ESC European Society of Cardiology
European Heart Journal (2021) **42**, 3767–3769
doi:10.1093/eurheartj/ehab513

EDITORIAL

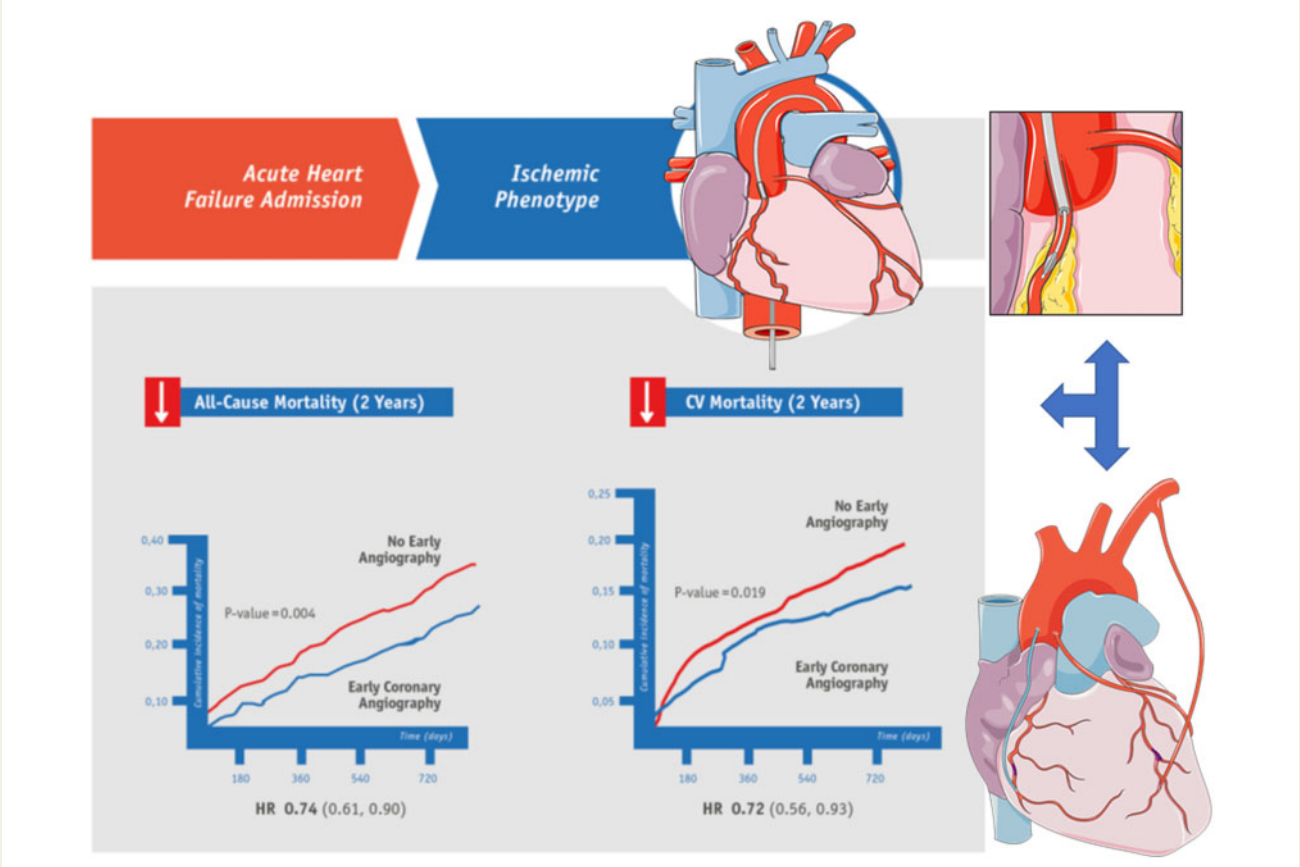
Does early angiography pave the way for improved outcomes in patients with acute heart failure?

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Online publish-ahead-of-print 31 August 2021

This editorial refers to 'Early invasive coronary angiography and acute ischaemic heart failure outcomes', by L.B. Kosyakovsky *et al.*, doi:10.1093/eurheartj/ehab423.



Graphical Abstract Narrative of acute ischaemic heart failure.

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Coronary angiography has been a traditional diagnostic imaging test for epicardial coronary artery disease (CAD) and it provides ease of tailored decisions for cardiologists. There are some strengths and weaknesses of coronary angiography. It might potentially improve outcomes of heart failure (HF) patients by revascularization of epicardial CAD, as shown in the Surgical Treatment for Ischemic Heart Failure (STICH) trial,[1] although it might potentially harm the patient by contrast nephropathy, radiation exposure, and bleeding complications. Hence, a relatively well-established indication for coronary angiography is that HF patients are amenable to surgical revascularization, since the publication of the STICH trial, in which coronary artery bypass grafting was superior to medical therapy alone by reducing all-cause mortality, cardiovascular (CV) mortality, and CV hospitalizations over up to 10 years of follow-up;[2] however, percutaneous revascularization might potentially offer an alternative approach.

