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► **To cite this version:**

Clément Delmas, Mathieu Pernot, Alexandre Le Guyader, Romain Joret, Stéphane Roze, et al.. Budget Impact Analysis of Impella CP® Utilization in the Management of Cardiogenic Shock in France: A Health Economic Analysis. *Advances in Therapy*, 2022, 10.1007/s12325-022-02040-5 . hal-03542918

HAL Id: hal-03542918

<https://hal.sorbonne-universite.fr/hal-03542918>

Submitted on 25 Jan 2022

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Budget Impact Analysis of Impella CP® Utilization in the Management of Cardiogenic Shock in France: A Health Economic Analysis

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Received: September 3, 2021 / Accepted: January 5, 2022
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ABSTRACT

Introduction: Early detection and treatment of cardiogenic shock (CS) is crucial to avoid irreparable multiorgan damage and mortality. Impella CP® is a novel temporary mechanical circulatory support (MCS) device associated with greater hemodynamic support and significantly fewer device-related complications compared with other MCS devices, e.g., intra-aortic balloon pumps (IABP) and venoarterial extracorporeal membrane oxygenation (VA-ECMO). The

present study evaluated the budget impact of introducing Impella CP versus IABP and VA-ECMO in patients with CS following an acute myocardial infarction (MI) in France.

Methods: A budget impact model was developed to compare the cost of introducing Impella CP with continuing IABP and VA-ECMO treatment from a Mandatory Health Insurance (MHI) perspective in France over a 5-year time horizon, with 700 patients with refractory CS assumed to be eligible for treatment per year. Costs associated with Impella CP and device-related complications for all interventions were captured and clinical input data were based on published sources. Scenario analyses were performed around key parameters.

Results: Introducing Impella CP was associated with cumulative cost savings of EUR 2.7 million over 5 years, versus continuing current clinical practice with IABP and VA-ECMO. Cost savings were achieved in every year of the analysis and driven by the lower incidence of device-related complications with Impella CP, with estimated 5-year cost savings of EUR 22.4 million due to avoidance of complications. Total cost savings of more than EUR 250,000 were projected in the first year of the analysis, which increased as the market share of Impella CP was increased. Scenario analyses indicated that the findings of the analysis were robust.

Conclusion: Treatment with Impella CP in adult patients aged less than 75 years in a state of refractory CS following an MI was projected to lead to substantial cost savings from an MHI

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perspective in France, compared with continuing current clinical practice.

Keywords: Budget impact; Cardiogenic shock; France; Impella CP®; Left-ventricular assist devices

Key Summary Points

Why carry out this study?

Early detection and treatment of cardiogenic shock (CS), a state of inadequate blood flow to vital tissues caused by cardiac dysfunction, is crucial in preventing irreparable organ damage and patient mortality, particularly as up to 20% of patients are non-responsive to pharmacologic therapies.

Impella CP® is a novel temporary mechanical circulatory support (MCS) device associated with greater hemodynamic support and significantly fewer device-related complications compared with other MCS devices such as intra-aortic balloon pumps (IABP) and venoarterial extracorporeal membrane oxygenation (VA-ECMO).

The aim of the present study was to evaluate the budget impact of introducing Impella CP versus continuing standard of care with ECMO and IABP in France.

What was learned from the study?

Projections indicated that the introduction of Impella CP for the treatment of adult patients aged less than 75 years in a state of refractory CS following an MI would lead to substantial cost savings from the perspective of the national health insurer in France over 5 years, compared with continuing current clinical practice with IABP and VA-ECMO.

Cost savings were achieved in every year of the analysis through a reduced incidence of device-related complications and fewer days spent in hospital for patients with CS.

INTRODUCTION

Cardiogenic shock (CS) is a state of inadequate blood flow to vital tissues due to cardiac dysfunction, with hypotension (systolic blood pressure [SBP] \leq 90 mmHg) in spite of adequate filling pressures representing a defining characteristic [1–3]. CS is a medical emergency and early detection and treatment is crucial in preventing irreparable organ damage and patient mortality. Acute myocardial infarction (MI) with left ventricular dysfunction represents the most common underlying cause of CS, accounting for up to 50% of cases [3–5].

In France, approximately 3% of acute MIs resulted in CS in 2015, while between 2005 and 2015, in-hospital mortality remained consistently high for both primary CS (42% and 38%, respectively) and secondary CS (57% and 59%, respectively), indicating that there is still a paucity of effective treatments [6]. Indeed, CS represents the most common factor relating to in-hospital mortality for patients with MI, particularly for patients with refractory CS where mortality rates of up to 70% at 1 month have been observed [4, 7]. First-line pharmacologic treatments for CS typically include vasopressors and inotropes, but up to 20% of patients remain resistant to these therapies and often require more invasive interventions [8, 9].

Devices that provide mechanical circulatory support (MCS) represent vital interventions for managing patients with refractory CS. Temporary MCS devices are crucial for stabilizing patients with CS over the short term following an acute MI, providing time to either allow the patient to recover or for more permanent measures, such as placement of long-term MCS devices or heart transplantation, to be implemented. The most widely used temporary MCS approaches over the past few decades include the intra-aortic balloon pump (IABP) and venoarterial extracorporeal membrane oxygenation (VA-ECMO), but the ongoing, high levels of mortality in patients with CS indicate a need for more effective interventions [10]. For example, intervention with IABP has been shown to not significantly reduce 30-day mortality in patients with CS following acute MI

[11, 12]. Indeed, IABP has been withdrawn from the European treatment guidelines following the results of the IABP-SHOCK II trial [1, 11].

Impella CP[®] is a temporary MCS device that received the CE mark for marketing in Europe in 2012, and was developed to provide left ventricular support and sustain systemic perfusion for up to 5 days in patients with CS occurring immediately (less than 48 h) following acute MI or other adverse cardiovascular events or surgeries [13]. Impella CP is a microaxial left ventricular assist device (LVAD) that is positioned in the heart via a percutaneous approach, pumping blood from the dysfunctional left ventricle to the aorta [13]. In lieu of normal cardiac function, this perfuses vital tissues and stabilizes hemodynamics, while also unloading the left ventricle and reducing myocardial workload and oxygen demand, providing an opportunity for recovery of the native heart [13–15]. Impella CP has been associated with greater hemodynamic support compared with IABP in several studies, and significantly fewer device-related complications (17% versus 40%, $p < 0.01$) compared with VA-ECMO in a recent retrospective analysis [16–20]. Moreover, a key advantage of Impella CP is that it can be used in secondary treatment centers that do not contain a cardiac surgery department, as it is designed as an interventional cardiology procedure.

