

## Ten-Year Outcomes Following Revascularization Strategies for Non-ST-Segment Elevation Myocardial Infarction and Multivessel Disease

### ST Segment Yükselmesi Olmayan Miyokard Enfarktüsü ile Başvuran Çoklu Damar Hastalarında Revaskülarizasyon Stratejilerinin On Yıllık Sonuçları

#### ABSTRACT

**Objective:** There remain conflicting recommendations regarding revascularization strategies for patients with non-ST-segment elevation myocardial infarction (NSTEMI) and multivessel disease (MVD). This study aimed to compare the long-term outcomes of different revascularization strategies.

**Method:** Patients with similar characteristics were categorized into three groups: immediate complete revascularization (ICR), staged complete revascularization (SCR), and non-complete revascularization (NCR). The SCR group was further divided based on the time interval between the index and staged procedures: SCR  $\leq$  24 hours and SCR  $>$  24 hours. Cardiac composite outcomes included the total number of cardiac deaths and recurrent myocardial infarction during the follow-up period.

**Results:** Out of 14,511 screened patients, 316 were included in the analysis. The results showed a significant difference in risk between SCR and ICR (hazard ratio [HR] (95% confidence interval [CI]): 0.27 (0.15–0.47);  $P = 0.001$ ). There was no significant difference between NCR and SCR (HR (95% CI): 1.06 (0.61–1.84);  $P = 0.832$ ). The SCR group was divided into two groups based on the time interval from the first to the second procedure (time interval [TI]  $\leq$  24 hours in the SCR1 group, and TI  $>$  24 hours in the SCR2 group). The frequency of cardiac composite outcomes was lower in SCR1 compared to SCR2 (16.7% vs. 47.1%;  $P = 0.038$ ).

**Conclusion:** Our findings support the use of ICR and SCR completed within 24 hours due to their favorable long-term outcomes in patients with MVD and NSTEMI.

**Keywords:** Complete revascularization, infarct-related artery, multivessel disease, revascularization strategies, non-ST-segment elevation myocardial infarction

#### ÖZET

**Amaç:** ST segment yükselmesi olmayan miyokard enfarktüsü (NSTEMI) ve çok damar hastalığı olan hastalar için revaskülarizasyon stratejileriyle ilgili çelişkili öneriler devam etmektedir. Çalışmamızda revaskülarizasyon stratejilerinin uzun vadeli sonuçlarını karşılaştırmayı amaçladık.

**Yöntem:** Benzer özelliklere sahip hastalar üç gruba ayrıldı: hemen tam revaskülarizasyon (ICR), aşamalı tam revaskülarizasyon (SCR) ve tam olmayan revaskülarizasyon grubu (NCR). SCR grubu, indeks ve aşamalı prosedürler arasındaki zaman aralığına göre iki gruba bölündü: SCR  $\leq$  24 saat ve SCR  $>$  24 saat. Kardiyak bileşik sonuçlar, takip süresi boyunca toplam kardiyak ölüm ve tekrarlayan miyokard enfarktüsü sayısını içeriyordu.

**Bulgular:** Taranan 14.511 akut koroner sendrom hastasından 316 NSTEMI hastası analize dahil edildi. SCR ve ICR arasında kardiyak bileşik sonuç riski açısından anlamlı bir fark olduğunu gösterildi (HR (95% CI): 0,27 (0,15–0,47);  $P = 0,001$ ). NCR ve SCR arasında anlamlı bir fark olmadığı gösterildi (HR (95% CI): 1,06 (0,61–1,84);  $P = 0,832$ ). SCR grubu, ilk işlemten ikinci işleme kadar geçen zaman aralığına (TI) göre iki gruba ayrıldı (SCR1 grubunda TI  $\leq$  24 saat ve SCR2 grubunda TI  $>$  24 saat). Kardiyak bileşik sonuç sıklığı, SCR1 grubunda SCR2 grubuna göre daha düşüktü (%16,7 ve %47,1;  $P = 0,038$ ).

