International Journal of Cardiology xxx (xxxx) xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Clinical expert consensus document on the use of percutaneous left ventricular assist support devices during complex high-risk indicated PCI Italian Society of Interventional Cardiology Working Group Endorsed by Spanish and Portuguese Interventional Cardiology Societies

Alaide Chieffo [a], Francesco Burzotta [b], Federico Pappalardo [c], Carlo Briguori [d], Roberto Garbo [e], Giulia Masiero [f], Elisa Nicolini [g], Flavio Ribichini [h], Carlo Trani [b], Belén Cid Álvarez [i], Oriol Rodríguez Leor [j], Raúl Moreno [k], Ricardo Santos [l], António Fiarresga [m], João Brum Silveira [n], Armando Pérez de Prado [o], Giuseppe Musumeci [f], Giovanni Esposito [p], Giuseppe Tarantini [q,*]

[a] Interventional Cardiology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[b] Institute of Cardiology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy
[c] Advanced Heart Failure and Mechanical Circulatory Support Program, San Raffaele Scientific Institute, Vita Salute University, Milan, Italy
[d] Interventional Cardiology Unit, Mediterranea Cardiocentro, Naples, Italy
[e] S.G. Bosco Hospital, Turin, Italy
[f] Cardiovascular Department, Ospedale Santa Croce e Carle, Cuneo, Italy
[g] Unità di Emodinamica, Ospedali Riuniti di Ancona, Ancona, Italy
[h] Department of Cardiology, University of Verona, Verona, Italy
[i] Hospital Universitario De Santiago de Compostela, A Coruña, Spain
[j] Hospital Universitario Germans Trias i Pujol, Badalona, Spain
[k] Hospital Universitario La Paz, IDIPAZ, Madrid, Spain
[l] Centro Hospitalar de Setúbal, Setúbal, Portugal
[m] Centro Hospitalar Lisboa Central, Hospital de Santa Marta, Lisboa, Portugal
[n] Centro Hospitalar e Universitário do Porto, Hospital de Santo António, Porto, Portugal
[o] Hospital Universitario de León, León, Spain
[p] Department of Advanced Biomedical Sciences, Divisions of Cardiology and Cardiothoracic Surgery, Federico II University, Naples, Italy
[q] Department of Cardiac, Thoracic and Vascular Science, University of Padova, Italy.

ARTICLE INFO

Article history:
Received 1 February 2019
Received in revised form 18 May 2019
Accepted 23 May 2019
Available online xxxx

ABSTRACT

Percutaneous coronary intervention (PCI) is establishing as the last remaining revascularization option in an increasing number of patients affected by complex coronary artery disease not suitable for surgery. Over the past decade, percutaneous left ventricular assist device (pLVAD) has increasingly replaced intra-aortic balloon pump to provide hemodynamic support during such non-emergent complex high-risk indicated procedures (CHIP) averting the risk of circulatory collapse and of adverse events in long lasting and/or complicated procedures. This review article aims to report the key factors to define CHIP, to summarize the available pLVAD which have CE mark for temporary mechanical LV support and to discuss the rationale of their use in this subset of patients. Based on the expertise of the Italian Society of Interventional Cardiology working group, with the endorsement from Spanish and Portuguese Society of Interventional Cardiology working groups, it will provide several practical suggestions in regards to the use of pLVAD in different clinical CHIP scenarios.

1. Introduction and objective

Over the past decades the indication for percutaneous coronary interventions (PCI) has progressively widened to involve those patients with high-risk characteristics requiring advanced technologies and longer procedure times. Although the guidelines recommend coronary artery bypass grafting (CABG) for patients with high complexity coronary artery disease (CAD), PCI can represent the last remaining revascularization option in an increasing number of patients not suitable for

Abbreviations: PCI, percutaneous coronary interventions; CABG, coronary artery bypass grafting; CAD, coronary artery disease; IABP, intra-aortic balloon pump; CHIP, complex high-risk indicated procedures; pLVAD, percutaneous left ventricular assist device; LVEF, left ventricular ejection fraction; LMCA, unprotected left main coronary artery; MAE, major adverse events; RCT, randomized control trial; MVD, multivessel disease; MAE, major adverse event.

* Corresponding author at: Department of Cardiac, Thoracic and Vascular Science, University of Padova, Via Giustiniani 2, 35128 Padova, Italy.
E-mail address: giuseppe.tarantini.1@gmail.com (G. Tarantini).

https://doi.org/10.1016/j.ijcard.2019.05.065
0167-5273/

surgery [1]. Historically the intra-aortic balloon pump (IABP) has been used to provide hemodynamic support during complex high-risk indicated procedures (CHIP). However, it has never demonstrated to be superior to conventional treatment [2]. Over the past decade, novel percutaneous left ventricular assist device (pLVAD) has increasingly replaced the IABP during such procedures. Consequently, a preventive strategy of protected PCI has been proposed in an increasingly number of patients with highly complex CAD requiring revascularization [3].

However, the rapid expansion of the use of these devices during high risk PCI without clear recommendations from European Society of Cardiology [1] lead the working group on pLVAD of the Italian Society of Interventional Cardiology (GISE), with the endorsement from Spanish and Portuguese Society of Interventional Cardiology working groups, to write a Clinical Expert Consensus Document on the Use of pLVAD during High-Risk PCI.

Therefore, this report discusses rationale, indications, patient selection and practical suggestions in regards to the use of pLVAD during non-emergent CHIP based on the expertise of three working groups. The writing committee was composed of interventional cardiologists selected from the national societies according to an acknowledged expertise in the field. They identified several different clinical high-risk PCI scenarios based on available literature review reaching a final agreement on protected PCI management through an exchange of opinions based on evidence during conference calls and face-to-face meetings.

