Author’s response to reviews

Title: Trends in aortic aneurysm- and dissection-related mortality in the state of Sao Paulo, Brazil, 1985-2009: multiple-cause-of-death analysis

Authors:

Augusto H Santo (auhsanto@usp.br)
Pedro Puech-Leão (drpuech@usp.br)
Mariana Krutman (mari.krutman@ig.com.br)

Version: 6 Date: 25 August 2012

Author’s response to reviews: see over
To BMC Public Health

Please find attached the revised manuscript of the paper entitled "Trends in aortic aneurysm- and dissection-related mortality in the state of São Paulo, Brazil, 1985-2009: multiple-cause-of-death analysis", submitted to BMC Public Health. We would like to express our appreciation and gratitude for the comments and suggestions of the reviewers and the BMC Public Health Editorial Team. All comments of the reviewers were taken into account and properly included in the text of the manuscript. Please find below a point-by-point response to the reviewers’ comments to the last version of the manuscript.

Version: 5 Date: 8 August 2012
Reviewer: Janet Powell
Reviewer’s report:

The analysis of this complex data set remains muddled. There are great opportunities, but these have not been fully exploited.

1* In comparison to mortality data from other countries, the mortality from dissection (versus aneurysm) is very high. This requires both analysis and comment eg is hypertension poorly treated in Brazil?

We were aware of the high mortality related to dissection when compared to aneurysms. One factor that may explain this problem is the adjectivalization of aneurysm as “dissecting” by physicians when completing death certificates. The following paragraph had already been included in the discussion part of the manuscript: “However, specific limitations occur with aortic aneurysm and dissection as a mentioned cause-of-death. An abdominal, thoracic or of unspecified site aortic aneurysm may be informed as an "dissecting aneurysm" by physicians when completing the death certificate; the "dissecting" adjective may lead the cause-of-death to be understood as being a dissection instead of an aneurysm. Therefore, the observed values of dissection mortality rates may be overestimated.”

At the same time, we agree with the reviewer’s comment about hypertensive diseases as a factor that is responsible for the higher mortality related to dissection. The prevalence of hypertension in Brazil is very high, accounting, in 1996, around 21.6% (24.4% in women and 18.4% in men) and for those aged 65 years and over 57.7% (61.5% in women and 51.7% in men). These data were included in the discussion part of the manuscript but recent similar estimates for 2011 can be downloaded from the site of the Ministry of Health, (http://portal.saude.gov.br/portal/saude/profissional/area.cfm?id_area=152), looking for Vigitel 2011.

2* Although it is acceptable to present combined mortality from aneurysm and dissection, it is much better if the two are considered separately since these 2 disorders have rather different risk factors. Also aneurysm repair has been available for many years but endovascular intervention for dissection is a much more recent
We can understand and agree with the reviewer’s concerns. Nevertheless, other factors also have determined our decision to study aortic aneurysm and dissection at the same time. We have used the structure of the International Classification of Diseases to study mortality data since all cause-of-death are prepared according WHO guidelines. In most developed countries and in Brazil, mortality statistics are produced by means of automated processing to identify the underlying cause-of-death and store all other conditions mentioned by physicians on the death certificate. The elementary unit of the classification is the category, described as “The basic ICD is a single coded list of three-character categories, each of which can be further divided into up to ten four-character subcategories” (see International Classification of Diseases and Related Problems, Tenth Revision, Volume 2, Instruction manual). We acted in accordance with this design and used ICD-9 and ICD-10 categories “441” and “I71”, that included both aortic aneurysm and dissection. The use of ICD category structure allowed the study of their subcategories, discriminating aortic dissections, and thoracic, abdominal, thoracoabdominal and of unspecified sites aortic aneurysms. Another advantage of ICD structure to our study was the possibility of regrouping ruptured and without mention of rupture aneurysms, fact that permitted to describe and analyse their epidemiological characters, like age at death, sex, and associated causes of death. We must also remember that the categories of the International Classification of Diseases are used for international comparisons of mortality statistics, as well as for epidemiological and administrative uses. For instance, the dissection and aortic aneurysm ICD category is includes as one class in the List of 113 Selected Causes of Death in the United States of America to rank leading causes of death.

Being the first study in Brazil was a prevalent factor that imported to use the combined mortality of aortic aneurysm and dissection. This argument was already presented to respond the comments of reviewers to the original version of the manuscript, as follows: “This is the first study in Brazil (and to our knowledge in Latin America), mainly with a epidemiological perspective (instead of clinical) to describe mortality trends of all the range of conditions included as aortic aneurysm and dissection with the use of multiple-cause-of-death methodology. Such data were not known among us, contrasting to England & Wales, where the studies of Fowkes, Macintyre and Ruckey and of Filipovic, Goldacre, Roberts, Yeates, Duncan and Mozaffari have before shed light on the epidemiology of aortic aneurysm and dissection. The authors have not missed the importance of abdominal aortic aneurysm; but aimed mainly to see the forest in spite of the trees.”

3* Combining data for underlying causes of mortality and secondary causes is unacceptable. This is because secondary causes reported depend on the level of case ascertainment. For some disorders eg abdominal aortic aneurysm, case ascertainment has increased rapidly and ultrasonography is used to detect even small aneurysms that do not warrant repair. Therefore, the potential inclusion of abdominal aortic aneurysm as a co-existent disorder can only be interpreted in the context of both case ascertainment, volume and outcome of elective aneurysm repairs and clinical practice
guidelines in Brazil. The authors should focus only on the primary underlying cause of death. There are sufficient interesting data to allow this.

