NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Percutaneous insertion of a temporary heart pump for left ventricular haemodynamic support in high-risk percutaneous coronary interventions

Some people having elective or urgent high-risk procedures to their heart arteries (percutaneous coronary interventions) may need support with circulatory blood flow support devices in PCI to reduce the risk of their heart and circulation failing during the operation. In this procedure, a catheter (a thin tube) with a pump in the end is put into the heart through a large artery (usually in the groin or arm pit). The aim is to help the heart pump blood round the body during a heart operation.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety

and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in April 2018.

Procedure name

- Percutaneous insertion of a temporary heart pump for left ventricular hemodynamic support in high-risk percutaneous coronary interventions.

Specialist societies

- The British Cardiovascular Intervention Society (BCIS)
- The British Cardiovascular Society (BCS)
- Society of Cardiothoracic Surgeons of Great Britain and Ireland
- Royal College of Physicians
- Royal College of Surgeons.

Description of the procedure

Indications and current treatment

Additional support for the heart is not usually needed with angioplasty or percutaneous coronary intervention (PCI). However, a subset of high-risk patients with extensive or complex coronary artery disease, (unprotected left main disease, last remaining vessel or multi-vessel disease), poor left ventricular function, ongoing myocardial ischemia, cardiogenic shock and co-morbidity may benefit from some form of heart support during their angioplasty procedure.

Temporary percutaneous mechanical haemodynamic support (MHS) can be used prophylactically in some elective high-risk angioplasty procedures or in urgent procedures. The aim is to support the patient's circulatory system, provide blood flow to increase cardiac output, unload the ventricle and improve blood flow to maintain haemodynamic stability. This minimises myocardial ischemia and reduces the risk of haemodynamic collapse during the procedure. Intra-aortic balloon pumps (IABPs) are the most common temporary percutaneous MHS devices used. Intra- or extra-corporeal pumps may also be used for temporary

hemodynamic support. Percutaneous left ventricular-assist devices for haemodynamic support are sometimes used instead of IABPs.

What the procedure involves

Inserting a temporary percutaneous MHS device can be done before, during or after PCI in selected high-risk patients, and is then taken out when the patient is stable.

The procedure is done under local anaesthesia. An introducer sheath is inserted into a large artery (usually the femoral or axillary artery) and a guidewire is passed into the left ventricle. A catheter with an integrated pump at its distal end is passed over the guidewire, into the ascending aorta and across the aortic valve into the left ventricle. Fluoroscopic imaging is used during the procedure. The catheter is then attached to an automated external console which controls the pump speed and monitors its function, allowing blood to be taken from the left ventricle and pumped into the ascending aorta.

Different miniature, catheter-based, intravascular devices are available and the precise implantation technique varies according to the device. One device needs a trans-septal puncture to be done.

Efficacy summary

Mortality

In an Ontario Health Technology Assessment (HTA), results from 10 studies (1 randomised controlled trial [RCT PROTECT II] and 9 observational studies [1 comparative [Boudoulas et al, 2012] and 8 non-comparative studies]) for high-risk PCI reported that compared with IABPs, temporary percutaneous mechanical hemodynamic support [MHS] (with Impella 2.5) showed no significant difference in mortality (GRADE low). In the RCT, 30 day mortality rate was not significantly different between the groups in intent-to-treat analysis (7.6% versus. 5.9% p=0.47) and per-protocol (6.9% versus. 6.2%; p=0.74) analysis. The 90-day mortality between temporary percutaneous MHS and IABP was similar (intent-to-treat analysis: 12.1% versus. 8.7%, p = 0.24; per-protocol analysis: 11.6% versus. 9.0%, p = 0.38). In a retrospective chart review of patients with acute coronary syndrome undergoing high-risk PCI treated with temporary percutaneous MHS (n = 13) or IABP (n = 62), at 1-year follow-up, mortality rates were 15.3% in the temporary percutaneous MHS group and 25.8% in the IABP group (p = 0.72) (Boudoulas 2012). The 30-day mortality rates ranged from 0% to 10% in the 8 observational studies. The 2 studies from the USpella registry (Cohen 2015; Miani 2012) reported in-hospital mortality rates of 2.8% to 3.4%.[1]

The HTA also reported results from 7 studies (1 RCT [ISAR-SHOCK trial] and 6 observational studies [1 comparative [Manzo-Silberman 2013] and 5 non-comparative studies]) for cardiogenic shock. Evidence from the RCT reported that there was no difference in 30-day mortality rates between temporary percutaneous MHS (with Impella) and IABP groups (46% versus 46%) (GRADE low). Similarly, in the comparative study there was no statistically significant difference in 30-day mortality rate between the temporary percutaneous MHS (with Impella) and IABP groups (23% versus 29.5%, p=0.61). In the non-comparative studies, the mortality rates at different follow-up periods largely varied.[1]

In a meta-analysis of 3 RCTs in patients with cardiogenic shock comparing temporary percutaneous MHS with IABP, the pooled 30-day all-cause mortality data showed no significant difference between the groups (Relative risk [RR]1.06, 95% CI 0.68 to 1.66).[2]

In a meta-analysis of 20 studies on the use of temporary percutaneous MHS during high-risk PCI, pooled 30-day mortality rate of 3.5% (95% confidence interval [CI] 2.2% to 4.8%; I^2 20%) and 8% (2.9%, 13.1%, I^2 55%) without significant heterogeneity between studies were reported in the 12 studies that used Impella and in the 7 studies that used TandemHeart, respectively.[3]

A systematic review of 20 studies (4 RCTs, 2 comparative observational studies, and 14 non-comparative observational studies) on temporary percutaneous MHS (with Impella) for high-risk PCI (including cardiogenic shock) reported that the 30-day rate of all-cause mortality was similar across groups in RCTs conducted in patients with cardiogenic shock or acute myocardial infarction undergoing emergency PCI (Syefarth 2009: 46% in both groups; Ouweneel 2016: 46% versus 50%). In 1 RCT (O'Neil 2012) it was not statistically significant (7.6% versus 5.9%, p=0.47). In most non-comparative studies the 30-day rates of all-cause mortality were generally low (range 3.7% to 10%). Higher rates ranging between 18 to 74% were seen in 4 cohort studies.[4]

Major adverse cardiac events (MACE) (including myocardial infarction, stroke, and revascularization)

In the Ontario HTA, results from 9 studies (1 RCT [PROTECT II] and 8 non-comparative observational studies) for high-risk PCI reported that compared with IABPs, temporary percutaneous MHS (with Impella 2.5) showed no significant difference in MACEs (GRADE low). In the RCT, the overall 30-day MACE rate was not significantly different between the groups in intent-to-treat analysis (35.1% versus. 40.1%; p=0.28) and per-protocol (34.3% versus. 42.2%, p=0.092) analysis. The 90-day overall MACE rate for temporary percutaneous MHS group was significantly lower than IABP group in per-protocol analysis (40% versus. 51%, p = 0.023) but not in the intention-to-treat analysis (40.6% versus. 49.3%, p

= 0.066). The stroke rates were significantly higher in the IABP group (ITT analysis 0% versus 1.8%, p=0.043). Six non-comparative observational studies reported an overall 30-day MACE rate of 5% to 20%.[1]

The HTA also reported results from 5 studies (1 RCT [ISAR-SHOCK trial] and 4 observational studies [1 comparative [Manzo-Silberman 2013] and 3 non-comparative studies]) for cardiogenic shock. In the RCT and comparative observational study, there was no difference in MACEs between temporary percutaneous MHS group (with Impella) and IABP group at 30-day follow-up (GRADE low). In 3 non-comparative studies, stroke rates varied between less than 2% to 6% and in 2 studies the rate of revascularisation ranged between 2.6% to 10.8%.[1]

In the meta-analysis of 20 studies on the use of temporary percutaneous MHS during high risk PCI, pooled 30-day myocardial infarction rate of 3.3% (95% CI 1.4% to 5.3%; I^2 79%) with significant heterogeneity between studies and 3.9% (0%, 7.8%, I^2 0%) without significant heterogeneity between studies were reported in the 12 studies that used Impella and in the 7 studies that used TandemHeart, respectively.[3]

In a retrospective case series of 891 patients from the global catheter-based ventricular assist device registry, the use of temporary percutaneous MHS (with Impella 2.5 or CP) during elective or urgent high-risk PCI in patients without severely reduced left ventricular ejection fraction (LVEF defined as more than 35%, n=230) was compared with patients with severely reduced LVEF (with LVEF less than 35%, n=661). The patients with LVEF more than 35% had severe comorbidities and complex angiographic features but the major adverse cardiovascular and cerebral event rates were similar with no significant differences between the 2 groups (3.78% versus 1.74%; p=0.193).[5]

The systematic review of 20 studies (4 RCTs, 2 comparative observational studies, and 14 non-comparative observational studies) on temporary percutaneous MHS (with Impella 2.5 or 5.0) for high-risk PCI (including cardiogenic shock) reported that in 2 RCTs (O'Neil 2012 and Ouweneel 2016), the rates of MACE was low and no significant differences were observed at 30 days, 90 days and 1 year follow-up (O'Neil 2012: MACE at 90 days [40.6% versus 49.3%, p=0.07]; revascularisation 3.6% versus 7.8%, p=0.06). The only significant difference was observed for stroke at 30 days (0% versus 1.8%, p=0.04). In non-comparative studies, rates of MACE were slightly higher (range 5% to 20%) and myocardial infarction varied greatly (range 0 to 64%). Rates of stroke (range 0 to 2%) and repeat revascularisation (range 0 to 6%) were low.[4]

Major adverse events (The composite endpoint components included: all-cause mortality, Q-wave or non–Q-wave myocardial infarction (MI), stroke or transient ischemic attack, any repeat revascularization procedure, need for cardiac or

vascular operation, acute renal insufficiency, severe intra-procedural hypotension requiring therapy, cardiopulmonary resuscitation or ventricular tachycardia requiring cardioversion, aortic insufficiency, and angiographic failure of PCI).

A prespecified sub-group analysis of PROTECT II RCT (comparing temporary percutaneous MHS [with Impella 2.5] versus IABP) during high-risk PCI evaluated the impact of device learning on the outcomes of PROTECT II trial (excluding the first patients in each group at each site). The analysis reported a trend toward higher major adverse events (MAEs) at 30 days for the subgroup of first (n=58) versus remaining patients with Impella 2.5 (n=167): 44.8% versus 31.7%, p = 0.072. MAE rates for the first (n=62) and remaining patients with IABP (n=161) were similar at 30 days. After exclusion of the first patient in each group, MAE rates for Impella 2.5 (n=167) and IABP (n=160) were 31.7% versus 40.0% (p = 0.119) at 30 days and 38.0% versus 50.0% (p = 0.029) at 90 days.[7]

Haemodynamic stability

In the HTA, results from 5 studies (1 RCT [PROTECT II trial] and 4 non-comparative observational studies) for high-risk elective or emergency PCI reported that compared with intra-aortic balloon pumps (IABPs), temporary percutaneous MHS (with Impella-2.5), improved hemodynamic parameters (GRADE low to very low). Various outcome measures were used to measure hemodynamic stability in these studies. In the RCT, patients with temporary percutaneous MHS had a significantly lower maximal decrease in cardiac power output than those using IABPs (Impella 2.5: −0.04 ± 0.24 W versus IABP: −0.14 ± 0.27 W; p =0.001). The 2 USpella registry studies (Cohen 2015, Miani 2012) reported that 3.4 to 7.1% of patients has transient hypotension during support. Similarly 2 other small studies (Dixon 2009, Ilidormitis 2011) have also reported 100% hemodynamic stability[1].

In the same HTA, results from 5 studies (1 RCT [ISAR-SHOCK trial] and 4 observational studies) for cardiogenic shock reported that compared with IABPs, temporary percutaneous MHS (with Impella 2.5) improved hemodynamic stability (GRADE very low). Various outcome measures were used to measure hemodynamic stability before and after support in these studies. Evidence from the RCT (Seyfarth 2008) showed patients with temporary percutaneous MHS had a significant increase in cardiac index after 30 minutes of support, compared with those using IABPs (Impella: 0.49 ± 0.46 L/min/m^2 versus IABP: 0.11 ± 0.31 L/min/m^2, p = 0.02). There was no significant difference in serum lactate between groups. All non-comparative studies (Casassus 2015, O'Neil 2014, Lauten 2013, and Griffith 2013) reported that patients with temporary percutaneous MHS have significantly improved hemodynamic parameters, including systolic and diastolic blood pressure, cardiac output, cardiac index, and pulmonary arterial pressure.[1]

In the meta-analysis of 3 RCTs in patients with cardiogenic shock (the majority of whom had PCI) comparing temporary percutaneous MHS with IABP, after device implantation patients with temporary percutaneous MHS had higher cardiac index (mean difference [MD] 0.35 L/min/m^2, 95% confidence interval [CI] 0.09 to 0.61, p<0.01), higher mean arterial pressure (MD 12.8 mmHg, 95% CI 3.6 to 22.0, p<0.01), and lower pulmonary capillary wedge pressure (MD −5.3 mm Hg, 95% CI −9.4 to −1.2, p<0.05) compared with IABP patients.[2]

The systematic review of 20 studies (4 RCTs, 2 comparative observational studies, and 14 non-comparative observational studies) on temporary percutaneous MHS (with Impella 2.5, 5.0) for high-risk PCI (including cardiogenic shock) reported improved hemodynamic outcomes. Across studies, the mean cardiac output was 2.1L/min and the mean arterial pressure increased. In 1 RCT (Seyfarth 2008), the mean arterial pressure increased from 78±16 mmHg before support to 87±18 mmHg after support (p=0.06). In 1 study (Dixon 2009) MAP decreased from baseline 84.5±14.3 mmHg to 76±11.9 mmHg (p=0.004) after support, and in another study (Miani 2012) MAP increased from baseline 83±18 mmHg to 89±18 mmHg (p<0.0001) after support.[4]

Acute kidney injury (AKI)

In a retrospective comparative case series of 230 patients with LVEF less than 35% (115 patients with temporary percutaneous MHS [with Impella 2.5] and 115 unsupported matched controls) who had high-risk PCI, the incidence of in-hospital AKI was less in temporary percutaneous MHS patients compared to that in unsupported control patients (5% [6/115] versus 28% [32/115], p<0.001). The use of Impella 2.5 during high-risk PCI was independently associated with a significant reduction (adjusted odds ratio, 0.13; 95% CI, 0.09–0.31; P<0.001) in the risk of developing AKI. This protective effect persisted in patients with temporary percutaneous MHS, despite pre-existing chronic kidney disease (CKD) or a lower left ventricular ejection fraction (LVEF), (adjusted odds ratio [OR], 0.63; 95% CI, 0.25–0.83; p=0.04 and adjusted OR, 0.16; 95% CI, 0.12–0.28; p<0.001, respectively).[6]

Safety summary

Bleeding complications (including access site hematoma and major bleeding needing transfusion)

In the Ontario Health Technology Assessment (HTA), bleeding complications were reported in 10 observational studies (1 comparative and 9 non-comparative studies) for high-risk PCI. In the comparative study [Boudoulas 2012], the in-hospital rate of blood transfusion due to major bleeding was not statistically different between IABP and temporary percutaneous MHS groups (GRADE very low). In the non-comparative studies, the rate of major bleeding needing blood

transfusion ranged from 9.7% to 34.2%. The rate of femoral hematoma ranged from 8.6 to 40%.[1]

In the same study, bleeding complications were reported in 1 RCT [ISAR-SHOCK trial] and 5 observational studies (1 comparative [Manzo-Silberman 2013] and 4 non-comparative studies) for cardiogenic shock. In the RCT, the rate of haemolysis significantly increased in the temporary percutaneous MHS (Impella) group when compared with IABP group (GRADE low). In the comparative study, more patients in the temporary percutaneous MHS group (with Impella) needed blood transfusion from major bleeding than patients in the IABP group (26% versus 9%, p=0.06). In the non-comparative studies the rates of bleeding needing blood transfusion (18 to 24%), needing surgery (2.6 to 4.2%) and haemolysis (6.3 to 10.3%) were similar.[1]

In the meta-analysis of 3 RCTs in patients with cardiogenic shock, bleeding was significantly more in patients with temporary percutaneous MHS compared with patients treated with IABP (relative risk [RR] 2.35, 95% CI 1.40–3.93, p<0.01).[2]

In the meta-analysis of 20 studies on the use of temporary percutaneous MHS during high-risk PCI, pooled clinical major bleeding rate of 7.1% (95% CI 4.3% to 9.9%; I^2 63%) with significant heterogeneity between studies and 3.6% (1.1%, 6.1%, I^2 0%) without significant heterogeneity between studies were reported in the 12 studies that used Impella and in the 7 studies that used TandemHeart, respectively.[3]

In the systematic review of 20 studies (4 RCTs, 2 comparative observational studies, and 14 non-comparative observational studies) on temporary percutaneous MHS (with Impella) for high-risk PCI, non-comparative studies reported that access site hematoma rates at 30 days were heterogeneous, with 3 studies reporting rates of 8% and 2 studies reporting higher rates (15.3% and 40%).[4]

Vascular complications

In the Ontario HTA, vascular complications were reported in 6 observational studies (1 comparative and 5 non-comparative studies) for high-risk PCI. In the comparative study [Boudoulas 2012], no significant difference was reported for in-hospital vascular complication rates between temporary percutaneous MHS group and IABP group (15.3% versus. 6.4%, p = 0.27) (GRADE low). In 2 non-comparative registry studies (Maini 2012, Cohen 2015), in-hospital rate for major vascular complications (defined as pseudo-aneurysm, arterio-venous fistula, or access site infection) was 4%. The rates for pseudo-aneurysm were 2.6% and 3% in 2 other non-comparative studies.[1]

In the same study, vascular complications were reported in 1 RCT [ISAR-SHOCK trial] and 4 observational studies (1 comparative [Manzo-Silberman 2013] and 3

non-comparative studies) for cardiogenic shock. In the comparative study, no significant difference was reported in vascular complication rates between temporary percutaneous MHS group (with Impella) and IABP group (3% versus 2%, p= 0.9). In 1 non-comparative registry study (O'Neil 2014), 10% patients had vascular complications (defined as surgical intervention on a pseudo-aneurysm, arteriovenous fistula, vessel dissection/perforation, or access site thrombosis) and 4% had limb ischemia. Limb ischemia was also reported in 10% patients in another study (Casassus 2015) and 1 patient in the temporary percutaneous MHS group (with Impella) in the RCT. Other events reported were aortic insufficiency (5.6%) and one case of vein patch rupture.[1]

In the meta-analysis of 3 RCTs in patients with cardiogenic shock, no significant difference was observed in incidence of leg ischaemia in patients with temporary percutaneous MHS compared with patients with IABP (RR 2.59, 95% CI 0.75–8.97, p=0.13).[2]

In the meta-analysis of 20 studies on the use of temporary percutaneous MHS during high-risk PCI, pooled clinical major bleeding rate of 4.9% (95% CI 2.3% to 7.6%; I^2 78%) with significant heterogeneity between studies and 6.5% (3.2%, 9.9%, I^2 0%, p=0.9 for heterogeneity) without significant heterogeneity between studies were reported in the 12 studies that used Impella and in the 7 studies that used TandemHeart, respectively.[3]

Fever or sepsis

In the meta-analysis of 3 RCTs in patients with cardiogenic shock, no significant difference was observed in incidence of fever or sepsis in patients with temporary percutaneous MHS compared with patients with IABP (RR 1.11, 95% CI 0.43 to 2.90).[2]

Mitral regurgitation

Mitral regurgitation a rare complication after temporary percutaneous MHS (with Impella) and unsuccessful PCI was reported in a patient with anterior ST elevation myocardial infarction. The support device was weaned off on day 3 but cardiac index declined. On investigation, new severe eccentric mitral regurgitation was seen and an urgent echocardiogram confirmed ruptured posterior chordae. Another temporary percutaneous MHS (TandemHeart) was placed and the patient was stabilised. Sepsis was resolved on day 8 and patient had mitral valve replacement.[8]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and

about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse event: mechanical interaction with mitral subvalvular apparatus causing mitral regurgitation. They considered that the following were theoretical adverse events: ventricle rupture during insertion and device thrombosis.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous insertion of a temporary heart pump for left ventricular hemodynamic support in high risk percutaneous coronary interventions. The following databases were searched, covering the period from their start to 29.01.2018: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	High-risk patients (including patients in cardiogenic shock) undergoing percutaneous coronary intervention (PCI).
Intervention/test	Percutaneous insertion of a temporary heart pump for left ventricular haemodynamic support in high-risk percutaneous coronary interventions
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 6581 patients from 4 systematic reviews (with prospective, randomised and non-randomised clinical studies and registry data)[1-4], 2 retrospective studies[5-6], 1 randomised controlled trial[7] and 1 case report[8]. There is an overlap of studies in all the systematic reviews.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on percutaneous insertion of a temporary heart pump for left ventricular hemodynamic support in high risk percutaneous coronary interventions

Study 1 Health Quality Ontario (2017)

Details

Study type	Systematic review
Country	Canada
Search period	January 1946 to December 2015 Databases searched: Ovid MEDLINE, Ovid Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), Centre for Reviews and Dissemination (CRD) Health Technology Assessment Database, National Health Service (NHS) Economic Evaluation Database. Health technology assessment websites, reference lists of included studies and other sources were also searched.
Study population and number	n= **18 studies (n=2223)** (**1 randomized controlled trial [RCT] and 10 observational studies for high-risk PCI and 1 RCT and 6 observational studies for cardiogenic shock**)
Age and sex	Not reported
Study selection criteria	Single RCT published in 2008 and all RCTs, systematic reviews, meta-analyses, health technology assessments, observational studies (retrospective chart review, prospective registry) published from 2009 onward, studies that examined Impella percutaneous assist devices in high-risk PCI or cardiogenic shock in English were included. Concurrent use of other mechanical circulatory systems that support blood flow, for example, intra-aortic balloon pump (IABP) or ECMO, case series, case reports, editorials, letters to editor, abstracts, non-systematic reviews, were excluded.
Technique	Temporary percutaneous mechanical hemodynamic support (MHS) devices in high-risk PCI or cardiogenic shock **Devices used in studies: Impella 2.5, Impella 5.0, TandemHeart** High risk PCI: 1 RCT (O'Neil 2012) Impella 2.5 versus IABP; 10 observational studies Cardiogenic shock: 1 RCT (Seyfarth 2008) Impella 2.5 versus IABP; 6 observational studies
Follow-up	**Varied**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: follow-up varied in studies included in the systematic review.

Study design issues: systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). Systematic searches were done, search strategy was peer-reviewed using the PRESS Checklist and screened by one reviewer. Evidence was appraised according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. The quality of evidence was assessed as low or very low. The 2 RCTs included were small, and one was terminated early for ineffectiveness. Most included studies were observational studies with many limitations. This systematic review did not pool data (due to different definitions of composite outcomes and varied time points of the outcomes between the studies) so conclusions were based on a qualitative review of the evidence. Experts were also consulted.

Other issues: There is overlap of patients in some studies. The study also has substantial overlap with the studies included in other systematic reviews. Cost- effectiveness data from this report has not been examined as it is outside the scope of IPAC remit.

Key efficacy and safety findings

Efficacy and Safety

Number of studies analysed: **18 studies**

High-risk PCI : 11 studies (1 RCT and 10 observational studies)

Hemodynamic stability

Studies	n	Outcomes*	Impella 2.5	IABP
O Neil 2012 RCT (PROTECT II study)	448 (IMP 225 vs IABP 223)	Maximal decrease in cardiac power output	−0.04 ± 0.24 W	−0.14 ± 0.27 W P=0.001
Cohen 2015 (USpella registry)	637	Transient hypotension during support	7.1% (5.1%–9.1%)	
Dixon 2009 (PROTECT I study)	20	Freedom from hemodynamic compromise	100%	
Iliodromitis 2011	38	Hemodynamic stability	100%	
Maini 2012 (USpella registry)	175	Transient hypotension during support	3.4%	

*various outcomes were used to measure haemodynamic stability.

Mortality

Studies	n	In-hospital	30-day	12-month
O Neil 2012 RCT (PROTECT II study)	448 (IMP225 vs IABP 223)	NR	ITT: 7.6% vs. 5.9% (P = .47) PP: 6.9% vs. 6.2% (P = .74)	NR
Boudoulas 2012	75 (IMP 13 vs IABP 62)	0% vs. 20.9% (P = .10)	NR	15.3% vs. 25.8% (P = 0.72)
Alasnag 2011	60	NR	5%	NR
Cohen 2015 (USpella registry)	637	2.8%	NR	NR
Dixon 2009 (PROTECT I study)	20	NR	10%	NR
Iliodromitis 2011	38	NR	2.9%	NR
Kovacic 2013	IMP 36+TH 32	0%	2.8%	NR
Maini 2012 (USpella registry)	175	3.4%	4%	12%
Schwartz 2011	IMP 13+32TH +5 IABP	NR	0%	NR
Sjauw 2009 (Europella registry)	144	NR	5.5%	NR

Major adverse cardiac events (-myocardial infarction, stroke, revascularization)

Studies	In-hospital		30-day	

	Overall	Individual events	Overall	Individual events
O Neil 2012 RCT (PROTECT II study)	NR	NR	ITT 35.1% vs 40.1% (p=0.28) PP: 34.3% vs 42.2% (p=.092)	**ITT** MI 13.8% vs 10.4% (p=0.29) Stroke 0% vs 1.8% (p=043) RR 1.3% vs 4.1% (p=0.29) **PP** MI: 13.4% vs. 10.9% (*P* = 0.43) Stroke: 0% vs. 1.9% (*P* = 0.042) RR: 1.4% vs. 4.3% (*P* = 0.072)
Alasnag 2011	NR	NR	5%	
Cohen 2015 (USpella registry)	NR	MI 1.3%, RR 0.78%	NR	MI 0%, stroke 0%, RR 0%, urgent CABG 0%
Dixon 2009 (PROTECT I study)	NR	NR	20%	MI 10%
Iliodromitis 2011	NR	MI 63.6%	NR	NR
Kovacic 2013	NR	MI 6%	8.3%	NR
Maini 2012 (USpella registry)	NR	MI 1.1%, stroke 0.6%	8%	MI 1.1%, stroke 0.6%, RR0.6%
Schwartz 2011	NR	NR	15%	MI-0%, stroke 0%
Sjauw 2009 (Europella registry)	NR	NR	12.4%	Stroke 0.7%

Bleeding complications

Studies	In-hospital		30-day	
	Femoral hematoma	Bleeding needing transfusion	Femoral hematoma	Bleeding needing transfusion
Boudoulas 2012	NR	38.4% vs 32.2%(P=0.74)	NR	NR
Alasnag 2011	NR	NR	8.3%	10%
Anusionwu 2012	8%	NR	NR	NR
Cohen 2015 (USpella registry)	11%	NR	NR	NR
Dixon 2009 (PROTECT I study)	40%	10%	NR	NR
Iliodromitis 2011	15.5%	34.2%	NR	NR
Kovacic 2013	3%	NR	NR	NR
Maini 2012 (USpella registry)	8.6%	9.7%	NR	NR
Schwartz 2011	8%	39%	NR	NR
Sjauw 2009 (Europella registry)	NR	NR	NR	5.5

Vascular complications

Studies	In-hospital		30-day
	Impella 2.5	IABP	
Boudoulas 2012	15.3%	6.4% (p=0.27)	NR
Maini 2012 (USpella registry)	4%	-	NR

(Europella registry)	4%	-	NR
Alasnag 2011	NR	-	0%
Iliodromitis 2011	2.6%	-	NR
Kovacic 2013	3%	-	NR

Cardiogenic shock : 7 studies (1 RCT and 6 observational studies)

Hemodynamic stability

Studies	**N**	**Outcomes***	**Impella 2.5**	**IABP**
Seyfarth 2008 ISAR-SHOCK trial	25 (IMP 12 vs IABP 13)	Change of cardiac index after 30 minutes of support	0.49 ± 0.46 L/min/m^2	0.11 ± 0.31 L/min/m^2 (p=0.02)
		Diastolic arterial pressure (after vs. before support)	Increased by 9.2 ± 12.1 mmHg	Decreased by 8.0 ± 13.1 mmHg (p=0.002)
		Serum lactate	123 ± 87 hrs over mmol/L	180 ± 147 hrs over mmol/L (p=0.12)
Non comparative studies			**Before versus after support**	
Casassus 2015	22	Cardiac index	2.2 ± 0.4 vs. 2.6 ± 0.7 L/min/m^2 (P = 0.047)	
		Cardiac power index	0.33 ± 0.1 vs. 0.49 ± 0.2 W/m^2 (P = 0.02)	
		Systolic blood pressure	88 ± 25 vs. 111 ± 22 mmHg (P = 0.003)	
		Diastolic blood pressure	55 ± 12 vs. 67 ± 10 mmHg (P = 0.009)	
		Mean arterial pressure	67 ± 15 vs. 82 ± 13 mmHg (P = 0.027)	
		Mean pulmonary arterial pressure	29 ± 10 vs. 21 ± 7 mmHg (P = 0.011)	
		Pulmonary capillary arterial pressure	24 ± 10 vs. 16 ± 7 mmHg (P = 0.027)	
Lauten 2013 Impella-EUROSHOCK registry	120	Plasma lactate	5.8 ± 5.0 vs. 2.5 ± 2.6 mmol/L (P = 0.023)	
O'Neill 2014 (USpella registry)	154	Systolic blood pressure	85.4 ± 25.6 vs. 126.7 ± 31.4 mmHg (P < 0.0001)	
		Diastolic blood pressure	50.8 ± 18.6 vs. 78.7 ± 21.1 mmHg (P < 0.0001)	
		Mean arterial pressure	62.7 ± 19.2 vs. 94.4 ± 23.1 mmHg (P < 0.0001)	
		Mean capillary wedge pressure	31.9 ± 11.2 vs. 19.2 ± 9.7 mmHg (p<0.0001)	
		Cardiac index	1.9 ± 0.7 vs. 2.7 ± 0.7 L/min/m^2 (P < 0.0001)	
		Cardiac power input	0.48 ± 0.17 vs. 1.06 ± 0.48 W (P < 0.0001)	
		Cardiac output	3.4 ± 1.3 vs. 5.3 ± 1.7 L/min (P < 0.0001)	
Griffith 2013 RECOVER I study Impella 5.0	16	Cardiac index	1.6 ± 0.4 vs. 2.5 ± 0.4 L/min/m^2 (P = 0.0001)	
		Mean arterial pressure	71.4 ± 12.5 vs. 83.1 ± 7.5 mmHg (P = 0.01)	
		Pulmonary artery diastolic pressure	28.0 ± 3.9 vs. 19.8 ± 3.2 mmHg (p<0.0001)	

Mortality

Study	**N**	**30-day**	**6-month**	**12-month**

Seyfarth 2008 (ISAR-SHOCK trial)	25 (IMP 12 vs IABP 13)	46% vs. 46%	NR	NR
Manzo-Silberman 2013	78 (35 IMP vs 43 IABP)	23% vs. 29.5% (p = 0.61)	NR	NR
Casassus 2015	22	NR	40.9%	45.5%
Lauten 2013 (EUROSHOCK registry)	120	64.2%	NR	71.7%
O'Neill 2014 (USpella registry)	154	49.3%	NR	NR
Engström 2013	46	60.5%	NR	NR
Griffith 2013 (RECOVER I study)	16	6.3%	19%	25%

Major adverse cardiac events (-myocardial infarction, stroke, revascularization)

Studies	**In-hospital**		**30-day**	
	Overall	**Individual events**	**Overall**	**Individual events**
Seyfarth 2008 (ISAR-SHOCK trial)	NR	NR	No difference in complex organ dysfunction scores	NR
Manzo-Silberman 2013	NR	NR	NR	Stroke: 0% vs. 0%
Lauten 2013 (EUROSHOCK registry)	NR	NR	15%	MI: 6.7% ; Re-PCI: 10.8% CABG: 2.5%; Stroke: 1.7%
O'Neill 2014 (USpella registry)	NR	Stroke 1.9%, RR 2.6%; Re-infarction 0.9%	NR	NR
Griffith 2013 (RECOVER I study)	NR	NR	12.5%	Stroke: 6.3%

Bleeding complications (in-hospital)

	Femoral hematoma	**Bleeding needing transfusion**	**Bleeding needing surgery**	**Haemolysis**
Seyfarth 2008 (ISAR-SHOCK trial)	NR	NR	NR	Significantly increased in the Impella group in first 24 hours
Manzo-Silberman 2013	NR	26% vs. 9% (P = 0.06)	NR	NR
Casassus 2015	10%	18.2%	NR	NR
Lauten 2013	NR	24.2%	4.2%	7.5%
O'Neill 2014 (USpella registry)	NR	17.5%	2.6%	10.3%
Griffith 2013 (RECOVER I study)	NR	NR	43.8%	6.3%

Vascular complications

Studies	**Impella 2.5**	**IABP**	**P value**
Seyfarth 2008 (ISAR-SHOCK trial)	Limb ischemia in 1	0	NR
Manzo-Silberman 2013	Vascular complications 3%	Vascular complications 2%	0.9
Casassus 2015	Limb ischemia 10% Aortic insufficiency 5.6%	-	-
O'Neill 2014 (USpella registry)	Limb ischemia 3.9% Vascular complications 9.7%	-	-
Griffith 2013 (RECOVER I study)	Vein patch rupture 1	-	-

Abbreviations used: CABG, coronary artery bypass graft; IABP Intra-aortic balloon pump; ITT, intention-to-treat; IMP, Impella; MI, myocardial infarction; NR, not reported; PP, per-protocol; RCT, randomised controlled trial; RR, repeat revascularisation; TH, TandemHeart; vs, versus.

Study 2 Cheng JM (2017)

Details

Study type	Meta-analysis
Country	The Netherlands
Search period	Inception to April 2009 Databases searched: MEDLINE, Embase, and Cochrane Central Register of Controlled Trials; clinical trials.gov, references of included trials and conference proceedings were also checked and experts were consulted.
Study population and number	n= **3 randomised controlled trials (n=100) on percutaneous left ventricular assist devices(PLVAD) for cardiogenic shock** **PLVAD (n=53) versus IABP counter pulsation (n=47)**
Age and sex	Mean age ranged between 63 to 66 years Sex: 8 to 16% male
Study selection criteria	All controlled trials using percutaneous LVAD in patients with cardiogenic shock, with follow-up of at-least 30 days, with no language restrictions were included. Trials without control group and trials using surgical LVADs were excluded.
Technique	Percutaneous left ventricular assist devices in the management of cardiogenic shock. **One RCT used the Impella device (Seyfarth 2008) and** **2 RCTs (Thiele 2005, Burkhoff 2006) used TandemHeart**. All patients were treated with inotropes or vasopressors, mechanical ventilation, and percutaneous coronary intervention.
Follow-up	**30-days**
Conflict of interest/source of funding	None declared

Analysis

Follow-up issues: complete follow-up in all included trials.

Study design issues: the number of patients included in the meta-analysis was small; 2 type of devices have been assessed in the included studies. For the meta-analysis, studies were screened and data was extracted by two reviewers, disagreements were resolved by consensus or by a third reviewer. Quality of studies was assessed in terms of randomisation, adequateness of sequence generation, concealment of allocation, blinding and handling of patient attrition. Patients were randomly assigned, but methods of sequence generation and allocation concealment was not reported properly. Data were extracted using standardised forms. Weighted mean differences were calculated for cardiac index, mean arterial pressure and pulmonary capillary wedge pressure. Relative risks were calculated for 30-day mortality, leg ischemia, bleeding and sepsis. In the main analysis, results were based on random effects approach.

Key efficacy and safety findings

Efficacy and Safety

Number of studies analysed: **3 studies**

Pooled analysis of outcomes

Outcome	Thiele 2005		Burkhoff 2006		Seyfarth 2008		Pooled (fixed effects model)		Pooled (random effects model)	
	PLVAD (n=21)	IABP (n=20)	PLVAD (n=19)	IABP (n=14)	PLVAD (n=13)	IABP (n=13)	Mean difference/relative risk	p-value	Mean difference/relative risk (95% CI)	p-value
Hemodynamics (weighted mean difference)										
CI+SD (L/min/m^2)										
Baseline	1.8±0.4	1.6±0.5	1.8±0.4	1.8±0.6	1.7±0.5	1.7±0.6				
After support	2.3±0.6	1.8±0.4	2.2±0.6	2.1±0.2	2.2±0.6	1.8±0.7	0.35 (0.14; 0.55)	<0.001	0.35 (0.09; 0.61)	<0.01
MAP+SD (mmHg)										
Baseline	62±14	65±13	70±16	67±15	78±16	72±17				
After support	76±10	70±16	91±16	72±12	87±18	71±22	12.1 (6.3; 17.9)	<0.001	12.8 (3.6; 22.0)	<0.01
PCWP+SD (mmHg)										
Baseline	20±4	26±7	25±8	28±6	22±8	22±7				
After support	16±5	22±7	16±4	25±3	19±5	20±6	-6.2 (-0.8, -4.3)	<0.001	-5.3 (-9.4; -1.2)	<0.05
Clinical outcome (relative risk)										
30-day mortality n (%)	9 (4.3)	9 (45)	9 (47)	5 (36)	6 (46)	6 (46)	1.06 (0.68; 1.66)	0.80	1.06 (0.68; 1.66)	0.80
Adverse events (relative risk)										
Leg ischemia n (%)	7 (33)	0 (0)	4 (21)	2 (14)	1 (1)	0 (0)	2.59 (0.75; 8.97)	0.13	2.59 (0.75; 8.97)	0.13
Bleeding n (%)	19 (90)	8 (40)	8 (42)	2 (14)			2.35 (1.40; 3.93)	<0.01	2.35 (1.40; 3.93)	<0.01
Fever or sepsis, n (%)	17 (81)	10 (50)	4 (21)	5 (36)			1.38 (0.88; 2.15)	0.16	1.11 (0.43; 2.90)	0.83

Abbreviations used: CI, confidence interval; CI, cardiac index; IABP Intra-aortic balloon pump; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; PLVAD, percutaneous left ventricular assist device; SD, standard deviation.

Study 3 Briasoulis A (2016)

Details

Study type	Systematic review and meta-analysis
Country	USA
Search period	Inception to April 2009 Databases searched: MEDLINE, PUBMED, EMBASE, and Cochrane with no language restrictions. Hand search of all included studies was done to identify all relevant studies.
Study population and number	n= **20 studies (n= 1512) in patients undergoing high-risk PCI** **1 randomised controlled trial (Impella versus IABP) and 18 observational cohort studies and registries**
Age and sex	Mean age ranged between 63 to 66 years Sex: 8 to 16% male
Study selection criteria	Prospective controlled trials and cohort studies of patients that received hemodynamic support with percutaneous left ventricular assist devices (PLVADs) for high-risk PCI were included. Studies using surgically implanted assist devices and extracorporeal membrane oxygenation, case reports and case series as well as studies with less than10 cases were excluded.
Technique	**12 studies (1 RCT and 11 cohort studies) with 1,346 patients underwent Impella 2.5 L device placement and** **8 cohort studies with 205 patients received TandemHeart device for high-risk PCI.**
Follow-up	**30-days**
Conflict of interest/source of funding	No conflicts of interest to disclose

Analysis

Follow-up issues: complete follow-up in all included trials.

Study design issues: Systematic review and meta-analysis was done in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. 2 type of devices have been assessed in the included studies. Studies were systematically searched, screened, quality assessed and data was extracted by two reviewers. Cochrane's risk of bias tool was used to quality assess the prospective randomized study. The Newcastle-Ottawa tool was used for the quality assessment of cohort studies. 5 cohort studies were found to be at high risk of bias while other studies were at low risk of bias. A pooled meta-analysis of studies was done using review manager software. Pooled effect of intervention was measured using odds ratio with 95% confidence interval. Studies were heterogeneous with different designs, populations, inclusion criteria, outcomes and follow-up periods. Therefore the results might be affected by selection bias and confounding. Various definitions were used for vascular complications, myocardial infarction and bleeding. Vascular complications included (1) access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arteriovenous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, or compartment syndrome) requiring blood transfusions or surgical intervention; (2) distal embolization and limb ischemia; or (3) failure of percutaneous access site closure requiring intravascular or surgical correction.

Other issues: There is overlap of patients in some studies. The systematic review also has substantial overlap with the studies included in other systematic reviews.

Key efficacy and safety findings

Efficacy and Safety

Number of studies analysed: **20 studies**

IMPELLA (12 studies, n=1346): 1 RCT-PROTECT II [Impella versus IABP]

Outcomes	No of events	OR	95% CI, p value
30 day mortality	54/1346	0.035	0.022, 0.048 (p=0.243)
Myocardial infarction	53/1308	0.033	0.014, 0.053 (p<0.001)
Major bleeding	126/1346	0.071	0.043, 0.099 (p<0.002)
Vascular complications	89/1346	0.049	0.023, 0.076 (p<0.001)

TandemHeart (8 cohort studies, n=252)

Outcomes	No of events	OR	95% CI (p value)
30 day mortality	22/212	0.080	0.029, 0.131 (P=0.030)
Major bleeding	11/205	0.036	0.011, 0.061 (p=0.581)
Vascular complications	15/205	0.065	0.032, 0.099 (p=0.865)

Abbreviations used: CI, confidence interval; IABP Intra-aortic balloon pump; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; PLVAD, percutaneous left ventricular assist device; SD, standard deviation.

Study 4 Ichou JA (2017)

Details

Study type	Systematic review
Country	Canada
Search period	Inception to February 2016 Databases searched: Ovid MEDLINE, Embase, and the Cochrane Library; hand search of relevant studies was also done.
Study population and number	n= **20 studies (n=1287) on Impella HSD for high-risk percutaneous coronary intervention (PCI)** **(4 RCTs [n=438]:**1 in high-risk patients with left main disease or multi-vessel disease undergoing PCI, 2 RCT in patients with cardiogenic shock and myocardial infarction (MI) and 1 RCT in patients with ST-elevation myocardial infarction[STEMI]) **2 controlled observational studies** [Impella versus IABP], **and 14 uncontrolled observational studies)**
Age and sex	Mean age ranged from 57.9 to 79.8 years; Sex: 59.1% to 100% male
Study selection criteria	RCTs and observational studies that evaluated the Impella devices (2.5 & 5.0) in high-risk patients undergoing PCI, reporting clinical outcomes: all-cause mortality, major adverse cardiac events (MACE), stroke, MI, repeat vascularisation or bleeding complications (including hematoma) at 20-30 days or longer follow-ups, or any of the angiographic or hemodynamic outcomes-duration of device support, cardiac output, angiographic success, mean arterial pressure (before and after support); studies in which more than 10 patients received the Impella device; both uncontrolled and controlled (versus intra-aortic-balloon pump [IABP]) studies, published in English or French were included. Other types of studies (reviews, meta-analysis, abstracts, commentaries, animal studies etc), with less than 10 patients were excluded.
Technique	**Impella device in high-risk patients undergoing PCI** **Elective PCI (n=10 studies), emergent (n=5 studies) and elective or emergent (n=4 studies)**
Follow-up	**Varied (ranging from 1 to 42 months)**
Conflict of interest/source of funding	Authors have no conflicts of interest.

Analysis

Follow-up issues: follow-up varied in studies.

Study design issues: systematic review was done according to a prespecified protocol and reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). Systematic searches were done, studies were screened and data was extracted by two reviewers, disagreements were resolved by consensus or by a third reviewer. The quality of evidence was assessed according to Cochrane risk of bias assessment tool for RCTs and non-randomised studies of interventions for observational studies. Three RCTs included were small and had insufficient statistical power. One RCT had high risk of bias because of wide inclusion criteria and early termination for insufficient recruitment. Most included studies were small observational studies with high risk of bias. Studies included were heterogeneous in study designs, study populations, and reporting of results. Data was not pooled due to different definitions of composite outcomes and varied time points of assessment.

Study population issues: study populations in included studies are different with multiple co-morbidities and were at high procedural risk. The percentage of patients with previous MI was variable, ranging from 24% to 76%. In comparative studies patient characteristics were similar between the 2 groups.

Other issues: There is an overlap of patients in some studies. This systematic review also has substantial overlap with studies included in the HTA and other systematic reviews.

