Dear Dr. Picano,

We are resubmitting the above entitled manuscript to be published in Cardiovascular Ultrasound. Substantive changes were performed to answer all reviewers' comments. In addition, some references were added and figure legends were corrected. We would like to thank you so much for your attention,

Sincerely,

Paulo Magno Martins Dourado

Reviewer 1's comments

Spelling errors were corrected.

Fig 4: in the graph the r values are reported (not p values)
Answer: We added the r values in Figure 4.

Fig 5 and 6: the legend does not correspond to the figure. There are 2 legends to figure 5. Please check and correct.
Answer: We apologize for this mistake. Legend and figure 5 were corrected in the revised manuscript.

Reviewer 2's comments

Major comments
The time point of adenosine infusion was 30 minutes after reperfusion of the occluded LAD. The authors should discuss this short time interval. Why have they chosen 30 minutes? This should include a critical comment on the optimal time after reperfusion to perform MCE.
Answer: The reviewer's comment was included in the limitation section on page 12: "IS estimation has been demonstrated limited immediately after reperfusion because of reactive hyperemia that occurs shortly after reperfusion and abates within hours. Previous studies have demonstrated that myocardial contrast echocardiography with intermittent harmonic imaging performed after twelve hours of reperfusion provides an accurate assessment of infarct size. One could argue that the period in which myocardial perfusion was evaluated in our study was too close after LAD reperfusion (30 min). However, the study was designed to determine the value of RTMCE in a period of time in which reactive hyperemia is known to occur."

In the section "clinical implications" the authors state, that adenosine is not necessary in every examination to analyze infarct size. Even without a vasodilator, IS can be assessed. This striking finding should be discussed.
because literature by Kaul (Kaul S, Heart 1999, 81:2-5) suggests that a vasodilator is inevitable to accurately assess IS. Answer: The initial studies using myocardial contrast echocardiography for determining infarct size were performed with different conditions of contrast infusion and echocardiographic imaging. More specifically, most studies reporting the need for vasodilators were performed with intermittent harmonic imaging. Although we have not elucidated the mechanism that would result in better IS determination using real-time myocardial contrast echocardiography, possible explanations are described in page 11 of the revised manuscript.

Furthermore, it would be interesting to discuss the literature concerning infarct size assessment by the use of cardiac MRI and peri-infarct ischemia (e.g. late enhancement). Recently, echocardiographic strain rate analysis was suggested as a method to assess myocardial viability (Zhang Y J Am Coll Cardiol. 2005 46(5):864-71). The authors should discuss the methodological aspects and compare the pro's and con's of each method. Answer: Reviewer's suggestions were included on page 12 of the revised manuscript: ' Magnetic resonance imaging with gadolinium-based contrast was been demonstrated a precise method for determining IS and its transmurality. Magnetic resonance imaging offers high spatial resolution and can identify non-viable tissue using delayed enhancement technique. However, its cost and availability limit the widespread use of this technique. RTMCE is a non-radiologic modality of imaging that permits the evaluation of patients at bedside, with rapid information regarding myocardial contraction and perfusion. Strain rate imaging is another echocardiographic imaging that has been recently shown useful for differentiating transmural from non-transmural myocardial infarction in a small number of patients."

The manufacturer of PESDA contrast agent should be named (or specify it was home-made) Answer: The method for preparing PESDA contrast agent is now described on page 5 of the revised manuscript.

Minor comments 
All the spelling errors were corrected.

Reviewer 3 ' s comments 

The real-time myocardial contrast echocardiography alone slightly underestimated the actual infarct size, however, the addition of adenosine in the majority of cases somewhat overestimated it. To this reviewer, the explanation of this finding was not too much explicit in the discussion section. Answer: We do agree that this is a conflicting issue and possible explanations for our findings are better described in page 11 of the revised manuscript (discussion section).

The Authors admit in the study limitations section that ?Although myocardial blood flow quantification can provide information about myocardial viability after reperfusion therapy, we considered that it was not necessary for the design of this study. Any explanation? Answer: Quantification of myocardial blood volume and velocity are now available using specific software. In this study, we sought to determine the infarct size by planimetry using RTMCE and correlate this area with TTC. For the purpose of our study, planimetry of the hypoperfused area seems good enough for determining the no-reflow area. The additional value that quantification would have still has to be addressed.

Minor comments 
Figure quality and legend were improved.