Author’s response to reviews

Title: The progression rate of peripheral arterial disease in patients with intermittent claudication. A systematic review

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Response to Reviewers

Reviewer reports:

Reviewer #1: This is a systematic review evaluating the current evidence base evaluating progression rate of symptomatic PAD. Overall this manuscript is well written and is easy to read. The review is well executed and is in an area of importance. Well done to all involved.

Background

In line 101 - you suggest that only 5% of patients with IC progress to CLTI, then in the following paragraph line 110 - you say a substantial amount of patients with IC progress to CLTI - this statements are contradictory?

Response: text amended

Are you planning on developing a predictive formulae for lower limb management in patients with IC? If so, you should state this here

Response: The intention of this review was not to develop a predictive formula but it highlighted gaps in knowledge which need to be filled in order identify predictors in these in patients for the predictive to be compiled.
Methods

Table 1 with your search strategy should include MESH headings so that it is clear and repeatable - perhaps outline your medline strategy and state it was adjusted to suit different databases?

Response: Text amended

Results

The first few sentences repeat what is already in the PRISMA diagram - so much of this section can be deleted and refer readers to the diagram - will make for easier reading.

Response: text amended

I am sorry but I don't like the bullet point summary of results in the middle of the results section. I wonder if this could be changed into a paragraph?

Response: text amended

Line 338 - patients of advanced age (>75 years) are also at higher risk of MAC, this should be included

Response: included in line 364

Numbers less than 100 need to be spelled out - this is throughout the manuscript

Response: text amended

Line 343 - a lot of these studies were published a long time ago, prior to the issues with ABPI being recognised, this is likely why it is not discussed as a limitation - I think this should be considered

Response: Text amended. Included in line 368
Discussion

I think the argument that progression is likely underestimated should be explained more clearly to the reader - the issues with selection bias and the fact that ABPI will likely underestimate the presence of disease - you could cite some of the diagnostic accuracy work that has been done in recent years - half of all disease is missed by ABPI, which explains the likely underestimation

Response: text amended and reference added lines 383-386

Limitations

Despite a thorough search you may have missed some papers - this should be added

Response: text amended

I think the future studies section should be removed or reduced significantly

Response: text amended

I look forward to seeing this manuscript in print

Reviewer #2: This is a very interesting article that clearly shows deficits in research reporting progression of peripheral arterial disease. I agree with the authors that this is possibly being under reported.

A few points that the authors may wish to elaborate further on, in order to substantiate their findings:

An annual change of 0.01 according to ABPI translates into a period of 10 years for perfusion to degrade by 0.1 - is this a reasonable amount of time, or do we perhaps see much faster rate of disease progression? Especially keeping in mind the authors' own statement that "TASC review indicate a more aggressive progression of PAD resulting in an amputation rate of 27% in those with IC." (lines 362-365).

Response: longitudinal studies longer than 5 years reported a high attrition rate and reports are unreliable therefore it is not known whether the rate increases along the years but there is some evidence suggesting that the most aggressive rate of progression is within the first year of diagnosis (McDermott et al 2004).
How reliable are the results of the quoted studies, given that they are based on ABI? It is well known that this test has inherent difficulties in reporting perfusion in the presence of calcification, which are not always immediately apparent.

Response: Text added 368-370

Since ABI testing is performed by different operators in the various studies quoted, can they be relied upon?

Response: Reliability of internal validity was reported in the studies

Highlighting the above points would make a more emphatic conclusion to the review

Response: Text added in lines 451-454