Assessing the association of appropriateness of coronary revascularization and 1-year clinical outcomes for patients with stable coronary artery disease in China

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Abstract

Background: The Chinese appropriate use criteria (AUC) for coronary revascularization was released in 2016 to improve the use of coronary revascularization. This study aimed to evaluate the association between the appropriateness of coronary revascularization based on the Chinese AUC and 1-year outcomes in stable coronary artery disease (CAD) patients.

Methods: We conducted a prospective, multi-center cohort study of stable CAD patients with coronary lesion stenosis ≥50%. After the classification of appropriateness based on Chinese AUC, patients were categorized into the coronary revascularization group or the medical therapy group based on treatment received. The primary outcome was a composite of death, myocardial infarction, stroke, repeated revascularization, and ischemic symptoms with hospital admission.

Results: From August 2016 to August 2017, 6085 patients were consecutively enrolled. Coronary revascularization was associated with a lower adjusted hazard of 1-year major adverse cardiovascular and cerebrovascular events (MACCEs; hazard ratio [HR]: 0.62; 95% confidence interval [CI]: 0.45–0.86; $P = 0.004$) than medical therapy in patients with appropriate indications ($n = 1617$). No significant benefit in 1-year MACCEs was found after revascularization compared to after medical therapy in patients with uncertain indications ($n = 2658$, HR: 0.81; 95% CI: 0.52–1.25; $P = 0.338$) and inappropriate indications ($n = 1810$, HR: 0.80; 95% CI: 0.51–1.23; $P = 0.308$).

Conclusions: In patients with appropriate indications according to Chinese AUC, coronary revascularization was associated with significantly lower risk of MACCEs at 1 year. No benefit was found in coronary revascularization in patients with inappropriate indications. Our findings provide evidence for using Chinese AUC to guide clinical decision-making.

Clinical trial registration: NCT02880605. https://www.clinicaltrials.gov.

Keywords: Stable coronary artery disease; Appropriate use criteria; Coronary revascularization

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Introduction

During the past few decades, randomized controlled trials have demonstrated that coronary revascularization relieves symptoms but fails to improve survival in patients with stable coronary artery disease (CAD).[1,2] Considering that no benefit to survival has been observed and the potential complications and extra cost from the procedures have remained, the appropriateness of coronary revascularization has frequently been highlighted in stable CAD patients.[3]

Thus, as a supplement to clinical guidelines and to optimize the quality of clinical practice, appropriate use criteria (AUC) for coronary revascularization has been released in the United States, Europe, Japan, and China.[4-6] As AUC integrates evidence, guidelines, and clinician experience to optimize physician decision-making, it is important to validate the association between AUC adherence and clinical outcomes before use is widespread. The international AUC (US AUC) was first released by the American College of Cardiology Foundation and six other societies in 2009 and then validated by real-world data to show that AUC adherence was associated with better outcomes and quality of life.[7,8] These studies have established the foundation for US AUC application in real-world practice.

In China, the rapid development of coronary revascularization and the imbalance ratio (17:1 in 2017) of percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) have rekindled interest in improving the appropriate indications for coronary revascularization.[9-11] However, US AUC may not be applicable to the Chinese population, as Chinese researches and high-frequency clinical scenarios may differ from those of US.[12] Thus, the Chinese AUC system was designed and published in 2016 according to Chinese clinical practice.[13] However, no study exists to validate Chinese AUC. Therefore, our study aimed to evaluate the association between the appropriateness of coronary revascularization based on Chinese AUC and long-term outcomes in patients with stable CAD.

Methods

Ethical approval

Our study protocol was approved by the Ethics Committees of all four participating centers (Fuwai Hospital, No. 2016-778; Peking University People's Hospital, No. 2016PHB134-01; Beijing Chao-Yang Hospital, No. 2016-160; Peking Union Medical College Hospital, No. B177). All eligible patients provided informed consent for this study before undergoing coronary angiography.

Development of the Chinese AUC

In China, a domestic AUC for coronary revascularization was published in 2016, which drew off of experience from the 2012 US AUC methodology [Supplementary Materials, http://links.lww.com/CM9/A154].[13,14] In consideration of differences in Chinese clinical practice, two major changes were made to the 2012 US AUC methodology: (1) a panel of 24 nationally recognized experts were recruited for final recommendations based on both Chinese and foreign literature including six interventional cardiologists, six cardiac surgeons, 12 non-interventional cardiologists, physicians, and statistical and clinical trial design experts; (2) stress test results were classified into "not performed," "positive findings," and "negative findings."

Study design

This study was a prospective, multi-center cohort study designed to evaluate the association between appropriate coronary revascularization based on Chinese AUC and 1-year outcomes. The study was registered at ClinicalTrials.gov (No. NCT02880605).

Participants

To be eligible for inclusion, patients needed to have stable CAD according to the National Cardiovascular Data Registry CathPCI criteria (stable angina, no or silent myocardial ischemia) and at least one coronary lesion stenosis ≥50% determined by elective coronary angiography. Exclusion criteria included prior CABG and those with no corresponding indications in the Chinese AUC. The study participants were enrolled from four big tertiary cardiac centers in Beijing, China. This study sample represented nearly 12% of all PCIs performed in the Beijing region at the time of the study.[15]

Study groups

After providing informed consent, eligible participants were consecutively enrolled in the study. All enrolled patients were divided into three groups according to Chinese AUC recommendations: the appropriate indication group, the uncertain indication group, and the inappropriate indication group. In each of the three groups, patients were then divided into the coronary revascularization group and the medical therapy group according to the treatment received. Two investigators who did not participate in data collection independently reviewed the clinical characteristics of each enrolled patient and classified them into appropriate, inappropriate, or uncertain indication according to Chinese AUC. Any disputes were settled via review by a third investigator, with decision by consensus.

Data collection

Well-trained research nurses interviewed patients during their index hospitalization to collect clinical information focused on data used in Chinese AUC that included: (1) clinical presentation; (2) Canadian Cardiovascular Society (CCS) class; and (3) intensity of anti-ischemic medical therapy. Other Chinese AUC-related data were collected by medical record abstraction, including extent of coronary disease, stress test results, and left ventricular ejection fraction. Patients' demographic, clinical, and procedural characteristics were collected via medical record.

Follow-up process

After 1 year, all participants in the present study were contacted by the research staff via telephone or mail using

standard procedures and forms. In the scenarios where participants reported any adverse events after hospital discharge, their medical records were reviewed for further confirmation. All adverse events of interest were carefully verified and adjudicated by independent clinicians.

Outcome measurements

The primary outcomes were major adverse cardiac and cerebrovascular events (MACCEs) at 1 year which were defined as a composite of all-cause death, non-fatal myocardial infarction, stroke, repeat revascularization, and ischemic symptoms with hospital admission. Secondary outcome measures included the following: (1) all-cause death, (2) non-fatal myocardial infarction, (3) stroke, (4) repeat revascularization, (5) ischemic symptoms with hospital admission. An independent clinical events committee (including cardiologists and cardiac surgeons) adjudicated on all the clinical outcomes. Definitions of the outcomes are provided in Supplementary Materials, http://links.lww.com/CM9/A154.

Statistical analysis

Data are presented as the mean ± standard deviation for continuous variables and as percentages for categorical variables. Baseline characteristics between the coronary revascularization group and the medical therapy group were compared using Chi-square or Fisher exact tests for categorical variables and *t* tests or the Mann-Whitney *U* test for continuous variables.

Univariate and multivariate Cox proportional hazards models were used to examine the associations between treatment appropriateness and clinical outcomes. Variables in baseline characteristics with a $P < 0.1$ in univariate analysis and clinically important variables were included in the multivariate models. In sensitivity analysis, a propensity score was generated for each patient by a multivariable stepwise logistic regression model using all baseline variables with treatment strategy (revascularization *vs.* medical therapy) as a binary outcome.

All comparisons were two-sided, with statistical significance defined as *P* less than 0.05. Analyses were calculated using SPSS version 22.0 (IBM Corp, New York, NY, USA).

Results

Study participants

Study enrollment is presented in Figure 1. There were 6330 patients with stable CAD and at least one coronary lesion stenosis ≥50% from August 2016 to August 2017. We excluded 150 patients with prior CABG, 80 patients without corresponding indications in Chinese AUC and 15 patients with a lack of CCS classification data. In the end, 6085 patients were enrolled in the present study, including 1617 patients (26.6%) in the appropriate indication group, 2658 (43.7%) in the uncertain indication group, and 1810 (29.7%) in the inappropriate indication group. Of the 1617 patients who had appropriate indications, coronary revascularization was performed on 1252 patients, with 1053 receiving a PCI and 199 receiving a CABG. Of the 2658 patient who had uncertain indications, coronary revascularization was performed on 1966 patients, with 1871 receiving a PCI and 95 receiving a CABG. Of the 1810 patients who had inappropriate indications, coronary revascularization was performed in 762 patients, with 753 receiving a PCI and 9 receiving a CABG.

