

New European guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction – what are the new and key messages

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The new European guidelines on the management of non-ST segment elevation acute coronary syndromes (NSTEMI-ACS) were published in June 2007, two months before the ACC-AHA guideline update on the same topic [1,2]. The ESC guidelines differ from the American guidelines on a certain number of points: the ESC document is much shorter, more practice-oriented and formulated specifically to provide the most relevant and up-to-date information to clinicians about the best management strategies for dealing with NSTEMI-ACS patients. Nevertheless, the two documents impart more or less the same messages, despite some minor differences in the level of recommendations for certain drugs or treatments.

These ESC guidelines incorporate all the recently published evidence as regards drug therapies and procedures, particularly invasive versus conservative strategies, and represent the most comprehensive summary currently available of diagnostic and therapeutic strategies for NSTEMI-ACS patients. However, the spirit in which these guidelines were written is completely different from previous guidelines on the same issue. Three unique new features are present in these new ESC guidelines that are the key to understanding how the recommendations were established.

The first originality is that the ESC guidelines take into account benefit-risk ratio, expressed as number needed to treat to avoid one event (NNT) and number needed to harm to produce one event (NNH) (Fig. 1). Secondly, the quality of the trials reviewed was scrutinised in great detail to establish the levels of recommendations. Trials with an appropriate and robust design (double-blind, placebo-controlled, randomised trials) using hard endpoints (myocardial infarction [MI], stroke or bleeding complications), with suitable sample-size calculations

and incorporating contemporary treatments, were used as the primary basis for the recommendations. Trials that did not fulfil any or all of these criteria were given lower priority.

Last but not least, for the first time, the efficacy-safety profile of drugs and treatments was taken into account for the gradation of recommendations. Until the recent past, only the efficacy and usefulness of a therapeutic approach was considered for recommendations. However, bleeding complications have emerged as a major contributor to the risk of death, MI and stroke at 30 days and 6 months. Many concordant reports have shown that major bleeding complications have led to a four- to fivefold increase in the risk of death at 30 days [3]. It is therefore no longer possible to recommend treatments on the sole basis of their efficacy, without taking into account the safety profile. This was rendered mandatory by a recent meta-analysis showing that reduced bleeding complications led to improved survival and a lower risk of death, death/MI and death/MI/stroke [4]. This means that the ESC recommendations were strongly influenced by this way of thinking.

Finally, a further new feature of the ESC guidelines is the inclusion (in addition to the major traditional chapters) of sections on the more practical aspects encountered in daily practice, such as management of special populations and situations: the elderly, women, diabetes, renal failure, anaemia. Furthermore, complications, and how to deal with them, are described in detail, focusing particularly on bleeding complications and thrombocytopenia.

The ESC guidelines on NSTEMI-ACS opens with chapters on epidemiology, natural history, and pathophysiology, and goes on to describe diagnosis and risk assessment. In this latter chapter, the use of a risk score calculator is promoted, in order to help clinicians in risk stratification of the patients. A risk score is just an aid to risk stratification, which should be based on clinical and electrocardiographic presentation, in addition to laboratory tests (troponin, presence of diabetes or renal failure). All types of treatment are reviewed in detail, particularly anticoagulants, anti-platelets, coronary revascularisation, as well as long term management and rehabilitation. A special chapter is dedicated to resistance to anti-platelet agents and