**Sonuç:** Çalışma sonuçlarımız, çok damar hastası NSTEMI hastalarında uzun dönem olumlu sonuçları sebebiyle ICR ve 24 saat içinde tamamlanan SCR stratejisini desteklemektedir.

**Anahtar Kelimeler:** Tam revaskülarizasyon, enfarkt ilişkili damar, çok damar hastalığı, revaskülarizasyon stratejileri, ST-segment yükselmesiz miyokard enfarktüsü

#### ORIGINAL ARTICLE KLİNİK ÇALIŞMA

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The combination of multivessel disease (MVD) and acute coronary syndrome is associated with a higher risk of major adverse cardiac events (MACEs).<sup>1</sup> In hemodynamically stable patients with ST-segment elevation myocardial infarction (STEMI) and MVD, complete revascularization is recommended either during the index percutaneous coronary intervention (PCI) procedure or within 45 days.<sup>2</sup> There is extensive evidence in the literature addressing MVD in patients presenting with STEMI. However, there is limited data to guide the management of MVD in patients presenting with non-ST-segment elevation myocardial infarction (NSTEMI). Studies comparing complete revascularization and infarct-related artery (IRA)-only PCI in NSTEMI patients are needed.

Observational and non-randomized studies suggest that complete revascularization is associated with fewer MACEs during follow-up. However, the findings of these studies leave gaps in the evidence. The current European Society of Cardiology (ESC) guidelines provide a Class IIa recommendation for complete revascularization, preferably during the index procedure, in patients with MVD presenting with NSTEMI.<sup>3</sup> This recommendation has not yet been elevated to Class I and is based on the SMILE trial (Impact of Different Treatment in Multivessel Non-ST Elevation Myocardial Infarction Patients: One Stage Versus Multistaged Percutaneous Coronary Intervention).<sup>4</sup> The SMILE trial demonstrated a lower risk of MACEs with immediate complete revascularization compared to staged complete revascularization. There remain conflicting recommendations for patients with NSTEMI and MVD regarding revascularization limited to the IRA versus revascularization of all significant stenoses during the index procedure. The optimal timing of non-IRA revascularization in an immediate or staged procedure remains unclear.<sup>3-6</sup> We aimed to compare the outcomes of immediate complete revascularization, staged complete revascularization, and IRA-only revascularization in patients with NSTEMI and MVD.

## Materials and Methods

The data of patients admitted to our hospital with a diagnosis of acute coronary syndrome (ACS) between 2014 and 2024 were retrospectively reviewed. MVD was defined as stenosis of  $\geq 50\%$  in at least two coronary arteries. Eligible patients were required to have at least one angiographically significant non-IRA lesion. Revascularization of the IRA or non-IRA was considered successful if the final residual stenosis after PCI was  $< 30\%$ . An interventional cardiologist with ten years of experience analyzed the angiography films using the hospital information-processing system. The cardiologist was blinded to the patients' identities and clinical outcomes. The determination of the IRA was based on angiographic visualization. Features such as intraluminal filling defects, acute occlusion, ulcers, dissection, intraluminal flaps, or irregularities were used to identify the IRA.

Patients presenting with unstable angina pectoris or STEMI were excluded from the study. Additionally, we excluded patients who did not undergo coronary angiography. Other exclusion criteria included patients with a history of prior PCI, coronary artery bypass grafting, or stroke. Patients with a glomerular filtration rate  $\leq 50$  mL/min/1.72m<sup>2</sup> or Killip class  $\geq 2$  (indicative of rales, pulmonary edema, or cardiogenic shock) at admission were also excluded to minimize confounding factors.

## ABBREVIATIONS

|                   |   |
|-------------------|---|
| ACS               | Acute coronary syndrome   |
| ESC               | European Society of Cardiology  |
| FFR               | Fractional flow reserve   |
| ICR               | Immediate complete revascularization  |
| IRA               | Infarct-related artery  |
| MACEs             | Major adverse cardiac events  |
| MVD               | Multivessel disease   |
| NCR               | Non-complete revascularization  |
| NSTEMI            | Non-ST-segment elevation myocardial infarction  |
| PCI               | Percutaneous coronary intervention  |
| SCR               | Staged complete revascularization   |
| SENIOR-RITA trial | Secondary Prevention in the Elderly: Randomized Intervention Trial of Angina  |
| SMILE trial       | Impact of Different Treatment in Multivessel Non-ST Elevation Myocardial Infarction Patients: One Stage Versus Multistaged Percutaneous Coronary Intervention |

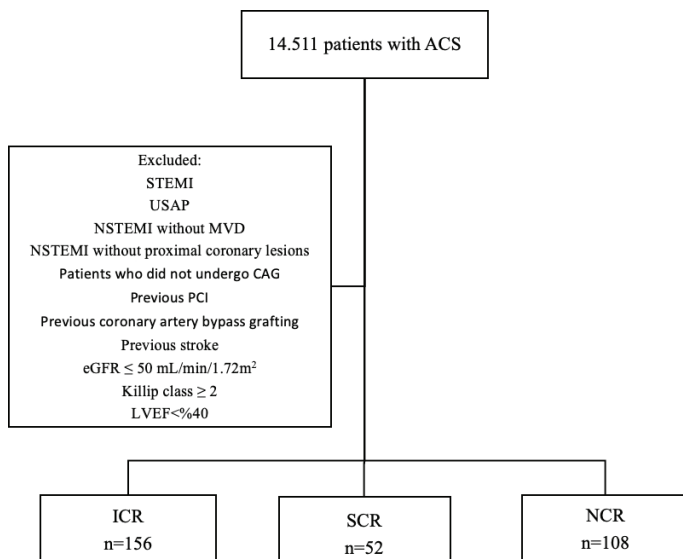
Three distinct groups were formed from the patient population: immediate complete revascularization (ICR), staged complete revascularization (SCR), and the non-complete revascularization group (NCR). The ICR and SCR groups were classified as having complete revascularization, while the IRA-only PCI group was categorized as having non-complete revascularization.

Revascularization strategies were determined for patients based on the following criteria:

- In our clinic, ICR is the primary consideration for all patients with MVD and NSTEMI.
- SCR was selected under specific circumstances, including prolonged duration of the index procedure, excessive use of contrast material, presence of complex lesions, puncture site bleeding, hypotension, patient noncompliance, or preference to perform the staged procedure during regular daytime hours. SCR was defined as complete revascularization performed within 30 days after IRA, as no definitive guideline exists in the literature regarding this timeline.
- Patients who declined the second PCI were included in the NCR group.
- The choice of access site and procedural details, including stent type, diameter, and length, was left to the discretion of the invasive cardiologist.
- Dual antiplatelet therapy was maintained for at least one year, followed by aspirin monotherapy beyond the initial 12 months.

## Study Endpoints

Data were obtained from the hospital information system and death certificates. Clinical events were analyzed from the follow-up period after the last procedure in the SCR group and after the index procedure in the ICR and NCR groups. The follow-up outcomes included the cardiac composite outcome, all-cause mortality, cardiac death, recurrent myocardial infarction (MI), and any rehospitalization. The cardiac composite outcome was defined as the sum of cardiac death and recurrent MI. Angina accompanied by elevated troponin levels was classified as recurrent MI.



**Figure 1.** The study population selection and the patients included and excluded in the present study are shown.

ACS, Acute Coronary Syndrome; CAG, Coronary Angiography; eGFR, Estimate Glomerular Filtration Rate; LVEF, Left Ventricular Ejection Fraction; ICR, Immediate Complete Revascularization; SCR, Staged Complete Revascularization; STEMI, ST-Elevation Myocardial Infarction; NCR, Non-Compleat Revascularization; NSTEMI, Non-St-Elevation Myocardial Infarction; USAP, Unstable Angina Pectoris; PCI, Percutaneous Coronary Intervention.

