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Editorial

Dual antiplatelet therapy duration in patients with ACS undergoing PCI: The "12 months tenet" is soundly questioned

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The dual antiplatelet therapy (DAPT) ensured the safeguarding of coronary stents at the end of the 1990s. Furthermore, the benefits of DAPT beyond the protection of stent thrombosis were soon evident, when extended up to 12 months in patients with acute coronary syndrome (ACS).

With the arrival of the first generation of drug-eluting stents (DES), DAPT extended for 12 months came to the rescue of DES lowering the risk of late thrombosis. The new generations of DES have shown systematically less late thrombosis rates than the first generation [1], and led to investigation of shorter DAPT periods. Pooled analysis of trials showed that short DAPT (3–6 months) was not inferior to 12 months DAPT in terms of ischemic events while reducing bleeding rates. On the other hand, DAPT periods over 12 months reduced thrombotic events but at the cost of increasing bleeding [2,3].

Although in many of these trials a meaningful proportion of patients with ACS was included, the application of the short DAPT strategies was limited in practice to the setting of stable angina, given the safety reserves that existed to reduce DAPT after an ACS.

The topic reached such importance that, in order to guide the medical community, task force documents and guidelines on DAPT after PCI were published [4,5]. These guidelines recommend DAPT after PCI for 12 months in patients with ACS, being reasonable to shorten these periods in the presence of a high hemorrhagic risk (i.e. PRECISE DAPT score ≥ 25) to 6 months.

Parallel or subsequent to the publication of these guidelines, new trials have been conducted comparing different durations of DAPT but focused exclusively on the ACS population. As expected, several meta-analyses focused on ACS have been recently published, however these studies did not include the latest trials carried out specifically in the population with ACS [6–8].

The manuscript published in this issue of the IJC [9], shows the results of a meta-analysis that includes all the trials that have assessed different durations of DAPT in patients with ACS, whether they are specific ACS trials or had subgroups of patients with ACS. The primary efficacy endpoint was overall mortality and the primary safety endpoint was major bleeding. After the selection process, 17,941 patients from 11 trials (3 RCTs and 8 subanalyses of RCTs) were included. The authors excluded the PEGASUS trial because included patients who could have experienced the ACS up to 3 years before enrollment, and therefore not truly represented ACS population [10].

The main conclusion was the best safety profile of a short (3–6 months) duration of DAPT with less bleeding outcomes and similar rates of recurrent thrombotic complications, including mortality, as compared to the standard 12 months. On the other hand, longer DAPT regimens (>1 year) provide benefits in terms of ischemic events, but with excess in hemorrhagic complications, which explain the neutral effect on mortality.

Since some trials conducted with BMS were included in the analysis, the short DAPT periods could be 3 or 6 months, and the time of randomization could vary between trials, the authors performed a sensitivity analysis that showed similar results regardless of the type of stent, DAPT duration or time to randomization.

In this regard, the authors suggest that BMS are still frequently used in ACS and especially in older patients, but the truth is that this is no longer the case, and the use of DES has become dominant (>90%) by demonstrating better clinical outcomes even with the shorter DAPT periods applied in patients at higher risk of bleeding.

Regarding the 3 or 6 months, the smaller size of the group with 3 months could subtract statistical power from this subgroup analysis. In addition, of the two trials that evaluated 3 months DAPT, in RESET trial the DES used had a relatively high late luminal loss (Endeavor sprint®) and in the REDUCE trial a strong trend to a higher mortality was seen in the 3-months arm.

When dealing with patients from RCT these may not fully represent the population with ACS of the real practice, as shown by the quite

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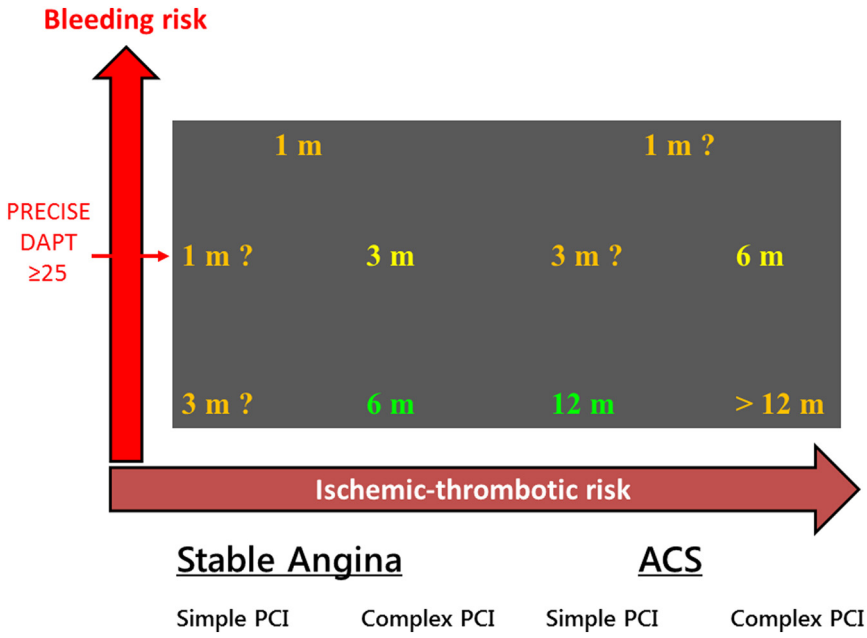

Fig. 1. Proposed algorithm by this author for decision making process on DAPT duration.

limited inclusion of the very elderly (62.2 ± 2.1 years). On the other hand, some high-risk characteristics, such as cardiogenic shock or left main lesions, were exclusion criteria in the RCT.

The risk-benefit balance of the DAPT is dynamic and changes over time, especially after an ACS in which the risk of thrombosis is high at the beginning and progressively reduced over time. It is evident that there are many factors that influence upon the risk-benefit balance that a given duration of DAPT can offer to the patient undergoing PCI after an ACS. To cite the most relevant, the different type of ACS (elevated or not elevated ST), the extension of coronary disease (SYNTAX score), the complexity of the PCI, the type of DES, the drug used in the DAPT (Clopidogrel vs. Ticagrelor or Prasugrel) and finally the risk of bleeding. The present meta-analysis is not at patient level and hence it is not possible to define subgroups in which the results may differ significantly.

Having said all this, the 12 months DAPT strategy for all ACS patients no longer can be systematically applied. Since risk profiles may change or events may occur during follow-up, it is also relevant to consider that the decision for duration should be reassessed during the course of the initially selected treatment strategy. The use of bleeding risk scores, such as the PRECISE DAPT score, may help in the decision-making process, but clinical judgment is irreplaceable when assessing the trade-off between the potential benefit of reducing ischemic outcomes and the risk of increased bleeding associated with DAPT.

Like for many others fields in medicine, an individualized approach is mandatory though properly evidence informed. (Fig. 1) This is more demanding for the cardiologist but studies like the discussed herein may provide aid.

Declaration of conflicts of interest

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