Reviewer's report

Title: Low fat intake is associated with pathological manifestations and poor recovery in patients with hepatocellular carcinoma

Version: 1 Date: 21 January 2013

Reviewer: Srinivasan Dasarathy

Reviewer's report:

This is a very interesting paper by Yamada et al on the impact of dietary interventions in HCC. This is a highly significant area in clinical hepatology with a broad applicability and the authors have used innovative methods to document the dietary intake and carefully evaluated the energy requirements. A few concerns however detract from the significant impact this work is likely to have and are stated below.

1. The authors state that “energy from fat intake was positively correlated with npRQ” in their “Results” section but this is counter to known data that the contribution of different sources of energy (fat, carbohydrate and protein) is determined by npRQ. So it is surprising that the authors found a positive and direct correlation between npRQ and fat energy because as the fat energy increases, one would expect the npRQ will decrease.

2. The authors in their “Methods” section page 8 that the REE or BEE was multiplied by stress and activity coefficients (1.1 and 1.3) but they do not provide any data on how these were decided. Was this based on an activity score or stress level? How was stress determined?

3. They use a single criterion for recovery based on the INR. However, after interventions for HCC, there is likely to be some hepatocellular decompensation and this may affect the INR rather than the nutritional status. This needs to be discussed and the data interpreted with this limitation explicitly stated. Did the authors consider any other recovery pattern outcome measure e.g. Hospitalization, decompensation etc since it is recognized that complications of cirrhosis are more frequent and severe in malnourished than well nourished subjects?

4. The authors have used BIA as a single measurement tool for quantifying body composition but its validity in cirrhosis especially those with fluid overload may have limitations. Even though a number of authors have suggested that BIA is reliable in cirrhosis, were any other measures like skin fold thickness, arm area, CT measures of muscle and fat, or DEXA used to determine the functional impact of energy malnutrition at least at baseline?

5. The authors interpret their npRQ to show that patients had protein and energy malnutrition. Using only a small number of control subjects to define cut offs, define energy needs based on prediction equations is fraught with limitations and these need to be acknowledged.
6. The tables with the clinical details are very unwieldy, it could be summarized and summary data provided so that the 2 tables can perhaps be summarized into one.

7. The authors also have 2 distinct measures that include response to therapy and minimal HE. The relation between these 2 with HCC is also not clear. The rationale for this needs to be clarified. The authors state that minimal HE alters food intake but is there evidence that it specifically alters fat intake or metabolism and if so what is the mechanism for this?

8. The selection bias in this is also not taken into consideration. How were these patients chosen? Were they consecutive patients or was there a reason for selecting these subjects?

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have not competing interests.