Author's response to reviews

Title: The Prognostic Value of Dobutamine Stress Echocardiography Amongst British Indian Asian and Afro-Caribbean Patients: A Comparison with European White Patients.

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Author's response to reviews: see over
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Dr Eugenio Picano  
Dr Rosa Sicari  
Editors-In-Chief, Cardiovascular Ultrasound.

Dear Dr’s Picano and Sicari,

We would like to resubmit our manuscript entitled: ‘The Prognostic Value of Dobutamine Stress Echocardiography Amongst British Indian Asian and Afro-Caribbean Patients: A Comparison with European White Patients’ by O’Driscoll, J et al. for consideration of publication into the Research section of Cardiovascular Ultrasound. Also enclosed are 5 tables and 3 figures.

The following revisions have been made as recommended by the reviewers and editorial board:

Reviewer: Professor Albert Varga

1. My major concern is regarding the AIM of the present analysis. The Authors should convincingly explain why they think that there should be ANY difference in response to dobutamine stress (or in predictive power of DSE regarding fatal or non fatal future cardiovascular events) in patients with different ethnicity? DSE is a diagnostic imaging modality for the assessment of hemodynamically significant coronary artery disease. Positive DSE occurs when there is a significant stenosis in a certain coronary artery. According to my knowledge, there are no data in the literature that there is any significant difference in coronary artery stenoses in different ethnic populations. If yes, the Authors should explain the previous findings in the introduction section and discuss their own findings in the discussion section comparing the present data with the previous findings. For instance, do the Authors have any data about the differences in predictive power of other diagnostic tests (such as perfusion scintigraphy or exercise ECG) in different ethnic populations? I do understand that there are differences in the OCCURRENCE and PRESENTATION of coronary artery disease in different ethnic populations. These differences had already been abundantly studied and described (as was acknowledged by the Authors); therefore the majority of the results of the present study can be considered as confirmatory.

Within the UK, Afro-Caribbean, Caucasian, and Indian Asian patients have differing ages to the presentation for cardiovascular events. The exact mechanisms of this are unclear. Differing prevalence of diabetes and hypertension may in part explain these differences, although other mechanism may exist. Whilst we completely agree that there is no reason why DSE
should differ as a diagnostic tool in different ethnic groups, we do feel it is important to determine whether ischaemia and ischaemic burden have the same prognostic power in these different ethnic groups. We have included this information on page 5, lines 6-8.

Previous research demonstrated a significant difference in survival between White, Black and Hispanic patients undergoing exercise treadmill testing. The Hispanic group exhibited improved survival over White and Black ethnic groups despite adjustment for demographic, baseline ECG, cardiovascular disease co-morbidities, cardiac risk factors, and exercise test findings. We have included this information with a supporting reference on page 4, lines 19-22. We have also discussed this finding on Page 15, lines 20-22 in the discussion section.

2. NFCE should be explained also in the Abstract

In the abstract on page 2, line 9, non-fatal cardiac events has been defined.

3. The description of the dobutamine protocol is too long

The description of the dobutamine protocol has been reduced.

4. According to my understanding the Authors did not administer beta blockers after the termination of the dobutamine infusion. According to the recent recommendations, an antidote should be given in all patients at the end of the test regarding its outcome (positivity or negativity).

The authors recognise that some centres do use intravenous beta-blockade routinely in patients who receive dobutamine. However that is not the practice in our centre and is in accordance with current European Association of Echocardiography (a registered branch of the European Society of Cardiology) and American Heart Association guidelines for the application of stress echocardiography, which details that beta-blocker therapy may be administered to reverse the side effects of dobutamine.

5. The sensitivity of the test was surprisingly high (94%), the specificity was acceptable (84%). Please give an explanation

We agree that the sensitivity of the DSE result in our study was high. The result may be impacted upon by a referral bias and we have noted this in our limitations section on page 17, lines 22-23.

6. The “European white” patients where significantly older, however, the all cause mortality in this group did not differ from the mortality observed in the other groups. According to many studies the Age is a powerful predictor of all cause mortality therefore an explanation is needed at this point.

We agree that age is a powerful independent predictor of outcome. Our results show that older age was an independent predictor of outcome in all-ethnic groups studied for non-fatal cardiac events and all-cause mortality. Prior research has demonstrated that ethnic minority groups, in particular South
Asians have coronary artery disease at an earlier age compared to Caucasian populations. However, major adverse cardiac and cerebrovascular events are reported to be similar despite this difference in age. Our results compare to this. This has been supported in our discussion on page 16, lines 19-24.

Reviewer 2: Professor Patrizio Lancellotti

1. The present study examined the prognostic importance of dobutamine stress echocardiography (DES) in three ethnic groups in the UK. DSE was performed on 5329 consecutive patients (2676 Indian Asian, 2219 European white and 434 Afro-Caribbean). Among the three ethnic groups, ischemia on DSE was associated with 2 to 2.5 times the risk of non-fatal cardiac events and 1.2 to 1.4 times the risk of all-cause mortality. Peak wall motion score index was the strongest independent predictor of non-fatal cardiac events and all-cause mortality in all groups. So, the authors concluded that no major differences among racial and ethnic groups in the predictive value of DSE were detected. The paper is well written and provides interesting data, though DSE is known to stratify the risk of patients. It would be of interest to know if the territory of ischemia affected the outcome similarly in the 3 groups. Also were these patients living for long in UK? It would also be interesting to know the pre-test probability of CAD in each group. Also could the authors more info on the influence of pre-treatment on DSE results.

The territory of ischaemia was characterised according to an overlap model:
Left anterior descending artery (LAD) – anterior wall, anteroseptum, mid and apical inferoseptum; Circumflex artery (Cx) – mid inferolateral wall, basal and mid lateral wall; Right coronary artery (RCA)/Cx Artery – inferior wall, basal inferolateral wall, basal inferoseptum. This has been included on page 7-8, line 22-23 (page 7) and 1-3 (page 8). There were no significant differences between ethnic groups and this has been included on page 12, line 6-7.

Afro-Caribbean patients had been resident in the UK for 38±15 years and Indian Asian 41±17 years and European whites were born in the UK. We have included this information on page 10, lines 6-8.

The pre-test probability of coronary artery disease did not significantly differ between ethnic groups. We have included the method of determining pre-test probability of CAD on page 6, lines 13-16 and results on page 10, lines 17-18. We have also included the results in Table 1.

We have analysed the data to ascertain if there were any differences in anti-anginal medication (defined as any treatment alone or in combination of beta-blockers, calcium antagonists, or nitrates medication) before DSE. There were no significant differences in the proportion of patients prescribed anti-anginal medication pre-DSE between ethnic groups. We have included this information on page 11, lines 1-3.
We are grateful for the insightful and elaborate comments from the editor’s and reviewers, and we have replied to all issues. We believe that the manuscript has been improved by the changes. If so instructed, the authors are willing to modify the text further.

All authors have read and approved the manuscript resubmission. The manuscript has not been published and is not being considered for publication elsewhere in whole or part in any language except as an abstract. There are no conflicts of interest for any of the authors involved.

Please be in touch if you have any questions.

Yours sincerely,

Dr Rajan Sharma (corresponding author)