Scisense PV Technical Note

Hemodynamic Measurements of Left Ventricle (LV) Function Post Myocardial Infarct (MI) using Pressure Volume (PV) Loops in Rodents

When using invasive methods to measure hemodynamic parameters in rodents, most researchers studying chronic myocardial infarct are using permanent suture-induced descending coronary artery occlusion. Usually, they perform the Pressure-Volume (PV) Catheter study at 4 weeks (28 days) post-MI (3, 4, 8). Some researchers extend the artery occlusion study time another 2 weeks (1, 2) to study the effect of chronic heart failure/animal survival.

Cardiac remodeling at 28 days after the onset of MI is characterized by the structural changes of the LV having impact on whole heart, such as infarcted regional-wall thinning, chamber dilatation, and hypertrophy in the viable region the severity of these changes are based on position of occlusion (1, 3, 7). Signs of early post-infarction remodeling taking place in mouse heart are described in the table below. Due to strain-dependency and genetic background of animals and also with the position of coronary artery occlusion, the post-MI mortality varies. For more information on factors related to MI models including cellular and genetic influence please see Translational Physiology of Myocardial Infarct (RPV-12-tn).

STAGE POST-MI	BEGINNING	DEVELOPMENT	TIME FRAME	CHANGES OF MYOCARDIUM	VENTRICULAR MECHANICS	VENTRICULAR FUNCTION
Coronary artery occlusion	Acute ischemia	Infarct enlargement	Minutes - hours	Disorder of structural proteins	Passive myocardium	Impaired systolic function
Infarct stiffening	Necrosis progression	Collagen formation	Hours - days	Edema, necrosis, and degradation	Increased stiffness and strength; infarct expansion	Impaired systolic function
Collagen formation	Fibrosis	Decreasing collagen formation	7 - 28 days	Increase in collagen content (scar formation)	Maximum stiffness	Impaired diastolic function
Decreased collagen formation	Remodelling	Scar thinning; the rest of myocardium hypertrophy	28 days +	Scar shrinkage and collagen cross-linking	Decrease in stiffness; scar anisotropy	Improved LV function

*Post-infarction stages in mouse based on work of Shioura et al. (1)

When cardiac hemodynamics are measured by PV catheterization at 4 weeks post-MI, the load dependent parameters of cardiac function (e.g. SV, SW, CO, EF, dP/dt max/min, τ) are reduced as compared to intact animals (1). At the same time, compensatory hypertrophy of surviving myocardium occurs roughly up until 6 weeks post-MI, after which decompensation occurs. LV decompensation is marked by a significant decrease of developed pressure, strikingly reduced SV, SW and CO and development of diastolic dysfunction. A noticeable negative outcome of diastolic dysfunction is seen in the rise in end-diastolic pressure (EDP). It is also common for the left atrial and pulmonary venous pressures to elevate leading to pulmonary congestion and edema.

COMPARING MAJOR SYSTOLIC AND DIASTOLIC LOAD INDEPENDENT INDICES (CONTROL VS. POST-MI)

Systolic properties are characterized by the load-independent End Systolic Pressure-Volume Relationship (ESPVR) which is composed of the slope or end systolic elastance (Ees), and the volume axis intercept (V0). ESPVR can be characterized by either the quadratic or the linear equation. Generally, ESPVR is assumed to be influenced by afterload impedance (9), and when analyzed

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over wider ranges of contractile states it was found to be non-linear (10) and the volume axis intercept is better estimated using quadratic rather than linear equation (11). For this reason when ESPVR (systolic functional contractility parameter) in rodents post-MI is compared to a control group, a simple t-test cannot be applied as it fails to account for covariance and statistical interdependence between Ees and V0. Therefore, it is best to report changes occurring in volume axis intercept (V0) and slope (Ees). To compare post-MI and control groups, analysis of covariance (ANCOVA) with dummy variable should be instituted (12). For further discussion of ESPVR comparison of groups see Burkhoff et. al 2005 (13).

