Relationship Between Early Diastolic Intraventricular Pressure Gradients, an Index of Elastic Recoil, and Improvements in Systolic and Diastolic Function

Michael S. Firstenberg, MD; Nicholas G. Smedira, MD; Neil L. Greenberg, PhD; David L. Prior, MD, PhD; Patrick M. McCarthy, MD; Mario J. Garcia, MD; James D. Thomas, MD

Background—Early diastolic intraventricular pressure gradients (IVPGs) have been proposed to relate to left ventricular (LV) elastic recoil and early ventricular “suction.” Animal studies have demonstrated relationships between IVPGs and systolic and diastolic indices during acute ischemia. However, data on the effects of improvements in LV function in humans and the relationship to IVPGs are lacking.

Methods and Results—Eight patients undergoing CABG and/or infarct exclusion surgery had a triple-sensor high-fidelity catheter placed across the mitral valve intraoperatively for simultaneous recording of left atrial (LA), basal LV, and apical LV pressures. Hemodynamic data obtained before bypass were compared with those with similar LA pressures and heart rates obtained after bypass. From each LV waveform, the time constant of LV relaxation (τ), +dP/dt_\text{max}, and −dP/dt_\text{max} were determined. Transesophageal echocardiography was used to determined end-diastolic (EDV) and end-systolic (ESV) volumes and ejection fractions (EF). At similar LA pressures and heart rates, IVPG increased after bypass (before bypass 1.64±0.79 mm Hg; after bypass 2.67±1.25 mm Hg; P<0.01). Significant improvements were observed in ESV, as well as in apical and basal +dP/dt_\text{max}, −dP/dt_\text{max}, and τ (each P<0.05). Overall, IVPGs correlated inversely with both ESV (IVPG=−0.027[ESV]+3.46, r=−0.64) and EDV (IVPG=−0.027[EDV]+4.30, r=−0.70). Improvements in IVPG correlated with improvements in apical τ (Δτ =5.93[ΔIVPG]+4.76, r=0.91) and basal τ (Δτ =2.41[ΔIVPG]+5.13, r=−0.67). Relative changes in IVPGs correlated with changes in ESV (ΔESV=−0.97[ΔIVPG]+23.34, r=−0.79), EDV (ΔEDV=−1.16[ΔIVPG]+34.92, r=−0.84), and EF (ΔEF=0.38[ΔIVPG]−8.39, r=0.85).

Conclusions—Improvements in LV function also increase IVPGs. These changes in IVPGs, suggestive of increases in LV suction and elastic recoil, correlate directly with improvements in LV relaxation and ESV. (Circulation. 2001; 104[suppl 1]:I-330-I-335.)

Key Words: diastole ■ surgery ■ physiology ■ ventricles

In 1930, Katz¹ speculated that the actively relaxing left ventricle (LV) has the ability to “exert a sucking action to draw blood into its chamber.” Despite these early speculations that diastole was not entirely a passive process, it was not until 1979 that Ling et al² demonstrated in a canine model the presence of regional diastolic intraventricular pressure gradients (IVPGs) between the base and apex of the LV. It was speculated that these gradients resulted in the active “sucking” of blood into the LV from the left atrium.² Courtois and colleagues subsequently validated these findings in 1988³ and later demonstrated, also in a canine model, a reduction in IVPG with myocardial ischemia induced by acute coronary occlusion.⁴ In this later study, they demonstrated a strong relationship between diastolic IVPG and systolic function, with regional ischemia-induced changes in LV function having a direct effect on IVPG. This observation led them to speculate that IVPGs were related to regional elastic recoil, or the potential energy stored during systole of the LV, and that impairments in regional systolic function would have a significant adverse effect on LV “suction.” Expanding on these concepts, Nikolic and colleagues⁵ later confirmed the relationship between IVPG and the elastic restoring forces of the LV in an intermittently nonfilling LV canine model (the mitral valve was intermittently mechanically occluded during diastole). They showed that IVPG was linearly related to the suction volume of the LV, that it was directly influenced by global geometric changes of the LV, particularly in the longitudinal plane, and that it could exist in the absence of LV filling. Nikolic et al⁶ had previously demonstrated that volumes below the equilibrium volume (the volume of the

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LV when fully relaxed at zero pressure), which they defined as the suction volume, were directly related to the magnitude of LV elastic recoil, or potential energy, forces. Therefore, these experiments suggested that IVPGs are directly related to LV geometry and are influenced by the regional and global effects of elastic recoil and that overall, they reflect the potential energy stored during systole and represent a mechanism by which the LV can adequately fill under low filling pressures.

Although these animal studies demonstrated that decreases in IVPG correlate with decreases in LV function during acute myocardial ischemia, little is known regarding the potential for increasing these gradients with interventions that improve LV function. Furthermore, although it has been suggested that IVPGs also exist in humans,7 data are lacking on the magnitude of these gradients and the influence of perturbations in systolic and diastolic function. Therefore, the goals of the present study, which was conducted in humans undergoing revascularization and/or surgical changes in geometries in systolic and diastolic function. Therefore, the goals of the present study, which was conducted in humans undergoing revascularization and/or surgical changes in geometries in systolic and diastolic function. Therefore, the goals of the present study, which was conducted in humans undergoing revascularization and/or surgical changes in geometries in systolic and diastolic function. 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Figure 1. Representative intracardiac waveforms. A, Representative waveforms obtained before operative intervention. B, Representative waveforms obtained after operative intervention. For both, top panel illustrates simultaneous full-scale recording of left atrial (LA) and LV pressures. Middle panel focuses on LV basal and apical waveforms during diastole, with gradient between them demonstrated in bottom panel. Peak of early diastolic intraventricular gradient is shown.

formed to evaluate the relationship between the change in IVPG before and after operative intervention and the relative or absolute changes in these indices. For all statistics, P values <0.05 were considered statistically significant.

Results
LV Systolic and Diastolic Function Before and After Surgery
Left atrial pressures, heart rates, and SVs before and after operative interventions (all P=NS) were similar overall. However, there were significant improvements in ejection fraction and ESV (both P<0.05; Table). Although EDV decreased after patients were weaned from CPB (pre-bypass 79.7±38.7 versus post-bypass 66.9±22.6 mL), this change was not statistically significant overall (P=0.13) except in the 4 patients undergoing IES, in whom EDV decreased from 111.9±38.1 to 76.5±30.4 mL (P=0.03). In the other 4 patients, EDV increased insignificantly from 56.6±15.0 to 59.7±15.6 mL (P=0.36). In addition, from the pressure transducers, LV basal +dP/dt max improved from 890±101 mm Hg/s (range 761 to 1075 mm Hg/s) to 1128±220 mm Hg/s (range 826 to 1426 mm Hg/s, P<0.01 versus pre-bypass); similarly, LV apical +dP/dt max improved from 909±114 mm Hg/s (range 758 to 1100 mm Hg/s) to 1094±221 mm Hg/s (range 788 to 1455 mm Hg/s, P<0.01 versus pre-bypass).

Similar to the improvements in systolic function, diastolic function also improved after operative intervention. Apical −dP/dt max and τ both improved after intervention (−830±207 to −984±267 mm Hg/s and 62.5±12.2 to 51.6±8.3 ms, both P<0.05 pre-bypass versus post-bypass), as did basal −dP/dt max and τ (−857±199 to −971±255 mm Hg/s and 55.2±13.4 to 47.6±12.0 ms, both P<0.05 pre-bypass versus post-bypass).

LV IVPGs Before and After Intervention
In all cases, peak IVPG was positive and occurred toward the end of relaxation, during which LV pressures were at their minimum. Peak IVPG before CPB was 1.64±0.79 mm Hg (range 0.50 to 2.80 mm Hg) and increased to 2.67±1.25 mm Hg (range 1.20 to 5.14 mm Hg) after patients were weaned from CPB (P<0.01). Similarly, mean IVPG increased from 0.92±0.64 to 1.51±0.74 mm Hg (P<0.01). Overall, all patients increased their peak IVPG by 1.03±0.75 mm Hg (37.9±20.8%).

Overall, pre-bypass and post-bypass IVPG correlated inversely with both EDV (IVPG=−0.027[EDV]+4.30, r=−0.70, P<0.001; Figure 2, top) and ESV (IVPG=−0.027[ESV]+3.46, r=−0.64, P<0.001; Figure 2, bottom). In addition, similar inverse correlations were observed between mean IVPG and EDV (r=−0.62) and ESV (r=−0.54). A linear relationship was observed between IVPG and both apical and basal +dP/dt max (r=0.54 and r=0.57, respectively, both P<0.01). Although no correlation was observed between IVPG and apical or basal τ or −dP/dt max, or the apical to basal differences in these values, improvements in IVPG correlated with improvements (ie, shortening) in apical τ (∆τ=5.93[ΔIVPG]+4.76, r=0.91, P<0.001; Figure 3) and, to a lesser extent, basal τ (∆τ=2.41[ΔIVPG]+5.13, r=0.67, P<0.001; Figure 3). In addition, improvements in the percent increase in IVPG correlated linearly with volume indices of LV systolic function, namely, ESV (∆ESV=−0.97[ΔIVPG]+23.34, r=−0.79, P<0.001; Figure 4), EDV (∆EDV=−1.16[ΔIVPG]+34.92, r=−0.84, P<0.001; Figure 4), and EF (∆EF=0.38[ΔIVPG]−8.39, r=0.85, P<0.05; Figure 5).

Discussion
Our findings confirm the existence of a quantifiable IVPG during early diastolic filling in humans. Furthermore, we demonstrate that improvements in LV systolic and diastolic...
function, through operative myocardial revascularization and/or LV remodeling, result in increases in these gradients. These findings complement previous animal experiments that demonstrated reductions in IVPG secondary to acute ischemia and impairments in LV systolic function.