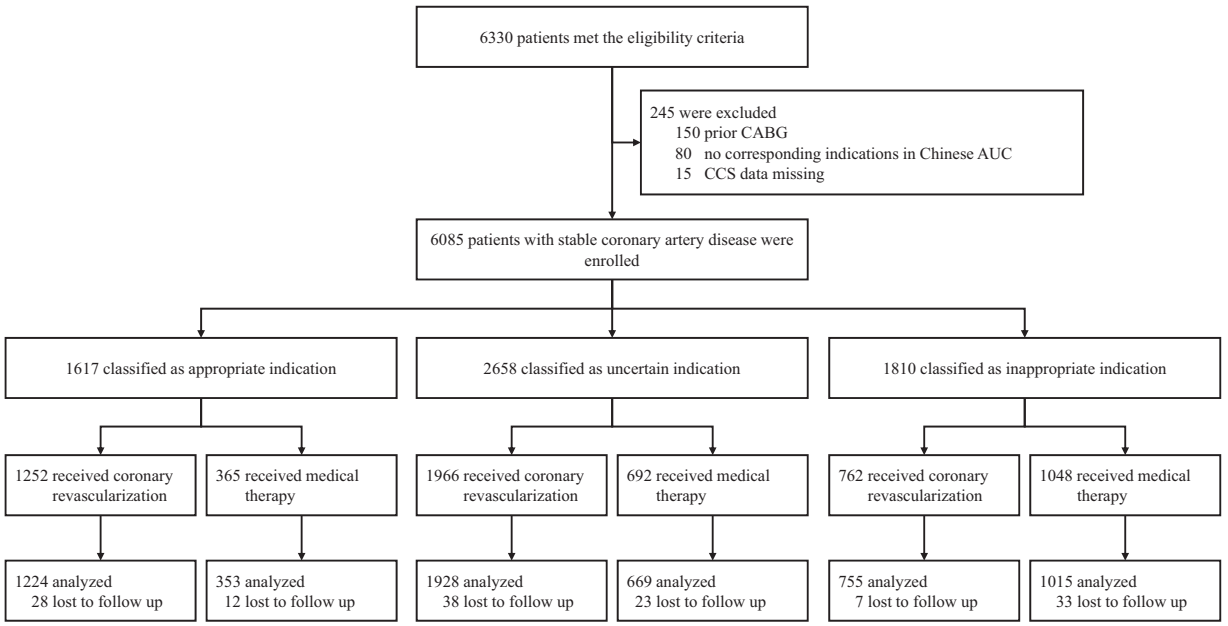

Figure 1: Study flowchart for this prospective, multi-center cohort study of stable CAD patients with coronary lesion stenosis ≥50%. AUC: Appropriate use criteria; CABG: Coronary artery bypass graft; CCS: Canadian Cardiovascular Society; PCI: Percutaneous coronary intervention; CAD: Coronary artery disease.

Table 1: Clinical characteristics according to appropriateness categories and initial treatment.

