Reviewer’s report

Title: Admission Hypoxia-inducible Factor 1alpha Levels and In-Hospital Mortality in Acute Decompensated Heart Failure Patients

Version: Date: 25 March 2015

Reviewer: Armando Pucciarelli

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Comment by Armando Pucciarelli
The authors evaluated the impact of serum levels of HIF-1# (hypoxia-induced factor) on the short term clinical outcomes of patients affected by acute decompensated heart failure (ADHF). HIF-1# detected in the serum was not identified as a predictor of short-term prognosis in the ADHF, when using the Cox proportional hazards multivariate analysis. However, a significantly higher level of this factor was demonstrated in the serum of patients dead during ADHF compared to the one found in survivors. Moreover, its levels were higher in heart failure patients with reduced left ventricular ejection fraction compared to those found in patients with preserved ejection fraction. A significant correlation of HIF-1# with serum levels of NTproBNP was detected.

Major Compulsory Revisions.
- The paper is written in bad English and it cannot be accepted for publication in its current form; it needs a heavy editing for the removal of the very numerous spelling and grammar errors.

Other criticisms are outlined below.

- Abstract, Conclusions, row 22: The sense of this sentence is understandable, however probably it should be written in a more correct manner, as follows: “It may become a prognostic biomarker of heart failure, however this potential role needs to be convalidated by means of further prospective studies in the future”

- Introduction page 1, row 4. “Some researchers have been proved that the synthesis of BNP was directly caused by hypoxia mediated through HIF-1# independent mechanism without the stimulation of hemodynamic and neurohormone, which was based on ventricular myocyte model system in vitro”. The sentence is poorly written and needs to be reworked. Please correct “Some researchers have demonstrated...”

The grammar and spelling mistakes are so numerous that they require a heavy revision of the text for improving the language. This could be achieved by requesting the assistance of a specialized service for copyediting of academic and scientific manuscripts. This recommendation is aimed to avoid regrettable rejection of this very interesting manuscript.

- Results page 7, row 2: The levels of HIF-1 are very high in this series, due to the
existence of a condition of cardiac acute decompensation. However, the reader needs to be adequately informed about the normal range of the serum level of HIF-1 among healthy subjects as well as patients with systolic or diastolic dysfunction; in addition, exhaustive information should be provided about the serum levels of HIF-1 among patients with ADHF. This information could be provided within a table, or, alternatively, it could be given in the text of the Results, so as to enable the reader to understand the meaning of the values (expressed as pg/ml or ng/ml or ng/liter). Please report the requested information about the normal and pathological serum levels of HIF-1 under the various conditions (healthy individuals, left ventricular dysfunction [systolic or diastolic], left ventricular failure).

- Results, page 7, row 7: "HIF-1 levels positively correlated with NT-proBNP (r = 0.337, P<0.001), TnT (r = 0.357, P<0.001), and negatively correlated with LVEF (r = -0.332, P<0.001) and SBP (r = -0.145, P=0.013). " Please add the correlation plots in order to better describe the correlations that have been found between HIF-1 and NTproBNP, HIF-1 and TnT, HIF-1a and LVEF, HIF-1a and SBP (four scatter plots on the whole).

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**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.