Reviewer's report

**Title:** Risk factors for the progression of atherosclerosis after primary CABG: Gene polymorphisms in the APOE, NOS3, and LIPC genes predispose to adverse events

**Version:** 1  **Date:** 26 April 2009

**Reviewer:** Angel L Fernandez

**Reviewer's report:**

**Major Compulsory Revisions**

**Title.**

In my opinion the title does not reflect the content of the article. The title proposed by the authors may assume that in this article adverse events after primary CABG are secondary to progression of atherosclerosis. However it is known that adverse events may be secondary not only to atherosclerosis progression but also to vein graft atherosclerosis and graft thrombosis. In my opinion a title as “Gene polymorphisms in the APOE, NOS3 and LIPC genes are risk factors for cardiac adverse events after primary CABG” may be shorter and clearer.

**Methods.**

The authors define CAD progression as the need for reoperation, re-intervention (PCI and/or hospital admission for myocardial infarction) or angina at the time of follow up. However in the medical literature CAD defines only native-vessel coronary artery disease. This means that reoperation, PCI and angina should not be proposed as clinical surrogates for CAD because vein graft atherosclerosis, graft occlusion and incomplete surgical revascularization may be cause of reoperation, CPI and angina. In my opinion the expression CAD should be suppressed from the manuscript since no data about native-vessel coronary artery disease progression are reported. The expression “CAD progression” could be replaced by another one as “cardiac adverse events”.

**Results.**

Preoperative risk factors of CAD and its progression.

The authors asseverate “Obviously, patients were postoperative fairly efficiently treated for their classical risk factors, so that these risk factors did not develop a more significant influence”. I disagree with the authors. It has not been demonstrated that patients were postoperative efficiently treated for their classical risk factors. Only 50% of patients received statins at the time of follow up and in my opinion this is a very low rate because 75% of patients presented with hypercholesterolemia at the time of first CABG. The treatment of classical
risk factors is appropriate only if therapeutic goals are achieved. Plasma concentration of cholesterol at the time of follow up should be displayed as well as glycosylated hemoglobin in diabetic patients. In my opinion only if these risk factors were appropriately managed it may be assumed that they not exerted a significant influence in the postoperative evolution and therefore this asseveration should be modified.

Gene polymorphisms and the progression of CAD.

The distribution of the patients according to polymorphisms should include any data concerning the status of classical risk factors (levels of LDL cholesterol, presence of diabetes etc) in each polymorphism subgroup indicating if any significant difference was observed between the subgroups.

Discussion.

In the sixth paragraph the authors asseverate “Certainly medical therapy, particularly lowering of low density lipoprotein cholesterol levels, has been proven to reduce the advancement of CAD after CABG (19). Due to the design of our retrospective study we were unable to prove the beneficial effects of medical therapy, because therapy after primary CABG was determined by the cardiologist and patients with recurrent syndromes received intensified medical therapy. Likewise, the role of classical risk factors on the CAD progression is difficult to interpret. Risk factors at the time of primary CABG were medically treated………..Therefore, these classical risk factors lost their predictive value”. I disagree with the authors. It has not been demonstrated that patients with recurrent syndromes received intensified medical therapy and as a matter of fact only 50% of patients received statins. It has not been demonstrated that neither the control of risk factors was difficult to interpret nor the classical risk factors lost their predictive value. The reduction of cardiovascular events and the need for repeat coronary revascularization in patients with previous CABG by lowering LDL-cholesterol has been clearly demonstrated in large groups of patients (Shah SJ et al. Intensive lipid-lowering with atorvastatin for secondary prevention in patients after coronary artery bypass surgery. J Am Coll Cardiol 2008; 51: 1938-43). However no data are shown about the level of LDL cholesterol at the time of follow up. We do not know if an appropriate control of hypercholesterolemia was achieved in any case. Only 50% of patients received statins but 75% presented hypercholesterolemia at the time of the first CABG. In my opinion the authors should modify this paragraph.

Minor Essential Revisions

Introduction.

In my opinion the introduction is should be shortened.

In the first paragraph the sentence “We hypothesized that classical risk factors of atherosclerosis…..”. is repeated again in the last paragraph “We hypothesized…..”. One of the sentences should be suppressed.
In the fifth paragraph the authors asseverate “We investigated the T202T polymorphism ....”. This sentence belongs to the Methods section instead to the introduction and should be suppressed.

Methods.

In the first paragraph the authors explain that “perioperative data and postoperative therapies are listed in table 1. However the therapy is not showed in table 1 and should be included.

In the first line of the Statistics the word "und" should be replaced by the word "and".

Results.

Preoperative risk factors of CAD and its progression.

Documented risk factors at the time of primary CABG do not include the presence of diabetes mellitus. It should be of great value to indicate the number of diabetic patients were included in the study and the possible impact of diabetes on the clinical evolution. The authors showed risk factors at the time of primary CABG but there are no data about risk factors along the follow-up. The presence of hypertension, diabetes and plasma concentration of LDL cholesterol should be reported at the time of the follow-up visit.

Discussion

In the second paragraph 17th line the word "und" should be replaced by "and".
In the second paragraph 18th line the word "after" should be replaced.

Discretionary Revisions

Results.

Perioperative parameters and progression of CAD.

It should be interesting to study the impact of the graft used either internal thoracic artery or saphenous vein on symptoms recurrence, reoperation and PCI.

References.

All references were published before 2005. Any substantial articles have been published since then. They should be included and discussed in the manuscript.


Silbert BS et al. The apolipoprotein E4 allele is not associated with cognitive dysfunction in cardiac surgery. Ann Thorac Surg 2008; 86: 841-8
**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests