Reviewer's report

**Title:** Matrix-metalloproteinases-1, -2, -3, -9, their inhibitors TIMP-1, -2, and the MMP1/TIMP1-complex in blood plasma as markers for transitional cell carcinoma of the bladder

**Version:** 3  **Date:** 24 January 2006

**Reviewer:** Andrew Roddam

**Reviewer's report:**

This review comments solely on the statistical aspects of this manuscript and the following are only minor essential revisions which the authors need to make.

1. In Table 1 I suggest that all values shown are medians with an appropriate summary range in brackets – the authors should simply chose either the 5th to 95th or the IQR to display and be consistent for cases and controls.
2. It is not clear to me why there are tests for normality of the data if the authors then go on to use non-parametric test statistics. For clarity wouldn’t it be simpler just to state that non-parametric tests were used throughout due to the small sample sizes.
3. In the methods section it says that the Mann Whitney U test and the Wilcoxon test for paired and unpaired samples was used. However its not immediately obvious which samples are paired – I thought that all the samples were unpaired and in essence these two tests are the same. Could the authors clarify the analysis section to describe what they actually did.
4. Prior to investigating the diagnostic accuracy of the various proposed classifiers the authors should include the correlations between the MMPs and their inhibitors – its perhaps more important to see this than the correlation with TNM.
5. In the methods section it states that logistic regression models were used to evaluate odds ratios but none are displayed/described in the paper – please correct.
6. The authors should note a limitation in the discussion with reference to their analyses of diagnostic prediction – that is they are determining a cut-off and then testing how well it performs in the same data set. This is well known to over estimate the ability of the marker as a diagnostic test – in an ideal situation you would split your data into two, estimate the cut-off in one half and test it in the other.
7. I am quite concerned that the logistic regression analysis could be very misleading especially if the markers are highly correlated as there could be a great deal of overfitting. I strongly suggest either deleting the results or playing down their interpretation both in the summary of the paper and in the abstract, unless the authors can clearly demonstrate that the results do not occur due to overfitting or excess internal correlations between the MMPs and their inhibitors.

**What next?:** Accept after minor essential revisions

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

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests