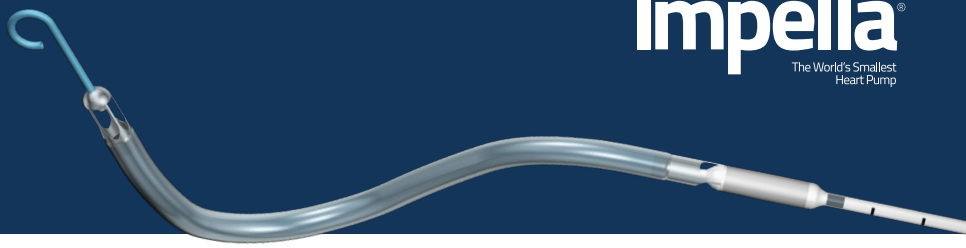
PRODUCT UPDATE

January 2019



Impella RP® Heart Pump Bulletin

Impella RP received full Pre-Market Application approval (PMA) in September 2017 for use in patients who suffer right heart failure after LVAD implantation or after open heart surgery, heart transplant, or AMI cardiogenic shock. This followed a separate HDE approval study, completed in January 2015.

The results of both studies are as follows:

RECOVER RIGHT Study Results (N=30)

- RECOVER RIGHT was an FDA-approved, prospective, multicenter, single arm study designed to evaluate the safety and probable benefit of the Impella RP in patients with right ventricular failure (RVF) refractory to medical treatment and deemed to require hemodynamic support.
- The 30 patients enrolled in the RECOVER RIGHT trial were categorized into two patient cohorts. Cohort A included patients who developed RVF within 48 hours after implantation of a left ventricular assist device (LVAD). Cohort B examined patients who developed RVF within 48 hours of post-cardiotomy shock or post-acute myocardial infarction (AMI) shock. The primary endpoint was patient survival at 30 days, hospital discharge, or bridge to the next therapy.
- The clinical trial results from RECOVER RIGHT were announced in October 2014 at the annual Transcatheter Cardiovascular Therapeutics (TCT) 2014 scientific meeting in Washington, DC. Overall, the survival rate was 73% in the entire population at 30 days. Cohort A showed a survival rate of 83.3% and Cohort B showed a 58.3% survival rate at 30 days.

Journal of Heart and Lung Transplant, December 2015(34).

Impella RP PMA Cohort (N=60)	Survival
PMA Subjects (RR + CAP + HDE PAS) – full cohort (N=60)	73% (44/60)
Cohort A (N=31)	77% (24/31)
Cohort B (N=29)	69% (20/29)

Journal of Heart and Lung Transplant, December 2018(37).

There are no other devices currently approved by FDA under a PMA as safe and effective for these patients with right ventricular failure (i.e. ECMO, TandemLife are 510(k) systems cleared for <6 hours of hemodynamic support, have not completed any FDA IDE studies, and are not approved for any indication. Centrimag is a surgical device with HDE approval on the right side and conducted an HDE study meeting the criteria of safe with probable benefit. Centrimag on the left side has a 510(k) clearance for <6 hours of hemodynamic support).

FDA Post-Market Approval Study (PAS) and Patient Monitoring:

Abiomed is committed to the quality assurance of all Impella products and as a result tracks commercial use with our Impella Quality Database (IQ) as well as conducts a cVAD Study at approximately 30 hospitals utilizing IRB and prospective data collection with FDA definitions from prior studies. As part of the PMA process, a Post Approval Study (PAS) is required to follow RP patients and their outcomes to discharge. Devices cleared by the 510(k) process are not required to conduct or report post-market surveillance to the FDA on device safety or patient outcomes.

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Abiomed has been collecting data from cVAD sites on all Impella RP cases as part of the required FDA Post-Approval Study (PAS). In the company's recent review of the data collected to date in the study (n=23 patients), the survival-to-discharge rates for both the LVAD cohort and the right heart failure due to cardiogenic shock cohort are different in the PAS centers, 73% survival in the PMA cohort (n=60 patients) to 17% survival in the PAS cohort (n=23 patients). Of these 23 patients in the PAS cohort, only 7, or 30%, would meet the criteria from the FDA study, the additional 70% qualify as a salvage attempt or last resort implantation. The table below shows the statistical differences in the patient characteristics or timing of treatment:

Characteristics	RP PMA (N=60 Patients)	RP PAS 12M Report (N=23 Patients)	P-Value
Age			
MEAN±SD(N)	58.58±15.12 (60)	65.61±13.72 (23)	0.056
Did the patient experience an in-hospital cardiac arrest prior to Impella implant	0.00% (0/60)	56.52% (13/23)	<.001
At the time of Impella implant did the patient receive CPR/ACLS	5.00% (3/60)	30.43% (7/23)	<.001
Was there evidence of hypoxicischemic brain injury prior to Impella implant	0.00% (0/60)	14.29% (3/21)	0.016
Was the patient supported with inotrope or vasopressors prior to Impella implant	98.33% (59/60)	86.96% (20/23)	0.063
If yes, Indicate total number of inotrope or vasopressors			
Mean±SD(N)	3.37±1.24 (59)	4.38±1.56 (13)	0.014
Median	3.00	4.00	
Range (Min, Max)	(1.00,6.00)	(2.00,8.00)	
Patients in shock >=48 hours	0.00% (0/34)	26.09% (6/23)	<.001
IABP used prior to Impella implant	0.00% (0/60)	30.43% (7/23)	<.001

This technical bulletin discusses Abiomed's investigation into the reason for this change, and how physicians can ensure that patients selected for Impella RP treatment are those most likely to benefit from Impella RP support, as compared to profound shock salvage utilization. The FDA studies demonstrated that the proper use and timely implantation of the Impella RP yields higher survival with the potential for recovery of the right ventricle. These protocols are captured in multiple physician and hospital publications, and identified as best practices. In addition, over the last 12 months, Abiomed has hosted more than 200 physicians at our Heart Recovery Institute and trained them on improving outcomes specific to identifying hemodynamic failure for left, right, and biventricular patients. Education regarding newer hemodynamic parameters for RV hemodynamic assessment such as PAPI are increasingly being utilized for simplifying and aiding clinicians in more rapid identification of RV dysfunction of patients in need of right side hemodynamic support. These best practices are early identification of right ventricular failure and the need for invasive hemodynamic monitoring.

The dominant change that was observed in the PAS (n=23), was prolonged time in shock (>24 hours) before placement of the Impella RP device in these patients. This review of patients in cVAD detailed frequent use of the device after periods of RV failure of more than 48 hours, up to several weeks post-LVAD implant, post-open heart surgery, or post-myocardial infarction with cardiogenic shock. Abiomed strongly recommends adherence and compliance to the inclusion/exclusion criteria used in the PMA cohort to ensure optimal outcomes.

In order to specifically address this, Abiomed has attached a new checklist that you should use to determine if Impella RP support is an appropriate treatment for your patient, or if the patient is not likely to benefit from Impella RP support. Abiomed advises all clinicians to review the PMA study inclusion and exclusion criteria and asks that physicians recognize that patients falling outside of those criteria may be too ill to benefit from the device. If you are still considering use of the device in salvage, last attempt, patients who do not meet the checklist appropriate use criteria, Abiomed suggests that the decision to use the Impella RP be preceded by a discussion with the patient's family regarding the expected outcome of a critically ill patient, with high risk of mortality. In the best interest of the patient, we would expect this same conversation to occur prior to the use of alternative devices (i.e. ECMO, TandemLife, Centrimag, etc.) that are not subject to post-approval studies or FDA reporting.

In addition, please note that Abiomed has set up a 24-Hour RP Hotline within our Clinical Support Center (CSC) to aid Impella RP users in proper patient selection and management (800-422-8666).

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Impella RP® Heart Pump Patient Selection Criteria Checklist

Treatment with the Impella RP System is appropriate for patients with a body surface area >1.5 m^2, who develop signs of acute right ventricular failure:

1. Post-implantation of an FDA approved surgical LVAD; or
2. Post-heart surgery, post-heart transplant or post-myocardial infarction

The checklists below are based on the exclusion criteria for the Impella RP pre-market clinical study. These checklists are provided to help you determine if Impella RP support is an appropriate treatment for your patient, and may predict whether your patient is likely to benefit from Impella RP support.

