Reviewer’s report

Title: Association of Fascin-1 with Cancer-Specific Mortality, Disease-free Survival and Metastasis in Carcinomas: a Systematic Review and Meta-analysis

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Reviewer: Cord Langner

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The manuscript by Tan and co-workers reports on a systematic meta-analysis exploring the prognostic value of Fascin-1 expression in different cancer tissues. The authors restrict themselves to the analysis of breast, colorectal, gastric, lung and esophageal cancers, as these are the most extensively studied.

In general, the study design is appropriate and the study appears to be well performed, although I am not a biostatistician. There are however some major and minor comments that have to be made and taken into consideration, respectively.

Major Compulsory Revisions

The authors should make clear already in the methods section, that significance is achieved only when p-values are below 0.05. Thus, there is no statistically significant association, when p-values are 0.05 or even higher. I would like to give an example: The use of the term “weak association” (already present in the abstract) for p-values of 0.09 or even 0.24 is discouraged. This is “no association”.

The authors should more clearly sum-up the limitations of their analysis at the end of the discussion. Patient numbers are relatively small for meta-analyses, and the dataset is deeply influenced by case (and study) selection. The authors comment upon tumor heterogeneity only regarding different histological subtypes of breast cancer and different stages of colorectal cancer. Anyhow, these are all adenocarcinomas. There are possibly, however, much more important implications regarding the other types of cancer, even if no heterogeneity between the studies was noted (this might merely confer that Fascin-1 acts independent from morphological subtype, tumor histogenesis and molecular background) : In the esophagus we have squamous cell carcinoma and Barrett’s adenocarcinoma, and there is no basis to lump these together. In the lungs, we have small cell and non-small cell carcinomas, and in the stomach, we have diffuse cancer related to E-cadherin inactivation/mutation and the intestinal subtype, all of these having different genetic backgrounds. Thus, pooling data of these biologically different tumors which by some chance arise within the same organ is a matter of debate and should be commented upon in appropriate way.

“We assumed that “death” referred to cancer-specific mortality and not to all-cause mortality” (on page 7). I do not agree. Every investigator who has ever
related morphological findings in cancer tissues to outcome knows that it is comparably easy to find out whether a patient is dead or still alive. But if he/she is dead (perhaps years ago) it is difficult to assess the reason. Thus, if the authors of a given paper do not report on “cancer-specific mortality” (if they do, this is improved quality) they most probably only checked the overall status, dead or alive.

Minor Essential Revisions

Please do not use the abbreviated names as you currently do it. The abbreviated terms should only be given in brackets, e.g., one of us (XYZ). In addition, reference [2] is by Hashimoto and colleagues not only by “JCA” (last line of page 5).

The authors should go into more detail, whether the reported studies were performed on full sections or (only) on TMAs (I am sorry, I cannot open the supplemental material due to some technical problems and do therefore not know whether this information is provided there, but brief data on this topic are needed already within the main text).

Likewise we need at least some overview data on the length of follow-up in the assessed studies, as this should be a criterion to include or exclude a specific investigation.

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

**Declaration of competing interests:**

I have no competing interest to declare.