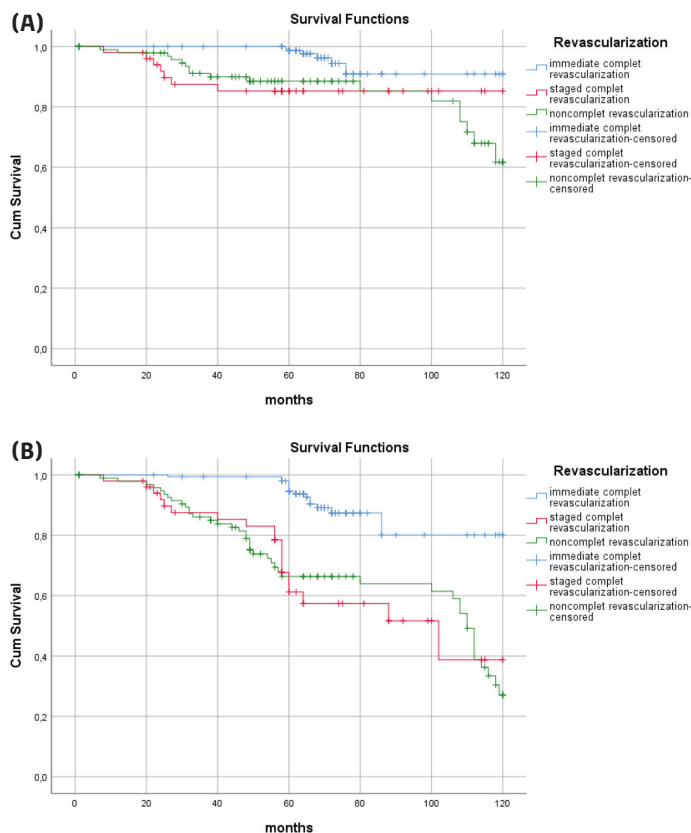
Ethical approval was obtained from the Tekirdağ Namık Kemal University Non-Interventional Clinical Research Ethics Committee (Approval Number:2024.228.07.03, Date: 30.07.2024). All patients provided written informed consent for the use of their data in the study. The study was conducted in accordance with the guidelines of the Declaration of Helsinki. Artificial intelligence-assisted technologies, such as large language models, chatbots, or image generators, were not utilized in the production of this submitted work.

### Statistical Analysis

The statistical analyses of the collected data were performed using the Statistical Package for the Social Sciences software (version 22.0, IBM Corp., Armonk, NY, USA, 2016). Descriptive statistics for variables were presented as mean  $\pm$  standard deviation for normally distributed data and as median (minimum–maximum) for non-normally distributed data. Categorical variables were expressed as percentages and compared using the chi-square test or Fisher's exact test. The distribution of the data was assessed using the Kolmogorov-Smirnov test. Comparisons among the ICR, SCR, and NCR groups were conducted using one-way analysis of variance with Tukey post-hoc correction or the Kruskal-Wallis test with Dunn's post-hoc correction, as appropriate. Kaplan-Meier survival curves were constructed to compare the three groups. A P value of  $\leq 0.05$  was considered statistically significant.

### Results

A total of 14,511 patients presenting with ACS were screened. Patients were stratified according to the revascularization strategy to create similar groups in terms of demographic and baseline characteristics. Ultimately, 316 patients were included in the analysis (Figure 1).



**Figure 2.** The primary outcomes are (A) cardiac death, and (B) myocardial infarction. A difference in favor of immediate complete revascularization is presented as a positive value.

### Baseline Characteristics

The study population had a mean age of 71.1 years, with 63% of participants being men. A total of 108 patients (34.2%) underwent IRA-only PCI (NCR), while 208 patients (65.8%) underwent complete revascularization. The ICR, SCR, and NCR groups were similar in terms of baseline characteristics (Table 1).

### Long-Term Clinical Outcomes

The median time between the index and staged procedures in the SCR group was 10.1 days (1–30). The median follow-up period from the last procedure in the SRC group and the index procedure in the ICR and NCR groups was  $63 \pm 28$  months, with a maximum follow-up period of 120 months. The clinical outcomes during follow-up are presented in Table 2. The risk of cardiac composite outcomes was lower in the ICR group compared to the SCR and NCR groups (12.8%, 36.5%, and 40.7%, respectively;  $P = 0.001$ ). Similarly, the ICR group demonstrated a lower risk of recurrent MI (9.6%, 36.5%, and 39.8%, respectively;  $P = 0.001$ ), rehospitalization (16.7%, 50%, and 41.7%, respectively;  $P = 0.000$ ), cardiac death (3.8%, 13.5%, and 15.7%, respectively;  $P = 0.003$ ), and all-cause mortality (7.1%, 26.9%, and 23.1%, respectively;  $P = 0.002$ ).

In the SCR group, 18 patients underwent the staged procedure within 24 hours after the index procedure. The SCR group was further divided into two subgroups based on the time interval between the first and second procedures: time interval (TI)  $\leq 24$  hours (SCR1) and TI  $> 24$  hours (SCR2). The frequency of cardiac

**Table 1. Baseline Clinical, Lesional, and Procedural Characteristics**

| Variables                               | ICR         | SCR          | NCR         | P     |
|---|-------------|--------------|-------------|-------|
| Age, (years)                            | 69.5 ± 9    | 75.1 ± 7     | 72.2 ± 11   | 0.081 |
| Male, n (%)                             | 100 (64.1)  | 33 (63.5)    | 69 (63.9)   | 0.532 |
| Hypertension, n (%)                     | 81 (51.9)   | 28 (53.8)    | 60 (55.5)   | 0.231 |
| Diabetes mellitus, n (%)                | 51 (32.6)   | 19 (36.5)    | 37 (34.2)   | 0.188 |
| Dyslipidemia, n (%)                     | 82 (52.5)   | 24 (46.1)    | 48 (44.4)   | 0.268 |
| Current smoking, n (%)                  | 68 (43.5)   | 25 (48)      | 46 (42.5)   | 0.421 |
| <b>Laboratory findings at admission</b> |             |              |             |       |
| HGB (g/dL)                              | 12.6 ± 1.52 | 12.3 ± 0.7   | 12 ± 1.22   | 0.522 |
| eGFR (mL/min/1.72m <sup>2</sup> )       | 84.3 ± 13.2 | 81.5 ± 10.3  | 75.7 ± 9.2  | 0.084 |
| Troponin T (ng/L)                       | 22.1 ± 8.1  | 26.2 ± 7.7   | 25.5 ± 2.9  | 0.287 |
| CRP (mg/L)                              | 35.9 ± 12.2 | 27.4 ± 8.2   | 31.5 ± 11.2 | 0.098 |
| NT-pro BNP (pg/mL)                      | 112.1 ± 22  | 118.2 ± 19.1 | 120.3 ± 9.2 | 0.285 |
| GRACE risk score                        | 129.5 ± 21  | 138.7 ± 11   | 134.3 ± 19  | 0.092 |
| LVEF, (%)                               | 48.2 ± 3.2  | 50.6 ± 4.9   | 47.2 ± 2.8  | 0.103 |
| SYNTAX score                            | 21.0 ± 5.4  | 17.8 ± 2.2   | 19.5 ± 3.8  | 0.091 |
| TI (hours)                              | 16.8 ± 4.1  | 17.9 ± 3.2   | 16.1 ± 9.6  | 0.611 |
| <b>Location of the IRA, n (%)</b>       |             |              |             | 0.193 |
| LMCA                                    | 9 (5.8)     | 3 (5.8)      | 7 (6.5)     |       |
| LAD                                     | 98 (62.8)   | 35 (67.3)    | 66 (61.1)   |       |
| Proximal                                | 87 (88.2)   | 30 (85.7)    | 59 (89.3)   |       |
| Mid                                     | 55 (56.1)   | 18 (51.4)    | 35 (53)     |       |
| Distal                                  | 4 (4.1)     | 1 (2.8)      | 2 (3)       |       |
| RCA                                     | 30 (19.2)   | 8 (15.4)     | 18 (16.7)   |       |
| Proximal                                | 12 (40)     | 3 (37.5)     | 6 (33.3)    |       |
| Mid                                     | 23 (76.6)   | 6 (75)       | 12 (66.6)   |       |
| Distal                                  | 2 (6.6)     | 1 (12.5)     | 2 (11.1)    |       |
| CX                                      | 19 (12.2)   | 6 (11.5)     | 17 (15.7)   |       |
| Proximal                                | 15 (78.9)   | 4 (66.6)     | 12 (70.5)   |       |
| Mid                                     | 8 (42.1)    | 2 (33.3)     | 6 (35.2)    |       |
| Distal                                  | 1 (5.2)     | 1 (16.6)     | 3 (17.6)    |       |
| Stent length for IRA (mm)               | 24.5 ± 8.1  | 16.1 ± 1.2   | 17.8 ± 4.7  | 0.041 |
| Stent diameter for IRA (mm)             | 2.7 ± 0.5   | 2.6 ± 0.2    | 2.6 ± 0.4   | 0.822 |
| Three-vessel disease, n (%)             | 82 (52.5)   | 27 (51.9)    | 58 (53.7)   | 0.475 |
| Pre-TIMI flow of culprit vessel, n (%)  |             |              |             |       |
| II-III                                  | 91 (58.3)   | 34 (65.3)    | 64 (59.2)   | 0.215 |
| Post-TIMI flow of culprit vessel, n (%) |             |              |             |       |
| II-III                                  | 156 (100)   | 52 (100)     | 108 (100)   |       |
| Total number of implanted stents        | 3 (2-5)     | 3 (2-5)      | 1 (1-2)     | 0.453 |
| Glycoprotein IIb/IIIa inhibitor         | 17 (10.8)   | 6 (11.5)     | 19 (17.5)   | 0.021 |
| <b>Medications at discharge</b>         |             |              |             |       |
| Clopidogrel                             | 120 (76.9)  | 41 (78.8)    | 82 (75.9)   | 0.241 |
| Ticagrelor, n (%)                       | 36 (23)     | 11 (21.1)    | 26 (24)     | 0.351 |
| ACEi/ARBs, n (%)                        | 102 (65.3)  | 36 (69.2)    | 78 (72.2)   | 0.562 |
| Beta-blocker, n (%)                     | 128 (82)    | 42 (80.7)    | 84 (77.7)   | 0.835 |
| Statin, n (%)                           | 132 (84.6)  | 43 (82.6)    | 87 (80.5)   | 0.328 |
| Oral anticoagulant, n (%)               | 16 (10.2)   | 6 (11.5)     | 11 (10.1)   | 0.640 |

