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Acute Left Ventricular Unloading Reduces Atrial Stretch and Inhibits Atrial Arrhythmias

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ABSTRACT

BACKGROUND Left atrium (LA) physiology is influenced by changes in left ventricular (LV) performance and load.

OBJECTIVES The purpose of this study was to define the effect of acute changes in LV loading conditions on LA physiology in subacute myocardial infarction (MI).

METHODS MI was percutaneously induced in 19 Yorkshire pigs. One to 2 weeks after MI, 14 pigs underwent acute LV unloading using a percutaneous LV assist device, Impella. The remaining 5 pigs underwent acute LV loading by percutaneous induction of aortic regurgitation. A pressure-volume catheter was inserted into the LA using a percutaneous transseptal approach, and LA pressure-volume loops were continuously monitored. Atrial arrhythmia inducibility was examined by burst-pacing of the right atrium. Nicotinamide adenine dinucleotide phosphate oxidase (NOX) levels and ryanodine receptor phosphorylation were examined in LA tissues to study the potential effect of stretch-dependent oxidative stress.

RESULTS MI resulted in reduced LV ejection fraction and increased LV end-diastolic pressure with concomitant increase in LA pressure and volumes. Acute LV unloading resulted in a reduction of LV end-diastolic pressure, which led to proportional decreases in mean LA pressure and maximum LA volume. LA pressure-volume loops exhibited a pump flow-dependent, left-downward shift. This was associated with reduced LA passive stiffness, suggesting the alleviation of the LA stretch that was present after MI. Prior to acute unloading of the LV, 71% of the pigs were arrhythmia-inducible; LV unloading reduced this to 29% ($p = 0.02$). Time to spontaneous termination of atrial arrhythmias was decreased from median 55 s (range 5 to 300 s) to 3 s (range 0 to 59 s). In contrast, acute LV loading with aortic regurgitation increased LA pressure without a significant effect on arrhythmogenicity. Molecular analysis of LA tissue revealed that NOX2 expression was increased after MI, whereas acute LV unloading reduced NOX2 levels and diminished ryanodine receptor phosphorylation.

CONCLUSIONS Acute LV unloading relieves LA stretch and reduces atrial arrhythmogenicity in subacute MI.
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The negative consequences of acute myocardial infarction (MI) include decreased left ventricular (LV) function, pulmonary congestion, and increased arrhythmogenesis. Located upstream of the LV, the left atrium (LA) has unique roles including as a reservoir, a pump, and supraventricular electrical conduction. Acute MI leads to hemodynamic derangements that result in pressure-volume overload of not only the LV, but also the LA, leading to myocardial stretch of both chambers. LA stretch makes it difficult to expand further, and can lead to congestion of the lung through impaired reservoir function. Furthermore, stretch provides an arrhythmogenic substrate in the setting

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of ischemia (1). Atrial tachycardia (AT) and atrial fibrillation (AF) are commonly observed in patients after acute MI and are associated with increased morbidity and mortality. Indeed, recent data shows new-onset AF after acute coronary syndrome is associated with a 4.4-fold increase in in-hospital mortality (2).

