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Effects of Mechanical Left Ventricular Unloading by Impella on Left Ventricular Dynamics in High-Risk and Primary Percutaneous Coronary Intervention Patients

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Objectives: We studied online left ventricular (LV) dynamic effects of mechanical LV unloading directly after percutaneous coronary intervention (PCI). **Background:** Limited clinical information is available on the direct LV dynamic consequences of LV unloading in patients undergoing high-risk PCI and primary PCI for acute ST-elevation myocardial infarction. **Methods:** The effects of the Impella LP2.5 device on LV dynamics were studied in 11 patients (elective high-risk PCI, $n = 6$; primary PCI, $n = 5$). LV pressure and volume were continuously assessed by a pressure-conductance catheter at 4 different support levels of the Impella, from 0 L/min at baseline to 2.5 L/min at maximal support. **Results:** The response to increased LV unloading was not different between both groups of patients. The pooled data showed no change on global and systolic LV function during increased LV unloading, while diastolic function showed improvement as indicated by an increased LV compliance in all patients. There was a decrease in end-diastolic pressure from 22 ± 12 to 13 ± 9 mm Hg ($P = 0.0001$), in end-diastolic elastance from 0.134 ± 0.060 to 0.091 ± 0.064 mm Hg/mL ($P = 0.009$), and in end-diastolic wall stress from 84 ± 50 to 47 ± 39 mm Hg ($P = 0.004$). **Conclusions:** LV unloading decreases end-diastolic wall stress and improves diastolic compliance dose-dependently. Our results indicate beneficial LV unloading effects of Impella during high-risk and primary PCI.

Key words: left ventricular function; hemodynamics; angioplasty; heart-assist device; pressure-volume relations

INTRODUCTION

Left ventricular (LV) support and unloading may be beneficial for patients with compromised LV function undergoing high-risk percutaneous coronary intervention (PCI) [1,2], and for patients treated by primary PCI for acute ST-elevation myocardial infarction (STEMI) [3,4]. The Impella LP2.5 (Impella) is a novel percutaneous microaxial blood pump that directly unloads the LV by continuously aspirating blood from the LV cavity and expelling it into the ascending aorta. The design is based on the 14F percutaneous Hemopump. Initial clinical experience with the Hemopump in the late nineties, showed a decrease in pulmonary capillary wedge pressure and the maintenance of sufficient mean aortic pressure during cardiac arrest [5]. The unloading mechanism is essentially different than that of intra-aortic balloon pumping (IABP) [6,7].

In the clinical setting, the IABP showed afterload reduction and limited LV unloading [7], an increase in coronary flow [8,9], and conflicting data on pulmonary capillary wedge pressure and cardiac index [10–12]. In experimental studies, the Impella showed an effective

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LV unloading and an improved coronary perfusion [6,13]. Furthermore, the Impella showed to be easy to use in the setting of high-risk [2] and primary PCI [3]. However, there is limited clinical information on LV dynamics during direct and profound LV unloading as effected by true LV assist devices in this setting. Previously, we reported that Impella support resulted in an improved coronary perfusion and a decreased coronary microvascular resistance in high-risk PCI patients [14].

Therefore, the aim of our present study was to test the hypothesis that direct LV unloading by the Impella results in an improvement in cardiac performance and a concomitant decrease in end-diastolic pressure and wall stress in elective high-risk PCI patients with compromised LV function, and in nonshock STEMI patients treated by primary PCI.

METHODS

Patients

The whole study consisted of two patient groups with a total of 11 patients.

Group 1—Elective high-risk PCI patients: High-risk PCI. This cohort consisted of six consecutive patients with stable angina, who underwent an elective high-risk PCI with circulatory support by the Impella. All patients had a decreased LV function (ejection fraction 28% ± 14%), as determined by echocardiography or nuclear scintigraphy. Patients were included if the planned PCI was considered high-risk on the basis of a poor LV function combined with left main coronary artery, last remaining vessel or equivalent PCI procedure [2]. All patients were pretreated with aspirin, clopidogrel and heparin before the PCI. PCI was performed following routine procedures, after which LV measurements were performed (see "Study Protocol").

Group 2—Acute STEMI patients: Primary PCI. This cohort consisted of five consecutive patients who presented with their first acute anterior STEMI within 6 hours after onset of symptoms. Patients were pretreated with aspirin, clopidogrel, and heparin before PCI. Primary PCI was performed following routine procedures. After primary PCI of the occluded left anterior descending artery (LAD), the Impella was inserted and LV measurements were performed (see "Study protocol"). Exclusion criteria was cardiogenic shock defined as a systolic blood pressure $\leq$90 mm Hg for at least 30 minutes or vasopressors required to maintain blood pressure >90 mm Hg.

General exclusion criteria for both groups were significant valvular disease and LV thrombus, as assessed by echocardiography before catheter insertion into the LV. The study complied with the Declaration of Helsinki and was approved by the institutional research and ethics committee. All subjects gave written informed consent.

Instrumentation

The Impella LP2.5 (Abiomed Europe GmbH, Aachen, Germany) was inserted retrogradely into the LV across the aortic valve via the femoral artery. The Impella is a pigtail catheter-based microaxial flow device that continuously aspirates blood from the LV cavity and expels it into the ascending aorta. It has nine support levels, producing a flow of up to 2.5 L/min. The differential pressure sensor at the tip of the cannula allows proper positioning of the pump and continuously registers the intracavitary and aortic pressure to derive pump flow and control its rotational speed.

The 7F pigtail equipped combined pressure-conductance catheter (CD Leycom, Zoetermeer, The Netherlands) was placed in the LV via the contralateral femoral artery. The Swan Ganz catheter was placed in the pulmonary artery via the femoral vein. Blood resistivity rho was determined by a 5 mL blood sample, cardiac output was determined by thermodilution and parallel conductance was determined by hypertonic saline injections to calibrate the volume signals of the conductance catheter [15]. An echocardiogram was repeated when both Impella and conductance catheter were operational to assess possible aortic valve regurgitation.

Study Protocol and Analysis

LV dynamics were recorded continuously during 4 incremental and decremental Impella support levels (ranging from 0 L/min at level 1 to 2.5 L/min at level 9). The duration of support at each level was at least 2 minutes. Data were analyzed off line. Per-beat averages of the recorded variables were calculated as the mean of all beats during a steady state of at least 30 s. The following indices were obtained: heart rate (HR), cardiac index (CI), ejection fraction (EF), stroke volume (SV), stroke work as the area of the PV-loop (SW), end-systolic and end-diastolic volume (ESV, EDV), end-systolic and end-diastolic pressure (ESP, EDP), maximal rate of pressure change (dP/dt_{max}), and the relaxation time constant Tau, defined as that time required for the cavity pressure at dP/dt_{min} to be reduced by half. Effective arterial elastance (E_A), an index of LV afterload, was calculated by ESP/SV. End-systolic elastance (E_{ES}) was estimated by ESP/ESV [16], and end-diastolic stiffness (E_{ED}) by EDP/EDV. Subsequently, the ventricular-arterial coupling ratio was calculated by E_{ES}/E_A, which describes the interaction between LV performance and the systemic arterial system [17]. End-diastolic

wall-stress (WS_{ED}) was calculated from the instantaneous LV pressure (P) and volume (V) signals, and from LV mass (LVM) as derived from echocardiography, by P·(1 + 3·V/LVM) [18].

Statistical Evaluation

Data are expressed as mean ± SD or *n* (%). Intergroup differences were tested for significance by the twotailed independent samples t-test. Hemodynamic measurements at different support levels of the Impella were compared with the situation of no support and with the previous support level using the within subjects variance component of ANOVA with repeated measures, followed by linear contrast analysis. Correlations were tested using the twotailed Pearson correlation. SPSS release 15.0.1 statistical software package for windows (SPSS, 2006, Chicago, Illinois) was used for analyzes. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

The baseline characteristics are shown in Table I. The high-risk PCI patients show a positive history of cardiac disease, multiple risk factors for and presence of extensive coronary artery disease (CAD), increased LV mass [19], and severely compromised left ventricles with elevated levels of NT-proBNP and subsidiary medical therapy. The STEMI patients had no cardiac history, but show several risk factors for CAD, and appeared to have compromised left ventricles as observed by the low EF and large infarct size indicated by the high cardiac necrosis markers.

In all patients, no or only minimal additional aortic valve regurgitation was present when both the Impella and conductance catheter were positioned across the aortic valve. In both patient groups there was one patient with disturbed volume signals, allowing assessment of pressure-derived indices only in these two patients.

LV Dynamic Data

The response of LV dynamics to increasing and decreasing Impella support levels occurred almost immediately (within a few heart beats) and then remained constant at each support level. There was a similar dose-dependent response to increasing and decreasing support. Between the high-risk PCI and STEMI group, baseline LV dynamic data were only different for SV (52 ± 8 versus 40 ± 6 mL, respectively, $P = 0.04$) and for dP/dt_{max} (987 ± 197 versus 1362 ± 179 mm Hg/s, respectively, $P = 0.01$). Since there were no differences between both groups in LV dynamic responses to changes in Impella support, LV dynamic data were pooled in Table II.

In Table II, the LV dynamic data of all patients are listed for the different support levels of the Impella. The left panel shows that the baseline values of global, systolic and diastolic function are generally impaired. Global function parameters show a relatively low SV, CI, and SW, an increased E_A, and a mismatch in ventricular-arterial coupling [20]. Systolic function shows a high ESV, and a low EF, E_{ES}, and dP/dt_{max}. Diastolic function shows a high EDV, EDP, E_{ED}, and WS_{ED}, and an impaired relaxation and filling.

The mean aortic pressure remained unchanged from 110 ± 23 mm Hg at minimal support to 106 ± 25 mm Hg at maximal support ($P = 0.1$). The right panels of Table II show that global and systolic LV function remained unchanged at increasing support levels, while diastolic function improved. There was a marked decrease in EDP by 42% ± 24% ($P = 0.0001$), and in WS_{ED} by 40% ± 26% ($P = 0.004$) as also illustrated in Figure 1. LV compliance increased, as indicated by a decrease in E_{ED} by 29% ± 38% ($P = 0.009$). The decrease in WS_{ED} correlated to the decrease in EDP ($r = 0.75$, $P = 0.02$).

Figure 2 illustrates the shift of the PV-loop induced by the Impella in two STEMI patients. The left- and downward shift of the PV-loop (Figure 2A), assumingly on its diastolic compliance curve, was observed in 2 out of 5 high-risk PCI and 2 out of 4 STEMI patients. The right- and downward shift of the PV-loop (Figure 2B), indicating a changed compliance curve, was observed in 3 out of 5 high-risk PCI and 2 out of 4 STEMI patients. Between the patients in the high-risk PCI group, we found no explanatory factors that correlated with the type of PV-loop shift. On the other hand, in the STEMI group differences in residual ischemia were related to differences in PV-loop shift. Both patients with the downwards shifted compliance curve had a TIMI flow grade 2 after primary PCI versus a TIMI flow grade 3 in the other patients.

DISCUSSION

In this study, we demonstrated direct beneficial effects of mechanical LV unloading on end-diastolic wall stress, diastolic compliance, and on the intrinsic mechanical properties of the LV during diastole, in high-risk PCI and STEMI patients.

LV Unloading

Our study shows that in all patients, the Impella leads to direct diastolic wall stress reduction, which is

TABLE I. Patient Characteristics

	High-risk PCI ($n = 6$)	STEMI ($n = 5$)
Clinical characteristics and risk factors		
Age, *y*	72 ± 13	56 ± 13
Male gender	4 (67)	4 (80)
Diabetes	1 (17)	1 (20)
Hypertension	2 (33)	2 (40)
Hypercholesterolemia	2 (33)	2 (40)
Family history of CAD	5 (83)	1 (20)
Current smoking	4 (67)	4 (80)
Previous myocardial infarction	6 (100)	0 (0)
Previous coronary artery bypass grafting or PCI	1 (17)	0 (0)
Canadian cardiovascular society class ≥3	6 (100)	5 (100)
Physical and diagnostic tests		
Heart rate, bpm	76 ± 15	76 ± 16
Mean systolic blood pressure, mm Hg	123 ± 22	131 ± 15
Mean diastolic blood pressure, mm Hg	66 ± 15	83 ± 9
[a]Left ventricular ejection fraction, %	28 ± 14	29 ± 7
[a]Left ventricular mass, *g*	246 ± 68	191 ± 67
[a]Left ventricular dilatation	5 (83)	2 (40)
[a]Aortic valve insufficiency grade ≥2	1 (17)	0 (0)
[a]Mitral valve regurgitation grade ≥2	5 (83)	0 (0)
NT-proBNP, ng/L	2336 ± 1995	3001 ± 5254
Treatment-related characteristics		
Target lesion in LAD	2 (33)	5 (100)
Target lesion in LCx	3 (50)	0 (0)
Target lesions in LM, LAD and LCx	1 (17)	0 (0)
Dukes jeopardy score ≥8 (of maximal 12)	6 (100)	2 (40)
Three vessel disease, %	6 (100)	2 (40)
Last remaining vessel, %	2 (33)	0 (0)
Presence of a chronic total occlusion	3 (50)	0 (0)
TIMI flow grade 3 after PCI, %	6 (100)	3 (60)
Cardiac markers after primary PCI		
Peak NT-proBNP, ng/L	N/A	5120 ± 6106
Peak CK-MB, μg/L	N/A	277 ± 162
Peak Troponin T, μg/L	N/A	14.6 ± 11.5

Values are *n* (%) or mean ± SD. PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; CAD, coronary artery disease.

[a]Assessed before high-risk PCI and assessed after primary PCI; NT-proBNP, N-terminal part of the pro-B-type natriuretic peptide; LAD, left anterior descending artery; LCx, left circumflex; LM, left main; TIMI, thrombolysis in myocardial infarction; CK, creatine kinase.

related to the level of LV unloading. Such direct and marked effects may be the expected advantage over the IABP, since the Impella directly removes blood from the LV. LV unloading by the Impella has previously been shown to be more effective than by the IABP in the experimental setting [6], and in the clinical setting by limited data obtained from right heart catheterization [3]. Clinical data on surgically implanted pulsatile and nonpulsatile LV assist devices show a decrease in pressure assessed by right-heart catheterization, and in dimensions assessed by echocardiography [21].

Incremental Impella support caused improvement in LV compliance by shifting the PV-loop left- and downwards on the compliance curve in half of the patients, regardless of the extent of LV impairment after primary PCI. This PV-loop shift on the compliance curve is expected to occur when filling pressures decrease due to mechanical unloading as in line with experimental studies [13].

The observed right- and downward shift of the PV-loop in the other high-risk PCI and STEMI patients indicates that the compliance curve itself shifted downwards, thereby improving the intrinsic mechanical properties of the LV during diastole. For decades it has been known that CAD as well as acute myocardial infarction negatively influence LV function by a decrease in LV compliance, indicated by an upward shift of the compliance curve [22]. Recently it was shown that primary PCI immediately causes an improvement in diastolic function by shifting the compliance curve downwards [23]. Therefore, our

TABLE II. LV Dynamic Changes During LV Support by the Impella LP 2.5 in 11 Patients

	Impella support level				
	1 0 L/m	3 1.5 L/m	6 2.0 L/m	9 2.5 L/m	*P*-value (linear)
Global function					
HR, bpm	74 ± 12	75 ± 12	75 ± 12	75 ± 12	0.3
SV, mL	47 ± 9	45 ± 10	49 ± 15	50 ± 19	0.3
CI, L/min	1.9 ± 0.5	1.8 ± 0.4	1.8 ± 0.4	1.7 ± 0.5	0.3
SW, mm Hg·L	4.53 ± 0.88	4.55 ± 0.89	4.92 ± 1.16	4.62 ± 1.17	0.3
E_A, mm Hg/mL	2.62 ± 0.45	2.81 ± 0.64	2.61 ± 0.77	2.60 ± 1.28	0.5
E_{ES}/E_A	0.39 ± 0.12	0.35 ± 0.07	0.41 ± 0.19	0.50 ± 0.35	0.7
Systolic function					
ESV, mL	120 ± 51	121 ± 54	118 ± 46	114 ± 35	0.4
EF, %	26 ± 6	25 ± 3	27 ± 7	30 ± 12	1.0
ESP, mm Hg	110 ± 23	112 ± 26	110 ± 26	106 ± 25	0.1
E_{ES}, mm Hg/mL	1.02 ± 0.36	0.99 ± 0.33	0.99 ± 0.29	1.07 ± 0.41	0.7
dP/dt_{max}, mm Hg/s	1158 ± 266	1145 ± 301	1114 ± 279	1116 ± 282	0.1
Diastolic function					
EDV, mL	179 ± 43	167 ± 57	167 ± 48	158 ± 45	0.2
EDP, mm Hg	22 ± 12	17 ± 13	16 ± 11	13 ± 9	0.0001
E_{ED}, mm Hg/mL	0.134 ± 0.060	0.107 ± 0.068	0.092 ± 0.058	0.091 ± 0.064	0.009
τ, ms	48 ± 6	48 ± 6	47 ± 6	46 ± 6	0.07
WS_{ED}, mm Hg	84 ± 50	67 ± 57	56 ± 43	47 ± 39	0.004

