

Comments on the 2023 ESC guidelines for the management of acute coronary syndromes

Authors:

Grupo de Trabajo de Comentarios a la Guía ESC 2023 de Síndrome Coronario Agudo:

Rut Andrea (1)*, Ana Viana-Tejedor (2)*, Albert Ariza (3), Gemma Berga (4), Roberto Martín-Asenjo (5), Sandra O. Rosillo (6)

Affiliations:

- (1) Acute Cardiac Care Section, Cardiovascular Institute, Hospital Clinic Barcelona, University of Barcelona, IDIBAPS, Barcelona, Spain.
- (2) Acute Cardiac Care Unit. Cardiovascular Institute. Hospital Clínico San Carlos. Madrid. Spain.
- (3) Unidad de Cuidados Intensivos Cardiológicos, Servicio de Cardiología, Hospital Universitario de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain.
- (4) Interventional Cardiology, H.Santa Creu i Sant Pau Barcelona, University of Barcelona, IIB Sant Pau
- (5) Unidad de Cuidados Críticos Cardiológicos. Servicio de Cardiología. Hospital 12 de Octubre
- (6) Acute Cardiac Care Unit. Cardiovascular Institute. University Hospital la Paz, Madrid. IdiPAz.

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***Authors for correspondence and workgroup's coordinators:**

Dra. Rut Andrea MD, PHD

Acute Cardiac Care Section, Cardiovascular Institute, Hospital Clinic Barcelona
Villarroel. 170, 08036, Barcelona, Spain

E-mail address: randrea@clinic.cat

Dra. Ana Viana-Tejedor MD, PHD

Acute Cardiac Care Unit, Cardiovascular Institute, Hospital Clínico San Carlos.
Calle del Prof Martín Lagos, S/N, 28040, Madrid, Spain.

E-Mail address: ana_viana_tejedor@hotmail.com

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INTRODUCTION

The European Society of Cardiology (ESC) has achieved quite a success by releasing a single document for the management of acute coronary syndromes (ACS)^[1], as patients presenting with ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation (NSTEMI-ACS) share many common pathways such as those of initial diagnostic work-up, antithrombotic regimes or secondary prevention strategies, so it conforms more closely with the clinical setting. Moreover, new guideline is more dynamic and has many figures that can help physicians with their daily practice and an animated central figure useful to disseminate key messages.

NOVELTIES

The main new 37 recommendations and/or significant changes can be categorized into several sections.

Antithrombotic therapy

On this topic, we want to emphasize two new recommendations. First, it is strongly recommended (I-C) to resume dual antiplatelet therapy (DAPT) for at least 12 months, after an ACS treated with either coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI) or conservative strategy. Second, it is not recommended to de-escalate antiplatelet therapy within first 30 days after an ACS (III-B).

One of the most controversial aspects of these guidelines was downgrading, from I-A to IIb-B pre-treatment with P₂Y₁₂-inhibitors in STEMI patients undergoing PCI, based on results of the ATLANTIC trial^[2], where pre-treatment with ticagrelor during transfer (31 minutes before PCI) failed to show benefit versus administration immediately before angioplasty. Yet, there was indeed a reduction of stent thrombosis (ST) and no increased bleeding risks. Also, pre-treatment with prasugrel was not explored.

Invasive strategy: timing and technical aspects

Previous controversy derived from NSTEMI-ACS guidelines recommendation of an early invasive strategy (within first 24 hours) in high-risk patients has been solved and it has now been downgraded from I-A to IIa-A, as it has not proven benefit when universally applied.

Regarding technical aspects, for the first time, this guideline recommends PCI in patients with spontaneous coronary artery dissection only if there are signs/symptoms of ongoing ischemia, a large area of myocardium in jeopardy and/or reduced anterograde flow (I-C).

Cardiac arrest

Also, as a novelty, there is a dedicated section for cardiac arrest (CA), where CA centres' role has been enhanced by recommending transport of all patients with CA secondary to ACS to those facilities (IIa-C). Furthermore, evaluation of neurological prognosis should be performed after 72 hours (I-C).

Two previous recommendations have been modified. First, routine immediate angiography is no longer recommended in haemodynamically stable patients without persistent ST-segment elevation (III-A) in the light of several clinical trials, including the multicentre Spanish COUPE^[3], as it does not provide survival benefit over delayed angiography. Second, temperature control for patients remaining unresponsive after return of spontaneous circulation is still recommended, but target has been relaxed to active prevention of fever (i.e., > 37.7 °C) for at least 72 hours (I-B).

Management of non-infarct related artery in patients with multivessel disease

The results of the COMPLETE trial^[4] have influenced the new guideline, moving from IIa-A to IA the recommendation to perform complete revascularization either during hospital admission or after discharge (within 45 days), as there were no differences between both strategies.

A few days after guidelines' publication, MULTISTAR-AMI trial (immediate versus staged PCI) was presented, showing a significant reduction in the incidence of primary endpoint at 1 year, for immediate (8.5%) vs. staged PCI (16.3%)^[5]. However, this great difference was mainly driven by higher periprocedural MI in staged PCI.

Cancer patient with ACS

In cancer patients, invasive PCI strategy improves survival^[6] and therefore should be preferred if ≥ 6-months survival is expected (I-B). Conversely, in lower expected survival and/or very high bleeding risk, a conservative strategy should be considered (IIa-C).

In order to reduce bleeding risks in this setting, three new antithrombotic recommendations have been made (III-C) based on patients' platelet count: Avoid a) aspirin if $<10,000/\mu\text{L}$; b) clopidogrel if $<30,000/\mu\text{L}$; c) prasugrel/ticagrelor if $<50,000/\mu\text{L}$.

Finally, temporary interruption of cancer therapy and urgent multidisciplinary approach is recommended when it is suspected to be a contributing cause of ACS (I-C).

Patients' perspective

As a novel and truly positive aspect, it is worth noting that the guideline includes a section on patients' perspectives, shared decision-making, informed consent, Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs). It recommends individualizing care of ACS patients by considering their needs, beliefs values and preferences, and ensuring shared decision-making (I-B). "Teach back" technique is suggested to ensure their comprehension.

CONSEQUENCES OF THE IMPLEMENTATION IN OUR ENVIRONMENT

Class I recommendations have been synthesized and Class III have kept the same proportion as in the previous guideline, thus there are more Class II recommendations (36%) forcing physicians to a more challenging decision-making process.

Antithrombotic therapy

Even though interventional cardiology and stents have changed the prognosis of patients presenting with an ACS, there are still some drawbacks, including patients' persistent ischemic risk due to ST. DAPT has been the cornerstone for reducing thrombotic complications. The late onset of action of oral P_2Y_{12} -inhibitors is their Achilles' heel. As there was evidence supporting P_2Y_{12} -inhibitors pre-treatment's safety and due to its effect on the reduction of rates of definite ST², it has been part of the routine care of patients presenting with STEMI. Yet, whether this strategy improves patients' clinical outcomes or coronary reperfusion is still unknown.

Discouraging routine pre-treatment with oral P_2Y_{12} -inhibitors in patients with both STEMI and NSTEMI-ACS, might indirectly promote use of alternatives such as cangrelor, first and

only intravenous P₂Y₁₂-inhibitor approved by European Medicines Agency. There is a growing body of evidence of real-world setting studies which include updated protocols combining intravenous cangrelor plus oral transition to prasugrel/ticagrelor showing its safety and efficacy [7]. This shift of paradigm might be reasonable in STEMI when time-elapsing between diagnosis and PCI is expected to be short. Possible cost-effectiveness of a more widespread use of cangrelor is unknown. Despite its high costs, savings might be driven from a reduced use of GP IIb/IIIa-inhibitors, shorter in-hospital wash-out periods of surgical candidates and decreased ischemic complications. However, a challenging period of transition is needed to confirm above issues in our environment.

Improvements in stent technology (polymer-free stents, biodegradable polymers stents, etc) have fuelled debate on optimal duration of DAPT after index ACS revascularization. Patients' risk of developing either thrombotic or bleeding complications is dynamic, and DAPT duration should be individualized and re-assessed. This guideline has been very consistent with this statement and presents alternative antithrombotic regimes which better fit patients' clinical characteristics.

Invasive strategies

The role of the nurse is pivotal in early diagnosis and treatment of ACS. In our setting, nurses lead triage of patients, so it is essential to emphasize their education and raise awareness of importance of minimizing delays [8].

Downgrading recommendation for early invasive strategy of patients with high risk NSTEMI-ACS is more appropriate when considering that health-care systems have limited resources (i.e., weekends, night shifts) and that current evidence has shown its lack of benefit. However, delayed revascularization linked to the absence of pre-treatment could translate in more thrombotic events, so prospective registries will be needed if those recommendations are fully applied.

Novelties on the technical aspects of invasive strategies support the development of intravascular imaging, which will further aid PCI-decision making process and might improve PCI-related outcomes in upcoming years.

Management of non-infarct related artery in patients with multivessel disease

Invasive epicardial functional evaluation of non-infarct related arteries is growing, however, its superiority over angiographic imaging is controversial. The latter is recommended to evaluate lesion's severity (I-B). Net benefit for patients and health systems of performing systematic second-time coronary angiographies might be questioned if main utility of functional evaluation is to discard revascularization.

Cardiac arrest

In the past years, hyperinvasive strategies such as routine immediate angiography in stable patients without persistent ST-segment elevation or therapeutic hypothermia, were thought to provide survival benefits to patients recovered from a CA. Currently, new evidence has provided principles to establish a more contemporary post-resuscitation care and has reminded us the need of searching new lines of investigation in this field, even if trial results could not be fully extrapolated to all clinical CA scenarios (i.e. lower rates of bystander resuscitation and use of automatic defibrillators). We believe, the role of CA centres could be the solution to standardize management and to perform the right treatment in the right patient.

Cancer patients

As the proportion of ACS patients with cancer-diagnosis is rising (3%)[9], we need to be prepared to offer them strategies that reduce all-cause mortality such as PCI (especially in expected survival ≥ 6 months) and appropriate antithrombotic regimes (adjusted to coexisting thrombotic/haemorrhagic risks). Quality-care of this population will certainly demand specialization and creation of multidisciplinary teams.

Patients perspective

Global access to information has improved patient's knowledge of different cardiology conditions and treatments and has favoured the building of shared decision-making processes. Person-centred care instead of patient-centred care must be gold-standard of clinical practice. In order to achieve it, health-care systems must also provide health-care related personnel with necessary time and resources.

Secondary prevention

Current guideline maintains the recommendation to participate in a cardiac rehabilitation program following an ACS (I-A) as soon as possible and to adopt a healthy lifestyle (I-

B). As referral rates, participation, and implementation continue to be low, tele-rehabilitation is presented as an optimal alternative^[10]. It is important to optimize the use of our resources in order to accomplish educational, medical, and pharmacological adherence and improve cardiovascular outcomes during follow-up.

GAPS IN KNOWLEDGE

Regarding the levels of evidence, only 29% are A and 38% C, reflecting that despite accumulation of scientific evidence since previous guidelines, there still are many gaps in evidence.

Diagnosis accuracy and management in STEMI and NST-ACS

A significant proportion of patients in whom a STEMI diagnosis is suspected and for whom the reperfusion network is activated, have normal coronary arteries. Optimizing STEMI diagnosis in these patients could reduce need for transfer between hospitals and promote a more rational use of healthcare resources. In this sense, research about the use of machine learning techniques for improving ECG diagnosis of STEMI is warranted^[11].

