Renal Protection During Impella®-Supported PCI in Patients With High-Risk Complex Coronary Artery Disease

BY MICHAEL P. FLAHERTY, MD, PHD, FACC, FSCAI

Acute kidney injury (AKI) after percutaneous coronary intervention (PCI) is associated with a higher risk of acute myocardial infarction, increased bleeding, extended length of stay, increased cost, and up to a 12-fold increased risk of mortality.[1-3] AKI rates after PCI are a quality metric that may impact overall reimbursement. Patients with complex coronary artery disease are at increased risk of AKI due to coexisting risk factors (older age, gender, left ventricular [LV] ejection fraction [LVEF], chronic kidney disease, acute coronary syndrome, etc), longer procedure times with greater contrast volume, and associated hemodynamic instability. Furthermore, the risk of AKI surrounding high-risk PCI may limit procedural quality and/or complete revascularization, which results in staged future vessel interventions and increases adverse event rates at intermediate-term follow-up.[4-7] Although surgical revascularization is an option for some patients, it is associated with a higher AKI risk than PCI, reaching up to a 4.5-fold higher risk in patients with advanced baseline chronic kidney disease (CKD).[8-10]

Current AKI prevention strategies in high-risk patients focus on expanding intravascular volume via intravenous hydration while attempting to minimize contrast volume use. In addition, particularly in patients with low LVEF, AKI prevention focuses on pharmacologic hemodynamic support in hopes of optimizing renal perfusion by increasing cardiac output and maintaining a favorable mean arterial pressure (MAP). However, the use of inotropes and vasopressors for hemodynamic support does carry an increased mortality risk.[11-13] Furthermore, increasing MAP does not itself protect against AKI and may not translate into a mortality benefit and does not obviate the need for renal replacement therapy (RRT).[14] Methods to reduce AKI risk have demonstrated only a modest reduction in AKI incidence, without an observed mortality benefit.[15,16]

The Impella heart pump (Abiomed, Inc.) provides continuous-flow mechanical hemodynamic support while simultaneously unloading the left ventricle, thereby enhancing forward cardiac flow. Its unique mechanism of action may provide renal protection against AKI or drastically reduce the severity of renal injury. The impact of Impella support versus no support was studied in a sick cohort of 230 patients with LVEF ≤ 35% undergoing high-risk PCI.[17] One hundred fifteen patients who received Impella 2.5 support were compared to a matched cohort of 115 patients without Impella support. Patients in the Impella arm had a greater number of comorbidities, longer procedure times, and received a higher contrast volume. Despite these risks, Impella-supported patients experienced a fivefold reduction in AKI compared to unsupported patients (5.2 vs 27.8%; $P = .001$) (Figure 1) and fewer required hemodialysis (0.9% vs 6.1%; $P < .05$).[17] AKI reduction with Impella support was also observed when these authors' stratified analyses based on AKI Network (AKIN) stages and severity of baseline CKD. Moreover, Impella support was found to be an independent predictor of reduced AKI risk (odds ratio, 0.13; 95% CI, 0.09-0.31; $P < .001$) after adjusting for other risk factors, including LVEF, estimated glomerular filtration rate, procedure time, and contrast volume.[17]

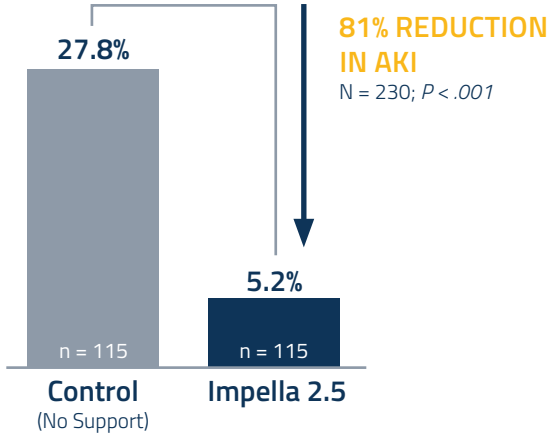

Figure 1. Incidence of AKI in high-risk PCI without hemodynamic support versus use of Impella 2.5®.

