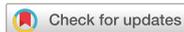


State of the Art Review



2021 Korean Society of Myocardial Infarction Expert Consensus Document on Revascularization for Acute Myocardial Infarction

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AUTHOR'S SUMMARY

The characteristics of patients with acute myocardial infarction (AMI) and its disease patterns in Korea have gradually changed, and revascularization practices have also improved dramatically. Several characteristics associated with revascularization in Korean patients differ from those in other countries. The sophisticated methods of AMI revascularization have led to the need for an expert consensus among interventional cardiologists in Korea. The Task Force on Expert Consensus Document of the Korean Society of Myocardial Infarction has comprehensively reviewed previous literature, and this comprehensive review led to the development of expert consensus.

ABSTRACT

Acute myocardial infarction (AMI) is a fatal manifestation of ischemic heart disease and remains a major public health concern worldwide despite advances in its diagnosis and management. The characteristics of patients with AMI, as well as its disease patterns,

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Conflict of Interest

The authors have no financial conflicts of interest.

Data Sharing Statement

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have gradually changed over time in Korea, and the outcomes of revascularization have improved dramatically. Several characteristics associated with the revascularization of Korean patients differ from those of patients in other countries. The sophisticated state of AMI revascularization in Korea has led to the need for a Korean expert consensus. The Task Force on Expert Consensus Document of the Korean Society of Myocardial Infarction has comprehensively reviewed the outcomes of large clinical trials and current practical guidelines, as well as studies on Korean patients with AMI. Based on these comprehensive reviews, the members of the task force summarize the major guidelines and recent publications, and propose an expert consensus for revascularization in patients with AMI.

Keywords: Fibrinolysis; Myocardial infarction; Percutaneous coronary intervention; Reperfusion; Stents

INTRODUCTION

The characteristics of patients with acute myocardial infarction (AMI), as well as its disease patterns, have gradually changed in Korean patients over time. Moreover, methods and outcomes of revascularization have improved dramatically. For example, the number of patients with non-ST-segment elevation myocardial infarction (NSTEMI) has gradually increased, with these patients exceeding the number of patients with ST-segment elevation myocardial infarction (STEMI) in 2012 (**Figure 1**).¹⁾ This phenomenon can be explained by the introduction of high-sensitivity cardiac troponin assays and improved awareness and management of coronary risk factors. Results from the Korea Acute Myocardial Infarction Registry (KAMIR), nationwide multicenter registry of Korean patients with AMI, have shown that the age of patients presenting with AMI has gradually increased, to a mean 65.0 years in 2018 (**Figure 2**).¹⁾ Patients with NSTEMI are more likely to present with multivessel diseases than patients with STEMI (**Table 1**).

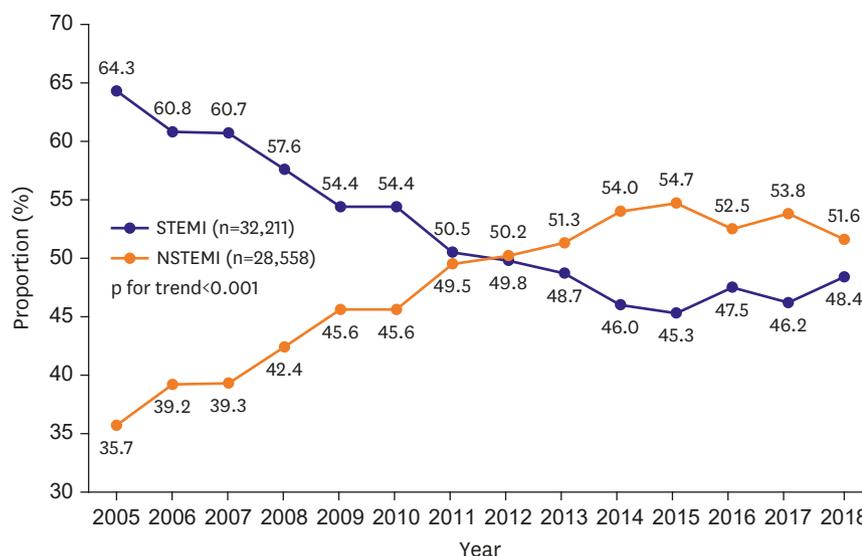


Figure 1. Proportions of acute myocardial infarction patients in Korea with STEMI and NSTEMI from 2005 to 2018. Reproduced with permission from Kim et al. Korean J Intern Med 2019;34:1-10.¹⁾ NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction.

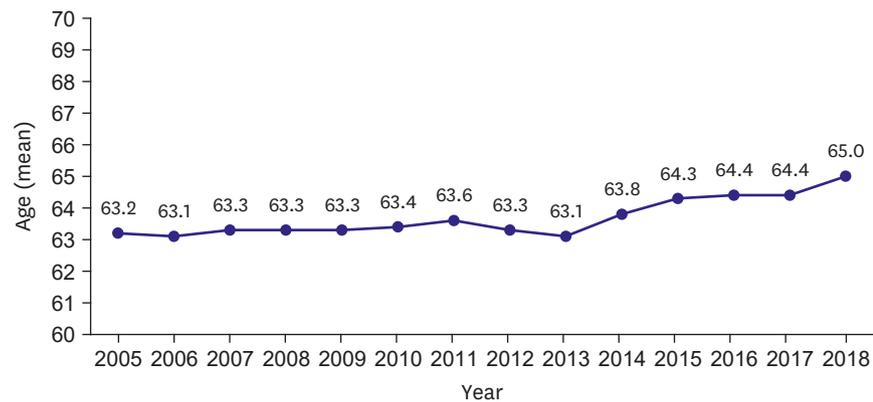


Figure 2. Temporal trends in mean ages of Korean patients with acute myocardial infarction from 2005 to 2018. Reproduced with permission from Kim et al. Korean J Intern Med 2019;34:1-10.¹⁾