Early work investigating the determinants of IVPG by Courtois et al.4 demonstrated significant decreases in IVPG with acute coronary occlusion from 1.2±0.5 to 0.6±0.6 mm Hg, changes that are consistent with our in situ observations. In addition, they demonstrated a relationship between decreases in IVPG and extensive regional systolic dysfunction. These findings, in conjunction with their previous work, 3 contributed to their speculation of the relationship between IVPG and the elastic recoil of the LV and provide a mechanism to maintain LV filling at lower diastolic pressure. Through impairments in regional systolic function, less energy would be released during diastole, which in turn would result in decreased or abnormal intraventricular flow. These observations are consistent with our findings of not only a relationship between IVPG and ESV but also of a relationship between the change in IVPG and changes in ESV, thereby validating the hypothesis relating the elastic recoil of the LV to IVPG. Furthermore, the lack of a relationship between IVPG and left atrial pressures (y = −0.052x+2.47, r = 0.27, P > 0.05) combined with the observations by Nikolic et al in their nonfilling LV model5 suggest that although these early gradients may exist in the absence of LV filling, they may represent intrinsic properties of the LV and transmitral pressure gradients.

To elaborate on the relationship between diastolic filling and IVPG, Steine and colleagues11 compared results of color M-mode echocardiography, a technique that allows for noninvasive visual estimation of LV filling patterns, with invasively obtained pressure gradients. In their canine model of LV dysfunction, using coronary microembolization, IVPG decreased from 1.9±0.9 to 0.7±0.5 mm Hg. In addition to also observing an inverse relationship to ESV (r = −0.95, P < 0.01), they demonstrated that IVPG was inversely related
been attributed in part to improvements in both systolic and diastolic function or whether the 2 properties are synergistically linked (ie, ESV) can occur independently of changes in diastolic function or whether the 2 properties are synergistically linked by the elastic recoil properties of the LV. Clinical observations show that systolic and diastolic impairments often coexist. Although isolated diastolic dysfunction can exist with preserved systolic function (and vice versa), our findings suggest a relationship of early LV relaxation and diastolic filling with ESV and elastic recoil. CABG is a well-established strategy for myocardial revascularization in patients with symptomatic coronary artery disease. Although we did not seek to prove the benefits or effects of the surgical interventions used during the present study, we did find a linear correlation between the shortening of both basal and apical τ and an increase in IVPG. In part, this finding may be because τ, dP/dt max, and IVPGs reflect different parameters of LV regional and global relaxation. Our findings suggest that myocardial revascularization and LV remodeling result in improvements in ventricular relaxation that are related to changes in LV elastic recoil. However, it is unclear from these findings whether isolated changes in systolic function (ie, ESV) can occur independently of changes in diastolic function or whether the 2 properties are synergistically linked by the elastic recoil properties of the LV. Clinical observations show that systolic and diastolic impairments often coexist. Although isolated diastolic dysfunction can exist with preserved systolic function (and vice versa), our findings suggest a relationship of early LV relaxation and diastolic filling with ESV and elastic recoil.

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Conclusions

These techniques have been shown to accurately measure transmural pressure gradients in a canine model and more recently in humans. The ability to directly and noninvasively quantify this index of LV function may allow for better assessment of cardiac function in response to various interventions, such as pharmacological echocardiographic stress testing or intraoperative assessment of surgical interventions, or as a component of serial examinations of functional status.

Figure 4. Relationships between relative changes in IVPG and relative changes in EDV (solid circles) and ESV (open circles).

Figure 5. Relationships between relative change in IVPG and EF.

Study Limitations

There are several significant limitations to our human study. Although we suggest that improvements in IVPG coincide with improvements in elastic recoil through an inverse relationship with ESV, we did not actually measure either the elastic recoil of the LV or the suction volume. The suction volume is defined as the difference between the smallest measured LV volume and LV volume at zero pressure, a property that may be technically difficult to determine precisely in humans. In addition, although it has been suggested that IVPGs reflect the elastic recoil and release of potential energy, it is yet to be demonstrated whether this process is secondary to a passive release of stored energy or whether this “suction” is an active energy-consuming component of early diastole. Another limitation is our intraoperative model. Although the effects of an intact pericardium are known to affect diastolic filling and alter end-diastolic LV pressure-volume relationships, the timing of these influences during diastole is such that they should have little influence on early-diastolic physiology. In addition, despite the limited number of patients studied and the different operative procedures performed, our results nonetheless validate the physiological relationships observed.

Potential Clinical Applications

Recent advances in color Doppler echocardiography may allow for noninvasive measurements of IVPG. By abstraction of the spatiotemporal velocity characteristics of color M-mode echocardiography, a pressure gradient along an imaging scan line, such as mitral inflow, can be derived. These techniques have been shown to accurately measure transmural pressure gradients in a canine model and more recently in humans. The ability to directly and noninvasively quantify this index of LV function may allow for better assessment of cardiac function in response to various interventions, such as pharmacological echocardiographic stress testing or intraoperative assessment of surgical interventions, or as a component of serial examinations of functional status.

Conclusions

IVPGs, a previously demonstrated index of LV elastic recoil and early diastolic suction, increase with operative interventions that improve both systolic and diastolic function.
Furthermore, changes in these gradients are directly related to improvements in ESV, an index of LV contractility, and, an index of LV relaxation.

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