Key efficacy and safety findings

Efficacy and Safety

Number of studies analysed: **20 studies**

Hemodynamic stability

Study	Angiographic success (%)	Duration of support mean (SD) (minutes)	Lesions treated mean (SD)	Cardiac output (SD) (L/minute)	Mean arterial pressure, mean (SD) (mmHg)		
					Before support	During support	After support
RCTs							
O' Neil 2012	-	114 (162)	2.9 (1.4)	-	-	-	-
Ouweneel 2016	-	2940 (1680-4560)	-	-	-66(15)	-	-
Ouweneel 2016 [STEMI]	-	2940 (2,220)	-	6.4 (1.6)	-	-	-
Seyfarth 2008	90	1500 (3600-2460)	-	-	-78 (16)	-	87 (18)
Observational studies							
Miani 2012	99	60 (6-4320)	2.2(1.1)	2.1 (0.2)	83 (18)	101 (20)	89 (18)
Sjauw 2009	100	87.8 (50.7)	-	-	-	-	-
O'Neil 2014	-	23.7 (3.5-62.7)	2.33 91.40)	4.4 (2.2)	67.9 (20.7)	94.5 (21.3)	-
Alasnag 2011	96	38 915)	3 (1)	2.1 (0.2)	-	-	-
Venugopal 2014	98	-	2 (1)	-	-	-	-
Ilidormitis 2011	97.4	120.1 (45.4)	-	-	-	-	-
Kovacic 2013	99	41.7 (38.7)	2.5 (1.0)	-	-	-	-
Engstorm 2011	-	-	-	-	68 (22)	-	-
Ferreiro 2010	96.3	90 (60-110)	2.3 (1.2)	2.2 (0.2)	-	-	-
Anusionw 2012	100	603 (1523)	-	-	-	-	-
Casassus 2015	-	2130 (1338)	1.8 (1.0)	-	67 (15)	82 (13)	-
Dixon 2009	100	96 (36)	2.4 (0.9)	2.2 (0.3)	84.5 (14.3)	89 (14.8)	76 (11.9)
Henriques 2006	100	-	-	-	-	-	-
Boudoulas 2012	-	-	-	-	-	-	-
Schwartz 2011	100	-	-	-	-	-	-
Burzotta 2008	-	-	1.6	-	-	-	-

Complications rates in comparative studies

Study	N		All-cause mortality n (%)		Stroke n (%)		MI n (%)		MACE n (%)		Repeat revascularisation n (%)	
	IMP	IABP	IMP	IABP	IMP	IABP	IMP	IABP	IMP	IABP	IMP	IABP
30-day follow-up												
O' Neil 2012	225	223	17 (7.6)	13 (5.9)	0	4 (1.8)	31 (13.8)	23 (10.4)	79 (35.1)	89 (40.1)	3 (1.3)	9 (4.1)
Ouweneel 2016	24	24	11 (46)	12 (50)	-	-	-	-	-	-	-	-
Seyfarth 2008	13	13	6 (46)	6 (46)	-	-	-	-	-	-	-	
Schwartz 2011	13	5	2 (15)	0	0	0	0	1 (20)	2 (15)	2 (40)	-	-

3 months follow-up												
O' Neil 2012	225	223	27 (12.1)	19 (8.7)	2 (0.9)	6 (2.7)	27 (12.1)	31 (14.2)	91 (40.6)	108 (49.3)	8 (3.6)	18 (7.8)
Ouweneel 2016	24	24	12 (50)	12 (50)	1 (40	1(4)	1 (4)	2 (8)	-	-	-	-
Ouweneel 2016 [STEMI]	12	9	3 (26)	1 (11)	1 (8)	0	-	-	3 (26)	3 (33)	-	-
12 months follow-up												
Boudoulas 2012	13	62	2 (15.3)	16 (25.8)	-	-	-	-	-	-	-	-
Ouweneel 2016	12	9	3 (26)	1 (11)	1 (8)	0	-	-	4 (37)	4 (47)	-	-

Complications rates in non-comparative studies

Study	Lost to follow-up	All-cause mortality n (%)	Stroke n (%)	MI n (%)	MACE n (%)	Repeat revascularisation n (%)	Hematoma n (%)
30-day follow-up							
Miani 2012	0	7 (4)	1 (0.6)	2 (1.1)	14(8)	1(0.6)	-
Sjauw 2009	-	8 (5.5)	1 (0.7)	0	-	-	-
O'Neil 2014	9	23 (42.6)	-	-	-	-	-
Alasnag 2011	0	3(5)	0	0	3(5)	-	5(8.3)
Venugopal 2014	0	8(18)	1(2)	1(2)	-	-	-
Iliodormitis 2011	0	1(2.86)	0	21(63.6)	-	-	6(15.8)
Kovacic 2013	0	0	0	2(6)	-	0	3(8)
Engstorm 2011	8	25(7.4)	-	-	-	-	-
Ferreiro 2010	0	1 (3.7)	-	6(22.2)	3 (11.1)0	0	-
Anusionwu 2012	0	-	-	-	-	-	2(8)
Dixon 2009	0	2(10)	0	2(10)	4(20)	0	8(40)
Henriques 2006	0	4(21)	-	-	-	-	-
Burzota 2008	0	1(10)	-	-	3(30)	2(20)	-
6-months follow-up							
Maini 2012	-	16(9)	-	-	-	-	-
Casassus 2015	0	(40.9)	-	-	-	2(10)	-
12-months follow-up							
Maini 2012	-	21(12)	-	-	-	-	-
Casassus 2015	0	10(45.5)	-	-	-	-	-
Burzotta 2008	0	1(10)	-	-	3(30)	2(20)	-

Abbreviations used: IABP Intra-aortic balloon pump; ITT, intention-to-treat; IMP, Impella; MI, myocardial infarction; MACE, major adverse cardiac events; NR, not reported; RCTs, randomised controlled trials; SD, standard deviation; STEMI, ST-elevation myocardial infarction.

Study 5 Alaswad K (2018)

Details

Study type	**Retrospective case series (global CVAD registry)**
Country	USA
Study period	2007-2015
Study population and number	n= **891 patients with non-severely reduced left ventricular function** (defined as left ventricular ejection fraction [LVEF]> 35%) **who received mechanical circulatory support (MCS) in high-risk percutaneous coronary intervention (PCI)** **severely reduced LVEF <35% : 75% (661/891); non-severely reduced LVEF >35%: 26% (230/891)** Predicted surgical mortality: STS score (6.37±7.11 versus 4.87±5.84; p=0.007 Predicted surgical morbidity: STS score (31.95±17.17 versus 25.50±15.55; p<0.001
Age and sex	Mean 96.57 years; 75% male
Study selection criteria	Patients without cardiogenic shock from the catheter-based ventricular assist device registry, who underwent elective or urgent PCI with an Impella device (2.5 or CP) were included. Patients who received MCS after the start of PCI were excluded from the analysis.
Technique	**Impella device (2.5 or CP) implanted during elective or urgent high-risk PCI** The indication for PCI, decision to use MCS before the PCI, and choice of device were made by the operator. Elective PCI: LVEF>35% (51.74%) versus LVEF<35% (37.52%); p=<0.001.
Follow-up	**To discharge**
Conflict of interest/source of funding	Authors report no conflicts of interest. 3 authors were consultants for different manufacturers.

Analysis

Follow-up issues: limited follow-up only.

Study design issues: data/events recorded until hospital discharge from the ongoing multicentre global catheter-based ventricular assist device (cVAD) registry was analysed. Registry is limited to patients who had Impella only. Major adverse cardiovascular and cerebral events (MACE) include all-cause death, myocardial infarction (MI), stroke or transient ischemic attack and repeat revascularisation.

Study population issues: patients with non-severely reduced LVEF when compared with patients with severely reduced LVEF, tended to be older (72.12±11.70 years versus 68.68±11.01 years; p<0.001), had more extensive coronary artery disease with more diseased vessels (91.90±0.71 versus 1.73±0.79; p=0.005), more multi-vessels treated (1.74±0.69 versus 1.55±073; p<0.001), more lesions treated (1.87±00.80 versus 1.67±0.76; p=0.001) and significant use of rotational atherectomy (21.21% versus 14.90%; p=0.046). They also had high prevalence of renal failure (25%), diabetes (45%), congestive heart failure (33%), previous MI (30%) and previous PCI (42%) or previous coronary artery bypass grafting (CABG) (29%) and high predicted mortality and morbidity scores.

Key efficacy and safety findings

Efficacy and safety

Number of patients analysed: **891**

Outcomes after PCI

Adverse events	All patients (n=891) %	LVEF<35% (n=661) %	LVEF>35% (n=230) %	P value
MACE	4.26	4.54	3.48	0.574
Death	3.25	3.78	1.74	0.193
Myocardial infarction	0.56	0.30	1.30	0.112
Acute renal dysfunction	5.16	6.05	2.61	0.055
Revascularisation (including emergent CABG)	0.79	0.61	1.30	0.383
Acute hepatic failure	0.34	0.30	0.43	1.000
Bleeding requiring surgery	0.67	0.76	0.43	1.000
Bleeding needing transfusion	6.62	5.75	9.13	0.090
Device malfunction	0.11	0.15	0.00	1.000
Hematoma	4.15	3.33	6.52	0.053
Vascular complication needing surgery	1.35	1.06	2.17	0.201
Vascular complication not needing surgery	2.47	2.57	2.17	1.000
Acute bowel ischemia	0.22	0.15	0.43	0.450
Need for cardiac, thoracic or abdominal vascular operation or femoral artery bypass graft	0.22	0.15	0.43	0.450
Hypotension during support	4.60	4.39	5.22	0.587
Infection	2.13	1.66	3.48	0.114
Cardiopulmonary resuscitation or ventricular arrhythmia	3.03	3.48	1.74	0.263
Failure to achieve angiographic success (as residual stenosis <30% after stent implant)	0.45	0.30	0.87	0.275

Abbreviations used: CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular and cerebral events; PCI, percutaneous coronary intervention.

Study 6 Flaherty MP (2017)

Details

Study type	**Retrospective comparative case series**
Country	USA
Study period	2011-14
Study population and number	**n= 230 patients with left ventricular ejection fraction (LVEF) < 35% undergoing high-risk percutaneous coronary intervention (PCI) with temporary mechanical hemodynamic support** (Impella 2.5). (**115 percutaneous mechanical hemodynamic-supported patients and 115 unsupported matched-controls)**
Age and sex	Age: median 68 years; sex: 66% (130/230) male
Study selection criteria	Patients with Impella 2.5 support and LVEF less than 35% were included in the analysis. Patients treated with an intra-aortic balloon pump (IABP) or those on haemodialysis before PCI were excluded from this study. 22 patients who had electrophysiology procedures, 9 with Impella CP, 4 with an LVEF more than 35%, and 3 who did not undergo PCI were also excluded from the analysis.
Technique	Impella 2.5 support during elective or urgent high-risk PCI. PCI was done according to standard clinical practice. No patients received bicarbonate or N-acetylcysteine. However, patients with estimated glomerular filtration rate (eGFR in mL/min per 1.73 m2) less than 60 received intravenous hydration and high dose statins per institutional protocol when feasible. Non-ionic and low-osmolar contrast and were used. The use of potential nephrotoxic medications, such as angiotensin-converting enzyme inhibitors, loop-diuretics, and nonsteroidal anti-inflammatory drugs, were similar between groups.
Follow-up	**In-hospital outcomes**
Conflict of interest/source of funding	The first author received a research grant and speaker honoraria from the manufacturer

Analysis

Follow-up issues: limited follow-up only.

Study design issues: single centre retrospective study with large patient cohort. The primary outcome was incidence of in-hospital acute kidney injury (AKI) according to AKI network criteria. Baseline estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation. Patients were stratified based on normal baseline renal function (eGFR >60), mild chronic kidney disease (CKD; eGFR 45–60), moderate chronic kidney disease (CKD) (eGFR 30–45), or severe CKD (eGFR <30). Logistic regression analysis determined the predictors of AKI (primary outcome). Operators were not blinded to baseline creatinine.

Study population issues: The unsupported control group used for comparison was matched for age (42–85 years), sex, LVEF (10%–35%), level of acuity, and contrast load (170–775 mL). Baseline clinical characteristics were similar between unsupported and Impella-supported patients. More Impella supported patients had moderate CKD (17% versus 8%; P=0.05) at baseline.

Key efficacy and safety findings

Safety

Number of patients analysed: **230**

Procedural outcomes

	Total (n=230)	Impella (n=115)	Control (n=115)	p value
Procedure time, minutes, median (IQR)	152 (100–171)	149 (121–183)	123 (105–142)	0.01
Impella 2.5 support time (hours) mean±SD		1.87±0.62		
Length of stay, days, mean±SD	4.6±3.0	3.5±1.4	5.7±3.7	<0.001
LM disease (or last remaining conduit), n (%)	39 (17)	30 (26)	9 (6)	0.00
3-vessel disease, n (%)	90 (39)	54 (47)	36 (31)	0.02
Multi-vessel disease, n (%)	214 (93)	105 (91)	109 (95)	0.31
Surgical candidate, n (%)	140 (61)	41 (36)	99 (86)	0.00
Volume of contrast, mL, median (IQR)	260 (210–280)	287 (225–320)	250 (210–281)	0.05

In-hospital peri-procedural outcomes

	Total (n=230)	Impella (n=115)	Control (n=115)	p value
Primary outcome				
AKI* n (%)	38 (17)	6 (5)	32 (28)	0.001
Secondary outcomes				
Need for haemodialysis (AKI-HD)^ n (%)	8 (4)	1 (0.9)	7 (6)	0.031
Death n (%)	2 91)	0	2 (2)	0.156
Maximum change in creatinine, mg/dL, mean ± SD, (% increase)	1.65±0.84 (30)	1.36±0.44 (5)	1.94±1.03 (50)	0.000
Maximum change (% decrease) in eGFR, mL/min per 1.73 m^2	20	6	51	0.001
Major vascular complications, n (%)	7 (3)	4 (4)	3 (3)	0.651
Surgical repair n (%)	0	0	0	-
Ultrasound-guided compression, stent graft deployment, n (%)	1 90.4)	1	0	-
Ipsilateral limb ischemia, n (%)	2 (1)	1 (1)	1 (1)	-
Access site-related bleeding (haemoglobin drop ≥3 g/dL), n (%)	2 (1)	2 (2)	2 (2)	-

*defined as an increment increase of serum creatinine within a period of 72 hours post procedure (beginning at the time of contrast exposure in those exposed): AKI classified using AKI network criteria (AKI stage 1, ≥0.3 mg/dL absolute or 1.5 to 2.0-fold relative increase in serum creatinine; AKI stage 2, >2- to 3-fold increase in serum creatinine; AKI stage 3, >3-fold increase in serum creatinine or serum creatinine >4.0 mg/dL with an acute increase of >0.5 mg/dL).

^ defined as acute or worsening renal failure, necessitating new renal dialysis.

Peri-procedural incremental change in creatinine

	Total (n=230)	Impella (n=115)	Control (n=115)	p value
Baseline creatinine, mg/dL, mean		1.29±0.37	1.26±0.24	0.52
Post-procedure day 3 Creatinine mg/dL, mean		1.19±0.33, 5.6% decrease; P=0.04	1.67±0.81, 30% increase P<0.001	

Incidence of AKI based on severity of baseline CKD

There was no difference in CKD severity and incidence of AKI in Impella supported patients. In unsupported patients the post-procedure incidence of AKI was significantly greater and correlated with the severity of CKD. In patients with mild baseline CKD (eGFR 45–60 mL/min per 1.73 m2) the incidence of AKI when compared with percutaneous mechanical hemodynamic supported patients was 6% versus 0.9% (P<0.05), respectively, and continued to increase with CKD severity.

Overall, when compared with Impella supported patients, unsupported patients presenting with severe CKD at baseline (eGFR <30 mL/ min per 1.73 m2) had the highest incidence of both AKI and AKI-HD (20.5% versus 2.7% and 3.6% versus 0.9%, respectively; P<0.05).

Predictors of acute kidney injury (AKI) in Impella 2.5 supported versus unsupported control patients after high-risk PCI (multi-variate logistic regression)

Independent predictors	AOR	95% CI	P value
Impella support	0.13	0.09 to 0.31	<0.001
Ejection fraction (%)	0.16	0.12 to 0.28	<0.001
eGFR	0.63	0.25 to 0.83	0.038
Procedural time (minutes)	0.98	0.71 to 1.13	0.072
Contrast volume (50 ml)	2.14	1.28 to 5.14	<0.001

Abbreviations used: AKI, acute kidney injury; AK-HD, acute kidney injury needing haemodialysis; AOR, adjusted odds ratio; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, inter-quartile range; SD, standard deviation

Study 7 Henriques J PS (2014)

Details

Study type	**RCT (PROTECT II trial)- prespecified sub-group analysis**
Country	USA and Europe (74 sites)
Study period	2007-10
Study population and number	**N=328 patients supported during high risk percutaneous coronary intervention (PCI)** **Patients with Impella 2.5, excluding first patients at each site (n=161)** versus **Patients with Intra-aortic balloon pump (IABP), excluding first patients at each site (n=167)**
Age and sex	Mean age: Impella group: 67 years, IABP group 68 years Sex: 8% male in both groups.
Study selection criteria	Patients eligible for enrolment required hemodynamic support, as determined by the treating physician, during non-emergent PCI. Eligible patients were scheduled for PCI of an unprotected left main artery or last patent coronary vessel and had a left ventricular ejection fraction (LVEF) less than35%, or had 3-vessel disease and a LVEF less than 30%.
Technique	**Insertion of a temporary mechanical hemodynamic) support device (Impella 2.5) or IABP during elective or urgent high-risk PCI.** Patients underwent right and left heart catheterization and vascular access suitability was assessed. Patients were randomized to either the Impella 2.5 or a commercially available IABP. Revascularization was performed using standard equipment and techniques, leaving the use of drug-eluting or bare metal stents as well as adjunctive therapies such as rotational atherectomy and antiplatelet therapy to the discretion of the treating physician. Hemodynamic support was discontinued in the catheterization laboratory if the patient was deemed hemodynamically stable.
Follow-up	**30 and 90 days post procedure**
Conflict of interest/source of funding	Study was funded by the manufacturer.

Analysis

Follow-up issues: The study was discontinued early for futility after review of the planned interim data.

Study design issues: A prespecified subgroup-analysis of PROTECTII trial (excluding the first Impella [n=58] and IABP patients [n=62] in each group) was done to assess the impact of device learning curve on outcomes of PROTECT II. Patients were excluded from both the intention to treat and per-protocol patient populations. Experience with IABP prior to PROTECT II study was wide compared to Impella 2.5. At the end of the study, 38 sites did not enrolled any patients.

The primary endpoint of the PROTECT II trial was the composite rate of 10 major adverse events (MAEs) at discharge or 30-day follow-up, whichever was longer. Treatment comparisons were performed using $\chi 2$ test. Kaplan–Meier estimates of the cumulative incidence of MAE through 30 and 90 days were performed, and a log-rank test was used to compare the curves between the 2 study arms at these time points.

Study population issues: baseline characteristics were similar between the first and remaining Impella patients, except for higher incidence of cardiomyopathy in the first Impella patients.

Key efficacy and safety findings

Efficacy and Safety

Number of patients analysed: **327 (167 Impella versus 161 IABP)**

Major adverse events (MAE), Impella 2.5 compared with IABP patients, excluding first patients at each site, ITT analysis

	30 days			90 days		
	Impella 2.5 (n=167)	**IABP (n=161)**	**P value**	**Impella 2.5 (n=167)**	**IABP (n=161)**	**P value**
Composite of major adverse events, % (n)	31.7 (53)	40.0 (64)	0.119	38.0 (63)	50.0 (79)	0.029
Death, % (n)	6.0 (10)	5.6 (9)	0.888	10.8 (18)	8.2 (13)	0.424
Stroke/TIA, % (n)	0	1.9 (3)	0.075	0.6 (1)	2.5 (4)	0.159
Myocardial infarction, % (n)	13.2 (22)	10.0 (16)	0.371	12.7 (21)	13.3 (21)	0.864
Repeat revascularization, % (n)	1.8 (3)	31.5 (5)	0.437	4.2 (7)	8.9 (14)	0.90
Need for cardiac or vascular operation, % (n)	0.6 (1)	1.3 (2)	0.537	1.2 (2)	1.3 (2)	0.960
Acute renal dysfunction, % (n)	4.8 (8)	5.0 (8)	0.930	4.2 (7)	5.1 (8)	0.717
Cardiopulmonary resuscitation or ventricular arrhythmia requiring cardioversion, % (n)	2.4 (4)	1.9 (3)	0.745	2.4 (4)	3.2 (5)	0.679
Aortic valve damage/increase in aortic insufficiency, % (n)	0	0	-	0	0	-
Severe hypotension requiring treatment, % (n)	3.0 (5)	10.6 (17)	0.006	1.8 (3)	7.6 (12)	0.013
Angiographic failure, % (n)	0	0.6 (1)	0.306	0	0	-

Major adverse events (MAE), first Impella 2.5 patients at each site compared to remaining Impella 2.5 patients, ITT analysis

	30 days			90 days		
	First Impella 2.5 patients (n=58)	**Remaining Impella patients (n=167)**	**P value**	**First Impella 2.5 patients (n=58)**	**Remaining Impella patients (n=167)**	**P value**
Composite of major adverse events, % (n)	44.8 (26)	31.7 (53)	0.72	48.3 (28)	38.0 (63)	0.168
Death, % (n)	12.1 (7)	6.0 (10)	0.131	15.5 (9)	10.8 (18)	0.347
Stroke/TIA, % (n)	0	0	-	1.7 (1)	0.6 (1)	0.434
Myocardial infarction, % (n)	15.5 (9)	13.2 (22)	0.656	10.3 (6)	12.7 (21)	0.642
Repeat revascularization, % (n)	0	1.8 (3)	0.304	1.7 (1)	4.2 (7)	0.379
Need for cardiac or vascular operation, % (n)	1.7 (1)	0.6 (1)	0.431	1.7 (1)	1.2 (2)	0.767
Acute renal dysfunction, % (n)	1.7 (1)	4.8 (8)	0.305	3.4 (2)	4.2 (7)	0.797
Cardiopulmonary resuscitation or ventricular arrhythmia requiring cardioversion, % (n)	1.7 (1)	2.4 (4)	0.765	1.7 (1)	2.4 (4)	0.761
Aortic valve damage/increase in aortic insufficiency, % (n)	0	0	-	0	0	-
Severe hypotension requiring treatment, % (n)	10.3 (6)	3.0 (5)	0.025	10.3 (6)	1.8 (3)	0.004
Angiographic failure, % (n)	1.7 (1)	0	0.089	1.7 (1)	0	0.090

Major adverse events (MAE), first IBP patients at each site compared to remaining IABP patients, ITT analysis

	30 days	90 days

	First IABP patients (n=62)	Remaining IABP patients (n=160)	P value	First IABP patients (n=61)	Remaining IABP patients (n=158)	P value
Composite of major adverse events, % (n)	40.3 (25)	40.0 (64)	0.965	47.5 (29)	50.0 (79)	0.744
Death, % (n)	6.5 (4)	5.6 (9)	0.814	9.8 (6)	8.2 (13)	0.705
Stroke/TIA, % (n)	1.6 (1)	1.9 (3)	0.895	3.3 (2)	2.5 (4)	0.761
Myocardial infarction, % (n)	11.3 (7)	10.0 (16)	0.777	16.4 (10)	13.3 (21)	0.555
Repeat revascularization, % (n)	6.5 (4)	3.1 (5)	0.260	4.9 (3)	8.9 (14)	0.328
Need for cardiac or vascular operation, % (n)	1.6 (1)	1.3 (2)	0.834	3.3 (2)	1.3 (2)	0.319
Acute renal dysfunction, % (n)	3.2 (2)	5.0 (8)	0.567	3.3 (2)	5.1 (8)	0.571
Cardiopulmonary resuscitation or ventricular arrhythmia requiring cardioversion, % (n)	6.5 (4)	1.9 (3)	0.080	6.6 (4)	3.2 (5)	0.257
Aortic valve damage/increase in aortic insufficiency, % (n)	0	0	-	0	0	-
Severe hypotension requiring treatment, % (n)	3.2 92)	10.6 (17)	0.077	0	7.6 (12)	0.027
Angiographic failure, % (n)	0	0.6 (1)	0.533	0	0	-

Abbreviations used: IABP, intra-aortic balloon pump; ITT, intention-to-treat; TIA, transient ischemic attack.