A comparison of revascularization for AMI patients in Korea and other countries identified several aspects in Korea that may be considered strengths. First, 99.1% of STEMI patients in Korea underwent primary percutaneous coronary intervention (PCI) in 2018 (**Figure 3A**).¹⁾ Second, drug-eluting stents (DESs), almost exclusively newer-generation DESs, were implanted in 99.6% of patients with primary PCI (**Figure 3B**).¹⁾ Thus, nearly all STEMI patients underwent primary PCI with newer-generation DES, in accordance with recent European Society of Cardiology (ESC) guidelines.²⁾ Third, 25.1% of STEMI patients, compared with 49.6% of NSTEMI patients, underwent primary PCI by the transradial approach (**Table 1**). In addition, one third of STEMI patients underwent thrombus aspiration,

Table 1. Characteristics of Korean patients in the KAMIR-NIH registry study with STEMI and NSTEMI

Variables	STEMI (n=5,895)	NSTEMI (n=5,693)	p-value
Age (years)	62.6±12.8	64.7±12.2	<0.001
Male (%)	4,611 (78.2)	4,084 (71.7)	<0.001
Single-vessel disease	3,110 (52.8)	2,520 (44.3)	<0.001
Multivessel disease	2,785 (47.2)	3,173 (55.7)	0.005
Transradial approach	1,482 (25.1)	2,825 (49.6)	<0.001
Thrombus aspiration (%)	2,158 (36.6)	692 (12.2)	<0.001
Glycoprotein IIb/IIIa inhibitor use (%)	1,269 (21.5)	495 (8.7)	<0.001
BMS	176 (3.0)	178 (3.1)	0.659
First-generation DES			
Paclitaxel-eluting stent	4 (0.1)	8 (0.1)	0.224
Sirolimus-eluting stent	70 (1.2)	76 (1.3)	0.477
Second generation DES			
Zotarolimus-eluting stent	1,240 (21.0)	1,180 (20.7)	0.684
Everolimus-eluting stent	2,720 (46.1)	2,576 (45.2)	0.335
Biolimus-eluting stent	768 (13.0)	756 (13.3)	0.689
Other second generation DES	604 (10.2)	476 (8.4)	<0.001
PCI strategy			
Primary PCI strategy in STEMI	5,704 (96.8)		
Early invasive strategy in NSTEMI		3,386 (59.5)	
Early conservative strategy in NSTEMI		2,095 (36.8)	
Complete revascularization (%)	4,070 (69.0)	3,958 (69.5)	0.574
Additional testing			
Intravascular ultrasound	1,074 (18.2)	1,268 (22.3)	<0.001
Fractional flow reserve	38 (0.6)	119 (2.1)	<0.001
Optical coherence tomography	119 (2.0)	152 (2.7)	0.020

BMS = bare-metal stent; DES = drug-eluting stent; KAMIR-NIH = Korean Acute Myocardial Infarction Registry-National Institute of Health; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

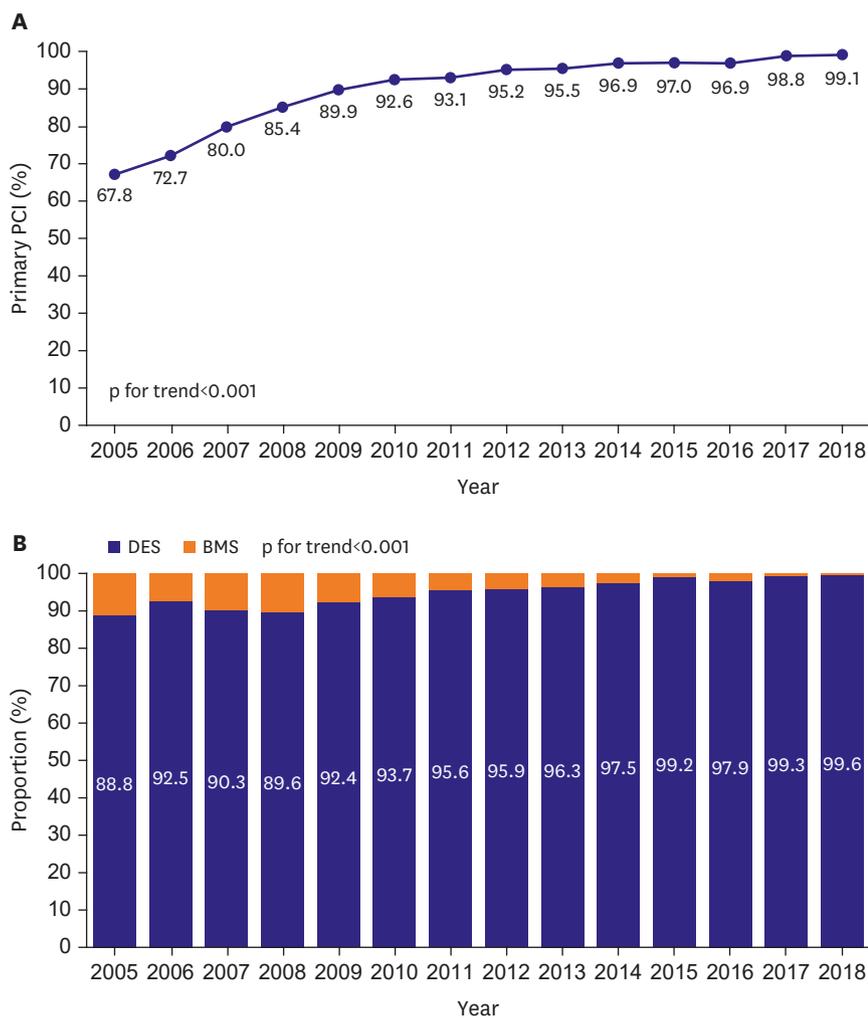


Figure 3. (A) Annual rate of primary PCI in Korean patients with STEMI from 2005 to 2018. (B) Proportions of Korean patients with STEMI implanted with DESs and BMSs from 2005 to 2018. Reproduced with permission from Kim et al. Korean J Intern Med 2019;34:1-10.¹⁾
 BMS = bare-metal stent; DES = drug-eluting stent; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

and one fifth were treated with glycoprotein IIb/IIIa inhibitors. Based on the sophisticated state of AMI revascularization in Korea, an expert consensus is proposed, based on global revascularization guidelines with the integration of Korean data.

