Reviewer's report

Title: Diagnostic Accuracy of Pleural Fluid NT-pro-BNP for Pleural Effusions of Cardiac Origin: A Systematic Review and Meta-analysis

Version: 1  Date: 23 September 2010

Reviewer: Thomas Mueller

Reviewer's report:

The authors of this meta-analysis aimed to evaluate the diagnostic accuracy of NT-proBNP pleural fluid concentrations for the identification of pleural effusions caused by heart failure. This topic is of scientific interest. However, each single study published on this topic so far is pointing to the same view that the determination of natriuretic peptides is useful for establishing of whether a pleural effusion is caused by heart failure or whether it is attributable to other diseases. Thus, the result of the present meta-analysis, namely that NT-proBNP measurements are useful in this diagnostic setting, is expected. Nevertheless, this meta-analysis seems to be appropriately performed and publication of the results is worth while. Several issues, however, should be addressed by the authors in a revised version.

1. The authors evaluate the diagnostic accuracy of NT-proBNP concentrations in pleural fluid. Why didn’t the authors consider investigating the diagnostic accuracy of BNP concentrations in pleural fluid as well and to compare both results? This would be of interest as there is currently a debate of whether one of these analytes might perform better than the other one in the setting of pleural effusions as correctly mentioned by the authors in the current version of the manuscript. What about other members of the cardiac natriuretic peptide family (e.g., ANP, NT-proANP, and MR-proANP)?

2. From the clinical point of view it might be very useful to measure BNP or NT-proBNP in plasma but not in pleural fluid. There are published data that this approach provides at least the same diagnostic accuracy as determining those same analytes in pleural fluid. Thus, it might be advantageous to obtain BNP or NT-proBNP concentrations from plasma/serum samples because thoracentesis is not necessary at this stage. To my opinion, there are two possibilities for a diagnostic approach in patients with pleural effusions of unknown origin: i) in first instance thoracentesis and diagnosis of a transudate or exudate by Light criteria, in second instance BNP determinations (in plasma or pleural fluid) in all uncertain cases; ii) in first instance BNP determinations (in plasma, determination in pleural fluid is not necessary with this approach) and diagnosis of heart failure as the cause of the pleural effusion, in second instance (if heart failure is most likely not the cause of the effusion) thoracentesis and diagnosis of a transudate or exudate by Light criteria with establishing the correct final diagnosis. The second approach is probably advantageous. However, these issues should be discussed more comprehensively in the manuscript.
3. The authors of papers included into the present meta-analysis state that they enrolled patients with pleural effusions and indication for thoracentesis for diagnostic purposes or symptom relief. This is not appropriate. As those studies deal with the diagnostic accuracy, only patients with thoracentesis for diagnostic purposes should have been considered. The authors should comment on these issues in their manuscript.

4. Furthermore, diagnostic procedures such as thoracenteses are only indicated in case of diagnostic uncertainty. E.g., since more than 80% of pleural effusions caused by heart failure are bilateral, of similar size and afebrile, a trial of diuresis can be undertaken, and only if the effusions persist, thoracentesis is indicated. Therefore, the indication used can influence the study population and may bias the corresponding findings. Thus, again the authors of the present meta-analysis are advised to comment on these problems.

5. The main question of whether a diagnostic strategy based on natriuretic peptide measurements adds diagnostic information to clinical variables or the clinician’s initial diagnostic impression remains unanswered. Can the authors provide information, to what extent BNP measurements add diagnostic information to clinical variables or the clinician’s initial diagnostic impression? To my opinion, this topic should be discussed in the manuscript.

6. I am not familiar with statistical procedures in meta-analyses. The methods applied should be reviewed by a statistician.

7. The authors describe that 8 of the 10 studies included into this meta-analysis used the Roche assay. However, it is not stated of whether the methods applied refer to the first or second generation Roche assay – this should be clarified. In addition, 2 studies used the competitive assay from Biomedica and as demonstrated in reference #31, NT-proBNP serum concentrations are appr. 10-fold higher with the Biomedica assay compared with the Roche assay. Although the proportional bias is unclear for the specimen pleural fluid, this issue might have considerable impact on the cut off values in the 2 studies of the present meta-analysis using the Biomedica assay.

8. In the discussion of this manuscript, the authors point out that “three studies (references 23, 25, 32) have examined the diagnostic accuracy of pleural fluid BNP in pleural effusions of cardiac origin”. This is not true because in reference #32, BNP was measured in plasma only but not in pleural fluid.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.