When considering interventions for reimbursement, payers must consider both clinical and economic aspects of novel therapies. Ease of use and improved clinical outcomes relating to device-related complications must therefore be balanced with costs of introducing the device. Indeed, costs of new devices often represent a barrier to uptake in many countries, particularly as healthcare systems come under increasing budgetary pressures worldwide. This is especially pertinent in France, where healthcare expenditure represented one of the highest proportions of gross domestic product in Europe (approximately 12%) in 2013 [21]. Universal coverage is provided in France via statutory health insurance (SHI), which covers 75% of healthcare expenditure and is funded by taxation as well as employee and employer contributions [21]. Nonetheless, supplementary

insurance is often considered by patients looking to reduce copayments or cover areas of treatment that SHI may not reimburse [21]. The present study therefore aimed to evaluate the budget impact of introducing Impella CP, versus continuing standard of care with ECMO and IABP in France, for the treatment of adult patients aged less than 75 years in a state of CS following an MI, refractory to pharmacologic therapy and not exhibiting refractory respiratory failure requiring extracorporeal assistance and/or severe multiple organ failure.

METHODS

Modeling Approach

A budget impact model was developed in Microsoft Excel (Redmond, WA), to evaluate Impella CP versus IABP and VA-ECMO treatment from a Mandatory Health Insurance (MHI) perspective in France. All modeled scenarios included both IABP and VA-ECMO as comparator treatments, as per clinical practice in France (data on file). The model comprised two clinical pathways, termed the care pathway before Impella CP and the care pathway after Impella CP.

The first pathway was developed in collaboration with six leading clinical experts (one cardiologist-intensivist, four cardiac surgeons, one pharmacist) and one health economist working within the French healthcare system, and modeled patients from CS to the treatment decision for one of the available interventions (Impella CP, IABP, or VA-ECMO; Fig. 1). As this module was upstream of the studied interventions, all transition states and probabilities, as well as cost outcomes, were identical regardless of the treatment arm. The main objective of this module was to accurately model clinical practice, to estimate the average cost per patient prior to the treatment decision.

The second care pathway estimated the costs and outcomes associated with Impella CP, IABP, or VA-ECMO treatment (Fig. 2). This component captured the probability of myocardial recovery, as well as the likelihoods of heart transplantation, insertion of a long-term LVAD,

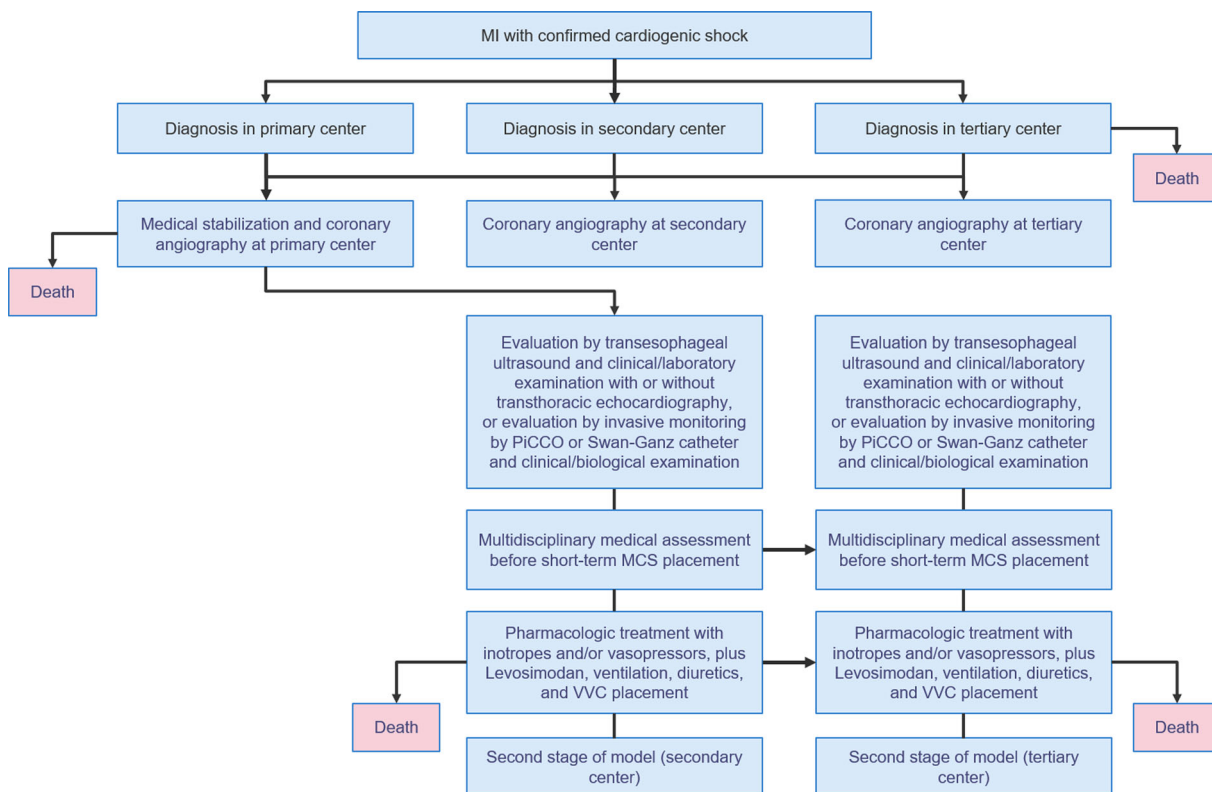


Fig. 1 Treatment pathway prior to Impella CP, IABP, and VA-ECMO. *MCS* mechanical circulatory support, *PiCCO* pulse contour cardiac output, *VVC* ventricular vascular coupling

or palliative care in patients not experiencing myocardial recovery. Mortality was captured throughout the pathway. Event probabilities for all treatment arms were based on clinical expert opinion, the published literature, and data from the Bordeaux University Hospital (Table 1) [11, 12, 20, 22–24]. The modeled care pathway was designed in line with guidance from the six previously described clinical experts working within the French healthcare system to accurately represent current clinical practice in France. Patients entered this module in two treatment center type states: secondary and tertiary. Secondary treatment centers were modeled to contain an interventional cardiology department but no cardiac surgery department, comprising one cardiac catheterization room, one trained interventional cardiologist, one intensive care and cardiac resuscitation unit, one general intensive care unit and/or coronary care unit, trained nurses, and a 24/7 assistance service provided by Abiomed.

Tertiary treatment centers were modeled to contain both interventional cardiology and cardiac surgery departments (encompassing all treatment modalities such as heart transplantation and long-term MCS placement). The differentiation between the two treatment center types aimed to capture the advantage of Impella CP as an interventional cardiology procedure. Patients were subsequently treated with one of the interventions, according to two scenarios that reflected current practice (without Impella CP) and potential future practice (with Impella CP). The estimated annual costs for these two scenarios were calculated by multiplying the number of eligible incident patients by the total annual cost associated with each treatment pathway. Outcomes were evaluated over a 5-year time horizon, and no discounting was applied, in line with national recommendations and budget impact analysis guidelines published by the International

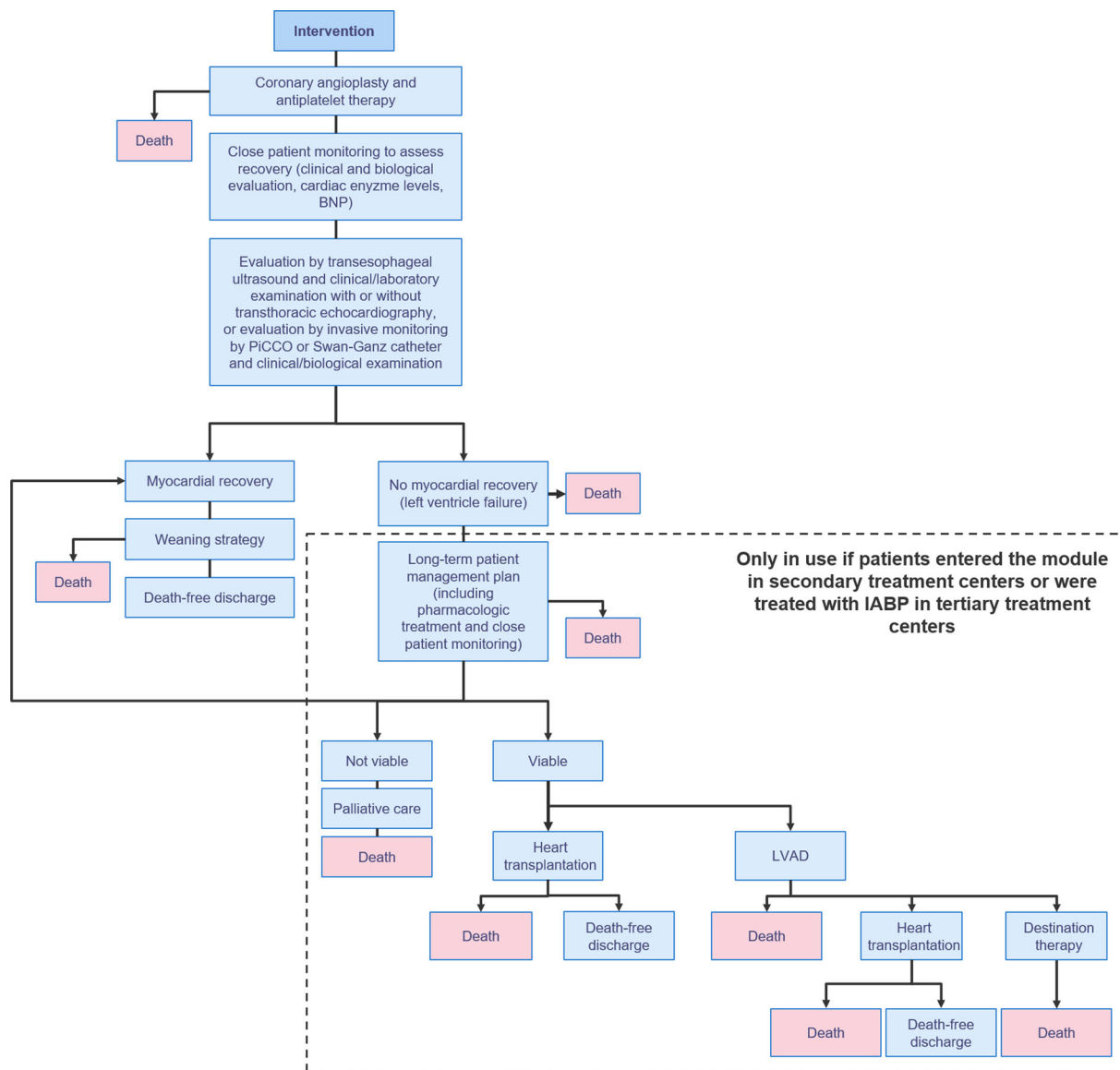


Fig. 2 Treatment pathway after decision to use Impella CP, IABP, or VA-ECMO. *BNP* brain natriuretic peptide, *LVAD* left ventricular assist device, *IABP* intra-aortic balloon pump

Society for Pharmacoeconomics and Outcomes Research (ISPOR) [25, 26].

In the scenario evaluating potential future practice, the projected market share for Impella CP was assumed to increase over the 5-year time horizon in both the secondary and tertiary centers (Table 2). In secondary centers, market share was projected to gradually increase from 20% in year 1 to 70% in year 5, while in tertiary centers, market share was projected to increase from 20% in year 1 to 40% in year 3, after which

it remained at 40% for years 4 and 5 (Table 2). Market share projections were based on internal Abiomed data.

The target population for Impella CP in France was based on data from the medicine, surgery, and obstetrics department of the Medical Information System Program (PMSI-MCO), with the definition for CS based on a published study [27, 28]. A total of 6432 patients diagnosed with CS following an MI were identified, of which 6421 were aged 18 years or more. In

Table 1 Clinical input data

Outcome	Impella CP	IABP	VA-ECMO	Source
Median (IQR) LoS in ICU, days	6 (3–14)	7 (4–13)	16 (9–30)	[11, 12, 20]
Median (IQR) time device used, days	3 (2–6)	1.6 (no IQR applied)	6 (3–8)	[11, 20, 24]
Vascular access site infection, %	1.1	31.9	15.8	[12, 20]
Amputations, %	0.0	0.0	4.7	Abiomed data on file, Cheng et al. [23]
Acute renal injury, %	15.0	0.0	55.6	Abiomed data on file, Cheng et al. [23]
Median time dialysis required, days	0	2	0	Calculated from 7 out of 24 patients requiring dialysis, median 7 days per patient (rounded up from 1.7 days) [24]
Requiring blood products, %	62.8	33.0	97.4	[11, 20]
Requiring long-term left VAD, %	1.1	4.0	13.2	[11, 20]
Use of additional IABP, %	4.4	0.0	55.3	[20]
Stroke, %	4.4	3.1	10.5	[12, 20]

ICU intensive care unit, IABP intra-aortic balloon pump, IQR interquartile range, LoS length of stay, VAD ventricular assist device, VA-ECMO venoarterial extracorporeal membrane oxygenation

line with a 2018 position statement published by the Emergency and Acute Cardiac Care working group of the French Society of Cardiology (SFC), patients were excluded in a step-wise manner on the basis of the following criteria: aged more than 75 years, aged less than 18 years, at least one absolute contraindication to use of Impella CP (severe aortic insufficiency, an aortic mechanical valve, or left ventricle thrombus), no previous angioplasty, and at least one relative contraindication to use of Impella CP (stroke, cardiac arrest, or neurological conditions such as paralysis or dementia) [9]. This yielded a target population of less than 706 patients. A total of 700 patients with refractory CS were therefore assumed to be eligible for one of the treatment options during each year of the

analysis, yielding a cumulative total of 3500 patients.

Cost Data

Costs were accounted from an MHI perspective in France and expressed in euros (EUR). The analysis captured the costs of each intervention, cardiac surgery, circulatory support withdrawal strategy, and heart transplantation, as well as non-diagnosis-related group (DRG) costs for device-related complications, including amputation of lower limbs, dialysis, and stroke. Costs of daily supplements, such as stays in intensive care units (with and without resuscitation), and long-term LVAD implantation were also captured (Table 3). Costs were derived from data

Table 2 Projected market share estimates in the base case analysis

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Number of patients	700	700	700	700	700
Market share, scenario 1: Without Impella CP in secondary center, %					
Impella CP	0	0	0	0	0
IABP	95	95	95	95	95
VA-ECMO	5	5	5	5	5
Market share, scenario 1: Without Impella CP in tertiary center, %					
Impella CP	0	0	0	0	0
IABP	20	20	20	20	20
VA-ECMO	80	80	80	80	80
Market share, scenario 2: With Impella CP in secondary center, %					
Impella CP	20	30	50	60	70
IABP	75	65	45	35	25
VA-ECMO	5	5	5	5	5
Market share, scenario 2: With Impella CP in tertiary center, %					
Impella CP	20	30	40	40	40
IABP	10	10	10	10	10
VA-ECMO	70	60	50	50	50

IABP intra-aortic balloon pump, *VA-ECMO* venoarterial extracorporeal membrane oxygenation

from the National Health Insurance (NHI) and the Agency for Hospital Information (ATIH) in France, as well as published sources [29–31]. Hospital costs were expressed in 2019 values and add-on list prices in 2020 values, while cost data relating to amputations were sourced from published literature and inflated to 2019 values [29, 31]. Costs associated with the management of stroke over the 5-year period were sourced from 2017 data [30]. Due to the perspective of the analysis, intra-DRG costs were not captured within the budget impact calculation.

Subgroup and Scenario Analyses

A number of deterministic subgroup and scenario analyses were performed to assess the robustness of the base case findings regarding

changes in input parameters. These included performing separate analyses in the subgroups of patients treated in secondary and tertiary centers; excluding the costs of device-related complications; applying higher costs for VA-ECMO treatment (increased from EUR 0 to EUR 3000 and EUR 6000 in separate analyses, based on data from the Public Assistance department of the Hospital of Paris); and increasing the market share of Impella CP [32]. Multiway deterministic scenario analyses were also performed with combinations of these settings, including combinations of subgroups with exclusion of complication costs, increased market share of Impella CP with higher costs of ECMO treatment, and increased market share of Impella CP with higher costs of ECMO treatment and exclusion of complication costs.

Table 3 Cost data applied in the base case analysis

Item	Cost, EUR	Source
Unit costs		
Impella CP	14,850.00	Abiomed, data on file
IABP	–	Intra-DRG ^a
VA-ECMO	–	Intra-DRG ^a
Supplement for ICU stay (resuscitation unit), per day	805.36	ATIH [29]
Supplement for ICU stay, per day	403.15	ATIH [29]
Supplement for dialysis session	44.84	ATIH [29]
Complication costs		
Hospitalization in ICU, per day	403.15	ATIH [29]
Device-related vascular access site infection	–	Intra-DRG ^a
Amputation of lower limbs within 5 years	11,010.00	Halimi et al. [31]
Acute renal injury	–	Intra-DRG ^a
Supplement for dialysis session	44.84	ATIH [29]
Need for labile blood products	–	Intra-DRG ^a
Need for long-term LVAD	83,187.00	Ameli.fr [30]
Use of additional IABP	–	Intra-DRG ^a
Stroke within 5 years	23,520.00	Ameli.fr [30]

ATIH Agency for Hospital Information, DRG Diagnosis Related Group, EUR euros, IABP intra-aortic balloon pump, NHI National Health Insurance, LVAD left ventricular assist device, VA-ECMO venoarterial extracorporeal membrane oxygenation

^aAs the payer perspective was that of mandatory health insurance, intra-DRG costs were not accounted in the budget impact calculation

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

RESULTS

Base Case Analysis

Projections indicated that, over a 5-year time horizon, introducing Impella CP for the treatment of patients with refractory CS would yield

cost savings of EUR 2.7 million versus continuing current clinical practice with IABP and VA-ECMO alone. The total costs of introducing Impella CP were estimated to be approximately EUR 92.6 million, while continuing current clinical practice (without Impella CP) was estimated to cost a total of EUR 95.4 million (Table 4). Cost savings were achieved during every year of the analysis, with annual cost savings of EUR 258,413 in the first year (with a 20% market share for Impella CP in both secondary and tertiary centers) gradually increasing to EUR 850,668 in the fifth year (with a 70% market share in secondary centers and 40% market share in tertiary centers for Impella CP).