PART 1. PRIMARY PERCUTANEOUS CORONARY INTERVENTION FOR ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

Reperfusion therapy

Summary of the major guidelines and recent publications

Transmural ischemia caused by complete obstruction of a coronary artery is the major pathophysiology of STEMI. The most important strategy in preventing ongoing myocardial

Table 2. Important time targets in patients with STEMI

Intervals	Time targets
FMC to STEMI diagnosis	≤10 min
Maximum expected delay from STEMI diagnosis to primary PCI	≤120 min
FMC to device crossing	≤90 min
STEMI diagnosis to start of fibrinolysis	≤10 min
Start of fibrinolysis to evaluation of its efficacy	≤90 min
Start of fibrinolysis to angiography	Up to 2–24 hours

FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

necrosis is to restore blood flow of obstructed coronary arteries using PCI or fibrinolytic agents. The shorter the time to reperfusion, the lower the risk of myocardial damage, necrosis, and microvascular damage. Thus, the time from symptoms to reperfusion is one of the most important factors in determining prognosis in patients with STEMI.

Primary PCI within 12 hours of symptom onset is the preferred reperfusion strategy in patients with STEMI because it was found to be superior to thrombolytic therapy in reducing mortality, reinfarction, and stroke events.^{2,3)} Cardiovascular centers that perform primary PCI should organize skilled teams that require experienced support personnel as well as interventional cardiologists. A delay between symptom and initiation of PCI can reduce the benefits of myocardial salvage, with the survival advantage of primary PCI being maintained for delays of up to 60 or 120 minutes.³⁾ However, because most studies were performed in the 1990s or early 2000s, their results require careful interpretation because of subsequent advances in procedural factors, treatment strategies after thrombolysis, intensive care during the acute periods, and secondary preventive treatment. The important time targets, based on previous studies and guidelines, are summarized in **Table 2**.

If primary PCI cannot be performed within 120 minutes, then fibrinolytic therapy is recommended within 12 hours of symptoms onset in patients without contraindications.^{2,4)} On-site fibrinolytic treatment becomes preferable in a center not capable of performing primary PCI, as the former has been associated with a lower risk of mortality compared with transfer for PCI resulting in a delay longer than 120 minutes.⁵⁾ Following initiation of thrombolysis, it is recommended to transfer to a center capable of performing primary PCI in all patients. Rescue PCI is indicated immediately when fibrinolysis has failed, whereas re-administration of fibrinolytic treatment has not been shown to be beneficial.⁶⁾ Following successful fibrinolysis, defined as a <50% ST-segment resolution at up to 60–90 minutes, typical reperfusion arrhythmia, and disappearance of chest pain, routine early angiography is recommended because it is associated with better prognosis than watchful waiting strategy.^{7,8)} Very early angiography (<2 hours) was not associated with clinical benefits,⁹⁾ with trials showing a median delay between the start of lysis and angiography of up to 2–17 hours.^{10,11)} Therefore, angiography up to 2–24 hours after successful lysis is recommended if there are no contraindications.

There is no general agreement for routine primary PCI strategy in patients starting >12 hours after symptom onset. Primary PCI is indicated for patients with symptoms lasting over 12 hours in the presence of recurrent pain or dynamic electrocardiogram (ECG) changes, suggesting ongoing ischemia, hemodynamic instability, or life-threatening arrhythmias. Studies testing the effects of late recanalization of an occluded infarction-related artery (IRA) found that reperfusion was not beneficial.¹²⁾ Routine PCI of an occluded IRA starting over 48 hours after the onset of STEMI is not indicated.

Evidence from Korea

Data from KAMIR-National Institute of Health (NIH) registry, a nationwide prospective registry that enrolled AMI patients in major university hospitals of South Korea, found that the median door-to-balloon time was 59 minutes, with 92.2% of patients having a door-to-balloon time of <90 minutes. For STEMI patients, door-to-balloon time was independently associated with all-cause mortality (adjusted hazard ratio [HR] per 1 hour increase, 1.90; 95% confidence interval [CI], 1.51–2.39; $p < 0.001$). Shortening door-to-balloon time showed significant survival benefits in Korean STEMI patients.¹³⁾

Data from KAMIR also compared the clinical impact of a pharmacoinvasive strategy with primary PCI in STEMI patients. Most patients ($n=8,878$) underwent primary PCI at a median 105 minutes after symptom onset, whereas 708 patients underwent thrombolysis and subsequent PCI. The 12-month incidences of death (4.4% vs. 4.1%) and major adverse cardiac events (MACE) (7.5% vs. 7.8%) were similar in the 2 groups.¹⁴⁾

Recommendations

- Primary PCI is recommended in patients with STEMI and ischemic symptoms lasting <12 hours.
- Primary PCI is recommended in STEMI patients presenting >12 hours after initial ischemic symptoms, especially in patients with continuing symptoms or dynamic ECG changes suggestive of ongoing ischemia, hemodynamic instability, or life-threatening arrhythmias.
- Primary PCI is not recommended in asymptomatic STEMI patients presenting >48 hours after ischemic symptoms.
- Fibrinolytic therapy is recommended in patients with STEMI and ischemic symptoms of <12 hours duration when primary PCI cannot be performed within 120 minutes.
- Rescue PCI is indicated immediately when fibrinolysis has failed. By contrast, coronary angiography and subsequent PCI are recommended 2 and 24 hours after fibrinolysis in successfully reperfused STEMI patients if there are no contraindications.
- If admitted to a non-primary PCI-capable center, STEMI patients with ischemic symptoms of <12 hours duration are recommended to transfer to a primary PCI-capable center. If timely primary PCI cannot be performed within 120 minutes, the on-site fibrinolytic and transfer strategy should be considered.

