Effects of Impella on Coronary Perfusion in Patients With Critical Coronary Artery Stenosis

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***Background*—**Mechanical circulatory support devices are used to maintain hemodynamic stability during high-risk percutaneous coronary interventions. Little is known on the effects of such devices on coronary hemodynamics in patients with significant coronary stenosis. We sought to investigate whether mechanical circulatory support in the form of Impella (Abiomed Inc, Danvers, MA) can improve coronary hemodynamics in the presence of a critical coronary stenosis.

***Methods and Results*—**We examined coronary perfusion pressures and coronary pressure distal to a critical stenosis using a coronary pressure wire in 11 patients (12 coronary lesions) undergoing high-risk percutaneous coronary interventions with the use of mechanical circulatory support. Systemic, ventricular, and coronary hemodynamics were obtained at both minimum and maximum support levels before high-risk percutaneous coronary interventions. All patients had obstructive lesions with angiographically estimated diameter stenosis between 70% and 99% and distal coronary artery pressure to aortic pressure ratios between 0.44 and 0.88. When compared with minimum support, maximum support resulted in a decrease in the left ventricular end-diastolic pressure (27.3±8.6 versus 21.5±5.2 mm Hg; P=0.002) and increases in the mean systemic blood pressure (77.6±13.5 versus 88.2±12.2 mm Hg; P<0.001) and mean distal coronary pressure (51.8±20.2 versus 60.8±18.1 mm Hg; P<0.001). Effective coronary perfusion pressure (mean aortic pressure–left ventricular end-diastolic pressure) significantly increased with maximum support (49.8±15.7 versus 67.2±13.6 mm Hg; P<0.001). Diastolic perfusion pressure (diastolic blood pressure–left ventricular end-diastolic pressure) also significantly increased with maximum support (32.9±13.4 versus 52.0±11.6 mm Hg; P<0.001).

***Conclusions*—**Mechanical circulatory support with Impella can improve distal coronary pressure and coronary perfusion pressures in the presence of critical coronary stenosis. **(*Circ Cardiovasc Interv*. 2018;11:e005870. DOI: 10.1161/CIRCINTERVENTIONS.117.005870.)**

Key Words: arterial pressure ■ blood pressure ■ coronary vessels ■ heart ■ hemodynamics

Mechanical circulatory support (MCS) devices are frequently used to maintain systemic perfusion in cardiogenic shock, acute myocardial infarction, and high-risk percutaneous coronary intervention (HRPCI). Historically, intra-aortic balloon pump (IABP) has been the most frequently used support device and has been shown to improve systemic blood pressure and increase coronary blood flow in nonstenotic arteries.[1,2] Several studies, however, have demonstrated that IABP does not improve coronary hemodynamics in the presence of a significant stenosis.[1–4] Given a significant portion of patients undergoing HRPCI have obstructive, multivessel, coronary artery disease (CAD), we evaluated whether a more robust form of MCS (Impella, Danvers, MA) could improve coronary perfusion in the presence of significant obstructive CAD. The Impella catheter is a transvalvular percutaneous MCS device that unloads the left ventricle directly by aspirating blood from the left ventricle into the ascending aorta.[5,6] Impella has been shown to improve systemic hemodynamics, including mean arterial pressure, cardiac output, and cardiac power[6–8]; however, its impact on coronary hemodynamics especially in the presence of critical CAD remains unknown. We sought to examine the effect of MCS in the form of Impella on coronary pressures and perfusion across significant coronary stenosis during HRPCI.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Patients

We enrolled 11 consecutive patients from November 2015 to November 2016 who underwent elective Impella-assisted HRPCI at a single tertiary center. Mean age was 75±11 years, 64% were men, and mean left ventricular ejection fraction was 40%±20% (Table 1). The decision to use MCS was based on high-risk features, such as severe systolic left ventricular dysfunction, unprotected left main disease, or a last patent conduit, similar to the criteria used in the PROTECT II trial

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WHAT IS KNOWN

- Prior studies have demonstrated that intra-aortic balloon pump counter pulsation improves coronary hemodynamics in nonstenotic coronary arteries.
- Yet in the presence of significant stenosis has not been shown to significantly improve coronary hemodynamics.

WHAT THE STUDY ADDS

- Mechanical circulatory support, in this case using Impella, demonstrated improved coronary hemodynamics in the setting of a significant coronary stenosis.

(Prospective, Randomized Clinical Trial of Hemodynamic Support With Impella 2.5 Versus Intra-Aortic Balloon Pump in Patients Undergoing High-Risk Percutaneous Coronary Intervention).[7] Four patients had normal left ventricular ejection fraction; however, use of MCS device was deemed necessary given high-risk anatomy (eg, severe distal left main calcification) and need for atherectomy. All patients had obstructive lesions with angiographically estimated diameter stenosis between 70% and 99% and distal coronary artery pressure to aortic pressure ratios (Pd/Pa) between 0.44 and 0.88 (Figure 1; Table 2). The study was approved by the institutional review board, and all subjects gave informed written consent.

Procedure

All patients received aspirin and a loading dose of a second antiplatelet agent (clopidogrel or ticagrelor) before PCI. Heparin was used in all cases for anticoagulation. Three arterial access points were obtained, bilateral femoral arteries and a radial artery. Subsequently, the Impella device was placed in the standard fashion after obtaining a femoral angiogram to confirm adequate vessel caliber. Procedural sheath was placed in the contralateral femoral artery, and a pigtail catheter was placed in the left ventricle via the radial artery and kept in during the procedure to continuously record left ventricle pressures. The Impella CP was used in 10 patients, and the Impella 5.0 was used in 1 patient, and device choice was based on the primary operators discretion. Impella 5.0 was used in 1 patient given perceived need by the clinician for a more robust hemodynamic support.

Hemodynamic Measurements

After placement of the Impella, confirmation of adequate position was obtained using fluoroscopic guidance and with confirmation of an adequate positioning signal on the device console, after which we proceeded with hemodynamic assessment. A 0.014-inch pressure wire (Philips Volcano, Andover, MA) was balanced outside of the body and then placed distal to the coronary lesion after normalizing the pressure wire with the guiding catheter pressure. In cases where severe calcification or tortuosity was present, we first passed a workhorse 0.014-inch wire distally and then exchanged that for the pressure wire after performing the standard pressure normalization.

Subsequently, we recorded the distal coronary pressure (via the pressure wire), left ventricular end-diastolic pressure (LVEDP; via the pigtail catheter), and systemic blood pressure (via the procedural guiding catheter), and all measurements were displayed simultaneously on the hemodynamic screen (Figure 2). Measurements were performed at 2 Impella flow settings, maximum support level (P8 flow, >3 L/M) and minimum support level (P2 flow < 1 L/M). When switching between flow levels, measurements were performed after at least 3 minutes to allow for adjustments in systemic and coronary hemodynamics. After obtaining the aforementioned measurements, we calculated the effective coronary perfusion pressure (CPP) as mean systemic blood pressure subtracted by LVEDP. We calculated the diastolic coronary pressure gradient as diastolic blood pressure subtracted by LVEDP. After completion of hemodynamic measurements, PCI was performed. All procedures were completed by the authors to minimize technical error and maximize adherence to the protocol. All hemodynamic variables were reviewed and independently measured, and discrepancies were either averaged between the 2 readers or reviewed by an additional independent reader.

Statistical Analysis

Numeric data were summarized as mean±SD. The differences between the maximum and minimum support levels were evaluated using paired *t* testing for normally distributed data and Wilcoxon signed-rank testing for non-normally distributed data (LVEDP was the singular variable measured in this manner). Categorical data were

Table 1. Baseline Characteristics

Age, y	Sex	Indication	No. of Vessels	Lesion Studied	Angiographic Lesion Severity	LVEF	Added Complexity	MCS Used
90	Female	USA	3	RCA	99	25	Rotational atherectomy	CP
90	Male	SA	3	LCx	85	50	Rotational atherectomy	CP
87	Female	NSTEMI	3	LCx	99	69	Rotational atherectomy	CP
73	Male	USA	2	LAD	80	63	Rotational atherectomy	CP
74	Male	USA	2	LAD	99	74		CP
				Diag	70			
62	Male	SA	3	LCx	70	19	CTO PCI	5.0
59	Male	SA	2	RCA	70	30		CP
73	Male	SA	1	RCA	90	35	Rotational atherectomy	CP
82	Female	NSTEMI	3	LAD	90	30	Rotational atherectomy	CP
64	Male	SA	3	LAD	95	15		CP
74	Female	NSTEMI	3	LAD	90	34	Rotational atherectomy	CP

CP indicates Impella CP; CTO PCI, chronic total occlusion percutaneous intervention; Diag, first diagonal coronary artery; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; LVEF, left ventricle ejection fraction; MCS, mechanical circulatory support; NSTEMI, non–ST-segment–elevation myocardial infarction; RCA, right coronary artery; SA, stable angina; and USA, unstable angina.

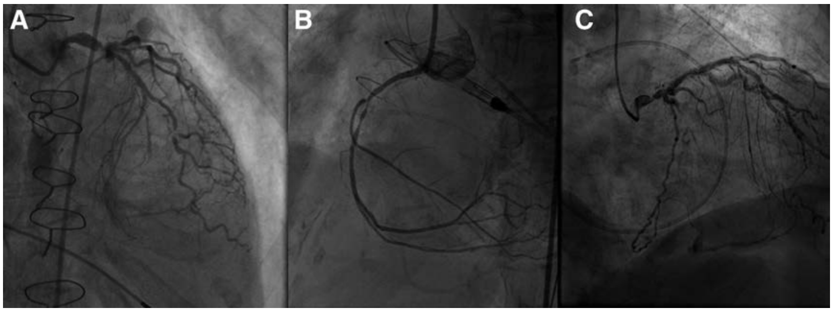

Figure 1. Coronary angiograms of select cases used to determine the effects of mechanical circulatory support on coronary perfusin in patients with critical coronary stenosis.

presented as frequencies or percentages. Two-sided $P<0.05$ was considered statistically significant.

Results

Patient Characteristics

We included 11 patients in this single arm study with 12 total lesions studied, and baseline characteristics are shown in Table 1. Mean patient age was 75±11 years, 64% were men, and mean left ventricular ejection fraction was 40%±20%. All procedures were performed electively for unstable angina, non–ST-segment–elevation myocardial infarction, or class III/IV angina refractory to medical therapy. Exclusion criteria included cardiogenic shock, severe aortic stenosis, and ST-segment–elevation myocardial infarction. No patient had complications during coronary pressure measurement.

Systemic Hemodynamics

Maximum hemodynamic support with the Impella device compared with minimum support resulted in statistically higher systolic aortic blood pressures (111.3±19 versus 119.3±17 mm Hg; $P=0.001$; 7% increase), diastolic aortic blood pressures (59.9±11 versus 72.3±11 mm Hg; $P<0.001$; 21% increase), and mean aortic blood pressures (77.6±13 mm versus 88.2±12 mm Hg; $P<0.001$; 14% increase; Figure 3; Table 2). LVEDP was lower during maximum Impella support (27 [25% quartile=21; 75% quartile=33] versus 22 [25% quartile=18; 75% quartile=24] mm Hg; $P=0.002$; 19% decrease).

Coronary Hemodynamics

Mean distal coronary pressure beyond a critical lesion increased significantly during maximum support with the Impella device (51.8±20.2 versus 60.8±18.1 mm Hg; $P<0.001$; 17% increase). Both effective CPP (49.8±15.7 versus 67.2±13.6 mm Hg; $P<0.001$; 35% increase) and diastolic CPP (32.9±13.4 versus 52.0±11.6 mm Hg; $P<0.001$; 58% increase) increased significantly during maximum hemodynamic support (Figure 4; Table 2). There was no significant change between Pd/Pa at minimum and maximum levels of support (0.65±0.17 versus 0.68±0.16; $P=0.514$).

Discussion

The main finding of our study is that Impella device can improve CPPs in patients with critical coronary artery stenosis. This was demonstrated using an intracoronary pressure wire to directly measure the coronary pressure distal to a critical stenosis present in the proximal to midsegment of a major epicardial coronary artery. Subsequent measurements of systemic and coronary hemodynamics were performed with the Impella at minimum and maximum support levels. Impella-assisted HRPCI resulted in a significant increase in systemic hemodynamics (mean, systolic, and diastolic pressures) similar to previous reports.[8,9] However, we demonstrated for the first time that an Impella device has a favorable effect on the mean coronary pressure distal to a critical coronary lesion, as well as a significant improvement in diastolic and effective CPPs.