Values are mean ± SD. HR, heart rate; SV, stroke volume; CI, cardiac index; SW, stroke work; E_A, effective arterial elastance; E_{ES}/E_A, ventricular-arterial coupling ratio; ESV, end-systolic volume; EF, ejection fraction; ESP, end-systolic pressure; E_{ES}, end-systolic elastance; dP/dt_{max}, maximal rate of left ventricular pressure change; EDV, end-diastolic volume; EDP, end-diastolic pressure; E_{ED}, end-diastolic stiffness; Tau, relaxation time constant; WS_{ED}, end-diastolic wall stress.

data suggest that the Impella may dissolve the "demand ischemic state" of the impaired ventricles in the high-risk PCI patients and the "long-term occlusion ischemia" in the STEMI patients with suboptimal reperfusion (i.e. TIMI <3 flow), corresponding to 'demand ischemia' studied previously during pacing [24].

Impella-unloading decreased wall stress in all of the patients. When considering that immediately after primary PCI for STEMI there is an increased microvascular resistance in the infarct and noninfarct related artery [25], which is related to LV filling pressures [26], our data suggest that wall stress reduction by LV unloading decreases coronary microvascular resistance and increases coronary flow velocity, as previously shown during Impella support [14].

In line with wall stress reduction interventions such as IABP unloading and surgical cardiomyoplasty, Impella unloading may also reduce mechanical dyssynchrony by decreasing wall stress in patients with advanced CAD or after primary PCI [27,28].

Cardiac Support

As previously shown in the experimental setting [6], an improved cardiac function at maximum support of the Impella depends on the preassist cardiac output, since the device is a parallel pump across the aortic valve, total cardiac output constitutes of flow output through the pump plus the output from the heart. We found no increase in cardiac output at incremental support levels, presumably due to the fact that our study population had sufficient pre-assist cardiac output. In line with this finding, active diastolic relaxation was only mildly prolonged and only mildly, but not significantly improved by the unloading device. Cardiac performance seemed to be down-regulated at incremental Impella support, assumingly related to reduced oxygen demand, since total output remained unchanged. Nonetheless, when cardiac performance is insufficient, such as in cardiogenic shock, the Impella may contribute to the total cardiac output [29].

LV support by the widely used IABP is induced by LV afterload reduction by decreasing impedance to LV ejection [7]. Our findings of the fact that the Impella-induced effects on LV dynamics occur at constant afterload, as shown by a constant E_A, suggest that further pharmacological or mechanical afterload reduction on top of Impella support [13] could be of additional value in STEMI patients, specifically in case of no-reflow or severe LV impairment.

Limitations

There are a few limitations of our study with respect to the interpretation of the data. We did not measure myocardial oxygen consumption and lactate metabolism to determine whether the Impella support