Variables	Appropriate indications			Uncertain indications			Inappropriate indications		
	Coronary revascularization ($n=1252$)	Medical therapy ($n=365$)	P	Coronary revascularization ($n=1966$)	Medical therapy ($n=692$)	P	Coronary revascularization ($n=762$)	Medical therapy ($n=1048$)	P
Age (years)	60.2 ± 10.0	61.8 ± 10.4	0.011	58.7 ± 10.0	60.9 ± 9.7	<0.001	57.4 ± 10.1	59.4 ± 9.9	<0.001
Men	956 (76.4)	274 (75.1)	0.611	1563 (79.5)	491 (71.0)	<0.001	607 (79.7)	779 (74.3)	0.008
Extent of coronary disease			<0.001			<0.001			<0.001
Mild disease (50%–69%)	0 (0)	0 (0)		1 (0.1)	40 (5.8)		11 (1.4)	598 (57.1)	
1 vessel	138 (11.0)	41 (11.2)		818 (41.6)	352 (50.9)		430 (56.4)	327 (31.2)	
2 vessels	128 (10.2)	32 (8.8)		797 (40.5)	214 (30.9)		321 (42.1)	123 (11.7)	
3 vessels	593 (47.4)	131 (35.9)		350 (17.8)	86 (12.4)		0 (0)	0 (0)	
Left main stenosis	393 (31.4)	161 (44.1)		0 (0)	0 (0)		0 (0)	0 (0)	
Number of anti-anginal medications			0.682			0.332			0.969
0	283 (22.6)	78 (21.4)		663 (33.7)	213 (30.8)		239 (31.4)	330 (31.5)	
1	332 (26.5)	108 (29.6)		680 (34.6)	265 (38.3)		244 (32.0)	337 (32.2)	
2	486 (38.8)	139 (38.1)		486 (24.7)	167 (24.1)		222 (29.1)	309 (29.5)	
3	151 (12.1)	40 (11.0)		137 (7.0)	47 (6.8)		57 (7.5)	72 (6.9)	
Stress test			0.583			0.006			0.919
Positive	45 (3.6)	14 (3.8)		19 (1.0)	11 (1.6)		5 (0.7)	6 (0.6)	
Negative	5 (0.4)	3 (0.8)		5 (0.3)	8 (1.2)		17 (2.2)	26 (2.5)	
Not performed	1202 (96.0)	348 (95.3)		1942 (98.8)	673 (97.3)		740 (97.1)	1016 (96.9)	
Severity of chest pain*			<0.001			<0.001			<0.001
No angina	230 (18.4)	106 (29.0)		618 (31.4)	173 (25.0)		749 (98.3)	744 (71.0)	
CCS class I	320 (25.6)	73 (20.0)		573 (29.1)	237 (34.2)		5 (0.7)	132 (12.6)	
CCS class II	480 (38.3)	126 (34.5)		718 (36.5)	220 (31.8)		8 (1.0)	172 (16.4)	
CCS class III	171 (13.7)	43 (11.8)		48 (2.4)	41 (5.9)		0 (0)	0 (0)	
CCS class IV	51 (4.1)	17 (4.7)		9 (0.5)	21 (3.0)		0 (0)	0 (0)	
Left ventricular ejection			0.001			0.003			0.502
≤35%	13 (1.0)	13 (3.6)		9 (0.5)	11 (1.6)		5 (0.7)	7 (0.7)	
36%–50%	103 (8.2)	44 (12.1)		81 (4.1)	21 (3.0)		42 (5.5)	62 (5.9)	
>50%	1107 (88.4)	301 (82.5)		1819 (92.5)	630 (91.0)		693 (90.9)	935 (89.2)	
Not assessed	29 (2.3)	7 (1.9)		57 (2.9)	30 (4.3)		22 (2.9)	44 (4.2)	
Cardiac history									
Previous MI	62 (5.0)	31 (8.5)	0.011	69 (3.5)	42 (6.1)	0.004	34 (4.5)	60 (5.7)	0.232
Previous heart failure	3 (0.2)	1 (0.3)	1.000	2 (0.1)	3 (0.4)	0.115	1 (0.1)	3 (0.3)	0.643
Previous PCI	42 (3.4)	17 (4.7)	0.243	57 (2.9)	53 (7.7)	<0.001	24 (3.1)	53 (5.1)	0.047
Cerebrovascular disease	170 (13.6)	47 (12.9)	0.729	245 (12.5)	86 (12.4)	0.981	81 (10.6)	128 (12.2)	0.298
Peripheral vascular disease	68 (5.4)	23 (6.3)	0.526	85 (4.3)	49 (7.1)	0.004	40 (5.2)	53 (5.1)	0.855
Cardiac risk factors and medical comorbidities									
Hypertension	787 (62.9)	229 (62.7)	0.967	1185 (60.3)	441 (63.7)	0.109	433 (56.8)	631 (60.2)	0.149
Hyperlipidemia	763 (60.9)	218 (59.7)	0.675	1230 (62.6)	467 (67.5)	0.020	501 (65.7)	680 (64.9)	0.704
Diabetes	430 (34.3)	132 (36.2)	0.521	623 (31.7)	214 (30.9)	0.710	230 (30.2)	301 (28.7)	0.500
COPD	14 (1.1)	4 (1.1)	1.000	16 (0.8)	13 (1.9)	0.020	3 (0.4)	13 (1.2)	0.057
Smoked during the last year	580 (46.3)	156 (42.7)	0.226	967 (49.2)	329 (47.5)	0.457	396 (52.0)	475 (45.3)	0.005
CAD family history	219 (17.5)	71 (19.5)	0.390	343 (17.4)	133 (19.2)	0.295	159 (20.9)	203 (19.4)	0.432

Data were presented as n (%) or mean ± SD. *Severity of chest pain is defined as the symptom status prior current hospitalization according to the National Cardiovascular Data Registry CathPCI criteria. CCS: Canadian Cardiovascular Society; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; COPD: Chronic obstructive pulmonary disease; CAD: Coronary artery disease; SD: Standard deviation.