Diastolic properties are characterized by the load-independent End Diastolic Pressure-Volume Relationship (EDPVR). EDPVR is characterized by a non-linear curve fit of the change of ventricular pressure relative to change in ventricular volume (dP/dV). Post-MI changes characterized by an increase of collagen formation and scar cross-linking and shrinkage (see table) greatly influences final myocardial PV properties thus the position of the EDPVR . Slope of this relationship is called beta, also termed as chamber stiffness constant. When comparing EDPVR relationship post-MI one approach is to linearize it and use linear regression analysis with dummy variables or ANCOVA similar to ESPVR (12, 13).

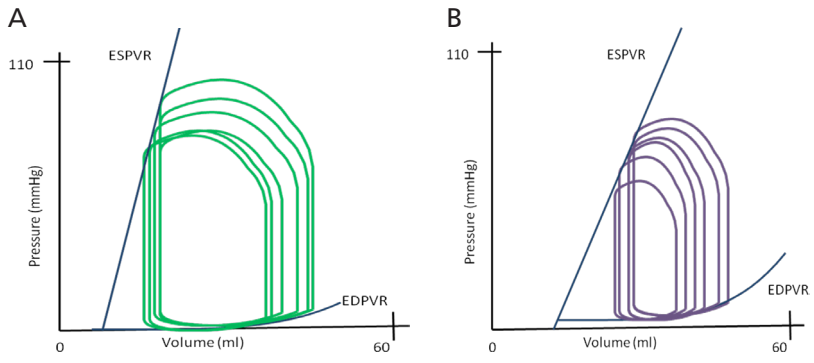

Fig. 1: Representative drawing of load-independent PV loops post-IVC occlusion at (A) beginning of study (control) and (B) at 4 weeks post-MI. At 4 weeks post-MI the purple PV loops shows characteristic rightward shift with decreased slope of ESPVR. ESPVR is progressively worsening and continues to decline with time following MI. LV chamber remodelling post-MI leads to increased stiffness with decreased filling capacity during diastole as seen in changes to the EDPVR. The rise of EDP at 4 weeks post-MI leads to increased effort of LV muscle against which heart has to work during the filling phase. Additionally, rodents with healed infarcts operate at higher EDV at 6-10 weeks MI post as compared to healthy hearts.

As load independent parameters are measured, using pre-load reduction by temporary occlusion of inferior vena cava (IVC), a rightward shift of PV loops is observed (Fig. 1). As a good internal control, it is imperative to select for analysis only those samples of IVC occlusion that were performed by similar technique including method of occlusion and vena cava location of preload reduction. Additionally, parameter such as ESPVR, EDPVR, time varying elastance (E_{max}), PRSW, dP/dt_{max} vs. EDV are all declining post-MI. PRSW (SW vs. EDV) deterioration reveals changes in systolic function independent of chamber geometry. Time-varying elastance indicates the LV chamber adjustments leading to decrease of compliance, defined by the proportionality between intraventricular pressure and volume. Left ventricular end-systolic elastance / effective arterial elastance increases at 4 weeks post MI indicating a worsening coupling ratio

Using Admittance technique to assess load dependent and independent parameters in post-MI injured rodent heart has several distinct advantages over the traditional conductance method. There is no need for volume calibration of the catheter or hypertonic saline injection for parallel conductance determination with Admittance which saves time and reduces sources of error (6). By using Admittance method in rodent post-MI, an appropriate correction of the parallel conductance of injured cardiac muscle is achieved in real-time based on blood conductance calibrated to end systolic and end diastolic blood conductance and aortic flow. This occurs instantaneously while discarding the injured muscle parallel conductance (6). Admittance is also more insensitive to the impact of changes in heart geometry which may occur as a result of MI due to the ability to place the catheter in the center of the LV using Phase and Magnitude signals (5). See the PV Catheter Positioning Guide for placement methodology. Unguided conductance catheters can end up in an off centered position which gives inaccurate results (5).

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