Reviewer's report

Title: Age-dependent defective TGF-beta1 signaling in patients undergoing coronary artery bypass grafting.

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Reviewer: Carlos G Santos-Gallego

Reviewer's report:

The authors intend to study the age-dependent development of atherosclerosis and test the hypothesis that it is due to defective TGF-β signaling with increasing age. The authors find 1) TGF-β expression inversely correlates with age in conditioned medium from VSMC obtained from mesenteric arteries from abdominal surgery patients; 2) TGF-β plasma levels in CABG patients; 3) the expression of p27 (one of the main pathways of TGF-β) also inversely correlates with age in tissue from internal mammary arteries from CABG patients.

The article is interesting. It has a clear hypothesis, the design is simple but elaborated to answer the research question, the samples size is large (and importantly it involves real-life patients) and the results confirm the hypothesis of the age-dependent reduction in TGF-β favouring atherosclerosis development.

Major Compulsory Revisions: None

Minor Essential Revisions:
- In the abstract, it is not clear which patients (CABG or abdominal patients) provide which sample (arteries, plasma,...). The reader has to go to the Methods and Result section to get that information. Please rephrase the abstract to clarify. How many abdominal surgery patients?
- Is there a relationship between TGF-β levels and pharmacological treatment (ie, do statins/ACEI/betablockers affect TGF-β signaling) in this population?

Discretionary Revisions (recommendations for improvement which the author can choose to ignore):
- Is there any relationship between TGF-β levels and severity of atherosclerosis (eg, % of maximal stenosis in coronary angiography, number of coronary segments affected, Framingham score, Agatston score,..., or rough estimates such as LVEF or wall motion score index or positivity of conventional stress tests -echo, nuclear-) even after adjusting by age? This result would greatly enhance the message conveyed by the authors.
- Since TGF-β acts mainly through the SMAD pathway, the finding of age-dependent SMAD signaling pathway in the internal mammary arteries would also reinforce the results.
Level of interest: An article of importance 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 do not have any conflict of interest regarding this manuscript