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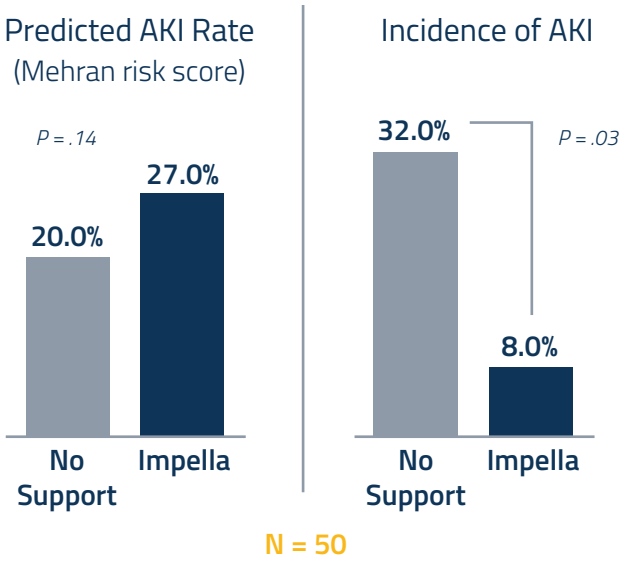

Figure 2. The patients on Impella support had a lower incidence of AKI.

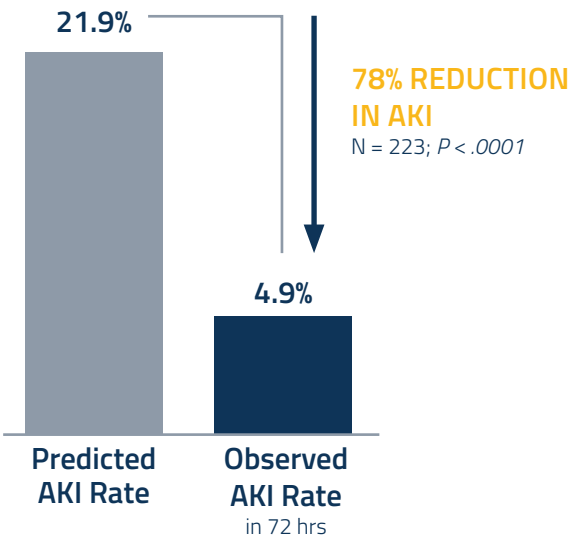

Figure 3. Impella support resulted in a 78% lower incidence of AKI compared to the predicted rate of AKI.

Current guidelines recommend AKI prevention protocols guided by Mehran risk score, which identifies patients at high risk for periprocedural AKI.[18] A recent report that utilized the Mehran risk score demonstrated that despite similar predicted AKI risk between Impella-supported high-risk PCI and nonsupported PCI (27% vs 20%; *P* = .14), Impella-supported patients experienced lower AKI risk (8% vs 32%; *P* = .03) (Figure 2).[19] Further evidence from the prospective, multicenter, global cVAD Renal Protection Study showed 78% lower observed AKI compared to the predicted risk from the Mehran AKI risk score (4.9% vs 21.9%) (Figure 3).[20]

The renoprotective effect of Impella was further validated in the PROTECT III substudy presented during Transcatheter Cardiovascular Therapeutics 2019. One hundred six Protected PCI patients were compared to 106 propensity-matched patients without Impella support. Patients with Impella support had a 77% lower incidence of AKI (5.7% vs 24.5%; *P* = .0002) along with a lower severity of AKI (Figure 4).[21]

Other mechanical circulatory support devices, such as intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation (ECMO), have been used to provide hemodynamic support for high-risk procedures, although existing data have failed to demonstrate any benefit from either in protecting against AKI. In fact, IABP was identified as an independent predictor for AKI in a propensity-matched analysis of a ST-segment elevation myocardial infarction population.[22] A recent meta-analysis revealed a significantly increased risk of AKI when ECMO support was used. In this study, those who had AKI requiring RRT while on ECMO had a 3.7-fold higher risk of death.[23] In contrast, a significantly lower incidence of AKI was observed in a single-center experience when Impella-supported high-risk PCI was compared with ECMO support (12% vs 55%; *P* = .03) in patients with similar predicted Mehran risk scores (31% vs 35%; *P* = .55) (Figure 5).[24]

With regard to the renoprotective mechanisms accounting for AKI risk reduction with Impella support, these appear to be multifactorial. Putative mechanisms point to Impella-mediated maintenance of continuous renal perfusion during PCI, thereby reducing ischemic tubular necrosis and providing an estimated glomerular

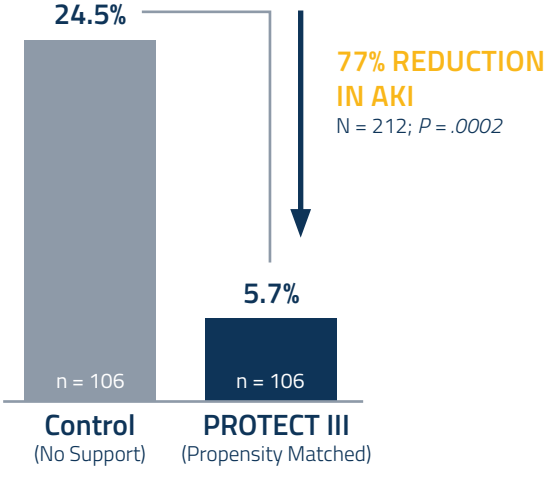

Figure 4. Impella support resulted in a 77% lower rate of AKI.

