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Adverse Events and Modes of Failure Related to Impella RP: Insights from the Manufacturer and User Facility Device Experience (MAUDE) Database

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ABSTRACT

Background/purpose: Right ventricular (RV) mechanical circulatory support remains an important adjunctive therapy for RV failure refractory to medical therapy. Impella RP (Abiomed, Danvers, MA) is approved for providing temporary RV support for patients with acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery. Robust data on the most commonly reported complications and failure modes for the Impella RP are lacking. We analyzed the post-marketing surveillance data from the Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database to assess these endpoints.

Materials/methods: The MAUDE database was queried for the time period January 1, 2009, through December 31, 2018, for Impella devices by Searching for the following event types: "injury", "malfunction", "death", and "other". The search yielded 436 device reports. Impella RP medical device reports were screened, and 35 reports were included for the final analysis.

Results: In cases of reported complications, Impella RP was placed most commonly for right ventricular failure (RVF) developing in postcardiotomy patients (20%). The most commonly reported complications included bleeding (42.9%) and vascular complications (22.8%). The modes of failure included damage or fracture of the device elements (34.2%); thrombus, or clot in the system (17.1%); and device detachment (8.6%).

Conclusions: Findings from the MAUDE database highlight the failure modes of the Impella RP device that should be addressed in order to improve the device performance and obtain improved clinical outcomes when utilized for RVF.

1. Introduction

Right ventricular failure (RVF) can develop in patients with advanced heart failure, pulmonary embolism, pulmonary hypertension, acute myocardial infarction, or after major cardiac surgery (left ventricular assist device implantation [LVAD] or heart transplantation) [1]. RVF significantly increases morbidity and mortality, escalating associated health-care costs. Medical therapy includes optimization of fluid status, pulmonary vasodilators, inotropes, and vasopressors. Cases refractory to these interventions may require short-term mechanical support with surgical or percutaneous right ventricular assist devices (RVADs) [1]. Surgical RVADs include CentriMag pump or right atrium to pulmonary artery cannulation with either a thoracotomy or an open sternotomy. Percutaneous options include extracorporeal centrifugal flow devices such as Tandem-Heart, venoarterial extracorporeal membrane oxygenation (VA-ECMO), or axial flow devices, e.g., Impella RP [1]. The Impella RP® (Abiomed, Danvers, MA) is a percutaneous RVAD approved by the Food and Drug Administration (FDA) on September 20, 2017, for providing temporary support in patients with acute RVF [2–4]. In a recent FDA communication, higher mortality rates were noted for patients treated with the Impella RP in the interim post-approval study analysis than the rate previously observed in the premarket clinical studies [5]. Although hemodynamic benefits have been demonstrated in the pivotal studies related to the Impella RP [2–4], limited safety data are available since its market introduction. We, therefore, analyzed the United States FDA Manufacturer and User

Abbreviations: FDA, Food and Drug Administration; MAUDE, Manufacturer and User Facility Device Experience; RV, right ventricle; RVF, right ventricular failure.

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Facility Device Experience (MAUDE) database to report these endpoints.

2. Methods

2.1. Study device

The Impella RP is a 22 Fr microaxial pump mounted onto an 11 Fr catheter capable of generating flow up to 4.6 l/min at 33,000 rpm [6]. The device is delivered percutaneously through a 23 Fr peel-away sheath over a 0.025-inch guide-wire. The Impella RP system consists of the following (from distal to proximal – Fig. 1): a) 6 Fr pigtail that stabilizes the catheter in the correct position in the pulmonary artery; b) outlet area; c) 22 Fr cannula; d) inlet area; e) 11 Fr catheter shaft; f) repositioning sheath (consisting of an 11 Fr sheath with a hemostatic valve to allow repositioning of the catheter); and g) introducer or check valve [6]. The Impella RP catheter is advanced under fluoroscopic guidance in an antegrade fashion through the femoral vein and inferior vena cava across the tricuspid and pulmonic valves. The inflow cage of the device is positioned in the inferior vena cava, while the outflow cage is positioned in the pulmonary artery just proximal to the pulmonary artery bifurcation. A chest X-ray of the Impella RP System Catheter is provided in Fig. 2. The Impella RP is approved to provide short-term support to the failing right ventricle (RV) for up to 14 days in patients with a body surface area ≥ 1.5 m^2 [6].