2. Definition of high-risk and protected PCI and the role of the Heart Team

The definition of CHIP has been evolving in the most recent years. There is a growing consensus that in order to define PCI complexity several factors have to be taken into account: hemodynamic status of the patient (shock or severely depressed left-ventricular function), patient clinical characteristics and comorbidities and complexity of coronary anatomies/lesions [3]. High-risk clinical characteristics and comorbidities are defined as: advanced age (>75 years), diabetes mellitus, heart failure with left ventricular ejection fraction (LVEF) ≤ 35%, acute coronary syndromes (ACS), previous cardiac surgery, peripheral vascular disease, advanced chronic kidney disease (glomerular filtration rate < 30 ml/min/1.73 m^2), chronic obstructive pulmonary disease, concomitant severe aortic valvulopathy or severe mitral regurgitation. Complexity of coronary anatomies/lesions includes: unprotected left main disease (LMCA), degenerated saphenous vein grafts, severely calcified lesions with need for rotational atherectomy, last patent conduit, and chronic total occlusions (CTO) in patients with multivessel disease (MVD). A PCI is therefore considered as high-risk in patients satisfying at least one clinical and one anatomical high-risk criteria as defined above [4,5]. It is important to consider that all these factors come into play in this heterogeneous population ranging from patients presenting with ACS and cardiogenic shock to clinically much more stable patients presenting with heart failure or angina with markedly reduced LVEF and complex CAD [4,5].

Based on these findings, the working group definition of non-emergent CHIP is a percutaneous revascularization in the context of complex CAD especially in case of severe ventricular dysfunction (LVEF <35%) (Fig. 1) [4,5]. In this particular setting (defined in different clinical scenarios) the rate of complications is not only increased but also associated to a significant increase of major adverse events (MAE) during the procedure, due to the rapid worsening of the already compromised LV function. This anticipated risk of hemodynamic compromise has to be prevented or supported [4,5].

CHIP requires a multidisciplinary team approach with the involvement of Heart Team and application of current guidelines [1]. Most of the patients involved in such procedures are refused by cardiac surgeons. However, not only an expert interventional cardiologist and cardiac surgeon are involved in this process but also dedicated anesthesiologists, cath-lab staff and, if required, intensive care personnel with the knowledge and experience required to handle ventricular support. A serious question that needs to be addressed and should be considered by hospital administration is how to best train physicians and staff to assure competencies when indicating, performing and monitoring these procedures.

3. CE MARK pLVAD and current available evidences

The available pLVAD with CE mark for high surgical risk patients with complex CAD and significantly reduced LVEF are described in details in the Supplementary appendix.

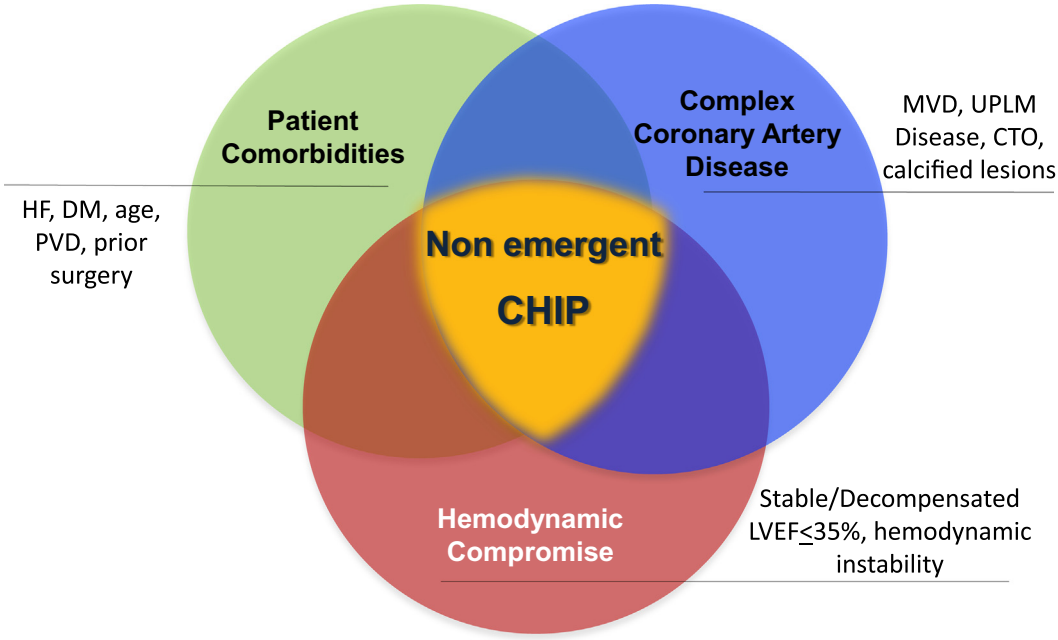

Fig. 1. Non emergent complex high-risk indicated procedures definition according to the hemodynamic status of the patient (shock or severely depressed left-ventricular function), patient clinical characteristics and comorbidities and complexity of coronary anatomies/lesions.

Please cite this article as: A. Chieffo, F. Burzotta, F. Pappalardo, et al., Clinical expert consensus document on the use of percutaneous left ventricular assist support device..., International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2019.05.065

4. Clinical need and device selection

The physiologic effects of an LV-aortic support, as Impella device, are: first, the unloading of the left ventricle, reducing LV end-diastolic pressure and LV wall tension and decreasing LV work and myocardial oxygen demand (Fig. 2); secondly, it increases the mean arterial pressure, diastolic pressure, cardiac output and thus cardiac power output, leading to improved systemic perfusion and increased coronary flow. Differently, the active deflation of the IABP immediately before the onset of systole reduces peak LV systolic and diastolic pressures and LV afterload, increasing LV stroke volume. Otherwise, an ECMO system, a continuous peripheral pump against cardiac flow, without a LV venting strategy increases LV systolic and diastolic pressure, while reducing LV stroke volume and increasing in LV afterload. The net effect could be a worsening of the myocardial oxygen consumption (Fig. 2). Current strategies of LV unloading while on VA-ECMO include: central percutaneous cannulation of the left atrium and utilization of an IABP as well as concomitant implantation of an Impella device [6].

Due to the lack of large randomized trials on comparison among mechanical cardiac support (MCS) devices in CHIP, current European guidelines exclusively consider pLVAD use in refractory cardiogenic shock and as a bridge therapy to recovery or decision in carefully selected patients with acute heart failure [1]. However, the rationale for the use of pLVAD in CHIP setting is to achieve an adequate forward cardiac output and increase mean arterial pressure to ensure vital organ perfusion while decreasing afterload and ventricular filling pressures. This may guarantee a more stable hemodynamic condition and prevent circulatory collapse in long lasting and/or complicated coronary complex PCI (see clinical scenarios below). The greater is the complexity of PCI the greater is the risk of complications. Complete revascularization for CHIP may require the use of multiple high-pressure balloon inflations or other techniques, such as rotational atherectomy in case of severe calcified CAD, that can lead to coronary and systemic hypoperfusion potentially resulting in circulatory collapse. The use of pLVAD (especially in critically ill patients) allows the operator to complete the procedure in optimal hemodynamic conditions and with low risk of peri-procedural complications. As a matter of facts, differently from European guidelines, the American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions acknowledged the pLVAD use in HR PCI with a Class IIb recommendation since 2011 [7,8] Similarly, the National Institute for Health and Care Excellence (NICE) updated in the 2018 its interventional procedures program guidance by recommended temporary and prophylactic use of pLVAD in selected elective high-risk angioplasty procedures [9].

Currently available pLVAD proved different efficacy and safety in clinical studies and their specific use should be evaluated on the basis of individual patient characteristics and clinical conditions assessed by a multidisciplinary team (Fig. 3) [5,10]. However, the early initiation of hemodynamic support prior to PCI could be reasonably associated with more complete revascularization and fewer adverse events, as suggested by several studies on pLVAD use in emergent and acute settings [11,12].

Based on the available evidence and safety data shown above, the committee focuses the following recommendations on the use of the Impella 2.5 and CP pumps in different practical clinical settings, if not contraindicated. Absolute or relative contraindications to Impella use include: mural thrombus in the LV, mechanical aortic valve or heart constrictive device, severe aortic valve stenosis or moderate to severe insufficiency, severe peripheral arterial disease, significant right heart failure, acute aortic dissection, recent stroke or contraindication to anticoagulation [7]. Furthermore, Impella pumps devices might be associated with complications as below described, especially for Impella CP and prolonged placement. Accordingly, the panel advices to carefully consider these possible hazards during the Heart-team evaluation, as: bleeding complications, including access site hematoma and major bleeding needing transfusion or surgery (incidence range from 7% to 40%), major vascular complications including pseudo-aneurysm, arterio-venous fistula, limb ischemia or access site infection (3–10%), sepsis [9].

The patient and access management and the health economics evaluation of Impella use are described in details in the Supplementary appendix.

5. Clinical scenarios for pLVAD use during CHIP

5.1. Unprotected left main and severe coronary artery disease (SYNTAX score > 22)

According to current ESC guidelines patients with LM disease and SYNTAX score > 22 have a class IIa recommendation for PCI [1]. A high proportion of patients with distal LM have also MVD and left ventricle dysfunction [13] adding additional risk to the procedure. The higher

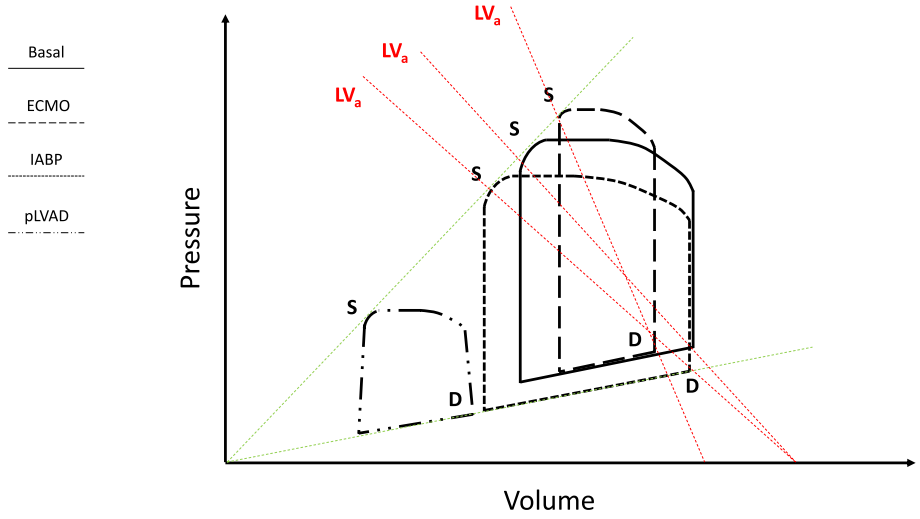

Fig. 2. Pressure volume (PV) loops during normal conditions and after LVAD activation. Points D indicate the end-diastolic pressure-volume point, while points S indicate the end-systolic pressure-volume point. Stroke volume (SV) is represented by the volume difference between end-systolic and end-diastolic volumes. The left-ventricular afterload (LVa) derives from the ratio of end-systolic pressure and stroke volume (red dot lines). Intra-aortic balloon pump (IABP) counter pulsation reduces peak LV systolic and diastolic pressures and LVa and increases LV SV. Veno-arterial extra-corporeal membrane oxygenation (ECMO) without a LV venting strategy increases LV systolic and diastolic pressure, while reducing LV stroke volume and increasing in LVa. The net effect could be a worsening of the myocardial oxygen consumption. Percutaneous LV assist devices (pLVAD), as Impella and TandemHeart, significantly reduce LV pressures, volumes, stroke volume and cardiac workload. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Please cite this article as: A. Chieffo, F. Burzotta, F. Pappalardo, et al., Clinical expert consensus document on the use of percutaneous left ventricular assist support device..., International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2019.05.065

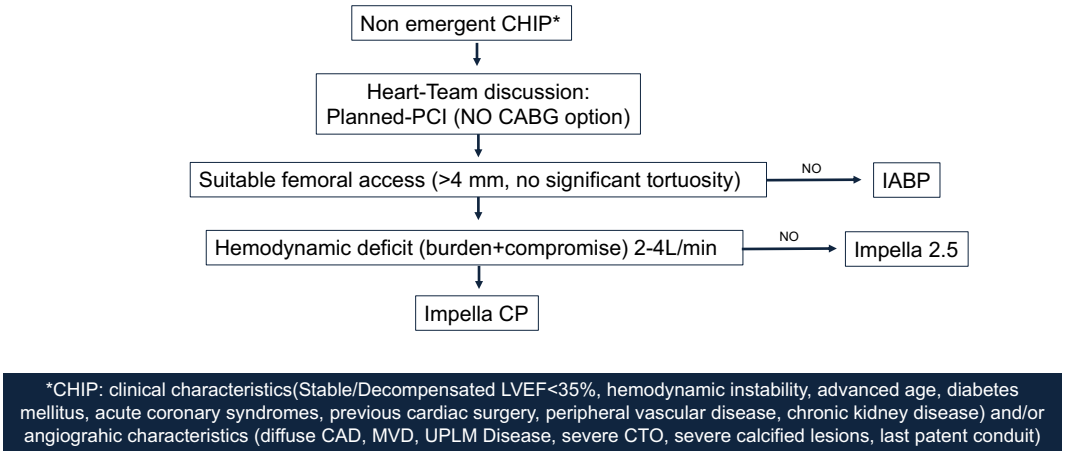

Fig. 3. Proposed flow-chart for percutaneous left ventricular assist devices selection in complex high-risk indicated procedures according to patient characteristics and clinical conditions.

the syntax score in the context of LM disease, the stronger the indication for myocardial revascularization (either CABG or PCI) over medical treatment [2]. To this regard, although PCI has a class III, level of evidence B indication when SYNTAX score is >32, it is not infrequent to consider PCI for these patients because of surgical contra-indication or refusal due to clinical and anatomic conditions (porcelain aorta, ACS or severe comorbidities). In the context of CHIP (Table I) several studies reported the safety, feasibility, and potential benefits of Impella 2.5 and Impella CP in the treatment of unprotected LMCA disease and severely depressed LVEF. In particular, a sub-analysis from the USpella Registry, on 127 patients who received hemodynamic support for LM PCI (mean age 69.98 ± 10.7 years, 71% men, and mean LVEF 28.74 ± 15.55%), showed that in-hospital and 30-days mortality rates were 1.43% and 2.1% respectively. The average baseline and post PCI (residual) SYNTAX scores were 31.4 and 7.86, respectively ($p < 0.001$) [14]. Additionally, there are also some initial evidence that a pLVAD might be indicated in case of PCI for distal unprotected LMCA and intermediate-high SYNTAX score irrespective of LVEF [15,16].

Based also on the available evidence, the consensus of the panel is that a pLVAD is strongly encouraged in case of unprotected distal LMCA associated with SYNTAX score ≥ 33 and severe LV dysfunction (LVEF < 35%) when surgical approach is not an option (heart team decision). Moreover, the panel suggest to consider a pLVAD in case of non-emergent CHIP for unprotected distal LMCA associated with SYNTAX score > 22 and severe LV dysfunction (LVEF < 35%).

5.2. Complete revascularization

Growing evidence confirms the benefits of CR on clinical outcomes, suggesting that it should be the goal of therapy whenever possible, especially in MVD and LVEF dysfunction [17]. The current European Society Guidelines identified the anticipated completeness of revascularization as one of the most important criteria for decision-making with respect to the type of revascularization CABG and PCI, especially in high-risk stable patients and in those with heart failure and systolic left ventricular dysfunction [1]. Both anatomical and functional criteria have been used to define the completeness of revascularization [18–20]. CR is often a challenge in patients undergoing high-risk, MVD PCI [21,22]. CR usually requires longer procedural times, challenging techniques such as CTO and rotational atherectomy, a technique with additional risk for acute vessel occlusion, low-flow or distal embolization, with subsequent myocardial necrosis. These complex procedures might increase the rate of intraprocedural complications as shown in clinical studies [21,23] (Table I).

This consensus group is aware of the current limitation of the available evidence for mechanical support in CR PCI. However, hemodynamic support by pLVAD pre PCI is indicated in patients undergoing non emergent CHIP, in case of complex procedures in patients with severe LV dysfunction in the attempt to obtain CR.

5.3. Complex CTO

Technical success rate of CTO PCI has improved in the recent years due to better equipment and amelioration of procedural techniques. Nevertheless, the high-risk profile of patients with impaired LVEF remains a significant barrier to treatment. Obviously, the main indication to proceed to CTO PCI in this complex anatomical and clinical setting is the presence of large myocardium viability and/or ischemia in the territory of chronically occluded vessel. Need for Mechanical Circulatory Support (MCS) device for complex CTO PCI also depends upon the

Table I
Summary of the main available clinical data on non-emergent high-risk PCI with Impella cardiac support.

Study	Sample size (n)	Pump type	Age (years)	CHIP type	Mean Syntax score (n)	Mean LVEF (%)	ACS (%)	Follow-up	MAE (%)	Death (%)
PROTECT II RCT	452	Impella 2.5 vs IABP	68	3VD/ULMCA, low LVEF	30 ± 13	24 ± 6	0	90 days	41 vs 49 ($p = 0.07$)[a]	12 vs 9 ($p = 0.2$)[a]
German Impella Registry	154	Impella 2.5 e CP	73	Complex anatomy, comorbidities, low LVEF	32 ± 13	NA (30% of pts. < 30%)	NA	In-H	NA	2.6
USPELLA Registry	637	Impella 2.5	70	Complex anatomy, comorbidities, low LVEF	NA	30 ± 15	NA	In-H	NA	2.8
cVAD Registry	891	Impella 2.5 e CP	70	Elective/urgent HR-PCI	NA	30 ± 16	34%	In-H	4.3	3.3

CHIP: complex high-risk indicated procedures; ACS: acute coronary syndrome; MAE major adverse events; 3VD: 3 vessel disease; ULMCA: unprotected left main coronary artery disease; RCT: randomized control trials; in-H: in hospital; HR-PCI: high-risk percutaneous coronary intervention.
[a] Intention-to-treat analysis.

Please cite this article as: A. Chieffo, F. Burzotta, F. Pappalardo, et al., Clinical expert consensus document on the use of percutaneous left ventricular assist support device..., International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2019.05.065

hemodynamic condition at the time of PCI, the anticipated risk of hemodynamic compromise during the procedure, and the need for hemodynamic support after revascularization [5] (Table I).

Even though there are not clinical evidence in dedicated randomized trials, based on practice supported PCI by Impella, mainly CP, is recommended before PCI in patients with low LVEF (<35%) together with ≥1 of the following high-risk features: complex CTO PCI needing retrograde approach (ischemic time of donor vessel), CTO PCI with rotational atherectomy and hemodynamic instability. Even though LVEF >35% is not an indication to pLVAD, it may be useful when a complex CTO procedure requires retrograde approach through last remaining patent conduit in patient with double CTO or in case of significant hemodynamic instability that precluded completing PCI at first attempt. ECMO have to be considered as bail-out strategy in case of acute hemodynamic compromise during the complex procedure.

The consensus of the panels is that the pLVAD use in CTO non emergent PCI is indicated as preventive strategy in symptomatic or ischemic patients with 1) severely reduced LVEF and complex anatomical setting, if not amenable for surgery, including high-risk CTO features; 2) less than severe LVEF and complex anatomical settings as second attempt after a failed CTO-PCI because of hemodynamic instability or CTO-PCI retrograde from last remaining vessel.

5.4. Last remaining vessel

Last remaining vessel is defined as a sole remaining conduit, native artery or bypass graft, with occlusion of the native and bypass supplies to the remaining two coronary territories. Here, the PCI is recommended when chronic occlusion revascularization is judged not feasible due to either clinical and angiographic consideration, or uncertainty of ischemia or viability in the myocardial territory subtended by the occluded coronary artery. However, this is a CHIP due to large territory involved and anticipated risk of hemodynamic compromise during the procedure. In fact, transient interruption of coronary blood flow with a balloon may cause severe hypotension or collapse. Furthermore, any dysrhythmia, a no-reflow phenomenon, intervals of ischemia-reperfusion injury, or any procedural complication may be life-threating. For all the above reasons, pLVAD protected PCI is needed in this setting. In a selected group of patients with severe co-morbidities, complex angiographic features or when high-pressure dilatations or atherectomy were required, an hemodynamic support may be deemed necessary even in absence of severely LV dysfunction [5] (Table I).

The consensus of the panels is that in case of non-emergent last remaining vessel revascularization non amenable for CABG associated with LVEF dysfunction a pLVAD protected PCI, is strongly indicated as life-saving strategy.

5.5. Diffuse and calcified lesions

In order to achieve an optimal result when treating lesions characterized as high anatomical complexity (chronic total occlusions, diffuse or severely calcific lesions) prolonged PCI balloon inflations, high pressure balloon dilation, radio-frequency or laser-based technologies and rotational atherectomy are often needed. Moreover no-reflow phenomenon is more frequently observed in this setting (see below). This can lead to hypotensive events [23] and therefore hemodynamic collapse. Patients with moderate or severe systolic function depression are at higher risk. Interestingly, the use of rotational atherectomy in the PROTECT II trial was significantly higher in the Impella group [23] (Table I).

Data are largely missing. Notwithstanding, the consensus is that the pLVAD non emergent protected PCI of diffused and calcified lesions is indicated in patients considered at risk because of the coronary disease (see above) and severe LV dysfunction especially when rotational atherectomy is required.

5.6. High-risk slow-no reflow including saphenous vein grafts

Coronary slow- or no-reflow is a phenomenon which may complicate a PCI, either in the context of stable coronary artery disease or ACS, leading to poor procedural and short-term outcome [24]. It is estimated that its incidence is up to 60% after primary PCI for ST-elevation ACS [25]. Furthermore, this phenomenon is particularly frequent when PCI is performed in degenerated saphenous vein grafts (SVGs) [26]. Predictors of PCI-related coronary anatomical or functional slow/no-reflow include both lesion-specific features, such as high thrombotic burden, long disease, post-dilatation in the context of large plaque burden, SVG disease, and patient-specific features, such as time to reperfusion, low systolic blood pressure or left ventricular dysfunction at presentation [27]. Given the absence of effective therapies in this setting, the adoption of a protected PCI may play a role, not only when the risk slow/no reflow is high but also when the related hemodynamic compromise is significant, especially in patients with complex anatomy and severe LV dysfunction (Table I).

