Reviewer's report

Title: Clinical predictors of statins prescription in acute ischemic stroke patients: findings from the Lombardia Stroke Registry

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Reviewer: Danielle Ni Chroinin

Reviewer's report:

Thank you for the opportunity to review 'Clinical predictors of statins prescription in acute ischemic stroke patients: findings from the Lombardia Stroke Registry.'

This paper reports the prevalence of statin prescription in the Lombardia Stroke Registry, stratified by multiple patient clinical factors, and utilises a Classification Tree to describe the variables associated with statin use in a step-wise fashion. The authors report suboptimal use of statins, and lack of adherence to existing guidelines.

This paper is topical, and the suboptimal practice described echoes recent publications that have described compliance with the Get With the Guidelines-Stroke in other populations [Hseih et al. Circulation 2010; 122(11): 1116-1123; de Carvalho et al. Cerebrovasc Dis Extra 2012; 2(1): 26-35]

Essential Revisions:

- Methods and Results

  How was dyslipidemia defined? Previous physician diagnosis? History of lipid drug treatment? Pre or post-stroke lipid levels?

  Was NIHSS assessment standardised/evaluated by trained personnel?

  Patient factors such as patient preference or agreement to treatment are not addressed, and may have affected rates of statin use at discharge.

  The authors do not report the treating speciality, or how many patients were admitted to a Stroke Unit, or under the care of a specialist stroke team. It would be interesting to know if these factors are associated with statin prescription.

  The separate analysis of large artery strokes is helpful, given that several guidelines differentiate LDL targets on the basis of stroke of atherosclerotic origin, and that SPARCL limited patients to those with stroke/TIA with non-cardioembolic stroke. Potentially the latter fact should be highlighted.

  As a hospital-based registry, the study will have inherent biases, which should be acknowledged at some point.

- Discussion
Rather than individually cite each variable associated with statin prescription (or not), and detail potential barriers for each one, the authors might consider an overview of barriers to guideline adherence, referring to the appropriate variables.

The gender bias is notable, whereby women are less likely to receive statins. However, the authors almost appear to excuse the lack of guideline adherence in women, attributing it to the "well-known higher risk of cardicerebrovascular pathologies in men", which may or may not have been their intent? Of note, a similar gender bias was seen as regards to lipid management guideline in stroke patients in the North Dublin Population Stroke Study, reported at the European Stroke Conference, May 2013.[Ni Chróinín et al Cerebrovascular Dis 2013; 35(Suppl 3)]


The authors attribute the association between stroke severity and statin non-prescription, and between antithrombotic use and non-statin use, to a concern on the part of the physician re non-compliance or higher risk of bleeding (with larger infarcts or haemorrhagic transformation). It is more likely that this represents a 'non-prescribing' bias where patients who have had severe strokes and a poor prognosis are not commenced on secondary preventativiv therapies, e.g. in the context of palliation, or a recognition on the part of the physician that RCTs on which guidelines are based often exclude patients with significant disability or poor life-expectancy.

It is interesting that despite the higher rates of statin prescription in patients with DM or hypertension (though still suboptimal), risk factors traditionally associated with small vessel disease, small vessel strokes per se were not associated with rates of statin prescription.

"The classification tree applied on the subgroup of LVD patients lets us to conclude that statins, in the absence of dyslipidemia, are almost randomly prescribed even in the presence of well-defined atherosclerosis." The fact that the rate approximated randomisation 2:1 does not necessarily justify the implication that physicians are 'randomly' assigning statin treatment. There may be some rationale, but the factors influencing such decision-making have not been explored in this study.

"Unexpectedly, thrombolytic treatment...seems to enhance statin prescription": This most likely represents a marker of better stroke care and probably increased
specialist input in patients who have received thrombolysis, which should be mentioned.

It would be worth including a brief paragraph outlining the authors' own ideas as to the strengths and weaknesses of the current study.

It is also probably worth referencing THRAST in relation to IV lysis and statin use.[Cappellari et al. Neurology. 2013 Feb 12;80(7):655-61. doi: 10.1212/WNL.0b013e318281cc83]

-Conclusion

The authors conclude that there is 'need for consensus on the matter, in order to get improved and precise guidelines, easier to put into practice by physicians'. This fails to acknowledge that there are guidelines in existence that are both evidence-based and directive. This study shows failure to adhere to well-established parameters for statin initiation, the problem would seem to reflect a failure on the part of treating physicians to utilise existing guidelines. It is possible that physicians may be unaware of the guidelines, believe them to be inappropriate for individual patients, or perceive them as imprecise, but this study did not investigate this further.

Other comments/Discretionary revisions:

While the authors present an analysis of the clinical factors associated with statin use, information regarding other physician-related factors influencing adherence to guidelines would also be of interest. If unable to provide such information, the authors might develop this more in the discussion. They do not really characterise the "factors interfering with statin prescription" as is suggested in the Introduction, and the focus should be made clearer.

Do the authors have information regarding statin use post-discharge? Might primary care physicians have introduced statins following hospital discharge? Might patients who went home on statin not have continued it post-discharge?

-Figures

Figure 1 could potentially be placed online as supplemental material, or incorporated into Figures 4 or 5.

Figure 2 is probably unnecessary, as the increased rate of statin prescription is mentioned in the text.

Additional comments:

There are a number of grammatical and phrasing errors that may represent inexact translations to English (particularly in the abstract and Intro), which should be corrected if for publication.

A qualitative study investigating physician factors influencing statin prescription
would be of interest, and maybe should be considered for future study?

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

No conflicts of interest to declare.