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ORIGINAL ARTICLE

Incremental prognostic value of the SYNTAX score to late gadolinium-enhanced magnetic resonance images for patients with stable coronary artery disease

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Abstract The prognostic significance of the SYNTAX (Synergy between PCI with Taxus and cardiac surgery) score has recently been demonstrated in patients with stable multivessel or left main coronary artery disease (CAD). The present study determines whether adding the SYNTAX score to Framingham risk score (FRS), left ventricular ejection fraction (LVEF) and presence of myocardial infarction (MI) by late gadolinium enhancement (LGE) magnetic resonance imaging can improve the risk stratification in patients with stable CAD. We calculated the SYNTAX score in 161 patients with stable CAD (mean age: 66 ± 10 years old). During a mean follow-up of 2.3 years, 56 (35 %) of 161 patients developed cardiovascular events defined as cardiovascular death, non-fatal MI, cerebral infarction, unstable angina pectoris, hospitalization due to heart failure and revascularization. Multivariate Cox regression analysis selected triglycerides [hazard ratio (HR): 1.005 (95 % confidence interval (CI): 1.001–1.008), $p < 0.008$], presence of LGE [HR: 6.329 (95 % CI: 2.662–15.05), $p < 0.001$] and the SYNTAX score [HR: 1.085 (95 % CI: 1.044–1.127), $p < 0.001$] as risk factors for future cardiovascular events. Adding the SYNTAX score to FRS, EF and LGE significantly improved the net reclassification index (NRI) [40.4 % (95 % CI: 18.1–54.8 %), $p < 0.05$] with an increase in C-statistics of 0.089 (from 0.707 to 0.796). An increase in C-statistics and significant improvement of NRI showed that adding the SYNTAX score to the FRS, LVEF and LGE incrementally improved risk stratification in patient with stable CAD.

Keywords The SYNTAX score · Late gadolinium enhancement · Magnetic resonance imaging · Coronary artery disease · Prognosis

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Introduction

The Synergy between PCI with Taxus and cardiac surgery (SYNTAX) score is an angiographic scoring system based on X-ray coronary angiography (CAG) which can evaluate anatomical complexity of the coronary arterial plaque [1]. Recently, the prognostic significance of the SYNTAX scores to predict future cardiovascular event has been demonstrated in patients with stable multivessel or left main coronary artery disease (CAD) [2] and acute coronary syndrome (ACS) [3]. Late gadolinium-enhanced (LGE) MRI allows for the accurate assessment of irreversible myocardial injury such as myocardial infarction (MI) or myocardial fibrosis [4, 5]. The transmural extent is useful as a marker of myocardial viability in infarcted myocardium [6]. Furthermore, presence of LGE is a strong prognostic predictor in patients with various cardiovascular diseases such as acute MI, stable CAD, unrecognized MI and cardiomyopathy [7–14].

