Reviewer’s report

Title: Differences in Presentation of Symptoms between Women and Men with Intermittent Claudication

Version: 1 Date: 7 March 2011

Reviewer: Gavin Bryce

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Major Compulsory Revisions

1. Methods, Paragraph 1 – The methodology is not clear. Would it be possible to explain the purpose of Parts A and B?

2. Methods, Paragraph 3 – Could you expand on the self-reporting of concomitant diseases? Was there any systemic enquiry or case note review or was this based on voluntary information only?

3. Methods - There is a lot of detail on DUS and Echo. This section could be reduced in size considerably with only 2 or 3 short lines to describe the tests used. [Please note you describe left ventricular ejection fraction in the area for DUS and not Echo]

4. Methods - Where you describe serum markers you call these systemic markers. Including these highly specialised serum markers which individually have a great deal written about them might be counterproductive to this paper. Unless felt essential to the aims of the paper it might be reasonable to consider removing these from both the methods and results so as not to confuse the key aim of the paper. Even more so as the results of these markers in such a small number of patients result in no significant findings.

5. Results – Please include patient numbers, proportions and p-values in the main text when describing all results.

6. Results – There is one line describing ‘classic IC symptoms’ between men and women. As this is where the general purpose of the paper is aimed are there more results relating to differing symptom presentations that could be included, rather than mostly QOL measures?

7. Results, Paragraph 1 - In 2nd sentence comparison groups are not indicated. Which patients were older and had lower ABI's and compared to whom? If this is group 1 vs group 2 there appears to be no statistical comparison in results section or table 2 to validate this.

8. Results, Paragraph 2 - Sentence 2 suggests walking ability declined according to WIQ and references Table 3, however Table 3 reports on the Intermittent Claudication Questionnaire in group 3 and does not show change over time as suggested in results section. There is no detailing of results of WIQ in group 3 or reference to time intervals in results section or tables. Can this be added?

9. Results, Paragraph 3 - It is described that according to the ICQ that men
experienced more leg pain and that men spent longer thinking about the pain. According to Table 3 it is in fact women who spent more time thinking about pain, and there was only a statistical significance in respect to time spent thinking about leg pain. Whilst it would be ok to say that men were more likely to have severe leg pain that this was not statistically significant and this should be noted. Again p values in text would help.

10. Results, Paragraph 3 - In sentence 3 both DUS and echo are reported as similar and figure 1 is referenced. Figure 1 does not show Echo results and it may be best to separate these two. In this sentence report on DUS findings alone and give some figures including p values and then reference Figure 1. Comment on Echo results in next sentence (the results of which are not similar).

11. Results, Paragraph 4 - In which interview/questionnaire did men describe more classic IC symptoms? Please give more details if possible.

12. Discussion, Paragraph 2 - I do not think that the text from the sentence ‘One question that emerges...’ to the end of paragraph 2 raises an obvious relevant point. I understand the suggestion that the Rose questionnaire may not accurately identify those with IC, however this would need supported by referenced studies to support or otherwise. Further, I am not aware of any study stating that a deterioration of ABI over time identifies or diagnoses those with IC. Symptomatically 50% would be expected to improve and 25% stay the same (J Vasc Surg 2000, 31:S5-S35), and although much of this is due to collateral vessel formation in what is essentially a progressive disease an absolute reduction in ABI in all with IC is not expected (although I would be happy to be proven otherwise). It may be beneficial to cut much of this area of discussion.

13. Discussion, Paragraph 3 - It is discussed that men, but not women, had deterioration in WIQ scores over time; however although alluded to this is not detailed with data in the results. If correct there is once again an assumption that walking impairment worsens in all with IC. As described above this would only be expected in 25% of patients with IC. Are there other reasons for this difference? Gardner et al (J Vasc Surg 2010, 52(5):1204-10) conclude that women with IC ambulate slower than men. Is it possible that this is why there is a less marked deterioration? Misdiagnosis is a possibility with reports of increased prevalence of spinal stenosis in women (J Am Geriatr Soc. 2003, 51(2):222-8). It is reported in this study that men are more likely to suffer LV systolic dysfunction – is this a reason for further reduced walking impairment in men? Please expand where possible.

14. Discussion, Paragraph 5 - Sentence 2 is not completely clear. While diagnosis of peripheral vascular disease is important for CVS risk reduction measures there will be those with asymptomatic PAD that are not aware of this need regardless of sex. If there is a suggestion that women present later than men then this needs supported by data/references. Also, this sentence appears to be contradictory as it describes those that do not require symptomatic treatment, but then describes health care allocation to provide symptomatic relief. Can this sentence/point be clarified?

15. Discussion, Paragraph 7 - In sentence 5 you say that Group 3 was an
acceptable approximation of the demographics of Group 2. If this is the case then this needs to be detailed in the results section. Could this be done in a separate table or with additional columns in Table 2?

16. Discussion, Paragraph 7 - Other Limitations that should be included are:
• The group sizes of Group 1 and Group 2 are very different (10 times) and therefor statistical differences in Group 2 may not be apparent in Group 1 due to the smaller numbers. This detracts slightly on direct comparison between group 1 and 2, although does not preclude comparison.
• The use of self-reported co-morbidity is not common practice and makes any conclusions based on these particular results impractical. This seems to be a major limitation.

