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BRIEF COMMUNICATION

Improved clinical outcomes associated with the Impella 5.5 compared to the Impella 5.0 in contemporary cardiogenic shock and heart failure patients

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A redesigned surgically implanted heart pump incorporates several design changes from the prior device generation, but no published comparative data demonstrate if these changes translate to improved outcomes. We retrospectively compared clinical characteristics and outcomes, drawn from an FDA-mandated QA database, for contemporary patients treated with the Impella 5.5 or Impella 5.0 for acute myocardial infarction complicated by cardiogenic shock (AMICS), cardiomyopathy, or postcardiotomy cardiogenic shock (PCCS). A total of 1238 patients at 290 US sites were included for analysis. Patients receiving the Impella 5.5 had significantly higher survival through explant (i.e., successfully weaned or bridged to heart replacement therapy) than those receiving the Impella 5.0 in all 3 settings: AMICS (70.5% vs 56.8%; $p = 0.005$), cardiomyopathy (88.1% vs 76.9%; $p = 0.001$), and PCCS (76.1% vs 55.7%; $p = 0.003$). Duration of support was significantly longer for Impella 5.5 patients with AMICS (9.2 vs 6.1 days; $p = 0.008$) and cardiomyopathy (10.7 vs 8.1 days; $p < 0.001$).
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Since the Impella 5.5 (Abiomed, Danvers, MA) was commercially released in the United States (US) in October 2019, it is increasingly being used as a bridging device to heart transplantation or durable left ventricular assist device, or for native heart recovery. This surgically implanted heart pump differs from the prior generation device, the Impella 5.0, in its device rigidity, shorter motor, and lack of a pigtail (Figure 1). The Impella 5.5 has also been designed to allow for longer support duration, which enables its use as a bridging device to either heart recovery or replacement. Initial reports have demonstrated good

Abbreviations: AMICS, acute myocardial infarction complicated by cardiogenic shock; ECMO, extracorporeal membrane oxygenation; PCCS, post-cardiotomy cardiogenic shock; QA, quality assurance

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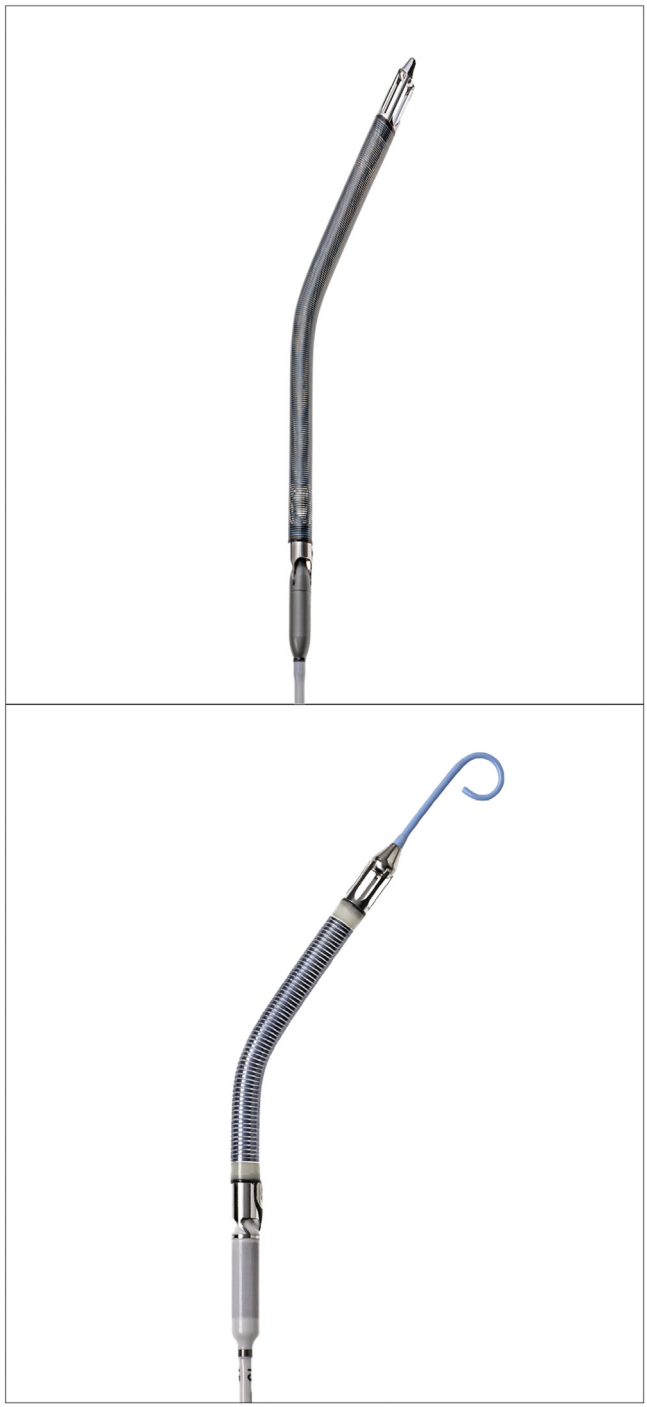

