Author's response to reviews

Title: Clinical Characteristics and Outcomes of Patients with Acute Myelogenous Leukemia Admitted to Intensive Care: A Case-Control Study

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Author's response to reviews: see over
Dear Professor Norton,

Re: Manuscript Re-submission titled “Clinical Characteristics and Outcomes of Patients with Acute Myelogenous Leukemia (AML) Admitted to Intensive Care: A Case-Control Study” (MS ID 1552851702365376)

Thank you for the opportunity to re-revise and resubmit our manuscript. As you will see, we have responded and addressed each of the Reviewer’s comments from your letter dated September 10, 2010. We appreciate the Reviewer’s detailed review of our manuscript and recognize the contributions they have made to its quality.

Response to Reviewer 1 Comments:
1. The authors state that the hazards of death in the AML cases were significantly higher than the AML controls and the ICU controls. However, the reference is stated to be the AML controls, suggesting that both populations (AML cases and ICU controls) were compared to ICU controls. Please confirm that the HR of 1.67 (95% CI, 1.1 - 2.55) stated in the abstract is the HR of AML cases compared to ICU controls (and not ICU controls compared to AML controls). If this is the case, table 5 should be changed accordingly stating 1. the HR of AML cases compared to AML controls and 2. the HR of AML cases compared to ICU controls. In addition, the text (results page 11) states only one HR for two comparisons, showing up in table 5 as the HR of the comparison of AML cases vs AML controls. Since this message is also part of the key messages, this might also be changed accordingly.

The HR have now been clarified. For these analyses, the reference variable was AML controls (HR 1.0) – Table 5 is currently correct.

2. Since ref. 16 has been introduced, the part of the introduction needs to be updated (p. 4, change the sentence starting with 'Only three studies' to 'only four studies' and update the following sentences accordingly.

This has been updated.

3. Results (p. 10, demographic, clinical and diagnostic characteristics of AML) and Table 1: The text states that 'Co-morbid illness was more common in ICU controls when...', whereas table 1 states >90% of ICU controls having 0 or 1 comorbidity compared to much lower fraction in the AML cases and controls. Please check.

We have clarified this.

4. One spelling error: '...while in ICU HAS higher survival' (p. 12) change to:
while in ICU HAD...

This has been corrected.

5. Discussion, p. 15: It is stated that the adjusted risk of death remains higher in the AML cases during follow-up. However, the Kaplan-Meier plot (figure 1) suggests that at least the curves of AML cases and AML controls are running parallel from app. day 50 on. To detect a persistent worse prognosis after ICU discharge, I suggest an additional landmark survival analysis from the time of ICU discharge of the patients surviving the ICU stay. This is an excellent suggestion. To enable a conditional survival analysis as suggested, it would have to be conducted at hospital discharge to allow inclusion of both AML cases (who were admitted to ICU) and AML controls (who were not admitted to ICU). We have now included this analysis.

Discretionary revision:
6. I’d change the Hypothesis stated on page 16: 'These observations would suggest that prognosis for AML patients receiving active chemotherapy may be better than perceived'. Hypothetically, the reason for better survival of pts receiving active therapy might have also been a selection of only patients with a good prognosis being offered chemotherapy by their treating physician.

We have revised this statement.

Response to Reviewer 2 Comments:
1) This is a matter of preference for me, and therefore should be viewed as a discretionary revision. Since the final number of AML ICU patients was 45, I would find it helpful to have the analyses performed using the 45 non-ICU AML patients that were matched to these patients, rather than all 50 non-ICU AML patients that were originally matched. While I suspect that the results would not change substantially, for me it would be a more logical analysis to undertake (especially since the non-AML ICU controls were matched 1:5 with the 45 AML ICU patients).

We appreciate the reviewer’s comment. In our methods, we matched 1:1 AML cases and AML controls; however, as outlined 5 patient charts were unavailable. The subsequent analyses were not in fact “paired” but rather were performed as subgroups. We then matched 1:5 with ICU controls – arriving at our current numbers. We believe the exclusion of patient observations at this point is unnecessary – as we risk it being non-random and potentially impacting our statistical power.

2) In Table 4, the reported n is 50 for the non-AML ICU controls, whereas it should be 225.
This has been corrected.

The manuscript has been approved by all authors. The manuscript has not been previously published and is not being considered for publication elsewhere.
If there are any further questions or concerns, please contact us at your convenience. We hope the Editor’s now find our manuscript satisfactory for publication in *BMC Cancer* and look forward to your review.

Sincerely,

[Signature]

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