17. Conclusion - The conclusion does not summarise the main findings of the study. I think these are:
• Objectively men and women have similar severity of PAD
• Despite this women appear to have greater walking impairment when questioned, especially with regards walking speed, and women spend more time thinking about their pain
• Men claim to suffer more severe pain (although not significantly so) when questioned

What does this mean with regards clinical practice today and what further research could help with this? Can there be more discussion and emphasis in the conclusion on the differing presentation of symptoms in IC?

18. Abstract - In the results the prevalence is reported for IC in different sexes, however this is not reported in the main results text. In the results of the abstract the p-value for walking speed is incorrect according to Table 2, and there are no reported results on joint problems in the main text.

19. Table 3 - Is this the correct table (see point 8 above)?

Minor Essential Revisions
1. Background, Paragraph 1, Sentence 2 describes definite conclusions about prevalence of PAD and IC in differing sexes, however different studies report varying findings. It would be best to refer to the paper/study that these results come from in the text rather than just reference by number. It could say ‘Findings of the ……study reveal that when based on ABI alone women are more likely to suffer from PAD, however when diagnosis relies on additional assessment of symptoms (ie intermittent claudication) there is at least equal distribution [2].’

2. Background, Paragraph 1 - ABIs are Ankle-Brachial’ Indices’ and not ‘Indicies’ (too many i’s).
3. Background, Paragraph 1 - Please reference prevalence of IC in elderly.
4. Background, Paragraph 2 - Last sentence should read ‘A correct diagnosis is also essential to enable appropriate modification of cardiovascular (CV) risk factors and to prevent CV morbidity and death [5].’
5. Methods, Paragraph 2 - There is confusion between present and past tense.
Formality would normally use past tense unless indicated otherwise. So should read: ‘The Part A cohort was derived from the Swedish PAD Prevalence Study (SPPS). This population based point-prevalence study was conducted in 4 Swedish Regions during 2004 and included questionnaire results of 5080 men and women taken from 8000 randomly selected participants aged 60-90 years. Questionnaire data collected included details of walking ability, concomitant diseases.......

6. Methods, Paragraph 3 2nd last sentence should read ‘ABI was defined as’ and not ‘..was measured defined as..’.

7. Methods, Paragraph 4 – No data on death rate or cause of death is reported in the results and therefore this should be deleted.

8. Results, Paragraph 1 - Difficult to read part of sentence ‘with more men with a smoking history’. Say ‘with an increased likelihood of a smoking history in men (Group 1 p =0.001, Group 2 p<0.001)’ or something similar.

9. Results, Paragraph 3 - Sentence 4 would read better as ‘Left ventricular systolic dysfunction was more common in men, with a reduced ejection fraction in 41% of men compared to 15% of women (p=0.06), although this was not statistically significant’.

10. Discussion, Paragraph 1 - What does ‘distinct’ mean? Does this mean ‘men are more likely to have suffered from a cardiovascular disease than women’.

11. Discussion, Paragraph 5 – In sentence 2 ‘does’ is missing from ‘....mild IC in women that does not require symptomatic...’

12. Discussion, Paragraph 5 - Sentence 8 should read ‘Our data reports a similar disease distribution between the sexes....in women, opposing the notion that women have less severe PAD, and it is difficult....’

13. Discussion, Paragraph 7 - It is not strictly correct to say it is ‘probable’ that large differences between sexes would be detected. It might be appropriate to say ‘It is possible, however, that larger and more significant differences between the sexes would have been identified if a larger cohort had been recruited.

14. Table 2 - Please include headings ‘Group 1’ with IC and ‘Group 2’ with control group for ease of understanding, as detailed in results section.

15. Table 3 - P values should have ‘.’ marks rather than ‘,’. Should be 0.067 and not 0.067. Subheading ‘Score Median and Quartiles (Q)’ is not positioned correctly and may be best if taken out.

Discretionary Revisions

1. Background, Paragraph 1 – ‘Affecting’ would be preferable to ‘Afflicting’.

2. Background, Paragraph 2 - ‘and the extent of reduction determines if there is indication for surgical treatment’ would possibly read better as ‘and the extent of reduction increases the likelihood of surgical intervention.’

3. Background, Paragraph 3 - In sentence 1 ‘signs’ in the literature are described. It would be better to say ‘reports’ or ‘publications’.

4. Methods, Paragraph 2 – This would be easier to read if ‘SPPS’ was described
rather than ‘2004’ as in sentence 1 which could say …'living in one of the regions included in the SPPS.'

5. Methods, Paragraph 4 – The sentence on the 'supervising nurse providing verbal support' seems unnecessary and could be taken out.

6. Discussion, Paragraph 1 - ‘Study’ would be more appropriate than ‘investigation’ in sentence 1.

7. Discussion, Paragraph 1 - The end of sentence 2 would read better if ‘regardless of the presence of IC.’

8. Discussion, Paragraph 2 - Sentence 1 would read better if ‘Men have a greater CV disease burden than women in the present study, which is a common finding throughout the current published literature.’

9. Discussion, Paragraph 2 - Sentence 3 might read easier if ‘ones’ is replaced by ‘publications’.

10. Discussion, Paragraph 4 - Do you mean ‘misdiagnosing’ or ‘under-diagnosing’?

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

**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:**

I declare that I have no competing interests.