made on the basis of data that subsequently become available. In the discussion, we describe a 2% to 12% 30-day or hospital mortality among patients undergoing rescue angioplasty, but it is clear from the reference section that this includes data from studies published after initiation of the MERLIN trial.

It is extraordinary for the authors to suggest that we made the comment that 3,000 patients would be needed to show mortality benefit and that, knowing this, we went on to perform a trial on 300 patients. First, this comment does not actually appear in our study, having been removed (not at our request) during the review and editing process. Second, the figure of 3,000 is an estimation of the number required in each of the two arms in order to demonstrate significant reduction in coronary mortality at the levels we observed (11% conservative vs. 8.5% rescue). Their comments imply that the authors have not understood our power calculation and also that they have either reviewed our original study and been subsequently unaware of changes made by the editorial team, or been given the wrong draft to comment on in the editorial process.

We have not stated that the primary end point in the MERLIN trial is negative, but instead that we failed to demonstrate mortality benefit. Presentation of the results in open forum suggests that those in favor of rescue angioplasty have seen a slight benefit in mortality, as well as the perceived advantages of the combined end point, and interpret this as a reason to continue a rescue program. Conversely, skeptics interpret our results as confirming their belief that rescue angioplasty is performed too late to be beneficial.

We agree that the majority (56%) of our patients had nonanterior infarction, but this is not the same as inferior infarction and does not imply anything about infarct size. The investigators state that randomized trials and American Heart Association/American College of Cardiology guidelines suggest that clinical benefit from rescue angioplasty is confined to anterior myocardial infarction (MI). However, this is based almost entirely on data from the RESCUE trial (3), with its limitations as described. No randomized trial has demonstrated lack of benefit from rescue angioplasty in patients with nonanterior MI.

Despite the above comments, we suspect there is no major conflict. A successful rescue angioplasty frequently benefits the patient: the vessel opens, flow is restored, the ST segments come down, and there are no complications. However, it is an omission to make no comment on the potential for harm. The challenge is to identify those patients with most to gain and the lowest risk of harm.

We have not abandoned rescue angioplasty, and certainly not abandoned the open-artery hypothesis. We believe that primary angioplasty is the best treatment for ST-segment elevation myocardial infarction. However, while patients continue to receive fibrinolytics for ST-segment elevation myocardial infarction, the question of rescue remains. Our approach is a selective one, in line with the editorial view. Our current focus is on how to deliver primary angioplasty to a large population in the northeast of England with equitable access to care for all patients. If this can be achieved, the unanswered dilemmas of rescue angioplasty will become relatively less important.

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REFERENCES


REPLY

We thank Drs. Sutton and Belder for their interest in our paper (1) and again wish to compliment Sutton et al. (2) on undertaking the largest rescue angioplasty trial conducted to date. It appears that we were using an earlier version of the study when commenting on the required sample size of 3,000 patients, and for this we apologize. But all parties agree that one could not expect a significant reduction in mortality given the small sample size and control group mortality of only 11%.

Although we can debate whether nonanterior myocardial infarction (MI) is the same as inferior MI, it is clear that patients who present with inferior ST-segment elevation have a smaller infarct size (3) and better prognosis than patients with anterior MI (4). Moreover, given the low baseline risk of inferior MI patients, it has been difficult to prove a mortality advantage with reperfusion therapy compared to placebo (4).

So what have we learned from the MERLIN trial? It is clear that rescue angioplasty has room for improvement. Consistently, rates of Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 after rescue percutaneous coronary intervention (PCI) are lower than those reported after primary PCI. We had hoped that extraction of thrombosis or use of distal protection devices would improve perfusion and clinical outcomes. Yet large, randomized trials using distal protection (EMERALD trial) or thrombectomy (AIMI trial) showed no improvement in TIMI flow grades, myocardial blush scores, infarct size, or major adverse cardiac events compared to PCI alone (5). The lack of benefit may have been due to embolization with saline agitation, advancing the device past the thrombotic lesion or diverting emboli into proximal side branches. Therefore, it is possible that use of lower-profile thrombectomy catheters, filters, or proximal protection devices may be of benefit.

We agree with the MERLIN investigators that the focus should not be on rescue PCI, but on how to deliver primary angioplasty to a larger population. Performance of primary PCI (by an experienced PCI operator) in a diagnostic-only catheterization laboratory would increase availability enormously. We should work toward a goal of performing prehospital electrocardiography and transferring patients with ST-segment elevation myocardial infarction from home, directly to a primary PCI center.
Definition of Failed Lysis May Have Influenced Outcome in the MERLIN Trial

We note with great interest the findings of the recent MERLIN trial (1). We congratulate the investigators on their attempts to evaluate prospectively the efficacy of rescue angioplasty in this randomized controlled trial. We would, however, like to point out a few potential confounding factors that may have had an important effect on the findings.

We note that the definition used for failed lysis was “a second ECG [electrocardiogram] at 60 min after onset of lytic therapy, showing failure of the ST-segment elevation in the worst lead to have resolved by 50%, as compared with the pre-treatment ECG, as well as the presence of an accelerated idioventricular rhythm at the time of the 60-min ECG.” We believe this definition of failed lysis may have clearly influenced the outcome of the trial. As acknowledged in the accompanying editorial (2), the time of 60 min may have led to more patients being taken for coronary angiography than if 90 min were used. It is possible that a number of patients who were entirely pain free may have undergone angiography; these patients might have been exposed to a procedure with a risk involved and hence affected the outcome parameters assessed.

We acknowledge the lack of large randomized trials in this field, and once again congratulate the investigators on their attempt to answer this important question. We hope further studies in this area will add to the emerging evidence regarding rescue angioplasty.

REFERENCES


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REPLY

We thank Dr. Osman and colleagues for their interest in the MERLIN trial report (1). We would like to address their comments on potential confounding factors.

First, they appear to have misread the protocol definition for failed fibrinolysis, which was “a second ECG [electrocardiogram] 60 min after the onset of fibrinolytic therapy showing failure of the ST-segment elevation in the worst lead to have resolved by 50% by comparison to the pre-treatment ECG as well as the presence of an accelerated idioventricular rhythm at the time of the 60-min ECG.”

Second, we debated the most appropriate method of diagnosing failed fibrinolysis, specifically the timing of the second ECG. In a previous study we assessed the ability of a 2-h ECG, performed immediately before coronary angiography, to predict flow in the infarct-related vessel (2). In the MERLIN trial we elected to diagnose failed fibrinolysis at 60 min for the following reasons: a) time is muscle, particularly when the initial reperfusion strategy is ongoing chest pain. When assessing the possibility of failed lysis we, at our institution, always assess whether the patient has ongoing chest pain. This forms an important part of the evaluation of whether a patient is taken for angiography in the first place. Continual chest pain is regarded as a very good indicator of failed lysis and recommended as an important noninvasive marker for defining failed lysis (3). Some of the patients in the MERLIN trial who were entirely pain free may have undergone angiography; these patients might have been exposed to a procedure with a risk involved and hence affected the outcome parameters assessed.

We acknowledge the lack of large randomized trials in this field, and once again congratulate the investigators on their attempt to answer this important question. We hope further studies in this area will add to the emerging evidence regarding rescue angioplasty.