Reviewer’s report

Title: The influence of statin exposure on inflammatory markers in patients with early bacterial infection: pilot prospective cohort study.

Version: 2 Date: 28 May 2014

Reviewer: Erik B Kistler

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This study by Shankar-Hari, is a prospective observational study seeking to determine risk factors for illness after infection in a low-risk hospitalized patient population, including the use of statins. As a preliminary hypothesis-generating study this prospective trial reasonably collected data and then, by regression analysis, attempted to find significant variables of interest that might be possible risk factors for inflammation and further illness. The statin angle appears to have been an afterthought, but is of some clinical interest.

Major concerns

The manuscript would be improved by either bringing statin use (did all patients on statins previously receive them in hospital? Were some discontinued their statins? Did patients previously not on statins have statins started in hospital?) to the forefront or decreasing the emphasis on them and then changing the title to reflect this.

The study population is interesting, if somewhat unusual. Subjects were enrolled based antibiotic coverage after admission and followed until admission to a high-dependency or IC unit, or for 10 days. 30 day disposition was also recorded. Although it is appreciated that a power analysis was not conducted, the result is somewhat predictable. Unless there was postulated to be a huge effect size for statins, early infection with limited mortality would likely not show a difference in this sample size.

What is the makeup of the 12% of patients who were given antibiotics but who did not display SIRS-like symptoms? From the inclusion criteria these patients apparently had either proven or suspected infection(?) What about those patients who may have become septic but were not given antibiotics (i.e., were missed until ICU)? Were there any patients subsequently admitted to ICU or who died who did not receive antibiotics until they reached the ICU? It is possible that this group, if statin use is a surrogate for reasonable out-patient care, contained a preponderance of non-statin users?

The 30 day follow-up revealed approximately 20% morbidity/mortality with mortality at 5.7%. To this reviewer this group is more interesting than the statin result. Was there any constant in this group? (Here’s where enlarged a priori variable definition might have been helpful – but can still be done as a post hoc analysis). At present the manuscript simply reads that ‘it wasn’t the statins’ but leaves no further understanding for mechanisms of poor outcome. A sentence or
two describing this subgroup would elevate considerably interest in this manuscript.

The sentence in Methods that reads, “...we aimed to enrol [sic] all possible study subjects during the period of availability of the data collectors.” should be explained. If this is a summer collection period this should be stated. Alternatively, if data is only collected, for example in the morning hours, this too should be noted. Sick patients have a tendency to be admitted at inopportune moments, and diurnal data collection (if this is the case) may have skewed the data towards a) less ill patients or perhaps b) better diagnosis (i.e., diagnosis not missed in the early morning hours because of staffing, etc.)

Although it is appreciated that the a priori selected predictors are appropriate, there are several others, including race, type of infection (i.e. PNA vs urologic infection), APACHEII/SOFA (or some scale attesting to acuity of illness not included in Charlson score), that since this study was a hypothesis-generating one might have included (and presumably one has the data available for at least some of these predictors).

Minor points:

It is noted that data was collected in 2008. Not that 6 year-old data is invalid, but this gives the flavor of an after-thought of a study, not one that was designed to answer a particular research question.

Idle question: is it routine for the institution where the study was conducted to obtain a daily CRP on all patients admitted with routine or suspected infection? Or is this data-set part of a larger interventional trial that specifically collected CRPs? If so, this aspect of study design should be acknowledged.

Figures 1,2 and 3 need a legend

Overview: The result that statin use did not alter CRP or WCC or results of any kind is of some interest. However, as this was a hypothesis-generating study there was no a priori hypothesis and thus no power analysis, and it is not possible to make a definitive statement from this manuscript, only state that in the convenience sample collected there was no difference in outcome between groups. As it stands, the manuscript is relatively superficial and of limited interest in its bird’s eye view of patients with low-acuity infection. It is suspected, however, that there may be some genuinely interesting outcomes from this study (already collected and presumably not already published) that would at least inform to a hypothesis-driven RCT; it would be of great interest to see these results, inconclusive though they may be (what kinds of infections pre-disposed to long hospital stay? Any commonality in mortality or ICU admission? Any particular SIRS component that seemed more or less predictive in this population? Etc.).

Level of interest: An article of limited interest

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 no competing interests