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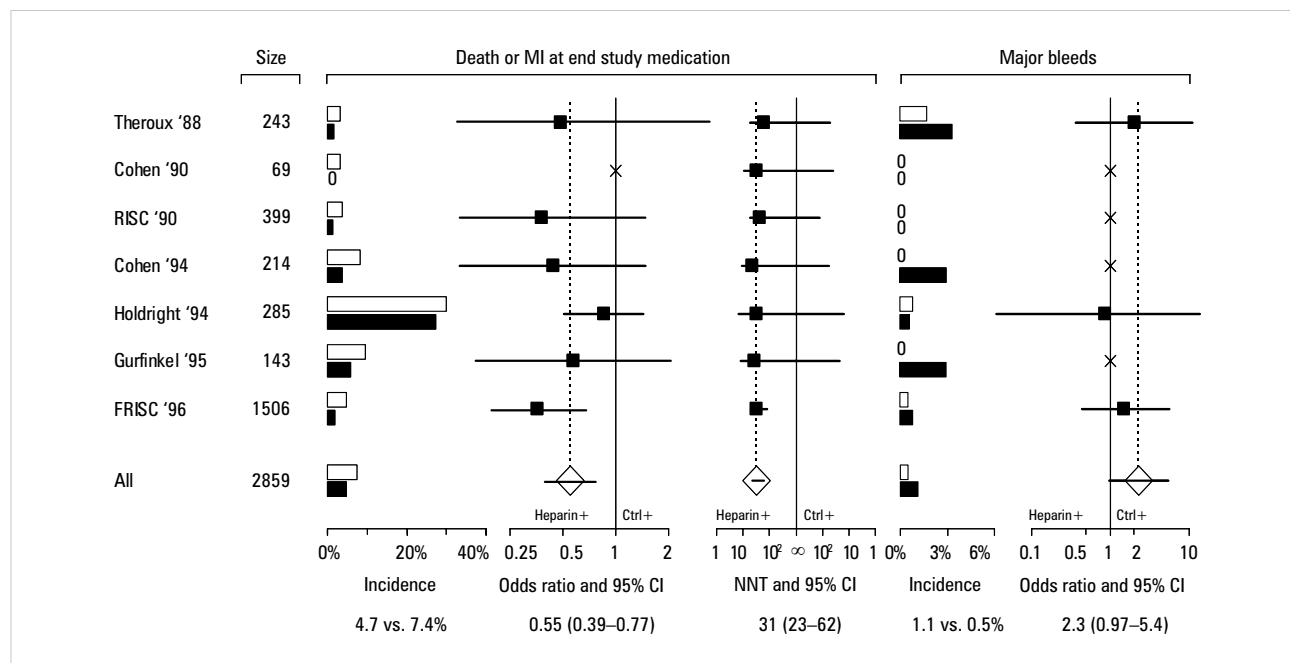


Fig. 1. Death, myocardial infarction and major bleeds at the completion of study medication in randomized trials of UFH/LMWH (dark bars) vs. control (open bars) [from: *Eur Heart J.* 2007; 28: 1611, with permission of the publisher]. NNT = number of patients who needed to be treated to avoid one event

drug interactions, covering also withdrawal of antiplatelet agents in patients under dual antiplatelet therapy.

A clear management strategy is proposed on the basis of initial risk stratification, distinguishing three different levels of risk: life-threatening conditions, moderate to high risk patients, or low risk patients. Patients presenting in life-threatening conditions are rare, and represent only 4 to 5% of the total NSTEMI-ACS population. These patients are at very high risk of death or further myocardial infarction: The features are recurrent or refractory angina, with major ST segment modifications and/or clinical symptoms of heart failure or hemodynamic instability, and/or life threatening arrhythmias during angina attacks. These patients should be managed very rapidly (within 2 hours after referral) with invasive strategy. Moderate to high risk patients are those with elevated troponins, dynamic ST changes, permanent ST depression, diabetes mellitus, reduced renal function (with $GFR < 60 \text{ ml/min/1.73m}^2$), depressed left ventricular function, early post-MI angina, PCI within the last 6 months, or prior CABG, and intermediate to high risk according to a risk calculator. In the ESC guidelines, the GRACE risk score is proposed [5]. These patients should be taken to the catheterisation laboratory within 72 hours for angiography, and revascularisation whenever possible. Lastly, patients at low risk are those without recurrence of chest pain, no signs of heart failure, no ECG changes on 2 recordings at 6 to 12 hours interval, and no troponin elevation on 2 samples taken at 6 to 12 hours interval. These patients should be managed conservatively, and submitted to non-invasive evaluation to demonstrate the presence of ischemia. They may be submit-

ted to invasive strategy if it judged necessary, but not as first-line option. For these three different risk situations, the use of drugs (anti platelet agents, anticoagulants) before, during and after the cathlab is clearly explained.

If these guidelines are adequately implemented, they may help to considerably improve patient outcome. It has been shown in many registries that implementation of guidelines leads to better outcome. The question is particularly relevant in Central and Eastern Europe, where coronary artery disease, and particularly acute coronary syndromes, have reached epidemic proportions. Recent reports have shown that the rate of coronary artery disease, and death caused by coronary artery disease, is three- to fourfold higher in Central and Eastern Europe, as compared to western Europe. Lifestyle habits, particularly diet, cigarette smoking, incidence of diabetes, hypertension, lipid disorders and abdominal obesity, may account for this higher risk of coronary artery disease in these regions. The rate of cardiovascular disease represents a major burden for society and has important public health implications [6-8].

