similar MACE rates (2/14 = 14.3% vs. 9/51 = 17.6%). This outcome was influenced by several factors, including ischemic burden, the number of coronary vessels involved, revascularization methods, LV systolic function, as well as the type of surgery and anesthetic considerations. Additionally, in our univariable Cox regression analysis,

Table 4. Additive value of CMR variables on the predictive value of RCRI score for predicting in-hospital or 30 days MACE.

	C-index (95%CI)	NRI (95%CI)	*p*-value	IDI (95%CI)	*p*-value
RCRI	0.61 (0.43-0.79)	Reference	Reference	Reference	Reference
RCRI + LVEF	0.73 (0.55-0.92)	0.35 (0.009-0.61)	***0.02***	0.08 (0.01-0.25)	***<0.001***
RCRI + Presence of inducible ischemia	0.77 (0.64-0.91)	0.58 (0.20-0.75)	***<0.001***	0.07 (0.02-0.20)	***<0.001***
RCRI + Presence of LGE	0.73 (0.57-0.89)	0.38 (0.01-0.64)	***0.01***	0.03 (0.003-0.11)	***0.01***

A *p*-value <0.05 (bold-italic) indicates statistical significance.
95%CI: 95% confidence interval; C-index: concordance index; CMR: cardiac magnetic resonance; IDI: integrated discrimination index; LGE: late gadolinium enhancement; LVEF: left ventricular ejection fraction; MACE: major adverse cardiovascular events; NRI: net reclassification improvement; RCRI: Revised Cardiac Risk Index.

revascularization between CMR and surgery was not significantly associated with MACE. However, our study population was limited, and the study was not specifically designed to evaluate this issue.

Overall, our research demonstrates the prognostic value of stress perfusion CMR in predicting MACE in patients undergoing major noncardiac surgery. Future studies with larger populations or prospective and multicenter designs will be useful, as our CMR protocol and analysis are aligned with the SCMR protocol, making it feasible for reproducible or multicenter studies.

Study limitations

This study has several limitations. First, not all patients referred for major noncardiac surgery underwent stress perfusion CMR imaging, leading to potential selection bias. Second, 83 patients were excluded for reasons primarily related to surgery being canceled due to CMR findings, as well as not undergoing non-cardiac surgery within 180 days of the CMR. These exclusions may reflect the typical complexity and high volume of patients referred to a tertiary academic center, which may have resulted in a missed estimation of the event rate. Third, our single-center study was limited by the relatively small number of patients, which affected the precision and statistical power of our analysis, necessitating confirmation in a larger patient population. The small number of adverse events also precluded a valid multivariable analysis; however, we adjusted for conventional risk factors and factors known to be associated with MACE instead. Fourth, we defined the primary outcome as MACE during the index hospitalization and up to 30 days after discharge. The outcomes of previous studies varied, including postoperative outcomes without specific duration [7], outcomes at 30 days post-surgery [6,9], outcomes during the index hospitalization and up to 30 days post-discharge [26], and up to 3 months after surgery [27]. The MACE risk is highest within the first 30 days after surgery but is still frequent within the first 3–5 months after surgery [1]; therefore, our outcome period was reasonable to assess the effect of surgery. Finally, one-fifth of our cohort consisted of patients who underwent cancer surgery, which is often time-sensitive and may have influenced clinicians to refrain from performing coronary revascularization prior to surgery. However, current evidence suggests that routine coronary revascularization before noncardiac surgery, even for high-risk surgeries such as vascular surgery, does not alter outcomes [25]. Additionally, current guidelines do not recommend routine revascularization before major noncardiac surgery [5,24].

Conclusions

In this retrospective cohort study, inducible myocardial ischemia detected by stress perfusion CMR in patients evaluated prior to major noncardiac surgery was associated with MACE during the index hospitalization for surgery or within 30 days post-discharge. However, further research, particularly larger prospective or multicenter studies, is needed to validate these findings and assess their generalizability.

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Author contributions

CRediT: **Ngamsiree Sukprasert**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing; **Kasinee Wanitchung**: Data curation, Investigation, Software, Visualization, Writing – review & editing; **Sumet Prechawuttidech**: Data curation, Investigation, Software, Visualization, Writing – review & editing; **Sasima Tongsai**: Formal analysis, Resources, Supervision, Validation, Writing – review & editing; **Yodying Kaolawanich**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University. Written informed consent from the patients was waived by the SIRB due to the retrospective nature and confidentiality-preserving design of the study.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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ORCID

Yodying Kaolawanich http://orcid.org/0000-0003-1262-9212

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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