In prior studies mainly studying cardiopulmonary resuscitation,[10,11] CPP was calculated as the difference between mean aortic pressure and right atrial pressure. However, the coronary circulation is unique because flow is subjected to extravascular compression forces during systole and diastole resulting from both myocardial contraction and elevated intraventricular pressure. It has been suggested that when assessing CPP simply using the right atrial pressure may not be adequate because it does not account for those extravascular and intraventricular forces,[12] and the downstream pressure is related not only to the right atrial pressure but also to the LVEDP.[13] Hence in our study, we placed a catheter in the left ventricle to measure LVEDP directly and subsequently calculate the effective CPP based on the LVEDP measurement as opposed to right atrial pressure despite increased procedural complexity.

The improvement in the effective CPP observed in this study was because of a combination of both increased mean and diastolic blood pressures, as well as a concomitant reduction in LVEDP. In comparison, to the best of our knowledge, there is no human clinical data to support that IABP significantly reduces LVEDP, and animal models have shown no significant effect of IABP on LVEDP.[14,15] In addition, it has been shown in multiple studies that in comparison to IABP, Impella provides superior systemic hemodynamic support, including higher mean aortic pressures.[7,9] In combination, the aforementioned differences in hemodynamic effects between the 2 devices help explain why a favorable effect on CPP was seen in our study with Impella but not shown in prior studies with IABP. The results of our study may also explain why the subgroup of multivessel CAD in the PROTECT II trial[16] had more intraprocedural hemodynamic stability with the Impella device compared with IABP irrespective of the number of vessels treated. Patients treated with IABP with multivessel disease had a

Table 2. Invasive and Coronary Hemodynamics

Patient	Power Level Setting	sLV	dLV	LVEDP	sAo	dAo	mAo	mPd	eCPP	dCPP	Pd/Pa
1	2	93	9	16	93	58	70	33	54	42	0.47
	8	89	12	14	90	61	71	37	57	47	0.52
	Δ	−4	−3	−2	−3	+3	+1	+4	+3	+5	+0.05
2	2	n/a	n/a	n/a	127	57	83	67	n/a	n/a	0.81
	8	n/a	n/a	n/a	130	60	83	79	n/a	n/a	0.95
	Δ	n/a	n/a	n/a	+3	+3	0	+12	n/a	n/a	+0.14
3	2	145	28	47	134	72	97	66	50	25	0.68
	8	161	22	25	149	82	108	70	83	57	0.64
	Δ	+16	−6	−22	+15	+10	+11	+4	+33	+32	−0.04
4	2	121	13	28	104	52	69	35	41	24	0.51
	8	139	13	24	119	62	80	40	56	38	0.5
	Δ	+18	0	−4	+15	+10	+11	+5	+15	+14	−0.01
5	2	125	11	25	131	62	82	39	57	37	0.47
	8	118	11	15	122	85	100	58	85	70	0.58
	Δ	−7	0	−10	−9	+23	+18	+19	+28	+33	+0.11
5	2	131	16	23	131	65	88	77	65	42	0.88
	8	130	16	22	130	70	90	78	68	48	0.87
	Δ	−1	0	−1	−1	+5	+2	+1	+3	+6	−0.01
6	1	n/a	n/a	26	93	61	72	47	46	35	0.65
	9	n/a	n/a	20	111	83	88	54	68	63	0.61
	Δ	n/a	n/a	−6	+18	+22	+16	+7	+22	+28	+0.04
7	2	134	12	19	134	81	104	92	85	62	0.88
	8	139	13	19	139	89	110	96	91	70	0.87
	Δ	+5	+1	0	+5	+8	+6	+4	+6	+8	−0.01
8	2	135	23	27	102	55	65	48	38	28	0.73
	8	135	14	24	122	62	79	63	55	38	0.8
	Δ	0	−9	−3	+20	+7	+15	+15	+17	+10	+0.07
9	2	97	19	33	95	44	59	26	26	11	0.44
	8	104	20	22	103	63	76	48	54	41	0.63
	Δ	+7	+1	−11	+8	+19	+17	+22	+28	+30	+0.19
10	2	80	28	35	80	69	74	57	39	34	0.77
	8	95	28	33	95	83	87	66	54	50	0.76
	Δ	+15	0	−2	+15	+14	+13	+9	+15	+16	−0.01
11	2	116	12	21	112	43	68	35	47	22	0.51
	8	126	12	18	122	68	86	41	68	50	0.48
	Δ	+10	−1	−3	+10	+25	+18	+6	+21	+28	−0.03
Mean	1–2	117.7	17.2	27.3	111.3	59.9	77.6	51.8	49.8	32.9	0.65
SD	1–2	21.1	7.0	8.6	19.3	11	13.5	20.2	15.7	13.4	0.17
Mean	8–9	123.6	16.1	21.5	119.3	72.3	88.2	60.8	67.2	52	0.68
SD	8–9	22.3	5.5	5.2	17.3	11.1	12.2	18.1	13.6	11.6	0.16
	Δ	+5.9	−1.1	−5.8	+8	+12.4	+10.6	+9	+17.4	+19.1	+0.03

Δ indicates change; dAO, diastolic aortic pressure; dCPP, diastolic coronary perfusion pressure; dLV, diastolic left ventricular pressure; eCPP, effective coronary perfusion pressure; LVEDP, left ventricular end-diastolic pressure; mAo, mean aortic pressure; mPd, mean distal pressure; n/a, not applicable; Pd/Pa, mean distal pressure/mean aortic pressure; sAO, systolic aortic pressure; and sLV, systolic left ventricular pressure.

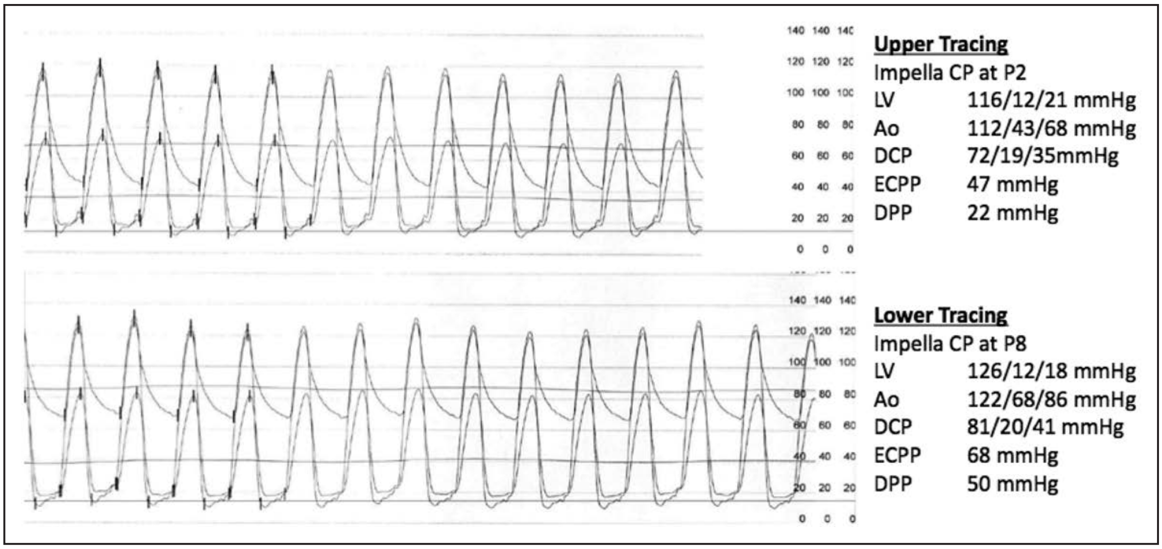

Figure 2. A case example of distal coronary pressure (as measured by the pressure wire), left ventricular (LV) end-diastolic pressure (as measured by the pigtail catheter), and systemic blood pressure (as measured by the procedural guiding catheter) simultaneously displayed at low and high level of support. Ao indicates aortic pressure systolic/diastolic/mean; DCP, distal coronary pressure, systolic/diastolic/mean; DPP, diastolic perfusion pressure that is the diastolic aortic pressure subtracted by the left ventricular end-diastolic pressure; and ECPP, effective coronary perfusion pressure that is the mean aortic pressure substracted by the left ventricular end-diastolic pressure.