Pre-Implant Assessment: Post LVAD Insertion	Pre-Implant Assessment: Post Heart Surgery, Transplant or Acute Myocardial Infarction
☐ Time (hours) to insertion post LVAD implant _____ hrs	☐ Time (hours) to insertion post completion of cardiac surgery or heart transplant, or presentation with acute myocardial infarction _____ hrs
☐ INTERMACS I patients (crash and burn with worsening lactate levels or acidosis)	☐ Patients in profound cardiogenic shock, i.e., SBP < 75mmHg and CI < 1.3 l/min/m^2 despite two or more high dose inotropes, PH<7.1 not corrected by 100 Ml NaHCO3, DIC, anoxic brain Injury or CGS >24 hrs
☐ Evidence of end-organ failure (bilirubin >5 or creatinine >4 within 24 hrs of implant)	☐ AMI with acute mechanical complication (VSD, ventricular rupture or pap rupture)
☐ Evidence of acute neurologic injury	☐ Unsuccessful revascularization of RCA
☐ Active infection defined as two of the following (WBC >12,5000 or positive blood culture or fever)	☐ Active infection defined as two of the following (WBC >12,5000 or positive blood culture or fever)
☐ RA, RV or PA thrombus	☐ RA, RV or PA thrombus
☐ Prosthetic valves In the right heart	☐ Prosthetic valves in the right heart
☐ Structural tricuspid disease	☐ Structural tricuspid disease
☐ ASD or PFO (unrepaired)	☐ ASD or PFO (unrepaired)
☐ Pulmonary valve stenosis or insufficiency	☐ Pulmonary valve stenosis or insufficiency
☐ Severe pulmonary hypertension (PAS>60mmHg)	☐ Severe pulmonary hypertension (PAS>60mmHg)
☐ Documented DVT and/or presence of IVC filter	☐ Documented DVT and/or presence of IVC filter
☐ Anatomic abnormalities precluding insertion	☐ Anatomic abnormalities precluding insertion
☐ PA conduit	☐ PA conduit
☐ Patients on right-sided support or ECMO	☐ Patients on right-sided support or ECMO
☐ Current Pulmonary Embolism	☐ Current Pulmonary Embolism
☐ Aortic Dissection or Marfan Syndrome	☐ Aortic Dissection or Marfan Syndrome
☐ Allergy or intolerance to contrast	☐ Allergy or intolerance to contrast
☐ HIT or sickle cell disease	☐ HIT or sickle cell disease
☐ Existing congenital heart disease that would preclude placement	☐ Existing congenital heart disease that would preclude placement
BEST CANDIDATE: Time to insertion < 48 hours AND no boxes checked	**BEST CANDIDATE: Time to insertion < 48 hours AND no boxes checked**

Right Ventricular Failure (RVF) is defined as:

- A cardiac index <2.2 l/min/m^2 despite continuous infusion of high dose inotropes
- ***AND ANY OF THE FOLLOWING***:
  - CVP > 15 mmHg or
  - CVP/PCWP or LAP > 0.63 or
  - Moderate to severe global RV dysfunction on echocardiography defined as one of the following criteria:
    - Global RV hypokinesis
    - TAPSE score of ≤ 14 mm
    - Right ventricular diameter at basis > 42 mm
    - Right ventricular short axis (or mid-cavity) diameter > 35 mm

High dose inotropes is defined as:

- Dobutamine of ≥ 10 µg/kg/min or equivalent for more than 15 minutes (120 minutes for milrinone) and/or administration of more than one inotrope/ vasopressor medication

If you have questions about the appropriate selection of a patient for Impella RP support, or patient management, contact Abiomed's 24 Hour Clinical Support Center at (800-422-8666)

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Right-Side Support
The Impella RP® System is indicated for providing temporary right ventricular support for up to 14 days in patients with a body surface area ≥1.5 m^2, who develop acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery.

Important Risk Information for Impella RP System

CONTRAINDICATIONS
The Impella RP System is contraindicated for patients with the following conditions: Disorders of the pulmonary artery wall that would preclude placement or correct positioning of the Impella RP device. Mechanical valves, severe valvular stenosis or valvular regurgitation of the tricuspid or pulmonary valve. Mural thrombus of the right atrium or vena cava. Anatomic conditions precluding insertion of the pump. Presence of a vena cava filter or caval interruption device, unless there is clear access from the femoral vein to the right atrium that is large enough to accommodate a 22 Fr catheter.

POTENTIAL ADVERSE EVENTS
The potential adverse effects (eg, complications) associated with the use of the Impella RP System: Arrhythmia, Atrial fibrillation, Bleeding, Cardiac tamponade, Cardiogenic shock, Death, Device malfunction, Hemolysis, Hepatic failure, Insertion site infection, Perforation, Phlegmasia cerulea dolens (a severe form of deep venous thrombosis), Pulmonary valve insufficiency, Respiratory dysfunction, Sepsis, Thrombocytopenia, Thrombotic vascular (non-central nervous system) complication, Tricuspid valve injury, Vascular injury, Venous thrombosis, Ventricular fibrillation and/or tachycardia.

In addition to the risks above, there are other **WARNINGS** and **PRECAUTIONS** associated with Impella RP. Learn more visit:
www.abiomed.com/important-safety-infomation

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