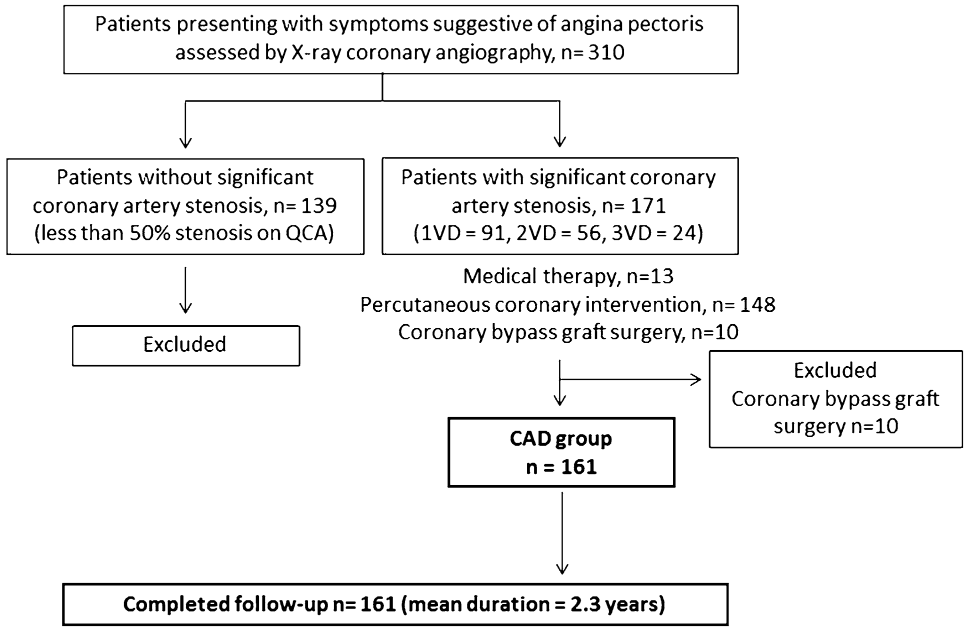

Fig. 1 Flow chart of patient enrollment. *QCA* quantitative coronary angiography, *VD* vessel disease, *CAD* coronary artery disease

In the current study, we hypothesized that adding the SYNTAX score to LGE MRI would improve the ability to predict the future cardiovascular events among patients with stable CAD. The purpose of this study was to investigate the incremental prognostic value of the SYNTAX score over LGE MRI in patients with stable CAD.

Materials and methods

Patients

Figure 1 shows a flow chart of the study enrollment. Among 310 patients who were initially enrolled in this study, X-ray CAG confirmed the presence and absence of significant coronary artery stenosis in 139 and 171 patients. Significant coronary artery stenosis was defined as ≥50 % luminal narrowing on quantitative coronary angiography (QCA) images. All patients underwent cardiac MRI to evaluate their cardiac function and myocardial infarction. We excluded 139 patients without CAD from analysis. Ten patients each who were treated by coronary artery bypass graft surgery (CABG) were excluded. Finally, 161 stable CAD patients were enrolled in the final analysis (Fig. 1). This study was approved by the institutional review board, and all patients gave written informed consent to participate in this study.

Acquisition of MR images

We acquired MRI images using a 1.5-T MR scanner equipped with 32 channel cardiac coils (Achieva, Philips Healthcare, Best, The Netherlands). Cine MRI and LGE MRI were imaged in the entire study population.

Acquisition of cine MR images

Vector-electrocardiographic (VCG) monitoring leads were attached to supine patients and scout images were acquired in three orthogonal planes for cardiac orientation. Vertical and horizontal long-axis slices of cine MR images of the LV were acquired using a steady-state free precession (SSFP) sequence. The volume and mass of the LV were calculated from short-axis cine MR images acquired from the apex to the base of the LV (repetition time, 4.1 ms; echo time, 1.7 ms; flip angle, 55°; field of view, 350 × 350 mm; acquisition matrix, 128 × 128; slice thickness, 10 mm; number of phases per cardiac cycle, 20).

Acquisition of LGE MR images

The patients were injected with 0.15 mmol/kg of gadopentetate dimeglumine (Magnevist; Bayer Healthcare, Leverkusen, Germany). LGE MRI images were acquired 15 min after in the same planes as the cine images using inversion recovery—prepared gradient-echo sequences. The imaging parameters for late gadolinium-enhanced imaging were as follows: repetition time, 4.3 ms; echo time, 1.3 ms; flip angle, 15°; field of view, 380 × 380 mm; acquisition matrix, 256 × 180; and slice thickness, 10 mm. We detected the null point of the normal myocardium using a Look–Locker sequence.

X-ray coronary angiography

An observer who was blinded to the cardiac MRI results interpreted conventional X-ray CAG images using QangioXA quantitative software (Medis Inc., Raleigh, NC, USA). Patients received an intracoronary administration of isosorbide dinitrate (2–3 mg), then contrast agent was injected and the degree of coronary arterial stenosis was evaluated on the images using quantitative coronary angiography (QCA) analysis. Significant coronary arterial stenosis was defined as ≥50 % reduction in luminal diameter by QCA.

Data analysis

Analysis of cine MR and LGE MR images

Two observers used an Extend MR WorkSpace workstation (Philips Healthcare) to analyze the cine MR and LGE MR images. All images were rendered innominate and reviewed in random order. The LV epi- and endocardial borders on the short axis of cine MR images were manually traced with exclusion of the papillary muscles that encompassed the LV myocardium. The LV mass was then calculated by the consensus of two observers as the sum of the myocardial volume areas multiplied by the specific gravity (1.05 g/mL) of the myocardial tissue [15].