Figure 1 The Impella 5.5 device (top panel) and Impella 5.0 device (bottom panel). Notably, the Impella 5.5 device lacks the pigtail on the catheter and has a shorter motor, as well as more rigid cannula.

outcomes with the Impella 5.5 in the US and Germany,[1-3] yet no published comparative data exist to determine whether these changes lead to improved outcomes compared to the Impella 5.0.

In a retrospective analysis of the IQ registry, an FDA-mandated quality assurance database, we compared clinical characteristics and outcomes in contemporary US patients treated with the Impella 5.5 and 5.0 heart pumps in the settings of acute myocardial infarction complicated by cardiogenic shock (AMICS), postcardiotomy cardiogenic shock (PCCS), and cardiomyopathy (an IQ database category that aimed to capture non-AMI shock). Patients treated with extracorporeal membrane oxygenation (ECMO) before or during Impella use were excluded. IRB submission and informed consent were not required, as no private health information or source data were extracted.

Clinical outcomes were reported through device explant. Device survival was defined as successful weaning off support or bridging to destination therapy. Mortality was defined as expiring on support or withdrawal of care. Adverse events (AEs) through device explant were recorded by field representatives, with no source adjudication. Oversight of data quality was limited to sponsor review of correctly input indications, and periodic Quality Control of inputted outcomes and AEs. Those with aborted placement or unknown outcome were not included for assessment of clinical outcome or duration of support. Statistical comparison was performed with Fisher's exact test for categorical data and unpaired t tests for continuous data. RStudio was used for statistical comparison.

A total of 1238 patients treated at 290 US centers from October 2019 to December 2020 were included for analysis. There was no significant difference in gender distribution, baseline left ventricular ejection fraction (LVEF), or pulmonary artery catheterization use (Table 1). Impella 5.5 patients treated for AMICS were significantly younger (median, 62 vs 66 years; $p = 0.002$). Insertion site was similar in AMICS and cardiomyopathy patients; however, PCCS patients treated with the 5.5 were more likely to have the device placed via ascending aorta (40.0% vs 11.1%; $p = 0.001$), whereas 5.0 patients were more likely to have axillary access (76.2% vs 55.0%; $p = 0.031$). Rate of aborted placement was similar in AMICS and cardiomyopathy patients, but significantly lower with the 5.5 in PCCS patients (4.8% vs 13.2%; $p = 0.033$).

Impella 5.5 patients had significantly higher survival through device explant for all 3 indications: AMICS (70.5% vs 56.8%; $p = 0.005$), cardiomyopathy (88.1% vs 76.9%; $p = 0.001$), and PCCS (76.1% vs 55.7%; $p = 0.003$) (Table 2). Cardiomyopathy patients had similar rates of successful weaning off support, but a significantly higher percentage of Impella 5.5 cardiomyopathy patients were successfully bridged to heart replacement therapy (54.4% vs 41.8%; $p = 0.005$). PCCS patients had similar rates successfully bridged to heart replacement therapy, but Impella 5.5 PCCS patients had a significantly higher rate of successful weaning (70.1% vs 52.3%; $p = 0.013$). Duration of support was significantly longer in Impella 5.5 AMICS patients (median 9.2 vs 6.1 days; $p = 0.002$) and Impella 5.5 cardiomyopathy patients (median 10.7 vs 8.1 days; $p = 0.0008$).

Rates of hemolysis, cerebrovascular accident, bleeding, and vascular injury were similar in AMICS and PCCS patients, with significantly lower hemolysis rates in Impella 5.5 cardiomyopathy patients (3.0% vs 9.3%; $p = 0.003$). This may owe to the removal of the pigtail catheter and increased ease of repositioning.

