Author's response to reviews

Title: Left ventricular non-compaction: clinical features and cardiovascular magnetic resonance imaging

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Author's response to reviews: see over
Reviewer 1 report
This work shows a large number of patients with non-compaction but has several bias of inclusion: all patients that come to make a magnetic resonance in a specialized center are selected for symptoms. Is natural that the case does not present the selected data according to the guidelines of the current literature that show a high proportion of asymptomatic subjects in patients with non-compaction. This important finding must be reported in the discussion.

We thank the reviewer for this important point, which has been addressed in the discussion.

It should also be noted that the reported increased cardiovascular events, such as stroke and arrhythmias, were evaluated in patients presenting significant co-morbidity that may justify the presence of symptoms such as atrial fibrillation or dilated cardiomyopathy.

We thank the reviewer for this important point, which has been addressed in the discussion.

The statistical analysis performed including tests such as ANOVA and not been described in the methods.

Thank you – this has been addressed.

In conclusion, the data may have some interest, but the discussion of the work must be completely rewritten by dividing the data of the sampling and reviewing case by case, the burden of morbidity.

We thank the reviewer for this point. Having considered this point in detail, we think that this would make the manuscript too unwieldy and detract from the central message.

Useful to add a more current bibliography.

Thank you, this has been updated.

Furthermore, if possible, a comparison between the spongy and compact dell'ecocardiogramma of resonance.

Thank you for this point. We feel this may be extrapolating our data too much.

Reviewer 2 report
Minor Essential Revisions
It's an interesting paper about LV non-compaction: clinical features and CMRI. It sounds strange the low suspicion of NC raised by echo, just in 10% of the exams. How were these echos done?
Thank you for this point. The echocardiograms were carried out by experienced sonographers and reviewed by cardiologists. However, contrast was not administered.

Abstract: please change trans-thoracic for transthoracic

Thank you – this as been corrected.

Reviewer 3 report
This interesting study describes clinical and ECG characteristics of 42 patients inwhom left ventricular noncompaction (NC) was diagnosed by cardiac magnetic resonance imaging (CMRI) and compares the findings with 22 control patients without NC. To improve its impact, the manuscript should be revised according to the following points:

Major comments
Introduction:
It should be mentioned
• that NC is not only congenital but may develop or even disappear during lifetime,
• that NC is frequently associated with neuromuscular or other inherited disorders,
• how many of the studies about diagnosing NC by CMRI are anatomically controlled by cardiac surgery, heart transplantation or autopsy.

Thank you. These point are now included.

Methods:
• Which echocardiographic machines were used? How was left ventricular systolic function measured echocardiographically?

Thank you this has been addressed in the methods. As some patients were referred specifically for CMR at this centre, echocardiographic evaluation was obtained from the referring centre. Thus the echocardiographic features were not performed in one centre. However, the focus of this manuscript is on CMR.

• According to which criteria were the control patients selected? In the abstract it is mentioned that they were age-matched, however no details are given in the methods.

Thank you this has been addressed in the methods.

• In NC planimetry is sometimes difficult or even impossible, due to the ventricular trabeculations, regardless if echocardiography or CMRI is used. How did the authors overcome this problem?

This has now been addressed. In fact, this did not present a problem during analysis.
• Were interobserver studies carried out for diagnosis of NC, measurement of EF, x:y ratio and NC area?

One author, FL, decided if patients met the criteria for NC. No inter-observer studies were conducted.

• How were abnormal trabeculations, indicative for NC, differentiated by CMRI from papillary muscles, false tendons and aberrant bands?

These could be differentiated without difficulty on the CMR scans.

• Why were the NC patients not investigated neurologically to look for neuromuscular disorders?

Any patient with symptomatic neuromuscular disease would be referred. However, in the UK all cardiologists must have trained and been assessed in neurology, and undertake general medical on call duties.

Results
• Did the MR machine or the study protocol change during the study period? If yes, did the change of the machine or study protocol influence the prevalence of NC or NC-measurements?

Thank you. The same machine and protocols were used.

• What was the indication for CMRI in the study patients?

This is now a standard investigation for heart failure, and is carried out in all new diagnoses.

• What was the indication for CMRI in the control patients?

These patients were referred for investigation of other pathologies such as excluding coarctation, who were subsequently found to have normal scans.

• What was the NYHA class of heart failure in the study patients at the time of CMRI?

This was not recorded, as the scans took place after the original clinic visit. This is retrospective data, and so may not be as useful or complete as prospective data.

• How long was the interval between echocardiography and CMRI?

Thank you. These were carried out within 2 months.

• Were the echocardiograms re-read after CMRI? In how many patients was NC also visible echocardiographically after having established the diagnosis by CMRI?

This was not systematically carried out in this retrospective case series.
• Quantification of NC was carried out at end-diastole. It is known that the duration of diastole is influenced by the heart rate. Thus, it would be interesting to know the heart rate during CMRI and if there was an association with NC-measurements.

Thank you for this point. The heart rate was not systematically recorded throughout the study. The machine averages over 8 to 15 seconds, dividing each cardiac cycle into 20 phases, and CMR diastole appears to reflect anatomical volume.

• Were any follow-up CMRIs carried out and did NC change qualitatively or quantitatively?

As this was a series of cases, we were not able to offer complete follow up studies to the patients.

Discussion
• The article by Boyd et al. is referenced in a misleading manner. Boyd studied the anatomical distribution of abnormal trabeculations during autopsy and never stated that 70% of healthy subjects have some degree of NC. Please clarify!

This has now been changed and we thank you for this point.

• How to explain that 25 males but only 17 females were diagnosed with NC?

Thank you. We are reluctant to draw too much attention to this as it may be due to chance or referral bias.

• I agree with the authors that there is little consensus on the diagnostic criteria of NC, especially regarding CMRI. That stresses the need for anatomically controlled studies, as mentioned above. This point should be included in the discussion.

Thank you we have now included this in the discussion.

Minor comments
• According to the abstract, 5% suffered from stroke, in the results 4%. Please clarify! Thank you it is 4.7%, rounded up to 5.

• According to the methods patients were studied over a 6 year period, in the results they were identified over a 4 year period. Please clarify! This is a four year study.

• According to results 6 patients were asymptomatic, in table 1 are 5 asymptomatic patients. Please clarify!

• Please correct “routne” in line 1 of the “study limitations”. Thank you this has been removed.
• **Table 1 – what is “CAF”?** Thank you this should read AF.

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
I have no competing interests