Study 8 Bhatia N 2016 (2017)

Details

Study type	Case report (poster presentation)
Country	USA
Study period	2016
Study population and number	n= **1 patient with anterior ST elevation myocardial infarction (MI)**
Age and sex	52 year old man
Study selection criteria	
Technique	Patient had an unsuccessful percutaneous coronary intervention. Impella CP was placed for support and patient was transferred to main center for coronary artery bypass grafting (CABG).
Follow-up	**10 days**
Conflict of interest/source of funding	Not reported

Key efficacy and safety findings

Safety
Number of studies analysed: **1** **Mitral regurgitation (MR) after Impella® placement (rare catastrophic complication)** After placement of Impella CP and enroute to hospital, patient developed aspiration pneumonia and acute respiratory distress syndrome. On day 3, Impella was weaned to P1 (lowest pump level) with cardiac index (CI) 3.5 L/min/m^2 and removed. In an hour, cardiac index declined to 1.5 L/min/m^2. A new holosystolic murmur was heard at apex. Tall v waves were seen on wedge tracing from Swan-Ganz catheter. Echocardiogram (TTE) showed new severe eccentric mitral regurgitation (MR), not present on admission TTE. Due to rapid decompensation after removal of Impella, iatrogenic MR from mechanical damage to mitral valve (MV) was the top differential along with mechanical complications of MI, i.e., free wall rupture, ventricular septal defect or worsening hypoxic respiratory failure. An urgent transoesophageal echocardiogram confirmed ruptured posterior chordae. Septic shock and bacteraemia precluded MV replacement. Tandem Heart® was placed to decompress his left atrium and patient was stabilized. Sepsis resolved on day 8 and patient had MV replacement with CABG.
Abbreviations used: CABG, coronary artery bypass grafting; IABP Intra-aortic balloon pump; ITT, intention-to-treat; ; MI, myocardial infarction; NR, not reported; SD, standard deviation.

Validity and generalisability of the studies

- Different devices are used for a number of indications (Impella 2.5, Impella CP/3.5 and Impella 5.0, TandemHeart, iVCAL2 and HeartMate).
- The focus of this overview is on devices used for temporary percutaneous mechanical hemodynamic support before, during and after urgent or elective high-risk PCI including cardiogenic shock.
- The majority of the studies were on Impella 2.5 and TandemHeart only.
- The randomised controlled trials (RCTs) mainly compared Impella 2.5 or TandemHeart with IABP in high-risk PCI and cardiogenic shock and have shown superior hemodynamic support but no difference in mortality rates. There is no evidence directly comparing Impella CP or 5.0 with IABP.
- There are no studies comparing one type of temporary percutaneous mechanical hemodynamic support device with another.
- There is very little evidence on Impella 3.5/CP.
- Pilot studies on iVCAL2 and PHP HeartMate have been added to appendix.
- Follow-up in studies included in the systematic reviews varied (ranging from 1 to 42 months).

Existing assessments of this procedure

The American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions Guidelines for PCI[9] recommend percutaneous mechanical circulatory support in two clinical settings: as an adjunct to high-risk PCI (class IIb) and for cardiogenic shock in patients presenting with ST-elevation with myocardial infarction (STEMI) (class IIb). In addition an expert consensus document endorsed by multiple societies supported the use of percutaneous mechanical circulatory support devices for elective high-risk PCI.[9]

- A hemodynamic support device is recommended for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy. (Class I, Level of Evidence: B)

- Elective insertion of an appropriate hemodynamic support device as an adjunct to PCI may be reasonable in carefully selected high-risk patients

(Class IIb, Level of Evidence: C). High-risk patients include: unprotected left main or last remaining conduit PCI, cardiogenic shock, PCI of a vessel subtending a large territory on a background of severely depressed left ventricular function.

- IABP can be useful for patients in cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy (Class IIa, Level of Evidence: B). Alternative left ventricular assist devices for circulatory support may be considered in patients with refractory cardiogenic shock (Class IIb, Level of Evidence: C).

European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic heart failure (2016). The Task Force for the diagnosis and treatment of acute and chronic heart failure of the ESC developed the below recommendations with the special contribution of the Heart Failure Association (HFA) of the ESC[10]

13.1.1 Mechanical circulatory support (MCS) in acute heart failure

'To manage patients with acute heart failure (AHF) or cardiogenic shock (INTERMACS level 1), short-term mechanical support systems, including percutaneous cardiac support devices, extracorporeal life support (ECLS) and extracorporeal membrane oxygenation (ECMO) may be used to support patients with left or biventricular failure until cardiac and other organ function have recovered. Typically the use of these devices is restricted to a few days to weeks. Evidence regarding the benefits of temporary percutaneous MCS in patients not responding to standard therapy, including inotropes, is limited. In a meta-analysis of three randomized clinical trials comparing a percutaneous MCS vs. intra-aortic balloon pump (IABP) in a total of 100 patients in cardiogenic shock, percutaneous MCS appeared safe and demonstrated better haemodynamics, but did not improve 30-day mortality and was associated with more bleeding complications. In a randomized trial on high-risk PCI in patients with impaired left ventricle (LV) function (PROTECT II trial), the 30-day incidence of major adverse events was not different for patients with IABP or a haemodynamic support device. Based on these results, temporary percutaneous MCS cannot be recommended as a proven or efficacious treatment for acute cardiogenic shock. In selected patients it may serve as a bridge to definite therapy. A difficult decision to withdraw MCS may need to be made when the patient has no potential for cardiac recovery and is not eligible for longer-term MCS support or heart transplant'.

European Society of Cardiology (ESC) guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (2015): The task Force for the Management of Acute

Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the ESC recommends[11]

- Immediate PCI for patients with cardiogenic shock if coronary anatomy is suitable (class I, level of Evidence B)
- IABP insertion should be considered in patients with haemodynamic instability/cardiogenic shock due to mechanical complications (Class IIa, Level of Evidence C).
- Short-term mechanical circulatory support in patients with cardiogenic shock may be considered (Class IIb, Level of Evidence C)
- Routine use of IABP in patients with cardiogenic shock is not recommended (Class III, level of Evidence B).

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Medtech Innovation Briefing

- Impella 2.5 for haemodynamic support during high-risk percutaneous coronary interventions. NICE MedTech innovation briefing 89 (2016). Available from https://www.nice.org.uk/advice/mib89

Interventional procedures

- Optical coherence tomography to guide percutaneous coronary intervention. NICE interventional procedures guidance 481 (2014). Available from https://www.nice.org.uk/guidance/ipg481

Technology appraisals

- Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes. NICE technology appraisal guidance 317 (2014). Available from http://www.nice.org.uk/guidance/TA317
- Cangrelor for reducing atherothrombotic events in people undergoing percutaneous coronary intervention or awaiting surgery requiring interruption of anti‑platelet therapy (terminated appraisal). NICE technology appraisal guidance 351 (2015). Available from http://www.nice.org.uk/guidance/TA351

NICE guidelines

- Myocardial infarction with ST-segment elevation: acute management. NICE guideline CG167 (2013). Available from http://www.nice.org.uk/guidance/CG167
- Unstable angina and NSTEMI: early management. NICE Guideline CG94 (2013). Available from http://www.nice.org.uk/guidance/CG94
- Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease. NICE guideline CG172 (2013). Available from http://www.nice.org.uk/guidance/CG172

NICE quality standards and pathways

- Acute coronary syndromes in adults. NICE quality standard 68 (2014). Available from https://www.nice.org.uk/guidance/qs68
- Myocardial infarction with ST-segment elevation. NICE pathway (2017). Available from https://pathways.nice.org.uk/pathways/myocardial-infarction-with-st-segment-elevation
- Chest pain. NHS pathway (2017). Available from https://pathways.nice.org.uk/pathways/chest-pain

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for percutaneous insertion of a temporary heart pump for left ventricular hemodynamic support in high risk percutaneous coronary interventions were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 3 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Impella LD and Impella RP are also available but are indicated for use during open chest surgery and for right heart failure respectively. These additional versions and indications are beyond the scope of this topic. Extracorporeal membrane oxygenation (ECMO) is also beyond the scope of this topic.
- Impella CP (the next generation of Impella 2.5 with a high flow rate) is used most widely in the UK.
- Impella devices are the only devices approved by FDA.
- HeartMate PHP is not currently available on the market.
- Ongoing RCTs
  - NCT01633502: Effects of advanced mechanical circulatory support in patients with ST segment elevation myocardial infarction complicated by cardiogenic shock. The Danish Cardiogenic Shock Trial (DanShock) randomised controlled trial- comparing Impella 3.5 device to conventional circulatory support in patients with cardiogenic shock complicating MI. Primary end-point:6-month mortality, n=360 patients, estimated primary completion date: October 2017, Denmark.
  - NCT02468778: Supporting patients undergoing high-risk PCI using a high-flow percutaneous left ventricular support device (SHIELD II). To evaluate

the use of HeartMate PHP with Impella 2.5 as the active comparator for both the elective and urgent indications (suspended participant recruitment). Completion date October 2017.

- NCT02831881 PROTECT III: A prospective clinical trial for patients undergoing protected percutaneous coronary intervention with IMPELLA® 2.5 system. Currently recruiting participants, completion date November 2020.
- NCT03000270: Door to unloading with IMPELLA CP system in acute myocardial infarction (DTU) – currently recruiting patients to evaluate the use of delay v. immediate use of Impella, expected enrolment: n=50, estimated primary completion date: February 2019, USA.
- NCT02279979: Thoratec Corporation HeartMate PHP™ Cardiogenic Shock Trial (study terminated)

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Heart Failure Association (HFA) of the ESC. European Heart Journal. 14; 37(27):2129-2200.

11. Roffi M, Patrono C et al (2016). 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). European Heart Journal, Volume 37, Issue 3, 14 January 2016, Pages 267–315.

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	29/01/2018	Issue 1 of 12, January 2018
HTA database (Cochrane)	29/01/2018	Issue 4 of 4, October 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane)	29/01/2018	Issue 12 of 12, December 2017
MEDLINE (Ovid)	29/01/2018	1946 to Present with Daily Update
MEDLINE In-Process (Ovid)	29/01/2018	January 26, 2018
MEDLINE Epubs ahead of print (Ovid)	29/01/2018	January 26, 2018
EMBASE (Ovid)	29/01/2018	1974 to 2018 January 26
BLIC (British Library)	30/01/2018	n/a

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 "Meta-Analysis of Usefulness of Percutaneous Left Ventricular Assist Devices for High-Risk Percutaneous Coronary Interventions".fc_titl.
2 "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".fc_titl.
3 "Real-world use of the Impella 2.5 circulatory support system in complex high-risk percutaneous coronary intervention: the USpella Registry".fc_titl.
4 "Supported high-risk percutaneous coronary intervention with the Impella 2.5 device the Europella registry.".fc_titl.
5 "Percutaneous left ventricular assist device for high-risk percutaneous coronary interventions: Real-world versus clinical trial experience".fc_titl.
6 "Percutaneous Ventricular Assist Devices: A Health Technology Assessment".fc_titl.
7 or/1-6
8 Percutaneous Coronary Intervention/
9 (percutaneous adj2 (coronar* or heart* or cardiac*) adj2 (intervent* or revasculari?ation*)).tw.
10 ((percutaneous or catheter* or transcatheter* or microaxial* or micro axial*) adj4 (coronar* or heart* or cardiac*) adj4 (pump* or device* or assist* or bridge*)).tw.
11 (PCI or PCIs or HRPCI or HRPCIs).tw.
12 or/8-11

13 exp Heart-Assist Devices/
14 Assisted Circulation/
15 *Coronary Circulation/
16 Angioplasty, Balloon, Coronary/
17 ((coronar* or heart* or cardi*) adj2 balloon adj2 (dilat* or angioplast* or pump*)).tw.
18 ((coronar* or heart* or cardi*) adj2 (support* or assist* or device* or system* or pump*)).tw.
19 ((coronar* or heart* or cardi*) adj2 (continuous* or CF) adj2 (blood flow* or circulat*)).tw.
20 or/13-19
21 Ventricular Function, Left/
22 Ventricular Dysfunction, Left/
23 (left * adj4 (ventricul* or ventric*) adj4 (function* or dysfunct* or arrhythm* or tachyarrhythm*)).tw.
24 ?VAD.tw.
25 (LV adj4 (support* or assist* or device* or system*)).tw.
26 ((haemodynamic* or hemodynamic* or ventric* or circulator*) adj4 (support* or assist* or device* or system*)).tw.
27 or/21-26
28 Coronary Artery Disease/su
29 Shock, Cardiogenic/su
30 Heart Failure/su
31 Coronary Occlusion/
32 ST Elevation Myocardial Infarction/
33 Myocardial Infarction/su [Surgery]
34 Cardiac Output, Low/
35 (low adj2 cardi* adj2 (output* or syndrom*)).tw.
36 Ischemia/su [Surgery]
37 ((coronar* or heart* or cardi*) adj2 (circulat* or blood flow*) adj2 (collaps* or fail* or fontan*)).tw.
38 ((heart* or cardi* or myocardi* or corona*) adj2 (intervent* or revascular* or surg* or procedure* or operat*)).tw.
39 ((acute or ST elevat*) adj2 myocardi* adj2 infarct*).tw.
40 ((acute or ST elevat*) adj2 MI).tw.
41 STEMI.tw.
42 or/28-41
43 12 and 20 and 27 and 42
44 (heartmate and (Percutan* or PHP or ?VAD)).tw.
45 (Impella* and (Percutan* or PHP or ?VAD)).tw.
46 (IVAC2L or "Terumo interventional system").tw.
47 ((PROTECT I or PROTECT II or RECOVER I or RECOVER II or ISAR-SHOCK or SHIELD I or SHIELD II or DanShock) and (trial* or stud*)).tw.
48 (NCT02468778 or NCT02831881 or NCT03000270 or NCT01633502 or NCT02279979).tw.

49 or/43-48
50 animals/ not humans/
51 49 not 50
52 (news or comment or editorial or case reports).pt.
53 51 not 52
54 limit 53 to ed=20050101-20181231

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Abaunza M, Kabbani LS et al (2015). Incidence and prognosis of vascular complications after percutaneous placement of left ventricular assist device. J Vasc Surg;62:417-23.	Case series (prospective) N=90 patients who underwent placement of an Impella left ventricular assist device during PCI (in 87%). Cardiogenic shock was documented in 67 patients (74%).	The Impella was placed for an average of 1 day (range, 0-5 days). At least one vascular complication occurred in15patients (17%).Acute limb ischemia occurred in12 patients; of whom four required an amputation and six required open or endovascular surgery. Other complications included groin hematomas and one pseudoaneurysm. All patient 30-day mortality was 50%, which was not significantly associated with vascular complications. Female sex and cardiogenic shock at the time of insertion were associated with vascular complications (P=.043 and P=.018, respectively).	Larger studies included in table 2.
Agarwal H and Aggarwal K (2016). Mechanical circulatory support in percutaneous coronary interventions: expanding the possibilities. The Journal of invasive cardiology. 6 (20): 243-246.		Percutaneous VADs should be considered for use in patients undergoing high-risk PCI, with CS and biventricular failure.	commentary
Akhondi AB, and Lee MS (2013). The Use of Percutaneous Left Ventricular Assist Device in High-risk Percutaneous Coronary Intervention and Cardiogenic Shock. Rev Cardiovasc Med;14(2-4):e144-e149	Case report and review	This review outlines a case of severe cardiogenic shock and hemodynamic instability where high-risk PCI is a reasonable option.	Review
Alasnag MA, Gardi DO et al (2011). Use of the Impella 2.5 for prophylactic circulatory support during elective high-risk percutaneous coronary intervention. Cardiovasc Revasc Med. 12(5):299-303.	Single-centre retrospective chart review N= 60 consecutive elective high-risk PCI cases Impella 2.5 for partial circulatory support during elective PCI Follow-up: 20 months	Despite lesion complexity and high-risk factors, we achieved an angiographic success rate of 96%. Left main lesions were treated in 55% of the patients, and 83% of patients had multiple lesions treated. There was one procedural death. At 30 days post intervention, mortality was 5%, and rates of myocardial infarction, stroke, target vessel revascularization and urgent bypass surgery were 0%.	Included in HTA 2017 added to table 2.

Alabbady AM, Abdul-Al AS et al (2017). Left ventricular assisting devices in percutaneous coronary intervention.US Cardiology Review 11 (2), 86-94.	Review	We aim to review the percutaneously-placed left ventricular assisting devices available to catheterization laboratories in the US for use in high-risk PCIs, their indications, contraindications, limitations, and review of the most prominent literature.	Review
Alli OO, Singh IM, Holmes DR, Pulido JN, Park SJ, Rihal CS. Percutaneous left ventricular assist device with TandemHeart for high risk percutaneous coronary intervention: the Mayo Clinic experience. Catheter Cardiovasc Interv 2012; 80:728e734.	Retrospective cross-sectional analysis N=54 patients undergoing high-risk PCI using the TandemHeart device for support.	There was a significant decrease in right and left heart pressures ($P < 0.05$) with a concomitant increase in the cardiac output from 4.7 to 5.7 L/min ($P = 0.03$) during TandemHeart support. Left main and multivessel PCI was performed in 62% of patients, and rotablation was used in 48%. Procedural success rate was 97%, whereas 30-day and 6 month survival were 90% and 87%, respectively. Major vascular complications occurred in 13% of cases. None of our patients developed contrast induced nephropathy or needed dialysis.	Included in Briasoulis A 2017 meta-analysis added to table 2.
Al-Husmai W, Yturralde F et al (2008). Single-centre experience with the TandemHeart percutaneous ventricular assist device to support patients undergoing high-risk percutaneous coronary intervention.	Case series N=6 implanted the TandemHeart percutaneous ventricular assist device in 6 patients who underwent high-risk PCI	100% success rate with implantation of the THpVAD. Five of the 6 patients were alive at 30 days post procedure. One patient died 3 days after the procedure due to multiorgan failure. A vascular surgeon performed the removal of the devices with no associated complications.	Larger studies included in table 2.
Alkhouli M, Mustafa Al et al (2017). Mechanical circulatory support in patients with severe aortic stenosis and left ventricular dysfunction undergoing percutaneous coronary intervention. Journal of Cardiac Surgery 32 (4), 145-49.	Case report and review	We present a case in which Tandem Heart was used to support a patient with severe aortic stenosis, severe protected left main and circumflex disease and severe cardiomyopathy and review the literature on this subject.	Case report

Alkhatib B, Wolfe L et al (2016). Hemodynamic Support Devices for Complex Percutaneous Coronary Intervention. Interventional Cardiology Clinic 5, 187-200.	Review	Trial data, consensus documents, and guidelines currently recommend high-risk PCI aided by hemodynamic support devices, and this article discusses the patient populations who would benefit from such an approach, the available devices and strategies, and expected outcomes.	Review
Al-Rashid F, Nix C et al (2015). Tools & Techniques - Clinical: Percutaneous catheter based left ventricular support using the Impella CP. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 10(11):1247-9	Key differences and technique will be discussed. In addition, we will try to give more insight into technical specifications and try to provide some tips and tricks for the users.		Technique.
Anusionwu O, Fischman D, Cheriyath P (2012). The duration of Impella 2.5 circulatory support and length of hospital stay of patients undergoing high-risk percutaneous coronary interventions. Cardiol Res. 3(4):154-7.	Single-centre retrospective chart review N=25 Impella circulatory support during percutaneous coronary intervention Not reported if elective or emergency PCI Follow-up: 15 months	The Impella was successfully inserted in all cases with a median duration of support of 70 minutes (range, 4 - 5760 minutes). Bleeding complication occurred in 8%. Spearman's rank correlation coefficient between the duration of Impella support and hospital stay was 0.49 (P = 0.023) while it was 0.71 (P = 0.001) between Impella support duration and CCU days.	Included in HTA 2017 added to table 2.
Arroyo D and Cook S (2012). Percutaneous ventricular assist devices: clinical evidence. Clin. Pract. 9(1)	Review	Efficient therapy of cardiogenic shock and optimal protection in high-risk percutaneous coronary intervention are still orphaned to ideal management. Intra-aortic Balloon pump and the newer percutaneous ventricular assist devices, such as TandemHeart and Impella Recover LP 2.5, have diversified the therapeutic arsenal with which one can tackle these clinical dilemmas. This article describes the characteristics of these three devices as well as the clinical evidence available for optimal and adapted use.	Review

Atkinson TM, Ohman EM et al (2016). A practical approach to mechanical circulatory support in patients undergoing percutaneous coronary intervention. JACC; cardiovascular Interventions, 9(9), 871-83.	Statement from the interventional council of the American college of cardiology.	The goal of this paper is to provide a practical approach to percutaneous mechanical circulatory support in patients undergoing percutaneous coronary intervention with cardiogenic shock and/or high risk features to aid decision making for interventional cardiologists.	Review and statement
Bagai J, Webb D et al (2011). Efficacy and safety of percutaneous life support during high-risk percutaneous coronary intervention, refractory cardiogenic shock and in-laboratory cardiopulmonary arrest. The Journal of invasive cardiology 23(4):141-7.	Retrospective cohort study N=39 patients treated either with percutaneous left ventricular assist devices (pLVAD) or cardiopulmonary support (CPS) for support of high-risk PCI, cardiogenic shock or in-lab cardiac arrest. (Tandem-Heart in 19 and Multifunctional Percutaneous Heart (MPH) system in 20 for both CPS and pLVAD).	Procedural efficacy was 100%. Emergent institution of CPS, in the setting of cardiac arrest, was able to support 7 out of 8 patients and resulted in a 50% survival to hospital discharge rate. Overall, in-hospital death and 30-day major adverse cardiac event rates were 28.2% and 35.9%, respectively. The risk of vascular complications and bleeding was relatively small. pLVADs are effective in supporting patients during high-risk cardiac (coronary and structural heart) interventions, with a low risk of device-related complications. Further, the expeditious use of CPS in the catheterization laboratory can improve survival in a selected subset of patients with refractory cardiogenic shock and cardiac arrest.	Larger studies included in table 2.
Basir MB, Schreiber T et al (2018). Feasibility of early mechanical circulatory support in acute myocardial infarction complicated by cardiogenic shock: The Detroit cardiogenic shock initiative. Catheterization and cardiovascular interventions: official journal of the Society for Cardiac Angiography & Interventions. 91: 454-461.	N=41 patients acute myocardial infarction complicated by n cardiogenic shock mechanical circulatory support (MCS)- Impella 2.5, CP	Door to support times averaged 83 ± 58 minutes and 71% of patients were able to reduce the levels of inotropes and vasopressors within the first 24-hours of their index procedure. Pre-procedure cardiac power output (CPO) was 0.57 W and post-procedure CPO was 0.95 W, a 67% increase ($p < 0.001$). Survival to explant for the entire cohort was 85% a significant improvement from institutional historical controls (85% vs 51% $p < 0.001$) and survival to discharge was 76%.	Larger studies included in table 2.

