Early Versus Late Intervention in High Risk Patients with Non ST Elevation Myocardial Infarction

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Abstract: In this review we investigate the outcome of early vs. late intervention high-risk patients with non-ST-elevation acute coronary syndromes.

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Introduction

Acute coronary syndrome (ACS) is a spectrum of clinical manifestations ranging from unstable angina and non-ST-segment elevation myocardial infarction (NSTEMI) to ST-segment elevation myocardial infarction (STEMI) **(Jiang et al., 2012)**.

The optimal timing of revascularization in patients presenting with unstable angina or NSTEMI remains controversial. Some early invasive trials in ACS failed to show any benefit of revascularization, while others actually found that it was harmful, especially in the early non stent era **(de Winter et al., 2005).**

However, with improvements in percutaneous coronary intervention (PCI) and the advent of novel adjunctive pharmacotherapy agents (such as GP 2b/3a inhibitors, new antiplatelet agents, and intensive statin regimens), the safety and efficacy of early PCI in ACS has improved significantly **(Jiang et al., 2012)**.

Therefore, a routinely invasive strategy (angiography and revascularizationif applicable) is recommended by the current guidelines **(Hamm et al., 2011)** in high-risk patients with non-ST-elevation acute coronary syndrome (NSTE-ACS). The majority of trials and meta-analysis on this topic showed a reduction in the incidence of cardiovascular death and myocardial infarction (MI) in the medium to long term **(Fox et al., 2010)**.

A considerable number of these patients are initially hospitalized in non-PCI centers. After medical stabilization and coronary angiography, the patient is then transferred to the PCI center for revascularization, if needed. This makes generalizability of the study results to clinical practice questionable. Observational studies by **Van de Werf et al. (2005)** showed that patients admittedto a center with angiography and PCI facilities were more likely to receive an invasive strategy, had a lower riskfor refractory or recurrent angina at the cost of higher risk for stroke and major bleeding. No difference was found in the incidence of cardiovascular death, myocardial infarctionor stroke at 6 months **(Badings et al., 2016)**.

Thus, there remains an ongoing debate as to the optimal time for coronary angiography in NSTEMI patients who require "early" invasive management **(Jiang et al., 2012)**.

Invasive coronary angiography and revascularization

Invasive coronary angiography, followed if indicated by coronary revascularization, is performed in the majority of patients hospitalised with NSTE-ACS in regions with well-developed healthcare systems. The decision for an invasive strategy should carefully weigh the risks of invasive diagnostics and the benefits in terms of diagnostic accuracy, risk stratification and assessment of the risks related to revascularization. The decision for revascularization takes into account the risk in terms of morbidity and mortality associated with the proposed modality (PCI or CABG) and the benefits in terms of short- and long-term prognosis, symptom relief, quality of life and duration of hospital stay. The indication for an invasive approach, the timing for myocardial revascularization and the selection of the revascularization modality depend on numerous factors, including clinical presentation, comorbidities, risk stratification (as outlined in section 4), presence of high-risk features specific for a revascularization modality, frailty, cognitive status, estimated life expectancy and functional and anatomic severity as well as pattern of CAD **(Marco et al.,2015).**

Approaches to the use of cardiac catheterization and revascularization:

Two general approaches to the use of cardiac catheterization and revascularization can be taken in patients with NSTE-ACS:

(1) **Early invasive strategy** involving early cardiac catheterization, followed by PCI, CABG, or continuing medical therapy, depending on the coronary anatomy.

➢ It is recommended in:

- Patients with NSTE-ACS who have ST-segment changes and/or positive troponin on admission or in whom these high-risk features develop over the subsequent 24 hours.
- Other high-risk indicators, such as recurrent ischemia or evidence of congestive heart failure **(Hamm et al., 2011).**
- It is also advised in patients with NSTE-ACS previously treated with CABG **(Anderson et al., 2007).**
- patients who have had NSTE-ACS within 6 months of a previous PCI and in whom restenosis may be the cause **(Hamm et al., 2011).**

(2) **Amore conservative approach**, with initial medical management and catheterization being reserved for patients with recurrent ischemia either at rest or on a non-invasive stress test, followed by revascularization if the anatomy is suitable.