The consensus of the panels is that the pLVAD use in this setting is indicated as bail-out strategy in case of slow-no reflow not promptly responsive to drugs and associated with hemodynamic decay of the CHIP patients.

5.7. Hemodynamic instability

Hemodynamic instability is a condition of low blood pressure and inadequate organ perfusion that requires inotropic or mechanical support to ensure sufficient cardiac output. Severity of the hemodynamic impairment, as well as the effectiveness of circulatory support, can be assessed by the continuous monitoring of the heart rate, blood pressure, cardiac output, central venous pressure, urine output and pulmonary artery pressure.

Performing CHIP in patients with acute ischemia or severe LVEF dysfunction and hemodynamic instability bares a high-risk of hemodynamic crush with consequent risk of irreversible shock and death. Interventional cardiologists must be trained to identify such high-risk situations by understanding the importance of the medical history, the state of organ damage, the coronary anatomy, lesion's morphology and the nature of the acute clinical event. Proficiency on intensive care and LV mechanical support during interventions in such settings is key. Conventional therapy is largely driven by the use of inotropes and vasopressors, which have long been known to be associated with high mortality rates as both dosage and number is increased [2,28]. Recent randomized control trials (RCTs) have challenged the benefit of IABP in the setting of acute myocardial infarction with hemodynamic compromise or cardiogenic shock. Even basic hemodynamic benefit was not observed because IABP is only augmenting the native heart function, which is low or nonexistent in this population. Accordingly, current European Guidelines left uncertain the IABP role in setting different from ACS or in CHIP [1]. The introduction of percutaneous mechanical support systems adds a relatively easy to set-up alternative to the interventional toolbox and it has already been demonstrated the safety of the percutaneous systems and the effectiveness of their hemodynamic performance [28,29]. However, the evidence of clinical value remains under investigation mainly because of two reasons: the heterogeneity of the populations analyzed on the one hand, and the unsolved debate of starting hemodynamic support before or after revascularization on the other.

The consensus of the panel is for a preventive proficient use of pLVAD in situations of hemodynamic instability, but confirmatory clinical data is missing.

5.8. Severe left ventricular dysfunction (LVEF <35%) and/or heart failure

Severe LV systolic dysfunction (LVEF <35%) and congestive heart failure are key clinical features associated with increased morbidity and mortality during PCI [7]. Additionally, any history of previous PCI

Please cite this article as: A. Chieffo, F. Burzotta, F. Pappalardo, et al., Clinical expert consensus document on the use of percutaneous left ventricular assist support device..., International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2019.05.065

complicated by heart failure signs or hemodynamic compromise, should be evaluated as a warning sign even in moderate LV systolic dysfunction patients. The abovementioned studies on pLVAD have demonstrated superior hemodynamic support and maintenance of cardiac power, an independent predictor of mortality especially in this setting [5,23]. As a matter of fact, the PROTECT II trial showed that the hypotensive events occurred less often in the Impella group [23]. Data from registries have further validated the benefits of Impella in real-world patients undergoing CHIP, showing a marked improvement in residual SYNTAX score after intervention and a more CR rate associated with a significant improvement in LV systolic function [15]. ECMO provides excellent circulatory support, notwithstanding in clinical practice it is used as bail-out support and it's not an off-loading system (see above). On the contrary, the off-loading system Impella is used also electively.

The consensus of the panel is that in non-emergent CHIP patients with severe left ventricular dysfunction (LVEF <35%) and/or heart failure the pLVAD should be considered in a heart team approach and should be implanted prior to intervention in an effort to avoid "crashing onto support" and to enable CR when feasible in patients without a surgical revascularization option.

5.9. PCI in patients with severe concomitant heart valve disease

Patients with aortic stenosis and very poor LVEF undergoing balloon valvuloplasty may have high-risk of hemodynamic crash (especially in the case of aortic regurgitation development). Low LVEF patients with concomitant aortic valve disease and CAD undergoing CHIP may do not tolerate procedure-related ischemia [30].

Among the different available mechanical cardiac assistance devices, Impella has the unique feature of requiring a correct placement across the aortic valve, with its distal portion deeply seated into the left ventricle. Accordingly, the aortic valve function is systematically (transiently) affected and conflicts with the complex mitral valve apparatus may occur in the case of catheter malposition. In the past, such considerations suggested to rule out Impella use in patients with severe left heart valve disease. On the bases of both an increased experience with Impella in cardiogenic shock and percutaneous valve intervention procedures, some centers started to consider Impella in selected heart valve disease patients. To date, case reports have been published on the successful use of Impella to help stabilize patients with cardiogenic shock due to aortic stenosis, aortic regurgitation or mitral regurgitation.

Besides these heterogeneous and anecdotal experiences, Impella has started to be considered as a valuable option in selected aortic stenosis patients undergoing emergent balloon aortic valvuloplasty or prior to transcatheter aortic valve implantation TAVI. In particular, the following specific scenarios have been highlighted as promising: the stabilization and bridging to (surgical or percutaneous) valve replacement of aortic stenosis patients who crashed after balloon aortic valvuloplasty and the assistance of high-risk patients with aortic stenosis undergoing emergent balloon aortic valvuloplasty alone [31,32] or elective TAVI with combined complex CAD requiring PCI [33,30].

Impella might be also indicated in patients with severe mitral regurgitation and depressed LVEF undergoing PCI.

The evidence in the field is actually by far inconclusive and further studies are needed to establish the role of Impella in critically ill patients with valve heart disease.

The consensus of the panels is that non emergent pLVAD use in patients with severe heart valve disease is actually not recommended. Percutaneous LVAD bail-out use to stabilize patients who crushed after aortic valvuloplasty may be considered in experienced centers when further valve treatments are considered feasible.

6. Conclusions

Currently available CE mark pLVADs have shown different efficacy and safety in non-emergent CHIP patients and their specific use should be evaluated on the basis of patient characteristics and clinical conditions assessed by a multidisciplinary team. However, because of the paucity of data, in order to further validate pLVAd in this setting, RCTs and national and international registries with larger number of patients and longer clinical follow up are warranted.

Acknowledgments

None.

Funding

None.

Declaration of Competing Interest

AC and GT received speakers fees from Abiomed and GADA, FB and CT received speaker's fees from Abiomed, Abbott and Medtronic; FP, CB, RG, GM, EN, FR, BCA, ORL, RM, RS, AF, JBS, APDP, GM, GE have no conflicts to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.05.065.

References

[1] Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ECS/EACTS guidelines on myocardial revascularization. Eur. Heart J. 2018; doi:https://doi.org/10.1093/eurheartj/ehy394.PMID: 30165437.

[2] Thiele H, Zeymer U, Neumann FJ, et al; IABP-SHOCK II Trial Investigators. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N. Engl. J. Med. 2012 Oct 4; 367 (14): 1287–96. doi:https://doi.org/10.1056/NEJMoa1208410.Epub 2012 Aug 26. PubMed PMID: 22920912.

[3] Bass TA. High-risk percutaneous coronary interventions in modern day clinical practice: current concepts and challenges. Circ Cardiovasc Interv. 2015 Dec; 8(12): e003405. doi:https://doi.org/10.1161/CIRCINTERVENTIONS.115.003405. PubMed PMID: 26628592.

[4] Myat A, Patel N, Tehrani S, et al. Percutaneous circulatory assist devices for high-risk coronary intervention. JACC Cardiovasc Interv. 2015 Feb; 8(2): 229–244. doi:https://doi.org/10.1016/j.jcin.2014.07.030. Review. PubMed PMID: 25700745.

[5] Rihal CS, Naidu SS, Givertz MM, et al; Society for Cardiovascular Angiography and Interventions (SCAI); Heart Failure Society of America (HFSA); Society of Thoracic Surgeons (STS); American Heart Association (AHA), and American College of Cardiology (ACC). 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. J Am Coll Cardiol. 2015 May 19; 65 (19): e7-e26. doi:https://doi.org/10.1016/j.jacc.2015.03.036.Epub 2015 Apr 7. PubMed PMID: 25861963.

[6] F. Pappalardo, C. Schulte, M. Pieri, et al., Concomitant implantation of Impella on top of VA-ECMO may improve survival of patients with cardiogenic shock, Eur. J. Heart Fail. 19 (3) (2017 Mar) 404–412, https://doi.org/10.1002/ejhf.668 (Epub 2016 Oct 6).

[7] Atkinson TM, Ohman EM, O'Neill WW, et al; Interventional Scientific Council of the American College of Cardiology. A practical approach to mechanical circulatory support in patients undergoing percutaneous coronary intervention: an interventional perspective. JACC Cardiovasc Interv. 2016 May 9; 9(9): 871–83. doi:https://doi.org/10.1016/j.jcin.2016.02.046. Review. PubMed PMID: 27151604.

[8] Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation. 2011 Dec 6; 124 (23): e574-651. doi:https://doi.org/10.1161/CIR.0b013e31823ba622.Epub 2011 Nov 7. Erratum in: Circulation. 2012 Feb 28; 125(8): e412. Dosage error in article text. PubMed PMID: 22064601.

[9] https://www.nice.org.uk/guidance/ipg633/evidence/overview-final-pdf-6599454877.

[10] S.A. Rios, C.A. Bravo, M. Weinreich, et al., Meta-analysis and trial sequential analysis comparing percutaneous ventricular assist devices versus intra-aortic balloon pump during high-risk percutaneous coronary intervention or cardiogenic shock, Am. J. Cardiol. (2018)https://doi.org/10.1016/j.amjcard.2018.07.01130146099.

[11] Basir MB, Schreiber TL, Grines CL, et al. Effect of early initiation of mechanical circulatory support on survival in cardiogenic shock. Am. J. Cardiol. 2017 Mar 15; 119(6):

