Myocardial infarction in elderly patients: How to assess their bleeding risk?

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Ischaemic heart disease is one of the most prevalent causes of death in western societies. The overall risk to develop ischaemic heart disease is associated with a "Western life style" and estimated to occur about 10 years earlier in men than women with hypertension, diabetes, and lipid disturbances. About 85% of patients dying from ischaemic heart disease are more than 65 years old and the frequency and fatality of ischaemic heart disease increases with age in both men and women (1, 2). A subclinical vascular disease with features like an increased carotid intima-media thickness, an abnormal ankle brachial index, and abnormal echocardiograms are very common in people aged 65 and older, and they represent a risk for the occurrence of acute coronary syndromes or myocardial infarction (MI). The number of old and very old patients presenting with MI is rapidly growing (1) and is expected to grow even further due to increased overall life expectancy also based on improvements in health care and living conditions (3).

Diagnosis of elderly patients with MI can be more cumbersome than in younger patients because the description of symptoms is often "atypical" and differs from the classical ones of e.g. sub-ternal pressure with exertion (3, 4). Whether presenting a ST elevation MI (STEMI) or non-ST elevation MI (NSTEMI), the therapeutic options are aiming to limit the extent of MI, to salvage the ischaemic myocardium, and to re-perfuse the infarcted vessels (5, 6). If STEMI is present, the decision must be made quickly as to whether the patient should be treated with thrombolysis or with primary percutaneous coronary intervention (PCI) (7, 8). Patients with NSTEMI should receive anti-ischaemic therapy and may be candidates for PCI urgently or during admission (8, 9).

Results from several studies indicate that PCI improves the outcome from STEMI especially in elderly patients (10–16). In addition to PCI, an adjunctive anti-thrombotic therapy is also usually applied to the elder MI patients. Thereby aspirin (17–19), clopidogrel, or the combinations of clopidogrel with aspirin in STEMI patients are of utmost choice. Although PCI and combined antithrombotic drug therapies in the elder MI patients are appealing, these MI patients represent a high-risk group with frequent treatment-related complications including a strong increase of major bleeding events following reperfusion procedures and combined antithrombotic drug regimens (5, 20). Bleeding events complicate therapeutic options and are often the reason for an increased risk of in-hospital mortality as well as an adverse long-term prognosis of these patients (21–23). Consequently, an effective bleeding risk assessment is urgently needed in this vulnerable patient group (24–26). However, patients aged ≥80 years are underrepresented among many clinical trials (3, 6, 7) with the consequence that so far a bleeding risk assessment is difficult, if not impossible, which may complicate therapeutic decisions and management of elderly patients with MI (27, 28). A possible way out of this dilemma was indicated in the article of the current issue of Thrombosis and Haemostasis by Koller et al. (29) who did a retrospective analyses of 387 patients with a median age of 84 (interquartile range: 81–87) years who were diagnosed with STEMI/NSTEMI receiving dual antiplatelet therapy (ASS + Clopidogrel) at hospital admission. Despite the limitations of a retrospective study and a relatively low number of ≥80 years patients, the high number of endpoints, i.e. 74 patients (19%) who suffered from a major bleeding event during hospital stay according to ISTH (International Society on Thrombosis and Haemostasis) bleeding definition, ensured sufficient statistical power. The authors then assessed the efficacy of the CRUSADE risk score (range 1–100) which was designed to estimate the patient's likelihood for an in-hospital bleeding event (30, 31). It includes the sum of eight weighted scores for systolic blood pressure, haematocrit, eGFR, heart rate, peripheral vascular disease, diabetes mellitus, signs of congestive heart failure at admission, and sex. Moreover, the authors applied a bootstrap resampling procedure to improve the CRUSADE bleeding risk score with the best fitting variables. As almost expected and in line with other studies, the simple use of the CRUSADE risk score in the elderly cohort had a limited capacity to discriminate the patients risk for bleeding events.

However, the novelty aspect in the study of Koller et al., consists in the inclusion of two more parameters in the multivariate analysis. These parameters were: i) a history of bleeding, and ii) C-reactive protein (CRP) levels. Importantly, with a three-fold increase in risk, a history of bleeding appeared to be the strongest predictor of bleeding complications after reperfusion therapy. In addition, the inclusion of CRP was also an independent predictor of bleeding and improved the CRUSADE score. The authors also found a significant correlation of CRP with cardiogenic shock
which is in line with the findings that elevated CRP indicates disease severity in a number of pathological conditions. These findings may warrant investigating whether CRP may also serve as a marker for comorbidities associated with elevated bleeding risk, a question which could not be solved so far. However, a recent position document from the Study Group on Biomarkers in Cardiology of the Acute Cardiovascular Care Association of the European Society of Cardiology, implies that platelet function testing could even have a role, suggesting that one of a range of biomarkers could be surrogates for greater bleeding risk (32).

Although men are supposed to be more at risk of cardiac events, the current study containing 45.9% male and 54.1% female patients with bleeding events did not find a significant difference for gender. The authors also compared and validated their results according to bleeding definitions from the Bleeding Academic Research Consortium Definition (BARC; bleeding defined as BARC class ≥2) and definitions used in the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) study (30, 31). Altogether, the authors found that the improvement in discrimination by including history of bleeding events or CRP levels was consistent throughout all compared bleeding definitions. Another important aspect raised by the authors was that they observed a trend for bleeding risk in patients receiving glycoprotein IIb/IIIa receptor antagonists (abciximab, tirofiban, epifibatide) during PCI which would warrant further analyses and larger studies. Nonetheless, this also indicates that the advantages of a more aggressive anti-coagulation treatment needs to be carefully weighed against the risk of bleeding when considering PCI in elderly patients (33).

Despite the authors made all possible efforts to carefully acquire patient data, and to minimise the risk of bias, one limitation remains and that is the lack of confirmation of the score in an external cohort before routine use in clinical practice. Furthermore, we need to know if new and more potent antiplatelet strategies have an impact on increased bleeding risk (and its prediction) in such ACS patients (34).

Overall, it is evident that the cardiovascular care of elderly MI patients needs to be seen in conjunction with their multidimensional health status. In line, atypical clinical presentations, altered pharmacokinetics and the often altered cognitive and functional status of elderly patients complicate the treatment options. Nonetheless, reperfusion strategies are the most beneficial in MI patients even up to 85 years of age. Thereby, PCI or fibrinolytics are the method of choice and depending on presence or absence of cardiogenic shock, time from presentation, and comorbidities, the balance is often shifted towards PCI. Importantly, the safety and efficacy of reperfusion in association with bleeding events are issues that require further risk assessment. The authors of the present study found that including the history of previous bleeding and/or CRP levels into the CRUSADE algorithm improved the assessment of bleeding risk in addition to already available risk scores in patients with MI ≥80 years. Thus, these simple parameters are likely to identify patients on high risk for a reocurrence of bleeding events and should therefore become an indispensable component of bleeding risk assessment.

Conflicts of interest
None declared.

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References
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