Baseline characteristics according to treatment and appropriateness categories

The baseline characteristics of patients treated with coronary revascularization or medical therapy, stratified by appropriateness categories, are shown in Table 1. Among patients with appropriate indications, those who received coronary revascularization were younger, more likely to be male, more likely to have severe coronary diseases, lower CCS class, lower left ventricular ejection fraction (LVEF) and were less likely to have cardiac risk factors than those who received medical therapy. Similar trends were also observed in the baseline characteristics among patients with uncertain indications. Among patients with inappropriate indications, those who received coronary revascularization were younger, more likely to have three-vessel diseases, higher CCS class, higher LVEF, and fewer prior myocardial infarctions.

Association between coronary revascularization and outcomes according to appropriateness categories

Among patients who had appropriate indications for coronary revascularization, 1-year MACCEs rates among the coronary revascularization group and medical therapy group were 9.7% and 15.9% respectively [Table 2]. Coronary revascularization was associated with a lower hazard of MACCEs after adjusting for patient baseline characteristics (adjusted hazard ratio [HR]: 0.62, 95% confidence interval [CI]: 0.45–0.86; $P = 0.004$). At 1 year, coronary revascularization also significantly reduced the adjusted hazard of repeat revascularization (3.0% *vs.* 7.9%, adjusted HR: 0.36, 95% CI: 0.22–0.59; $P < 0.001$) and the development of ischemic symptoms with hospital admission (5.9% *vs.* 10.7%, adjusted HR: 0.51, 95% CI: 0.34–0.77; $P = 0.001$) compared with the medical therapy group.

Table 2: One-year outcomes according to appropriateness classification and initial treatment.

Outcomes	Appropriateness classification	Coronary revascularization	Medical therapy	Unadjusted		Adjusted	
				HR (95% CI)	*P*	HR (95% CI)	*P*
Primary outcome							
MACCEs	Appropriate	119 (9.7)	56 (15.9)	0.59 (0.43–0.82)	0.002	0.62 (0.45–0.86)	0.004
	Uncertain	137 (7.1)	50 (7.5)	0.92 (0.67–1.27)	0.609	0.81 (0.52–1.25)	0.338
	Inappropriate	32 (4.2)	54 (5.3)	0.79 (0.51–1.22)	0.277	0.80 (0.51–1.23)	0.308
Secondary outcome							
Death	Appropriate	17 (1.3)	8 (2.5)	0.53 (0.23–1.23)	0.138	0.65 (0.28–1.51)	0.315
	Uncertain	9 (0.5)	4 (0.6)	0.76 (0.23–2.45)	0.640	0.64 (0.23–0.18)	0.406
	Inappropriate	1 (0.1)	8 (0.8)	0.17 (0.02–1.33)	0.090	0.18 (0.02–1.42)	0.103
Myocardial infarction	Appropriate	28 (2.2)	6 (1.9)	1.18 (0.49–2.84)	0.719	1.24 (0.51–3.02)	0.641
	Uncertain	33 (1.7)	2 (0.2)	5.58 (1.34–23.24)	0.018	6.74 (1.47–30.91)	0.014
	Inappropriate	10 (1.3)	2 (0.2)	6.68 (1.47–30.51)	0.014	6.62 (1.45–30.22)	0.015
Stroke	Appropriate	8 (0.6)	1 (0.3)	1.99 (0.25–15.93)	0.516	2.29 (0.28–1.35)	0.437
	Uncertain	13 (0.7)	3 (0.5)	1.46 (0.42–5.11)	0.558	1.50 (0.43–5.20)	0.527
	Inappropriate	5 (0.7)	5 (0.5)	1.34 (0.39–4.61)	0.648	1.31 (0.38–4.53)	0.668
Repeated revascularization	Appropriate	38 (3.0)	25 (7.9)	0.36 (0.22–0.69)	<0.001	0.36 (0.22–0.59)	<0.001
	Uncertain	40 (2.1)	8 (1.2)	1.68 (0.79–3.58)	0.182	1.21 (0.45–3.28)	0.710
	Inappropriate	12 (1.6)	17 (1.7)	0.85 (0.45–1.95)	0.849	0.94 (0.45–1.96)	0.849
Ischemic symptom admitted to hospital	Appropriate	74 (5.9)	34 (10.7)	0.52 (0.35–0.78)	0.002	0.51 (0.34–0.77)	0.001
	Uncertain	77 (4.0)	36 (5.5)	0.71 (0.48–1.05)	0.089	0.57 (0.31–1.02)	0.059
	Inappropriate	17 (2.2)	37 (3.7)	0.58 (0.32–1.05)	0.072	0.58 (0.32–1.04)	0.066

Data were presented as *n* (%). HR to compare outcomes in all appropriateness categories were adjusted for all univariate variables with a $P < 0.1$ in baseline characteristics. HR: Hazard ratio; CI: Confidence interval; MACCEs: Major adverse cardiovascular and cerebrovascular events.

