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EDITORIAL COMMENT

Antiplatelet therapy in patients with acute coronary syndromes and thrombocytopaenia: awaiting for evidence

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This editorial refers to 'Management of acute myocardial infarction in a patient with idiopathic thrombocytopenia purpura: the value of optical coherence tomography - a case report' by L. Al-Lawati *et al.*, doi:10.1093/ehjcr/ytaa460.

The complexity of antithrombotic therapy for the treatment of both acute and chronic coronary syndromes has rapidly escalated over the last decade. Advances in antiplatelet therapies coupled with an early invasive management have led to a dramatic reduction in the rates of adverse events in patients with acute coronary syndromes (ACS).[1] Similarly, in patients with chronic coronary syndromes (CCS) the use of combined antithrombotic therapies is now proposed for the long-term management of a group of subjects at high ischaemic risk.[2] However, the use of more potent antithrombotic approaches has been counterbalanced by a parallel increase in the rate of haemorrhagic complications, making an accurate estimation of individual bleeding risk a mandatory step in daily practice.[1,3] Accordingly, in patients deemed at high bleeding risk, the use of more potent antithrombotic drugs is generally discouraged, and shorter periods of combined antithrombotic regimens have been proposed.[1]

While it is already known that both bleeding and thrombotic risks are related at large, there are some clinical settings in which the two are even more tightly linked. Specifically, ACS patients with thrombocytopaenia (defined as a platelet count $<150 \times 10^9$/L) are at high risk of both bleeding and ischaemic events and have significantly worse outcomes than patients with a normal platelet count.[4] Despite the absence of specific guideline recommendations on this topic, it is generally felt that no restrictions to general ACS treatment protocols should be enacted in the presence of a platelet count greater than 30–50 $\times 10^9$/L (defined as mild-to-moderate thrombocytopaenia), except for the suggested use (still on very limited evidence) of clopidogrel as the $P2Y_{12}$ inhibitor of choice instead of the more potent agents prasugrel or ticagrelor.[4–6] In this setting, in the absence of bleeding events, dual antiplatelet therapy (DAPT) should be best limited to 1–3 months.[1,4,6] Conversely, in subjects with a platelet count $<30 \times 10^9$/L (severe thrombocytopaenia), coronary revascularization and DAPT should be planned within a multidisciplinary evaluation.[5,7] Finally, even single antiplatelet therapy with low-dose aspirin should be avoided when the platelet count falls below 10–20 $\times 10^9$/L.[8] Considering these caveats, the management of ACS patients with severe thrombocytopaenia is obviously challenging, particularly when a percutaneous coronary intervention (PCI) is deemed necessary.[4,5] Al-Lawati *et al.* present the case of a young patient with ST-elevation myocardial infarction (STEMI) in the context of extreme fluctuations of platelet count (from 1 to 658 $\times 10^9$/L) due to treatment-resistant immune thrombocytopaenic purpura (ITP).[9] The patient experienced an ACS shortly after a rescue therapy with intravenous immunoglobulins, which resulted in transient rebound thrombocytosis. Diagnostic coronary angiography was here complemented by optical coherence tomography (OCT), which revealed the presence of a coronary erosion as the putative cause of the index ACS. Plain old balloon angioplasty (POBA) under OCT guidance was here successfully used to restore coronary patency without complications. At follow-up, despite the early interruption of DAPT (12 days after the POBA), no recurrent coronary events occurred.

The present case highlights two of the still unresolved aspects in the management of patients with ACS in the setting of severe thrombocytopaenia: the choice of the best interventional strategy, and the choice of the most appropriate antithrombotic regimen.

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Table 1 Treatment strategies in patients with ACS, thrombocytopaenia and no active bleeding

Platelet count threshold	Suggested management
>100 × 10^9/L	Standard care
Between (30)–50 and 100 × 10^9/L	Proceed to revascularization; DAPT (aspirin + clopidogrel) for 1–3 months followed by SAPT[1,4–6]
Between 10–20 and 30 × 10^9/L	Multidisciplinary evaluation needed (cardiologist/haematologist)[5,7,8] Revascularization if needed (POBA if feasible); shortest DAPT duration (≤1 month)
<10 × 10^9/L	No recommendation available: careful balance of the risks of thrombosis and bleeding

ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; POBA, plain old balloon angioplasty; SAPT, single antiplatelet therapy.

As a rule, when PCI is needed, current evidence suggests the superiority of newer generation drug-eluting stents (DES) over bare metal stents, also in patients at high bleeding risk.[1,2,6,10] However, patients with more-than-mild thrombocytopaenia were largely excluded from randomized controlled trials,[6] leaving even more relevant doubts on the generalizability of trial results to subjects with severely reduced platelet count. In addition, while newer generation DES may allow the shortening of DAPT duration down to 1 month,[11] even this brief time frame may become impractical in patients with severely reduced and/or fluctuating platelet count. Therefore, conservative management that avoids coronary stenting (i.e. POBA) might theoretically be preferred. Some recent evidence has even suggested the feasibility of a conservative strategy, with only optimal medical therapy, in patients with ACS caused by plaque erosion, avoiding coronary stenting in several such patients.[12,13] Here, however, adequately powered studies are needed.

In conclusion, despite some isolated reports, to date no conclusive evidence exists on the most appropriate management of patients with ACS and severe thrombocytopaenia. It would appear reasonable to pursue coronary revascularization (if feasible with POBA) in patients at high thrombotic risk (i.e. STEMI and very high-risk non-STEMI). However, in these instances a case-by-case decision is opportune and a multidisciplinary evaluation strongly advocated (*Table 1*). General measures to avoid bleeding and to guide an optimal choice of coronary revascularization options should be readily implemented (including radial access and mandatory intracoronary imaging). In this context, considering the clinical relevance of the topic and the lack of a clear consensus on the best treatment strategies, case reports like the one by Al-Lawati *et al.*[9] should stimulate discussion and prompt, because of the impracticality of randomized trials, the establishment of dedicated multi-national registries collecting information on the management of patients with ACS and severe thrombocytopaenia.

Lead author biography

Dr Riccardo Liga is a Cardiologist at the University Hospital of Pisa, Italy, and an expert in multimodality cardiac imaging. His research interests involve the pathophysiology of ischemic heart disease and heart failure, as well as the risk stratification of patients with coronary artery disease. He currently serves as Deputy Editor of the *European Heart Journal – Case Reports*.

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