Late gadolinium enhancement was visually assessed and interpreted by the consensus of two observers who were blinded to the information about the patients. The LGE mass was measured on short-axis slices using manual planimetry method. The total LGE mass was calculated by summing the LGE mass of all sections, and the ratio (%) of LGE is expressed as:

$$\text{LGE}(\%) = \text{Total LGE volume/Total LV wall volume} \times 100(\%)$$

None of the patients had atypical enhancement defined as mid-myocardial or sub-epicardial enhancement with multifocal distribution.

Calculation of the SYNTAX scores

Based on the quantitative CAG analysis, we defined significant coronary artery stenosis as ≥50 % narrowing of coronary artery diameter in at least one coronary artery. The SYNTAX score for each angiogram was independently evaluated by two experienced cardiologists who were blinded to the MRI results. Differences in opinion were resolved by the consensus of two cardiologists. Briefly, lesions that caused ≥50 % luminal narrowing in vessels ≥1.5 mm were defined based on the modified American Heart Association coronary tree segment classification and separately scored regarding bifurcations or trifurcations or aortic ostial localization, chronic occlusion, vessel tortuosity, length, calcification and thrombus formation. Finally, the lesion score was added to obtain the SYNTAX score for each patient. Observer who calculated the SYNTAX score was blinded to clinical information and MRI data. Occluded infarct-related arteries were scored as occlusions of unknown duration. A high SYNTAX score indicates complex coronary disease. We assessed the reproducibility of the SYNTAX scores in a random sample of 30 patients. The kappa values of assessment of the SYNTAX scores for intra- and interobserver agreement were 0.81 and 0.70, respectively.

Risk assessment calculated by FRS

Previous study using the FRS showed that 24.7 % patients with coronary artery disease or stroke will experience cardiovascular events during a 4-year follow-up [16]. We modified this risk assessment model and stratified the patients into low–intermediate, high or very high risk categories calculated as 2-year risk scores for primary and secondary prevention of <12 %, 12–25 % and >25 %, respectively.

Follow-up

Clinical information was obtained from hospital records and via telephone interviews of patients. Major adverse cardiac and cerebrovascular events included any of cardiovascular death, non-fatal MI, unstable angina requiring revascularization, cerebral infarction, hospitalization due to heart failure and revascularization (percutaneous coronary intervention or CABG). When a patient experienced more than one event, the first event was included in the analysis. When at least two events occurred simultaneously, the events were selected in the order of cardiovascular death > non-fatal MI > cerebral stroke > UAP > HF > revascularization.

Statistical analysis

Data were statistically analyzed using SPSS software, version 17.0 (SPSS, Inc., Chicago, IL, USA) and SAS version 9.2 (SAS Institute, Cary, NC, USA). Continuous values are shown as mean ± standard deviation (SD). Skewed values are presented as medians with interquartile ranges (IQR). Normality was determined using the Shapiro–Wilk test. Differences between groups were evaluated using an unpaired t test for normally distributed variables, and the Mann–Whitney U test for skewed variables. We calculated the cumulative incidence of events according to the presence or absence of LGE using the Kaplan–Meier method and compared the two curves using a log-rank test. We used Cox proportional hazards models to estimate HRs for cardiovascular events and 95 % confidence intervals (CI). Two-sided $P < 0.05$ was considered to indicate a significant difference. C-statistics for the Cox proportional hazards regression models were estimated. We evaluated whether adding the SYNTAX score to the FRS, EF and LGE incrementally improves the prediction of cardiovascular events using the net reclassification index. Low–intermediate, high risk and very high risk categories were defined as <12 %, 12–25 % and >25 %, respectively.

Results

Patient characteristics

Table 1 summarizes the characteristics of the patients (mean age, 66 ± 10 years), of whom 140 (87 %) were male. The prevalence of hypertension, dyslipidemia, diabetes mellitus, current smoking, family history of CAD and obesity were 65, 57, 21, 13, 7, 15 %, respectively. Blood test results for mean LDL cholesterol and mean HbA1c were 126 ± 36 mmol/L and 5.9 ± 1.2 %, respectively. Mean LVEF was 54 ± 15 %, and regional wall motion abnormalities (RWMA) were found in 31 (19 %) patients. Myocardial infarction was identified in 73 (45 %) patients and the mean % LGE was 8 ± 12 %. The mean FRS was 13 ± 6 and the mean SYNTAX score was 9 ± 7.

