How to Cite this article: Carl Walther, Andrew Civitello, Kenneth Liao, and Sankar Navaneethan, Nephrology considerations in the management of durable and temporary mechanical circulatory support, Kidney360, Publish Ahead of Print, 10.34067/KID.0003382021

Article Type: Review Article

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Key Points:

Abstract:
Durable and temporary mechanical circulatory support (MCS) use is growing for a range of cardiovascular indications. Kidney dysfunction is common in persons evaluated for or receiving durable or temporary MCS, and portends worse outcomes. This kidney dysfunction can be due to pre-existing kidney chronic kidney disease (CKD), acute kidney injury (AKI) related to acute cardiovascular disease necessitating MCS, AKI due to cardiac procedures, and due to acute and chronic MCS effects and complications.

Durable MCS, with implantable continuous flow pumps, is used for long-term support in advanced HF refractory to guideline directed medical and device therapy, either permanently or as a bridge to heart transplantation. Temporary MCS—encompassing in this review intra-aortic balloon pumps (IABPs), axial flow pumps, centrifugal flow pumps, and venoarterial ECMO—is used for diverse situations: high risk percutaneous coronary interventions (PCI), acute decompensated heart failure (HF), cardiogenic shock, and resuscitation following cardiac arrest.

The wide adoption of MCS makes it imperative to improve understanding of the effects of MCS on kidney health/function, and of kidney health/function on MCS outcomes. The complex structure and functions of the kidney, and the complex health states of individuals receiving MCS, makes investigations in this area challenging, and current knowledge is limited. Fortunately, the increasing nephrology toolbox of non-invasive kidney health/function assessments may enable development and testing of individualized management strategies and therapeutics in the future. We review technology, epidemiology, pathophysiology, clinical considerations, and future directions in MCS and nephrology.

Disclosures: A. Civitello reports the following: Consultancy Agreements: Medtronic; Honoraria: Medtronic, Abbott; Scientific Advisor or Membership: Medtronic Titan Medical Advisory Board. S. Navaneethan reports the following: Consultancy Agreements: Bayer, Boehringer Ingelheim, Vifor and Tricida; Research Funding: Keryx; Honoraria: Bayer, Boehringer Ingelheim, Vifor and Tricida; Scientific Advisor or Membership: AJKD, CJASN, CardioRenal Medicine, Current Opinion in Nephrology and Hypertension, American Journal of Nephrology and KDIGO: Guideline writing committee member. The remaining authors have nothing to disclose.

Funding: HHS | NIH | National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK): Carl P. Walther, K23DK122131

Author Contributions: Carl Walther: Conceptualization; Visualization; Writing - original draft; Writing - review and editing Andrew Civitello: Writing -review and editing Kenneth Liao: Writing - review and editing Sankar Navaneethan: Conceptualization; Supervision; Writing - review and editing

Data Sharing Statement:

Clinical Trials Registration:

Registration Number:
The information on this cover page is based on the most recent submission data from the authors. It may vary from the final published article. Any fields remaining blank are not applicable for this manuscript.
Nephrology considerations in the management of durable and temporary mechanical circulatory support

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Abstract

Durable and temporary mechanical circulatory support (MCS) use is growing for a range of cardiovascular indications. Kidney dysfunction is common in persons evaluated for or receiving durable or temporary MCS, and portends worse outcomes. This kidney dysfunction can be due to pre-existing kidney chronic kidney disease (CKD), acute kidney injury (AKI) related to acute cardiovascular disease necessitating MCS, AKI due to cardiac procedures, and due to acute and chronic MCS effects and complications.

Durable MCS, with implantable continuous flow pumps, is used for long-term support in advanced HF refractory to guideline directed medical and device therapy, either permanently or as a bridge to heart transplantation. Temporary MCS—encompassing in this review intra-aortic balloon pumps (IABPs), axial flow pumps, centrifugal flow pumps, and venoarterial ECMO—is used for diverse situations: high risk percutaneous coronary interventions (PCI), acute decompensated heart failure (HF), cardiogenic shock, and resuscitation following cardiac arrest.

The wide adoption of MCS makes it imperative to improve understanding of the effects of MCS on kidney health/function, and of kidney health/function on MCS outcomes. The complex structure and functions of the kidney, and the complex health states of individuals receiving MCS, makes investigations in this area challenging, and current knowledge is limited. Fortunately, the increasing nephrology toolbox of non-invasive kidney health/function assessments may enable development and testing of individualized management strategies and therapeutics in the future. We review technology, epidemiology, pathophysiology, clinical considerations, and future directions in MCS and nephrology.
Introduction

Mechanical circulatory support (MCS) encompasses devices and strategies to provide or support circulation over time spans ranging from the duration of a cardiac catheterization to years. Durable MCS is used for long-term support for persons with advanced heart failure (HF) refractory to guideline-directed medical and device therapy. Temporary MCS is used to provide hemodynamic support in several clinical situations: prophylactic hemodynamic support during high risk PCI, acute decompensated HF, cardiogenic shock, and resuscitation following cardiac arrest.

Implantable left ventricular assist device (LVADs) are the most commonly used durable MCS device type by far, and will be the main focus of the durable MCS portion of this review (Table 1). Currently used devices are small, long-lasting continuous flow devices, and in recent years centrifugal (third generation) pumps have begun to supplant axial flow (second generation) pumps. Centrifugal-flow pumps were designed to be smaller, more durable, and less thrombogenic and hemolytic than axial flow pumps. While LV support is the most common durable MCS use in advanced HF, a smaller number of individuals—those with severe biventricular failure or predominant right ventricular disease with substantial left ventricular failure—are treated with biventricular support. Durable biventricular support options include a total artificial heart and biventricular implantation of ventricular support devices. Finally, isolated durable right ventricular (RV) support (RVAD) is used in a small number of individuals with isolated RV dysfunction but preserved LV function.

Temporary MCS is used to improve systemic and myocardial perfusion, reduce cardiac filling pressures, and reduce cardiac workload in a less invasive manner than
with durable devices (Table 1). IABP and venoarterial ECMO were the first temporary MCS devices, and IABP remains the most commonly used. Newer devices include impeller-driven axial flow pumps, a left atrial-to-femoral artery bypass pump, extracorporeal centrifugal pumps, and new ECMO devices.

The high burden of cardiovascular disease in the US, along with technological innovations, have led to growing use of durable and temporary MCS. Kidney dysfunction is common in persons receiving MCS, due to systemic diseases and the reciprocal relationship between kidney and cardiovascular health, and relates strongly with adverse outcomes.

**Durable MCS**

LVAD utilization has transformed from rare use, primarily for bridge to heart transplantation, to more common use, primarily for destination therapy, with 3,198 LVAD implantations in 2019 per the Society of Thoracic Surgeons (STS) Intermacs database. Destination therapy was the goal in 73.1% of LVAD implantations in 2019, compared to bridge to transplantation in 8.9%. This was a substantial change from 2010, when the goal was destination therapy in 34.9% of implantations and bridge to transplantation in 28.6%. This evolution of LVAD use occurred with the widespread adoption of continuous flow pumps and FDA approval for destination therapy use. We separate nephrology considerations in durable MCS into the pre-implantation, early post-implantation, and prolonged MCS periods.

*Pre-implantation*

*Epidemiology*
Kidney dysfunction at the time of LVAD implantation is an important risk factor for mortality, and has been incorporated into several prognostic scores. It is challenging in LVAD studies to accurately assess degree and chronicity of pre-existing kidney disease. In part, this is due to limitations in current kidney health assessments, limited largely to endogenous filtration markers and proteinuria. Filtration markers, particularly serum creatinine concentration and derived estimated glomerular filtration rate (eGFR), are influenced by muscle mass and fluid balance, resulting in inaccurate estimates in advanced HF.\textsuperscript{14,15} Chronicity of kidney dysfunction is difficult to determine in large cohort studies and may be challenging to determine even in single-center studies where patient care may be transferred to LVAD implantation centers shortly before implantation. Despite these limitations, and highlighting the importance of kidney function to prognosis, pre-implantation creatinine and eGFR-based categorizations correlate with adverse outcomes following LVAD implantation.\textsuperscript{16,17} One large cohort found that 36\% of LVAD recipients had eGFR <60ml/min/1.73m\textsuperscript{2} and 6\% had eGFR <30ml/min/1.73m\textsuperscript{2}.\textsuperscript{16} Persons requiring pre-implantation dialysis, particularly those on dialysis classified as having kidney failure with replacement therapy (KFRT), have especially high mortality after LVAD implantation.\textsuperscript{18-21} The other widely assessed kidney biomarker, proteinuria, also relates strongly with adverse LVAD outcomes.\textsuperscript{22,23}

The relationship of pre-implantation kidney dysfunction with changes in kidney function following LVAD implantation is variable. Among LVAD recipients, lower pre-implantation eGFR is associated with greater increase in eGFR following implantation.\textsuperscript{24,25} In an analysis of a national database of LVAD recipients, those with pre-implantation eGFR<60 ml/min/1.73m\textsuperscript{2} were more than twice as likely to experience
a 50% eGFR rise at one month post-implantation than those with eGFR≥60 ml/min/1.73m$^2$ (52% vs. 22%, P<0.001). However, it is currently unclear to what extent this finding is driven by survival bias (with high short term mortality in those with lower kidney function), regression to the mean (pre-implantation eGFR estimates are often based on single measures with susceptibility to large fluctuations), and by endogenous filtration markers’ confounding by fluid and body composition changes.°

Severe CKD can be a contraindication to LVAD use, although guidance and clinical practices vary. A recent Centers for Medicare & Medicaid Services Medicare Coverage decision listed “irreversible renal disease” as an absolute contraindication. In contrast, the American College of Cardiology’s (ACC’s) HF and Transplant Member Section and Leadership Council recently stated “dialysis-dependent renal failure is no longer an absolute contraindication to LVAD insertion”. Some centers use LVADs in advanced CKD for bridge to combined heart/kidney transplantation. Individuals with advanced CKD—including KFRT—have received devices. These individuals have lower survival than those without KFRT, although many achieved >1 year survival.

Mechanisms and pathophysiology

The mechanistic underpinnings of the epidemiologic data is unclear, and discussion is dependent on extrapolation from studies of low cardiac output states, kidney ischemia, non-HF disease states, and conjecture. First, diverse disease processes may be present pre-implantation. Chronic kidney parenchymal disease may be driven by type 2 diabetes and atherosclerotic vascular disease in many individuals, and proteinuria or albuminuria measurements provide some information about glomerular aspects of parenchymal kidney health, in addition to reflecting endothelial
Chronic ischemic damage to the kidneys may be an important factor in some patients, with chronic tubular hypoxia potentiated by low cardiac output leading to inflammation and tubulointerstitial fibrosis. Elevated central venous pressure (CVP) may cause interstitial fibrosis in the kidneys by causing capillary pericytes to detach from vascular walls and transition to a profibrotic myofibroblast cell type. Neurohormonal responses to the failing heart likely play an important role in chronic damage, with activation of the renin-angiotensin-aldosterone system and sympathetic nervous system driving intrarenal inflammation and fibrogenesis.

Acute kidney injury (AKI) in the pre-implantation period may be driven by low cardiac output and high renal venous pressures, particularly in patients in cardiogenic shock prior to LVAD implantation. In addition to causing reduced GFR, these flow disturbances can cause structural ischemia-reperfusion injury to the kidney. A large portion of LVAD recipients have cardiogenic shock severe enough to be managed with temporary MCS prior to durable LVAD implantation, presenting additional kidney risks discussed later. A particularly important question for nephrology is to what degree kidney dysfunction and damage drives adverse outcomes in LVAD recipients versus being a marker of severity of cardiac and systemic illness.

Clinical considerations

Effective methods to improve pre-implantation kidney dysfunction currently lie in the years before a patient requires LVAD implantation, when therapies to improve kidney outcomes are available for many disease states. In the short term pre-implantation period, specific measures to improve kidney outcomes are not available beyond systemic hemodynamic optimization. Determination of potential reversibility of
kidney dysfunction after LVAD implantation is often desired. However, prediction of kidney function improvement currently relies on clinical judgment. Comprehensive evaluation may provide information about potential for improvement and susceptibility to potentially life-threatening kidney complications (Figure 1). Data about parenchymal kidney health and reserve can be obtained from a detailed history, including long-term eGFR and albuminuria trends, prior AKI episodes, review of any prior kidney procedures (e.g., lithotripsy, partial nephrectomy), urinalysis and sediment examination, and evaluation of the pre-implantation period (trends in urine output and endogenous filtration markers, systemic perfusion). Direct information about kidney parenchymal injury in the preimplantation period could be provided by an approved kidney biomarker score calculated from urinary concentrations of the cell cycle arrest markers insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases-2 (TIMP-2), although this biomarker score has not been validated in this setting.

