Reviewer's report

Title: Reduced expression of ezrin in urothelial bladder cancer signifies clinically advanced disease, tumour progression and an impaired survival: validatory study of two independent patient cohorts

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Reviewer: Caj Haglund

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The subject of the study is interesting and clinically relevant. The materials are quite large and well characterised. Ezrin has been previously studied in bladder cancer, but only in two reports. Further validation of the results are therefore needed. The association between ezrin and podocalyxin is particularly interesting.

I recommend the paper to be accepted, but some changes are needed before the manuscript is ready for publication:

1. Please make it more clear, that membranous and cytoplasmic staining of ezrin were analysed separately, since in many papers staining intensity and percentage of positive cells have been combined. Did the authors try to combine membranous and cytoplasmic staining?

2. The mean value of two spots were used. Since low expression represents more malignant behaviour, one could also consider the lower score value to be more representative of the most aggressive cell population. This should be discussed.

3. Interpretation of markers whose expression decreases in malignancies is always difficult, since most IHC samples include negative areas, that can be negative for technical reasons. When evaluating the cytoplasmic intensity of ezrin, the authors decided to choose the most intense area. If loss ezrin is a marker for malignant behaviour this might not be biologically the right choice? Please discuss this question.

4. Was there any correlation between membranous ezrin and cytoplasmic ezrin?

5. There are some careless mistakes in affiliations.

Level of interest: An article of importance in its field

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
no