2.2. MAUDE database

The MAUDE database is a publicly available electronic repository that stores medical device reports submitted to the FDA [7]. Reporting can be mandatory (for manufacturers, importers, and device user facilities) or voluntary (for health-care professionals, patients, and consumers). Established in the early 1990s, the database is updated monthly and the search within the database is limited to adverse events reported within the last 10 years. Each report outlines information regarding the device, event date, whether the device was returned to the manufacturer, the event's description by the provider and the manufacturer's narrative. The FDA and manufacturers routinely monitor these reports to identify and rectify device-related safety events in a timely fashion. If a device is deemed defective, the FDA can issue safety alerts or recalls. Although this surveillance system cannot be used to establish definitive event rates, it can provide important insight into the mechanisms of complications associated with novel cardiovascular devices [8–10].

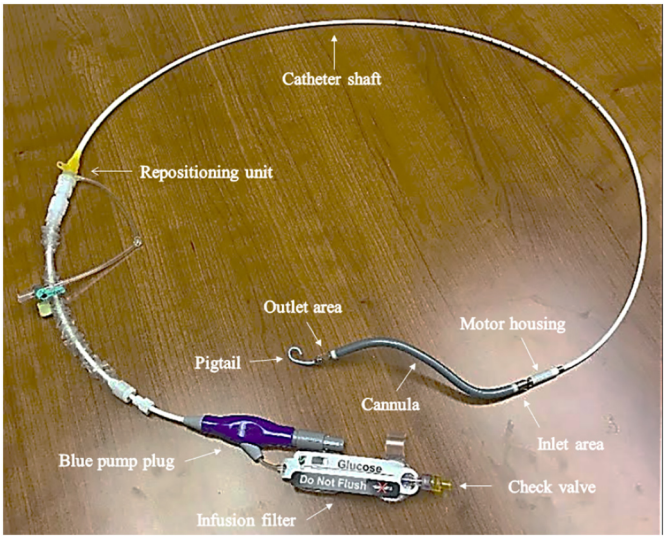

Fig. 1. Impella RP® System Catheter.

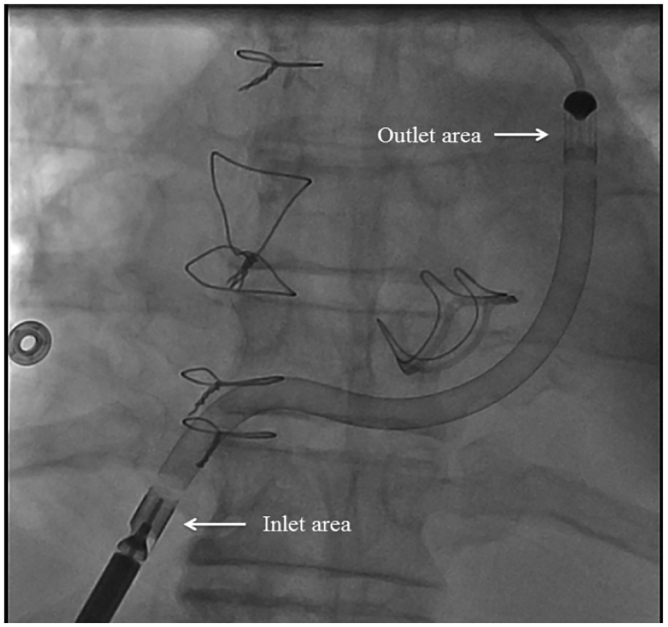

Fig. 2. Chest X-ray of the Impella RP System Catheter showing the inlet area positioned in the inferior vena cava and the outflow area positioned in the pulmonary artery just proximal to the pulmonary artery bifurcation.

2.3. Data collection

The MAUDE database was last accessed on December 31, 2018. Two independent reviewers (NK, ES) queried the database for the time period January 1, 2009, through December 31, 2018, for Impella devices yielding 436 reports. Impella RP cases were screened, resulting in 35 reports (classified in the database as injury = 20, malfunction = 10, and death = 5) that were included for final analysis. Commonly reported modes of failure and device-related adverse events were analyzed over the study period. Percentages represent the proportion of total submitted MAUDE reports. The study flow is summarized in Fig. 3.

3. Results

From our analysis, of the indications reported, the Impella RP was placed most commonly for RVF developing in postcardiotomy patients (20%). Other important indications included RVF developing as sequelae of myocardial infarction or its associated complications, post-LVAD placement, and orthotopic heart transplantation (Fig. 4). The most commonly reported complication was bleeding, occurring in 42.9% of cases, of which 80% of the patients required transfusion of blood products. Significant vascular complications were reported in 8 patients, and 5 of these required surgical repairs. Of the 35 Impella RP devices with reported complications, 16 were returned to the manufacturer for analysis. The most commonly reported failure mode of Impella RP was the structural damage of the different components of the device (34.2%). Other modes of failure included thrombus in the device, device detachment, and malfunction. Operator error was identified in 1 case because of improper technique, and the physician underwent retraining. A complete list of reported complications and failure modes is provided in Tables 1 and 2, respectively.

4. Discussion

There are very limited published data on the clinical feasibility and safety profile of the Impella RP. Initial experience with the Impella RP on 3 patients demonstrated improved hemodynamics [2]. The RECOVER RIGHT trial evaluated the safety and efficacy of Impella RP in

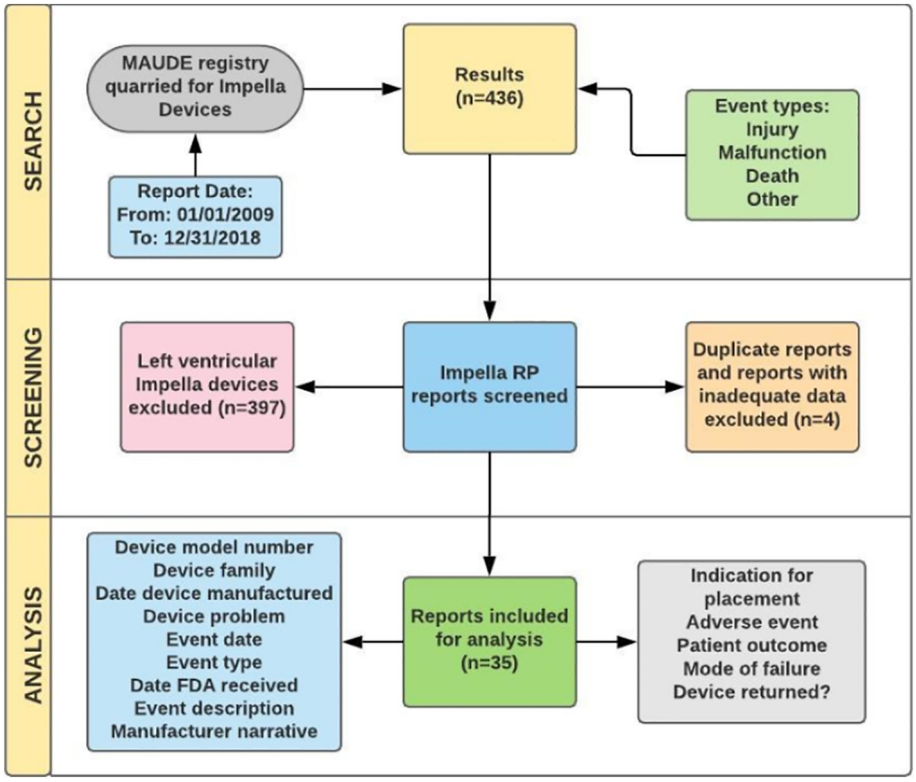

Fig. 3. Different indications for Impella RP placement among reports submitted to the MAUDE database. Results reported as N (%). Percentages represent proportion of total number of MAUDE reports. RV: right ventricular, LVAD: left ventricular assist device, OHT: orthotopic heart transplant, MI: myocardial infarction, VSD: ventricular septal defect, PE: pulmonary embolism, PHTN: pulmonary hypertension, CGS: cardiogenic shock.