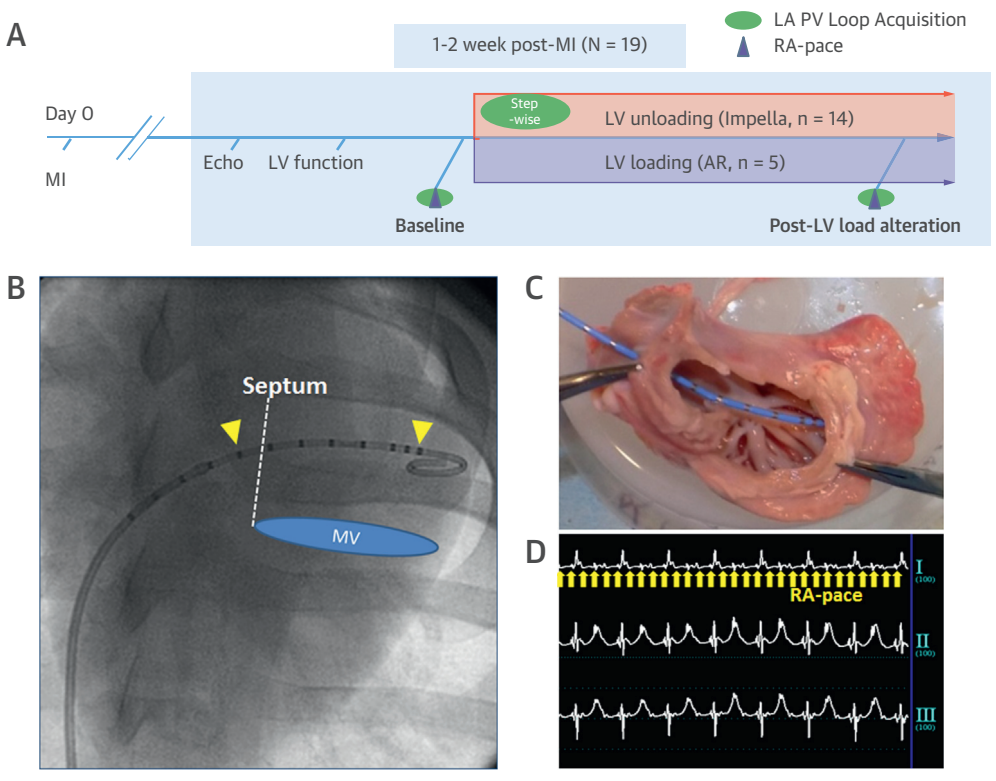
SEE PAGE 751

Recently, percutaneous left ventricular assist devices (pLVADs) have emerged as powerful options for managing post-MI patients (3,4), particularly those with cardiogenic shock. Clinical and preclinical studies show superior hemodynamic improvements over the intra-aortic balloon pump in this patient population (5–7), which has been the gold standard for nearly one-half of a century in managing MI patients who require hemodynamic support. Acute LV unloading by pLVADs is well-known to decrease wall stress by decreasing LV volume and pressure (8–11). Because the LA is hemodynamically linked with LV performance and load (12), unloading of the LV is expected to passively influence the LA, potentially decreasing its stretch and modifying arrhythmia propensity. However, no systematic studies exist that directly investigate this phenomenon, and little is known about the hemodynamics and physiological effects of changes in LV load on the LA. Therefore, we investigated the effects of LV unloading on the hemodynamic status of the LA and the ability of LV unloading to modify stretch-dependent AF in the setting of ischemia. We hypothesized that LV unloading using a percutaneous transaortic valve hemodynamic support device, Impella (Abiomed,

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
AR = aortic regurgitation
AT = atrial tachycardia
LA = left atrium/atrial
LV = left ventricle/ventricular
MI = myocardial infarction
NOX = nicotinamide adenine dinucleotide phosphate oxidase
pLVAD = percutaneous left ventricular assist device

FIGURE 1 Study Protocol and Methods for LA Physiology Evaluation



(A) Study protocol. Animals underwent LV unloading and loading experiments 1 to 2 weeks after MI, and changes in the LA physiology were studied by evaluating PV loop and arrhythmia inducibility by rapid pacing of the RA. **(B)** The PV catheter (Millar) was inserted into the LA through the atrial septum via femoral vein access. **Yellow arrowheads** indicate the excitation electrodes, and those in between were used for volume measurements. **(C)** Ex vivo simulation of the catheter location in the LA. Image is from the LV side looking up at the LA. **(D)** Electrocardiogram during the burst-pacing of the RA to induce atrial arrhythmia. **Yellow arrows** show the pacing stimuli. AR = aortic regurgitation; LA = left atrium; LV = left ventricle; MI = myocardial infarction; MV = mitral valve; PV = pressure-volume; RA = right atrium.