Alterations of left atrial function and substrate after myocardial infarction in relation to vulnerability for atrial fibrillation: A chronic porcine model

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Introduction: Atrial fibrillation (AF) is the most common arrhythmia in United States and is associated with atrial fibrosis. The reason for the development of atrial fibrosis is not understood but may be related to cardiac dysfunction from an array of causes. Atrial fibrosis is believed to contribute to both the generation and maintenance of AF. AF inducibility, tested by burst pacing of the atrium, is an index of vulnerability towards AF, and reflects electrical and/or structural remodeling. Our study focused on determining the acute effects of myocardial infarction (MI) on left atrial (LA) function and LA remodeling. We hypothesize that MI may lead to changes in atrial mechanics, which will result in acute inflammation and later fibrosis. Furthermore, we investigated whether AF inducibility after MI correlates to changes in the LA function and substrate.

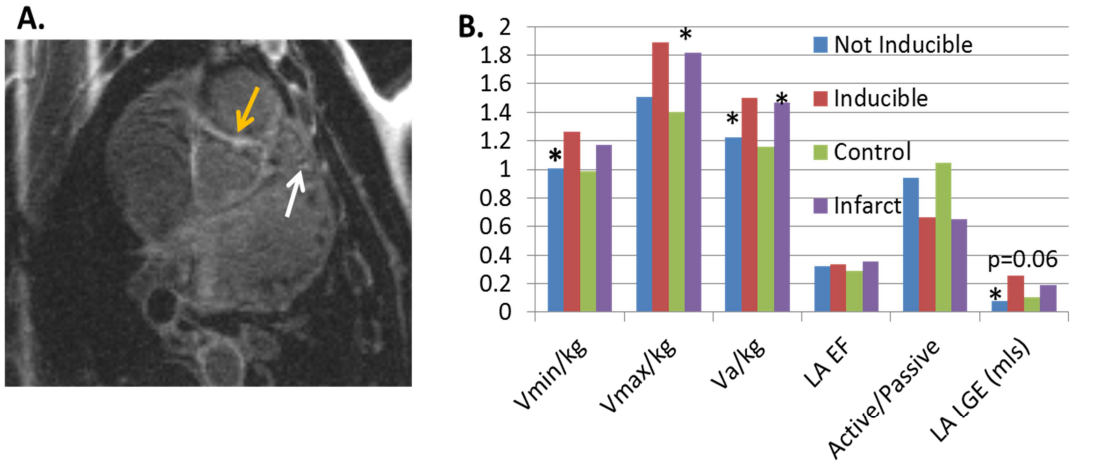

Figure 1: A) LGE image in post-MI pigs, showing enhancement of the aortic valve (orange arrow), and small area of the LA appendage (white arrow). B) Comparing inducible (N=6) to non-inducible (N=9) pigs, V^{min} and V^{a} were greater ($p<0.05$), and LA LGE volume was larger ($p=0.06$) in pigs with AF inducibility. Comparing controls and post-MI pigs, V^{max} and V^{a} were greater ($p<0.05$) post-MI.

Methods: Thirteen Yorkshire pigs were studied, including six control pigs, and nine pigs who were imaged one or two weeks after infarction (average weight 38± 7 kg). Transmural MIs were created by a percutaneous 90 min balloon occlusion of the coronary followed by reperfusion. All pigs were imaged on a 1.5T Siemens scanner (Siemens Healthcare, Erlangen, Germany). A stack of short-axis cine images covering the LA were obtained with balanced SSFP, with a 1.6 x 1.6 x 3 mm^3 spatial resolution (no gaps), and 25-30 frames, breath-holding and retrospective ecg-gating. Left ventricular (LV) cine images were also obtained. High resolution late gadolinium enhancement (LGE) of both the LA and LV was performed with ecg- and navigator-gating and 1.2 x 1.2 x 2.5 mm^3 resolution, approximately 20 minutes after injection of 0.2mmol/kg of gadobutrol. After MRI, all pigs were tested for AF inducibility, using a standard protocol of rapid burst (10 sec) atrial pacing at progressively shorter cycle lengths (300 to 100 msec). All image processing was performed in Matlab (v14) or 3D Slicer (v4.3.1). The cine images were segmented using thresholding and regions of interest, excluding the pulmonary veins, both in each slice and each time frame. The minimum volume (V^{min}), the maximal atrial volume (V^{max}), and the volume just prior to the atrial kick (V^{a}) were noted. From these we calculated other indices, including EF and the ratio of active to passive atrial emptying. All volume indices were normalized to body weight. The LV mass, volumes and infarct size were measured on the LV cine and LGE images. LA LGE images were blinded and randomized, and then LGE was segmented by including LA wall pixels with signal greater than the enhanced signal of the aortic valve (Figure 1A). Intra-observer error was assessed by segmenting the images again, 4 months later.

Results: No control pigs but 66% (6/9) of pigs post-MI were inducible. The mean infarct size was 15±7% of the LV, with microvascular obstruction (MO) involving 13±16% of the MI. Infarct size (16± 7% inducible vs. 12±.5%,p=0.2) and MO size (18± 9% inducible vs. 5± 5%, p=0.2) did not differ between inducible and non-inducible post-MI pigs. Of the LV indices of EF, volumes, and mass, only LVEDVI was greater post-MI (2.6±0.25 vs. 3.05±0.5 post-MI, p=0.05). Figure 1B summarizes the findings for atrial volumes, function and LGE, showing greater volumes post-MI, but similar LA EF. The active/passive ratio (i.e. contribution of the atrial kick to atrial emptying) did not significantly differ. There was increased atrial LGE enhancement volume in pigs with AF inducibility (p=0.06). All (6/6) inducible pigs had some atrial LGE enhancement, while only 38% of non-inducible pigs had some LGE. The intra-observer variability for atrial LGE volume measurements had reasonable correlation (R^2=0.79).

Discussion: We found evidence of atrial remodeling, including larger LA volumes post-MI, and a trend towards greater LGE enhancement in post-MI pigs with AF inducibility. LA enlargement has been reported in patients post infarct at a 12 day time-point (1). While fibrosis is unlikely to form one to two weeks post-MI, the LGE enhancement in the atrium may indicate myocardial injury of the atrium, similar to acute LV myocardial injury post-MI. Interestingly, we found much of the atrial LGE in the inferior portion of the LA appendage, where we have previously observed increased MMP activation—an index of inflammation.

References: 1) Popescu BA. American J Cardio 2004; 93: 1156.