Reviewer's report

Title: A randomized comparative study of patients undergoing myocardial revascularization with or without cardiopulmonary bypass surgery: The MASS III Trial

Version: 2 Date: 1 July 2008

Reviewer: Barry Davies

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1. Will the study design adequately test the hypothesis?
This is unclear for two reasons – the sample size calculation does not consider crossovers (which Figure 1 explicitly acknowledges) and there is no discussion of how endpoints, specifically the primary endpoint, are to be assessed. Is this going to be accomplished by a committee and in an unblinded fashion?

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?
There is some confusion as to the primary endpoint and its time frame

In Primary Composite End Points the protocol says
“The predefined primary end point was the incidence of cardiovascular mortality, cerebrovascular accident, nonfatal myocardial infarction, and refractory angina requiring revascularization.”

And in Methods it says “The sample size calculations are based on the assumptions that the actuarial freedom from cardiac event rate 3 years.”

BUT

In Primary Composite End Points the protocol says

“So, the primary end point in the comparison of surgery with and without cardiopulmonary bypass is also a cerebral event. This is defined as the proportion of patients free of the combined event of fatal and nonfatal cardiovascular accidents and cognitive dysfunction, whichever occurs first, to be determined in-hospital and during the 5 years of follow-up.”

These statements appear to be in conflict.

3. Is the planned statistical analysis appropriate?
The use of the Cox regression model appears to be appropriate although consideration should be given to testing the assumption of proportional hazards since the immediate effects versus the long-term effects of the interventions may be different.

Interim analyses are mentioned but no details are provided. There is no mention of a Data and Safety Monitoring Board besides a listing of members at the end of
the document.

4. Is the writing acceptable?

It is acceptable. There are some typos and grammatical mistakes.
- Should read “…coronary surgery with and without of cardiopulmonary bypass
in…” (in ABSTRACT and Objectives)

- The primary endpoint should be a composite of cardiovascular mortality,
cerebrovascular accident, nonfatal myocardial infarction, and refractory angina
requiring revascularization rather than an incidence of … (in ABSTRACT and
Primary Composite End Points)

- In Author’s contributions

Should be “Principal investigator…”
Should be “Additionally, SAO,…”