In this retrospective analysis, we found significantly improved outcomes through device explant with the

Table 1 Baseline and Procedural Characteristics for AMICS, Cardiomyopathy, and PCCS Patients Treated with the Impella 5.5 or 5.0

	AMICS			Cardiomyopathy			PCCS		
	Impella 5.5 (N=169)	Impella 5.0 (N=305)	*p*-value	Impella 5.5 (N=287)	Impella 5.0 (N=245)	*p*-value	Impella 5.5 (N=126)	Impella 5.0 (N=106)	*p*-value
Age									
Mean ± SD (N)	59.5 ± 12.5 (168)	63.7 ± 10.8 (303)	<0.001	55.3 ± 13.6 (283)	57.5 ± 12.4 (244)	0.059	65.0 ± 10.6 (123)	66.4 ± 10.0 (106)	0.324
Median (range)	62 (17-82)	66 (28-88)		59 (9-82)	59 (21-91)		66 (35-99)	67.5 (34-84)	
Female gender	31/167 (18.6)	45/301 (15.0)	0.360	59/285 (20.7)	41/241 (17.0)	0.316	19/122 (15.6)	22/106 (20.8)	0.388
LVEF									
Mean ± SD (N)	18.8 ± 10.2 (135)	17.9 ± 9.0 (226)	0.403	16.3 ± 7.2 (205)	16.5 ± 6.9 (191)	0.865	26.1 ± 11.8 (89)	23.1 ± 11.3 (72)	0.092
Median (range)	18 (5-75)	15 (5-50)		15 (5-45)	15 (5-55)		25 (10-60)	20 (10-60)	
PAC use	161/169 (95.3)	287/305 (94.1)	0.677	276/287 (96.2)	234/245 (95.5)	0.828	120/126 (95.2)	99/106 (93.4)	0.578
Insertion site									
Axillary	68/76 (89.5)	131/148 (88.5)	>0.99	106/111 (95.5)	132/137 (96.4)	0.756	22/40 (55.0)	48/63 (76.2)	0.031
Femoral	4/76 (5.3)	15/148 (10.1)	0.312	4/111 (3.6)	3/137 (2.2)	0.704	1/40 (2.5)	7/63 (11.1)	0.146
Ascending aorta	2/76 (2.6)	2/148 (1.4)	0.606	1/111 (0.9)	1/137 (0.7)	>0.99	16/40 (40.0)	7/63 (11.1)	0.001
Other	2/76 (2.6)	0/148 (0.0)	0.114	0/111 (0.0)	1/137 (0.7)	>0.99	1/40 (2.5)	1/63 (1.6)	>0.99
Aborted placement	10/169 (5.9)	15/305 (4.9)	0.671	11/287 (3.8)	7/245 (2.9)	0.634	6/126 (4.8)	14/106 (13.2)	0.033

AMICS, acute myocardial infarction complicated by cardiogenic shock; LVEF, left ventricular ejection fraction; PAC, pulmonary artery catheterization; PCCS, postcardiotomy cardiogenic shock; SD, standard deviation.
Categorical data is presented as numerator/denominator (percentage); continuous data as mean ± standard deviation (denominator), and median (range).
p values were calculated with Fisher's exact test for categorical data and unpaired t tests for continuous data.

Table 2 Clinical Outcomes through Device Explant in AMICS, Cardiomyopathy, and PCCS Patients Treated with the Impella 5.5 or 5.0

	AMICS			Cardiomyopathy			PCCS		
	Impella 5.5 (N=156)	Impella 5.0 (N=278)	*p*-value	Impella 5.5 (N=270)	Impella 5.0 (N=225)	*p*-value	Impella 5.5 (N=117)	Impella 5.0 (N=88)	*p*-value
Successfully weaned or bridged to heart replacement therapy	110/156 (70.5)	158/278 (56.8)	0.005	238/270 (88.1)	173/225 (76.9)	0.001	89/117 (76.1)	49/88 (55.7)	0.003
Successfully weaned	78/156 (50.0)	118/278 (42.4)	0.133	91/270 (33.7)	79/225 (35.1)	0.776	82/117 (70.1)	46/88 (52.3)	0.013
Bridged to therapy	32/156 (20.5)	40/278 (14.4)	0.108	147/270 (54.4)	94/225 (41.8)	<0.001	7/117 (6.0)	3/88 (3.4)	0.521
Expired on support or withdrawal of care	46/156 (29.5)	120/278 (43.2)	0.005	32/270 (11.9)	52/225 (23.1)	0.001	28/117 (23.9)	39/88 (44.3)	0.003
Expired on support	21/156 (13.5)	58/278 (20.9)	0.069	10/270 (3.7)	15/225 (6.7)	0.152	13/117 (11.1)	27/88 (30.7)	<0.001
Withdrawal of care	25/156 (16.0)	62/278 (22.3)	0.134	22/270 (8.1)	37/225 (16.4)	0.005	15/117 (12.8)	12/88 (13.6)	>0.99
Hemolysis	5/156 (3.2)	10/278 (3.6)	>0.99	8/270 (3.0)	21/225 (9.3)	0.003	2/117 (1.7)	1/88 (1.1)	>0.99
CVA	5/156 (3.2)	3/278 (1.1)	0.143	6/270 (2.2)	2/225 (0.9)	0.301	2/117 (1.7)	1/88 (1.1)	>0.99
Bleeding	1/156 (0.6)	5/278 (1.8)	0.426	3/270 (1.1)	5/225 (2.2)	0.478	3/117 (2.6)	6/88 (6.8)	0.177
Vascular injury	1/156 (0.6)	0/278 (0.0)	0.359	0/270 (0.0)	1/225 (0.4)	0.455	0/117 (0.0)	0/88 (0.0)	>0.99
Duration of support, days									
Mean ± SD (N)	13.2 ± 20.2 (156)	8.7 ± 9.5 (278)	0.008	15.1 ± 13.4 (270)	11.4 ± 10.6 (225)	<0.001	10.2 ± 23.5 (117)	6.6 ± 8.3 (88)	0.127
Median (range)	9.2 (0.04-233.3)	6.1 (0.01-87.1)		10.7 (0.03-71.1)	8.1 (0.3-64.1)		6.0 (0.0007-245.9)	4.4 (0.02-49.2)	