greater drop in mean aortic pressure with each subsequent vessel treated. One may hypothesize this may be secondary to intraprocedural ischemia and was observed less in patients treated with Impella.[16]

The mean Pd/Pa in our study was 0.65 (range, 0.44–0.88), suggesting that lesions treated were indeed hemodynamically significant. Prior studies have shown that a resting Pd/Pa ratio ≤0.86 had a 100% correlation with a fractional flow reserve ≤0.80.[17] As one may expect, the Pd/Pa ratio did not significantly differ between minimum and maximum support levels with Impella. This is because of both distal coronary pressure (Pd) and aortic pressures simultaneously increasing with the use of Impella, leaving the overall ratio unchanged. Furthermore, the Pd/Pa ratio is significantly influenced by blood pressure and heart rate,[18] both of which will change with the use of MCS. Therefore, we believe that even though Pd/Pa ratio can be useful in assessing coronary stenosis, changes in this ratio will not necessarily correlate with changes in coronary perfusion gradients.

Therapeutic options currently available to clinicians to treat hemodynamic instability during HRPCI include pharmacotherapy and MCS (IABP, Impella, Tandem Heart, and extracorporeal membrane oxygenator). Unfortunately, not all of these modalities can actually improve systemic and coronary perfusion simultaneously. Inotropic and vasopressor therapy can improve systemic blood pressure and cardiac output; however, paradoxically can impair myocardial oxygen supply and increase demand secondary to increased contractility, tachycardia, and coronary vasoconstriction.[13,19] Extracorporeal membrane oxygenator can substantially improve cardiac output and systemic perfusion, however, can result in elevation of filling pressure, afterload, and increased myocardial oxygen demand.[5,20,21] Prior studies have demonstrated worsening left ventricular wall motion in regions subtended by a stenotic coronary artery during extracorporeal membrane oxygenator support.[22] IABP can increase the cardiac output and diastolic blood pressure,[5,20] as well as improve coronary blood flow in nonstenotic arteries.[5,23] However, several prior studies have examined the effects of IABP on coronary hemodynamics in the presence of a significant stenosis using different modalities, including thermodilution catheter methods,[1] coronary pressure wire,[2] epicardial Doppler probe,[4] and coronary Doppler wire,[3,24] and all have failed to show a consistent improvement in coronary blood flow or coronary pressure distal to a stenosis with IABP support. As a result, it has been suggested that the effect of IABPs on ischemia is largely related to reduction in ventricular afterload and wall stress as opposed to augmenting coronary blood flow or coronary pressure distal to a stenosis.[3,4]

As a result of recent advances in PCI technology and experience, accompanied by a noticeable increase in patients' age and comorbidities, physicians are currently treating more complex multivessel CAD.[13,25] There is a rising need for MCS during HRPCI to ensure patient safety and to optimize procedural outcomes. It is, therefore, desirable to have an MCS device that improves coronary hemodynamics despite the presence of coronary stenosis while performing PCI. Improving coronary perfusion in this setting can potentially improve patient's tolerability of ischemia and improve outcomes.

Limitations

Coronary blood flow is primarily determined by the CPP and coronary vascular resistance, the latter being controlled by a myriad of endothelial, myogenic, and neuro-hormonal factors.[12,26] Therefore, CPP is an essential, but not the sole factor, in determining coronary blood flow. In this study, we did not measure coronary flow beyond the stenosis directly, rather we measured coronary pressures. Based on the basic law of fluid dynamics, an increase in the driving pressure

