Topic Brief: Ventricular Assist Devices for High-Risk Percutaneous Coronary Intervention

Date: 09/11/2019
Nomination Number: 0854

Purpose: This document summarizes the information addressing a nomination submitted on May 5, 2019 through the Effective Health Care (EHC) Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: Interventional cardiologists have been employing the use of percutaneous Ventricular Assist Devices (PVADs) to provide hemodynamic support in patients undergoing high-risk percutaneous coronary intervention (PCI) even in the absence of cardiogenic shock. It is unclear whether using these devices leads to better clinical outcomes or whether they are unnecessary in this particular subset of patients. A systematic review on effectiveness and harms of use of PVAD in this specific setting would help the nominator, a health plan, make better decisions regarding coverage of these devices.

Key findings

- This nomination meets all selection criteria.
- A new systematic review is feasible and would not be duplicative. We did not find any existing review that was up-to-date or any in-process review that would be accessible to meet the needs of the nominator.
- Most primary studies looked the Impella device, which was the initial focus of the nomination.
- Based on the results of our targeted literature search we estimate a small systematic review. We are aware of additional studies of TandemHeart published outside of our search window; and additional study designs not included in our targeted search (case series for example) that might report additional harms.

Program Decision: Though the scope of this topic met all EHC Program selection criteria and was considered for a systematic review. However, it was not selected.

Background

Percutaneous coronary intervention (PCI), also known as coronary angioplasty, is a nonsurgical procedure that improves blood flow to the heart. Interventional cardiologists perform PCI to open coronary arteries that are narrowed or blocked by the buildup of atherosclerotic plaque in patients with unstable angina, acute myocardial infarction, and multi-vessel coronary artery disease.[1] According to the National In-patient Sample, approximately 550,000 such procedures are performed annually in the United States.[2] To protect the myocardium from ischemia and support cardiac function during PCI, interventional cardiologists have been using ventricular assist devices (VADs), mechanical pumps used to support heart function by facilitating blood flow usually from the left ventricle to the aorta and coronary vessels leading to increased end organ perfusion.[1] Early versions of VADs were bulky and cumbersome but improvements in miniaturization technology have led to development of small percutaneously inserted versions such as Impella VADs (Abiomed, Danvers, MA).[3] The other percutaneous VADs that may be used is TandemHeart Percutaneous Ventricular Assist Device (pVAD)™ system (CardiacAssist, Pittsburgh, PA) or HeartMate Left Ventricular Assist System (Abbott, Chicago, IL). For purposes of this topic brief, we use the acronym "PVAD" as a collective term for all of these devices.

PCI (also termed 'high-risk PCI') with PVAD can be performed on either an emergent or elective basis.[4-7] In the emergent setting, the patient is usually decompensated and in cardiogenic shock.[4, 7] In contrast, high-risk PCI with PVAD can also be performed in an elective setting on stable patients with reduced ejection fraction but are *not* in shock to relieve symptoms such as chest pain. [5, 6] Use of PVAD during high-risk PCI can be costly but is covered by Medicare and insurance carriers when the patient is in established cardiogenic shock. Whether PVAD is necessary or improves clinical outcomes and quality of life among patients undergoing high-risk PCI who are *not* in cardiogenic shock is unclear. Existing guidelines published in 2011 by the American College of Cardiology Foundation, the American Heart Association, and the Society for Cardiovascular Angiography and Interventions state that "hemodynamic support device" (such as Impella VAD or TandemHeart Percutaneous Ventricular Assist Device (pVAD)™ system) "as an adjunct to PCI *may be reasonable* in carefully selected high-risk patients".[8] This lack of definitive practice guidance contributes to an ongoing decisional dilemma concerning coverage for health plans and insurance carriers.

Nomination Summary

This topic was nominated by the Interim Chief Medical Officer of Independent Health, a not-for-profit health plan that covers nearly 400,000 members residing in eight counties in Western New York [https://www.independenthealth.com]. Both Medicare and their organization cover use of Impella VAD in high-risk PCI in patients with cardiogenic shock as the clinical indication is clear. In contrast, whether Impella VAD is necessary in patients undergoing high-risk PCI who are *not* in cardiogenic shock is not established leading to uncertainty whether coverage is justifiable. Coverage decisions are further complicated by the high cost of Impella VAD, which adds $50,000 to $80,000 per procedure as communicated by nominator who plans to use a completed AHRQ systematic review to inform their coverage decisions.

Because we found a small number of studies specific to Impella VAD we broadened to scope to include the other commonly used PVADs, such as TandemHeart.