30 patients, which comprised 2 cohorts: Cohort A (n = 18) included patients who developed RVF after LVAD placement, and Cohort B (n = 12) included patients with RVF after myocardial infarction and cardiotomy [3]. The primary endpoint of survival to 30 days was achieved in 73.3% of the patients. A pooled analysis of the RECOVER RIGHT trial, Continuous Access Protocol and Post-Approval Study provided a real-world experience of Impella RP in 60 patients. Results showed that Impella RP was associated with expeditious hemodynamic benefit and favorable survival [4]. Reported complications rates in this study included major bleeding (48.3%), postoperative bleeding (43.3%), hemolysis (21.7%), and death (26.7%). The major limitation of this analysis, as well as the RECOVER RIGHT trial, was the lack of a control group, without which we cannot predict the 30-day mortality rate of patients treated without Impella RP use (i.e., medical therapy alone). In comparison to a 30-day survival rate of 73.3% in the premarket clinical studies of Impella RP, interim results from the post-approval study demonstrated a 30-day survival rate of only 17.4% [6]. The root cause for this increased mortality remains unknown and may include: patient selection, lack of adjustment

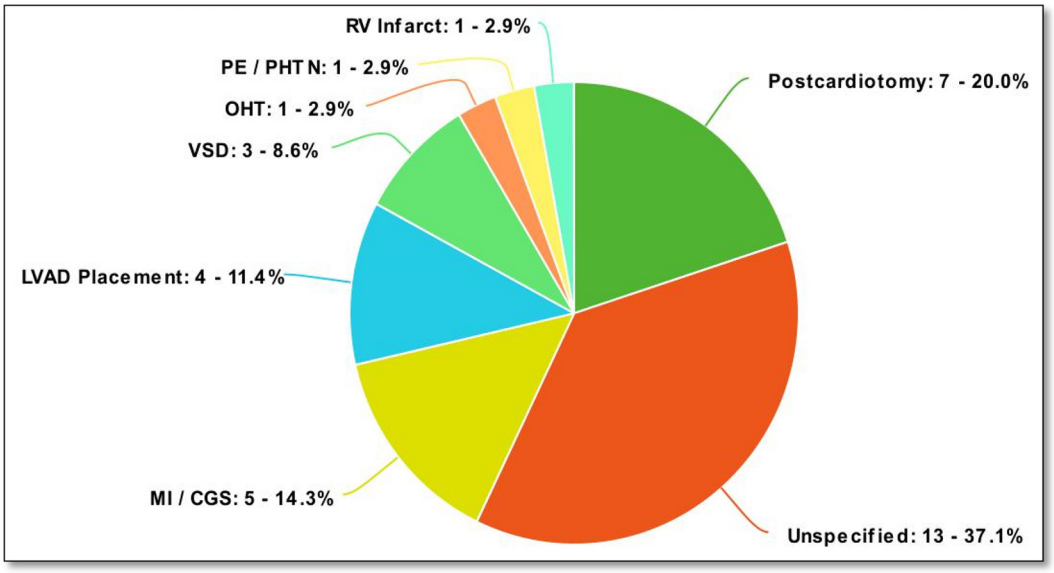

Fig. 4. Study flow chart of the data extraction from the FDA MAUDE database. FDA: Food and Drug Administration, MAUDE: Manufacturer and User Facility Device Experience.

Table 1
Summary of complications among reports submitted to the MAUDE database. Results reported as N (%). Percentages represent proportion of total number of MAUDE reports.