Adjunctive therapy

Summary of the major guidelines and recent publications

1) Stenting

Coronary stenting is an essential technique in primary PCI. Compared with balloon angioplasty, bare-metal stent (BMS) implantation was found to reduce the rates of reinfarction and target vessel revascularization.¹⁵⁾¹⁶⁾ DES implantation showed a reduced risk of target vessel revascularization compared with BMSs.¹⁷⁾ In addition, new-generation DESs have shown greater safety and efficacy than first-generation DESs, reducing stent thrombosis and target vessel revascularization rates.¹⁸⁾ These new-generation DESs also resulted in a lower risk of 5 year all-cause mortality than the BMS group.¹⁸⁾¹⁹⁾ Although an alternative strategy of deferred stent implantation into the IRA after 48 hours may reduce microvascular obstruction and improve microcirculatory function, this strategy did not reduce rates of the composite of all-cause mortality, heart failure, myocardial infarction (MI), or repeat revascularization.²⁰⁾

2) Access route

Traditionally, the transfemoral approach has been considered the primary vascular access

route for PCI in STEMI patients. However, the transradial approach has become more common in patients with STEMI, as it has shown favorable clinical outcomes. Transradial intervention has been associated with reduced risks of not only access site bleeding, vascular complications, and transfusion, but also major bleeding and all-cause mortality.²¹⁾²²⁾

3) Thrombus aspiration and glycoprotein IIb/IIIa inhibition

The benefit of routine thrombus aspiration was demonstrated in small trials and meta-analysis. By contrast, large-scale randomized controlled trials showed that routine thrombus aspiration was not superior to conventional PCI.²³⁾²⁴⁾ In addition, thrombus aspiration increased the risk of stroke in the Trial of Routine Aspiration Thrombectomy with PCI vs. PCI Alone in patients with STEMI (TOTAL) trial.²⁵⁾ A subgroup analysis in a meta-analysis of an individual patients found that thrombus aspiration in certain patients, including those with a high thrombus burden, tended to reduce the rate of cardiovascular death while increasing the rates of stroke and transient ischemic attack.²⁶⁾

Studies on the efficacy of glycoprotein (GP) IIb/IIIa inhibitors in patients with STEMI were mainly conducted before the era of oral dual antiplatelet therapy. In recent trials, however, the routine upstream use of GP IIb/IIIa inhibitors before primary PCI did not improve clinical outcomes.²⁷⁾²⁸⁾ By contrast, the use of GP IIb/IIIa inhibitors in bailout therapy has been considered in patients with angiographic evidence of a large thrombus, slow- or no-reflow, and other thrombotic complications.

Evidence from Korea

1) Stenting

A comparison in 687 Korean patients with STEMI showed that DESs significantly reduced the risks of target vessel failure (a composite of cardiac death, non-fatal MI, and target vessel revascularization) compared with BMSs (17.8% vs. 34.5%, $p < 0.01$).²⁹⁾ DES implantation into large vessels (≥ 3.5 mm) has been associated with a reduced need for repeat revascularization compared with BMS implantation.³⁰⁾ An analysis of 509 STEMI patients from the KAMIR between 2009 and 2012 showed that, although the rates of target vessel failure did not differ significantly in patients implanted with DESs and BMSs, the rate of stent thrombosis was significantly lower in the DES group.³¹⁾

Compared with immediate stenting, routine deferred stenting did not significantly reduce infarct size or microvascular obstruction in the Impact of Immediate Stent Implantation vs. Deferred Stent Implantation of Infarct Size and Microvascular Perfusion in Patients With STEMI (INNOVATION) trial, although deferred stenting strategies were safe.³²⁾ Large randomized trials are necessary to confirm the potential benefits of deferred stenting in patients with anterior wall STEMI.

2) Access route

In the KAMIR-NIH registry, transradial intervention significantly reduced the rate of 1 year major cardiocerebrovascular events (MACCEs) (7.1% vs. 10.1%, $p < 0.001$) by reducing the rate of major bleeding (0.6% vs. 2.2%, $p < 0.001$), when compared with transfemoral intervention. Moreover, transradial intervention was associated with significantly lower 1 year rates of MACCE (7.9% vs. 11.3%, $p < 0.001$) and major bleeding (0.6% vs. 2.2%, $p < 0.001$) than transfemoral intervention without a vascular closure device, although 1 year rates of MACCE (7.5% vs. 8.1%, $p = 0.437$) and major bleeding (0.6% vs. 1.0%, $p = 0.409$) were comparable in patients who underwent transradial intervention or transfemoral intervention with a vascular

closure device.³³⁾ Results from the registry of transradial intervention working group showed that transradial intervention was associated with lower incidence of access site hematoma and repeat revascularization in patients with STEMI undergoing primary PCI with DESs.³⁴⁾

3) Thrombus aspiration and glycoprotein IIb/IIIa inhibition

Two studies using the KAMIR data found that thrombus aspiration in patients with STEMI undergoing primary PCI was not clinically beneficial. Subgroup analysis, however, showed some interesting findings in Korean patients. When classified according to total ischemia time, a U-shaped relationship was observed between thrombus aspiration and clinical outcomes, with thrombus aspiration being beneficial in patients who presented with a total ischemia time of 4 to 6 hours.³⁵⁾ Another study showed better clinical outcomes in patients treated concomitantly with GP IIb/IIIa inhibitor and thrombus aspiration, and when the left anterior descending artery was the culprit lesion.³⁶⁾

In contrast to their provisional use, upstream treatment with glycoprotein IIb/IIIa inhibitors may not significantly reduce cardiac events following primary PCI. Major bleeding was higher in patients receiving upstream treatment with glycoprotein IIb/IIIa inhibitors.³⁷⁾

Recommendations

- Stenting with newer-generation DES is recommended over balloon angioplasty or implantation of BMS.
- Routine use of deferred stenting is not recommended. However, it may be considered for some patients, such as those with anterior wall STEMI.
- Radial access is recommended over femoral access. Femoral access can be considered, however, depending on the expertise of the operator or the patient's condition. If femoral access is performed, the use of a percutaneous closing device should be considered.
- Routine use of thrombus aspiration is not recommended. However, it may be considered in lesions with a large thrombotic burden.
- Routine use of glycoprotein IIb/IIIa inhibitors is not recommended. However, they may be considered as bailout therapy for some patients, such as those with no-reflow phenomenon, a high risk of thrombus-related complications, or evidence of a large thrombus.

PART 2. REVASCULARIZATION STRATEGY FOR NON-ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

Summary of the major guidelines and recent publications

In patients with NSTEMI, a routine invasive strategy is commonly performed, unless otherwise indicated.³⁸⁾ A meta-analysis of seven randomized trials that included 8,375 patients with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) showed that an early invasive strategy was associated with lower risks of death, MI, and rehospitalization for unstable angina at a mean follow-up of 2 years.³⁸⁾ Another meta-analysis of eight randomized trials that included 10,412 patients with NSTEMI-ACS found that routine invasive therapy significantly reduced the composite endpoint of death, MI, and recurrent ACS in patients with NSTEMI.³⁹⁾ Although these randomized trials were performed before the development of advanced PCI techniques, before newer-generation DESs and potent P2Y₁₂ inhibitors became available, and also included patients with unstable angina in addition to NSTEMI, routine and earlier implementation of invasive approaches was favored over conservative treatment, especially in patients with NSTEMI.

Table 3. Recommendations of major guidelines for the timing of invasive strategy in patients with NSTEMI-ACS

	2020 ESC Guidelines	2014 ACC/AHA Guidelines
Immediate invasive (<2 hours)	<ol style="list-style-type: none"> 1. Hemodynamic instability 2. Cardiogenic shock 3. Recurrent/refractory chest pain despite medical treatment 4. Life-threatening arrhythmia 5. Mechanical complication of MI 6. Acute heart failure clearly related to NSTEMI-ACS 7. ST-segment depression >1 mm/6 leads plus ST-segment elevation aVR and/or V1 	<ol style="list-style-type: none"> 1. Refractory angina 2. Signs or symptoms of heart failure or new or worsening mitral regurgitation 3. Hemodynamic instability 4. Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy 5. Sustained ventricular tachycardia or ventricular fibrillation
Early invasive (<24 hours)	<ol style="list-style-type: none"> 1. Established NSTEMI diagnosis 2. Dynamic new or presumably new ST/T-segment changes (symptomatic or silent) 3. Resuscitated cardiac arrest without ST-segment elevation of cardiogenic shock 4. GRACE risk score >140 	<ol style="list-style-type: none"> 1. Temporal change in troponin 2. New or presumably new ST depression 3. GRACE risk score >140

ACC = American College of Cardiology; AHA = American Heart Association; aVR = augmented vector right; ESC = European Society of Cardiology; GRACE = Global Registry of Acute Coronary Events; MI = myocardial infarction; NSTEMI-ACS = non-ST-segment elevation acute coronary syndrome; NSTEMI = non-ST-segment elevation myocardial infarction.

The ESC guidelines for the management of NSTEMI-ACS subdivided the timing of invasive strategies as immediate (<2 hours), early (<24 hours), and delayed (<72 hours).⁴⁰⁾ Immediate invasive strategy for NSTEMI-ACS is recommended in the situations shown in **Table 3**. Because very high-risk NSTEMI patients were generally excluded from randomized clinical trials, recommendations for immediate invasive strategy were mostly based on expert consensus. In the Timing of Intervention in Acute Coronary Syndrome (TIMACS) trial, the largest randomized trial to date assessing the optimal timing of intervention in ACS, a comparison of routine early intervention (<24 hours) with delayed intervention (>36 hours) found that the former did not reduce the composite of death, MI, or stroke at 6 months, but did reduce the rates of secondary outcomes, such as death, MI, and refractory ischemia.⁴¹⁾ This trial also revealed that early intervention was superior to delayed intervention in high-risk patients, defined as those with a Global Registry of Acute Coronary Events (GRACE) score >140. A recent meta-analysis of 8 randomized trials that included 5,324 patients with NSTEMI-ACS also found that early invasive strategy may be beneficial for high-risk patients.⁴²⁾

Recommendations for routine invasive strategy and optimal timing of intervention were derived from meta-analyses of randomized trials conducted prior to the introduction of high-sensitivity cardiac troponin assays. The high-sensitivity troponin tests have significantly increased the number of patients diagnosed with NSTEMI. A recent randomized trial of 2,147 patients with NSTEMI-ACS and elevated high-sensitivity troponin levels showed that early (<12 hours) invasive coronary evaluation did not improve overall long-term clinical outcomes compared with evaluation within 2–3 days in patients with NSTEMI. By contrast, early invasive therapy improved long-term outcomes in high-risk patients, defined as those with GRACE scores >140.⁴³⁾

In summary, routine invasive strategy is recommended for NSTEMI patients, and immediate intervention may be required for very high-risk NSTEMI patients. The optimal timing for invasive strategies should be guided by risk stratification in individual patients.

