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EDITORIAL

Avoiding invasive angiography in non-ST-elevation MI patients: are coronary CT angiography and FFR-CT the answer?

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The population of patients diagnosed as having non-ST-elevation myocardial infarction (NSTEMI) is heterogeneous. This diversity has been magnified by the routine use of high-sensitivity troponin (hsTrop) assays, since these facilitate, and thereby expand, the diagnosis of Type 1 and Type 2 myocardial infarction (MI) and myocardial injury[1]. Increasingly, this presents frontline clinical staff with a management dilemma in patients with a history of chest pain and troponin elevation, given that international guidelines recommend, on the basis of symptom improvement and prognostic advantage, invasive coronary angiography (ICA) with a view to revascularisation, where appropriate, in patients with Type 1 MI. There is, by contrast, no evidence of such advantages to the invasive strategy in other categories of NSTEMI.

This background helps to explain the consistent observation that a substantial proportion of cases with NSTEMI who undergo ICA do not have significant coronary artery stenosis(es). Given that ICA induces a degree of discomfort, anxiety and risk for the patient and carries a financial and bed occupancy cost to the healthcare system, such procedures can be deemed inappropriate. Strategies that seek to reduce the number of inappropriate ICA in this group are therefore conceptually attractive. Coronary computed tomography angiography (CCTA) is a candidate test around which to build such a strategy, taking into account its diagnostic performance in chronic coronary syndrome patients and the subsequent prognostic advantage seen using disease-modifying therapy in those patients with demonstrable atheroma[2]. Furthermore, fractional flow reserve (FFR) derived from CCTA (FFR-CT) has been shown in multiple observational and randomised studies to consistently yield significantly lower rates of ICA, and fewer ICA that yield unobstructed coronaries, without any compromise in safety in terms of clinical events[3-5].

In this issue of EuroIntervention, Meier et al present an observational study in which 151 patients with NSTEMI, who were classified as high risk by virtue of symptoms of ischaemia and elevated hsTrop, underwent (i) CCTA and FFR-CT followed by (ii) ICA and invasive FFR of all stenoses of 30-90%, all within 24 hours of admission[6]. Using the reference of significant coronary disease at ICA, defined as (i) a stenosis of 90% or more, or (ii) stenosis of <90% with an invasive FFR of ≤0.8, the primary endpoint was "the ability of FFR-CT and CCTA to rule out the presence of significant lesions... i.e., the negative predictive value... at the patient level". Unfortunately, the study, which was powered for 250 patients, was terminated early, apparently mainly due to pandemic-related recruitment issues. Nevertheless, it has yielded some interesting results that provide much food for thought.

Article, see page 73

Firstly, in this study population, guideline-directed therapy resulted in 34% of the patients having no significant coronary stenosis(es) at ICA, thereby highlighting the potential for better diagnostic strategies in this heterogeneous NSTEMI population. By contrast, the rate of potentially avoidable ICA (i.e., true negatives) would have been 19% with a CCTA-based strategy and 22% with an FFR-CT-based strategy. This is, in itself, an important observation and is completely consistent with existing data that confirm a significantly lower requirement for ICA in NSTEMI patients with upfront CCTA[7]. However, the mechanics of a CCTA-first strategy deployed routinely in NSTEMI patients is likely to be challenging outside the confines of a small study. Specifically, such an approach would require routine and rapid access to the CT scanner for a large, new population of patients who are generally not currently scanned, and a double-contrast load for the two-thirds who still need ICA after the CT. In the United Kingdom's National Health Service (NHS) system, certainly, this would be logistically challenging. In RAPID-CTCA, a multicentre trial that randomised NSTEMI patients

to early CCTA or routine care[7], there was a median increase in hospital stay of 0.21 days, but with a wide variation. Nevertheless, the rate of ICA was significantly lower in the CCTA group (54.0%) than in the standard care group (60.8%) (p=0.001), which is consistent with the current study. If this strategy could be achieved without putting the CCTA patients at a potential disadvantage in terms of length of stay, renal dysfunction or clinical outcome, then it is likely to be dominant from a patient satisfaction point of view. The cost efficacy of an upfront CCTA strategy would also need to be fully assessed.

Secondly, the Meier et al study invites us to question whether FFR-CT could have an additional advantage above and beyond CCTA alone in the investigation and management of NSTEMI patients. There is a paucity of data in this area. Chinnaiyan et al reported that FFR-CT did facilitate deferral of ICA and revascularisation in a cohort of patients with acute chest pain attending the emergency department (ED), but this population is not predominantly one consisting of NSTEMI patients[8]. The results in the current paper do not make a strong case for an additional advantage in an NSTEMI population from the point of view of the primary endpoint, which was the ability of FFR-CT and CCTA to rule out ICA+FFR-defined significant lesions at a patient level. In this regard, there was no significant difference between CCTA alone and FFR-CT. However, given the early termination of recruitment, with the inevitable lack of power that accompanies this, robust interpretation is impossible. Despite this, the overall diagnostic accuracy of FFR-CT was significantly greater than CCTA at a vessel level, as defined by the area under the curve. The latter observation, and the relatively small numbers in this study, speaks to the need for a large and randomised trial that assesses the relative value of CCTA alone and CCTA+FFR-CT in NSTEMI patients as arbiters of the need for medical therapy and ICA, with or without subsequent revascularisation. Such a trial would need to assess logistical feasibility (access times to scanner and catheter lab, length of stay, etc.), cost efficacy, patient satisfaction/quality of life, and safety, as well as clinical outcomes. Furthermore, the generalisability of such a result would be highly debatable; even within the United Kingdom, the waiting time for CCTA and ICA for inpatients is highly variable, and the relative waits would be a dominant consideration when estimating potential benefit even after a positive trial. For example, in our centre, the access time for ICA is less than 24 hours for NSTEMI patients, whereas the waiting time for CCTA is significantly longer. Thus, even for patients who avoid an unnecessary ICA, their hospital stay may be longer, and in fact the majority of the CCTA patients would be at the biggest disadvantage because they would still need ICA afterwards. There are few existing data with regard to the additional potential advantage of FFR-CT above and beyond CCTA alone. A substudy of the FORECAST trial that compares the outcome of patients in the usual care group who had CCTA with the test group who had CCTA plus selective FFR-CT is currently underway, but there are no other randomised data to address this question.

In summary, if it were logistically feasible to offer CCTA as the first test to patients with NSTEMI, this test would significantly reduce the number of patients who are offered ICA, and in particular, would reduce the proportion of ICA patients who have no significant coronary disease. The addition of FFR-CT in NSTEMI patients offers greater lesion-level diagnostic accuracy at the least, but specific clinical trials are now warranted to assess the impact accurately.

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Conflict of interest statement

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