Cardiovascular events during follow-up

During a mean follow-up period of 2.3 years, 56 patients experienced cardiovascular events as follows: 2 cardiovascular death, 11 UAP, 2 cerebral infarction, 4 heart failure requiring hospitalization, 37 revascularization. Figure 2 shows Kaplan–Meier survival curves stratified by presence of LGE and the SYNTAX score. All patients ($n = 161$) were assigned to groups based on LGE and median SYNTAX score of 8. Kaplan–Meier survival curves for 161 patients with CAD revealed a significant difference in cumulative survival between those with and without LGE ($p < 0.001$; log-rank test) and with SYNTAX score >8 and ≤8 ($p < 0.001$; log-rank test). Figure 3 shows the Kaplan–Meier survival curves for patients with CAD assigned to groups based on median SYNTAX score and LGE [group 1, LGE (−) and the SYNTAX score ≤8; group 2, LGE (−) and the SYNTAX score >8; group 3, LGE (+) and the SYNTAX score ≤8; group 4, LGE (+) and the SYNTAX score >8]. Outcome was significantly better and significantly worse for groups 1 and 4, respectively, compared with the other groups (Fig. 3). Table 2 summarizes the results of Cox proportional hazard analyses for cardiovascular events. Univariate analysis selected triglycerides (HR, 1.004; 95 % CI, 1.001–1.008; $p = 0.021$), RWMA (HR, 2.160; 95 % CI, 1.247–3.743; $p = 0.006$), LGE (HR, 5.841; 95 % CI, 3.012–11.33; $p < 0.001$) and the SYNTAX score (HR, 1.104; 95 % CI, 1.070–1.139; $p < 0.001$) as significant predictors of cardiovascular events. Multivariate analysis selected triglycerides (HR, 1.005; 95 % CI, 1.001–1.008; $p = 0.008$), LGE (HR, 6.329; 95 % CI, 2.662–15.05; $p < 0.001$) and the SYNTAX score (HR, 1.085; 95 % CI, 1.044–1.127; $p < 0.001$).

Net reclassification index and C-statistics for Cox proportional hazard models to predict cardiovascular events

Table 3 shows the results of C-statistics for Cox proportional hazard analysis to predict cardiovascular events. Adding the STNTAX score to the FRS, EF and presence of LGE resulted in an increase in the C-statistics. C-statistics for FRS + EF + LGE + the SYNTAX score was 0.796 (95 % CI, 0.723–0.865).

Table 4 shows reclassification according to the SYNTAX score in addition to FRS and EF. Adding the SYNTAX score significantly improved the net reclassification index (NRI) for those with CAD (60.1 %; 95 % CI, 38.7–81.5, $p < 0.001$). Table 5 show reclassification by adding the SYNTAX score to the FRS, EF and LGE MRI. Adding the SYNTAX score significantly improved the NRI in CAD patients (40.4 %; 95 % CI, 22.5–58.4; $p < 0.001$).

Discussion

To the best of our knowledge, this is the first study to assess the incremental increase in the prognostic significance of adding the SYNTAX score to LGE MRI, FRS and LVEF to predict cardiovascular events. The results in the current study indicated that the simultaneous assessment of extent of myocardial infarction by LGE MRI and coronary arterial atherosclerosis by the SYNTAX score would help to stratify patients with CAD who are at risk for cardiovascular events.

Prognostic value of the SYNTAX score in recent studies

The SYNTAX score was originally conceived as a mean of evaluating the complexity and severity of atherosclerosis of the coronary artery visualized by X-ray coronary CAG in patients with CAD [1]. Recent studies have shown that the SYNTAX score has prognostic significance for future cardiovascular events in patient with stable CAD, triple-vessel CAD and left main coronary arterial stenosis and ACS [2, 17–22]. Palmerini et al. [3] analyzed 2627 patients with non-ST segment elevation ACS who were treated by PCI from a subgroup of the

Table 1 Patients' characteristics

Characteristics	All patients ($n = 161$)
Age (years)	66 ± 10
Male [*n* (%)]	140 (87 %)
Body mass index (kg/m^2)	24.1 ± 3.4
Systolic BP (mmHg)	132 ± 24
Diastolic BP (mmHg)	79 ± 17
Heart rate (bpm)	75 ± 19
Coronary risk factors, *n* (%)	
Hypertension	105 (65 %)
Dyslipidemia	92 (57 %)
Diabetes mellitus	34 (21 %)
Current smoking	21 (13 %)
Family history of CAD	12 (7 %)
Obesity	24 (15 %)
Blood test results	
Total cholesterol (mmol/L)	199 ± 40
LDL cholesterol (mmol/L)	126 ± 36
HDL cholesterol (mmol/L)	51 ± 16
Triglyceride (mmol/L)	147 ± 73
Hemoglobin (g/dL)	14.3 ± 1.7
HbA1c (%)	5.9 ± 1.2
eGFR (mL/min/1.73 m^2)	72 ± 18
CRP (mg/dL)	0.54 ± 1.13
BNP (pg/dL)	106 ± 169
Medication use	
Statins	92 (57 %)
Antiplatelet agents	138 (86 %)
Calcium channel blockers	26 (16 %)
β blockers	63 (39 %)
ACE/ARB	96 (60 %)
ECG abnormalities, *n* (%)	
Left bundle branch block	3 (2 %)
Left ventricular hypertrophy	2 (1 %)
Resting ST segment change	25 (16 %)
Pathologic Q wave	25 (16 %)
Cardiac MRI findings	
LV ejection fraction (%)	54 ± 15
LVEDV (mL)	134 ± 65
LVESV (mL)	68 ± 63
LV mass (g)	100 ± 35
Regional wall motion abnormality [*n* (%)]	31 (19 %)
LGE [*n* (%)]	73 (45 %)
% LGE	8 ± 12
Risk scores	
FRS (%)	13 ± 6
SYNTAX score	9 ± 7

Values are shown as mean ± standard deviation (SD)

ACE angiotensin converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *BNP* brain natriuretic peptide, *BP* blood pressure, *CAD* coronary artery disease, *CRP* C-reactive protein, *ECG* electrocardiography, *eGFR* estimated glomerular filtration rate, *FRS* Framingham risk score, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *LGE* late gadolinium enhancement, *MRI* magnetic resonance imaging

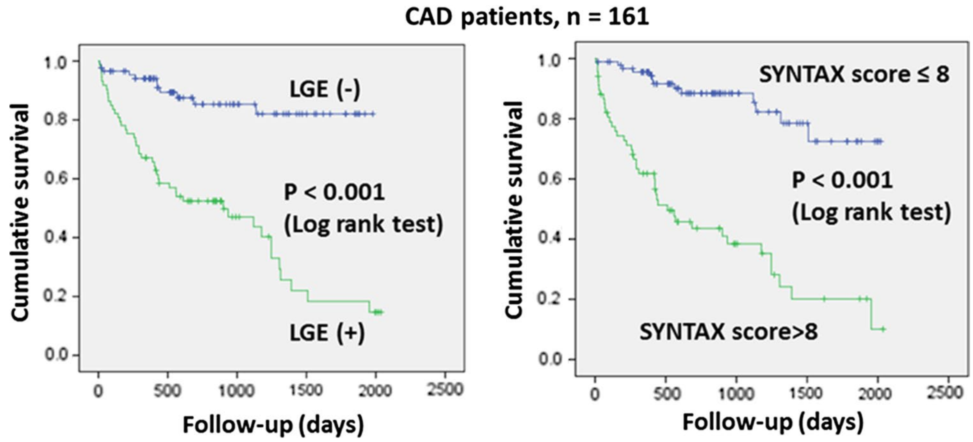

Fig. 2 Kaplan–Meier survival curves stratified by the SYNTAX score and LGE. Patients were divided into two groups based on presence or absence of LGE and median value of the SYNTAX score. Median value of the SYNTAX score was 8 for CAD patients. *LGE* late gadolinium-enhanced magnetic resonance imaging, *CAD* coronary artery disease

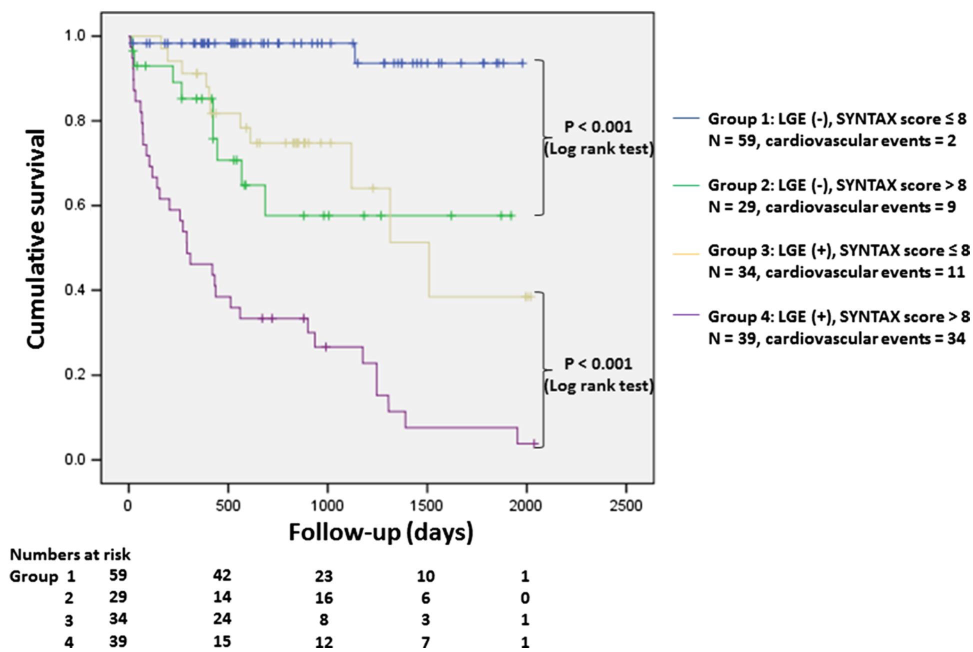

Fig. 3 Kaplan–Meier survival curves for patients with CAD ($n = 161$). Patients were allocated to four groups by LGE and the SYNTAX score. Median value of the SYNTAX score was 8 for CAD patients. *LGE* late gadolinium-enhanced magnetic resonance imaging

ACUITY (acute catheterization and urgent intervention triage strategy) trial and found that the SYNTAX score is an independent and significant predictor of 1-year rates of death, cardiac death, MI and target vessel revascularization. However, to date, the number of evidences regarding prognostic significance of the SYNTAX score is relatively limited. Therefore, we conducted this study to investigate the prognostic value of the SYNTAX score in CAD patients and to compare directly with established prognostic marker, severity of myocardial infarction by LGE MRI.

Deleterious effects of LGE in cardiovascular diseases

Irreversible myocardial injury can be assessed accurately by LGE MRI. The spatial resolution of LGE MRI is higher than that of myocardial single-photon emission computed tomography (SPECT) imaging [6]. Previous studies showed that the presence of LGE is a powerful prognostic marker of various cardiovascular diseases [23–25]. For example, myocardial scar on LGE is associated with a poor response to beta-blocker therapy [26] and revascularization (PCI or CABG) [4, 27]. Scott et al. [28] reported that the extent of LV scar quantified by LGE MRI is associated with spontaneous ventricular arrhythmia in patients with CAD and implantable cardiac defibrillators (ICD). Moreo et al. [29] showed a significant relationship between diastolic dysfunction evaluated by Doppler echocardiography and LGE on MRI and Wong et al. [30] showed a relationship between LGE and hospitalization of heart failure. Furthermore, unrecognized MI detected by LGE MRI has prognostic value in patients without clinical evidence of MI [7, 14]. The hazardous effect of LGE MRI was also observed in the current study.

Table 2 Cox proportional hazards analysis of cardiovascular event in patients with CAD

	Univariate analysis			Multivariate analysis		
	HR	95 % CI	*P*	HR	95 % CI	*P*
Age (per year)	0.994	0.970–1.019	0.63	Not selected		
Female (yes)	0.632	0.252–1.558	0.33	Not selected		
Body mass index (per kg/m^2)	0.983	0.905–1.067	0.68	Not selected		
Heart rate (per bpm)	0.998	0.978–1.018	0.82	Not selected		
Hypertension (yes)	1.043	0.605–1.796	0.88	Not selected		
Dyslipidemia (yes)	0.781	0.448–1.364	0.39	Not selected		
Diabetes mellitus (yes)	0.665	0.313–1.411	0.29	Not selected		
Current smoking (yes)	1.587	0.798–3.157	0.19	Not selected		
Family history of CAD (yes)	1.266	0.455–3.524	0.65	Not selected		
Obesity (yes)	0.972	0.999–1.026	0.11	Not selected		
Total cholesterol (per mmol/L)	1.002	0.995–1.008	0.67	Not selected		
LDL cholesterol (per mmol/L)	0.996	0.988–1.005	0.42	Not selected		
HDL cholesterol (per mmol/L)	1.012	0.997–1.028	0.11	Not selected		
Triglyceride (per mmol/L)	1.004	1.001–1.008	0.021	1.005	1.001–1.008	0.008
Hemoglobin (per g/dL)	1.011	0.870–1.176	0.89	Not selected		
HbA1c (per %)	1.147	0.912–1.442	0.24	Not selected		
eGFR (per mL/min/1.73 m^2)	0.998	0.983–1.013	0.78	Not selected		
CRP (per mg/dL)	0.937	0.693–1.267	0.67	Not selected		
BNP (per pg/dL)	1.000	0.999–1.002	0.50	Not selected		
Left bundle branch block (yes)	1.040	0.963–1.123	0.32	Not selected		
Resting ST segment change (yes)	0.695	0.314–1.536	0.37	Not selected		
Pathologic Q wave (yes)	1.538	0.825–2.870	0.18	Not selected		
LV ejection fraction (per %)	0.988	0.972–1.004	0.15	Not selected		
LVEDV (per mL)	1.002	0.999–1.005	0.20	Not selected		
LVESV (per mL)	1.002	0.999–1.005	0.13	Not selected		
LV mass (per g)	1.006	0.999–1.013	0.095	Not selected		
RWMA (yes)	2.160	1.247–3.743	0.006	0.992	0.533–1.848	0.98
Presence of LGE (yes)	5.841	3.012–11.33	<0.001	6.329	2.662–15.05	<0.001
% LGE (per %)	1.040	1.024–1.056	<0.001	Not selected		
FRS (per %)	0.986	0.947–1.026	0.49	Not selected		
SYNTAX score (per 1)	1.104	1.070–1.139	<0.001	1.085	1.044–1.127	<0.001

ACE angiotensin converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *BNP* brain natriuretic peptide, *BP* blood pressure, *CAD* coronary artery disease, *CRP* C-reactive protein, *ECG* electrocardiography, *eGFR* estimated glomerular filtration rate, *FRS* Framingham risk score, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *LGE* late gadolinium enhancement, *MRI* magnetic resonance imaging

Table 3 C-Statistics for Cox proportional hazards models to predict cardiovascular events

	C-statistics (95 % CI)	Increment in C-statistics
CAD patients ($n = 161$)		
FRS	0.557 (0.503–0.641)	
FRS + the SYNTAX score	0.752 (0.659–0.860)	0.195 (0.066–0.306)
FRS + EF	0.532 (0.520–0.702)	
FRS + EF + the SYNTAX score	0.748 (0.669–0.861)	0.217 (0.066–0.306)
FRS + presence of LGE	0.679 (0.648–0.780)	
FRS + presence of LGE + the SYNTAX score	0.792 (0.728–0.858)	0.114 (0.028–0.148)
FRS + EF + presence of LGE	0.707 (0.638–0.785)	
FRS + EF + presence of LGE + the SYNTAX score	0.796 (0.732–0.860)	0.089 (0.032–0.152)

CI confidence interval, *EF* ejection fraction, *FRS* Framingham risk score, *LGE* late gadolinium enhancement