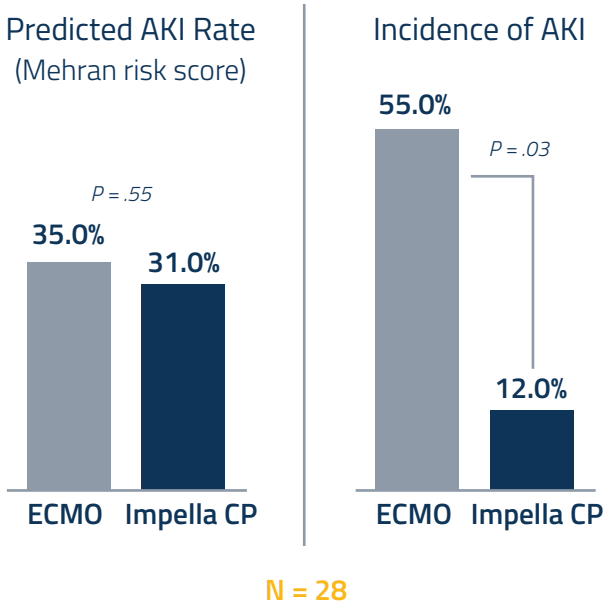

Figure 5. The patients supported with Impella CP® had a lower incidence of AKI.

filtration rate sufficient to prevent stagnation of nephrotoxic contrast in the renal tubules.[17] Other investigators suggest a novel finding that demonstrates a clear mechanistic link between Impella LV unloading and protective attenuation of the proinflammatory cardiorenal response to myocardial ischemia.[25]

CONCLUSION

In addition to increased mortality risk, AKI is associated with adverse outcomes after high-risk PCI. The incidence of AKI in Impella-supported patients relative to unsupported patients is significantly decreased during high-risk PCI. Relative to an individual's predicted AKI risk, Impella support mitigates that risk and protects against AKI. This decrease in AKI incidence with Protected PCI persists despite reduced LVEF or baseline renal dysfunction. Finally, Protected PCI with Impella lowers the incidence of AKI when compared to high-risk PCI in ECMO-supported patients and demonstrates a lower AKI rate than the overall predicted AKI risk in this population. Therefore, Impella-mediated hemodynamic support should be considered as an AKI risk reduction strategy during high-risk PCI in order to allow for more durable and complete revascularization and prevent staging of interventions. Perhaps most importantly, AKI incidence reduction achieved with Impella-supported high-risk PCI may potentially reduce in-hospital mortality, myocardial infarction, bleeding rates, and length of stay. ■

