Reviewer's report

Title: The Relation Between Neutrophil-to-Lymphocyte Ratio and Coronary Chronic Total Occlusions

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Reviewer: Vikram Agarwal

Reviewer's report:

In their manuscript titled, “The Relation Between Neutrophil-to-Lymphocyte Ratio and Coronary Chronic Total Occlusions”, the authors Demir et al. have tried to answer an interesting and complex question in the field of cardiology, to evaluate if the relatively easily available and cheap test of neutrophil/lymphocyte ratio can be utilized as a marker of CTO.

In the recent past there has been considerable interest in investigating increasing applications of neutrophil/lymphocyte relationship based on the fact that this ratio has been implicated to be associated with worse outcomes in a variety of cardiovascular conditions. This is rooted in its association with underlying inflammatory processes (acute and chronic). However, the exact pathophysiology behind this is still being completely understood.

While the question posed by Demir et al. is definitely interesting, the conclusions drawn by the authors of the obtained results need to be scrutinized carefully.

1. The authors find that NLR ratio is higher in CTO patients as compared to patients with underlying CAD. However pts with CTO also have higher Syntax and Gensini scores? Does this mean that pts with CTO just have a higher burden of CAD?

Is it possible that when pts with similar Syntax and Gensini scores in CAD and CTO groups are compared in the 2 groups, their NLR ratios would be similar?

It may be more appropriate to compare pts with same complexity of underlying CAD, other than the CTO, be compared when trying to answer this question?

2. Patient selection – How did the authors choose the pts? How were they left with exactly 75 pts in each arm of the study? Could there be selection bias?

3. Positive correlation between NLR and syntax score has been cited with a bivariate correlation analysis, r value is 0.16 and p-value is 0.05. This is very weak correlation at best and the p-value is statistically significant at <0.05, while the reported p-value is 0.05. This is not statistically significant.

4. The NLR cut off of 2.09 is derived from ROC analysis. However in a prior major study published on a similar topic, “Arbel, Yaron (12/2012). "Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography". Atherosclerosis (0021-9150), 225 (2), p. 456.” The cut off of 3 was associated with more severe disease as compared to values between 2-3. There is too much overlap between
the values with regards to severe CAD and CTO, which is the theme of the current manuscript

5. Baseline medications – there is no mention of the treatment the pts were on before the cath. Certain medications may have influenced the NLR ratio, e.g. statins. This needs to be addressed.

6. Pts with CTO had lower ejection fraction as compared to pts with underlying CAD (55% vs 51%). However, this was not significant on multivariate analysis. This is interesting and needs to be discussed more in discussion section

**Level of interest:** An article of limited interest

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests