Reviewer's report

Title: Diabetes mellitus impacts risk of macrovascular invasion in patients undergoing transplantation for hepatocellular carcinoma

Version: 1 Date: 19 February 2012

Reviewer: Abid Suddle

Reviewer's report:

This is an interesting study based upon a retrospective analysis of a prospectively collected database. As outlined by the authors, there is epidemiological data indicating an increased incidence of Hepaticellular Carcinoma in diabetic patients and worse outcomes in this patient group.

The diagnosis of diabetes at the time of transplant is not quite as tight as it may have been if the study had been conducted prospectively. The authors allude to this point. The study populations appear relatively well matched, although diabetic patients were older at the time of transplant. This may have implications for the stage of disease at the time of diagnosis/ transplant.

The radiologic staging at the time of transplant is similar for both groups. Transplant wait-list times seem reasonably short, although standard deviations are not given for this parameter. Bridging loco-regional therapy is used with similar frequency in both groups. Serum AFP is similar for both groups.

My major criticism of the study relates to pathologic analysis of explanted livers. We are told that the number of tumours and size of the dominant tumour nodules is similar for both groups. Size of tumours is known to be a surrogate marker for the risk of vascular invasion. However, no details are provided regarding the histologic staging of tumours; ie whether tumours are well, moderately or poorly differentiated, associated with potential satellite nodules of associated with divergent differentiation. These factors are potentially associated with vascular invasion and/or a higher risk of tumour recurrence.

Allowing for this, the authors have shown a higher risk of macrovascular invasion in diabetic patients. The risk with diabetes is, perhaps surprisingly, higher than for total tumour diameter. Post-transplant HCC recurrence was not higher in the diabetic group, but overall survival was poorer.

In the discussion, the authors outline potential reasons why diabetes would be associated with macrovascular invasion. Molecular profiling of explanted livers, in order to determine if diabetes is associated with a different gene signature profile, would have been interesting. The authors also outline potential limitations of the study.

Overall, I think the conclusions from the study provide an interesting and potentially clinically important observation which warrants further study for validation and to provide insight into potential mechanisms.

1. I do not feel the study requires major compulsory revisions.
2. Discretionary reviews. The conclusions from the study may be further validated if details relating to the full pathologic analysis of explanted livers, as outlined above, are included.

**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