Reviewer's report

Title: Elevated level of plasma Endothelin-1 in patients with atrial septal defect.

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Reviewer: Silvia Favilli

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The Authors investigate the ET-1 levels in patients with atrial septal defect (ASD) before and after closure; the aim of the study was to identify a new diagnostic and prognostic parameter to identify proper candidates for ASD closure.

The discussion analyses the data providing two main conclusions: 1) ET1 levels are higher in ASDs pts than in healthy controls and decrease after closure; 2) in ASD pts ET-1 levels are correlate with age, enlargement of right cavities and pulmonary artery pressure (but the early decrease after closure depends on the reduction of pulmonary blood flow, probably irrespective of pulmonary resistances).

The main criticism concerns the clinical value of the data provided by the Authors. The indications to ASD closure depend on several clinical, echocardiographic and sometimes hemodynamic parameters which are well defined in most patients.

It remains some ‘grey zones’ (older patients, with diastolic dysfunction; patients with moderately high pulmonary artery resistances) for which new ‘predictive’ parameters would eventually be useful, but a possible role of ET-1 in these challenging cases has not been discussed in the paper.

I agree that the possible additional informations provided by ET-1 plasma levels in populations with congenital heart disease deserve to be investigated (as it has been for NT-pro BNP, which is now increasingly used also in this particular subset of patients), but we need to define the aim of a prospective study. An incremental value of ET-1 levels in the decision making about closure of ‘asymptomatic patients older than 40 years of age, with normal pulmonary artery pressure’ (where the presence of right cavities overload remains the main criteria for intervention) is not demonstated by the present study.

Analysis of results and discussion should be modified in order to suggest (if it is possible, on the basis of Authors preliminary experiences) a possible role of ET-1 for the therapeutic choices:

a) do the Authors propose a medical follow-up (versus closure) in pts with small ASDs and low ET-1 levels?

b) do higher ET-1 levels before closure predict higher pulmonary artery pressure/resistances after closure?

c) could ET-1 dosage be considered in different populations with congenital heart
disease, where the decision or the timing for intervention is still under debate (eg, pts with operated Tetralogy of Fallot and pulmonary regurgitation)?

**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