Reviewer's report

**Title:** The Importance of Achieving a Target Heart Rate to Determine the Normal Limit Value of Coronary Flow Reserve in the Territory of the Left Anterior Descending Coronary Artery During Dobutamine Stress Echocardiography

**Version:** 1  **Date:** 16 December 2010

**Reviewer:** Patrick Meimoun

**Reviewer's report:**

The question addressed by the authors is important for practitioners performing stress echo and CFR during dobutamine stress echo (DSE). The interpretation of CFR with dobutamine stress should be made only when a delta heart rate of at least 50 bpm from baseline or at least 75% of maximum predicted heart rate is achieved.

The study is interesting, relatively well defined, the conclusion is clear, however some additional clarification and explanation is needed for the reader to understand clearly the study.

**Major compulsory revisions:**

Concerning the objective, the first point has already been published (the authors has listed the references in their manuscript, 9-11). Concerning the second point, which is indeed the main objective of the study, the authors should defined in the same section of the manuscript that they want to determine the NORMAL limit VALUE of CFR during DSE (which is clearly defined in the title). For this purpose they should define the population studied: without ischemic response during DSE.

Concerning the methods: Again, it is important to define more accurately the population studied: is a normal DSE test required to be included, or by chance the 33 patients were included because DSE was normal? In an unselected population, even at low risk of CAD, the frequency of normal test is not 100 %

Furthermore, in the section methodology, it is unclear if 1 or 2 equipment were used (page 6). About the Nyquist limit set at about 19 cms/s, it is not stated if it was changed during DSE. With increasing heart rate, the LAD flow velocity increased, and keeping the same low scale at high heart rates renders the visualization of the artery more difficult. For the reader, the authors should define if they changed gradually the scale of the color Doppler flow mapping during the test in order to better visualize the LAD. Furthermore, they should precise that they measured the flow velocity at the same position at each stage of DSE.

The definition of CFR was clearly defined on page 8, but the authors used the term CFR for all ratios of flow velocities at each stage of DSE along the manuscript, which is somewhat confusing. They should use CFR for the final
value clearly defined on page 8, and use the term “ratio of flow velocities” for all intermediate values measured during each stage of DSE, in order to improve the reading of the data.

On page 10, the “excellent concordance” is not a synonym of correlation. Furthermore, the p value for each correlation should be clearly defined. We can have a weak but significant correlation and vice-versa.

In the section discussion, the authors mentioned the effects of dobutamine on the coronary circulation which is important for the reader (page 11), but there is another mechanism by which the coronary flow increases during DSE, which is somewhat less important in this setting: the endothelium dependent flow mediated vasodilation (ref Kern et al, JACC 2003; 42: 1602-4, and Ghaleh et al Circulation 1995; 92: 2627-35 for instance).

The authors mentioned that they “have not found any study analyzing and measuring the relation between heart rate and CFR during DSE”, and they discussed briefly about the results of the reference 9 and 10 by comparison, and surprisingly not of the reference 11. However, the study mentioned in the reference 11 assessed CFR during DSE and compared it to the CFR obtained with adenosine in the same group of patient and found a good correlation and concordance between the tests, in a wide range of LAD disease (normal and abnormal tests were analysed). Although a clear cut-off of heart rate was not established in that study, it was emphasized along the manuscript that a maximal achievable target heart rate was necessary during DSE to obtain the good correlation and concordance between CFR-DSE and CFR-adenosine (which is a method of reference cited by the authors in introduction to measure CFR). Furthermore, a significant correlation was found in that study between CFR during DSE and change of rate-pressure product in patients with a normal DSE. In addition, the normal and abnormal values of CFR during DSE were clearly described in that study. A CFR < 2 with DSE was found in all patients who had a positive DSE in the LAD territory (n = 8) and interestingly the same low CFR < 2 was obtained with adenosine in these patients. Consequently, it would be interesting to discuss also briefly the results of the only available study in the literature comparing non invasive CFR with DSE and CFR with adenosine in order to emphasize the results of the current study.

Minor essential revisions

Concerning the Table 1, the reasons of ordering the study mentioned “diagnosis”. It should be stated briefly about which diagnosis the authors spoke.

Concerning the Figure 3, the legend does not correspond to the graph.

Concerning the Figure 4, it is unclear for the reader if we deal with a population with low and normal CFR or if for each patient the ratio of flow velocities was measured at each step of DSE? Furthermore, the final values of flow velocities (the real CFR) should be depicted in a different color (is it the white circle?) and the cut offs should be highlighted with dashed lines for better interpretation of the graph. The same comments are made for Figure 3 (after correction of the
In the Summary, the aim of the study is not clearly stated, the exact location of the measure of flow velocity is not depicted (proximal, distal?), and the definition of CFR is not given

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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' below