Patient related complications	(n = 35)
Bleeding/hematoma [n (%)]	15 (42.9)
Required transfusion	12 (34)
Postoperative bleeding	3 (8.6)
Vascular complications [n (%)]	8 (22.8)
Femoral vein dissection	1 (2.86)
Inferior vena cava tear	1 (2.86)
Iliac vein perforation	2 (5.7)
Pulmonary artery perforation	1 (2.86)
Hemolysis [n (%)]	3 (8.6)
Retroperitoneal bleeding [n (%)]	1 (2.86)
Thrombus/clot [n (%)]	4 (11.4)
Cardiac chamber perforation [n (%)]	2 (5.7)
Pericardial effusion [n (%)]	2 (5.7)
Death[a] [n (%)]	11 (31.4)
Care withdrawn	7 (20)

[a] Although 5 events were classified as death in the database, the actual reported deaths were 11 as noted in our analysis.

Table 2
Commonly reported proportions of failure modes for Impella. Results reported as N (%). Percentages represent proportion of total number of MAUDE reports.

Modes of device failure	(n = 35)
Fracture/kink/damage of different components [n (%)]	12 (34.2)
Introducer sheath	5 (14.2)
Valve	3 (8.6)
Outflow cage	1 (2.86)
Catheter	1 (2.86)
Other	2 (5.7)
Thrombus/clot/biomaterial in device [n (%)]	6 (17.1)
Device detachment [n (%)]	3 (8.6)
Retrieved surgically	1 (2.86)
Retrieved with snare device	1 (2.86)
Unable to retrieve	1 (2.86)
Device malfunction [n (%)]	2 (5.7)
Low purge pressure and decreased flow	1 (2.86)

of confounding variables or the different pre-implant characteristics of the patients in the premarket and the post-approval studies.

Given the paucity of data related to safety for this novel device, we highlight the most commonly encountered complications. Device-associated adverse events can be broadly classified into three categories based on the causative etiology: device malfunction, patient factors, and operator technique/skill. Certainly, an overlap exists between these categories. Areas for improvement for physicians lie within the latter two categories. Recognizing patient characteristics that increase the likelihood of device-related complications is a vital part of the evaluation process that should occur for each patient prior to device implantation. Operator skill/technique also plays an important role in device-related procedures. Identification of when either may have contributed to an adverse event is important to mitigate future events. Specifically, Abiomed reports that in cases involving adverse events identified as being potentially related to operator error, the physician underwent retraining on proper technique. Abiomed offers comprehensive operator training programs involving hands-on models, didactic sessions, and interactive sessions [11].

5. Limitations

Our analysis has some noteworthy limitations. Without on-site evaluation, it is difficult to establish a cause-and-effect relationship between device failure and adverse event. A minority of the devices were returned to the manufacturers for evaluation following the procedure, inhibiting a complete analysis of failure mode. Incidence rates for each complication could not be determined due to lack of denominator. Some general limitations of the MAUDE database include a) it is a passive surveillance registry that has incomplete and unverified data; b) given that the reporting is partially voluntary, an unknown number of complications remain unreported; and c) adverse events caused by clinician error may be underreported or inappropriately attributed to device failure.

6. Conclusions

The management of patients requiring RV hemodynamic support is evolving rapidly. With the development of multiple RVADs, ongoing surveillance of safety profiles, patient outcomes, and failure modes for these devices is imperative. MAUDE dataset serves as an important platform for both manufacturers and physicians to optimize device performance and clinical outcomes. Our analysis identifies complications associated with Impella RP devices. Judicious use, appropriate patient selection, and operator experience can all help mitigate these potential complications.

Conflicts of interest

Ron Waksman – Advisory Board: Abbott Vascular, Amgen, Boston Scientific, Medtronic, Philips Volcano, Pi-Cardia LTD, Cardioset; Consultant: Abbott Vascular, Amgen, Biosensors, Biotronik, Boston Scientific, Medtronic, Philips Volcano, Pi-Cardia LTD, Cardioset; Grant Support: Abbott Vascular, AstraZeneca, Biosensors, Biotronik, Boston Scientific, Chiesi; Speakers Bureau: AstraZeneca, Chiesi; Investor: MedAlliance.

Toby Rogers – Consultant: Medtronic; Proctor: Edwards Lifesciences.

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