Basir MB, Schreiber TL et al (2017). Effect of Early Initiation of Mechanical Circulatory Support on Survival in Cardiogenic Shock. Am J Cardiol;119:845e851	287 consecutive unselected patients enrolled in the catheter-based ventricular assist device registry presenting with AMICS who underwent percutaneous coronary intervention (PCI) were included in this analysis. All patients were supported with either the Impella 2.5 or Impella CP.	Survival to discharge was 44%. In a multivariate analysis, early implantation of a MCS device before PCI (p [0.04) and before requiring inotropes and vasopressors (p < 0.05) was associated with increased survival. Survival was 66% when MCS was initiated <1.25 hours from shock onset, 37% when initiated within 1.25 to 4.25 hours, and 26% when initiated after 4.25 hours (p [0.017). Survival was 68%, 46%, 35%, 35%, and 26% for patients requiring 0, 1, 2, 3, and ‡4 inotropes before MCS support, respectively (p <0.001).	Larger studies included in table 2.
Bhat et al (2011). Acute Complication Due to Impella 2.5 Device (Superficial Femoral Artery Thrombosis): Managed Successfully with Novel Aspiration Thrombectomy Catheter (Pronto V3). Clinical Medicine Insights: Cardiology. 5 17–21	Case report Impella recover LP 2.5 use in a high risk PCI	We report here the first case of a serious local vascular complication—superficial femoral artery thrombus formation during Impella recover LP 2.5 use in a high risk PCI which was managed successfully with novel aspiration thrombectomy catheter (Pronto V3), which in itself is the first reported use of Pronto V3 in such a vascular complication.	Larger studies included in table 2.
Alqaraqaz M, Bsir M et al (2018). Effects of Impella on Coronary Perfusion in Patients With Critical Coronary Artery Stenosis. Circ Cardiovasc Interv. 2018;11:e005870. DOI: 10.1161/	Case series N=11 patients (12 coronary lesions) undergoing high-risk percutaneous coronary interventions with the use of mechanical circulatory support Impella	When compared with minimum support, maximum support resulted in a decrease in the left ventricular end-diastolic pressure (27.3±8.6 versus 21.5±5.2 mm Hg; P=0.002) and increases in the mean systemic blood pressure (77.6±13.5 versus 88.2±12.2 mm Hg; P<0.001) and mean distal coronary pressure (51.8±20.2 versus 60.8±18.1 mm Hg; P<0.001). Effective coronary perfusion pressure (mean aortic pressure–left ventricular end-diastolic pressure) significantly increased with maximum support (49.8±15.7 versus 67.2±13.6 mm Hg; P<0.001). Diastolic perfusion pressure (diastolic blood pressure–left ventricular end-diastolic pressure) also significantly increased with maximum support (32.9±13.4 versus 52.0±11.6 mm Hg; P<0.001).	Results demonstrated in PROTECT II study-subgroup analysis of patients who had multi-vessel PCI.

Baumann S, Werner N et al (2018). Indication and short-term clinical outcomes of high-risk percutaneous coronary intervention with microaxial Impella® pump: results from the German Impella® registry. Clinial Research in Cardiology. https://doi.org/10.1007/s00392-018-1230-6	Observational, retrospective multi-center registry n=154 patients with complex coronary anatomy and comorbidities who have undergone protected high-risk PCI with Impella.	The majority were at a high operative risk illustrated by a logistic EuroSCORE of 14.7–17.4. The initial SYNTAX score was 32.0–13.3, indicating very complex CAD and could be reduced to 14.1–14.3 ($p < 0.0001$) after PCI. The main reasons for protected PCI were complex coronary anatomy (70.8%), personal impression (56.5%), reduced ventricular ejection fraction (49.4%), comorbidities (47.4%), and surgical turndown (30.5%). Four patients (2.6%) experienced an intrahospital death.	More relevant studies added to table 2.
Becher T, Bauman S et al (2017). Comparison of peri and post-procedural complications in patients undergoing revascularisation of coronary artery multivessel disease by coronary artery bypass grafting or protected percutaneous coronary intervention with the Impella 2.5 device. European Heart journal: acute cardiovascular care. published online: June 29, 2017.	Retrospective study N=54 patients with complex multivessel coronary artery disease undergoing either coronary artery bypass grafting before the implementation of a protected percutaneous coronary intervention programme with a peripheral ventricular assist device (n=28) or protected percutaneous coronary intervention with the Impella 2.5 device (n=26)	The major adverse cardiac and cerebrovascular event rate was numerically higher in the coronary artery bypass grafting group (17.9 vs. 7.7%; P=0.43) but was not statistically significant. The combined secondary endpoint was not different between the groups; however, patients undergoing coronary artery bypass grafting experienced significantly more peri-procedural adverse events (28.6 vs. 3.8%; P<0.05). Patients with complex multivessel coronary artery disease undergoing protected percutaneous coronary intervention with the Impella 2.5 device experience similar intrahospital major adverse cardiac and cerebrovascular event rates when compared to coronary artery bypass grafting.	More relevant and large studies included in table 2. CABG versus PCI with MHS device

Boudoulas KD, Pederzolli A et al (2012). Comparison of Impella and intra-aortic balloon pump in high-risk percutaneous coronary intervention: vascular complications and incidence of bleeding. Acute Card Care.14 (4):120-4.	Single-centre retrospective chart review N=13 (Impella 2.5) versus 62 (IABP) Included patients with cardiogenic shock (7.6% in Impella 2.5, 43.5% in IABP) Not reported if elective or emergency PCI Follow-up: 1 year	Post-procedure hematocrit was similar between groups. Blood transfusion occurred in 38.4% and 32.2% of patients in the Impella and IABP groups, respectively (*P* = NS); 65.3%, 30.7% and 3.8% of bleeding were due to vascular access site/procedure related, gastrointestinal and genitourinary, respectively. There was no statistical significant difference in vascular complications between the Impella and IABP groups (15.3% and 6.4% of patients, respectively); mesenteric ischemia (*n* = 1) and aortic rupture (*n* = 1) were only in the IABP group. In-hospital and one-year mortality were not statistically significant between groups.	Included in HTA 2017 added to table 2.
Blumenstein j, de Waha S et al (2016). Percutaneous ventricular assist devices and extracorporeal life support: current applications. EuroIntervention, 12:X161-67.	Review	Despite the lack of sufficient scientific evidence, the use of mechanical circulatory support devices has risen considerably in recent years. This educational article covers practical issues of IABP, LVAD, and ECLS with respect to patient and device selection, implantation technique, potential complications, and future perspectives.	Review
Burzotta F, Paloscia L et al (2008). Feasibility and long-term safety of elective Impella-assisted high-risk percutaneous coronary intervention: a pilot two-centre study. J Cardiovasc Med (Hagerstown) 9(10):1004-10.	Case series N=10 Impella® Recovery LP 2.5 high-risk PCI	Weaned 10/10 Survival 9/10 One patient died after removal due to acute stent thrombosis	Larger studies included in table 2
Burzotta F, Trani C et al (2015). Impella ventricular support in clinical practice: Collaborative viewpoint from a European expert user group. International Journal of Cardiology, 201, 684–691.	Review	A European expert user group review on the main theoretical principles of Impella. An up-to-date summary of the best practical aspects of Impella technology in a variety of clinical settings. A stepwise approach to plan, start and implement an Impella program.	Review

Burkhoff D, Cohen H et al (2006). A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock.	RCT N=42 patients with cardiogenic shock (CGS) treated in an initial roll-in phase (n = 9) or randomized to treatment with IABP (n = 14) or TandemHeart pVAD (n = 19). 30 patients (71%) had persistent CGS despite having an IABP in place.	Cardiogenic shock was due to myocardial infarction in 70% of the patients and decompensated heart failure in most of the remaining patients. The mean duration of support was 2.5 days. Compared with IABP, the TandemHeart pVAD achieved significantly greater increases in cardiac index and mean arterial blood pressure and significantly greater decreases in pulmonary capillary wedge pressure. Overall 30-day survival and severe adverse events were not significantly different between the 2 groups.	Included in systematic review by Cheng 2009 added to table 2.
Casassus F, Corre J, Leroux L, Chevalereau P, Fresselinat A, Seguy B, et al (2015). The use of Impella 2.5 in severe refractory cardiogenic shock complicating an acute myocardial infarction. J Interv Cardiol; 28(1):41-50.	Single-centre retrospective chart review N=22 patients with refractory CS from acute MI undergoing PCI and Impella 2.5 support refractory to first line therapy and IABP.	Hemodynamics improved significantly, end organ and tissue perfusion improved and a significant decrease in lactate levels after 2 days support. 13 patients successfully weaned off support and 4 were transitioned to another device. Function recovery of let ventricle when compared to baseline was seen 943 versus 27%, p<0.0001).the survival rate at 6 months and 1 year was 59% and 54.5%.	Included in HTA 2017 added to table 2.
Cohen MG, Matthews R et al (2015). Percutaneous left ventricular assist device for high-risk percutaneous coronary interventions: real-world versus clinical trial experience. Am Heart J. 170 (5):872-9.	USpella registry (funded by manufacturer-47 sites in US and 2 in Canada) Multicentre retrospective observational study N=637 elective and emergency PCI compared high-risk PCI supported by a microaxial pump (Impella 2.5) in a multicenter registry [n=339) versus the randomized PROTECT II trial (NCT00562016) [n=216]. Follow-up: in hospital outcomes (Overlaps data with Miani 2012)	Compared to the clinical trial patients, registry patients at hospital discharge, experienced a similar reduction in New York Heart Association class III to IV symptoms. Registry patients had a trend toward lower in-hospital mortality (2.7% vs 4.6, *P* = .27). Transient hypotension during PCI. In hospital mortality 2.8%.	Included in HTA 2017 added to table 2.

Cook A and Winecker S (2009). Percutaneous left ventricular assist devices during cardiogenic shock and high risk percutaneous coronary interventions. Current Cardiology Reports, 5, 369-376.	Review	This article reviews the growing evidence supporting the clinical use of left ventricular assist devices. Specifically, we discuss the use of left ventricular assist devices in patients with cardiogenic shock, in patients with acute ST-elevation myocardial infarction without shock, and during high-risk percutaneous coronary interventions.	Review
Cyrus T, Mathews SJ et al (2010). Use of mechanical assist during high-risk PCI and STEMI with cardiogenic shock. Catheterization and Cardiovascular Interventions 75 Suppl 1(S1):S1-6.	Review	Traditionally, intraaortic balloon-pumps have been used in acute MI with cardiogenic shock. As this modality has limited hemodynamic benefits, new developments have focused on active hemodynamic assist devices. These devices actively unload the left ventricle increasing cardiac output by 2.5–5 L/min and are increasingly easier to implant and monitor.	Review
Daubert MA, Massaro J et al (2015). High-risk percutaneous coronary intervention is associated with reverse left ventricular remodeling and improved outcomes in patients with coronary artery disease and reduced ejection fractionAm Heart J 2015;170:550-8.	Sub study of PROTECT II study. Among patients with quantitative echocardiography (LV volumes and biplane EF), we assessed the extent and predictors of reverse LV remodeling, defined as improved systolic function with an absolute increase in EF ≥5% and correlated these findings with clinical events. Quantitative echocardiography was performed in 184 patients at baseline and longest follow-up.	Mean EF at baseline was 27.1%. Ninety-three patients (51%) demonstrated reverse LV remodeling with an absolute increase in EF of 13.2% (P b .001). End-systolic volume decreased from 137.7 to 106.6 mL (P = .002).Nosignificant change in EF or end-systolic volume was seen among non-remodelers. Reverse LV remodeling occurred more frequently in patients with more extensive revascularization (odds ratio, 7.52; 95%CI [1.31-43.25]) and was associated with significantly fewer major adverse events (composite of death/myocardial infarction/ stroke/transient ischemic attack): 9.7% versus 24.2% (P = .009). There was also a greater reduction in New York Heart Association class III/IV heart failure among reverse LV remodelers (66.7% to 24.0%) than non-remodelers (56.3% to 34.4%), P = .045.	Sub study of PROTECT II study assessing reverse LV modelling and clinical outcomes

Dangas GD, Kini AS et al (2014). Impact of Hemodynamic Support With Impella 2.5 Versus Intra-Aortic Balloon Pump on Prognostically Important Clinical Outcomes in Patients Undergoing High-Risk Percutaneous Coronary Intervention (from the PROTECT II Randomized Trial)Am J Cardiol 2014;113:222e228.	RCT PROTECT II study intraaortic balloon pump (IABP, n[211]) or a left ventricular assist device (Impella, n[216]). Follow-up: 90 days	At 90 days, the rates of both composite end points were lower in the Impella group compared with the IABP group (MAE, 37% vs 49%, p [0.014 respectively; MACCE, 22% vs 31%, p [0.034 respectively). There were no differences in death or large myocardial infarction between the 2 arms. By multivariable analysis, treatment with Impella as opposed to IABP was an independent predictor for freedom from MAE (odds ratio[0.75 [95% confidence interval 0.61 to 0.92], p[0.007) andMACCE (odds ratio[0.76 [95% confidence interval 0.61 to 0.96], p[0.020) at 90 days postprocedure..	Sub study of PROECT II study - reexamined the outcomes of PROTECT II using a prognostically relevant definition of myocardial infarction (MI) and broadened the strength of analyses by including multivariable testing for predictors of cardiovascular adverse events.
Dandekar VK, AND Shroff AR (2011). Transradial Percutaneous Coronary Intervention in Patients Requiring Circulatory Assist Devices. Journal of Invasive Cardiology. 23, 11	Case report N=2 Impella 2.5	Here we present two cases in which the Impella 2.5 was used for hemodynamic support for elective PCI procedures done via the radial approach. Transradial access strategy for percutaneous coronary intervention is feasible even in cases where a percutaneous left ventricular assist device is utilized from a femoral artery approach.	Larger studies included in table 2.
Dudek D, Rakowski T et al (2016). Circulatory support with Impella CP device during high-risk percutaneous coronary interventions: initial experience in Poland. Adv Interv Cardiol 2016; 12, 3 (45): 254–257	prospective registry of all patients treated with the Impella CP during high risk PCI n=10 follow-up: 30 days	Thirty-day outcomes of patients treated for high-risk elective PCI were good, with no death during follow-up. Only in 1 patient was a small hematoma at the site of device insertion noted.	Larger studies included in table 2.

Dixon SR, Henriques JP, Mauri L, Sjauw K, Civitello A, Kar B, et al (2009). A prospective feasibility trial investigating the use of the Impella 2.5 system in patients undergoing high-risk percutaneous coronary intervention (the PROTECT I trial): initial U.S. experience. JACC Cardiovasc Interv. 2(2):91-6.	Multicentre prospective observational study (The PROTECT I Trial; NCT00534859) N=20 patients underwent high-risk PCI with minimally invasive circulatory support employing the Impella 2.5 system. Follow-up: 30 days	Device was implanted successfully in all patients. The mean duration of circulatory support was 1.7 ± 0.6 h (range: 0.4 to 2.5 h). Mean pump flow during PCI was 2.2 ± 0.3 l/min. At 30 days, the incidence of major adverse cardiac events was 20% (2 patients had a periprocedural myocardial infarction; 2 patients died at days 12 and 14). There was no evidence of aortic valve injury, cardiac perforation, or limb ischemia. Two patients (10%) developed mild, transient hemolysis without clinical sequelae. None of the patients developed hemodynamic compromise during PCI.	Included in HTA 2017 added to table 2.
Dens J, Meyns B et al (2006). First experience with the Impella Recover(R) LP 2.5 micro axial pump in patients with cardiogenic shock or undergoing high-risk revascularisation. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology (2) 1 84-90.	Case series N=40 patients presenting with cardiogenic shock (n=13) or scheduled for a high risk revascularisation (n=27) Impella Recover(R) LP 2.5 implanted.	In 3 patients the pump could not be placed in an adequate position, 5 had access related complications, 3 had malfunctions and early device-removal. The left ventricular filling pressures decreased in both groups (22 mmHg+/-7.5 to 16 mmHg+/-6 in the shock group, [p=0.0008] and over 6 hours from 14.3 mmHg+/-5.8 to 10 mmHg+/-2.9 in the high-risk revascularisation group,[p=0.0327]).	Larger studies included in table 2.
Doshi R, Singh A et al (2018). Gender difference with the use of percutaneous left ventricular assist device in patients undergoing complex high-risk percutaneous coronary intervention: From pVAD Working Group. European Heart Journal:acute cardiovascular care, published online: January 8, 2018, 1-10	Retrospective analysis 160 complex high-risk indicated patients with percutaneous left ventricular assist device use who were not in cardiogenic shock 9132 male and 28 female). Impella 2.5 or Impella CP (Abiomed Inc.) device was used as a left ventricular support device. In-hospital and 30-day follow-up	There was no difference in in-hospital mortality between the genders after performing a propensity score matched analysis (8.3% *vs*. 12.5%, *p*=0.54). Secondary outcomes of myocardial infarction, cardiogenic shock, congestive heart failure, dysrhythmia, major adverse cardiac events and composite of all complications were higher in males. Furthermore, 30-day survival was similar in males and females (88.9% *vs*. 87.5%, *p*=0.31). In addition, worse complications rates and survival were noted in patients with incomplete revascularization compared with those patients with complete revascularization in both gender.	More relevant studies included in table 2. Gender differences in clinical outcomes when LVAD support is used.

Eichhofer J, Osten M, Horlick E, Dzavik V. First Canadian experience with high-risk percutaneous coronary intervention with assistance of a percutaneously deployed left ventricular assist device. Can J Cardiol 2008 Nov;24(11):82-5.	Case report N=2 Impella® Recovery LP 2.5 high-risk PCI	Successful prophylactic use. % weaned : 1/1 % survival: 1/1	Larger studies included in table 2.
Engström AE, Granfeldt H, Seybold-Epting W, Dahm M, Cocchieri R, Driessen AHG, et al (2013). Mechanical circulatory support with the Impella 5.0 device for postcardiotomy cardiogenic shock: a three-center experience. Minerva Cardioangiol. 2013;61(5):539-46.	multicentre retrospective chart review n=46 patients with refractory cardiogenic shock after cardiotomy treated with Impella 5.0 pLVAD. Half of all patients had been treated with an intra-aortic balloon pump before 5.0-implantation.	The Kaplan-Meier estimate of overall 30-day survival was 39.5%. Thirty-day survival rates for patients with PCCS, refractory to aggressive conventional treatment and treated with the Impella 5.0 device, are comparable to those reported in studies evaluating surgically implantable VADs, whereas the Impella system is much less invasive.	Included in HTA 2017 added to table 2.
Engström AE, Piek JJ et al (2010). Percutaneous left ventricular assist devices for high-risk percutaneous coronary intervention. Expert Rev. Cardiovasc. Ther. 8(9), 1247–1255.	Review	Although many devices have been developed and randomized evidence is still pending, the Impella LP2.5 device seems to be promising as it is easily applicable, carries a low complication rate and provides adequate circulatory support.	Review
Engstrom A, Sjauw K et al (2011). Long-term safety and sustained left ventricular recovery: Long-term results of percutaneous left ventricular support with Impella LP2.5 in ST-elevation myocardial infarction. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 6(7):860-5	Case control study N= 10 patients with anterior ST-elevation myocardial infarction (STEMI) had Impella LP2.5 after PCI (cardiogenic pre-shock patients) Control group: n=10 comparable patients treated with routine care Mean duration of follow-up was 2.9±0.6 years in the Impella group and 3.0±0.3 years in the control group	No differences in aortic valve abnormalities and LVEF were demonstrated between the groups; nevertheless, LVEF increase from baseline was significantly greater in Impella-treated patients (23.6±8.9% versus 6.7±7.0%, P=0.008). Three-day support with the Impella LP2.5 is not associated with adverse effects on the aortic valve at long-term follow-up. LVEF was similar in both groups; however, recovery was significantly greater in the Impella group.	Larger studies added to table 2.

