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: Antonio Ciccarelli

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Comment by Antonio Ciccarelli

Major Compulsory Revisions

This study proposes an innovative classification of the heart failure syndrome subdivided according to the clinical profiles based on comorbidities. However, there are several points that led me to raise criticism and express some perplexities and requests for corrections.

- For example, the so-called "common" profile of chronic heart failure has not been outlined in a comprehensive manner. In fact, it seems to me that a detailed description of symptoms and signs is lacking for this pattern. The definition of the so-called "common" profile should be better presented.

- This classification was constructed on the basis of administrative data, that is, by evaluating and by numbering the principal diagnosis and secondary ones, as reported in an electronic database prepared by the hospital directorates; as such, it is adversely affected by the inaccuracy that is typical of large studies that do not include clinical data. Thus, my impression is that this classification may be useful for putting forward predictions about hospital costs and the financial management of disease; however, in my opinion, it does not bring much important information to the clinician who wants to schedule the therapeutic management of a patient with chronic congestive heart failure. In case the authors are in agreement on this point, a few comments about the lack of clinical data (e.g., left ventricular ejection fraction, estimated glomerular filtration rate, mean values of systolic blood pressure, the 6-min walking test, etc.) should be included in the "Strengths and Limitations". In other words, the authors should emphasize that, since clinical data are unavailable, the chance to extract useful information from summary administrative data is rather limited.

- The choice of codifying several profiles characterized by different clinical severity and developed on the basis of a simple list of concurrent diseases really offers a rather crude nosographic arrangement. In fact, with such a superficial classification of the comorbidities, the target of defining whether or not there is a causal relationship between chronic cardiac failure and the concomitant pathology is not reached. In other words, the renal dysfunction that occurs in the context of heart failure syndrome after prolonged vigorous diuretic therapy or ultrafiltration for the removal of interstitial fluid generally has a less severe significance compared to the impairment of renal function resulting from diabetic
glomerulopathy or nephroangiosclerosis, namely from diseases that are originally independent of chronic heart failure. Ascertaining whether the concomitant disease is a complication of heart failure, a predisposing condition or a simple pathological overlap without any causal relationship is sometimes very difficult or impossible in the presence of only administrative data. This issue should be addressed in the Discussion.

-A first clinical distinction is that between failure (dysfunction) of the left ventricle and that of the right ventricle; also, there is biventricular congestive heart failure in cases characterized by original left ventricular failure, which results over time in pulmonary venous hypertension and thereafter in pulmonary arterial hypertension causing overload and dysfunction of the right ventricle. Since the distinction between left and right or bilateral ventricular failure is often omitted from the electronic archives for administrative use, this important information is lost. In this regard, it should be considered that the renal dysfunction that occurs in left-sided chronic cardiac insufficiency is less frequent and far less serious than that which is realized in right ventricular or biventricular chronic heart failure. Also this issue could be addressed in the Discussion.

- Moreover, the nosographic discrimination between heart failure with reduced (HFrEF) and that with preserved left ventricular ejection fraction (HFpEF) is only very succinctly mentioned. The omission of the well-known distinction between HFpEF and HFrEF is recognized by the Authors, but they underrate the differences in clinical phenotype, judging by their statement that the comorbidities usually do not show any significant differences in comparison between HFrEF and HFpEF (please see the section "Strengths and Limitations": "We also did not differentiate between HF with preserved or unpreserved ejection fraction, although coupling of comorbidities do not seem to differ considerably between these subgroups of HF"). This is incorrect because the burden of co-morbidities is certainly greater in patients with HFpEF, if only for the fact that their mean age is higher. It is important to note that in HFpEF category, female sex, older age, poorly controlled hypertension, diabetes mellitus type II, atrial fibrillation and obesity are much more represented compared to HFrEF. The text should be changed accordingly in the section "Strengths and Limitations", and this issue should be adequately addressed in the Discussion.

- Therefore the subdivision by comorbidity profiles presented by the Authors does not take into account some established distinctive profiles of chronic heart failure, such as the distinction between left-sided, right and biventricular heart failure and that between HFpEF and HFrEF. In truth, each innovative classification should take into account those already existing, to demonstrate that the new proposed schema brings some advantages or additional information with respect to the existing categorizations. Thus, I would advise the Authors to elaborate in the Discussion a brief list of the clinical classifications adopted so far. Thereafter, it would be desirable to highlight the possible points of intersection and divergence with respect to their novel classification based on lists of comorbidities.

**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.