The Gp IIb/IIIa inhibitor numbers include a sum of the usage during the follow-up period. ACEi/ARB, Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers; CRP, C-Reactive Protein; CX, Circumflex Artery; eGFR, Estimated Glomerular Filtration Rate; HGB, Hemoglobin; ICR, Immediate Complete Revascularization; LAD, Left Anterior Descending Artery; LMCA, Left Main Coronary Artery; LVEF, Left Ventricular Ejection Fraction; NCR, Non-Complete Revascularization; NT-pro BNP, N-Terminal Pro-Brain Natriuretic Peptide; RCA, Right Coronary Artery; SCR, Staged Complete Revascularization; SYNTAX, The SYnergy Between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery; TI, Time Interval between the Diagnosis and Coronary Angiography; TIMI, Thrombolysis in Myocardial Infarction.

**Table 2. Follow-Up Outcomes**

|                                 | ICR       | SCR       | NCR       | P     |
|---------------------------------|-----------|-----------|-----------|-------|
| Cardiac composite outcome       | 20 (12.8) | 19 (36.5) | 44 (40.7) | 0.001 |
| Recurrent myocardial infarction | 15 (9.6)  | 19 (36.5) | 43 (39.8) | 0.001 |
| Cardiac death                   | 6 (3.8)   | 7 (13.5)  | 17 (15.7) | 0.003 |
| All-cause mortality             | 11 (7.1)  | 14 (26.9) | 25 (23.1) | 0.002 |
| Any rehospitalization           | 26 (16.7) | 26 (50)   | 45 (41.7) | 0.000 |

ICR, Immediate Complete Revascularization; NCR, Non-Complete Revascularization; SCR, Staged Complete Revascularization.

composite outcomes was lower in the SCR1 group compared to the SCR2 group (16.7% vs. 47.1%;  $P = 0.038$ ).

The Kaplan-Meier curves during follow-up are shown in Figure 2. No difference was observed in the cardiac composite outcomes between the staged complete revascularization and non-complete revascularization groups. However, a significant difference was identified in favor of the ICR group ( $P = 0.001$ ). Landmark analysis revealed that the difference in cardiac composite outcomes between the groups became distinctly apparent after 20 months. A significant reduction in risk was observed between the SCR and ICR groups (hazard ratio [HR] (95% confidence interval [CI]): 0.27 (0.15-0.47);  $P = 0.001$ ). In contrast, no significant difference was observed between the non-complete revascularization and staged complete revascularization groups (HR (95% CI): 1.06 (0.61-1.84);  $P = 0.832$ ).

## Discussion

This study was conducted as a three-arm investigation in patients with NSTEMI and MVD to compare the clinical benefits of ICR, SCR, and IRA-only revascularization. The results suggest that ICR reduces the incidence of cardiac composite outcomes over a 10-year follow-up period. No significant differences in clinical outcomes were observed between the SCR and NCR groups. However, when the SCR strategy was completed within 24 hours, outcomes were similar to those of ICR and superior to those of NCR. In routine clinical practice, accurately identifying the correct IRA can be challenging. Early and complete revascularization strategies may help mitigate the consequences of incorrect IRA identification.

The findings of our study align with the result of the SMILE trial, conducted in patients with MVD and NSTEMI. The SMILE trial demonstrated fewer major adverse cardiovascular events at one year in ICR compared to SCR. However, when comparing these results, the differences in study designs between the SMILE trial and our study must be taken into account. In our study, the median time between the first and second procedures was 10.1 days, which is longer than the mean of 4.8 days reported in the SMILE trial. Additionally, unlike the SMILE trial, a statistically significant difference in outcome curves was observed after the 20<sup>th</sup> month in our study.

A distinct mechanism that could explain the differing outcomes is the incorrect identification of the IRA during the index procedure. Difficulties in identifying the IRA in NSTEMI cases may have caused this result. In contrast, the culprit lesion in patients with STEMI is often angiographically evident. However,

accurately determining the IRA in patients with MVD and NSTEMI may be challenging. An important potential cause of conflicting evidence may be the challenges associated with accurately determining the IRA. New diagnostic methods are needed to improve IRA identification. Fractional flow reserve (FFR) is an increasingly utilized measurement, but during the acute phase, the functional evaluation of the IRA may underestimate the severity of stenosis.<sup>7</sup> In patients with ACS, IRA revascularization should not be delayed based on invasive functional assessments. For patients with MVD presenting with NSTEMI, FFR measurement is recommended for the hemodynamic evaluation of non-IRA lesions rather than for the IRA.<sup>8,9</sup> Previous studies have shown that delayed-enhancement cardiac magnetic resonance imaging has led to new IRA diagnoses in up to half of NSTEMI patients, with late gadolinium enhancement proving valuable in accurately identifying the IRA.<sup>10,11</sup>

Plaque vulnerability in non-IRA lesions may also contribute to the differing outcomes observed with revascularization strategies. Reduced antioxidant enzyme levels in ACS may increase oxidative stress and inflammation, leading to plaque instability. Several studies have demonstrated the presence of thin-cap fibroatheroma in non-IRA lesions of ACS patients with MVD.<sup>12-14</sup> Non-IRA plaque vulnerability was not fully evaluated in our study; however, its role in influencing outcomes cannot be excluded.