Table 3: One-year MACCEs according to appropriateness classification and initial treatment in patients without stress test results.

Appropriateness classification	Coronary revascularization	Medical therapy	Unadjusted		Adjusted	
			HR (95% CI)	*P*	HR (95% CI)	*P*
Appropriate	120 (9.9)	47 (15.7)	0.61 (0.43–0.85)	0.004	0.63 (0.45–0.88)	0.006
Uncertain	137 (7.1)	49 (7.7)	0.93 (0.67–1.28)	0.642	0.98 (0.70–1.36)	0.889
Inappropriate	31 (4.2)	54 (5.5)	0.76 (0.49–1.18)	0.222	0.76 (0.49–1.18)	0.225

Data were presented as *n* (%). HR to compare outcomes in all appropriateness categories were adjusted using the same model in primary outcome analysis. HR: Hazard ratio; CI: Confidence interval; MACCEs: Major adverse cardiovascular and cerebrovascular events.

In a sub-group analysis of patients without stress test results, coronary revascularization still reduced 1-year MACCEs compared with medical therapy in patients with appropriate indications [Table 3].

In the uncertain indication category, 1-year MACCE rates among the coronary revascularization group and medical therapy group were 7.1% and 7.5%, respectively. No significant reduction in 1-year MACCEs was observed in the coronary revascularization group compared with that in the medical therapy group (adjusted HR: 0.81, 95% CI: 0.52–1.25; $P = 0.338$). There were no significant differences in adjusted 1-year death, myocardial infarction, stroke, repeat revascularization, or development of ischemic symptoms with hospital admission between the coronary revascularization group and the medical therapy group [Table 2].

In the inappropriate indication category, 1-year MACCE rates among the coronary revascularization group and the medical therapy group were 4.2% and 5.3%, respectively. There was no significant difference in the adjusted 1-year MACCEs between the two groups (adjusted HR: 0.80, 95% CI: 0.51–1.23; $P = 0.308$). No significant differences were found in adjusted 1-year death, myocardial infarction, stroke, repeat revascularization, or ischemic symptoms with hospital admission between the two groups [Table 2].

In the sensitivity analysis using propensity score matching, there were no significant differences in baseline character-