The role of coronary angiography in acute HF (AHF) remains equivocal, however, in the guidelines. The 2016 European Society of Cardiology HF guidelines[3] state with a Class I indication that 'invasive coronary angiography is recommended in patients with HF and angina pectoris recalcitrant to pharmacological therapy or symptomatic ventricular arrhythmias or aborted cardiac arrest (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity', and with a Class IIa indication that 'invasive coronary angiography should be considered in patients with HF and intermediate to high pre-test probability of CAD and the presence of ischaemia in non-invasive stress tests (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity'. Of note, both recommendations are designated by level of evidence C as there were few data supporting them at the time of preparation of the document.

Hence, physicians remain reluctant to perform coronary angiography, particularly during the early period, in patients with AHF since acute decompensation brings about several issues to be considered and managed simultaneously.[4] Therefore, with the exception of ST-elevation myocardial infarction (MI), where immediate intervention saves lives, early or in-hospital coronary angiography and related intervention rates during index AHF admission remain low in the real-life setting.[5]

Of note, some might advocate to opt for non-invasive testing for ischaemia or viability rather than proceeding directly with coronary angiography as recommended in the guidelines. However, neither of these modalities has a well-established role to triage which patient is best suited for coronary angiography. More importantly, CAD is present in at least half of incident HF cases and, in one out of four of them, coronary angiography remains the sole method to identify the disease.[6] On the other hand, acute coronary syndrome (ACS) can be a precipitant factor in up to 50% of the AHF population,[7] rendering pre-test likelihood of these tests high and hence weakening the discriminatory role of non-invasive testing. In the European Society of Cardiology Heart Failure Long-Term (ESC-HF-LT) registry, 14% of all AHF patients were reported to present with ACS, 56.5% had ischaemic heart disease, and 30% had myocardial ischaemia as a precipitant factor.[8] Hence, in such a frequent setting, there is no strong justification to limit coronary angiography to those with recalcitrant angina, which may or may not co-exist with dyspnoea, and which might be classified as angina equivalent, though it is rarely attributed as such.

Things get more complicated at the molecular level. Myocardial injury is present when there is elevation of the cardiac troponin (cTn) value above the 99th percentile of the upper reference limit of normal (ULN),[9] If there is a rise and/or fall of cTn values alone, there is, by definition, acute myocardial injury in the setting of AHF rather than type 1 MI, or type 2 acute MI.[9] Also, AHF might be the primary diagnosis of either type 1 or type 2 MI.[10] Hence, different phenotypes with different outcomes might potentially exist in AHF patients depending on the presence or absence of chest pain, and troponin elevation.[11] In the absence of strong evidence-based recommendations, highly varying practices might exist in different centres and countries.

In this issue of the *European Heart Journal*, Kosyakovsky *et al.*[12] have performed an intriguing analysis. The authors identified 7239 AHF patients who were admitted to 70 emergency departments in Ontario from 2010 to 2013. Then, they intentionally selected 2994 'acute ischaemic HF patients', defined as those with previous MI, troponin elevation, or angina on presentation, and excluded patients with a most likely diagnosis of ACS and those with contraindications to coronary angiography.

Early angiography, which was defined as invasive angiography performed within 14 days of admission in this study, was reported in 52.3% and it was associated with 26% lower all-cause mortality [hazard ratio (HR) 0.74, 95% confidence interval (CI) 0.61–0.90, P = 0.002], 28% lower CV death (HR 0.72, 95% CI 0.56–0.93, P = 0.012), and 16% lower HF readmissions (HR 0.84, 95% CI 0.71–0.99, P = 0.042). These positive outcomes were linked to 2.58-fold higher rates of percutaneous coronary intervention and 2.94-fold higher rates of coronary artery bypass grafting within 2 years. Hence, AHF patients with ischemic phenotype seems to benefit early angiography (*Graphical Abstract*).

Although the authors pointed out that they excluded patients with ACS, troponin in the cohort was categorized as normal, greater than the ULN, or in the MI range as per hospital-specific assays. Of note, MI range troponin elevation was present in half of the group, along with troponin greater than the ULN in two-thirds of the population, and angina was present in almost half of the cohort. However, the authors reported that findings were consistent in those with troponin greater than the ULN or in the MI range, with no significant interactions for all-cause mortality (P for interaction = 0.322) and CV death (P for interaction = 0.797). Hence, not only the MI range but also troponin greater than the ULN range seems to somewhat indicate the ischaemic phenotype, though the exact role should be further scrutinized in those with or without angina or a previous history of MI.

The potential benefit of early angiography might be doubled either by removing the list of unnecessary medications such as antiplatelet and antianginal agents, which might jeopardize up-titration of critical HF medications among AHF patients with no epicardial disease, or by addition of critical agents, which improve prognosis of significant CAD in AHF.

In conclusion, anatomic evaluation of CAD via early angiography, which gives enough time in this analysis to let the patient tolerate the supine position for invasive testing, seems to yield improved outcomes for patients with AHF having ischaemic signals, i.e. elevation of troponin, angina, or previous history of MI, though the use of

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physiological evaluation remains debatable in AHF patients with considerable congestion with elevated venous pressure. Hence, differential identification of the ischaemic phenotype of AHF seems to enable early coronary angiography which is advantageous for patient outcomes, although it remains to be established whether there are more specific signals to be added, and further validation cohorts are needed.

Conflict of interest: none declared.

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