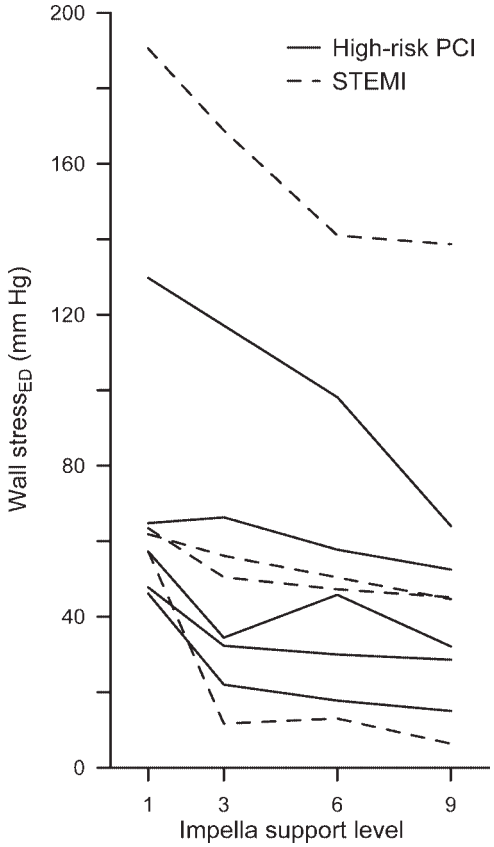

Fig. 1. Illustration of a decrease in end-diastolic wall stress in all patients during incremental Impella support. Each line represents the LV end-diastolic wall stress in a single patient. The four Impella support levels on the x-axis are indicated by 1 to 9, representing the lowest (0 L/min) to the highest (2.5 L/min) support level.

decreases myocardial metabolic demand. Furthermore, we assessed acute LV dynamic changes during short duration of Impella support and immediately after the PCI procedure, whereas influences on patient outcome may require longer periods of Impella support. This study was performed in high-risk compromised patients, whereas obviously, patients in cardiogenic shock may benefit most from LV assistance. Nevertheless, from our positive findings in hemodynamically stable patients more marked effects may be expected in shock patients.

Clinical Implications

The present study is the first clinical study to show that direct unloading of the LV has a beneficial effect on LV compliance, in high-risk PCI patients with severely impaired LV function and in STEMI patients treated by primary PCI, via assessment of online arithmetical and load-independent data from PV-loops. It may be expected that high-risk and primary PCI patients, with or without shock, will benefit from the above mentioned positive hemodynamic effects of the Impella to improve LV and patient recovery. Obviously, we cannot draw any conclusions on whether unloading by the Impella will have different effects on outcome than IABP.

CONCLUSIONS

LV support by Impella improves end-diastolic compliance and decreases end-diastolic wall stress by

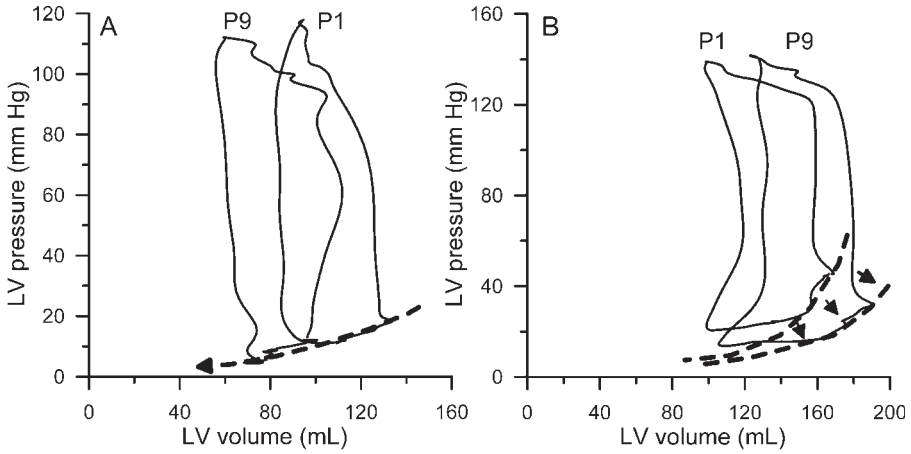

Fig. 2. Illustration of improved passive diastolic LV function by LV unloading in 2 ST-elevation myocardial infarction patients, indicated by a left- and downward shift of the PV-loop in patient A representing a decreased end-diastolic stiffness (A) or a right- and downward shift of the PV-loop in patient B representing an improved compliance curve (B). P1 represents an average PV-loop during support at the lowest pump level of the Impella LP2.5 device, whereas P9 represents the highest pump level.

effective LV unloading, and may improve the intrinsic diastolic properties of the LV by shifting the diastolic compliance curve downwards. Our results indicate beneficial LV unloading effects during high-risk and primary PCI, as assessed by online and load-independent data from PV-loops.