Table 4 Budget impact associated with the introduction of Impella CP in France

Parameter	Cost, EUR					
	Year 1	Year 2	Year 3	Year 4	Year 5	Cumulative
Base case analysis						
Total costs in scenario 1, without Impella CP	19,076,488	19,076,488	19,076,488	19,076,488	19,076,488	95,382,440
Total costs in scenario 2, with Impella CP	18,818,074	18,727,908	18,500,435	18,363,128	18,225,820	92,635,366
Overall budget impact	– 258,413	– 348,579	– 576,053	– 713,360	– 850,668	– 2,747,074
Subgroup analyses, overall budget impact						
Patients treated in secondary centers	– 274,615	– 411,922	– 686,537	– 823,844	– 961,152	– 3,158,070
Patients treated in tertiary centers	16,201	63,343	110,484	110,484	110,484	410,997
Patients treated in secondary centers, excluding complication costs	1,269,240	1,903,859	3,173,099	3,807,719	4,442,338	14,596,255
Patients treated in tertiary centers, excluding complication costs	550,300	878,305	1,206,309	1,206,309	1,206,309	5,047,531
Scenario analyses, overall budget impact						
Increased market share of Impella CP applied	– 395,720	– 623,194	– 713,360	– 850,667	– 987,975	– 3,570,918
Cost of VA-ECMO increased to EUR 3000	– 528,169	– 764,201	– 1,230,906	– 1,461,580	– 1,692,253	– 5,677,109

Table 4 continued

Parameter	Cost, EUR					
	Year 1	Year 2	Year 3	Year 4	Year 5	Cumulative
Cost of VA-ECMO increased to EUR 6000	- 797,924	- 1,179,822	- 1,885,760	- 2,209,799	- 2,533,839	- 8,607,145
Increased market share of Impella CP applied and cost of VA-ECMO increased to EUR 3000	- 758,842	- 1,225,547	- 1,461,579	- 1,692,253	- 1,922,926	- 7,061,149
Increased market share of Impella CP applied and cost of VA-ECMO increased to EUR 6000	- 1,121,964	- 1,827,901	- 2,209,799	- 2,533,839	- 2,857,878	- 10,551,381
Complication costs excluded	1,819,540	2,782,164	4,379,408	5,014,028	5,648,647	19,643,786
Increased market share of Impella CP applied and complication costs excluded	2,454,159	4,051,403	5,014,028	5,648,647	6,283,267	23,451,505
Cost of VA-ECMO increased to EUR 3000 and complication costs excluded	1,549,784	2,366,542	3,724,554	4,265,808	4,807,062	16,713,750
Cost of VA-ECMO increased to EUR 6000 and complication costs excluded	1,280,029	1,950,921	3,069,701	3,517,589	3,965,476	13,783,715

Table 4 continued

Parameter	Cost, EUR					
	Year 1	Year 2	Year 3	Year 4	Year 5	Cumulative
Increased market share of Impella CP applied, cost of VA-ECMO increased to EUR 3000, and complication costs excluded	2,091,037	3,449,049	4,265,808	4,807,061	5,348,315	19,961,273
Increased market share of Impella CP applied, cost of VA-ECMO increased to EUR 6000, and complication costs excluded	1,727,916	2,846,696	3,517,589	3,965,476	4,413,364	16,471,042

EUR euros, VA-ECMO venoarterial extracorporeal membrane oxygenation

Cost savings were a result of a reduced incidence of device-related complications with Impella CP, saving an estimated total of EUR 22.4 million over 5 years and entirely offsetting the cost of the device.

Subgroup and Scenario Analyses

Subgroup analyses demonstrated that the cost savings observed in the base case analysis were primarily a result of avoided complications in secondary treatment centers (Table 4). In the subgroup of patients treated only in secondary centers and without taking complications into account, introducing Impella CP was projected to cost EUR 14.6 million more than standard care with IABP and VA-ECMO over 5 years. Conversely, including the costs of complications in this subgroup led to 5-year cost savings of EUR 3.2 million with the introduction of Impella CP. When considering only patients

treated in tertiary centers and excluding costs of device-related complications, introducing Impella CP was associated with cost increases of EUR 5.0 million versus treatment with IABP and VA-ECMO, but this was partially offset when including the costs of treating device-related complications to yield more modest cost increases of EUR 410,997 over 5 years.

Scenario analyses relating to the cost of VA-ECMO and market share indicated that the conclusions from the base case analysis were robust to changes in these parameters. Excluding the costs of complications while increasing the cost of VA-ECMO consumables to EUR 3000 and EUR 6000 (based on data from the Public Assistance department of the Hospital of Paris), with market share values set to those used in the base case, led to increased costs of EUR 16.7 million and EUR 13.8 million, respectively, when introducing Impella CP [32]. Including the costs of treating complications in

these scenarios led to cost savings of EUR 5.7 million and EUR 8.6 million, respectively. Increasing the market share of Impella CP by 10% throughout the analysis led to increased costs of EUR 23.5 million when no complication costs were included, but cost savings of EUR 3.6 million when these costs were considered. Combination of these altered market share values with the increased unit costs of ECMO led to reduced incremental costs in the analyses excluding complication costs and increased cost savings in the analyses including complication costs.

DISCUSSION

Findings from the present budget impact analysis suggest that introduction of Impella CP for the treatment of adult patients aged less than 75 years in a state of refractory CS following an MI would likely lead to substantial cost savings from the perspective of the MHI in France, compared with continuing current clinical practice with IABP and VA-ECMO. Cost savings of up to EUR 10.6 million could be achieved over 5 years, a result of the reduced incidence of device-related complications with Impella CP, and increasing the market share of Impella CP was projected to further increase cost savings. Reduced device-related complications versus VA-ECMO were partially mediated through the percutaneous approach with Impella CP, a simpler and safer method compared with the extracorporeal approach of VA-ECMO. The proportion of patients in intensive care units in Paris experiencing CS was estimated to have increased by almost twofold between 1997 and 2012, demonstrating the importance of effective therapies for both clinicians and payers [33]. Combining an increasing market share of Impella CP with increasing numbers of patients with CS is also likely to lead to increasing cost savings versus continuing current clinical practice, particularly with regards to increased clinical expertise and improved post-implantation management as the devices become more widely used. Increased use of Impella CP would also allow more patients to be adequately treated in secondary centers, thereby improving

access to early MCS delivery—a 2018 single-arm, multicenter study demonstrated the importance of an adequate care management protocol, with emphasis on early delivery of MCS and invasive hemodynamic monitoring associated with rapid door-to-support times and improved survival in patients presenting with acute MI complicated by CS, with results consistent when the protocol was applied on a national level [34–36].

The scope of the present analysis, which took a budget impact approach, meant that pertinent ease-of-use benefits with Impella CP were likely not captured [37, 38]. Ease of use with Impella CP is particularly evident when compared with the logistical challenges, complexity, and high levels of medical resource use associated with VA-ECMO [20, 39]. The distinction between secondary and tertiary treatment centers in the modeling analysis was important to capture the advantage of Impella CP as an interventional cardiology procedure. While physicians' learning curves using the novel intervention, as well as the improved support provided for VA-ECMO owing to its wider use, were not taken into account, the design of Impella CP allows implantation at a secondary treatment center without a cardiac surgery department, which offers the twofold benefit of reduced burden on and need for patients to be treated at tertiary centers, and providing a temporary treatment option for patients in secondary centers requiring transfer to tertiary centers. Indeed, results from the present analysis showed that the majority of cost savings with Impella CP were achieved in secondary centers (Table 4). Moreover, associated quality-of-life benefits patients are likely to experience, such as those associated with a reduced number of treatment-related complications, were not captured, and a potential future cost–utility analysis could further explore the health economic impact of these benefits. Such an analysis would require robust clinical evidence demonstrating the magnitude of these benefits with Impella CP, and subsequent to the present analysis, a retrospective, propensity-score-matched study in 900 patients has associated use of Impella with improved clinical outcomes, fewer complications, shorter length of hospital stay, and lower

hospital cost compared to ECMO [40]. Upcoming prospective, multicenter randomized controlled trials, such as the ULYSS study (assessing early implantation of Impella CP versus conventional treatment in acute coronary syndrome complicated by CS [PHRC-19-0094]) and the DanGer Shock study (assessing survival with left ventricular MCS with Impella CP versus conventional guideline-driven treatment in patients with acute MI complicated by CS [NCT01633502]), should also help to elucidate potential benefits [41, 42]. Future cost–utility analyses balancing clinical outcomes from these trials against the costs of treatment should provide valuable information for both health-care payers and physicians.

The results of the present analysis should also be put into context in terms of the patient population. The use of an adult population aged less than 75 years was based on expert consensus in France, taking into account the balance between the associated cost–benefit of the studied interventions and individual patient factors. Moreover, while cost savings were observed in the population of patients in a state of refractory CS following MI, use of VA-ECMO is more appropriate in patients with multiple organ or respiratory failure [9]. It should also be noted that recent retrospective studies indicated that 11–32% of patients with either refractory left ventricle dominant CS or refractory left ventricle failure required treatment escalation with VA-ECMO, thereby requiring transfer to a tertiary treatment center and increased surveillance [43–45]. Nonetheless, the underlying mechanisms of the interventions should be considered during decision-making: a key advantage of both Impella CP and IABP is the unloading of the left ventricle and corresponding reduced myocardial workload. In contrast, VA-ECMO provides circulatory support and blood oxygenation without left ventricle unloading, which can lead to increased myocardial stress, delayed ventricular recovery, and pulmonary edema in up to 15% of cases [46–49]. Moreover, unloading of the left ventricle may be associated with a decrease in myocardial oxygen consumption, lowering the risk of a potentially fatal reinfarction and creating a more conducive setting for myocardial

recovery [50, 51]. Indeed, treatment with VA-ECMO has been linked to a poorer prognosis in patients treated for CS due to left ventricle failure [52]. However, recent evidence has also associated percutaneous cannulation for peripheral VA-ECMO with fewer local infections, similar rates of ischemia and sensory-motor complications, and improved 30-day survival compared to the surgical approach, indicating that the delivery method of each MCS therapy could also influence outcomes [53].

The clinical data sources applied in the present analysis should also be subject to rigorous evaluation given their importance to the results. The majority of the transition probabilities between modeled states were based on primary data from Bordeaux University Hospital, allowing the model to closely follow French clinical practice—this represents a key strength of the present study. Incidence of device-related complications (limb ischemia, access site bleeding, or infection) for Impella CP and VA-ECMO was based on the findings of a retrospective two-center study conducted in 128 patients with CS following acute MI, while the incidence of complications associated with IABP was based on a randomized, prospective trial enrolling 600 patients and a systematic review of randomized controlled trials including patients with acute MI complicated by CS [11, 12, 20]. The clinical data informing IABP-related complications, particularly the systematic review of several randomized controlled trials, represents a further strength of the present analysis. However, the clinical input data sourced from the analysis by Karami et al. could be seen as a limitation, with the study design being retrospective and observational in nature, rather than a randomized controlled trial or systematic review of the available evidence. That acknowledged, there is a paucity of randomized controlled trial data for Impella CP, due to its recent development and the logistical challenges of conducting these trials in critically ill patients [54]. Moreover, observational data are arguably more representative of real-world clinical practice than data from a study conducted in a controlled setting, and findings

of other observational studies were in line with those reported by Karami et al. [55, 56].

The exclusion of intra-DRG costs in the present analysis, particularly for IABP and VA-ECMO, should be noted. While this was based on the chosen perspective, Karami et al. reported that the proportions of patient receiving items covered by intra-DRG costs, such as labile blood products, were significantly higher for VA-ECMO than for Impella CP. Moreover, extensive medical resource use is required for VA-ECMO [39]. The exclusion of intra-DRG costs was therefore highly conservative from the perspective of Impella CP, and highlights that cost savings beyond those projected by the present analysis would likely be achieved should Impella CP be introduced into clinical practice.

CONCLUSIONS

The present budget impact analysis projected that the introduction of Impella CP for the treatment of adult patients aged less than 75 years in a state of refractory CS following an MI would lead to substantial cost savings from the perspective of the national health insurer in France, compared with continuing current clinical practice.

ACKNOWLEDGEMENTS

Funding. This study and the Rapid Service and Open Access fees were supported by funding from Abiomed.

Medical Writing, Editorial, and Other Assistance. Medical writing support and editorial assistance was provided by Samuel Malkin and William Valentine at Ossian Health Economics and Communications, Basel, Switzerland, which was supported by funding from SGE Consulting.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this

article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by SR and RJ. All authors contributed to the writing of the manuscript and read and approved the final version.

Disclosures. Romain Joret and Stéphane Roze are current employees of consultancy companies that have received consulting fees from Abiomed. Clément Delmas, Mathieu Perrot, Alexandre Le Guyader and Guillaume Lebreton have received Honoraria from Abiomed.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

1. Zeymer U, Bueno H, Granger CB, et al. Acute Cardiovascular Care Association position statement for the diagnosis and treatment of patients with acute myocardial infarction complicated by cardiogenic shock: a document of the Acute Cardiovascular Care Association of the European Society of Cardiology. *Eur Heart J Acute Cardiovasc Care*. 2020;9(2):183–97.
2. Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: this document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS). *Catheter Cardiovasc Inter*. 2019;94:29–37.
3. Chioncel O, Parissis J, Mebazaa A, et al. Epidemiology, pathophysiology and contemporary management of cardiogenic shock—a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2020;22(8):1315–41 (Erratum in: *Eur J Heart Fail*. 2021; 23(2):345).
4. van Diepen S, Katz JN, Albert NM, et al. (American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Mission: Lifeline) Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation*. 2017;136(16):e232–68.
5. Thiele H, Ohman EM, Desch S, Eitel I, de Waha S. Management of cardiogenic shock. *Eur Heart J*. 2015;36(20):1223–30.
6. Aissaoui N, Puymirat E, Delmas C, et al. Trends in cardiogenic shock complicating acute myocardial infarction. *Eur J Heart Fail*. 2020;22(4):664–72.
7. Ollivier J, Fresselinat A, Seguy B, et al. The use of Impella 5.0 in refractory cardiogenic shock: a medico-economic report. *Pharm J Medical Devices*. 2019. <https://www.euro-pharmat.com/la-revue-du-dm>. Accessed 17 Mar 2020.
8. van Diepen S, Thiele H. An overview of international cardiogenic shock guidelines and application in clinical practice. *Curr Opin Crit Care*. 2019;25(4):365–70.
9. Bonello L, Delmas C, Schurtz G, et al. Mechanical circulatory support in intensive care units: a position paper of the “Unité de Soins Intensifs de Cardiologie” group of the French Society of Cardiology, endorsed by the “Groupe Athérome et Cardiologie Interventionnelle” of the French Society of Cardiology. *Arch Cardiovasc Dis*. 2018;111(10):601–12.
10. Stretch R, Sauer CM, Yuh DD, Bonde P. National trends in the utilization of short-term mechanical circulatory support: incidence, outcomes, and cost analysis. *J Am Coll Cardiol*. 2014;64:1407.
11. Thiele H, Zeymer U, Neumann F-J, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367(14):1287–96.
12. Unverzagt S, Buerke M, de Waha A, et al. Intra-aortic balloon pump counterpulsation [IABP] for myocardial infarction complicated by cardiogenic shock. *Cochrane Database Syst Rev*. 2015;3:CD007398.
13. Abiomed. Impella CP. 2020. <https://www.abiomed.com/impella/impella-cp>. Accessed 5 Nov 2020.
14. Vasea H, Christensen S, Chistiansen A, et al. The Impella CP device for acute mechanical circulatory support in refractory cardiac arrest. *Resuscitation*. 2017;112:70–4.
15. Tepper S, Masood MF, Garcia MB, et al. Left ventricular unloading by Impella device versus surgical vent during extracorporeal life support. *Ann Thorac Surg*. 2017;104(3):861–7.
16. Jauw KD, Remmelink M, Baan J, et al. 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.
17. Engstrom AE, Cocchieri R, Driessen AH, et al. The Impella 2.5 and 5.0 devices for ST-elevation myocardial infarction patients presenting with severe and profound cardiogenic shock: the Academic Medical Center intensive care unit experience. *Crit Care Med*. 2011;39:2072.
18. Seyfarth M, Sibbing D, Bauer I, et al. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. *J Am Coll Cardiol*. 2008;52:1584.
19. Ouweneel DM, Engstrom AE, Sjaauw KD, et al. Experience from a randomized controlled trial with Impella 2.5 versus IABP in STEMI patients with cardiogenic pre-shock. Lessons learned from the IMPRESS in STEMI trial. *Int J Cardiol*. 2016;202:894.
20. Karami M, den Uil CA, Ouweneel DM, et al. Mechanical circulatory support in cardiogenic shock from acute myocardial infarction: Impella

- CP/5.0 versus ECMO. *Eur Heart J Acute Cardiovasc Care*. 2020;9(2):164–72.
21. Chevreul K, Berg Brigham K, Durand-Zaleski I, Hernandez-Quevedo C. France: health system review. *Health Syst Transit*. 2015;17(3):1–21.
 22. den Uil CA, Akin S, Jewbali LS, et al. Short-term mechanical circulatory support as a bridge to durable left ventricular assist device implantation in refractory cardiogenic shock: a systematic review and meta-analysis. *Eur J Cardiothorac Surg*. 2017;52(1):14–25.
 23. Cheng R, Hachamovitch R, Kittleson M, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. *Ann Thorac Surg*. 2014;97(2):610–6.
 24. Mejean C. Prise en charge du choc cardiogénique à la phase aiguë de l'infarctus du myocarde: Etude rétrospective, portant sur 50 cas [Management of cardiogenic shock in the acute phase of myocardial infarction: Retrospective study, covering 50 cases]. *Sciences du Vivant [q-bio]*. 2001. hal-01733636. Available at: <https://hal.univ-lorraine.fr/hal-01733636/document> Accessed 21 Jan 2022.
 25. Ghabri S, Autin E, Poullié AI, Josselin JM. The French National Authority for Health (HAS) guidelines for conducting budget impact analyses (BIA). *Pharmacoeconomics*. 2018;36(4):407–17.
 26. Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health*. 2014;17(1):5–14.
 27. Agence Technique de l'Information sur l'Hospitalisation. Formats PMSI 2016. 2017. <https://www.atih.sante.fr/formats-pmsi-2016>. Accessed 15 Dec 2020.
 28. Delmas C, Elbaz M, Bonello L, et al. Place de l'assistance circulatoire dans le choc cardiogénique en France en 2018: revue de la littérature et perspectives. *Méd Intensive Réa*. 2018;27:97–113.
 29. Agence Technique de l'Information sur l'Hospitalisation. Guide d'utilisation: Valorisation de l'activité 2018 par les tarifs 2018 et par les tarifs 2019. https://www.atih.sante.fr/sites/default/files/public/content/3592/guide_dutilisation_-_valorisation_de_lactivite_2018_par_les_tarifs_2018_et_tarifs_2019.pdf. Accessed 20 Feb 2020.
 30. Liste des Produits et Prestations Remboursables. <https://www.ameli.fr/sites/default/files/Documents/615994/document/lpp.pdf>. Accessed 18 Mar 2020.
 31. Halimi S, Benhamou PY, Charras H. Le cout du pied diabétique. https://www.fmc-tourcoing.org/PROGRAMME_FMC/DIABETE_10_00/DIABETEFMI/cout-pied-3.html. Accessed 6 Nov 2020.
 32. l'Assistance publique – Hôpitaux de Paris [Public Assistance—Hospital of Paris]. Le dispositif Cardiohelp®, un appareil ECMO portable ? [The Cardiohelp® device, a portable ECMO device?]. 2014. <http://cedit.aphp.fr/hospital-based-hta-levaluation-de-technologies-de-sante-a-lhopital/point-sur-le-dispositif-cardiohelp-appareil-ecmo-portatif/>. Accessed 8 Jun 2021.
 33. Puymirat E, Fagon JY, Aegerter P, et al. (Collège des Utilisateurs de Bases de données en Réanimation; CUB-Réa Group [Intensive Care Database User Group]). Cardiogenic shock in intensive care units: evolution of prevalence, patient profile, management and outcomes, 1997–2012. *Eur J Heart Fail*. 2017;19(2):192–200.
 34. Rab T, Ratanapo S, Kern KB, et al. Cardiac shock care centers: JACC review topic of the week. *J Am Coll Cardiol*. 2018;72(16):1972–80.
 35. Basir MB, Schreiber T, Dixon S, et al. Feasibility of early mechanical circulatory support in acute myocardial infarction complicated by cardiogenic shock: the Detroit cardiogenic shock initiative. *Catheter Cardiovasc Interv*. 2018;91(3):454–61.
 36. Hanson ID, Tagami T, Mando R, et al. SCAI shock classification in acute myocardial infarction: insights from the National Cardiogenic Shock Initiative. *Catheter Cardiovasc Interv*. 2020;96(6):1137–42.
 37. Esposito ML, Jablonski J, Kras A, Krasney S, Kapur NK. Maximum level of mobility with axillary deployment of the Impella 5.0 is associated with improved survival. *Int J Artif Organs*. 2018;41(4):236–9.
 38. Sassard T, Scalabre A, Bonnefoy E, Sanchez I, Farhat F, Jegaden O. The right axillary artery approach for the Impella Recover LP 5.0 microaxial pump. *Ann Thorac Surg*. 2008;85(4):1468–77.
 39. El Sibai R, Bachir R, El Sayed M. Outcomes in cardiogenic shock patients with extracorporeal membrane oxygenation use: a Matched Cohort Study in Hospitals across the United States. *Biomed Res Int*. 2018;2018:2428648.
 40. Lemor A, Dehkordi SHH, Basir MB, et al. Impella versus extracorporeal membrane oxygenation for acute myocardial infarction cardiogenic shock. *Cardiovasc Revasc Med*. 2020;21(12):1465–71.

