Author's response to reviews

Title: Anemia and chronic kidney disease are potential risk factors for mortality in stroke patients: a historic cohort study

Authors:

Patrizia Del Fabbro (p_delfabbro@yahoo.de)
Jean-Christophe Luthi (Jean-Christophe.Luthi@chuv.ch)
Emmanuel Carrera (Emmanuel.Carrera@chuv.ch)
Patrik Michel (Patrik.Michel@chuv.ch)
Michel Burnier (Michel.Burnier@chuv.ch)
Bernard Burnand (Bernard.Burnand@chuv.ch)

Version: 3 Date: 27 August 2010

Author's response to reviews: see over
Dear Dr. Norton,

Please find attached the revised version of our manuscript and, below, a point-to-point reply to your requests and the Referees’ Reports.

We trust that we have answered the various comments made by the Referees and hope that the manuscript can be accepted for publication in its revised format.

With best regards,

On behalf of all authors

Dr. Bernard Burnand

Lausanne, 25th August 2010

MS 1731854329376257
Point-to-point response to Editorial Requests and Referees’ Reports

<table>
<thead>
<tr>
<th>EDITORIAL REQUESTS</th>
<th>Answers provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of data – Please clarify if you received permission to use the data for this study. If permission was not required, please provide a statement to explain why permission was not needed. This must be included in the Methods section of the manuscript.</td>
<td>The use of the data is possible, since our Hospital benefits from a general authorisation for research protocols delivered by the Swiss Federal Data Protection and Information Commission within the framework of the Data Protection Law, any hospitalised patient having the possibility to oppose to the use of their data within the framework of research projects. Every patient gave his/her informed consent. This information has been added to the manuscript.</td>
</tr>
<tr>
<td>Reviewer 1</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Page 15, line 2, 48% of these</td>
<td>The corrections have been made</td>
</tr>
<tr>
<td>I think the results of the TREAT study with an almost doubling of stroke in those treated for the anemia should be discussed</td>
<td>We did already mention the TREAT study (Ref. 44, currently 43). Actually, the TREAT study was conducted in diabetic patients. Only 15% of our collective has diabetes. The positive association between anemia and the occurrence of stroke doesn’t mean that correcting anemia will reduce the occurrence of stroke.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reviewer 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major comments</strong></td>
<td></td>
</tr>
<tr>
<td>1) Methods: Why was a functional assessment scale “similar to Rankin scale” used and not Rankin scale itself? Please consider Rankin instead. Note: a significant difference exists between both scales as in the Rankin scale Stage VI is death whereas the used scale had only 5 stages.</td>
<td>We thank the reviewer for his comment and acknowledge that the functional scale described in the current manuscript is not commonly used in the stroke literature, contrary to the modified Rankin Scale (mRS). In fact, the functional scale described in the manuscript was used since the creation of the Lausanne Stroke Registry in 1978 and never modified thereafter to allow comparison between patients entered in the registry over the years. Unfortunately, the value of the mRS was not added as an item to the registry despite its wide use since the late 1980s to assess the functional status of stroke patients. However, and although formal validation of our scale has not been performed so far, we can consider that Stage I (LSR) corresponds to Stage 0-I (mRS), Stage II to Stage II, Stage III to Stage III-IV, Stage IV to Stage V and Stage V to Stage VI. Taking in account these considerations, we modified the manuscript as follows: 1. As suggested by the reviewer we removed the statement that our functional scale was “similar to Rankin scale” (page 8). 2. To clarify the use of our scale, we added the following sentences in the Methods section. «We did not use the widely used modified Rankin Scale (mRS) because our five-level scale was used since the creation of the LSR in 1978. At this time, the mRS had not yet been defined. In comparison, Stage I (LSR) corresponds to Stage 0-I (mRS), Stage II to Stage II, Stage III to Stage III-IV, Stage IV to Stage V and Stage V to Stage VI.</td>
</tr>
<tr>
<td>2) Statistics: the level of significance need to be defined, particularly, if as in Table 4 the authors label data as “p statistically significant”</td>
<td>The changes were done as proposed.</td>
</tr>
</tbody>
</table>
3) Results section: Prevalence data are presented in an unfavourable way. Please consider Figures at least for main variables GFR and Hb groups. We have clarified the presentation of prevalence data and added a figure that presents frequencies of patients by category of anemia according to GFR stages.

4) Results section: Univariate survival analysis should be performed by Cox proportional hazard analysis using Hb and GFR as continuous variables rather than subgroups for GFR and Hb. The current presentation of these data in several tables is confusing to the reader. We have added the results of analyses performed using Hb and GFR as continuous variables.

5) Table 4: Please, provide units of the variables used in the Cox analysis. Also p 14, first line: why is the probability of mortality calculated for 10g/L change in Hb (i.e. 1g/dl)? If g/dl is used here, please use this unit throughout the manuscript. The units of the variables used in the Cox analysis have been provided in Table 4. For Hb, we have used the units g/L throughout the manuscript.

6) The comment of HR of GFR should be omitted as the data is not significant. The comment has been deleted.

7) Discussion, p15: the statement “48% of patients had anemia” does not match with the data presented in the results section (p12: 17% had anemia). Also the statement “56% of stroke patients suffered from CKD” cannot be confirmed by the presented data in the results section. Please clarify. Thank you, we have made the corrections.

8) Referring to the previous comment and to Figure 1: The authors divide for patients with and without CKD but they report GFR subgroups. Please clarify. We have harmonised the results and comments, using GFR and K/DOQI CKD stages.

9) The figures are not acceptable and need careful revision for lay out, legends and readability in black and white printout. We have revised the figures to improve the quality, and revised the captions as well.

10) Please provide numbers of patients at risk in tables below the graphs. We have provided the numbers of patients at risk in the different subgroups in the Kaplan-Meier survival curves.

Minor points

Introduction, p. 5 “various degrees of end stage renal disease...” reads awkward and should be revised. Sentences 2 and 6 are largely redundant. The changes have been made.

The discussion should be shortened by 25%. Also, the reference list may shortened. We cut out a few sentences and words and dropped one reference.