Applicability of some guideline's recommendations to current clinical practice is challenging. A significant proportion of very high and high risk NST-ACS patients do not achieve an early invasive strategy, especially those admitted to non-PCI capable centres. Achieving this goal might require reorganization of networks, like those for STEMI.

ACS with unstable presentation

Cardiogenic shock (CS) is associated with a high mortality. Obtaining scientific evidence in this setting is extremely difficult, mostly because of complexity of including critical patients in randomized trials and their heterogeneity (cause/severity of shock). Regarding the role of IABP and MCS in patients with AMI-related CS, most trials have failed to show significant benefits. Probably better definition of CS phenotype (severity, presence of CA) would help when designing future trials. Likewise, better definition of aspects like unloading strategy in VA-ECMO patients, timing of percutaneous MCS support or selection of high-volume centres is needed.

As it has been said before, patients with CA are heterogeneous regarding aetiology and clinical profile. Assessing the potential impact of an emergent angiography according to

clinical profile and burden of cardiovascular risk factors might contribute to reduce areas of uncertainty. Notwithstanding, again artificial intelligence techniques when assessing ECG in patients with CA might identify patterns related to coronary artery occlusion.

Special populations: elderly and comorbid patients

While the management of robust elderly patients should be probably the same as younger, evidence about the optimal management in older patients with frailty and ACS is lacking. Benefit from a routine invasive strategy in older frail patients has been recently investigated in *MOSCA-FRAIL* trial [12]. An initial conservative approach demonstrated to be a reasonable alternative to routine invasive strategy among older frail patients with NST-ACS. These findings should be validated in larger, adequately powered trials, and interaction between burden of frailty and benefit from an invasive should be elucidated.

Moreover, proportion of comorbidities such as anaemia, chronic kidney disease and neoplasms among patients with ACS is expected to increase due to continuous ageing of population [13]. Most recommendations about ACS management in these special populations have level of evidence C since they are almost systematically excluded from clinical trials. Designing clinical trials including these complex patients to assess the impact of different antithrombotic strategies and role of an invasive strategy in this setting is warranted. In this sense, the role of blood transfusion among patients with anaemia and ACS remains poorly understood. *REALITY* trial [14], while waiting for powered trials, might be useful to improve clinical practice addressing potential effect of restrictive vs liberal strategy.

Finally, sex and gender differences are well known in ACS but there is a lack of evidence about the benefit, dose and timing of treatments in women as they are systematically underrepresented in clinical trials. More specific research is necessary in women with ACS in order to adapt their management and improve their outcomes.

Therapeutic adherence

Recently, *SECURE* trial [15] demonstrated an increase in therapeutic adherence and reduction of events among patients with ACS receiving polypill including aspirin, ramipril and atorvastatin. Multimodal assessment of therapeutic adherence is now highly recommended. Future studies should include adherence assessment by multimodal and objective methods.

Patients' centred outcomes

Most studies analysing prognosis and impact of antithrombotic drugs or invasive strategies in older patients with ACS have focused on cardiovascular events as the main endpoint (reinfarction, need for revascularization, or cardiovascular mortality). In this sense, it is important to note that in older ages clinical events are mostly due to non-cardiac causes, and assessing non-cardiac readmissions and their mortality is crucial. On the other hand, adapting endpoints to PROMS and PREMS (days alive out of hospital, quality of life, patients' experience) is currently a real need for obtaining solid scientific evidence and improving clinical outcomes of these complex patients in routine clinical practice.

CONCLUSIONS

These comments aim to highlight the new recommendations, improvements and queries of the implementation of these guideline in our environment, and to figure out the gaps in evidence about ACS. However, we encourage you to read full text of ESC 2023 guideline in order to go deeper on specific details to improve your daily practice.

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FIGURE LEGEND

Central Figure: New approach in ACS, person-centred, to individualize working diagnosis, invasive management, treatment and secondary prevention.