41. Haute Autorité de Santé (HAS). IMPELLA CP, dispositif d'assistance mécanique électrique percutanée, à flux axial, monoventriculaire gauche, de courte durée [IMPELLA CP, percutaneous mechanical electrical assistance device, axial flow, left single-ventricular, short duration]. Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé [National Commission for the Evaluation of Medical Devices and Health Technologies]. 2020. [https://www.has-sante.fr/upload/docs/evamed/CNEDIMTS-5861_IMPELLA%20CP_11_mars_2020_\(5861\)_avis.pdf](https://www.has-sante.fr/upload/docs/evamed/CNEDIMTS-5861_IMPELLA%20CP_11_mars_2020_(5861)_avis.pdf). Accessed 9 Jun 2021.
42. Udesen NJ, Møller JE, Lindholm MG, et al. Rationale and design of DanGer shock: Danish-German cardiogenic shock trial. *Am Heart J*. 2019;214:60–8.
43. Schurtz G, Rousse N, Saura O, et al. IMPELLA® or extracorporeal membrane oxygenation for left ventricular dominant refractory cardiogenic shock. *J Clin Med*. 2021;10(4):759.
44. Fagot J, Bouisset F, Bonello L, et al. Early evaluation of patients on axial flow pump support for refractory cardiogenic shock is associated with left ventricular recovery. *J Clin Med*. 2020;9(12):4130.
45. Tongers J, Sieweke J-T, Kühn C, et al. Early escalation of mechanical circulatory support stabilizes and potentially rescues patients in refractory cardiogenic shock. *Circ Heart Fail*. 2020;13(3):e005853.
46. Moazzami K, Dolmatova EV, Cocke TP, et al. Left ventricular mechanical support with the Impella during extracorporeal membrane oxygenation. *J Tehran Heart Cent*. 2017;12(1):11–4.
47. Schiller P, Vikholm P, Hellgren L. Experimental venoarterial extracorporeal membrane oxygenation induces left ventricular dysfunction. *ASAIO J*. 2016;62(5):518–24.
48. Ostadal P, Mlcek M, Kruger A, et al. Increasing venoarterial extracorporeal membrane oxygenation flow negatively affects left ventricular performance in a porcine model of cardiogenic shock. *J Transl Med*. 2015;13:266.
49. Rupperecht L, Flörchinger B, Schopka S, et al. Cardiac decompression on extracorporeal life support: a review and discussion of the literature. *ASAIO J*. 2013;59(6):547–53.
50. Curran J, Burkhoff D, Kloner RA. Beyond reperfusion: acute ventricular unloading and cardioprotection during myocardial infarction. *J Cardiovasc Transl Res*. 2019;12(2):95–106.
51. Stone GW, Selker HP, Thiele H, et al. Relationship between infarct size and outcomes following primary PCI: patient-level analysis from 10 randomized trials. *J Am Coll Cardiol*. 2016;67(14):1674–83.
52. den Uil CA, Jewbali LS, Heeren MJ, Constantinescu AA, Van Mieghem NM, Reis Miranda DD. Isolated left ventricular failure is a predictor of poor outcome in patients receiving veno-arterial extracorporeal membrane oxygenation. *Eur J Heart Fail*. 2017;19(Suppl 2):104–9.
53. Danial P, Hajage D, Nguyen LS, et al. Percutaneous versus surgical femoro-femoral veno-arterial ECMO: a propensity score matched study. *Intensive Care Med*. 2018;44:2153–61.
54. Bonello L, Delmas C, Gaubert M, Schurtz G, Ouattara A, Roubille F. Trials of mechanical circulatory support with percutaneous axial flow pumps in cardiogenic shock complicating acute myocardial infarction: mission impossible? *Arch Cardiovasc Dis*. 2020;113(6–7):448–60.
55. Lamarche Y, Cheung A, Ignaszewski A, et al. Comparative outcomes in cardiogenic shock patients managed with Impella microaxial pump or extracorporeal life support. *J Thorac Cardiovasc Surg*. 2011;142(1):60–5.
56. Ouweneel DM, de Brabander J, Karami M, et al. Real-life use of left ventricular circulatory support with Impella in cardiogenic shock after acute myocardial infarction: 12 years AMC experience. *Eur Heart J Acute Cardiovasc Care*. 2019;8(4):338–49.