Scope

1. What is the effectiveness and comparative effectiveness of percutaneous ventricular assist devices (PVAD) in providing hemodynamic support in patients undergoing high-risk percutaneous coronary intervention (PCI) who are not in established cardiogenic shock?

2. What are the harms and comparative harms of PVAD in providing hemodynamic support in patients undergoing high-risk PCI who are not in established cardiogenic shock?

Table 1. Questions and PICOTS (population, intervention, comparator, outcome, timing and setting)

Questions	1. Effectiveness	2. Harms
Population	Adults aged ≥18 years undergoing elective/non-emergent high-risk PCI who are not in established cardiogenic shock	
Interventions	PVAD including: ▪ Impella 2.5: a 12-F device with maximal flow rates of 2.5 L/min, placed through a femoral percutaneous approach ▪ Impella CP (cardiac power): a 14-F device with maximal flow rates of 3.5 L/min, placed through a femoral percutaneous approach ▪ Impella 5.0: a 21-F device with maximal flow rates of 5.0 L/min; placement requires an open femoral artery cut down ▪ TandemHeart Percutaneous Ventricular Assist Device™ system: a left atrial-to-femoral artery bypass system with flow rates up to 4.0 L/min ▪ HeartMate Left Ventricular Assist System: inserted through a 14 Fr sheath, deployed across the aortic valve expanding to 24 Fr and able to deliver up to 5 L/min	
Comparators	▪ Medical therapy ▪ Intra-aortic balloon pump (a device consisting of a long skinny balloon that controls blood flow through the aorta; used to support cardiac function)	
Outcomes	Primary outcomes • Mortality o All-cause o Cardiovascular mortality • Quality of life Secondary outcomes • Non-fatal myocardial infarction • Non-fatal stroke • Length of hospital stay	Primary outcomes • Serious adverse events o Vascular injury o Infection o Major bleeding • Other complications associated with use of device
Timing	All	
Setting	All elective/non-emergent hospital settings	

Abbreviations: F=french; PCI=percutaneous coronary intervention; PVAD=percutaneous ventricular assist device

Assessment Methods

See Appendix A.

Summary of Literature Findings

We found three systematic reviews that could address the scope, but they were not considered duplicative. One systematic review focused solely on Impella VAD and the search date range ended on February 15, 2016, which may be too old to be considered up-to-date.[9] We identified two additional systematic reviews that included both Impella VAD and TandemHeart VAD; however, these reviews also included individuals either with cardiogenic shock or undergoing ventricular tachycardia ablation.

Based on our searches of PVAD, we estimate 36 studies for inclusion in a small-sized systematic review. Most focused on Impella PVAD. A feasibility search for studies focused on the Impella PVAD from 2016 to August 20, 2019 yielded 349 citations. By reviewing a random sample of 200 abstracts, we project that 16 studies and added the number of relevant studies of Impella PVAD use in elective high-risk PCI cited in the previously mentioned systematic review (n=11; one RCT and 10 observational studies).[3, 5, 6, 10-16] A feasibility search broadly of PVAD identified 9 additional studies. Five focused on Impella PVAD and TandemHeart PVAD[17-21]; one focused on TandemHeart PVAD[22]; two focused on Impella[23, 24]; and one focused on HeartMate PVAD[25].

Nearly all abstracts reviewed were from observational studies mostly from patient registries or cohort studies and appeared to be relevant to both key questions except for one RCT which specifically examined loss of valvular integrity in the PROTECT II trial.[26] See Table 2, Primary studies column for the citations of included studies.

See Appendix A for the PubMed search strategy and links to the ClinicalTrials.gov search. See Appendix B for detailed assessments of all EPC selection criteria.

Table 2. Literature identified for each Question

Question	Systematic reviews (8/2016-8/2019)	Primary studies (1/2016-8/2019)
Question 1: Effectiveness	Total: 3 • Other - 3[9, 27, 28]	Total: 17 • RCT: 1[23] • Observational: 8[17-25, 29-36] Clinicaltrials.gov • Recruiting/Enrolling: 3 • Completed: 3 • Terminated: 3
Question 2: Harms	Total: 3 • Other - 3[9, 27, 28]	Total: 18 • RCT: 1[23, 26] • Observational: 8[17-22, 24, 25, 29-36] Clinicaltrials.gov • Recruiting/Enrolling: 3 • Completed: 3 • Terminated: 3

Abbreviations: RCT=randomized controlled trial

Summary of Selection Criteria Assessment

This nomination meets all selection criteria. We found three non-duplicative systematic reviews and estimate 36 primary studies covering PVAD use in high-risk PCI. We did not consider the systematic reviews duplicative because the search range was outdated or populations included

other conditions. A new systematic review could potentially shed light on whether PVAD use is safe and actually makes a difference in improving high-risk PCI outcomes in the non-emergent setting. A new review would be highly impactful and valuable since the nominator will use the findings to inform coverage decisions for their health plan. Moreover, existing non-definitive practice guidelines espoused by cardiology associations can be updated to provide more definitive guidance.

