Reviewer’s report

Title: Ventricular-arterial uncoupling after myocardial infarction in dogs - invasive versus echocardiographic evaluation

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Reviewer: Halliday Idikio

Reviewer’s report:

The authors have designed a dog model of myocardial infarction to investigate the patho-mechanistic features of post-MI heart failure and preserved left ventricular ejection fraction (LVEF)- defined as “diastolic heart failure in human patients with heart failure. The authors found ventricular –arterial uncoupling in dogs with MI.

The theme of left ventricular remodeling was introduced in the background and results. Left ventricular remodeling post-MI (JACC 2000;35:569-582. Circulation 1990;81:1161-1172) involves changes in LV geometry and sphericity and hypertrophy . These LV changes and other proposed mechanisms can impact many functions including mitral valve function (Europ J Echocard 2008; 9:207-221).


The authors effort to use the post-MI in dogs to model heart failure with preserved left ventricular ejection fraction (LVEF>50) is commendable. Hopefully this model can help expand our understanding of this form of human heart failure.

MAJOR COMMENTS

The Title does not reflect the effort the authors made in the experiment to provide an explanation for “Diastolic heart failure”. There is definition of “diastolic heart failure” in the background /introduction segment of the Abstract , but no direct reference to diastolic heart failure as one of the reasons for the experiment. From the conclusion in the Abstract, it appears the results explain post MI heart failure ; the statement “rather than by intrinsic diastolic heart failure” needs clarification. Neurohormal data are not summarized in the abstract- should be given for reader to know it was done.
1. In section Background, Line 3 ---“is frequently observed”—Should a percentage be given to help readers know the extent of the problem? It does appear that the authors are interested in finding an explanation for diastolic heart failure (lines 1-8) using the dog post-MI model.

In Line 12—limited coronary microembolization—needs clarification. The goal of the study needs to be clearly stated.

2. In the Methods/Animal Model, the LCA was ligated. Was this ligation of LCA permanent (non-reperfused) or removed after specified ischemic time (reperfused)? If reperfused, then the authors need to state duration of ischemic time and reperfusion. Also indicate what was done to “Controls”. 23 dogs were used for the experiment; the controls were only 6 versus 17 MIs- Can this impact the data interpretation? Please provide age as X+/−sd.

Also indicate time of measurement of baseline neurohormones.

3. In Methods/Echocardiography, the dogs were allowed to get used to the machine before getting data. When were “Baseline” measurements made- 6, 12 or 24 hrs after MI? Please indicate the interval between LCA ligation and baseline measurements.

The pressure-loop measurements required anaesthesia and echocardiographic measurements only needed sedation. There is concern that these measurements are not comparable. Please provide the catheter diameter and length used for transluminal valvuloplasty.

4. In Results/MRI, images showing the changes described for control and MI at baseline and 2months will make reading better (may be as Supplementary data). The infarct is 13%. Infarct size impacts the degree of remodeling and left ventricular dysfunction, as also described in animal models (J Nucl Med 2006; 47: 337-344). The changes in infarct sizes at baseline, 1week, 1month and 2months, are not known. Was infarct expansion noted (Remodeling includes infarct expansion). Can wall thickness be further reclassified into regions- Infarct zone (IZ) and Non-infarct zone (NIZ)?

In the result section remove statements of conclusion (i.e “These mitral--------LV filling pressure).

5. In Table 1 values for “Control Dogs” are not given for LV mass, and RWT. The results are compared between “Control and “MI at 2months”.

6. In Table 2, the “Baseline “ values are not provided for HR, CO,MAP and LVEDP as provided for controls in Table 1. In these comparisons, why are control values not used?

7. The Table 3, control values are not given for comparison with Baseline and MI at 2 months values.

8. The “Discussion” is centered around (Am J Physiol Heart Circ Physiol 2008; 294:H2313-2321) LV contractility. LV remodeling in general terms received less attention. How can the authors further clarify the statement that systolic uncoupling was found in the presence of “small infarcts”. The discussions are deemed adequate in light of the data provided.
MINOR COMMENTS
The manuscript will need some work for spelling errors, and trimming of long sentences. Under study design, Blood sampling --- delete sampling.

Declaration of competing interests:
I declare that I have no competing interests