Reviewer's report

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

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Reviewer: Adam Peets

Reviewer's report:

Thank you for the opportunity to review this study by Roze des Ordons et al. Using a retrospective case-control design, the authors describe the clinical course of 45 patients with acute myelogenous leukemia (AML) admitted to an academic Intensive Care Unit (ICU) over a 6 ½ year period and compared outcomes with both ICU controls and hospitalized AML patients not admitted to an ICU. They found that 11.7% of patients diagnosed with AML over the study period were admitted to the ICU and that these individuals had a significantly lower survival rate than patients in either of the control groups.

Overall, the authors should be congratulated for tackling this challenging area; one that I believe would be of interest to the readers of BMC Cancer. The results will help inform the design of future prospective studies and will add to the evolving literature describing optimal care of patients with hematologic malignancies and the role that ICU care can play in their management. At this point, my major concerns involve the matching of control patients (both the process used and the results of this process as presented in the manuscript); since comparisons with matched controls is one of the major strengths of this study, I have paid particular attention to this factor.

Major Compulsory Revisions:

1) Results: Given the importance of the matching process for this study, a few questions for the authors:
   a) The methods describe 1:1:1 matching. Why are there 50 patients in each of the control groups and only 45 AML patients?
   b) One of the criteria for matching the non-AML ICU patients was the patients’ sex. In Table 1, the authors report 46% of the patients in the control group were female, when only 26.7% of the ICU AML patients were female. Could the authors please clarify this discrepancy?

While I suspect that these issues are easily explained, they may also point to a more systematic issue with the matching process that would require further evaluation prior to publication.

Minor Essential Revisions:

1) Abstract: In the methods paragraph, the authors state that both control groups
are matched according to age, sex and illness severity. In the text, non-ICU hospitalized AML controls were matched for age and sex, but not illness severity. Please clarify.

2) Abstract: I don’t believe that the first sentence of the Conclusions is supported by the data presented. Since the authors do not have access to the details regarding those AML patients who received an ICU consult but were not admitted to the ICU, we are unsure of the exact number of patients who actually “required” ICU support during the study period (ie decision made to withdraw care on ward rather than admit to ICU). In addition, I can’t agree the use of the word “rare” when describing a phenomenon that affects nearly 12% of all patients diagnosed with AML. Granted, as a proportion of total ICU admissions, patients with AML are rarely admitted to the ICU; however, this has more to do with the patient case mix in that particular ICU, the number of admissions per year and the number of patients with AML in the catchment area. Stating both values is fine, but the authors should reword this sentence to improve clarity for the reader.

3) Results: While this is a personal viewpoint, I would also strongly encourage the authors to not use the term “trend” when referring to p values near but not below 0.05 (Lang and Secic, 2008, pg 58). (First sentence in the Baseline characteristics, physiology… paragraph and last sentence in Treatment intensity… paragraph). It is either statistically significant or not based on the criteria you have set a priori.

4) Discussion: Page 14, paragraph 2. In general, I like the concept that the authors are espousing. However, the first sentence needs to be reworded. There are a number of factors that will predict outcome for AML patients (or any other patient for that matter) prior to or at the time of ICU admission. For example, asystolic arrest. Even if the authors were referring to clinical factors related specifically to the AML (which the current wording of the sentence does not imply), my review of the current literature would not support the use of the term “probable” at this point. Softening it to “We believe…” or “It may be the case…” or “Perhaps…” would be more reasonable. The results of this study certainly add to the current understanding of prognostication, but given the limitations already identified by the authors, conclusions cannot be drawn.

5) Conclusion: Same concern with the first sentence of this section as outlined in the comments for the Abstract.

6) Key messages: Last bullet: I think the word ‘them’ is missing between ‘of’ and ‘survive’.

Discretionary Revisions:

1) Materials and Methods: One of the major strengths of this study is its use of controls to better understand the outcomes of AML patients admitted to the ICU. Therefore, the control groups and the process of matching are critical aspects of the study design. A few questions for the authors:

a)Realizing that the database for the AML patients only contained 386 patients,
could the matching process be more inclusive than simply age and sex? For example, are there enough patients to match by cytogenic prognosis or one of the other classification systems? (especially given the presence of 5 more “unknown” cytogenics in the ICU cases and that the control group had many more M3’s than the ICU cases (7 vs 1)).

b) Is there data available on where they are in their treatment course (ie pre-treatment, pre-transplant, or post-transplant)? Even if the patients could not be matched based on this variable, the information would help the reader interpret the results.

c) For the non-AML ICU controls, I suspect that there are a large number of admissions from which to draw controls. As it stands, I am not sure that ‘apples’ are currently being compared to ‘apples’. Are there enough patients in the ICU database to match the patients more closely? (For example, tightening the APACHE II limits to +/- 2, matching on co-morbidities, etc). This would allow the reader to be more confident that the differences are in fact attributable to the AML rather than other contributing factors.

If none of these is possible (I fully realize that this would involve a massive amount of work at this point), then mentioning something about the limitations of the matching process in the limitations paragraph would be appropriate.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests