CLINICAL RESEARCH

Preliminary experience with Impella Recover® LP5.0 in nine patients with cardiogenic shock: A new circulatory support system in the intensive cardiac care unit

Expérience préliminaire avec la pompe Impella Recover® LP5.0 chez neuf patients en choc cardiogénique. Une nouvelle assistance ventriculaire gauche en unité de soins intensifs cardiologicals

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Summary
Aim. — Cardiogenic shock is associated with high mortality. We report our experience with the short-term left ventricular axial pump Impella LP5.0 in nine patients with severe ischaemic heart failure.
Methods. — Six patients (group 1) presented with cardiogenic shock at the acute phase of an ST elevation myocardial infarction. Three patients (group 2) had severe ischaemic cardiomyopathy with temporary contra-indication to LVAD or transplantation. We measured haemodynamic and metabolic variables up to 96 hours and recorded morbidity, mechanical pump failures, and mortality up to one year postimplantation.

Abbreviations: CE, conformité européenne; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.
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Results. — In all patients the Impella LP5.0 was safely placed through the right subclavian artery. Cardiac power output increased from 0.64 (0.07) W to 0.94 (0.44) W and 1.02 (0.30) W at 24 and 72 hours, respectively. The Impella LP5.0 remained in place for 12 (7.2) days. In group 1, five patients were in INTERMACS Profile 3 at the time of pump insertion. Three could be weaned and survived. One patient in INTERMACS Profile 1 died of intractable heart failure within hours. In group 2, two of three patients underwent heart transplantation. Haemorrhage requiring transfusions was observed in four patients but only one case was directly related to the Impella LP5.0.

Conclusion. — Left ventricular assistance with the Impella LP5.0 appears to be well tolerated. It may be especially useful in patients with acute myocardial infarction complicated by cardiogenic shock who achieve INTERMACS Profile 3 with initial treatment.

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MOTS CLÉS
Infarctus du myocarde ; Choc cardiogénique ; Assistance ventriculaire gauche ; Pompe axiale

 Résumé
Objectif. — Le choc cardiogénique est associé à une mortalité élevée. Cette étude rapporte notre expérience avec la pompe axiale Impella LP5.0 chez neuf patients atteints d’insuffisance cardiaque sévère d’origine ischémique.

Méthodes. — Six patients (groupe 1) présentaient un choc cardiogénique à la phase aiguë d’un infarctus du myocarde avec sus-décalage du segment ST. Trois patients (groupe 2) étaient porteurs d’une cardiopathie ischémique sévère et n’étaient temporairement éligibles ni à une assistance ventriculaire gauche ni à une transplantation en urgence. Nous avons mesuré les variables hémodynamiques et métaboliques jusqu’à 96 heures après l’implantation du dispositif, ainsi que les défaillances de la pompe, la morbidité et la mortalité jusqu’à un an après l’implantation.

Résultats. — Chez tous les patients le dispositif LP5.0 Impella a été placé sans complication par voie sous-clavière droite. La puissance cardiaque a augmenté de 0,64 (± 0,07) W à 0,94 (± 0,44) W et 1,02 (± 0,30) W à respectivement 24 et 72 heures. Le dispositif est resté en place pendant 12 (± 7,2) jours. Dans le groupe 1, cinq patients présentaient un Profil INTERMACS 3 au moment de l’insertion de la pompe. Trois ont pu être sevrés et ont survécu. Un patient, qui présentait un Profil INTERMACS 1, est décédé d’insuffisance cardiaque réfractaire en quelques heures. Dans le groupe 2, deux des trois patients ont bénéficié d’une transplantation cardiaque. Quatre patients ont présenté une hémorragie nécessitant au moins une transfusion, mais seulement un cas d’hémorragie a été causé directement par la pompe.

Conclusion. — L’assistance ventriculaire gauche avec la pompe Impella LP5.0 semble être bien tolérée. Elle peut être particulièrement utile chez les patients présentant un infarctus aigu du myocarde compliqué de choc cardiogénique, qui atteignent un Profil INTERMACS 3 avec le traitement initial.

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Background
In patients with acute myocardial infarction and cardiogenic shock, treatment is based on revisualization, inotropes, IABPs and respiratory support, in order to ensure haemodynamic stabilization and allow partial recovery of left ventricular systolic function. In some patients, the outcome can be uneventful with quick recovery and fast weaning from support. In other patients, mechanical assistance is needed within hours [1]. These patients are described as Profile 1 in the INTERMACS classification [2]. A third group includes patients who, after initial improvement, are ‘stuck’ in a stable but precarious haemodynamic status; they remain stable, with mid-level or high doses of intravenous inotropic agents and/or an IABP (INTERMACS Profiles 2 or 3).

In patients with INTERMACS Profiles 1 to 3, additional short-term left ventricular support can provide important benefits. In recent years, several short-term left ventricular devices have been developed. They are often associated with complications that limit their usefulness [3].

The Impella LP5.0 (Abiomed Europe GmbH, Aachen, Germany) pump appears especially interesting. Relatively light and easy to implement, it provides a theoretical output of 4 L/min while unloading the left ventricle. Moreover, we have shown that the Impella LP5.0 can be inserted through the subclavian artery, which allows mobilization of the patient [4].

We report on the feasibility and the safety of the Impella LP5.0 based on our experience of its use in nine patients with ischaemic cardiogenic shock.

Methods
Patients
From November 2002 to November 2008, nine medical patients (seven men, two women), mean (standard
rated electrical motor and an inflow cannula (Fig. 1). The Impella LP5.0 consists of a rotor driven by an incorporated electrical motor and an inflow cannula (Fig. 1). The pump is placed through the aortic valve in the left ventricle, and drives blood from the left ventricle to the ascending aorta through the inflow cannula. The performance of the pump depends on the rotary speed (up to 32,000 rpm) and the pressure it is subjected to (aortic pressure minus left ventricular pressure). This pressure difference is continuously registered through a pressure sensor located in front of the rotor. The pump flow in physiological conditions is around 4 L/min. Rotational speed is set at nine increasing levels on the driving console. In Europe, the device is approved for short-term use, for up to 10 days (CE marked). In all patients, the pump was inserted through the subclavian artery. This method has been described elsewhere [4]. In brief, under general anaesthesia and heparinization, the right subclavian artery is exposed below the clavicle. An 8-mm vascular graft is sutured end-to-side and clamped closed to the anastomosis. A guidewire is introduced in the Impella LP5.0 pump through a specific lumen to the distal pigtail. The device is then introduced into the graft and an occluding plug around the 9-French driving cable is tied to prevent blood loss through the graft during the implantation manoeuvres. The guidewire and the pump are introduced into the subclavian artery to the left ventricle cavity, crossing the aortic valve, under fluoroscopic guidance or transoesophageal echocardiography. The correct position of the device is confirmed by fluoroscopy or transoesophageal echocardiography and the pressure signal at the console. The guidewire is then removed and the device is turned on. The graft around the cable is tied, closed to the anastomosis, cut off 1 cm further along, and removed. The surgical approach is closed and the driving cable with the sheath is allowed to exit from the subclavian wound. To remove the device, the same approach was used. Only the remaining graft is controlled; the ties around are removed and the device is gently pulled back and out. The graft is clamped and oversewn; then the surgical approach is closed.

Patient management

All patients had invasive arterial pressure monitoring. Five patients had a Swan Ganz catheter inserted just before Impella LP5.0 pump insertion. Patients were weaned from inotropic and vasopressor support as soon as possible. Filling volume was primarily triggered by the right atrial pressure and urine output. Organ perfusion was judged by clinical variables, urine output and evolution of blood lactate levels. The IABP remained in place until inotropic support was discontinued. Recovery of cardiac function was assessed by echocardiography. Angiotensin-converting enzyme inhibitors were introduced and their dose was increased as tolerated. Then low doses of beta-blocking agents were introduced. Weaning from the pump occurred over several days by reducing the pump speed from eight to two in 2–3 days.