The ESC guidelines promote drugs and therapies that may not be affordable for every patient in Central and Eastern Europe, depending on the healthcare system of a given country. This is particularly true as regards long term treatment with costly drugs such as clopidogrel and/or statins and/or ACE inhibitors. This is also true for invasive strategies. However, in Poland, access to care, especially access to invasive strategy and revascularisation, has tremendously improved in recent years as shown by registries. This is all the more important since revascularisation has been shown to offer a better prognosis,

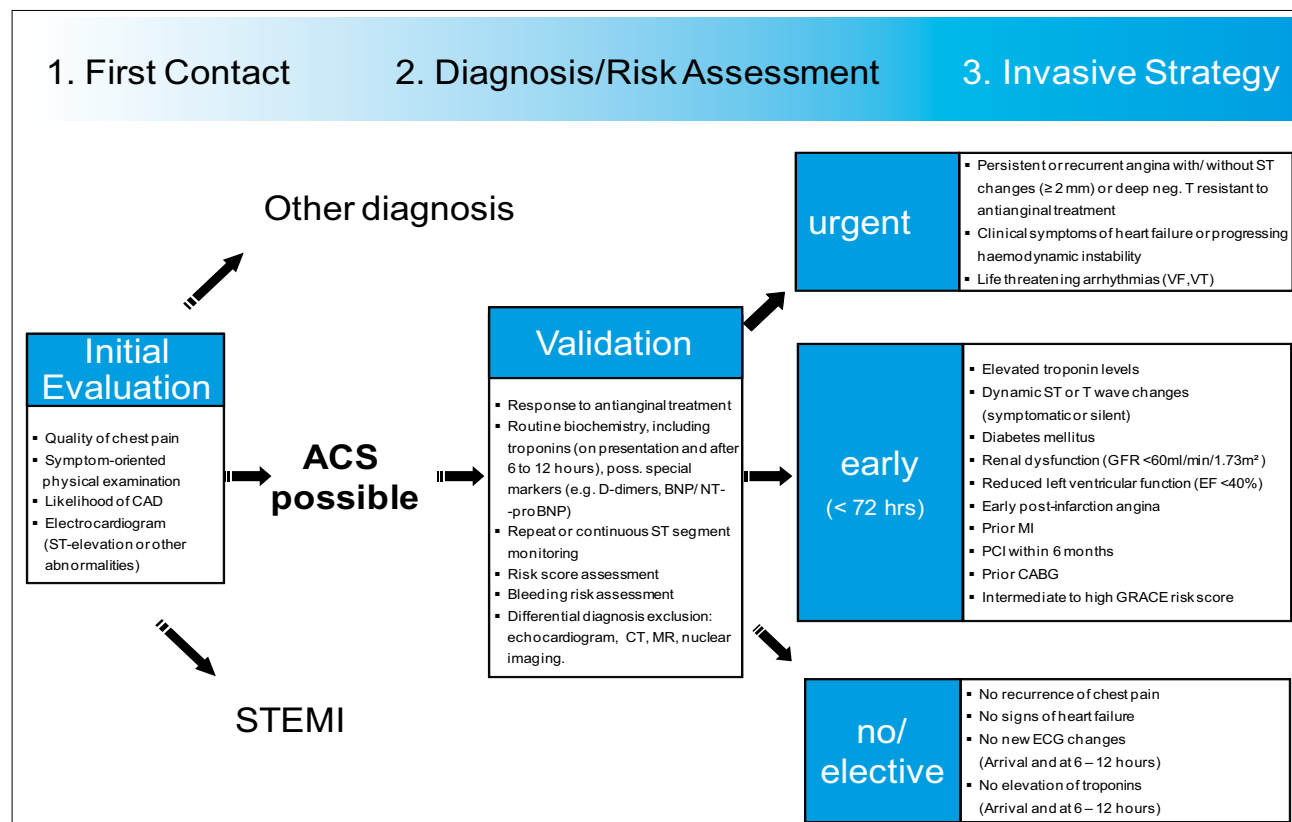


Fig. 2. Decision-making algorithm for the management of patients with NSTEMI-ACS (from: *Eur Heart J.* 2007; 28: 1642, with permission of the publisher). Abbreviations: ACS – acute coronary syndrome, CABG – coronary arterial by-pass graft, CAD – coronary artery disease, CT – computed tomography, EF – ejection fraction, GFR – glomerular filtrate rate, MI – myocardial infarction, MR – magnetic resonance, PCI – percutaneous coronary intervention, STEMI – ST segment elevation myocardial infarction, VF – ventricular fibrillation, VT – ventricular tachycardia

and is recognised as the mandatory approach for patients with life threatening conditions, and in patients at moderate to high risk, defined by troponin release, amongst other markers (Fig. 2).

The policy of the European Society of Cardiology has always been the same as regards guidelines, namely the Task Force in charge of writing the document takes into account scientific information only when grading their recommendations. In Europe, in view of the huge diversity in health care systems between the 50 different countries that make up Europe in its broadest geographical sense, the task of implementing guidelines in each country is left to the responsibility of local health authorities and doctors.

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