Reviewer's report

Title: Revascularization and cardioprotective drug treatment in acute coronary syndrome: How did they impact on patients' survival when delivered as usual care

Version: 1 Date: 17 February 2006

Reviewer: Valentin Fuster

Reviewer's report:

The authors present data on 9566 patients ≥65 years old surviving an acute coronary syndrome and present the associations of revascularization (percutaneous or surgical) and degree of use of recommended medications for secondary preventions (aspirin, statin, ACE inhibitors and betablockers) at discharge with total and cardiovascular mortality at 2 years. Survival was adjusted for age, gender, and a comorbidity score derived from the number of non-cardiovascular medications used by the patient. Data were obtained from central (hospital and province) databases. Adjusted survival was strongly associated to revascularization and, to a lesser extent, to the number of drugs prescribed.

1. General comments:

a) This is a well-written paper presenting interesting data on a large group of patients in the “real world”. The authors find some expected results, such as the improved survival derived from appropriate use of secondary prevention drugs (as previously demonstrated by Mukherjee et al; Circulation 2004). Some of the results are particularly surprising, like the better survival during the acute episode of those patients with more comorbidities (table 1) or the fact that patients with the lowest index of comorbidity had higher death rates at 2 years than sicker subjects (table 3). The finding that revascularization is the main determinant of survival, and even without subsequent therapy it appeared to be better than complete and correct medical treatment requires careful consideration. The reason for this finding might be that those patients without revascularization did not undergo catheterization because of different resources in different centers; therefore they would have been denied the potential benefits of this intervention. Or it might be that their coronary anatomy was not suitable for revascularization (because of low-grade or very advanced disease). Or because they had more comorbidities although this did not seem to be the case with the score employed by the authors. However, the “unexpected” results mentioned above together with reasonable uncertainty that those subjects taking more drugs have necessarily more severe diseases raises doubts on the validity of such an index. Finally, it might be possible that revascularization “per se” was necessarily better than medical treatment, as the survival curves appear to imply. Although this may be the case in the setting of STEMI (at least the restoration of coronary patency) it is still controversial in the case of NSTEMI or unstable angina. Unfortunately, we do not know the proportion of both. Therefore, reaching the latter conclusion requires great caution, as other studies better designed to confirm this hypothesis have yielded contradictory results. Looking at the data in this paper (figures 2-3), it would be possible to suggest that revascularization without subsequent treatment is a better option than correct medical therapy in a subject with unstable angina and one-vessel CAD. These considerations should be emphasized in the discussion to avoid sending a wrong message.

b) Another important issue is if revascularization and cardiovascular drugs had an impact in non-cardiovascular mortality (and if so why this could be) or if the whole benefit in total mortality came from the reduction in cardiovascular mortality alone. This should be included in the results.
2. Specific comments:

a) All abbreviations (ACE, ASA, etc) should be defined on first use.

b) Page 6, Methods, Studied population, line 4: what does “stable ACS cases” mean?

c) Page 7, Methods, Statistical Analysis, last line: The version, etc. of SAS needs not be included as a reference.

d) Table 1: Please add 2 additional columns: one with the total numbers for the population (such as in tables 2 and 3), and another one with the p values of the comparisons between survivors and deceased.

e) The statistical analysis in Tables 2 and 3 is confusing. For example, in table 2, does the asterisk in the first section apply to 2 groups (revascularization yes/no) or to types of revascularization? Similarly, in table 3, in the gender category, does the asterisk apply to only men (different groups ages) or men versus women, or both? These tables should be modified so that statistically significant differences are clear. In addition, what type of test was used for these comparisons (ANOVA, post-hoc test?) should be mentioned in the Methods. Also, the asterisk in the tables refers to p<0.0001: is the threshold employed by the authors to determine significance? (please explain).

f) Data shown in the tables needs not be repeated in the text (for example, a large part of the second paragraph of the methods, pages 8-9). If the authors want to emphasize one message, they should do so in the discussion.

g) Which survivals curves are significantly different from others? The scale of the survival curves graphs is somewhat misleading, as the lowest value in the y axis is very high. Figures 2-3 could be divided in 2 figures each, one showing the revascularization group and another one the non-revascularization group. In addition, if the age- and gender-adjusted curves were similar (as mentioned by the authors in the discussion) why did they choose to show the unadjusted (and less valuable) curves instead?

h) In table 4, adjusted hazard ratios are adjusted for what? All other 4 co-variables?

i) Why in the regression trees some of the “branches” include comorbidities but not others?

j) There is a typo in the first line of the Discussion. Also in page 11, paragraph 2, line 3.

I hope the above comments and suggestions are helpful to the authors.
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.