ESC European Society of Cardiology
European Heart Journal (2021) **42**, 352
doi:10.1093/eurheartj/ehaa927

High-risk NSTE-ACS: high time for robust data

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Online publish-ahead-of-print 14 November 2020

This commentary refers to '2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation', by JP Collet et al., doi:10.1093/eurheartj/ehaa575.

Collet *et al.*[1] in recently published ESC Guidelines addressed the issue of timing of invasive strategy in high-risk non-ST elevation acute coronary sydrome (NSTE-ACS) patients. Recommendations continue to mandate that invasive angiography within 24 h is the preferred approach when one high-risk criterion is met: (i) diagnosis of NSTE-ACS according to accepted definition, (ii) new or dynamic ST/T-segment changes, (iii) transient ST-segment elevation, or (iv) GRACE risk score >140.

Whilst agreeing with (ii) and (iii), we contend that currently available data are not sufficiently robust to support the Class 1A recommendation for (iv) GRACE Score >140. Although both the historic TIMACS[2] and more contemporary VERDICT[3] pre-specified GRACE risk score >140 Subgroup analyses did demonstrate a benefit from early revascularization, the findings in both overall unselected trial populations were neutral. These sub-studies may therefore be subject to confounding and their results must be interpreted with a degree of caution. It should also be noted that the Jobs *et al.*[4] meta-analysis, also cited by the Guideline committee to support its recommendation, comprised only 1519 patients (961 from TIMACS) and reported inconclusive tests for statistical interaction between invasive strategies, albeit hinting at a survival benefit in GRACE risk score >140 patients in the early invasive group. Furthermore, as all studies utilized conventional troponin or CK-MB for NSTE-ACS diagnosis, their results may not be translatable to the current era of high-sensitivity troponin use and greater detection of myocardial injury.

Widespread implementation of these recommendations will necessitate restructuring of current ACS system pathways and catheter laboratory resources which may be to the detriment of other patient populations—in particular those with STEMI—a condition with a robust evidence base underpinned by multiple prospective randomized studies and large meta-analyses. Therefore, the lack of high-quality evidence in high-risk NSTE-ACS should, in our opinion, be acknowledged in current Guidelines. The need for a prospective and robust randomized trial in order to definitively answer this important clinical question requires greater emphasis.

These data will be provided by our UK multi-centre British Heart Foundation funded RAPID N-STEMI trial of >1000 higher-risk patients (stratified by GRACE 2.0 risk score) randomized to very early 'STEMI-like' angiography vs. standard of care timing (ClinicalTrials.gov Identifier: NCT03707314).

Conflict of interest: T.A.K. declares that there is no conflict of interest. A.H.G. declares receipt of a grant from the British Heart Foundation that supports the RAPID N-STEMI trial (grant number: CS/17/1/32445).

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