845–851. doi:https://doi.org/10.1016/j.amjcard.2016.11.037.Epub 2016 Dec 18. PubMed PMID: 28040188.
[12] O'Neill WW, Schreiber T, Wohns DH, et al. The current use of Impella 2.5 in acute myocardial infarction complicated by cardiogenic shock: results from the USpella Registry. J. Interv. Cardiol. 2014 Feb; 27(1): 1–11. doi:https://doi.org/10.1111/joic.12080. Epub 2013 Dec 13. PubMed PMID: 24329756.
[13] Borges N, Kapadia SR, Ellis SG. Unprotected left main coronary artery disease: management in the post NOBLE and EXCEL era. Interv. Cardiol. 2017 Sep; 12(2): 92–96. doi: 10.15420/icr.2017:18:2. PubMed PMID: 29588736.
[14] Schreiber T, Wah Htun W, et al. Real-world supported unprotected left main percutaneous coronary intervention with Impella device; data from the USpella registry. Catheter. Cardiovasc. Interv. 2017 Oct 1; 90(4): 576–581. doi:https://doi.org/10.1002/ccd.26979.Epub 2017 Apr 18. PubMed PMID: 28417594. +.
[15] Maini B, Naidu SS, Mulukutla S, et al. Real-world use of the Impella 2.5 circulatory support system in complex high-risk percutaneous coronary intervention: the USpella Registry. Catheter. Cardiovasc. Interv. 2012 Nov 1; 80(5): 717–25. doi: https://doi.org/10.1002/ccd.23403.Epub 2012 Apr 25. PubMed PMID: 22105829.
[16] Cohen MG, Matthews R, Maini B, et al. Percutaneous left ventricular assist device for high-risk percutaneous coronary interventions: real-world versus clinical trial experience. Am Heart J. 2015; doi:10.1016/j.ahj.2015.08.009; PMID: 26542494.
[17] Sandoval Y, Brilakis ES, Canoniero M, et al. Complete versus incomplete coronary revascularization of patients with multivessel coronary artery disease. Curr Treat Options Cardiovasc Med. 2015 Mar; 17(3): 366. doi:https://doi.org/10.1007/s11936-015-0366-1. PubMed PMID: 25708977.
[18] Ong AT, Serruys PW. Complete revascularization: coronary artery bypass graft surgery versus percutaneous coronary intervention. Circulation 2006 Jul 18; 114(3): 249–55. PubMed PMID: 16847164.
[19] Zimarino M, Calafiore AM, De Caterina R. Complete myocardial revascularization: between myth and reality. Eur. Heart J. 2005 Sep; 26 (18): 1824–30. Epub 2005 Apr 11. Review. PubMed PMID: (15824076).
[20] Gössl M, Faxon DP, Bell MR, et al. Complete versus incomplete revascularization with coronary artery bypass graft or percutaneous intervention in stable coronary artery disease. Circ Cardiovasc Interv. 2012 Aug 1; 5(4): 597–604. doi:https://doi.org/10.1161/CIRCINTERVENTIONS.111.965509. Review. PubMed PMID:22896575.
[21] Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet 2013 Feb 23; 381 (9867): 629–38. doi:https://doi.org/10.1016/S0140-6736(13)60141-5. PubMed PMID: 23439102.
[22] Sarno G, Garg S, Onuma Y, et al; ARTS-II Investigators. Impact of completeness of revascularization on the five-year outcome in percutaneous coronary intervention and coronary artery bypass graft patients (from the ARTS-II study). Am. J. Cardiol. 2010 Nov 15; 106 (10): 1369–75. doi:https://doi.org/10.1016/j.amjcard.2010.06.069. Epub 2010 Oct 1. PubMed PMID: 21059423.
[23] O'Neill WW, Kleiman NS, Moses J, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. Circulation 2012; Oct 2; 126 (14): 1717–27. doi:https://doi.org/10.1161/CIRCULATIONAHA.112.098194; PMID: 22935569.
[24] Kunadian V, Giugliano RP, Newby LK, et al. Angiographic outcomes with early eptifibatide therapy in non-ST-segment elevation acute coronary syndrome (from the EARLY ACS Trial). Am. J. Cardiol. 2014 Apr 15; 113(8): 1297–305. doi:https://doi.org/10.1016/j.amjcard.2014.01.404. Epub 2014 Jan 31. PubMed PMID: 24607027.
[25] Ibanez B, James S, Agewall S, et al; ESC Scientific Document Group. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018 Jan 7; 39(2): 119–177. doi:https://doi.org/10.1093/eurheartj/ehx393.PubMed PMID: 28886621.
[26] Lee M, Kong J. Current state of the art in approaches to saphenous vein graft interventions. Interv. Cardiol. 2017 Sep; 12(2): 85–91. doi: 10.15420/icr.2017:4:2. PubMed PMID: 29588735; PubMed Central PMCID: PMC5808481.
[27] Lee MS, Park SJ, Kandzari DE, et al. Saphenous vein graft intervention. JACC Cardiovasc Interv. 2011 Aug; 4(8): 831–43. doi:https://doi.org/10.1016/j.jcin.2011.05.014.Review.PubMed PMID: 21851895.
[28] Samuels LE, Kaufman MS, Thomas MP, et al. Pharmacological criteria for ventricular assist device insertion following postcardiotomy shock: experience with the Abiomed BVS system. J. Card. Surg. 1999 Jul-Aug; 14(4): 288–93. PubMed PMID: 10874615.
[29] Kirtane AJ, Doshi D, Leon MB, et al. Treatment of higher-risk patients with an indication for revascularization: evolution within the field of contemporary percutaneous coronary intervention. Circulation. 2016 Aug 2; 134(5): 422–31. doi:https://doi.org/10.1161/CIRCULATIONAHA.116.022061. PubMed PMID: 27482004.
[30] Spiro J, Venugopal V, Raja Y, et al. Feasibility and efficacy of the 2.5 L and 3.8 L impella percutaneous left ventricular support device during high-risk, percutaneous coronary intervention in patients with severe aortic stenosis. Catheter. Cardiovasc. Interv. 2015 May; 85(6): 981–9. doi:https://doi.org/10.1002/ccd.25355.Epub 2014 Jan 31. PubMed PMID: 24408882.
[31] Karatolios K, Chatzis G, Luesebrink U, et al. Impella support following emergency percutaneous balloon aortic valvuloplasty in patients with severe aortic valve stenosis and cardiogenic shock. Hellenic J Cardiol. 2018 Mar 21. pii: S1109–9666 (17) 30541–9.
[32] Singh V, Yadav PK, Eng MH, et al. Outcomes of hemodynamic support with Impella in very high-risk patients undergoing balloon aortic valvuloplasty: results from the Global cVAD Registry. Int. J. Cardiol. 2017 Aug 1; 240: 120–125. doi:https://doi.org/10.1016/j.ijcard.2017.03.071.Epub 2017 Mar 22. PubMed PMID: 28377189.
[33] C. Briguori, A. Focaccio, C. D0Amore, et al., Elective mechanical circulatory support in the percutaneous treatment of patients with combined complex coronary artery disease and severe aortic valve stenosis, J Invasive Cardiol. 31 (3) (2019 Mar) 52–56 (PubMed PMID: 30819975).

Please cite this article as: A. Chieffo, F. Burzotta, F. Pappalardo, et al., Clinical expert consensus document on the use of percutaneous left ventricular assist support device..., International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2019.05.065