Evidence from Korea

A study of 6,134 NSTEMI patients from the KAMIR registry who underwent PCI between 2005 and 2011 found that an immediate invasive strategy, consisting of PCI within 4 hours, was not associated with improved 12-month clinical outcomes.⁴⁴⁾ However, the GRACE scores were 127±32 in the immediate PCI group and 127±30 in the non-immediate PCI group,

indicating that most of the study population were at intermediate risk. Another study, of 1,027 patients from the KAMIR-NIH registry with NSTEMI and acute heart failure between 2011 and 2015, found no significant differences in mortality, non-fatal MI, or rehospitalization for heart failure during the 12 month follow-up among groups that underwent immediate (<2 hours), early (2–24 hours), delayed (24–72 hours), and late (≥ 72 hours) PCI.⁴⁵⁾ These findings indicate that an immediate invasive strategy was not associated with improved clinical outcomes in NSTEMI patients with intermediate risk and acute heart failure. Further analyses are required to determine the optimal timing of invasive strategies, whether immediate or early, and to optimize risk stratification methods to guide revascularization strategies in patients with NSTEMI.

Recommendations

- Routine invasive strategy is recommended in patients with NSTEMI.
- Immediate invasive strategy is recommended in patients with NSTEMI at very high risk, including those with hemodynamic instability or cardiogenic shock (CS), refractory angina or recurrent ischemic chest pain, life-threatening ventricular arrhythmias, mechanical complications of MI, acute heart failure related to MI, and ST-segment depression >1 mm/6 leads plus ST-segment elevation augmented vector right (aVR) and/or V1.
- High-risk NSTEMI patients without indications for an immediate invasive strategy are recommended to undergo coronary angiography and subsequent PCI within 24 hours.
- The selection of the optimal timing of invasive strategy should be based on risk stratification of individual patients.

PART 3. REVASCULARIZATION STRATEGY FOR NON-CULPRIT LESIONS IN ACUTE MYOCARDIAL INFARCTION

Revascularization strategy for non-culprit lesions in acute myocardial infarction without cardiogenic shock

Summary of the major guidelines and recent publications

Approximately up to 40–50% of STEMI patients have multivessel disease, which is associated with poor prognosis.⁴⁶⁾⁴⁷⁾ Although immediate revascularization is recommended for patients with IRA, the optimum treatment of patients with non-IRA remains unclear. The 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for STEMI patients stated that the immediate revascularization of non-IRA during primary PCI is harmful (Class III).⁴⁸⁾ This recommendation was based on previous observational studies, which showed that there were safety concerns for multivessel revascularization due to the increased risk of procedural complications, increased procedure time, contrast-induced nephropathy, and stent thrombosis.⁴⁸⁾⁴⁹⁾ Later randomized clinical trials altered these recommendations, with the 2015 ACC/AHA guidelines stating that revascularization of non-IRA may be considered (Class IIb),⁵⁰⁾ and the 2017 ESC guidelines stating that revascularization of non-IRA should be considered (Class IIa).²⁾

Traditionally, significant non-IRA lesions were defined as those with >50% stenosis, but recent trials used different standards. For example, the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) and the Complete Versus Lesion-only Primary PCI Trial (CvLPRIT) trials set 50% stenosis as the revascularization threshold,⁵¹⁾⁵²⁾ whereas the Danish Study of Optimal Acute Treatment of Patients With STEMI: Primary PCI in Multivessel Disease (DANAMI-3-PRIMULTI) and the COMPARE-ACUTE trials set a fractional flow

reserve (FFR) of 0.80 as the criterion for revascularization.⁵³⁾⁵⁴⁾ The Complete vs. Culprit-Only Revascularization Strategies to Treat Multivessel Disease After Early PCI for STEMI (COMPLETE) used a diameter of ≥ 2.5 mm and visually estimated $\geq 70\%$ stenosis or $\text{FFR} \leq 0.8$ with a visual stenosis of $\geq 50\%$ as revascularization thresholds.⁵⁵⁾

The PRAMI trial of STEMI patients without CS found that immediate preventive PCI of non-IRA with $>50\%$ stenosis was associated with favorable clinical outcomes, including lower rates of cardiac death, MI, and refractory angina.⁵¹⁾ The CvLPRIT trial showed that in-hospital complete revascularization for non-IRA, performed either at the time of the first PCI or before discharge, significantly lowered the 12 month risk of MACE compared with an IRA-only strategy.⁵²⁾ Results from the DANAMI-3-PRIMULTI trial showed that complete revascularization with staged non-IRA PCI guided by FFR measurement was associated with a better prognosis than IRA-only treatment.⁵³⁾ The COMPARE-ACUTE trial found that the incidence of MACCE in the FFR-guided complete revascularization group was lower than in the IRA-only group of STEMI patients with multivessel disease.⁵⁴⁾ In the COMPLETE trial, which included 4,041 patients, the HR for the coprimary endpoint of cardiovascular death and recurrent MI in patients who underwent complete revascularization was 0.74 (95% CI, 0.60–0.91; $p=0.004$).⁵⁵⁾

In patients with STEMI without CS, there is no recommendation for the timing of revascularization for non-IRA: on-site vs. staged complete revascularization.²⁾ Results from the COMPLETE trial also showed that the timing of the second non-IRA intervention had no effect on clinical outcomes.⁵⁵⁾ In NSTEMI patients with multivessel disease, complete revascularization during index PCI may be considered.⁴⁰⁾ Results from the Impact of Different Treatment in Multivessel Non ST Elevation Myocardial Infarction Patients: One Stage Versus Multistaged Percutaneous Coronary Intervention (SMILE) trial, which enrolled 527 patients with multivessel NSTEMI showed that complete single-stage PCI resulted in fewer MACE events (HR, 0.55; 95% CI, 0.36–0.83; $p=0.004$).⁵⁶⁾ This benefit was largely determined by a significant reduction in repeat revascularization, with no significant between-group differences in cardiac death and MI rates.

Evidence from Korea

Results from the Incheon-Bucheon Cohort of Patients Undergoing Primary PCI for Acute STEMI (INTERSTELLAR) registry, which enrolled 705 STEMI patients with multivessel disease, showed that the incidence of MACE was lower in patients who underwent non-IRA PCI than in those who underwent IRA-only PCI alone (11.5% vs. 18.5%; HR, 0.56; 95% CI, 0.37–0.86; $p<0.01$; adjusted HR, 0.64; 95% CI, 0.40–0.99; $p=0.04$).⁵⁷⁾ A single-center study evaluating the impact of non-IRA PCI on 6 year clinical outcomes in propensity score matched groups found that non-IRA PCI did not reduce the incidence of ADHF (HR, 1.63; 95% CI, 0.63–4.22; $p=0.311$), whereas IRA-only PCI increased the risk of MACE (HR, 1.73; 95% CI, 1.09–2.74; $p=0.021$).⁵⁸⁾ Results from the KAMIR registry showed that multivessel revascularization in patients with NSTEMI achieved better clinical outcomes than culprit-only revascularization (HR, 0.66; 95% CI, 0.45–0.96; $p=0.031$).⁵⁹⁾

A study of 606 patients with STEMI and multivessel disease from the KAMIR-NIH registry who underwent complete revascularization found that multivessel multi-staged PCI was associated with better clinical outcomes than multivessel single-staged PCI (HR, 0.42; 95% CI, 0.19–0.92; $p=0.030$).⁶⁰⁾

Recommendation

- Multivessel complete revascularization for non-IRA should be considered in AMI patients without CS. Optimal timing of non-IRA intervention may be based on individual patient condition.

Revascularization strategy for non-culprit lesions in acute myocardial infarction with cardiogenic shock*Summary of the major guidelines and recent publications*

The ESC guidelines recommend that routine revascularization of non-IRA lesions should not be performed during primary PCI for patients with CS.⁶¹ Results from the Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial found that the 30-day risk of a composite of death or severe renal failure leading to renal replacement therapy was lower in those who initially underwent PCI of the IRA-only than in those who underwent immediate multivessel PCI.⁶²

Evidence from Korea

Analyses of data from the KAMIR and Korean Working Group in Myocardial Infarction (KorMI) registries showed that in-hospital mortality rates in patients with CS did not differ in those who underwent non-IRA and IRA-only PCI (31.7% vs. 24.5%; $p=0.247$).⁶³

Findings from the KAMIR-NIH registry showed that the risks of all-cause death and non-IRA repeat revascularization were significantly lower in the multivessel PCI group than in the IRA-only PCI group (HR, 0.59; 95% CI, 0.43–0.82; $p=0.001$; HR, 0.39; 95% CI, 0.17–0.90; $p=0.028$).⁶⁴ Patients undergoing non-IRA PCI during the index hospitalization were included in the multivessel PCI group, which showed favorable long-term clinical outcomes. In the CULPRIT-SHOCK study, however, 17.7% of patients in the IRA-only PCI group underwent staged multivessel revascularization. In the assessments of long-term outcomes, data from the KAMIR-NIH registry showed that the 3-year risks of recurrent MI ($p=0.030$) and non-IRA repeat revascularization ($p=0.017$) were significantly lower in patients who underwent multivessel than IRA-only PCI.⁶⁵ In addition, the 1-year risk of repeat revascularization in the CULPRIT-SHOCK study was significantly lower in the multivessel than in the IRA-only PCI group.⁶⁶

Recommendation

- In AMI patients with CS, emergent PCI of the culprit lesion is recommended, whereas routine immediate revascularization of non-IRA is not recommended. Staged multivessel PCI may be considered.

PART 4. MECHANICAL CIRCULATORY SUPPORT DEVICES IN ACUTE MYOCARDIAL INFARCTION COMPLICATED BY CARDIOGENIC SHOCK**Summary of the major guidelines and recent publications**

Despite advances in knowledge and treatment techniques, AMI, complicated by CS, remains a leading cause of death worldwide and a challenge for interventional cardiologists.⁶⁷ Temporary mechanical circulatory support (MCS) devices have been widely used as they can provide hemodynamic cardiopulmonary support until cardiac function recovers in patients with CS refractory to conventional medical therapy, such as fluid or vasopressive agents. Less is known,

Table 4. Recommendations of major guidelines for patients with acute myocardial infarction complicated by cardiogenic shock

	2017 ESC Guidelines	2013 ACC/AHA Guidelines 2017 Scientific Statement
Medical therapy	Inotropic/vasopressor agents may be considered for hemodynamic stabilization (Class IIb, LOE C)	Norepinephrine is associated with fewer arrhythmias and may be the vasopressor of choice in many patients with cardiogenic shock
IABP	1. IABP should be considered in patients with hemodynamic instability/cardiogenic shock due to mechanical complications (Class IIa, LOE C) 2. Routine use of IABP is not indicated (Class III, LOE B)	The use of IABP can be useful for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy (Class IIa, LOE B)
MCS	Short-term mechanical support may be considered in patients in refractory shock (Class IIb, LOE C)	1. Alternative left ventricle assist devices for circulatory support may be considered in patients with refractory cardiogenic shock (Class IIb, LOE C) 2. Temporary over durable MCS as a first-line device should be considered when immediate stabilization is needed to enable recovery of the heart and other organ systems 3. VA-ECMO may be the preferred temporary MCS option when there is poor oxygenation that is not expected to rapidly improve

