Peer Review File

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Reviewer A:
This observational, prospectively enrolled and retrospectively analysed cohort study looked at STEMI patients with a high thrombotic burden, managed initially with a minimalist immediate mechanical intervention (MIMI) strategy, who had repeat angiogram seven days or more beyond the initial angiogram, at which they were managed conservatively. It aimed to look at the long term outcome of these conservatively managed patients, with a mean follow-up period of 4.1 +/- 1.0 years. Key endpoints included definite or probable new thrombosis of the culprit lesion (7%), rate of culprit and clinically driven target lesion revascularisation (10.5%) and event free survival over the follow-up period (82.5%).

Comment 1: The inclusion criteria is a little unclear to me in relation to how patients without severe stenoses at the second angiogram were selected. The inclusion criteria for the SUPER-MIMI study design (section 2.1) doesn't mention this, and the patients included in this cohort were just those that were managed conservatively at the second angiogram. Is that because patients managed with stents all had severe residual stenoses and all patients managed conservatively did not, or because all patients in the SUPER-MIMI study had non-severe stenoses at second angiogram and patients treated with stent had plaque sealing of non-severe lesions? I suspect the former, but I think this should be said explicitly. It's eluded to in the introduction (line 76-77) but I think should be in the methods.

Reply 1: The SUPER-MIMI study aimed to determine, in STEMI patients with a high thrombus burden, if postponing the second angiogram for more than 7 days after restoration of a TIMI 3 flow in the culprit artery was safe. The primary endpoint was the rate of culprit artery reocclusion between the two procedures. There were no guidelines on how to manage the patient during the second procedure. As such, the decision to stent or to manage the culprit lesion conservatively during the second angiogram was at the operator's discretion.

In the retrospective SUPER-MIMI substudy, we aimed to assess the long-term outcomes of patients managed conservatively in the SUPER-MIMI study. The rate of conservatively managed patients in the SUPER-MIMI study was high (36.8%). We found that the reason of this conservative management was the absence of significant residual stenosis (illustrated by the residual stenosis in this population: all the DRS were below 50% DRS with 59.6% of DRS <30% and 40.4% of DRS between 30 and 50% as shown in Table 2). In contrast, patients who were stented in the SUPER-MIMI study had more significant residual stenosis, with 71.4% of stenoses ≥50% in patients who were stented.

Changes in the text: The methods section has been revised as follows (paragraph 2.2 /

line 103-106):
"In the SUPER-MIMI study, there were no guidelines on how to manage the patient during the second procedure. As such, the decision to stent or manage the culprit lesion conservatively during the second angiogram was at the discretion of the operator."

Comment 2: Furthermore, the first line of the section 2.3 (line 121) says, 'The SUPER-MIMI substudy includes the 57 of 155 patients (36.8%) in the SUPER-MIMI study who benefited from conservative treatment without stent implantation during the second procedure.' Benefited in comparison to what? In comparison to patients treated with stents to severe stenoses or stents to non-severe stenoses? Maybe just saying 'patients managed conservatively,' may be better as how they performed against another group in another study isn't relevant in the methods. Also, again, did they not receive stents because they had non-severe residual stenosis?

Reply 2: We agree that the formulation is not sufficient. We have modified it as advised.

Changes in the text: Method section / 2.3 SUPER-MIMI substudy / line 111:
"The SUPER-MIMI substudy includes the 57 of 155 patients (36.8%) in the SUPER-MIMI study who were managed conservatively without stent implantation during the second procedure."

Comment 3: Also, what was the threshold for a 'severe stenosis' (? visual angiographic assessment of 50% or 70% - table 2 suggests it's 50%, but not stated in the methods).

Reply 3: As mentioned in response to comment 1, there was no prespecified threshold because the SUPER-MIMI substudy was retrospective. There were no guidelines on how to manage patients during the second procedure in the SUPER-MIMI study. As such, the decision to stent or to manage the culprit lesion conservatively during the second angiogram was at the operator's discretion. However, we can see in the SUPER-MIMI substudy that these lesions were not significant (illustrated by the residual stenosis in this population: all the DRS were below 50%, with 59.6% of DRS <30% and 40.4% of DRS between 30% and 50% as shown in Table 2).

Comment 4: I think the point about how patients were selected to have no severe residual lesion is important because, as the authors note in limitations, the key limitation is the lack of a comparator group. If it's very clear that the other patients in SUPER-MIMI, not in this sub-study, had severe stenoses at their second angiogram, then they are not a particularly relevant comparator group and the lack of a comparator group becomes more justifiable. The numbers in this study are small, but clearly look at a less common clinical problem which is thus more difficult to recruit for - if patients treated with stent also had no severe coronary stenosis at second

angiogram, they I think they should be included as a comparator arm if possible.

Reply 4: This is a very relevant comment. As mentioned in response to comment 1, in comparison to patients who were managed conservatively, patients who were stented in the SUPER-MIMI study had more significant residual stenosis, with 71.4% of stenosis ≥50%.

Changes in the text: Results section / 3.2 / line 146-150
"3.2 Culprit lesion characteristics
The culprit lesion diameter residual stenoses (DRS) during the second angiogram were all below 50% (Table 2). In contrast to patients who were managed conservatively, patients who were stented in the SUPER-MIMI study had more significant residual stenosis with 71.4% of the culprit lesion DRS above 50%."

Comment 5: I think in trying to explain the high thrombosis rates in the discussion, the discussion about anatomical characteristics and selection of culprit lesions for conservative management was well done. However, baseline characteristics were also cited as a reason, but were then stated to be similar in patients included in other similar studies (presumably with lower thrombosis rates). Thus I didn't feel it explained higher thrombosis rates in comparison to other studies, given the patients were similar in both studies, but rather imparted commentary (good commentary) about what types of patients have non-obstructive residual plaque after thrombotic occlusion (younger, smokers and thus plaque erosion). Could this paragraph be re-framed?

Reply 5: We agree that the formulation is not adequate. We have reframed it as advised. We first described the baseline characteristics, which were similar to patients included in other studies. Then we discuss the anatomical characteristics and selection of culprit lesions for conservative management, which may explain the higher thrombosis rate.

Changes in the text: We have reframed the discussion as suggested.
"The baseline characteristics of our cohort are consistent with other populations of STEMI patients who have been managed conservatively, which have consistently included younger patients with higher rates of smoking and lower rates of diabetes and hypertension compared with a general population with ACS. The high rate of non-stenotic culprit lesions among younger patients with myocardial infarction might be explained by a different underlying mechanism in these patients, with a higher prevalence of erosive lesions that usually display relatively minor luminal narrowing. In a histopathological study, smoking history has also been reported as a prominent risk factor among younger patients with coronary thrombosis; and hypertension and diabetes were more prevalent in stable coronary artery disease.[18]

Two aspects should be discussed to explain the higher rate of re-thrombosis in our cohort: the anatomical characteristics and selection of culprit lesions eligible for

conservative management…"

Reviewer B:

Comment #1: please provide statement in the methods describing IRB approval and if applicable trial registration

Changes in the text: Methods section / 2.3 SUPERMIMI SUBSTUDY / line 114-116:

The study was conducted in accordance with the Declaration of Helsinki and was approved by the national ethics committee (CPP approval number L13-112).