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REFERENCES

1. Briguori C, Sarais C, Pagnotta P, Airoldi F, Liistro F, Sgura F, Spanos V, Carlino M, Montorfano M, Di Mario C, Colombo A. Elective versus provisional intra-aortic balloon pumping in high-risk percutaneous transluminal coronary angioplasty. Am Heart J 2003;145:700–707.
2. Henriques JP, Remmelink M, Baan J, Van Der Schaaf RJ, Vis MM, Koch KT, Scholten EW, De Mol BA, Tijssen JG, Piek JJ, De Winter RJ. Safety and feasibility of elective high-risk percutaneous coronary intervention procedures with left ventricular support of the Impella Recover LP 2.5. Am J Cardiol 2006;97: 990–992.
3. Sjauw KD, Remmelink M, Baan J, Lam K, Engstrom AE, Van Der Schaaf RJ, Vis MM, Koch KT, Van Straalen JP, Tijssen JG, De Mol BA, De Winter RJ, Piek JJ, Henriques JP. Left ventricular unloading in acute ST-segment elevation myocardial infarction patients is safe and feasible and provides acute and sustained left ventricular recovery. J Am Coll Cardiol 2008;51: 1044–1046.
4. Smalling RW, Cassidy DB, Barrett R, Lachterman B, Felli P, Amirian J. Improved regional myocardial blood flow, left ventricular unloading, and infarct salvage using an axial-flow, transvalvular left ventricular assist device. A comparison with intra-aortic balloon counterpulsation and reperfusion alone in a canine infarction model. Circulation 1992;85:1152–1159.
5. Scholz KH, Dubois-Rande JL, Urban P, Morice MC, Loisance D, Smalling RW, Figulla HR. Clinical experience with the percutaneous hemopump during high-risk coronary angioplasty. Am J Cardiol 1998;82:1107–1110.
6. Reesink KD, Dekker AL, Van Ommen V, Soemers C, Geskes GG, Van Der Veen FH, Maessen JG. Miniature intracardiac assist device provides more effective cardiac unloading and circulatory support during severe left heart failure than intraaortic balloon pumping. Chest 2004;126:896–902.
7. Schreuder JJ, Maisano F, Donelli A, Jansen JR, Hanlon P, Bovelander J, Alfieri O. Beat-to-beat effects of intraaortic balloon pump timing on left ventricular performance in patients with low ejection fraction. Ann Thorac Surg 2005;79: 872–880.
8. Ishihara M, Sato H, Tateishi H, Kawagoe T, Muraoka Y, Yoshimura M. Effects of intraaortic balloon pumping on coronary hemodynamics after coronary angioplasty in patients with acute myocardial infarction. Am Heart J 1992;124:1133–1138.
9. Kern MJ, Aguirre F, Bach R, Donohue T, Siegel R, Segal J. Augmentation of coronary blood flow by intra-aortic balloon pumping in patients after coronary angioplasty. Circulation 1993;87:500–511.
10. Taguchi I, Ogawa K, Oida A, Abe S, Kaneko N, Sakio H. Comparison of hemodynamic effects of enhanced external counterpulsation and intra-aortic balloon pumping in patients with acute myocardial infarction. Am J Cardiol 2000;86:1139–1141.
11. Thiele H, Sick P, Boudriot E, Diederich KW, Hambrecht R, Niebauer J, Schuler G. Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. Eur Heart J 2005;26:1276–1283.
12. Zehetgruber M, Mundigler G, Christ G, Merhaut C, Klaar U, Kratochwill C, Neunteufl T, Hofmann S, Heinz G, Maurer G, Siostrzonek P. Relation of hemodynamic variables to augmentation of left anterior descending coronary flow by intraaortic balloon pulsation in coronary artery disease. Am J Cardiol 1997; 80:951–955.
13. Sauren LD, Accord RE, Hamzeh K, De Jong M, Van Der Nagel T, Van Der Veen FH, Maessen JG. Combined Impella and intra-aortic balloon pump support to improve both ventricular unloading and coronary blood flow for myocardial recovery: an experimental study. Artif Organs 2007;31:839–842.
14. Remmelink M, Sjauw KD, Henriques JP, De Winter RJ, Koch KT, Van Der Schaaf RJ, Vis MM, Tijssen JG, Piek JJ, Baan J. Effects of left ventricular unloading by Impella recover LP2.5 on coronary hemodynamics. Catheter Cardiovasc Interv 2007; 70:532–537.
15. Baan J, Van Der Velde ET, De Bruin HG, Smeenk GJ, Koops J, Van Dijk AD, Temmerman D, Senden J, Buis B. Continuous measurement of left ventricular volume in animals and humans by conductance catheter. Circulation 1984;70:812–823.
16. Steendijk P, Tulner SA, Bax JJ, Oemrawsingh PV, Bleeker GB, Van Erven L, Putter H, Verwey HF, Van Der Wall EE, Schalij MJ. Hemodynamic effects of long-term cardiac resynchronization therapy: analysis by pressure-volume loops. Circulation 2006;113:1295–1304.
17. Sunagawa K, Maughan WL, Burkhoff D, Sagawa K. Left ventricular interaction with arterial load studied in isolated canine ventricle. Am J Physiol 1983;245:H773–H780.
18. Arts T, Bovendeerd PH, Prinzen FW, Reneman RS. Relation between left ventricular cavity pressure and volume and systolic fiber stress and strain in the wall. Biophys J 1991;59:93–102.
19. Lattanzi F, Di Bello V, Picano E, Caputo MT, Talarico L, Di Mario C, Landini L, Santoro G, Giusti C, Distante A. Normal ultrasonic myocardial reflectivity in athletes with increased left ventricular mass. A tissue characterization study. Circulation 1992;85:1828–1834.
20. Starling MR. Left ventricular-arterial coupling relations in the normal human heart. Am Heart J 1993;125:1659–1666.
21. Klotz S, Deng MC, Stypmann J, Roetker J, Wilhelm MJ, Hammel D, Scheld HH, Schmid C. Left ventricular pressure and volume unloading during pulsatile versus nonpulsatile left ventricular assist device support. Ann Thorac Surg 2004;77: 143–149.
22. Diamond G, Forrester JS. Effect of coronary artery disease and acute myocardial infarction on left ventricular compliance in man. Circulation 1972;45:11–19.
23. Remmelink M, Sjauw KD, Henriques JPS, Koch KT, Van Der Schaaf RJ, Vis MM, Tijssen JGP, De Winter RJ, Piek JJ, Baan J. Acute effects of primary percutaneous coronary intervention on left ventricular function by continuous pressure-volume loop analyses. J Am Coll Cardiol 2009;53:1498–1502.

24. Paulus WJ. Upward shift and outward bulge. Divergent myocardial effects of pacing angina and brief coronary occlusion. Circulation 1990;81:1436–1439.
25. Bax M, De Winter RJ, Koch KT, Schotborgh CE, Tijssen JG, Piek JJ. Time course of microvascular resistance of the infarct and noninfarct coronary artery following an anterior wall acute myocardial infarction. Am J Cardiol 2006;97:1131–1136.
26. Van Herck PL, Carlier SG, Claeys MJ, Haine SE, Gorissen P, Miljoen H, Bosmans JM, Vrints CJ. Coronary microvascular dysfunction after myocardial infarction: increased coronary zero flow pressure both in the infarcted and in the remote myocardium is mainly related to left ventricular filling pressure. Heart 2007;93:1231–1237.
27. Remmelink M, Sjauw KD, Piek JJ, De Winter RJ, Baan J. Effects of left ventricular unloading on reperfusion-related AIVR in acute myocardial infarction. Neth Heart J 2009;17:73–74.
28. Schreuder JJ, Steendijk P, Van Der Veen FH, Alfieri O, Van Der Nagel T, Lorusso R, Van Dantzig JM, Prenger KB, Baan J, Wellens HJ, Batista RJ. Acute and short-term effects of partial left ventriculectomy in dilated cardiomyopathy: Assessment by pressure-volume loops. J Am Coll Cardiol 2000;36:2104–2114.
29. Sjauw KD, Engstrom AE, Henriques JP. Percutaneous mechanical cardiac assist in myocardial infarction. Where are we now, where are we going? Acute Card Care 2007;9:222–230.