Reviewer's report

Title: Comorbidity Profiles and Inpatient Outcomes during Hospitalization for Heart Failure: An Analysis of the U.S. Nationwide Inpatient Sample

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Reviewer: Armando Pucciarelli

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Commentary by Armando Pucciarelli

Major Compulsory Revisions

The division into profiles of comorbidity, even though it is arbitrary, is effective in providing a new model of prognostication and an assessment of health care costs. In fact, the profiles are grouped according to a) the connection with lifestyles, b) the possible dominant role of renal dysfunction or c) the coexistence of acute ischemic coronary or cerebrovascular events. This is a very valuable way of attempting to accomplish a really new kind of nosographic scheme.

- However, we must emphasize that these profiles can imperceptibly evolve into one another with the progression of heart failure but also due to any pejorative trend which is restricted to co-morbidity and not primarily caused by the further deterioration of heart failure. For example, this may be the case of a lifestyle-related pattern, in which the presence of diabetes may lead to the development of diabetic glomerulopathy, even in the absence of pejorative evolution of pump failure. Thus, over time, the original pattern may come to display the clinical characteristics of heart failure including prominent renal dysfunction ('renal' profile). Therefore, these patterns should be considered as being rather dynamic entities which can vary considerably over time, so as to render an over-rigid categorization as being problematic in each of the proposed profiles. These concepts should be briefly addressed in the section ‘Limitations of the study’.

- Another limitation of this work is the lack of discrimination between patients with preserved and those with reduced left ventricular ejection fractions. In fact, according to several authors, the prevalence of diabetes mellitus, poorly controlled hypertension, obesity and atrial fibrillation is higher in heart failure patients with preserved ejection fraction (HFPEF) compared to those with reduced ejection fraction (HFREF). In this regard, see also Lam CS, Donal E, Kraigher-Krainer E, Vasan RS: ‘Epidemiology and clinical course of heart failure with preserved ejection fraction’. Eur J Heart Fail. 2011; 13:18-28. In studies that included both HFPEF and HFREF, patients with HFPEF were consistently found to be older, were more often female, more predominantly hypertensive, with a higher prevalence of atrial fibrillation but a lower prevalence of coronary artery disease compared with those with HFREF. This could also be highlighted in the section ‘Limitations of the study’ in order to be in keeping with reviews that tend to emphasize the existence of two distinct nosographic entities, namely HFPEF
and HFREF, without the mandatory evolution of the former toward to the latter.

- According to some authors (Lenzen MJ, et al., Eur Heart J. 2004 Jul; 25(14):1214-20; Owan TE, et al., N Engl J Med 2006;355:251–259; Lee DS et al., Circulation 2009; 119:3070–3077) considerably more interconnection has been evidenced between etiopathogenesis of HFPEF and diseases that could benefit from interventions in lifestyle, such as diabetes mellitus, obesity and hypertension. Thus, in order to prevent HFPEF in predisposed individuals (mostly hypertensive or diabetic patients) both the rationalization of food intake and regular practice of aerobic exercise is strongly recommended. Thus, in my opinion, the suggested addition would be useful in order to emphasize the complexity of the issues that underlie the ethiopathogenesis of these two types of chronic heart failure, whose potential relevance has been substantially disregarded in the new proposed categorization based on comorbidity profiles. Please express these considerations in the Discussion.

**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 declare that I have no competing interests