At the introduction part of our manuscript we have made reference to four papers that consider the use of multiple-cause-of-death methodology necessary to provide additional useful information to the conventional underlying-cause-of-death presented in the so called primary mortality statistics. Identified by their first authors, the papers of Lilienfed, and Gillum were population-based studies considering aortic aneurysm and dissection; the paper of Filipovic was population-based considering mainly abdominal aortic aneurysm but including also aortic aneurysm and dissection deaths and the paper of Rushton studied notified deaths from a cohort of men employed at eight oil refineries in the United Kingdom and includes a topic about aortic aneurysm and dissection deaths. The paper of Rushton, published in 1994, includes many concepts about multiple-cause-of-death methodology. All these papers testify the importance of the use of multiple-cause-of-death in the study of aortic aneurysm and dissection.

Right now, we would like to present the arguments of the reviewers’ concern about “case ascertainment” and Lilienfed’s similar fact “disease of interest”. Lilienfeld affirm that “The use of the underlying cause of death data as a proxy for incidence data has potential for much error, insofar as the disease of interest may be more common as a contributory or coexisting disease rather than an underlying cause. Investigations are needed of the degree to which such aortic aneurysms are listed as “contributory” or “coexisting”. We are confident that the questions proposed by the reviewer and by Lilienfeld were discussed in our manuscript with the use of the multiple-cause-of-death methodology. Our data have shown and confirm former results from other studies that ruptured aortic aneurysm and dissection are selected as underlying cause-of-death over 90% and 60% in deaths without mention of rupture. The manuscript also included in the discussion the results of studies about the high trustworthy of mortality statistics related to aortic aneurysm and dissection, as follows: “It may be argued how much actual aortic aneurysm and dissection are assumed as a cause-of-death. i.e., in other words, how trustworthy are mortality statistics. Few studies took care of the question. An unpublished review of the Mayo data disclosed that over 85% of Rochester residents diagnosed with aortic aneurysms that died between 1951 and 1980 had on their death certificate an aortic aneurysm as the underlying cause-of-death, and almost all based on radiographic findings [8]. In England, Oxford region, during 1979 and 1987, a linkage study between hospital and death certificate records disclosed that 86.5% of the people who died within four weeks of hospital admission with an aortic aneurysm as the main diagnosis included it mentioned on death certificates and among these ones 92.5% were identified as an underlying cause-of-death [47]“.

It was our privilege and honor to refer in the manuscript papers of Prof. Michael J. Goldacre as first author or as co-author. We would not find better words that the ones he has included in the paper “Trends in mortality rates comparing underlying cause and multiple cause coding in English population 1979-1998. Journal of Public Health Medicine 2003; 25(3):249-253”, as follows: “The two measures of all-mentions and of underlying-cause mortality, in combination, are
more useful than either alone. In people who die with multiple pathology, analysis of mentions identifies all deaths attributed to each disease. It also helps interpretation of underlying-cause mortality when the rules for assigning the latter have changed. However, certification practice in the number of causes certified per death may itself vary in time and place; and the contribution to mortality of an individual cause may be inflated or deflated in these respects. For this reason there are advantages in continuing to consider the underlying cause as well as mentions. To do so also unequivocally distinguishes the certifying doctor’s view that the decedent died from, as well as with, the disease; and it acknowledges the certifying doctor’s decision as to the single most important cause of death. Mortality statistics have a number of strengths, and weaknesses, in studying the occurrence of disease. Certification of death, and of the cause of death, is a legal requirement: unlike most epidemiological datasets, mortality data are complete in any population of interest in the developed world. A historical limitation of mortality statistics has been the restriction of coding and analysis to underlying cause. The introduction of routine multiple-cause coding and analysis of death certificate data is an important advance in medical statistics.”

4* It would be helpful to show the seasonal changes in mortality as a proportion of total mortality, to identify whether there are strong underlying seasonal effects on total mortality in Brazil.

The proportional mortality of aortic aneurysms (ruptured and non-ruptured) and of aortic dissection as an underlying cause-of-death was calculated. A new table was included with these results that confirm higher mortality in winter. The corresponding text in Results and Table are the following:

“Similarly, these data are presented by means of proportional mortality in Table 6, which once more establishes highest percentages of deaths mainly in winter aortic ruptured aneurysms and aortic dissection.”

Table 6 - Proportional mortality related to aortic aneurysms, ruptured and non-ruptured, and aortic dissection, as underlying cause-of-death, according to seasons of the year, state of São Paulo, Brazil, 1985 to 2009.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Summer</th>
<th>Autumn</th>
<th>Winter</th>
<th>Spring</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dissection</td>
<td>0.1987</td>
<td>0.2587</td>
<td>0.2610</td>
<td>0.2302</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Ruptured</td>
<td>0.2497</td>
<td>0.2990</td>
<td>0.3035</td>
<td>0.2734</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Non-ruptured</td>
<td>0.1194</td>
<td>0.1287</td>
<td>0.1221</td>
<td>0.1217</td>
<td>0.16265</td>
</tr>
</tbody>
</table>

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

The English text of the manuscript was entirely revised by the authors. Nevertheless, as English is not our native language, if corrections are so far
deemed necessary, we are ready to submit the manuscript to professional copydesk prior to publication.

Attentively

Augusto Hasiak Santo