AMICS, acute myocardial infarction complicated by cardiogenic shock; CVA, cerebrovascular accident; PCCS, post cardiotomy cardiogenic shock.

Categorical data is presented as numerator/denominator (percentage); continuous data as mean ± standard deviation (denominator), and median (range).

p values were calculated with Fisher's exact test for categorical data and unpaired t tests for continuous data.

Patients with aborted Impella placement, unknown outcome, or outcome of "on support" (i.e., unknown outcome) were not included in denominators for clinical outcomes nor calculation of duration of support values (63 patients had aborted placement, 35 had unknown outcome, and 6 remained on support [also unknown outcome]).

Other complications observed on support include hematoma, oozing, thrombus, ischemia, renal failure, systemic organ failure, arrythmia, and other.

Impella 5.5 in real-world AMICS, PCCS, and cardiomyopathy patients. This analysis does not allow the attribution of improved bridging and weaning rates to the device redesign, or unobserved differences in the patient populations.

The Impella 5.5 patients were supported for about 4 days longer than the 5.0 patients in all 3 settings, without an increased complication rate. We would speculate that the capability to provide robust longer-term support with the Impella 5.5 has resulted in higher successful use of the 5.5 as a bridge to heart replacement therapy, notably, a 14-percentage point increase in in cardiomyopathy patients. Longer support times also provide an increased opportunity for native heart recovery, which may have impacted the significantly higher successful weaning rates in the AMICS and PCCS populations.

We aimed to compare similar populations by restricting the analysis to the same time period for both devices and removing patients with concomitant ECMO, as the comparative efficacy of these devices for LV unloading with ECMO is a separate question that should be examined in further study. Importantly, the assessment of LVEF was nearly identical in the study populations. However, the IQ registry collects limited data, and confounding factors affecting clinical outcomes likely exist. In an analysis assessing prior implant experience (any indication) in the 2 cohorts, we found a significantly higher level of prior device experience in the 5.5 centers (mean 6 vs 4.8 years' experience; $p = 0.005$). However, this comparison was limited to prior 5.0 experience, as the market release of the 5.5 constituted the start of the study window for this analysis, and comprised the initial experience with the 5.5 for these centers. Any potential, as yet unstudied, learning curve with the 5.5 may also have impacted outcomes.

We are further limited by the nature of the IQ database, which only collects outcomes through device explant, and is per field representative reporting with limited oversight. This analysis challenges the heart failure community to conduct a prospective trial evaluating this device. Within the database and analysis limitations, in contemporaneous real-world patient populations, we observed a marked improvement in clinical outcome with the Impella 5.5 device compared to the Impella 5.0 as treatment for AMICS, PCCS, and cardiomyopathy.

Authorship contributions

D.R.—Study design, data analysis and manuscript writing. All co-authors contributed to data analysis and reviewed and approved the final manuscript.

Disclosure statement

D.R. reports honoraria from Abiomed, Medtronic, and Abbott. E.G. Soltesz reports honoraria from Abiomed. S.S. reports consulting fees from Abbott and Abiomed. M.D. reports funding for clinical trial work to the institution from Abiomed, Abbott, and TransMedics; travel support from Abbott and Abiomed for HM3 and Impella 5.5 Users Meetings, respsectively. M.K. reports consulting fees from Abiomed and CareDx. D.A.D'A. reports honoraria from Abiomed and Paragonix. Auxiliary medical writing services were provided by the device manufacturer (acknowledged above).

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