

## EDITORIAL COMMENT

# Don't Forget the Intervention in Very Elderly Persons With Acute Coronary Syndromes\*

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The most common admission indication in the cardiology practice is acute coronary syndrome (ACS) with or without ST-segment elevation. Antithrombotic and anti-ischemic therapies are the cornerstones in the medical management of these syndromes. In patients presenting with ST-segment elevation at the admission electrocardiogram, reperfusion therapy is instituted as fast as possible (1–3), which can be accomplished by primary percutaneous coronary intervention, fibrinolysis, or both. This results in a significant reduction in infarct size and improvement of short- and long-term prognosis (2,3). In patients with coronary syndromes presenting without ST-segment elevation on the admission electrocardiogram, anti-ischemic and antithrom-

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botic therapies are also of utmost importance. However, in the last decade a strong switch has been seen in the invasive approach of this condition. Risk stratification can be improved by angiography, and revascularization—if indicated—can be planned. Several randomized trials have evaluated a routine invasive strategy in comparison with a more selective invasive approach in these patients. The outcome results were mixed (4–6). Although these meta-analyses included trials from the pre-clopidogrel era, a routine invasive strategy has already shown a reduction in myocardial infarction and repeat intervention. The results with regard to early and long-term survival were variable. There seemed to be an early hazard for early mortality compensated by a later reduction (4).

The substrate of a non-ST-segment elevation myocardial infarction usually does not consist of an acutely occluded

epicardial coronary artery, like in ST-segment elevation myocardial infarction. In non-ST-segment elevation ACS there can be severe but non-occlusive coronary artery disease or no disease at all. In the large TACTICS-TIMI 18 (Treat angina with Aggrastat and determine Costs of Therapy with Invasive or Conservative Strategies—Thrombolysis in Myocardial Infarction 18) study, 43% of patients had left main or triple-vessel disease, and 13% had normal coronary arteries (7). In both instances reperfusion therapy is not indicated and only leads to harm by bleeding and excess myocardial infarction (8,9). In a meta-analysis of the 3 most recent large trials in this syndrome, it was shown that in only the highest-risk patients is there a mortality benefit by an early routine invasive approach, whereas the lower-risk patients have no mortality benefit at all (6). Therefore, current European and American guidelines on non-ST-segment elevation ACS do not recommend an early invasive strategy in low-risk patients (10,11). The strength of the latter meta-analysis is that it was based on individual patient data. The weakness is that it is constructed from trials, which are necessarily open by design and in which myocardial infarction is both an entry criterion and an endpoint at the same time.

In this issue of *JACC: Cardiovascular Interventions*, a highly interesting trial is presented on a routine invasive strategy versus a selective invasive strategy in non-ST-segment elevation ACS carried out exclusively in very elderly patients (over 80 years of age) (12). The appealing feature of this Italian study is that it is the first and only trial available performed specifically in very elderly patients with this syndrome. But the weakness is that the trial did not reach its aim with regard to the number of recruited patients. It clearly shows that in very elderly patients a routine invasive strategy can be helpful without clear excess harm. In the individual data meta-analysis mentioned in the preceding text (6), it was already shown that age is the strongest predicting factor for improved outcome by a routine invasive strategy, which is now confirmed by the current prospective study. These findings underscore that a factor identified in a meta-analysis can only be confirmed in a prospective randomized study in patients with such a feature.

Should all very elderly patients admitted with this syndrome undergo a routine invasive approach? Clearly, each case should be considered individually. Furthermore, in this Italian study only patients with a positive biomarker benefited from the therapy. This is a post hoc finding, the effect of which should be evaluated in a future prospective randomized trial, as pointed out in the preceding text. A good example of such an approach is the outcome of the large ICTUS (Invasive versus Conservative Treatment in Unstable coronary Syndromes) trial (13). In the years before the ICTUS trial, a positive biomarker indicated a higher risk for this group of patients. To prove this prospectively,

\*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

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the ICTUS trial included only patients with positive troponin levels. But it turned out that there was no benefit of a routine invasive approach in these high-risk patients, although 53% of the patients in the selective-invasive arm crossed-over to angiography like 51% of those patients in the TACTICS-TIMI 18 study (7).

So, the results of the current trial in very elderly patients should be repeated prospectively in similar patients but only in those with positive biomarkers. If that study should turn out to be positive, then together with the data presented today a routine invasive strategy would be strongly indicated in very elderly patients admitted with non-ST-segment elevation ACS and positive biomarkers.

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#### REFERENCES

1. Verheugt FWA. Reperfusion therapy starts in the ambulance. *Circulation* 2006;113:2377-9.
2. Keeley EC, Boura JA, Grines CL. Comparison of primary and facilitated percutaneous coronary intervention for ST-elevation myocardial infarct: quantitative review of randomized trials. *Lancet* 2006;367:579-88.
3. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994;343:311-22.
4. Mehta SR, Cannon CP, Fox KAA, et al. Routine versus selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. *JAMA* 2005;293:2908-17.
5. Qayyum R, Khalid R, Adomaityte J, Papadakos SP, Messineo FC. Systematic review: comparing routine and selective invasive strategies for the acute coronary syndrome. *Ann Intern Med* 2008;148:186-96.
6. Fox KA, Clayton TC, Damman P, et al. Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome a meta-analysis of individual patient data. *J Am Coll Cardiol* 2010;55:2435-45.
7. Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med* 2001;344:1879-87.
8. Antman EM, McCabe CH, Gurfinkel EP, et al. Enoxaparin prevents death and cardiac ischemic events in unstable angina/non-Q-wave myocardial infarction. Results of the thrombolysis in myocardial infarction (TIMI) 11B trial. *Circulation* 1999;100:1593-601.
9. Bar FW, Verheugt FW, Col J, et al. Thrombolysis in patients with unstable angina improves the angiographic, but not the clinical outcome. Results of UNASEM, a multicentre, randomised, placebo controlled clinical trial with anistreplase. *Circulation* 1992;86:131-7.
10. Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of acute coronary syndrome in patients presenting without ST elevation. *Eur Heart J* 2011;32:2999-3054.
11. Jneid H, Anderson JL, Wright RS, et al. 2012 ACCF/AHA focused update of the guideline of patients with unstable angina/non-ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2012;60:645-81.
12. Savonitto S, Cavallini C, Petronio AS, et al. Early aggressive versus initially conservative treatment in elderly patients with non-ST-segment elevation acute coronary syndrome: a randomized controlled trial. *J Am Coll Cardiol Intv* 2012;5:906-16.
13. De Winter RJ, Windhausen F, Cornel JH, et al. Early invasive versus selectively invasive management for acute coronary syndromes. *N Engl J Med* 2005;353:1094-104.

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**Key Words:** acute coronary syndrome ■ angioplasty ■ elderly ■ revascularization ■ treatment.