Data collection and statistics

Patient data were collected retrospectively from the medical records. Patients were classified according to the INTERMACS classification. This agency defined seven clinical profiles to describe patients included in its ventricular assist device registry [2]. These profiles provide convenient shorthand, which facilitates communication on the seriousness of acute heart failure and clarification of target populations for devices. Haemodynamic and laboratory data were collected before and up to 96 hours after Impella LP5.0 insertion. All causes of morbidity and mechanical failures were recorded. Acute renal failure was defined as urine output less than 30 mL/h. Mortality was recorded during hospitalisation, and at one month and one year postimplantation. Cardiac power output was measured as cardiac output times mean arterial pressure divided by 451 [5]. Continuous data are presented as mean (SD).

Results

Patients

Clinical characteristics are presented in Table 1. Mean age was 50.3 (14.0) years. The pump was inserted through the subclavian artery in all patients. In group 1, all but one patient were stabilized and relieved from shock but showed no sustained improvement. These INTERMACS
Profile 3 patients had the Impella LP5.0 implanted on a semi-urgent basis in the operating room. In one patient (P6), implantation occurred as a rescue operation in the catheterization laboratory after a failed primary percutaneous coronary intervention in an occluded left main artery.

In group 2, contraindications to a long-term assist device or urgent transplantation were history of stroke (P7), suspicion of colon cancer with sepsis (P9) and mental disorder (P8).

### Haemodynamic data

Haemodynamic data for the first 72 hours were complete in five patients (P1–P5; Table 2). Cardiac output increased from 4.0 (0.5) L/min with IABP and inotropic support to 5.88 (2.67) L/min and 5.84 (1.42) L/min, 24 hours and 72 hours after implantation, respectively. Cardiac power output increased from 0.64 (0.07) W to 0.94 (0.44) W and 1.02 (0.30) W, 24 hours and 72 hours after implantation, respectively. The cumulative diuresis during the 24 hours after the implantation of the pump was 4083 (1989) mL, with an hourly diuresis of 143 (81) mL.

### Clinical evolution

**Group 1 (n = 6)**

The Impella LP5.0 was implanted 4.7 (3.5) days after the onset of infarction (Table 3). One patient (P6) who required rescue implantation of the pump in the catheterization laboratory died of multiple-organ failure 48 hours later. Of the five patients alive 96 hours after implantation, one died of arrhythmic storm on the 10th day (P5). Four other patients were able to be weaned from dobutamine and norepinephrine. In these four patients, the IABP was withdrawn 4.0 (2.3) days after Impella LP5.0 implantation. One of these patients (P2) died on the 23rd day as the result of a sudden massive left haemothorax while still on the Impella LP5.0. The three other patients were able to be weaned from the Impella LP5.0. Thereafter, one received an implantable cardioverter-defibrillator one month later (P1), another underwent heart transplantation five months later (P4), and the last (P2) died of heart failure six months later. During Impella LP5.0 support, angiotensin-converting enzyme inhibitors were introduced in five patients and beta-blockers in four. At the time of pump removal, three patients were on angiotensin-converting enzyme inhibitors and three were on beta-blockers.
Table 2  Haemodynamic values before and after device implantation.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.5</td>
</tr>
<tr>
<td>2</td>
<td>4.0</td>
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<tr>
<td>3</td>
<td>3.6</td>
</tr>
<tr>
<td>4</td>
<td>4.5</td>
</tr>
<tr>
<td>5</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Before

| CO (L/min) | 4.0 (0.5) |
| CP (W)     | 0.64 (0.07) |

24-hour

| CO (L/min) | 5.88 (2.67) |
| CP (W)     | 0.94 (0.44) |

72-hour

| CO (L/min) | 5.84 (1.42) |
| CP (W)     | 1.02 (0.30) |

LV EF

| 0.3 (0.1) |

CO: cardiac output; CP: cardiac power; LV EF: left ventricular ejection fraction.

Table 3  Clinical course, complications and outcome.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Complications</td>
<td>Sepsis</td>
<td>+</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Survival

| Survival: in-hospital | + | 0 | + | + | 0 | 0 | + | + | 0 |
| Survival: 1 month | + | 0 | + | + | 0 | 0 | + | + | 0 |
| Survival: 1 year | + | 0 | 0 | + | 0 | 0 | + | + | 0 |

Group 2 (n = 3)

Of the three patients who had an Impella LP5.0 implanted due to contraindication to long-term assistance or urgent transplantation, one (P9) died of septic shock 14 days after implantation. The Impella LP5.0 had allowed further time to evaluate a bowel mass that eventually proved to be a diverticulitis. The other two patients had heart transplantation: one at 13 days (P8) and the other at six months (P7) after implantation.

Tolerance and complications

The Impella LP5.0 pump remained in place for 12.0 (7.2) days with extremes of 1–23 days. Overall, the pump was well tolerated and five patients were able to sit on a chair and even walk with it. Two pumps were damaged during implantation with kinking of the pump catheter. This was related in one case to calcifications and stenoses of the iliac artery during an initial left femoral attempt and in the other to difficult handling of the pump through direct left subclavian access. In both cases a new pump was successfully inserted through the right subclavian artery with the graft technique. One pump had a severe motor dysfunction 24 hours after implantation, probably related to a lack of proper lubrication by serum glucose; it required urgent removal. The flow sensors of two pumps failed beyond the first week. These pumps continued to function properly. One patient had a left haemothorax 23 days after implantation. Surgical thoracotomy showed diffuse bleeding not related to the aorta. All patients presented signs of inflammation or sepsis during their stay, which led to antibiotic coverage. Three patients had germs identified on blood culture during Impella LP5.0 assistance: pneumococci (P4), staphylococcus aureus (P1) and cytomegalovirus in sigmoid biopsies and bronchial aspiration (P9). Haemorrhage with anaemia requiring transfusions was observed in four patients: haemothorax (P2), haemoperitoneum (P9), upper gastrointestinal bleeding (P3), during insertion of the pump (P7). Haemolysis required transfusions occurred in one patient (P9) in the setting of inflammation and sepsis. Two patients experienced transient ischaemic stroke (P3, P7), related to air embolism in one case (P7). There was a systematic presence of thrombus on the proximal portion of the pump after withdrawal, which probably comes from the subclavian Dacron graft. One patient developed acute renal failure requiring dialysis (P5).

Discussion

Even if development of short-term left ventricular assist devices has accelerated in the past 10 years, few devices
are available [6]. The Impella LP5.0 is a miniaturized rotary blood pump that has the ability to unload the left ventricle with substantial pump capacity and to limit invasiveness. There are two CE-marked Impella Recover® systems. The smaller device, the Impella Recover® LP2.5 is introduced through a femoral percutaneous approach and can deliver an output of up to 2.5 L/min. It has been mainly used as support for patients undergoing high risk percutaneous coronary intervention [7,8].

In our series we used the larger device, the Impella LP5.0. The 21-French Impella LP5.0 provides a maximum 4.5 L/min output. It has been mainly used for haemodynamic support after heart surgery [9,10]. In these patients, the Impella LP5.0 was inserted directly through the ascending aorta. This route is cumbersome in patients with cardiogenic shock of medical aetiology. Insertion of the Impella LP5.0 through a surgical cutdown of a large peripheral artery — femoral or subclavian — is preferred. In all our patients, the Impella LP5.0 was inserted through the right subclavian artery. Experience with the Hemopump (Medtronic, Inc., Minneapolis, MN, USA), an axial pump with similar features, had shown that the femoral approach was associated with device-related complications such as catheter fracture and insertion difficulties [9]. We developed the subclavian approach because of failure of insertion through a calcified femoral artery and catheter fracture [4]. In our series, this route was well tolerated and allowed early mobilization of patients.