A meta-analysis of seven recent trials confirmed an overall significant 25% reduction in mortality and a 17% reduction in nonfatal MI after 2 years of follow-up in patients managed with an early invasive strategy **(Bavary et al., 2006).**

➢ **Indications for an initial conservative strategy**:

- patients with life-threatening comorbid conditions or in whom the risks outweigh the benefits,
- patients who do not wish to undergo an invasive procedure, and low-risk patients without recurrent symptoms **(Jneid et al., 2012).**

Table 1. **(Marco et al., 2015)**

Risk criteria mandating invasive strategy in NSTE-ACS

Very-high-risk criteria
• Haemodynamic instability or cardiogenic shock
• Recurrent or ongoing chest pain refractory to medical treatment
• Life-threatening arrhythmias or cardiac arrest
• Mechanical complications of MI
• Acute heart failure
• Recurrent dynamic ST-T wave changes, particularly with intermittent ST-elevation
High-risk criteria
• Rise or fall in cardiac troponin compatible with MI
• Dynamic ST- or T-wave changes (symptomatic or silent)
• GRACE score >140
Intermediate-risk criteria
• Diabetes mellitus
• Renal insufficiency (eGFR <60 mL/min/1.73 m²)
• LVEF <40% or congestive heart failure
• Early post-infarction angina
• Prior PCI
• Prior CABG
• GRACE risk score >109 and <140
Low-risk criteria
• Any characteristics not mentioned above

CABG = coronary artery bypass graft; eGFR = estimated glomerular filtration rate; GRACE = Global Registry of Acute Coronary Events; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; MI = myocardial infarction.

Timing of an Invasive Approach

(1) Early invasive strategy (average time to angiography ranging from 1.2 to 14 hours)

(2) Delayed invasive strategy (average time to angiography of 21 to 86 hours).

Mortality and MI rates in the two strategies did not differ **(Katritsis et al., 2011)** but the early invasive approach was associated with significant reductions in recurrent ischemia (41%) and duration of hospital stay (28%) and with favorable trends with respect to bleeding and the composite of cardiovascular death, MI, or stroke. This analysis lends support to an early invasive strategy, especially in high-risk patients such as those with continuing ischemia despite intensive medical therapy, as well as in patients with acute heart failure and ventricular tachyarrhythmias **(Marco et al., 2015).**

Risk assessment

Several risk scores that integrate clinical variables and findings on the ECG and/or from serum cardiac markers have been developed for patients with NSTE-ACS**. (Fox et al., 2006).**

- The TIMI (Thrombolysis In Myocardial Ischemia) risk score:
  - Identifies seven independent risk factors; their sum correlates directly with death or recurrent ischemic events. **(Antman et al., 2000)**.
  - This simple, rapid assessment of risk at initial evaluation identifies high-risk patients who can derive benefit from an early invasive strategy and more intensive antithrombotic therapy.
  - This risk score also predicts the severity of angiographic findings, including the extent of CAD **(Garcia et al., 2004)** thrombus burden, and flow impairment. **(Mega et al., 2005)**.
- An even simpler score, the TIMI risk index (age in decades × heart rate/ systolic blood pressure), predicts mortality in patients with NSTEMI. **(Wiviot et al., 2006).**
- The GRACE (Global Registry of Acute Coronary Events) risk score:
  - also identified risk factors that are independently associated with increased mortality**. (Fox et al., 2006)**.
  - Although perhaps more accurate, it is more complex than the TIMI risk score and is not easily calculated by hand. (Braunwald 2015).

Complications of coronary intervention.

Cardiac catheterization is a relatively safe procedure but has a well-defined risk for morbidity and mortality **(Bashore et al., 2012)**.

The potential risk for major complications during cardiac catheterization is often related to comorbid disease.

The use of low-osmolar and isosmolar contrast media, lower-profile diagnostic catheters, and reduced anticoagulation, as well as extensive operator experience, has reduced the incidence of complications. **(Bashore et al., 2012)**

Death related to diagnostic cardiac catheterization occurs in 0.08% to 0.75% of patients, depending on the population studied. Data from the Society for Cardiac Angiography identified subsets of patients with an increased mortality rate. **(Davidson et al., 2006)**

In an analysis of **(Underwood et al., 2004)** patients, multivariate predictors of significant complications were

1. moribund status.
2. advanced New York Heart Association functional class.
3. hypotension.
4. Shock.
5. aortic valve disease.
6. renal insufficiency.
7. unstable angina.
8. mitral valve disease.
9. acute myocardial infarction within 24 hours.
10. congestive heart failure.
11. cardiomyopathy.

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