An elevated troponin level is recognized as a high-risk criterion in the ESC guidelines, which recommend an invasive strategy within 24 hours.<sup>3</sup> The timing of IRA revascularization is crucial for high-risk ACS patients. In our study, staged revascularization procedures were completed within 24 hours in 18 patients, and a cardiac composite outcome was observed in three of these patients during the follow-up period. This rate is similar to that of the ICR group. Given the challenges of diagnosing the correct IRA during the index procedure, avoiding delays in revascularizing the correct IRA is critical. Therefore, performing a staged procedure within the first 24 hours is a reasonable approach. Additionally, misjudgment of the IRA could result in some acute plaques being left untreated, potentially triggering adverse outcomes between the index and second procedures. These factors may have contributed to the lack of differences in cardiac composite outcomes between the SCR and non-complete revascularization (non-CR) groups in our study.

An increasing number of patients with ACS are older adults, and advanced age is one of the primary predictors of adverse outcomes. However, data specific to older adults with ACS

are limited. According to the EARTH-STEMI study (Effective Acknowledgment of Complete Revascularization in Elderly Patients with ST-Segment Elevation Myocardial Infarction), complete revascularization was found to be superior to intervention limited to the IRA in patients aged 75 years or older with STEMI and MVD.<sup>15</sup> In contrast, the SENIOR-RITA trial (Secondary Prevention in the Elderly: Randomized Intervention Trial of Angina) reported that an invasive strategy did not result in a significantly lower risk of cardiovascular death or nonfatal MI compared to a conservative strategy over a median follow-up of 4.1 years.<sup>16</sup> In our study, 42% of patients were aged 75 years or older. Considering only patients aged  $\geq 75$  years, a significant reduction in cardiac composite outcomes was observed with a complete revascularization strategy compared to an incomplete revascularization strategy (13% vs. 28.3%;  $P = 0.001$ ). This result may be influenced by differences in age distribution (the oldest patient being 84 years old in our study compared to 103 years old in the SENIOR-RITA trial) and the smaller number of patients in our study. In the SENIOR-RITA trial, heart failure rates were higher in the non-invasive group than in the invasive group. To reduce confounding factors, patients with a left ventricular ejection fraction (LVEF)  $< 40\%$  were excluded from our study.

Many factors should be considered when determining the appropriate revascularization strategy. Early and complete revascularization may mitigate the consequences of incorrect IRA identification. However, renal complications are expected to be less frequent in the NCR and SCR groups. In our study, statistically lower renal failure rates in the SCR and NCR groups could not be observed, as patients with low estimated glomerular filtration rates (eGFR) at initial presentation or those with shorter follow-up periods were excluded. While the most significant advantage of ICR is its ability to minimize incorrect IRA identification, it is associated with a higher likelihood of renal complications.

### Study Limitations

Our study has several limitations. First, clinical markers could influence the risk of events. For instance, initial cardiac troponin levels and eGFR play a significant role in determining prognosis.<sup>17</sup> Additionally, N-terminal pro-B-type natriuretic peptide (N-terminal pro-BNP) provides prognostic information regarding the risk of left ventricular dysfunction. The Global Registry of Acute Coronary Events (GRACE) risk score is also an important tool for assessing mortality risk.<sup>18</sup> Due to the combined effects of these parameters, it was difficult to create comparable groups, which limited the number of patients included in the study. Second, FFR was not used for revascularization. Patients with NSTEMI could have been assessed using intracoronary physiology to determine the hemodynamic significance of intermediate-severity non-IRA stenoses. A physiology-guided approach might have reduced the number of coronary stents used. Furthermore, the identification of active infections could not be determined precisely due to the retrospective design of the study. However, C-reactive protein values were high and statistically similar across all three groups. One of the strengths of our study is the relatively small number of confounding factors.

### Conclusion

The clinical benefit of ICR was evident in terms of reducing cardiac deaths, MI, all-cause mortality, and rehospitalizations. The difference in cardiac outcomes between ICR and other revascularization strategies became apparent after the 20<sup>th</sup> month. The long-term outcomes of SCR completed within 24 hours were similar to those of ICR. These findings may reflect limitations in the accurate identification of the IRA with current diagnostic methods. Early and complete revascularization strategies could help mitigate the consequences of incorrect IRA identification.

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