Author's response to reviews

Title: Dobutamine stress echocardiography for assessing the role of dynamic intraventricular obstruction in left ventricular ballooning syndrome.

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To the Editors
Cardiovascular Ultrasound

Enclosed please find the revised version of the paper entitled: “DOBUTAMINE STRESS ECHOCARDIOGRAPHY FOR ASSESSING THE ROLE OF DYNAMIC INTRAVENTRICULAR OBSTRUCTION IN LEFT VENTRICULAR BALLOONING SYNDROME, which we would like to submit to Cardiovascular Ultrasound for publication.

The paper has been revised according to the suggestions and criticisms of the reviewers.

A detailed response to the reviewers’ comments is provided here.

REVIEWER N° 1 (Rosa Sicari)

1) All patients were included in the Italian Registry on Takotsubo syndrome. We used the diagnostic criteria proposed by the Mayo Clinic group in 2004 (Ann Intern Med 2004; 141:858-865).

2) All the required data on the recovery of WMA at the time of the test and on the number of patients who had a normalization or improvement of WMA with dobutamine or an ischemic response were added in the revised version. A table detailing the response to dobutamine in pts with and without obstruction has been added to clarify the results.

3) A brief comment on the clinical significance (or lack of) of dobutamine-induced intraventricular gradient has been added in the discussion.

4) The possible mechanisms of Takotsubo have been described in more details (see Discussion) and the possible role of coronary spasm during dobutamine stress has also been discussed.
5) In the discussion (Paragraph: clinical implications) it has been emphasized that the safety of the test in patients with Takotsubo should be assessed in larger populations.

6) All patients with a contractile reserve (as well as those without reserve) recovered at FU (see Results).

7) Yes, we think that a severe obstruction can cause myocardial ischemia by increasing myocardial oxygen consumption secondary to increased myocardial wall stress and by decreasing subendo-cardial perfusion in the apical region (see Discussion); the same mechanism is operative in patients with obstructive hypertrophic cardiomyopathy.

8) The 2 mentioned studies that used stress echo in pts with Takotsubo syndrome evaluated coronary reserve using dipyridamole in the acute phase and after recovery, but did not address the pathophysiological significance of dynamic obstruction in takotsubo; in the revised version they have been cited in the discussion on the pathophysiological mechanisms.

9) Images of 2 sample cases are shown in Fig. 1 and 2; we added 2 videos of 1 case illustrating the development of a severe mitral regurgitation and impaired apical wall motion secondary to dobutamine-induced dynamic obstruction.

REVIEWER N° 2 (E. Pasanisi)

1) We agree with the reviewer that betablocking treatment should be withdrawn > 24 hours before the test to better assess the response to dobutamine; however, for ethical reasons the period of betablockers withdrawal was as short as possible.

2) The 16-segment model used in this study is the model most commonly used for evaluation of regional wall motion in stress echo and we think that the use of a 17-segment model does not give any significant advantage nor modifies significantly the results of our study.

3) The criteria for stress echo positivity are described in the “Methods”: A new or worsening wall motion abnormality compared to baseline was considered diagnostic of myocardial ischemia.

4) The criteria for viability have been added in the “Methods”.

5) TFC has been specified.

6) The explanation for reduced end-diastolic volume during dobutamine has been given.

7) No correlation was found between the presence of LAD stenosis and stress echo positivity.

The ECGraphic changes observed in 4/6 patients with dynamic obstruction (depression...
in 1 pt and T wave positivity in 3 pts) were not typical for coronary artery spasm.

Looking forward to hearing from you soon.
Yours sincerely
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