Esfandiari S, Erickson L et al (2009). Technology Assessment Unit of the McGill University Health Centre. The Impella® percutaneous ventricular assist device [Internet]. Montreal (QC): McGill University; 2009. Available from: https://www.mcgill.ca/tau/files/tau/IMPELLA_FINAL_JUNE_2009.pdf	Systematic review 21 small case series 24 single reports Prophylactic use Rescue use	Prophylactic use. Impella® has been used “prophylactically” to provide vascular support during elective procedures such as PCI in dangerously compromised patients for a total of 143 cases. All of these patients were successfully weaned from the device and the estimated survival rate was 0.951(95% CI, 0.89-1.00). Rescue use. Impella® has been used as a "rescue" intervention in 131 cases of otherwise uncorrectable acute vascular collapse. Of these the rate of successful weaning from the pump was 0.82 (95%CI: 0.70- 0.94), and the survival rate 0.71 (95%CI: 0.52-0.89) .Significant complications were rare. Haemolysis, when reported, was mild. The Impella® device is clearly more clinically effective than IABP or ECMO.	More recent HTA added to table 2.
Ferreiro JL, Gómez-Hospital JA, Cequier AR, Angiolillo DJ, Roura G, Teruel L, Maristany J, Gómez-Lara J, Jara F, Bass TA, Esplugas E. Use of Impella Recover LP 2.5 in elective high risk percutaneous coronary intervention. Int J Cardiol 2010; 145:235e237.	Registry data review N=27 Impella Recover LP 2.5	Our study shows that the use of the Impella Recover LP 2.5 device is feasible, has an overall favorable safety profile, and may help prevent periprocedural and short-term complications derived from high-risk procedures	Included in Briasoulis A 2017 meta-analysis added to table 2.
Foresch P, Martinelli M et al (2011). Clinical use of temporary percutaneous left ventricular assist devices. Catheterization and Cardiovascular Interventions 78: 304-313.	Retrospective analysis N=75 patients with cardiogenic shock (n = 49) or high-risk percutaneous coronary intervention (n = 26). 42 patients with cardiogenic shock and 16 patients with high-risk PCI received a TandemHeart and 7 patients and 10 patients, respectively, received an Impella Recover LP 2.5.	One-month survival was 53% in patients with shock and 96% in patients with PCI. TPLVADs can support the failing heart with acceptable risk. Outcome is better in prophylactic use than in patients with cardiogenic shock.	Larger studies included in table 2.

Frisoli TM, Guerrero M et al (2016). Mechanical circulatory support with Impella to facilitate percutaneous coronary intervention for post-TAVI bilateral coronary intervention.	Case report	Successful deployment of Impella to restore hemodynamic stability facilitated definitive treatment with bilateral PCI.	Case report
Gimelli G, Wolff MR. Hemodynamically supported percutaneous coronary revascularization improves left ventricular function in patients with ischemic dilated cardiomyopathy at very high risk for surgery: a single-center experience. J Invasive Cardiol 2008; 20:642e646.	Retrospective case-series analysis N= 11 patients with prior myocardial infarction and ischemic cardiomyopathy underwent TandemHeart®-supported PCI. Indications for prophylactic support were depressed LVEF and a large myocardial mass at risk.	Baseline LVEF was 25 ± 8%, increasing to 41 ± 9% at a mean follow-up time of 15 ± 15 months ($p \leq 0.0004$). There were no in-hospital MACE and only 1 vascular complication requiring blood transfusion.	Included in Briasoulis A 2017 meta-analysis added to table 2.
Gimbolini C, Notaristefano S et al (2006). Percutaneous left ventricular assist device TandemHeart, for high-risk percutaneous coronary revascularization. A single centre experience. Acute Cardiac Care 8: 35-40.	Case series N= 6 patients underwent either emergency (n = 3) or elective (n = 3) placement of the TandemHeart device before a high-risk procedure.	Percutaneous transseptal ventricular assist device, TandemHeart, can be easily and rapidly deployed either in emergency or in elective high-risk PCI to achieve complete cardiac assistance.	Larger studies included in table 2.
Goldstein JA, Dixon SR et al (2017). Maintenance of valvular integrity with Impella left heart support. Results from the multicenter PROECT II randomized study. Catheterization and Cardiovascular Interventions 1-5.	RCT N=445 patients undergoing Impella (n=216) vs intra-aortic balloon pump (n=211) in the randomized PROTECT II. Echocardiographic analysis Follow-up: 90 days.	During Impella support there was no appreciable change in the degree of baseline valvular regurgitation. There were no cases of structural derangement of the mitral or aortic valve after use of the Impella device. At 90-day follow-up, there was an average 22% relative increase in LVEF from baseline (27% ± 9 vs. 33% ± 11, $P < 0.001$).	Echocardiographic analysis Sub study of PROTECT II study.

Gregory D, Scotti DJ, de Lissovoy G, Palacios I, Dixon S, Maini B, et al (2013). A value-based analysis of hemodynamic support strategies for high-risk heart failure patients undergoing a percutaneous coronary intervention. Am Health Drug Benefits; 6(2):88-99.	To compare the clinical and economic benefits of a percutaneous ventricular assist device versus an intra-aortic balloon pump (IABP) observed during the 90-day duration of the PROTECT II clinical trial, supplemented by a Markov model.	For high-risk patients with advanced heart failure undergoing PCI, the new pVAD reduced major adverse events, critical care and readmission length of stay, and readmission cost over the 90-day EOC, and was determined to be cost-effective over the longterm. These findings can assist decision makers in forming value-based judgments with regard to new hemodynamic support strategies.	Economic analysis –out of IP remit.
Griffith BP, Anderson MB, Samuels LE, Pae WE Jr, Naka Y, Frazier OH (2013). The RECOVER I: a multicenter prospective study of Impella 5.0/LD for postcardiotomy circulatory support. J Thorac Cardiovasc Surg;145(2):548-54.	Multicentre prospective study (RECOVER 1 study) N=16 patients with refractory cardiogenic shock after cardiotomy treated with Impella 5.0 pLVAD.	Hemodynamics improved immediately after the initiation of mechanical support: cardiac index, 1.65 versus 2.7 L/min/m2 (P = .0001); mean arterial pressure, 71.4 versus 83.1 mm Hg (P = .01); and pulmonary artery diastolic pressure, 28.0 versus 19.8 mm Hg (P < .0001). The pump provided an average of 4.0 ± 0.6 L/min of flow for an average duration of 3.7 ± 2.9 days (range, 1.7–12.6). The primary safety endpoint occurred in 2 patients (13%; 1 stroke and 1 death). For the primary efficacy endpoint, recovery of the native heart function was obtained in 93% of the patients discharged, with bridge-to-other-therapy in 7%. Survival to 30 days, 3 months, and 1 year was 94%, 81%, and 75%, respectively.	Included in HTA 2017 added to table 2.
Hatch J and Baklanov D (2014). Percutaneous hemodynamic support in PCI. Curr Treat Options Cardio Med 16: 293.	Review	With continued refinements in device technology, technique and application, it is anticipated that percutaneous device based procedures will continue to improve patient outcomes in the most critically ill and highest risk patients.	Review.
Henriques JP, Remmelink M et al (2006). Safety and feasibility of elective high-risk percutaneous coronary intervention procedures with left ventricular support of the Impella Recover LP 2.5. Am J Cardiol; 97(7):990-2.	Case series N=19 Impella® Recovery LP 2.5 high-risk PCI	Procedural success in all 19 patients No aortic valve regurgitation. Minor fall in Hb, No important device-related adverse events Weaning 19/19 Survival 19/19	Included in Ichou A 2017 added to table 2.

Henriques JPS, Classen BE et al (2015). Performance of currently available risk models in a cohort of mechanically supported high-risk percutaneous coronary intervention-From the PROTECT II randomized trial. International Journal of Cardiology 189: 272-278.	RCT Retrospective review N= 427 patients with unprotected left main disease, last remaining vessel or three-vessel disease with severely reduced left ventricular function underwent supported high-risk PCI with an intra-aortic balloon pump (IABP, N = 211) or a left ventricular assist device (Impella 2.5, N = 216) as part of the PROTECT II trial. Study examined the performance of the additive Euroscore, logistic Euroscore, STS mortality score, STS morbidity and mortality score, Mayo Clinic risk score and New York state PCI risk score on the endpoint of 90-day mortality in this unique high-risk population.	All-cause 90-day mortality was 10.4%. The scores were generally correlated ($p < 0.0001$ for all comparisons), with R2 values ranging from 0.28 (STS morbidity/mortality and Mayo Clinic) to 0.68 (logistic Euroscore and STS mortality). However, receiver–operator curves for 90-day all-cause mortality for all risk scores demonstrated poor discriminatory performance with c-statistics of 0.542–0.616. Calibration of the risk scores was not poor, but varied according to the specific score examined.	Risk assessment. Sub study of PROTECT II study.
Higgins J, Lamarche Y, Kaan A, Stevens LM, Cheung A (2011). Microaxial devices for ventricular failure: a multicentre, population-based experience. Can J Cardiol;27(6):725-30.	retrospective review N=35 patients with dilated cardiomyopathy (n = 13), acute myocardial infarction (n = 6), postcardiotomy shock (n = 6), and other etiologies (n = 12). Different models of Impella devices used (2 received Impella 2.5, 29 received Impella 5.0, and 6 received Impella RD/5.0).	Mean duration of support was 3.7 ± 3.0 days. In all, 49% were successfully weaned, and 22% were transferred to long-term mechanical support. Four patients have subsequently undergone successful cardiac transplantation. The 30-day mortality was 40%, and 6-month mortality was 49%. Complications included gastrointestinal bleeding (n = 1), hemoptysis (n = 1), and thrombocytopenia (n = 4).	Included in HTA 2017 added to table 2.

Ho KW, and Dzavik (2011). Haemodynamic Support Devices for Complex and High-risk Percutaneous Coronary Intervention. Interventional Cardiology, 2011;6(1):17–24	Review	Percutaneous haemodynamic support devices, including intra-aortic balloon counterpulsation pumps, percutaneous cardiopulmonary support and left ventricular assist devices, have been developed as adjunctive therapies during these complex procedures. Improvements in haemodynamic profiles with the use of these devices enhance procedural safety, allowing successful PCI to be performed in a more stable environment. Nevertheless, the use of these devices is associated with potentially serious complications and solid evidence for their routine use in high-risk PCI is lacking. Ongoing improvements in device designs and deployment techniques may eventually allow earlier, prophylactic use of support devices. Until then, the use of haemodynamic support devices should be individualised after careful consideration of the potential benefits and risks involved.	Review
Iliodromitis KE, Kahlert P et al (2011). High-risk PCI in acute coronary syndromes with Impella LP 2.5 device support. Int J Cardiol. 153(1):59-63.	Single-centre prospective observational study N=38 high-risk patients (mean age, 69.7±10.3 years, logistic EuroSCORE, 22.4±14.9%) with unstable angina pectoris or non-ST-segment elevation myocardial infarction and severe three-vessel-disease underwent emergency PCI [Patients with acute coronary syndrome required urgent revascularization] Follow-up: 30 days	Device insertion and explantation was feasible in all patients without vascular complications and continuous hemodynamic stability was obtained during PCI. PCI was uneventfully performed in all but one patient for technical reasons. One non procedure-related death occurred 7 days after the intervention, accounting for a total 30-day mortality of 2.86%. Other major cardiac or cerebrovascular events did not occur.	Included in HTA 2017 added to table 2.

Isgro F, Kiessling AH, Rehn E, Lang J, Saggau W. Intracardiac left ventricular support in beating heart, multi-vessel revascularization. J Card Surg 2003 May;18(3):240-4.	Prospective case series N=38 patients selected for coronary revascularization of beating heart 15 had a micro pump transaortically implanted in the left ventricle to support the heart during the operation with a flow rate of 2.5 to 3.9 l/min. 23 had no pump	Only one patient out of the left-ventricle-supported group had to be further operated on conventionally. There tended to be a higher blood loss recorded with the pump-supported patients. 8 patients operated on without pump support, the operation had to be converted to conventional methods.	Larger studies added to table 2.
Jones HA, Kalisetti DR et al (2012). Left Ventricular Assist for High-Risk Percutaneous Coronary Intervention. J INVASIVE CARDIOL 2012;24(10):544-550.	Review	The purpose of this report is to review the physiologic mechanism of action of the devices and discuss indications, limitations, and clinical outcomes during high-risk PCI.	Review
Joseph SM, Brisco MA et al (2016). Women With Cardiogenic Shock Derive Greater Benefit From Early Mechanical Circulatory Support: An Update From the cVAD registry. Journal of Interventional Cardiology. 29 (3), 248-256.	cVAD Registry analysis 180 patients who underwent percutaneous coronary intervention (PCI) and Impella 2.5 support for CS complicating an AMI	There was no difference in survival to discharge (P = 0.3). Patients receiving the Impella 2.5 pre-PCI had significantly lower inpatient mortality than those who received support post-PCI (P = 0.003). However, the magnitude of the survival benefit was significantly greater in women who received the Impella pre-PCI as compared to men. Overall, 68.8% of women survived with pre-PCI Impella 2.5 versus 24.2% post-PCI (P = 0.005) whereas 54.2% of men survived with pre-PCI Impella 2.5 versus 40.3% post-PCI (P = 0.1, p-interaction = 0.07). No differences in timing to intervention were found between men and women.	More relevant studies included in table 2. Data on sex differences in outcomes with mechanical circulatory support.

Kar B, Adkins LE, Civitello AB, Loyalka P, Palanichamy N, Gemmato CJ, Myers TJ, Gregoric ID, Delgado RM 3rd. Clinical experience with the TandemHeart percutaneous ventricular assist device. Tex Heart Inst J 2006;33:111e115.	Case series N=18 TandemHeart was used to support 18 patients (11 in cardiogenic shock and 7 undergoing high-risk percutaneous transluminal coronary angioplasty.	The patients in cardiogenic shock were supported for a mean of 88.8 ± 74.3 hours (range, 4-264 hr) at a mean pump flow rate of 2.87 ± 0.56 L/min (range, 1.8-3.5 L/min). The mean cardiac index improved from 1.57 ± 0.31 L/min/m2 before support to 2.60 ± 0.34 L/min/m2 during support. The mean duration of support for the high-risk percutaneous transluminal coronary angioplasty patients was 5.5 ± 8.3 hours (range, 1-24 hr). The mean flow rate was 2.42 ± 0.55 L/min (range, 1.5-3.0 L/min). The overall 30-day survival rate was 61%.	Included in Briasoulis A 2017 meta-analysis added to table 2.
Kar S (2018). Percutaneous mechanical circulatory support devices for high-risk percutaneous coronary intervention. Current Cardiology Reports 20: 2	Review	Percutaneous mechanical circulatory support devices (PMCSD) consist of the intra-aortic balloon pump (IABP), Impella, Tandem Heart, or extracorporeal membranous oxygenation (ECMO). They augment cardiac output, cardiac index, and cardiac power which allow the operator to mitigate hemodynamic perturbations during high-risk percutaneous coronary intervention (HR-PCI). This review discusses PMCSD and their contemporary literature.	Review
Kar B, Gregoric ID et al (2011). The percutaneous ventricular assist device in severe refractory cardiogenic shock. J Am Coll Cardiol 57, 688-96.	Case series N=117 patients with SRCS implanted with TandemHeart pVAD	The average duration of support was 5.8 ± 4.75 days. After implantation, the cardiac index improved from median 0.52 (interquartile range [IQR]: 0.8) l/(min·m2) to 3.0 (IQR: 0.9) l/(min·m2) ($p < 0.001$). The systolic blood pressure and mixed venous oxygen saturation increased from 75 (IQR: 15) mm Hg to 100 (IQR: 15) mm Hg ($p < 0.001$) and 49 (IQR: 11.5) to 69.3 (IQR: 10) ($p < 0.001$), respectively. The urine output increased from 70.7 (IQR: 70) ml/day to 1,200 (IQR: 1,620) ml/day ($p < 0.001$). The pulmonary capillary wedge pressure, lactic acid level, and creatinine level decreased, respectively, from 31.53 ± 10.2 mm Hg to 17.29 ± 10.82 mm Hg ($p <0.001$), 24.5 (IQR: 74.25) mg/dl to 11 (IQR: 92) mg/dl ($p < 0.001$), and 1.5 (IQR: 0.95) mg/dl to 1.2 (IQR: 0.9) mg/dl ($p < 0.009$). The mortality rates at 30 days and 6 months were 40.2% and 45.3%, respectively.	Larger and more relevant studies added to table 2.

Kern JM 2011. The Changing Paradigm of Hemodynamic Support Device Selection for High-Risk Percutaneous Coronary Interventions. Journal of invasive cardiology 23, 10,	clinical vignette	The clinical vignette is meant to illustrate the dilemma faced in daily practice with the most difficult high-risk PCI patients. the IABP was selected as the quickest way to obtain some degree of hemodynamic stabilization in the setting of AMI, As the procedure progressed, continuing hemodynamic compromise occurred. At this time, one should consider more powerful hemodynamic such as the Impella or TH. However, the team needed to institute the TH was not immediately available.	Review
Khera R, Cram P et al (2016). Use of Mechanical Circulatory Support in Percutaneous Coronary Intervention in the United States. Am J Cardiol;117:10-16.	Propensity score-matched analyses 5,031 patients who received a PVAD and 122,333 who received an IABP during PCI from the national inpatent sample.	Utilization of MCS increased from 1.3% of all PCIs in 2004 to 3.4% in 2012 (p trend <0.001), with increase in the use of both PVAD (<1/10,000 PCIs [2004 to 2007] to 38/10,000 [2012]) and IABP (132/10,000 PCIs [2004] to 299/10,000[2012] p <0.0001 for both). PVAD recipients were older (69 vs 65 years), more likely to have heart failure (68% vs 41%), chronic kidney disease (27% vs 11%, p <0.001 for all), and be admitted electively (30% vs 11%), but less likely to have acute myocardial infarction (52% vs 90%), cardiogenic shock (23% vs 50%), or need mechanical ventilation (16% vs 29%) compared with IABP recipients. Unadjusted in-hospital mortality was lower in PVAD compared with IABP recipients (12.8% vs 20.9%, p <0.001). However, in propensity-matched analyses (1:2), in-hospital mortality was similar in both groups (odds ratio 0.88, 95% confidence interval 0.70 to 1.09).	Data on all types of temporary MHS devices merged, not clear type of devices included.

Khera R, Cram P et al (2015). Trends in the Use of Percutaneous Ventricular Assist Devices: Analysis of National Inpatient Sample Data, 2007 Through 2012. JAMA Intern Med.; 175(6): 941–950	Retrospective study Patients who received a PVAD or IABP while hospitalized in the United States (2007-2012).	Utilization of PVADs increased 30-fold (4.6 per million discharges in 2007 to 138 per million discharges in 2012; P for trend < .001) while utilization of IABPs decreased from 1738 per million discharges in 2008 to 1608 per million discharges in 2012 (P for trend = .02). In 2007, an estimated 72 hospitals used PVADs, increasing to 477 in 2011 (P for trend < .001). The number of hospitals with an annual volume of 10 or more PVAD procedures per year increased from 0 in 2007 to 102 in 2011 (21.4% ofPVAD-using hospitals; P for trend < .001). Among PVAD recipients, 67.3% had a diagnosis of cardiogenic shock or acute myocardial infarction (AMI). There was a temporal increase in the use of PVADs in older patients and patients with AMI, hypertension, diabetes mellitus, and chronic kidney disease (P for trend < .001 for all). Overall, mortality in PVAD recipients was 28.8%, and mean (SE) hospitalization cost was $85 580 ($4165); both were significantly higher in PVAD recipients with cardiogenic shock (mortality, 47.5%; mean [SE] cost, $113 695 [$6260]; P < .001 for both). The PVAD recipients were less likely than IABP recipients to have cardiogenic shock (34.3% vs 41.2%; P = .001), AMI (48.0% vs68.6%; P < .001), and undergo coronary artery bypass graft surgery (6.2% vs 43.2%; P < .001), but more likely to undergo percutaneous coronary intervention (70.9% vs 40.4%; P < .001). In propensity-matched analysis, PVADs were associated with higher mortality compared with IABP (odds ratio, 1.23 [95% CI, 1.06-1.43]; P = .007).	Data on all types of temporary MHS devices merged, not clear type of devices included.

Kovacic JC, Nguyen HT, Karajgikar R, Sharma SK, Kini AS. The Impella Recover 2.5 and TandemHeart ventricular assist devices are safe and associated with equivalent clinical outcomes in patients undergoing high-risk percutaneous coronary intervention. Catheter Cardiovasc Interv. 2013; 82(1):E28-37.	Single-centre prospective observational study N=68 patients that underwent "high-risk" PCI with P-LVAD support 36 (Impella 2.5) versus 32 (TandemHeart) Not reported elective or emergency PCI (overlaps data with Cohen 2015)	PCI success rates were 99% in both groups, with similar in-hospital outcomes and a combined 7% major vascular access site complication rate. A single episode of left atrial perforation occurred during TH use. No patient required emergent CABG and no in-hospital deaths occurred. The 30-day MACE rate (death, myocardial infarction, target lesion revascularization) was 5.8%. There were no differences between the IR2.5 and TH groups with respect to short- or long-term clinical outcomes.	Included in HTA 2017 added to table 2. Included in Briasoulis A 2017 meta-analysis added to table 2.
Kovacic JC, Kini A et al (2015). Patients with 3-vessel coronary artery disease and impaired Ventricular Function Undergoing PCI with Impella 2.5 Hemodynamic Support Have Improved 90-Day Outcomes Compared to Intra-Aortic Balloon Pump: A Sub-Study of The PROTECT II Trial. J Interventional Cardiology 28:32-40.	RCT N=325 patients with left main/last patent vessel or 3-vessel coronary artery disease (3VD) in PROTECTII study undergoing PCI with hemodynamic support with IR2.5 compared to IABP. 167 Impella 2.5 (IR2.5) versus 158 intra-aortic balloon pump (IABP) Follow-up: 90 days	At 30 days after PCI, patients that received IR2.5 compared to IABP support trended toward a reduction in incidence of major adverse events (MAE): 32.9% vs. 42.4% (P = 0.078). At 90 days after PCI, there was a significant difference favoring IR2.5 for incidence of MAE: 39.5% vs. 51.0% (P = 0.039), with this effect being consistent across multiple clinical subgroups. Use of IR2.5 was an independent predictor of improved 90-day outcomes. Patients with 3VD and reduced LVEF show improved outcomes when PCI is performed with IR2.5 hemodynamic support.	Subgroup study of PROECT II study-assessing in 3-vessel disease and reduced LVEF patients.
Lauten A, Engström AE, Jung C, Empen K, Erne P, Cook S, et al (2013). Percutaneous left-ventricular support with the Impella-2.5-assist device in acute cardiogenic shock: results of the Impella-EUROSHOCK-Registry. Circ Heart Fail; 6(1):23-30.	Retrospective analysis Impella-EUROSHOCK multicentre registry N= 120 patients with cardiogenic shock from acute myocardial infarction receiving Impella 2.5 support, 10 patients upgraded to higher pump flow (Impella 5.0, ECMO, or surgical left ventricular assist device)	Thirty-day mortality was 64.2%. lactate levels decreased from 5.8±5.0 mmol/L to 4.7±5.4 mmol/L (P=0.28) and 2.5±2.6 mmol/L (P=0.023) at 24 and 48 hours, respectively. Early major adverse cardiac and cerebrovascular events were reported in 18 (15%) patients. Major bleeding at the vascular access site, hemolysis, and pericardial tamponade occurred in 34 (28.6%), 9 (7.5%), and 2 (1.7%) patients, respectively. age >65 and lactate level >3.8 mmol/L at admission were identified as predictors of 30-day mortality. After 317±526 days of follow-up, survival was 28.3%.	Included in HTA 2017 added to table 2.

Lee JM, Park J, Kang J, Jeon KH, Jung JH, Lee SE, et al (2015). The efficacy and safety of mechanical hemodynamic support in patients undergoing high-risk percutaneous coronary intervention with or without cardiogenic shock: Bayesian approach network meta-analysis of 13 randomized controlled trials. Int J Cardiol;184(1):36-46.	Systematic review and Bayesian network meta-analysis of RCTs comparing mechanical hemodynamic support devices (IABP [n=1410], pVAD [n=279]) versus medical therapy [n=1154] in high risk PCI populations.	Overall survival benefit was not significant with IABP (RR 0.84, 95% CI 0.56-1.24) or pVAD 9RR 0.95, 95% CI 0.42- 2.06) compared with medical therapy. Early survival benefit was also not seen. In terms of bleeding, pVAD was the worst (versus IABP RR 29.4, 95% CI 5.99-22.10, versus medical therapy RR 41.7, 95% CI 8.19-330.0) which was mainly driven by high incidence of bleeding in ECMO and TandemHeart, while IABMP was worse than MT (RR 1.41, 95% CI 1.01-2.08). the incidence of acute limb ischemia or vascular complication was not different between treatment groups.	Diverse studies on temporary MHS devices.included in the network meta-analysis (eg percutaneous cardiopulmonary bypass support-ECMO compared with IABP, emergency bypass system, Impella 2.5, TandemHeart) Evidence on IABP versus medical therapy is out of remit.
Lemaire A, Anderson MB, Lee LY, Scholz P, Prendergast T, Goodman A, et al (2014). The Impella device for acute mechanical circulatory support in patients in cardiogenic shock. Ann Thorac Surg; 97(1):133-8.	retrospective chart review N=47 patients with cardiogenic shock (n= 15) and postcardiotomy cardiogenic shock (n= 32). (38 had Impella 5.0 and 9 had Impella 2.5).	Ventricular function recovered in 34 of 47 patients (72%), and the device was removed, with 4 patients (8%) transitioned to long-term ventricular assist devices. The 30-day, 90-day, and 12-month mortality rates were 25%, 34%, and 36%, respectively. Complications occurred in 30% of the population and included device malfunction, high purge pressure, tube fracture, and groin hematoma	Included in HTA 2017 added to table 2.
Lamarche Y, Cheung A, Ignaszewski A, Higgins J, Kaan A, Griesdale DEG, et al (2011). Comparative outcomes in cardiogenic shock patients managed with Impella microaxial pump or extracorporeal life support. J Thorac Cardiovasc Surg;142(1):60-5.	retrospective chart review single centre 29 patients on Impella devices [Impella 5.0 (n = 24) and Impella RD (n = 5)] were compared with 31 patients on ECMO	There was no significant difference in 30-day mortality rate between the Impella group and ECMO group (37.9% vs. 43.8%). However, blood transfusion, as indicated by the amount of blood products used, was significantly less frequent in patients supported by Impella devices than those supported by ECMO (P < .001).	Included in HTA 2017 added to table 2.

Liu W, Mukku VK et al (2013). Percutaneous Hemodynamic Support (Impella) in Patients with Advanced Heart Failure and/or Cardiogenic Shock Not Eligible to PROTECT II Trial. Int J Angiol;22:207–212.	Case series N= 10 patients with extremely high surgical risk and hemodynamic instability (advance HF and/or cardiogenic shock) underwent urgent PCI with Impella 2.5 support. 3 patients were with cardiac arrest and 1 patient was with acute myocardial infarction.	All patients hadsuccessful Impella implantation and remained hemodynamically stable during high-risk PCI. Among the 10 patients 2 patients (20%) died within 1 month and 1 patient developed limb ischemia. In high-risk population with advance HF/cardiogenic shock, Impella could be an important tool for hemodynamic support to PCI or could be a bridge to left ventricle assist device to achieve good recovery.	Larger studies included in table 2.
Mahmoudi M, Syed AI et al (2011). The role of percutaneous circulatory assist devices in acute myocardial infarction and high-risk percutaneous intervention in the 21st century. Cardiovascular Revascularization Medicine 12: 237-242.	Review	Role of percutaneous circulatory assist devices in patients with acute myocardial infarction (MI) without hemodynamic compromise and elective high-risk PCI remains controversial. This is reflected by the lack of formal recommendations by the international bodies regarding the use of such devices outside the setting of cardiogenic shock. The purpose of this article was to review the current evidence for the use of these devices in patients presenting with acute MI without cardiogenic shock and in those undergoing elective high-risk PCI.	Review
Maini B, Naidu SS, Mulukutla S, Kleiman N, Schreiber T, Wohns D, et al (2012). Real-world use of the Impella 2.5 circulatory support system in complex high-risk percutaneous coronary intervention: the USpella Registry. Catheter Cardiovasc Interv. 80 (5):717-25.	Multicentre retrospective observational study (47 sites in US and 2 in Canada (USpella registry funded by manufacturer) N=175 patients who underwent high-risk PCI with prophylactic support of the Impella 2.5 (elective and emergency PCI) Follow-up: in hospital, 30 day and 12 months	Overall angiographic revascularization was successful in 99% of patients and in 90% of those with multivessel revascularization, resulting in a reduction of the mean SYNTAX score post-PCI from 36 ± 15 to 18 ± 15 ($P < 0.0001$) and an improvement of the ejection fraction (from 31 ± 15% to 36 ± 14%, $P < 0.0001$). In 51% of patients, the functional status improved by one or more NYHA class ($P < 0.001$). In hospital mortality 3.4%. At 30-day follow-up, the rate of MACE was 8%, and survival was 96%, 91%, and 88% at 30 days, 6 months, and 12 months, respectively.	Included in HTA 2017 added to table 2.

Maini B, Scotti DJ, Gregory D. Health economics of percutaneous hemodynamic support in the treatment of high-risk cardiac patients: A systematic appraisal of the literature. Expert Review of Pharmacoeconomics and Outcomes Research. 2014;14(3):403-16.	Systematic review of 6 studies on pLVAD for short-term hemodynamic support to high-risk patients with cardiogenic shock and percutaneous coronary interventions.	As the incidence of heart disease rises and the attendant economic burden of healthcare climbs, technologies for mitigating cardiovascular illness will be the target for more robust empirical evidence to justify the comparative value of minimally invasive hemodynamic support interventions in the armamentarium of treatment options available to physicians.	Economic impact out of IP remit.
Manzo-Silberman S, Fichet J, Mathonnet A, Varenne O, Ricome S, Chaib A, et al. Percutaneous left ventricular assistance in post cardiac arrest shock: comparison of intra aortic blood pump and Impella Recover LP 2.5. Resuscitation. 2013;84(5):609-15.	Single-centre retrospective registry n=78 patients with cardiogenic shock after cardiac arrest compared Impella 2.5 (n = 35) with IABP (n = 43)	Median “no flow” and median “low flow” were similar at admission as were hemodynamic parameters. The feasibility of IMPELLA implantation was good (97%). At 28 days, the survival rate without sequellae was 23.0% in the IMPELLA and 29.5% in the IABP group (p = 0.61). Vascular complications were observed equally in both groups (3 vs 2, p = 0.9). Serious bleeding complications occurred in 26% of IMPELLA patients vs 9% of IABP patients (p = 0.06).	Included in HTA 2017 added to table 2.
Martinez CA, Badheka AO et al (2012). Hemodynamic support in high-risk percutaneous coronary interventions and cardiogenic shock. Interv. Cardiol. 4(1), 125–136	Review on the three commonly used and approved percutaneous devices -Intra-aortic balloon pump (IABP), Impella® Recover 2.5 and TandemHeart®.	In the setting of peripheral vascular disease the device with the lowest vascular profile should be initially selected(IABP→Impella→Tandem Heart) in order to avoid vascular complications. Caution should be taken in the cases of Impella and TandemHeart use. Temporary LV assist devices have not been decisively shown to have mortality benefits and can be associated with increased complications, depending on their vascular profile. Nevertheless, they do provide crucial hemodynamic support.	Review

McCulloch B (2011). Use of the Impella 2.5 in High-Risk Percutaneous Coronary Intervention. Crit Care Nurse 2011;31 e1-e16.	Review	The Impella 2.5 is a percutaneously placed partial circulatory assist device that is increasingly being used in high-risk coronary interventional procedures to provide hemodynamic support. The Impella 2.5 is able to unload the left ventricle rapidly and effectively and increase cardiac output more than an intra-aortic balloon catheter can. Potential complications include bleeding, limb ischemia, hemolysis, and infection. One community hospital's approach to establishing amultidisciplinary program for use of the Impella 2.5 is described.	Review
Meraj PM, Doshi R et al (2017). Impella 2.5 initiated prior to unprotected left main PCI in acute myocardial infarction complicated by cardiogenic shock improves early survival. Journal of Interventional Cardiology.30:256-263.	Retrospective study N= 36 patients in the cVAD Registry supported with Impella 2.5 pLVAD for AMICS who underwent PCI on ULMCA culprit lesion Pre-PCI group (n = 20) and Post-PCI group (n = 16).	Non-ST segment elevation myocardial infarction and greater coronary disease burden were significantly more frequent in the Pre-PCI group but they had significantly better survival to discharge (55.0% vs 18.8%, P = 0.041). Kaplan-Meier 30-day survival analysis showed very poor survival in Post-PCI group (48.1% vs 12.5%, Log-Rank P = 0.004). Initiation of Impella 2.5 pLVAD prior to as compared with after PCI of ULMCA for AMICS culprit lesion is associated with significant early survival	More relevant studies included in table 2. MHS prior to PCI in AMICS
Mukku VK, Cai Q et al (2012). Use of Impella ventricular assist device in patients with severe coronary artery disease presenting with cardiac arrest. Int J Angiol; 21:163–166.	Case series N=3 CAD patients presenting with cardiac arrest underwent PCI with Impella support.	Impella VAD may play an adjunctive role in obtaining hemodynamic stability in these high-risk patients undergoing PCI. One of the patients was supported to left VAD implantation, and the other two had excellent neurological and functional recovery.	Larger studies included in table 2.
Myat A, Patel N et al (2015). Percutaneous circulatory assist devices for high-risk coronary intervention. JACC: Cardiovascular Interventions 8(2): 229-44.	Review on percutaneous cardiac assist devices such as the intra-aortic balloon pump, Impella, TandemHeart and extracorporeal membranous oxygenation.	Review examines the results of several randomized multicenter trials investigating their use in high-risk coronary intervention to determine which patients would benefit most from their implantation and whether there is a signal to delineate whether they should be used in an elective pre-procedure, standby, rescue, or routine post-procedure fashion.	Review

Nascimbene A, Loyalka P, Gregoric ID, Kar B. Percutaneous coronary intervention with the TandemHeart percutaneous left ventricular assist device support: six years of experience and outcomes. Catheter Cardiovasc Interv 2016; 87:1101e1110.	Retrospective analysis N=74 patients with TandemHeart™ percutaneous left ventricular assist device during percutaneous coronary intervention (PCI) in patients for whom conventional PCI and aorto-coronary bypass would pose substantial risk (eg cardiogenic shock or extremely risky intervention due to complex anatomy). Follow-up; 6 years	At 30 days after PCI, survival rates were 94%, 88%, 79%, and 55% in the elective, urgent, emergent, and emergent salvage groups, respectively. Survival rates at one year were at 75% in the elective, 64% in the urgent, 52% in the emergent, and 45% in the emergent salvage groups. Survival rates at 6 years were 68% in the elective, 53% in the urgent, 31% in the emergent, and 41% in the emergent salvage groups, respectively. In elective and urgent groups, successful weaning from mechanical support was possible in all patients. In the emergent and emergent salvage groups, successful weaning from mechanical support was possible in 84% and 55% of patients, respectively.	Included in Briasoulis A 2017 meta-analysis added to table 2.
O'Neill WW, Kleiman NS, et al (2012). 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. 126(14):1717-27.	Multicentre RCT PROTECT II trial 452 symptomatic patients with complex 3-vessel disease or unprotected left main coronary artery disease and severely depressed left ventricular function. ITT population 225 (Impella 2.5), versus 223 (IABP) Elective PCI (study funded by manufacturer) Follow-up: 90 days	Impella 2.5 provided superior hemodynamic support in comparison with IABP, with maximal decrease in cardiac power output from baseline of -0.04±0.24 W in comparison with -0.14±0.27 W for IABP (P=0.001). The primary end point (30-day major adverse events) was not statistically different between groups: 35.1% for Impella 2.5 versus 40.1% for IABP, P=0.227 in the intent-to-treat population and 34.3% versus 42.2%, P=0.092 in the per protocol population. At 90 days, a strong trend toward decreased major adverse events was observed in Impella 2.5-supported patients in comparison with IABP: 40.6% versus 49.3%, P=0.066 in the intent-to-treat population and 40.0% versus 51.0%, P=0.023 in the per protocol population, respectively.	Included in HTA 2017 added to table 2.

O'Neill WW, Schreiber T, Wohns DH, Rihal C, Naidu SS, Civitello AB, et al (2014). The current use of Impella 2.5 in acute myocardial infarction complicated by cardiogenic shock: results from the USpella Registry. J Interv Cardiol; 27(1):1-11.	Retrospective analysis of multicentre registry-38 centres in US USpella registry (funded by manufacturer) N=154 patients with cardiogenic shock from acute MI undergoing PCI and Impella 2.5 Before versus after support	Both groups were comparable except for diabetes (P¼0.02), peripheral vascular disease (P¼0.008), chronic obstructive pulmonary disease (P¼0.05), and prior stroke (P¼0.04), all of which were more prevalent in the pre-PCI group. Patients in the pre-PCI group had more lesions (P¼0.006) and vessels (P¼0.01) treated. These patients had also significantly better survival to discharge compared to patients in the post-PCI group (65.1% vs.40.7%, P¼0.003).Survival remained favorable for the pre-PCI group after adjusting for potential confounding variables. Initiation of support prior to PCI with Impella 2.5 was an independent predictor of in-hospital survival (Odds ratio 0.37, 95% confidence interval: 0.17–0.79, P¼0.01) in multivariate analysis. The incidence of inhospital complications included in the secondary end-point was similar between the 2 groups.	Larger studies included in table 2.
Ouweneel DM, Claessen BE et al (2015). The Role of Percutaneous Haemodynamic Support in High-risk Percutaneous Coronary Intervention and Cardiogenic Shock. International Cardiology Review.10 (1) 39-44.	Review	Despite the fact that percutaneous ventricular assist devices are used to treat a rather complex patient population, clinical testing remains important in order to evaluate their true impact on clinical outcome before being adopted into clinical practice. Therefore, this review shows an overview of the current experience and evidence of the available percutaneous cardiac assist devices.	Review

Patel NJ, Singh V et al (2015). Percutaneous Coronary Interventions and Hemodynamic Support in the USA: A 5 Year Experience. Journal of Interventional Cardiology. 25: 6, 563-573.	Cross sectional study (using Nationwide Inpatient Sample) n=18,094 patients who had percutaneous coronary interventions (PCIs) performed with intra-aortic balloon pump (IABP) (n=16,803) versus percutaneous ventricular assist devices (PVADs) (n=1069) such as Impella and TandemHeart and both IABP and PVAD (n=222).	On multivariable analysis, the use of PVAD was a significant predictor of reduced mortality (OR 0.55, 0.36–0.83, P = 0.004). This was particularly evident in sub-group of patients without acute MI or cardiogenic shock. The propensity score matched analysis also showed a significantly lower mortality (9.9% vs 15.1%; OR 0.62, 0.55–0.71, P < 0.001) rate associated with PVADs when compared to IABP. This largest and the most contemporary study on the use of hemodynamic support demonstrates significantly reduced mortality with PVADs when compared to IABP in patients undergoing PCI.	More relevant studies added to table 2.
Pershad A, Fraij G et al (2014). Comparison of the Use of Hemodynamic Support in Patients ‡80 Years Versus Patients <80 Years During High-Risk Percutaneous Coronary Interventions (from the Multicenter PROTECT II Randomized Study Am J Cardiol;114:657-664.	Comparative case series N=427 Outcomes were compared between patients >80 years (n=59) versus patients <80 (n=368) years enrolled in the PROTECT II trial (IABP versus Impella 2.5). Follow-up: 90 days	At 90 days, the composite end point of major adverse events and major adverse cerebral and cardiac events were similar between patients ‡80 and <80 years (45.6% vs 44.1%, p [0.823, and 23.7% vs 26.8%, p [0.622, respectively). There were no differences in death, stroke, or myocardial infarction rates between the 2 groups, but fewer repeat revascularization procedures were required in patients >80 years (1.7% vs 10.4%, p[0.032). Bleeding and vascular complication rates were low and comparable between the 2 age groups (3.4% vs 2.4%, p[0.671, and 6.8% vs 5.4%, p[0.677, respectively). Multivariate analysis confirmed that age was not an independent predictor of major adverse events (odds ratio [1.031, 95% confidence interval 0.459-2.315, p [0.941), whereas Impella 2.5 was an independent predictor for improved outcomes irrespective of age (odds ratio[0.601, 95%confidence interval 0.391-0.923, p[0.020).	Outcomes not reported separately for the 2 comparators.

Pulido JN and Rihal CS (2013). Usage of Percutaneous Left Ventricular Assist Devices in Clinical Practice and High-risk Percutaneous Coronary Intervention. Intervntional Cardiology Clinics, 2 (3), 417–428.	Review	This article reviews currently available mechanical circulatory support systems and portable extracorporeal oxygenation, describing hemodynamic and physiologic rationales, indications, strategies, and available evidence for their use in high risk PCI.	Review
Rajdev S, Krishnan P, Irani A, Kim MC, Moreno PR, Sharma SK, Kini AS. Clinical application of prophylactic percutaneous left ventricular assist device (TandemHeart) in high-risk percutaneous coronary intervention using an arterial preclosure technique: single-center experience. J Invasive Cardiol 2008; 20:67e72.	Case series N=20 patients undergoing high-risk PCI implanted with TandemHeart. Hospital outcomes.	The TH was successfully implanted in all 20 patients. Mean LV ejection fraction of the study patients was 38 ± 18%. Time-to-implantation of the TH, duration of hemodynamic support and mean flow of the TH device were 31 ± 9 minutes, 74 ± 40 minutes and 2.5 ± 1.3 L/minute, respectively. At the end of PCI, the TH was removed in all cases and Perclose sutures were deployed in 18/20 (90%) patients. There was only 1 minor vascular complication, and the average length of stay was 2 ± 1 days. Periprocedural and inhospital mortality was 0%.	Included in Briasoulis A 2017 meta-analysis added to table 2.
Remmelink M, Sjauw KD, Henriques JP et al (2010). Effects of mechanical left ventricular unloading by Impella on left ventricular dynamics in high risk and primary percutaneous coronary intervention patients. Catheter Cardiovasc Interv; 75:187-190.	Case series N=11 Impella® Recovery LP 2.5 high-risk PCI	Increased aortic and intracoronary pressure. Decreased cor. resistance,& cor flow reserve, hyperemic flow velocity and cor flow reserve. Weaning 11/11 Survival 11/11	Larger studies included in table 2.