Table 4 Reclassification of risk by the SYNTAX score in addition to FRS, EF in patients with CAD ($n = 161$)

Risk categories by FRS and EF	New risk categories using FRS and EF and SYNTAX scores		
	Low–intermediate	High	Very high
Patients with cardiovascular events, $n = 56$			
Low–intermediate	0	0	0
High	1	0	8
Very high	5	3	39
Patients without cardiovascular events, $n = 105$			
Low–intermediate	0	0	0
High	10	11	3
Very high	20	38	23

According to Framingham Risk Scores calculated for 2-year cardiovascular event risk, low–intermediate, and very high risk values were <12 %, 12–25 % and >25 %, respectively. Overall net reclassification index was 60.1 % (95 % CI: 38.7–81.5, $p < 0.001$)

EF ejection fraction, *FRS* Framingham risk score, *SYNTAX score* Synergy between PCI and Taxus and cardiac surgery scores

Table 5 Reclassification by SYNTAX score in addition to FRS, EF and LGE MRI in patients with CAD ($n = 161$)

Risk categories by FRS and EF, SYNTAX score	New risk categories using FRS, SYNTAX score and LGE		
	Low–intermediate	High	Very high
Patients with cardiovascular events, $n = 56$			
Low–intermediate	0	1	4
High	2	0	4
Very high	0	3	42
Patients without cardiovascular events, $n = 105$			
Low–intermediate	32	1	1
High	36	5	2
Very high	0	3	25

According to Framingham Risk Scores calculated for 2-year cardiovascular event risk, low–intermediate, and very high risk values were <12 %, 12–25 % and >25 %, respectively. Overall net reclassification index was 40.4 % (95 % CI: 22.5–58.4, $p < 0.001$)

EF ejection fraction, *FRS* Framingham risk score, *SYNTAX score* Synergy between PCI and Taxus and cardiac surgery scores

Clinical implications

Here, we showed that an integrated approach using FRS, EF, LGE MRI and the SYNTAX score can predict future cardiovascular events with C-statistics of 0.796 in patients with known CAD. Although the incremental prognostic value of the SYNTAX score was statistically significant, the magnitude of increment in C-statistics is relatively small (increment of C-statistics = 0.089, Table 3). We believe that main finding of this study is that the SYNTAX score is not necessarily useful as an isolated prognostic predictor, however, when we used the SYNTAX score combined with LGE MRI, it might be useful as a reliable marker which can identify patients who is going to have worse prognosis compared to patients without LGE and with low SYNTAX score.

Study limitation

This single-center retrospective study had a relatively small patient cohort and thus our results require clarification in a multicenter study of a larger population. Although LGE MRI is non-invasive and useful for risk stratification, MRI is contraindicated for patients implanted with pacemakers or cardiovascular defibrillators and those with claustrophobia. Such patients were excluded from the present study. In the study done by Kelle et al. [31], the presence of inducible wall motion abnormality and LGE independently identify patients at increased risk for subsequent cardiac events. The assessment of myocardial ischemia is vital for the risk stratification of CAD patients. Further study is necessary to investigate if the SYNTAX score has incremental prognostic significance over the myocardial ischemia detected by MRI imaging (e.g., inducible wall motion abnormality by cine MRI or pharmacological stress perfusion MRI). Another limitation of this study is that we excluded patients treated with CABG. In the current study, number of CABG patients was relatively small to assess the prognostic value. Therefore, we excluded these patients and focused to assess prognosis in patients with low to moderate SYNTAX score. Further study is necessary to elucidate if the SYNTAX score has incremental prognostic value over LGE MRI in patients with high SYNTAX score. In addition, not all the patients were treated with FFR-guided PCI. FFR can provide us an appropriate indication of PCI procedure. Further study is necessary to investigate if the combination of the SYNTAX score and LGE can predict the occurrence of PCI for FFR-evidenced myocardial ischemia.

Conclusion

An increase in C-statistics showed that adding the SYNTAX score to the Framingham risk model, LVEF and LGE MRI incrementally improved risk stratification. An integrated approach using LGE MRI and the SYNTAX score might be useful for predicting vulnerable patients to develop the future cardiovascular events.

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Conflict of interest There are no conflicts of interest to declare.

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