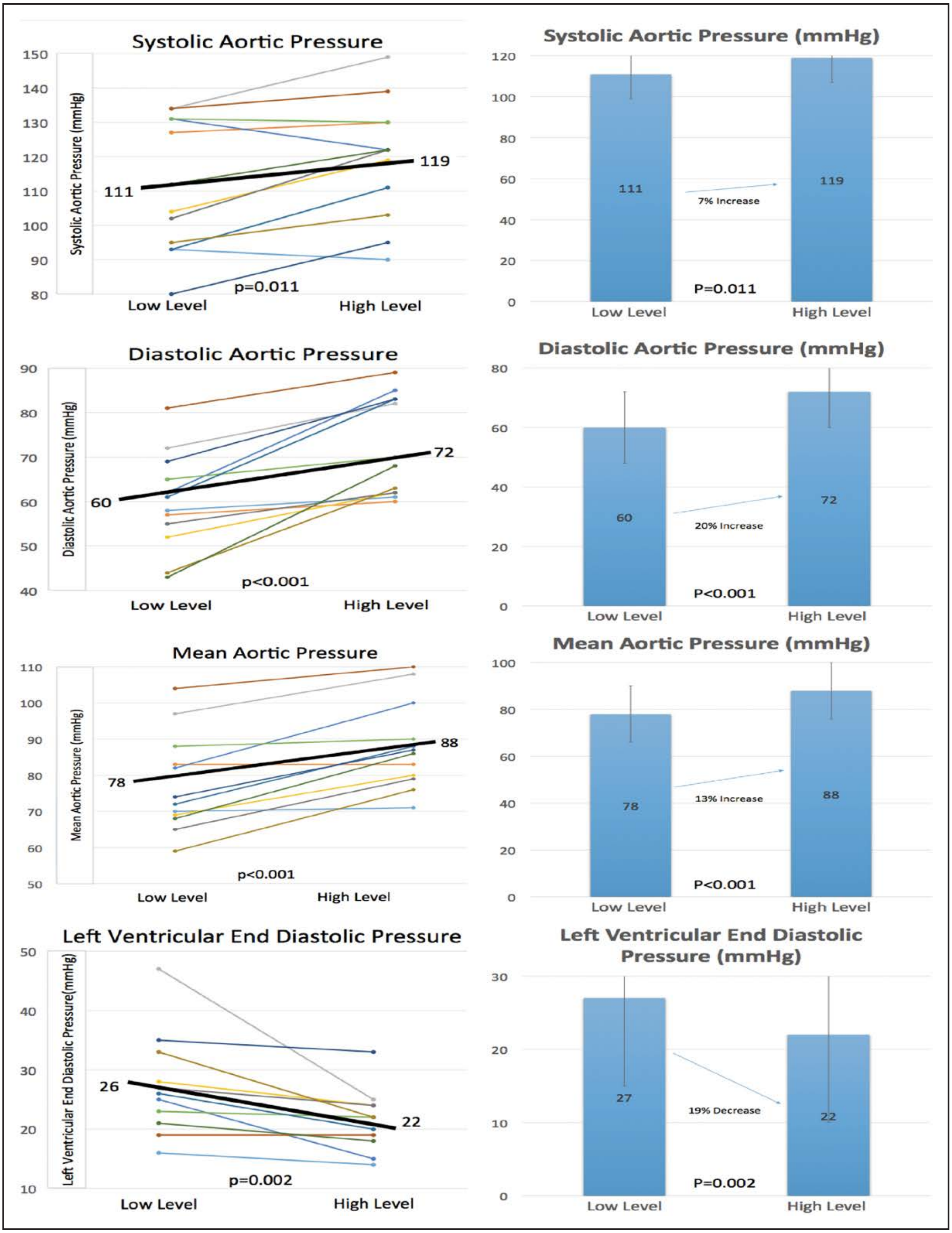

Figure 3. Systemic hemodynamics measured at low and high level of support.

gradient across the vascular bed if autoregulation is abolished is expected to result in increased blood flow.[13] In addition, passing the coronary pressure wire across the coronary lesion may have resulted in increased pressure gradient because of the wire itself; this effect, however, is likely to be relatively constant between the 2 study conditions. Because of the complexity of the procedure and time needed to perform initial hemodynamics, we did not remeasure coronary hemodynamics post-PCI. Last, given our sample size, we cannot directly associate the improvement in CPP with changes in clinical outcomes. Future studies with larger patient cohorts evaluating both coronary flow and pressures may be beneficial to expand the field of coronary hemodynamics and myocardial protection in supported HRPCI.