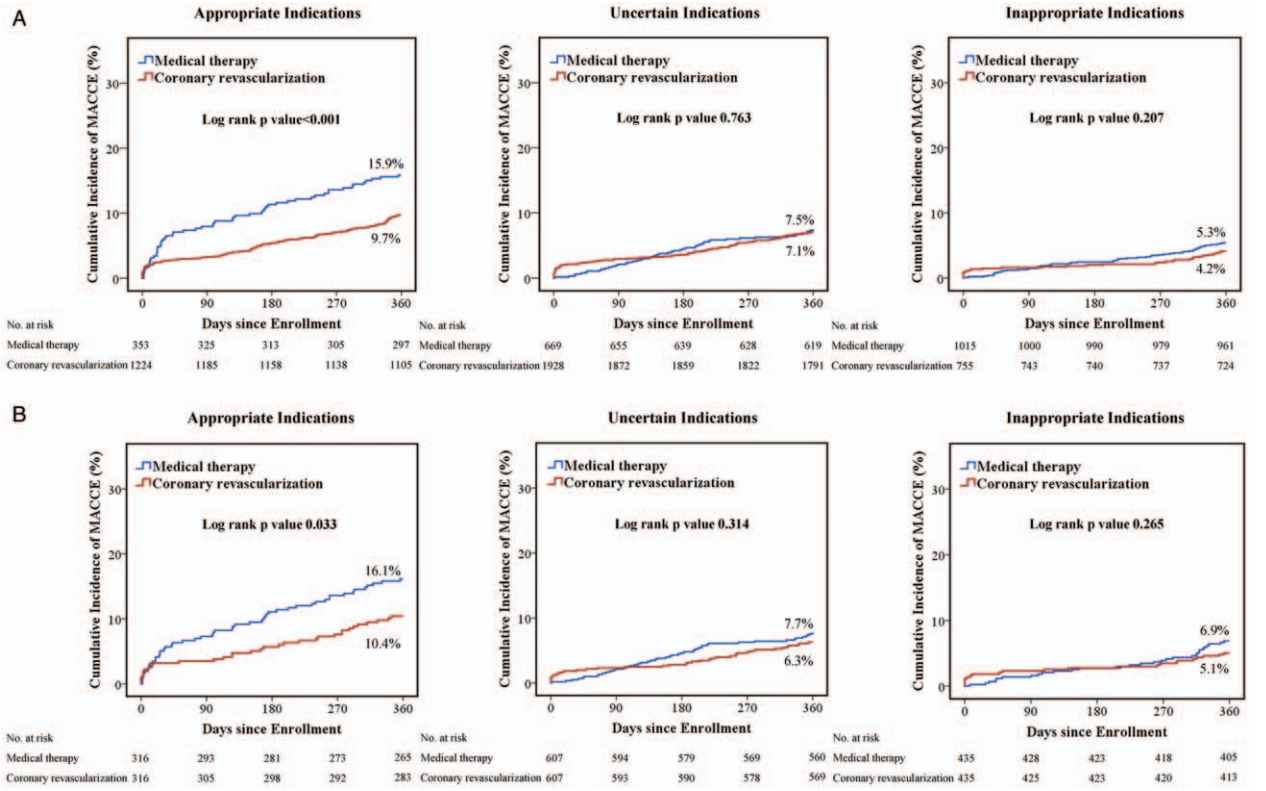

Figure 2: Cumulative incidence of the primary endpoint of initial and propensity score-matched cohorts. Kaplan-Meier curves are shown for 1-year MACCE among initial (A) and propensity score-matched (B) cohorts. HR: Hazard ratio; MACE: Major adverse cardiac events.

istics between the revascularization group and the medical therapy group among all AUC categories [Supplementary Table 1, http://links.lww.com/CM9/A154]. Compared with medical therapy, revascularization continued to be associated with a lower hazard of 1-year MACCEs in patients with appropriate indications [Figure 2]. And there were still no differences in 1-year MACCEs between the patients with either uncertain or inappropriate indications [Figure 2].

Discussion

In this prospective, multi-center, cohort study, we have provided validation for Chinese AUC by demonstrating that coronary revascularization among patients with appropriate indications was associated with significantly reduced risk of 1-year MACCEs compared with that in those who received medical therapy. In contrast, there were no significant differences in 1-year MACCEs between coronary revascularization and medical therapy in patients with uncertain or inappropriate indications.

AUC methodology has been widely accepted as a tool for determining the inappropriateness of coronary revascularization in both western and eastern countries.[4-6] In China, the rapid increase of revascularization procedures (nearly 800,000 in 2017) and disproportionate use of PCI over CABG (17:1 in 2017) has raised critical concerns about procedural inappropriateness.[9-11] Thus, the Chinese AUC was released in 2016, which followed the methodology of the 2012 US AUC with additional innovations. First, a larger and more comprehensive rating panel was invited to determine final appropriateness categories based on both Chinese and foreign literature. Second, the Chinese AUC added the category "stress test not performed" as limited medical resources and potential risks make stress test use in China rare. It is important to also note that the development of the Chinese AUC makes use of AUC methodology to standardize clinical practices that could be used in different regions.

Validating the AUC is an essential step for providing real-world support for AUC methodology.[16] Evaluation of the association between AUC adherence and improved outcomes is necessary, as many AUC scenarios lack high-quality evidence. Two studies previously validated the 2009 US AUC and observed that coronary revascularization was associated with a lower risk of adverse outcomes in stable CAD patients with appropriate indications.[7,8] Additionally, there were no significant differences in the adverse outcomes between coronary revascularization and medical therapy in the uncertain and inappropriate categories.[7,8] In the present study to validate the Chinese AUC, we demonstrated that AUC adherence was significantly associated with a lower adjusted hazard of 1-year MACCEs in patients with appropriate indications. We also found that the use of medical therapy for patients with uncertain and inappropriate indications may decrease the use of medical resources without increasing adverse events. These results were consistent with previous studies for US

AUC validation and demonstrated another successful practice of AUC methodology. However, as a tool of quality measurement, the clinical scenario design should be evaluated for its accurate representation of most situations seen by cardiovascular professionals.[17] In the present study, only 1.3% of patients were unmappable with the Chinese AUC, which demonstrated that the Chinese AUC was practical. The knowledge generated from our study has additional international value, as our successful assessment of the Chinese AUC could be a good example for incorporating AUC methodology at the local and national levels.