ACC = American College of Cardiology; AHA = American Heart Association; ECMO = extracorporeal membrane oxygenation; ESC = European Society of Cardiology; IABP = intra-aortic balloon pump; MCS = Mechanical Circulatory Support; LOE = level of evidence; STEMI = ST-segment elevation myocardial infarction; VA = veno-arterial.

however, about the benefits of percutaneous MCS, including the intra-aortic balloon pump (IABP), Tandem Heart® (Cardiac Assist, Inc., Pittsburgh, PA, USA), Impella® (Abiomed, Danvers, MA, USA), and extracorporeal mechanical oxygenation (ECMO). To evaluate the efficacy of IABP, the multicenter Intra-aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial randomized 600 AMI patients complicated with CS to IABP or no IABP; however, there were no between-group differences in 30-day mortality and long-term mortality.^{68,69} In real-world practice, Tandem Heart may not be useful in an emergency because it requires fluoroscopy-guided transeptal puncture to advance a 21 Fr inflow cannula into the left atrium. Furthermore, a small randomized trial comparing the efficacy of Impella CP and IABP found no difference in 30-day mortality rate in CS patients requiring mechanical ventilation.⁷⁰ To date, no randomized trial has shown that veno-arterial (VA)-ECMO is more effective than conventional therapy or other MCS devices. In our opinion, ECMO is more likely to have the greatest advantage in emergent situations because it can be readily inserted without delay, while providing full circulatory support. Current guidelines based on evidence of previous studies are described in **Table 4**.

Evidence from Korea

There are limited observational data on the efficacy of IABP and ECMO in Korean AMI patients, but there are no data on Impella or Tandem Heart as they are not yet commercially available in South Korea. An assessment of 1,359 patients in the KAMIR with AMI complicated by cardiac arrest from 2005 to 2014 found that the use of IABP had no clinical benefit after propensity score matching.⁷¹ Several retrospective, single-center studies have suggested that use of ECMO could improve survival in AMI patients complicated by CS.⁷² A comprehensive risk prediction model has also been developed from clinical and angiographic data of 145 AMI patients who were treated with VA-ECMO. The derived AMI-ECMO risk score can help to predict early prognosis in AMI patients undergoing VA-ECMO.⁷³ Recently, a dedicated multicenter CS registry named RESCUE was instituted and is expected to provide valuable information on the clinical aspects and prognosis of Korean AMI patients complicated by CS.

Recommendations

- Routine use of IABP is not indicated.
- IABP should be considered in patients with CS due to mechanical complications, such as mitral regurgitation, ventricular septal defect, or ventricular free wall rupture.
- Short-term mechanical supports may be considered in patients in refractory shock.
- VA-ECMO may be the preferred temporary MCS option when there is poor oxygenation or during cardiopulmonary resuscitation.

PART 5. MYOCARDIAL INFARCTION WITH NON-OBSTRUCTIVE CORONARY ARTERIES

Summary of the major guidelines and recent publications

The 2018 Fourth Universal Definition of Myocardial Infarction has defined myocardial infarction with non-obstructive coronary arteries (MINOCAs) as AMI without angiographic obstructive coronary artery disease (CAD) (<50% diameter stenosis in a major epicardial vessel).⁷⁴⁾ MINOCA is considered an ischemic mechanism, making it necessary to exclude nonischemic causes such as myocarditis or Takotsubo cardiomyopathy, and to confirm that obstructive CAD has not been inadvertently overlooked. MINOCA is thought to affect up to 6–8% of patients presenting with AMI and to be more common in women than in men.⁷⁴⁾ The possible mechanisms for MINOCA include rupture of atherosclerotic plaque, coronary thrombosis and emboli, microvascular disease, coronary spasm, and spontaneous coronary artery dissection. In addition to routine methods, such as electrocardiography, troponin assays, and invasive coronary angiography, further diagnostic modalities, such as provocation test for vasospasm, intravascular imaging, and cardiac magnetic resonance, may be considered. Treatment of MINOCA depends on the mechanism revealed by the abovementioned tests. A systematic review found that the 12-month all-cause mortality rate in patients with MINOCA was 4.7% (95% CI, 2.6–6.9%).⁷⁵⁾ Large-scale registry data suggest that treating patients with renin-angiotensin system (RAS) inhibitors and statins can reduce all-cause mortality in MINOCA patients.⁷⁶⁾

Evidence from Korea

Analysis of data from the KAMIR registry reported that clinical outcomes and prognosis in patients with MINOCA were similar to those in patients with 1- or 2-vessel CAD presenting with AMI, with 12 month MACE rates of 7.8% and 12.2%, respectively (p=0.359).⁷⁷⁾ In the KAMIR-NIH registry, a comparison of MINOCA and MI with obstructive CAD showed that the 2 year risks of all-cause mortality (9.1% vs. 8.8%, p=0.832) and recurrent MI (2.8% vs. 2.2%, p=0.528) were similar.⁷⁸⁾ Treatment of MINOCA patients with RAS inhibitors and statins was associated with significantly lower risks of all-cause mortality. Another analysis of data from the KAMIR registry showed that the rates of all-cause death (4.6% vs. 4.5%, p=0.941) and recurrent MI (0.2% vs. 0.5%, p=0.527) were similar in MI patients with vasospasm and patients with acute obstructive MI.⁷⁹⁾

Recommendation

- Because data on MINOCA remain insufficient, there is no general consensus on appropriate diagnostic and treatment methods. However, depending on the patient's clinical situation, the mechanism of MINOCA may be analyzed, using modalities such as provocation test for vasospasm, intravascular imaging, or cardiac magnetic resonance. Appropriated secondary preventive treatment may be considered accordingly.

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