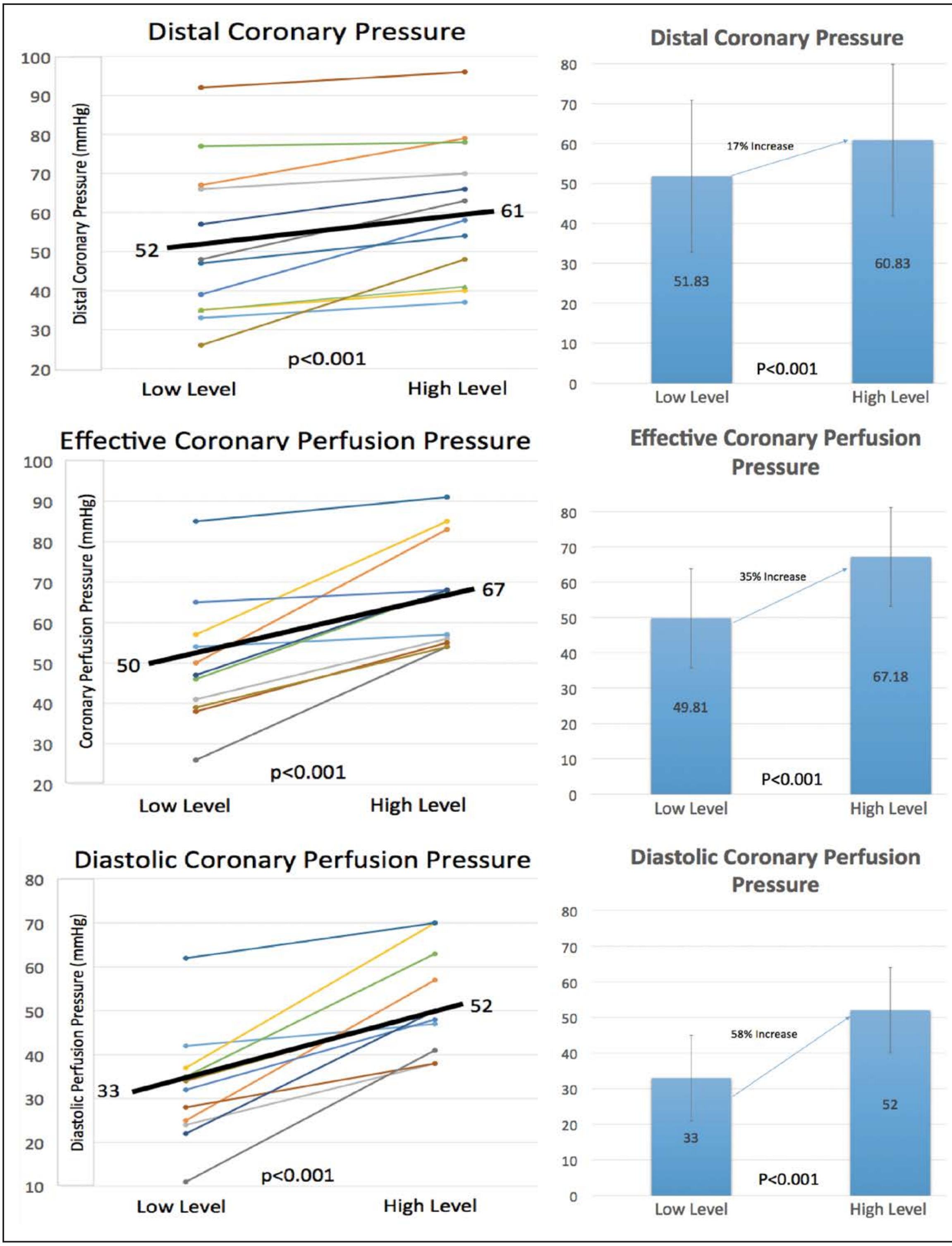

Figure 4. Coronary hemodynamic measured at low and high level of support.

Conclusions

To the best of our knowledge, this is the first study to demonstrate an increase in the invasively measured coronary pressure along with an improvement in the effective CPP with the use of MCS. This favorable effect on coronary hemodynamics may contribute to intraprocedural myocardial protection and minimize ischemia with its potential deleterious effects on clinical stability. These findings may help guide clinicians in selecting the appropriate hemodynamic support device when treating patients with critical multivessel CAD.

Disclosures

None.

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