It should be noted that revascularization was associated with an increased adjusted risk of myocardial infarction in patients with uncertain (1.4% *vs.* 0.2%) and inappropriate (1.2% *vs.* 0%) indications. These results were consistent with the COURAGE trial which demonstrated that periprocedural myocardial infarction was higher in the PCI group compared with the medical therapy group (3.0% *vs.* 0.8%).[1] However, there were no differences in the risk of myocardial infarction between the two groups in the final 4.6-year follow-up.[1] Thus, further results with longer follow-ups are still necessary to assess the association between revascularization and myocardial infarction in patients with uncertain and inappropriate indications.

The major difference between the Chinese and the US AUC was the addition of the "stress tests not performed" category in the Chinese AUC. Although the guideline for decision-making in patients with stable CAD recommends a risk stratification of stress, recent evidence demonstrates that coronary revascularization without guidance from non-invasive test results was also able to improve prognosis in stable CAD patients.[18] For example, compared with medical therapy, fractional flow reserve (FFR) guided PCI was found to reduce 1-year MACCEs in patients with stable CAD in the FAME II trial, and PCI was found to improve long-term prognosis during the 3.3-year follow-up in patients with stable low-risk CAD in the JSAP trial.[19,20] These results were consistent with sub-group analysis of patients without stress test results in the present study, showing that coronary revascularization reduced the risk of 1-year MACCEs compared with medical therapy in patients with appropriate indications [Table 3]. These results may further support the effectiveness of Chinese AUC.

Remarkably, only 26.6% of the patients in our study had appropriate indications for revascularization, whereas 43.7% had uncertain indications and 29.7% had inappropriate indications. This percentage differed quite dramatically from the previous Canadian study data demonstrating 60.9% of patients with appropriate indications, 20% with uncertain indications, and 19.1% with inappropriate indications.[7] This may be attributed to several factors. First, patients in our study were less likely to have severe angina symptoms and had fewer anti-anginal medications. According to the AUC or clinical guidelines, these patients were more likely to be recommended for intensive medical therapy.[4,14] Second, nearly 97% of patients had no stress test results in our study. Among all 36 of the Chinese AUC recommendations for patients without stress tests results, only 13 scenarios were categorized as appropriate indications [Supplementary Materials, http://links.lww.com/CM9/A154].[12] Thus only 17.5% (927/5298) of patients without stress test results were categorized as having appropriate indications, which reduced the total rate. These reasons might explain the lower rate of appropriate indications in our study. Furthermore, these results might partly reflect that pre-operative assessment for revascularization might be insufficient in China. Further study is still necessary to confirm these results and to improve the decision-making process.

The Chinese AUC may be applicable not only in China but also in many other countries. The recent 2017 US AUC emphasized non-invasive testing for ischemia and FFR to aid in decision making.[4] This may limit the utilization of the US AUC internationally. For instance, in India, Japan, and China, the lack of stress test results has made a large number of patients unmappable in the US AUC.[6,21,22] Additionally, the utilization of FFR was unattainable due to the cost.[4] Even in developed countries such as the USA, FFR-guided PCI accounted for only 2% of the PCIs performed in 2012.[23] Although the recent US AUC followed the most advanced evidence and guidelines, it may fail to represent most situations seen in clinical practices in regions with insufficient stress test and FFR utilization.[24] In these regions, use of the Chinese AUC may be considered more appropriate for decision-making or could be regarded as a quality measurement tool.

Our study has several limitations. First, patients in all cohorts were not randomized, and the heavy bias on grouping is worth noting. This point is further demonstrated by the differences in baseline characteristics between the revascularization and the medical therapy groups in Table 1. Thus, we have prospectively collected confounding variables and adjusted for these data in statistical analysis. Furthermore, we used both multivariate Cox proportional hazards and propensity score-matched models to adjust for the selection bias and confounding variables. Results from the two models drew the same conclusions. Second, we did not evaluate the benefit of quality of life and symptomatic relief after coronary revascularization in all the AUC categories. Third, as a physician-driven tool, the use of CCS classification should be regarded as a limitation. Thus, we trained research nurses to collect the most accurate symptom data possible from the patients by interviewing them during their index hospitalizations.

Using the Chinese AUC for coronary revascularization, we identified that coronary revascularization was significantly associated with lower risk of 1-year adverse outcomes in patients categorized as having appropriate indications. Coronary revascularization had no benefit in 1-year clinical outcomes in patients rated as having uncertain or inappropriate indications. These findings support the Chinese AUC to guide optimal decision-making for patients with stable CAD.

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Conflicts of interest

None.

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