Please see Appendix B for detailed assessments of individual EPC Program selection criteria.

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Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years up to September 13, 2019 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
  - AHRQ Evidence Reports https://www.ahrq.gov/research/findings/evidence-based-reports/index.html
  - EHC Program https://effectivehealthcare.ahrq.gov/
  - US Preventive Services Task Force https://www.uspreventiveservicestaskforce.org/
  - AHRQ Technology Assessment Program https://www.ahrq.gov/research/findings/ta/index.html
- US Department of Veterans Affairs Products publications
  - Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
  - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program https://www.healthquality.va.gov/
- Cochrane Systematic Reviews https://www.cochranelibrary.com/
- University of York Centre for Reviews and Dissemination database https://www.crd.york.ac.uk/CRDWeb/
- PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
- PubMed https://www.ncbi.nlm.nih.gov/pubmed/
- Epistemonikos https://www.epistemonikos.org/

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

Since we found a systematic review which had a search date range ending in February 2016 that was relevant to the initial focus of the nomination (Impella VAD), we conducted a limited literature search in PubMed from 2016 until the present. Because a large number of articles were identified, we reviewed a random sample of 200 titles and abstracts for each question for inclusion. We classified identified studies by question and study design, to assess the size and scope of a potential evidence review. We then calculated the projected total number of included studies based on the proportion of studies included from the random sample and the number of relevant studies included in the systematic review.

Because we found few studies specific to Impella VAD we broadened the search to PVAD, including searches specific to TandemHeart and HeartMate VADs (August 2014-September 2019). We reviewed all titles and abstracts from this additional search. We classified identified studies by question and study design, to assess the size and scope of a potential evidence review.

We also searched ClinicalTrials.gov for related trials.

Search Strategy

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to August 19, 2019
Date searched: August 20, 2019

#	Searches	Results
1	impella.ti,ab,kf.	651
2	limit 1 to yr="2016 -Current"	349
3	limit 2 to (adaptive clinical trial or clinical trial, all or comparative study or controlled clinical trial or equivalence trial or observational study or pragmatic clinical trial or randomized controlled trial)	20

Search for Percutaneous Ventricular Assist Device. Searchd September 13, 2019.
(percutaneous[All Fields] AND ("heart-assist devices"[MeSH Terms] OR ("heart-assist"[All Fields] AND "devices"[All Fields]) OR "heart-assist devices"[All Fields] OR ("ventricular"[All Fields] AND "assist"[All Fields] AND "device"[All Fields]) OR "ventricular assist device"[All Fields])) AND ("2014/09/15"[PDat] : "2019/09/13"[PDat])

"tandemheart"[All Fields] AND ("2014/09/15"[PDat] : "2019/09/13"[PDat])

"heartmate"[All Fields] AND PCI[All Fields] AND ("2014/09/15"[PDat] : "2019/09/13"[PDat])

ClinicalTrials.gov

Used search term "Impella" which returned 29 trials; other trials were excluded mostly due to inclusion criterion of cardiogenic shock

Used search term "HeartMate" which returned 37 trials. Other trials were excluded because they did not focus on high-risk PCI.

Used search term "TandemHeart" which returned 2 trials. One was a registry for use of the TandemHeart for any indication, and the other was withdrawn.

Value

We assessed the nomination for value. We considered whether or not the clinical, consumer, or policymaking context had the potential to respond with evidence-based change; and if a partner organization would use this evidence review to influence practice.

Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents interventions available in the United States.
1b. Is the nomination a request for an evidence report?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on effectiveness and comparative effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible and is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Approximately 550,000 PCI procedures are performed each year in the United States.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, evidence concerning effectiveness and safety of PCI will influence coverage decisions for a specific subset of patients who are not in cardiogenic shock.
2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes, this nomination addresses both benefits and potential harms of PVAD for protected high-risk PCI.
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, according to the nominator, use of an Impella PVAD increases the cost for PCI by $50,000 to $80,000 in their system.
3. Desirability of a New Evidence Review/Absence of Duplication	
3. A recent high-quality systematic review or other evidence review is not available on this topic	An existing up-to-date review is currently not available. We found one review of acceptable quality focused on Impella PVAD but the search range ended in February 2016.[9] We also found a review protocol in PROSPERO on Impella PVAD that was potentially relevant [**see URL in footnote*]. However, the contact for the review did not respond to our inquiries

	and a related abstract/article cannot be found on PubMed. We identified two SR on PVAD.[27, 28] Both included studies of Impella and TandemHeart. These were not considered duplicative because populations were not restricted solely to patients undergoing high-risk PCI. It would be possible however to examine the studies that did focus just on this population because of the very small numbers of studies included in each review. • Rios et al.[28] This 2018 review included patients undergoing high-risk PCI or with cardiogenic shock. This was not considered duplicative because the two groups were not analyzed separately. • Hu et al.[27] This 2018 review focused on patients undergoing high-risk PCI and ventricular tachycardia ablation. This was not considered duplicative because the two groups were not analyzed separately. We found one additional review published just before our search cut-off date. This review focused on both Impella and TandemHeart, and focused solely on the population of interest, patients undergoing high-risk PCI.[37] This review included 20 studies. We include this as it may be useful to the nominator.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, guidance is inconsistent and based on limited evidence. The 2011 ACCF/AHA/SCAI Guideline for PCI states that "Elective insertion of an appropriate hemodynamic support device as an adjunct to PCI *may be reasonable* in carefully selected high-risk patients." New evidence may clarify the risk-benefit ratio for this clinical situation and lead to a more definitive recommendation. Targeted updates of their guidelines for PCI have not addressed this issue. National Institute for Health and Care Excellence (NICE) updated in the 2018 its

	guidance by mentioning selected high-risk populations. The guidance notes that the device should only be used with special arrangements for clinical governance, consent, and audit or research. Specific populations mentioned include those with extensive or complex coronary artery disease, poor left ventricular function, ongoing myocardial ischemia, cardiogenic shock and comorbidity, in whom revascularization may not otherwise be possible. (https://www.nice.org.uk/guidance/ipg633)
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, there is practice variation but likely due to the non-definitive nature of the guideline rather than a gap in implementation.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	*Size/scope of review:* We anticipate that the size of the review will be small. We estimate about 36 studies. Recent reviews identified in our duplication search included 6-20 studies. We estimate that the total size of the relevant literature on the Impella PVAD may be approximately 27 studies across the two key questions (low confidence). By reviewing a random sample of 200 abstracts, we extrapolated the number of articles requiring full text review published during the current search period to be 16 and added the number of relevant studies of Impella PVAD use in elective high-risk PCI cited in the previously mentioned systematic review (n=11; one RCT and 10 observational studies). These would mostly be observational studies. Except for studies which focused on a specific type of harm (ex. valvular regurgitation), nearly all studies reported on clinical outcomes of survival at set time points (ex. 30-, 90-day survival) and MACE. Presence of other AEs such as bleeding (VADs usually requires anticoagulation) and insertion site complications were also reported. Impella PVADs were usually compared with IABP. Our additional search for PVAD identified 9 additional studies. Five studied Impella and TandemHeart PVAD; two focused on

	Impella; one focused on TandemHeart PVAD; and one focused on HeartMate PVAD. All but one were observational studies. In all the usual comparison was IABP. *ClinicalTrials.gov*: We found nine trials relevant to both key questions. **KQ1/KQ2** • Recruiting/Enrolling NCT02831881 (Impella) NCT03200990 (Impella) NCT02468778 (HeartMate) • Completed NCT03000270 (Impella) NCT00534859 (Impella) NCT02156609 (HeartMate) • Terminated NCT00562016 (Impella) (due to futility) NCT00972270 (Impella) (due to insufficient enrollment) • Withdrawn NCT02164058 (TandemHeart)
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, this topic will inform coverage decisions for PVAD use in patients undergoing non-emergent PCI.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes, the nominator plans to use the findings of the report for coverage decisions and guidelines within their health plan.

Abbreviations: ACCF= American College of Cardiology Foundation; AE=adverse event;AHA=American Heart Association; AHRQ=Agency for Healthcare Research and Quality; IABP=intra-aortic balloon pump; MACE=major adverse cardiovascular events; PCI=percutaneous coronary intervention; SCAI=Society for Cardiovascular Angiography and Interventions; PVAD=percutaneous ventricular assist device; VAD=ventricular assist device

**https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=35441*