1. Valle JA, McCoy LA, Maddox TM, et al. Longitudinal risk of adverse events in patients with acute kidney injury after percutaneous coronary intervention: insights from the National Cardiovascular Data Registry. Circ Cardiovasc Interv. 2017;10:e004439. doi: 10.1161/CIRCINTERVENTIONS.116.004439
2. Kooiman J, Seth M, Nallamothu BK, et al. Association between acute kidney injury and in-hospital mortality in patients undergoing percutaneous coronary interventions. Circ Cardiovasc Interv. 2015;8:e002212. doi: 10.1161/CIRCINTERVENTIONS.114.002212
3. Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol. 2005;16:3365-3370. doi: 10.1681/ASN.2004090740
4. Gaffar R, Habib B, Filion KB, et al. Optimal timing of complete revascularization in acute coronary syndrome: a systematic review and meta-analysis. J Am Heart Assoc. 2017;6(4):e005381.
5. Gershlick AH, Khan JN, Kelly DJ, et al. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CULPRIT trial. J Am Coll Cardiol. 2015;65:963-972. doi: 10.1016/j.jacc.2014.12.038
6. Rosner GF, Kirtane AJ, Genereux P, et al. Impact of the presence and extent of incomplete angiographic revascularization after percutaneous coronary intervention in acute coronary syndromes: the ACUITY trial. Circulation. 2012;125:2613-2620. doi: 10.1161/CIRCULATIONAHA.111.069237
7. Vaidya SR, Devarapally SR, Arora S. Infarct related artery only versus complete revascularization in ST-segment elevation myocardial infarction and multi vessel disease: a meta-analysis. Cardiovasc Diag Ther. 2017;7:16. doi: 10.21037/cdt.2016.08.06
8. Gaipov A, Molnar MZ, Potukuchi PK, et al. Acute kidney injury following coronary revascularization procedures in patients with advanced CKD. Nephrol Dial Transplant. 2019;34:1894-1901. doi: 10.1093/ndt/gfy178
9. Investigators SoS. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the stent or surgery trial): a randomised controlled trial. Lancet. 2002;360:965-970. doi: 10.1016/S0140-6736(02)11078-6
10. Hannan EL, Wu C, Walford G, et al. Drug-eluting stents vs. coronary artery bypass grafting in multivessel coronary disease. N Engl J Med. 2008;358:331-341. doi: 10.1056/NEJMoa071804
11. Levy B, Clere-Jehl R, Legras A, et al. Epinephrine versus norepinephrine for cardiogenic shock after acute myocardial infarction. J Am Coll Cardiol. 2018;72:173-182. doi: 10.1016/j.jacc.2018.04.051
12. Aljundi AHS, Mohammed SFK, Patel A, et al. Inotropic agents use in patients hospitalized with acute decompensated heart failure: a retrospective analysis from a 22-year registry in a Middle Eastern Country (1991-2013). BMC Cardiovasc Disord. 2016;16:47. doi: 10.1186/s12872-016-0223-5
13. Léopold V, Gayat E, Pirracchio R, et al. Epinephrine and short-term survival in cardiogenic shock: an individual data meta-analysis of 2583 patients. Intensive Care Med. 2018;44:847-856. doi: 10.1007/s00134-018-5222-9
14. Asfar P, Meziani F, Hamel JF, et al. High versus low blood-pressure target in patients with septic shock. N Engl J Med. 2014;370:1583-1593. doi: 10.1056/NEJMoa1312173
15. Brar SS, Shen AY, Jorgensen MB, et al. Sodium bicarbonate vs sodium chloride for the prevention of contrast medium-induced nephropathy in patients undergoing coronary angiography: a randomized trial. JAMA. 2008;300:1038-1046. doi: 10.1001/jama.300.9.1038
16. Garcia S, Bhatt DL, Gallagher M, et al. Strategies to reduce acute kidney injury and improve clinical outcomes following percutaneous coronary intervention a subgroup analysis of the PRESERVE Trial. JACC Cardiovasc Interv. 2018;11:2254-2261. doi: 10.1016/j.jcin.2018.07.044
17. Flaherty MP, Pant S, Patel SV, et al. Hemodynamic support with a microaxial percutaneous left ventricular assist device (Impella) protects against acute kidney injury in patients undergoing high-risk percutaneous coronary intervention. Circ Res. 2017;120:692-700. doi: 10.1161/CIRCRESAHA.116.309738
18. Levine GN, Bates ER, Blankenship JC, et al. ACCF/AHA/SCAI guideline for percutaneous coronary intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2011;58:e44-e122. doi: 10.1016/j.jacc.2011.08.007
19. Westenfeld R, et al. End organ perfusion & kidney protection. Why use percutaneous ventricular assist devices? Presented at the meeting of the European Society of Cardiology Congress; August 2018; Munich, Germany.
20. Flaherty MP, Moses JW, Westenfeld R, et al. Impella support and acute kidney injury during high-risk percutaneous coronary intervention: the Global cVAD Renal Protection study. Catheter Cardiovasc Interv. 2020;95:1111-1121. doi: 10.1002/ccd.28400
21. Popma J, et al. PROTECT III first look: high-risk PCI outcomes in 800 Impella-supported patients. Presented at the annual Transcatheter Therapeutics (TCT) meeting; September 2019; San Francisco, California.
22. Caspi O, Habib M, Cohen Y, et al. Acute kidney injury after primary angioplasty: is contrast-induced nephropathy the culprit? J Am Heart Assoc. 2017;6:e005715. doi: 10.1161/JAHA.117.005715
23. Thongprayoon C, Cheungpasitporn W, Lertjitbanjong P, et al. Incidence and impact of acute kidney injury in patients receiving extracorporeal membrane oxygenation: a meta-analysis. J Clin Med. 2019;8:981. doi: 10.3390/jcm8070981
24. Wiora J, Horn P, Jung C, et al. Impella is associated with shorter time-to-support and reduced incidence of contrast-induced nephropathy compared to VAECMO in high-risk PCI. Abstracts of the 2017 A-CURE Symposium. J Cardiovasc Translational Res. 2018;11:58-70.
25. Qiao X, Swain L, Reyelt L, et al. VA-ECMO increases urinary levels of the biomarker kidney injury marker-1 (KIM-1) in a preclinical model of acute myocardial infarction. Abstract presented at the American Heart Association's Scientific Sessions; Aug 2, 2019; Boston, Massachusetts.

Michael P. Flaherty, MD, PhD, FACC, FSCAI
Structural and Coronary Interventional Cardiologist
Baptist Health
Louisville, Kentucky
mpflah01@gmail.com
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