Reviewer's report

Title: Risk factors for delirium in acutely admitted elderly patients: a prospective cohort study

Version: 1 Date: 14 February 2005

Reviewer: E Wesley Ely

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General

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The question posed by the authors is an important one. The authors do point out, however, that they are not the first investigators to study risk factors for delirium in elderly hospitalized patients. They state that the results of previous studies “were not conclusive.” The specifics of this statement should be described in the introduction.

2. The distinction between delirium that is present upon admission (prevalent delirium) and delirium that develops in during the hospitalization (incident delirium) has been clearly described [Elie M, et al. J Gen Intern Med 13:204]. This distinction should be outlined clearly in the introduction as the authors are making a case that previous studies did not adequately examine risk factors for prevalent delirium, which is the aim of the current study. This aim should be more clearly stated.

3. The authors state that informed consent was obtained “following enrollment.” Is this correct? If informed consent was obtained prior to enrollment, as it should have been, this needs to be clearly stated.

4. The authors should describe the number of patients over 65 years of age admitted to the medicine service during the enrollment period (number of patients screened), the number consented and enrolled, and the number excluded for each pertinent exclusion criteria.

5. A number of validated tools were used to evaluate for risk factors, and the authors should be commended for choosing to use such instruments. However, a more structured method of collecting data regarding medication exposure could have been utilized. For instance, in addition to recording the number and class of medications used, estimated doses could have been recorded as well. This information is likely important in understanding the propensity of psychoactive medications to induce or exacerbate delirium. This should be listed in the discussion as a limitation of the current study. Also, were any efforts made to verify that the patients were actually taking the medications and the doses that they were taking? Again, the uncertainty of the accuracy of this data should be outlined in the discussion. Future studies should document the type and dose of medications taken and attempt to confirm compliance with the prescribed regimen.

6. The authors state that delirium they are detecting “could have been already present at admission, or developed within 48 hrs after admission.” They should speak to whether delirium present admission is the same as delirium developed on hospital day 2 with regard to risk factors, outcomes, etc. This may be addressed in a paragraph on study limitations, since they did not distinguish between delirium occurring at these different timepoints.

7. The authors give no explanation in the statistical analysis section regarding sample size calculations. How was the sample size determined? With 126 patients enrolled and over 15 risk factors being studied, it is likely that the analysis is subject to overfitting, i.e., some variables may be identified as significantly associated simply by chance. Typically, a study should enroll 10-15 cases (i.e., patients with delirium) for every risk factor being evaluated. Using this rule, the current study should have enrolled approximately 500 patients assuming delirium occurred in 30%. This limitation
should be clearly described in the discussion. [Harrell FE, Regression Modeling Strategies]

8. The association between delirium and a decreased number of leukocytes is not expected and warrants more discussion.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. There are no leukocytes in serum. The authors should simply state that the leukocyte count was recorded.
2. The authors report that 36 patients (29%) had delirium within 48 hours of admission. How many of these patients had delirium at admission, and how many developed it after admission?
3. Please define the term “psychopharmacama.” In table 2, the percentage of patients without delirium who received psychopharmacama should be listed.
4. The authors state that cognitive impairment was the strongest risk factor for delirium in the current study. However, table 5 shows that the unadjusted Hazard ratio for a Katz ADL score of >7 is higher than the ratio for cognitive impairment. Please explain this discrepancy or modify the discussion appropriately.

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Discretionary Revisions (which the author can choose to ignore)

1. Were those collecting data on risk factors (e.g., completing the IQCODE and KATZ-ADL via surrogate) blinded to the presence or absence of delirium in the patient? This should be stated in the methods.
2. The authors state in the discussion that some studies found an increased risk associated with anticholinergic drugs while others did not. Some discussion of the limitations of the cited studies is warranted. For example, Francis et al. found that anticholinergic drugs were more common among patients who developed delirium, but this was not statistically significant. It is possible that the study was underpowered to show this association. This holds true for the study reported by Marcantonio et al. as well. Schor et al. reported that anticholinergic medications were less common among patients who developed delirium. However, the majority of delirious patients studied by Schor et al. developed delirium after 48 hours of hospitalization while the majority of delirious patients studied by Francis et al. developed delirium earlier in the hospital stay. The risk factors for these two populations may be significantly different.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.