Roos JB, Doshi SN, Konorza T, Palacios I, Schreiber T, Borisenko OV, et al. The cost-effectiveness of a new percutaneous ventricular assist device for high-risk PCI patients: Mid-stage evaluation from the European perspective. J Med Econ. 2013;16(3):381-90.	Cost effectiveness of pVAD compared to IABP-European perspective-decision tree model and Markov model used.	Compared with IABP, the pVAD generated an incremental quality-adjusted life-year (QALY) of 0.22 (with Euro-registry data) and 0.27 (with US-registry data). The incremental cost-effectiveness ratio (ICER) of the device varied between €38,069 (with Euro-registry data) and €31,727 (with US-registry data) per QALY compared with IABP.	Cost effectiveness out of IP remit.
Sandhu A, McCoy LA et al (2015). Use of Mechanical Circulatory Support in Patients Undergoing Percutaneous Coronary Intervention Insights From the National Cardiovascular Data Registry. Interventional Cardiology. Circulation.132:1243-1251	Retrospective review N=76 474 patients who underwent PCI in the setting of cardiogenic shock at one of 1429 National Cardiovascular Data Registry CathPCI participating hospitals. No mechanical circulatory support was used in 41 286 (54%) patients, 29 730 (39%) received IABP only, 2711 (3.5%) received O-MCS only, and 2747 (3.6%) received both IABP and O-MCS.	At the start of the study period, 45% of patients undergoing PCI in the setting of cardiogenic shock received an IABP and 6.7% received O-MCS. The proportion of patients receiving IABP declined at an average rate of 0.3% per quarter, whereas the rate of O-MCS use was unchanged over the study period. The predicted probability of IABP use varied significantly by site. The probability of O-MCS use was <5% for half of hospitals and >20% in less than one-tenth of hospitals.	Change in patterns of use of devices.
Sarkar K, Kini AS et al (2010). Percutaneous left ventricular support devices. Cardiology Clinics 28: 168-184.	Review	The authors discuss percutaneous circulatory support devices available and used, the technical aspects with insertion and removal, relevant data from systematic reviews, meta-analyses, randomised trials, and registries about the benefits from their use in patients with cardiogenic shock complicating STEMI and in those with significant left ventricular systolic dysfunction undergoing complex PCI.	Review

Shreenivas SS and Wilensky RL (2012). Percutaneous circulatory support during percutaneous coronary intervention. Inetrv Cardiol 4 (4), 449-460.	Review	There are several percutaneous devices, such as the intra-aortic balloon pump, Impella®, TandemHeart® and extracorporeal membrane oxygenation, that can provide circulatory support during planned percutaneous coronary intervention, support cardiogenic shock during a large myocardial infraction and salvage a patient who is in cardiac arrest. Although none of these devices have been shown to have a mortality benefit, the use of these devices allows for operator comfort by providing a 'safety net'. In cases of cardiac arrest, these devices are frequently the only means of restoring adequate perfusion.	Review
Seyfarth M, Sibbing D et al (2008). 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. Journal of the American College of Cardiology (52) 19 1584-8.	Randomised controlled trial (ISAR-SHOCK trial) N= 26 patients with cardiogenic shock caused by acute myocardial infarction 13 Impella® 2.5 versus 13 IABP Follow-up: 30 days	1 patient died before implantation. Greater increase in cardiac index and BP with Impella® than with IABP Impella 6/12 weaned IABP 4/13 weaned Impella 6/12 survived IABP 4/13 survived Overall 30-day mortality was 46% in both groups	Included in HTA 2017 added to table 2.
Schwartz BG, Ludeman DJ, Mayeda GS, Kloner RA, Economides C, Burstein S (2011). High-risk percutaneous coronary intervention with the TandemHeart and Impella devices: a single-center experience. J Invasive Cardiol; 23(10):417-24.	Single-centre retrospective chart review N=50 13 (Impella 2.5), 5 (IABP), 32 (TandemHeart) Device selection of Impella 2.5 or TandemHeart based on disease severity. Elective PCI	All devices (100%) were initiated successfully. Angiographic success was achieved in 96% (80% IABP, 100% Impella, 97% TandemHeart). Of the 38 patients not in cardiogenic shock, death occurred in 1 (2.6%), recurrent ischemia in 3 (8%), and stroke in 0%. Shortly after device removal, systolic blood pressure (mean increase, +5 ± 22 mmHg) and ejection fraction (mean increase, +7.4 ± 11%; p = 0.0006) increased in all 3 groups, suggesting a beneficial effect on the myocardium. 30 day MACE rate was 15%.	Included in HTA 2017 added to table 2.

Sjauw KD, Konorza T, Erbel R, Danna PL, Viecca M, Minden HH, et al (2009). Supported high-risk percutaneous coronary intervention with the Impella 2.5 device. The Europella registry. J Am Coll Cardiol; 54(25):2430-4.	Multicentre retrospective observational study Europella registry (Funded by manufacturer- 10 sites in Europe) N=144 Elective PCI Follow-up: 30 days	Mortality at 30 days was 5.5%. Rates of myocardial infarction, stroke, bleeding requiring transfusion/surgery, and vascular complications at 30 days were 0%, 0.7%, 6.2%, and 4.0%, respectively.	Included in HTA 2017 added to table 2.
Shah AP, Retzer EM et al (2015). Clinical and Economic Effectiveness of Percutaneous Ventricular Assist Devices for High-Risk Patients Undergoing Percutaneous Coronary Intervention. J INVASIVE CARDIOL; 27(3):148-154.	Review of all randomized control trials of the pVADS (Impella and TandemHeart) vs IABP in patients with cardiogenic shock and undergoing high-risk percutaneous coronary intervention (PCI). Retrospective analysis of 2010-11 Medicare MEDPAR data files was also performed to compare procedural costs and hospital length of stay.	Based on available trials (2 RCTs compared TandemHeart versus IABP, 1 RCT compared Impella 2.5 versus IABP in patients with cardiogenic shock and 1 RCT compared Impella 2.5 versus IABP in patients undergoing high risk PCI) there is no significant clinical benefit with pVAD compared to IABP. Use of pVADs is associated with increased length of Intensive Care Unit stay and a total longer LOS. The incremental budget impact for pVADs was $33,957,839 for the United States hospital system (2010-2011).	Narrative analysis of RCTs already included in HTA 2017 added to table 2. No meta-analysis done. Economic analysis out of remit.
Shah R, Thomson A et al (2012). Percutaneous left ventricular support for high-risk PCI and cardiogenic shock: who gets what? Cardiovascular Revascularization Medicine. 13, 2, 101-105.	Case series N=74 patients undergoing high-risk PCI (57) and those with CS (17) receiving IABP, Tandem Heart, Impella device. For the high-risk PCI cohort (n=57), 22 received PLVAD and 35 received IABP. For the CS cohort (n=17), 4 received PLVAD and 13 received IABP. In-hospital outcomes assessed.	Patients receiving PLVAD support were more likely to have a prior MI, had a lower ejection fraction, underwent treatment of more coronary lesions, and received more coronary stents compared to those receiving IABP support. The primary (in-hospital major adverse cardiovascular events) and secondary (in-hospital vascular complications) end points were similar between both groups.	Larger and more comprehensive studies added to table 2.

Shavelle DM, Kirtane AJ et al (2016). Impact of surgical correction on outcomes in hemodynamically supported high-risk percutaneous coronary intervention: insights from PROTECT II randomized study. Journal of Invasive Cardiology 28(5): 187-192.	n=427 patients with multivessel coronary artery disease or unprotected left main disease and severely reduced left ventricular systolic function undergoing PCI assisted by hemodynamic support (intraaortic balloon pump or Impella) from the PROTECT II randomized trial. Patients in whom surgical consultation was requested prior to PCI (n = 201) were compared with those in whom surgical consultation was not requested (n = 226).	Demographic and procedural variables were similar between patients receiving surgical consultation and patients not receiving surgical consultation, with the exception that the prevalence of prior coronary artery bypass graft surgery was significantly higher in patients not receiving surgical consultation (42.0% vs 25.4%; P<.001); MACCE rate at 90 days was similar in patients receiving surgical consultation compared with patients not receiving surgical consultation (23.4% vs 29.0%, respectively; P=.19). Clinical outcome was not associated with an antecedent request for surgical consultation. Whether the use of hemodynamically supported PCI can lessen the risk conferred by surgical ineligibility requires further study.	Association between request for surgical consultation prior to PCI and clinical outcomes assessed.
Shavelle DM, Clavijo L et al (2011). Percutaneous devices to support the left ventricle. Expert Rev Med Devices 8(6), 681-694.	Review	Summarizes the current status of three percutaneous left ventricular assist devices, review technical details involving device components and device insertion, discuss the hemodynamic changes that occur with device implantation and summarize published and ongoing clinical trials evaluating these devices in patients undergoing high-risk percutaneous coronary intervention and those with cardiogenic shock.	Review
Sibbald M, and Dzavik V (2012). Severe hemolysis associated with use of the Impella LP 2.5 mechanical assist device. Catheterization and Cardiovascular Interventions 80: 840-844.	Case report N=1	A 66-year-old woman with hemodynamic collapse during an elective PCI was successfully resuscitated with an Impella device. She developed marked biochemical evidence of intravascular hemolysis. This necessitated device removal which resulted in prompt resolution of the hemolysis. Routine measurement of biochemical markers of hemolysis and serial hemoglobin values during Impella device support to allow timely detection and treatment of this important complication was advised.	Larger studies included in table 2.

Spiro J, Venugopal V et al (2015). 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 aortic stenosis.	Case series N=5 patients with severe AS and left ventricle impairment who underwent PCI during Impella support. Follow-up: 30 days	The Impella catheter traversed the aortic valve (AV) unassisted in only one patient, with four cases requiring balloon-assist techniques. All patients underwent planned revascularisation; mean procedure time 177 minutes, mean number of stents 3.4, with 3 patients requiring rotational atherectomy. All procedures were well tolerated, with absence of arrhythmia, hypotension, pulmonary edema, stroke, or myocardial infarction. One patient died 48 hr post-PCI of multi-organ failure. The four remaining patients were well at 30 days.	Novel techniques described.
Spiro J and Doshi SN (2014). Use of left ventricular support devices during acute coronary syndrome and percutaneous coronary intervention. Curr Cardiol Rep 16:544	Review	This update discusses recent data describing the use of PVADs to support patients with AMI with or without cardiogenic shock and during high-risk PCI. It focuses on the unique features of each device, highlighting strengths, weaknesses and frequently encountered complications, which may be important when tailoring the most appropriate PVAD therapy to an individual patient's need.	Review
Susen S, Rauch A et al (2015). Circulatory support devices: fundamental aspects and clinical management of bleeding and thrombosis. Journal of Thrombosis and Haemostasis. 13: 1757-67.	Review	The review focuses on thrombotic and bleeding complications, and describes how the risk of thrombosis and bleeding may vary according to the clinical indication, but also according to the type of device. It describes the current knowledge of the mechanisms underlying the occurrence of these complications, provide some guidance for choosing the most appropriate anticoagulation regimen to prevent their occurrence for each type of device and indication, and provide some recommendations for the management of patients when the complication occurs.	Review

Sukiennik A, Kasprzak M et al (2017). High-risk percutaneous coronary intervention with Impella CP hemodynamic support. A case series and method presentation. Adv Interv Cardiol 13, 1 (47): 67–71	Case series N=5 elderly high-risk patients who underwent complex PCI supported by the Impella CP.	Hemodynamic support with the Impella CP device was effective, safe and easily removable. Good angiographic result without intra-procedural complications. Clinical status has improved in all patients and there were no deaths during 30-day follow-up. It appears to be a feasible strategy in patients undergoing high-risk PCI.	Larger studies included in table 2.
Syed AI, Kakkar A et al (2010). Prophylactic use of intra-aortic balloon pump for high-risk percutaneous coronary intervention: will the Impella LP 2.5 device show superiority in a clinical randomized study? Cardiovascular Revascularization Medicine, 11: 91-97.	Cohort study (retrospective analysis) N=85 patients undergoing non-emergent, high-risk PCI with IABP for hemodynamic support.	The overall in-hospital and 30-day event rates were low (15.3% and 21.3%, respectively) with a low major vascular complication rate (5.9%). Therefore, for the Impella Recover LP 2.5 device to demonstrate superiority over IABP with a treatment effect of 33.3% and 80% power, the Protect II trial will require a total of 908 patients. With the current sample size of 654 patients, the Protect II trial is underpowered, with only 66% power.	IABP study retrospectively comparing and questioning benefit of Protect II study.
Tanawuttiwat T, Chaparro SV et al (2013). An unexpected cause of massive hemolysis in percutaneous left ventricular assist device. Cardiovasc Revasc Med; 14(1):66-7	Case report	24 year-old patient developed massive hemolysis shortly after percutaneous left ventricular assist device, Impella 2.5, was placed. The hemolysis occurred without device alarm while the device was in the correct position. Further investigation of the device revealed fiber wrapped around the tip of the device, as a culprit. This case emphasizes on the special caution applied during device preparation to minimize the possible adverse events.	Adverse event reported in table 2.
Tayal R, Barvalia M et al (2016). Totally percutaneous insertion and removal of Impella device using axillary artery in the setting of advanced peripheral artery disease. Journal of Invasive Cardiology 28 (9):374-380.	Case report N=3	A new entirely percutaneous technique utilizing the axillary artery for delivery of Impella 2.5 (13.5 Fr) and CP (14 Fr) cardiac-assist devices for protected percutaneous coronary intervention in the setting of prohibitive peripheral artery disease.	Case report

Thiele H, Sick, P et al (2005). Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. European heart journal (26) 13 1276-83.	RCT N=41 Patients in ischemic cardiogenic shock after acute myocardial infarction with intended percutaneous coronary intervention of the infarcted artery, were randomized to either IABP (n=20) or percutaneous ventricular assist device support [Tandem Heart] (n=21). Follow-up: 30 days	Cardiac power index, as well as other haemodynamic and metabolic variables, could be improved more effectively by VAD support from 0.22 [interquartile range (IQR) 0.19-0.30] to 0.37 W/m2 (IQR 0.30-0.47, P<0.001) when compared with IABP from 0.22 (IQR 0.18-0.30) to 0.28 W/m2 (IQR 0.24-0.36, P=0.02; P=0.004 for intergroup comparison). Complications like severe bleeding (n=19 vs. n=8, P=0.002) or limb ischaemia (n=7 vs. n=0, P=0.009) were encountered more frequently after VAD support, whereas 30 day mortality was similar (IABP 45% vs. VAD 43%, log-rank, P=0.86).	Included in Chang 2009 added to table 2.
Ternus BW, Jentzer JC et al (2017). Percutaneous mechanical circulatory support for cardiac disease. Temporal trends in use and complications between 209 and 2015. Journal of Invasive Cardiology. 29 (9):309-313.	Retrospective analysis patients with ABP or Impella device N=778	The mean number of evcies placed per year was 111. There was no statistically significant trend in total number of devcies placed overall, but the rate of Impella placement declined over time (p=0.04). There was a significant trend toward less use before high-risk percutaneous coronary intervention (PCI) (P=.04). The composite secondary endpoint occurred in 59.4% of patients, with no significant difference between patients treated with an IABP or Impella (P=.66). There were 37 device-related complications, which occurred more commonly with the Impella (12.5%) than with the IABP (3.7%; P<.01).	More relevant studies included in table 2.
Valgimili M, Steendijk P et al (2006). Use of Impella Recover® LP 2.5 left ventricular assist device during high-risk percutaneous coronary interventions; clinical, haemodynamic and biochemical findings. EuroInterv.2:91-100.	Case series N=10 Impella Recover® LP 2.5 left ventricular assist device during elective high risk percutaneous coronary interventions (HR-PCI).	Impella catheter was used for 144±88 minutes and was removed immediately after the procedure in all but one patients. In 6, 3 and 2 patients, fHb levels increased above 1, 5 and 10 times the upper limit of normal. The PV analysis showed the occurrence of an acute volume increase in the majority of patients immediately after Impella insertion that tended to persist even at maximal pump speed.	Larger studies included in table 2.
Van Mieghem NM, Daemen J et al (2018). Design and principle of operation of the HeartMate PHP (percutaneous heart pump). EuroIntervention 2018;13:1662-1666	Thoratec HeartMate PHP (percutaneous heart pump) in 8 patients with high-risk PCI.	This technical report discusses: (i) the HeartMate PHP concept, (ii) the implantation technique, (iii) the haemodynamic performance in an in vitro cardiovascular flow testing set-up, and (iv) preliminary clinical experience in 8 patients	Technical report with very little clinical data.

Uil, C.A.D. (Corstiaan A. Den), Daemen, J, Lenzen, M.J, Maugenest, A.M, Joziasse, L. (Linda), van Geuns, R.J.M, & van Mieghem, N.M. (2017). Pulsatile iVAC 2L circulatory support in high-risk percutaneous coronary intervention. EuroIntervention, 12(14), 1689–1696. doi:10.4244/EIJ-D-16-00371	transfemoral PulseCath iVAC 2L (PulseCath, Amsterdam, The Netherlands pilot study enrolling 14 patients who underwent high-risk PCI under protection with the iVAC 2L.	Implantation of the iVAC 2L was successful in 13 (93%) patients. Median device flow was 1.4 (1.1-2.0) L/min. Total support time was 67 (23-149) minutes. The use of iVAC 2L support was associated with a better mean arterial pressure and cardiac output during the procedure. Angiographic success was 100%. There was one major procedural complication related to the 19 Fr access sheath. There were no major adverse events at three-month follow-up.	Pilot study.
Vavalle JP, and Ohman EM (2013). Left ventricular support systems for high-risk percutaneous coronary interventions. How can we improve outcomes for rare procedures? Circulation, 127:162-164.	Editorial	Although the use of prophylactic IABP or Impella can improve outcomes compared with a more stand-by approach, we must recognize that newer support devices may be on the horizon. The data from BCIS-1 and PROTECT-II that demonstrate more robust differences in the treatment arms with longer follow-up should be a call to investigators that future studies of hemodynamic support devices must include long-term follow-up.	Editorial
Vranckx P, Schultz CJ, Valgimigli M, Eindhoven JA, Kappetein AP, Regar ES, Van Domburg R, Serruys PW. Assisted circulation using the TandemHeart during very high-risk PCI of the unprotected left main coronary artery in patients declined for CABG. Catheter Cardiovasc Interv 2009; 74:302e310.	Retrospective review N=9 very high risk patients undergoing elective PCI for the novo lesions on the unprotected left main coronary artery with TandemHeart support. Follow-up: 6 months.	Technical success rate was 100%. The median (range) time for implementation of circulatory support was 27 min (24-30). A median (range) pump flow up to 4.36 (3.40-5.54) L/min was achieved with significant reduction of left ventricular filling pressures, pulmonary capillary wedge pressure and a small increase of systemic arterial pressures. Median (range) duration of support was 93 min (50.4-102). Successful weaning was achieved in all patients. There was no in hospital death, survival at 6 months was (89%), whereas vascular access site complications were seen in 4 patients (44.4%).	Included in Briasoulis A 2017 meta-analysis added to table 2.

Vranckx P, Meliga E et al (2008). The TandemHeart, percutaneous transeptal left ventricular assist device: a safeguard in high-risk percutaneous coronary interventions. The six year Rotterdam experience. EuroIntervention, 4: 331-337.	Case series N=23 patients for high risk, emergency or elective PCI. Implanted with TandemHeart.	Successful implantation was achieved in all. The mean time for implementation of circulatory support was 35 minutes. The index PCI was successful in all patients except two. A pump flow up to 4L/min was achieved with significant reduction of left ventricular filling pressures, pulmonary capillary wedge pressure and with significant increase of systemic arterial pressures. Duration of support ranged from 1-222 hours. Five patients died with the TandemHeart in place, four of whom were in irreversible cardiogenic shock at admission. Mild to moderate access site bleeding was seen in 27% of patients. One patient experienced a loge syndrome of the leg. Core temperature decreased to <36.5 degrees C in six patients, profound hypothermia (Ct <35 degrees C) was observed in two patients. There was no technical device failure.	Larger studies included in table 2.
Vecchio S, Chechi T, Giuliani G et al (2008). Use of Impella Recover 2.5 left ventricular assist device in patients with cardiogenic shock or undergoing high-risk percutaneous coronary intervention procedures: experience of a high-volume center. Minerva Cardioangiol; 56(4):391-9.	Case series N=11 Impella® Recovery LP 2.5 5 high-risk PCI (6 cardiogenic Shock) 5 patients with PCI and 6 with cardiogenic sock Follow-up: 30 days	Impella® proved successful in only 2 patient with shock whereas all PCI patients were safely discharged. Weaining –PCI 5/5 Cardiogenic shock (4/6) Survival PCI 5/5 (Cardiogenic shock 4/6) Bleeding occurred in 7, renal failure in 4, and thrombocytopenia in 1.	Larger studies included in table 2.
Venugopal V, Spiro J, Zaphiriou A, Khan S, Townend JN, Ludman PF, et al (2015). Percutaneous mechanical ventricular support in acute cardiac care: a UK quaternary centre experience using 2.5L, 3.8L and 5.0L Impella catheters. Cardiol Ther; 4(1):47-58.	Retrospective chart review N=45 patients at high risk PCI who had Impella devices (34 had Impella 2.5 and 10 had Impella 3.8/Impella CP)	Outcomes of all devices reported together. The 30-day outcomes for mortality, bleeding requiring blood transfusion, stroke, and periprocedural myocardial infarction were 18%, 5%, 2%, and 2%, respectively. No vascular complications were reported.	Included in HTA 2017 added to table 2.

Verma S, Burkhoff D et al (2016). Avoiding hemodynamic collapse during high-risk percutaneous coronary intervention: advanced hemodynamics of Impella support. Catheterization and cardiovascular interventions 89: 672-675.	Case report Impella device implaced in a patient during high risk PCI.	Complete hemodynamic collapse during PCI was avoided by mechanical support provided by the Impella device. Further a comprehensive model was used to predict ventricular function and patient hemodynamics.	Larger studies included in table 2.
Vetrovec GW (2017). Hemodynamic support devices for shock and high-risk PCI; when and which one. Curr Cardiol Rep 19: 100,	Review on devices and uses of hemodynamic support in management of high risk PCI and AMI with cardiogenic shock.	Hemodynamic support most often using Impella support, improves outcomes via providing hemodynamic stability to allow complete revascularization and optimal lesion treatment. Regarding shock, preliminary data suggests that a concept of early left ventricular unloading before PCI maybe the critical factor for improving the outcome for acute MI complicating MI.	Review
Wohns D, Muthusamy P et al (2014). Economic and Operational Implications of a Standardized Approach to Hemodynamic Support Therapy Using Percutaneous Cardiac Assist Devices. Innovations 2014;9:38Y42.	Retrospective study to compare the costs and resource use of Impella 2.5 (n=35) and intra-aortic balloon pump (IABP) support (n=295). Propensity score matching done.	As compared with IABP, Impella offered a more predictable course of treatment/resource consumption and was not associated with any extreme cost outliers (17.1% vs 0.0%, respectively; P = 0.025). The mean admission and 90-day episode of care total costs for Impella were 5.5% ($67,681 vs $71,608, P = 0.79) and 4.2% ($70,680 vs $73,476, P = 0.85) lesser than that for IABP, respectively. Although not statistically significant, Impella patients had a trend toward lower rehospitalization rates (11.4% vs 20%), lesser mean index length of hospital stay (11.2 vs 13.7), and 90-day (11.7 vs 14.2) episode of care length of hospital stay.	Costs out of IP remit.