An IABP is the reference short-term left ventricular assist device [5,11,12]. The Impella LP2.5 has been compared with an IABP in a randomized trial and provided similar haemodynamic support [13]. Our series has important differences. First, the Impella LP5.0 has twice the output of the Impella LP2.5. Second, in most of our patients, the Impella LP5.0 was associated with an IABP that had been inserted in the catheterizations laboratory at the time of angioplasty. The association of an IABP with the Impella LP5.0 offers some advantages by providing unloading of the left ventricle combined with higher aortic diastolic pressure. Experimental studies have shown that, compared with the Hemopump alone (a device similar to the Impella LP5.0), adding an IABP was associated with similar unloading features, an improved subendocardial flow that returned to normal in the ischaemic region but a slight reduction of the pump output [14].

Our study looked at the feasibility, efficacy and safety of the Impella LP5.0 and gives no insight into possible indications. Data on indications and optimal timing of insertion of short-term left assist devices remain scant among heterogeneous populations [3,9,15]. The Impella LP5.0 is not a substitute for ECMO, which is very effective in providing emergency mechanical pulmonary and circulatory assistance. In fact, the Impella LP5.0 pump does not add its output (around 4 L/min) to that of the failing heart but largely substitutes for it [10]. The additional work and output of the left ventricular assist device is actually associated with a lower endogenous cardiac output [16]. Compared with an IABP, overall cardiac output is only slightly higher with the Impella LP2.5 [13]. In a postcardiotomy series evaluating the Impella LP5.0, patients with a residual cardiac output of 1 L/min or more above the pump flow (estimated residual cardiac function) had a 10% mortality rate, as opposed to 88% in those with a residual cardiac function of 1 L/min or less (P < 0.001) [10]. In our series, the patient (P6) who remained in cardiogenic shock despite inotropes, ventilation and an IABP would probably have benefited more from an ECMO.

Within the limits of our descriptive report, INTERMACS P3 patients (pulled out of shock state, haemodynamically stable but still dependent on inotropes and an IABP [2]) may represent a population where the Impella LP5.0 device is especially attractive. The Impella LP5.0 appears to be relatively safe. As in our series, other series with Impella pumps have underlined the low rates of complications, bleeding and embolism that contrast with other short-term left ventricular assist devices [17—19]. Haemodynamic support is not the only way in which the Impella pump might benefit patients. Through reduced end-diastolic pressure, the Impella pump improves left ventricular remodelling and coronary perfusion in patients with myocardial infarction and might ease recovery of cardiac function [20].

Experimentally, support by a Hemopump has lead to a reduction of infarct size [21]. This reduction correlated with the degree of unloading during reperfusion. In a recent clinical series, left ventricular unloading with the Impella LP2.5 after an acute myocardial infarction resulted in a marked left ventricular recovery, suggesting a possible beneficial effect of mechanical unloading on postinfarct adverse remodelling [22]. Presumably, a larger and longer left ventricular discharge with the Impella LP5.0 could be associated with further improvement in left ventricular remodelling and speed up left ventricular recovery. These hypotheses are currently being tested in a randomized study assessing the clinical and economic consequences of the Impella LP5.0 in INTERMACS Profile 3 patients with acute myocardial infarction.

**Conclusion**

Left ventricular assistance for up to three weeks with the Impella LP5.0 inserted through the right subclavian artery appears to be safe and well tolerated. This strategy may improve haemodynamic status and allows further time in patients who have a transitory contraindication to transplantation or long-term assistance. Based on this series, a randomized study is currently assessing the benefit of this device on outcome and left ventricular function in patients with acute myocardial infarction complicated by cardiogenic shock who achieved INTERMACS Profile 3 with initial treatment.

**Disclosure of interest**

Didier Bresson: none; Franck Sibellas: none; Fadi Farhat: none; Olivier Jegaden: none; Gilbert Kirkorian: none; Eric Bonnefoy is coordinator of a research project on Impella LP5.0 in patients with acute myocardial infarction and cardiogenic shock.

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