Future investigations

Syndromic, filtration marker-and albuminuria-dependent AKI and CKD classifications are insufficient to understanding the complexity of kidney disease. This is particularly relevant to complex LVAD recipients. Investigations into cellular and molecular processes of kidney pathology are addressing this critical barrier to progress in many disease states, with analysis of kidney tissue and body fluids. Obtaining kidney tissue from LVAD recipients would be ideal for understanding kidney pathophysiology in this group, but kidney biopsy is seldom performed in these patients because of their often tenuous states. Thus, improved non-invasive assessments of kidney health are crucial to this patient population. Growing availability of urine and
blood biomarkers reflecting different aspects of kidney health/function, and growing use of omics-based systems investigations in many areas of medicine, may enable important non-invasive insights into kidney health in MCS. Pre-LVAD implantation parenchymal biomarkers may enable accurate assessment of kidney damage and differentiation of damage from flow-mediated functional reductions, yielding prognostic information on likelihood of kidney function recovery. Multi-omics studies of blood and urine samples in the pre-implantation period have the potential to further elucidate heterogeneity and mechanistic processes underlying kidney health states in these complex patients. Analysis of exosomes (membrane-derived, 50-200 nm diameter vesicles) from the urine may provide a non-invasive window into kidney cellular processes. In addition to accurate diagnosis and prognosis, movement of kidney health understanding from broad syndromes to accurate molecular mechanistic understanding is a crucial step towards therapies.

**Early post-implantation**

**Epidemiology**

LVAD recipients are at high risk of AKI in the early post-operative period. A recent meta-analysis estimated the incidence of AKI in >63,000 LVAD recipients at 36.9% when AKI was assessed using standardized criteria. The incidence of AKI treated with kidney replacement therapy (KRT) was 12.6%. With AKI, odds of death more than tripled in the first 30 days, and more than doubled over 1 year. With AKI treated with KRT, odds of death increased more than 7-fold in the first 30 days, and more than 5-fold in the first year.
Mechanisms and pathophysiology

AKI in LVAD recipients has many potential contributing factors. LVAD implantation is a major cardiac surgery with prolonged cardiopulmonary bypass (CPB).\textsuperscript{43} Cardiac surgery is thought to damage the kidney through ischemia-reperfusion injury, inflammatory and oxidative injuries, microembolic injury, toxin-mediated injury, and neurohormonal activation.\textsuperscript{44} Much of this information has come from animal models, although non-invasive data from humans supporting many of these mechanisms is accruing.\textsuperscript{44-46} LVAD recipients, given their often tenuous pre-implantation status, may be particularly susceptible to these insults.

Another potential cause of AKI is RV dysfunction, through elevated CVP. RV dysfunction is a common complication of LVAD implantation, and can occur anytime, although early appearance is most common.\textsuperscript{43} LVAD support reduces LV volume, which can shift the interventricular septum, distorting RV geometry and reducing function.\textsuperscript{43} The severity can vary from mild (manageable with inotropes, inhaled nitric oxide or intravenous vasodilators), to severe (requiring temporary or permanent RV MCS).\textsuperscript{47}

Clinical considerations

Specific interventions to reduce the risk of AKI and improve kidney outcomes in the early post-operative period are not available. Critical care nephrology practices are essential, with review of operative details, close monitoring of urine output, and frequent measurement of electrolytes and acid-base status, to detect any impending kidney failure or severe derangements (Figure 1). Diuretic use or ultrafiltration may be required for volume management. Urine microscopy may provide information, as presence of
numerous granular casts may suggest a severe acute tubular necrosis. Urine cell-cycle arrest biomarker score measurement ([TIMP2]*[IGFBP7]) may provide additional information about parenchymal kidney injury.

**Future investigations**

Detailed non-invasive assessments of parenchymal health using biomarker panels may enable accurate diagnosis of kidney injury sustained during surgery. In general cardiac surgery settings, with the [TIMP2]*[IGFBP7] score has enabled early identification and targeted management of AKI. Other biomarkers (Basic Fibroblast Growth Factor, Kidney Injury Molecule-1, N-terminal pro-B-type natriuretic peptide, and Tumor Necrosis Factor Receptor) measured early in the post-operative period are associated with development of CKD following general cardiac surgery. Mult-omics approaches hold the promise of more granular insights into kidney health. Improved understanding of the molecular mechanisms of kidney dysfunction in the early post-operative period has the potential to inform therapeutic development, and to identify individuals who may benefit from specific treatments.

**Prolonged MCS**

**Epidemiology**

LVADs tend to improve macrocirculatory parameters, increasing cardiac output and decreasing CVP, and disordered macrocirculation may be the primary driver of pre-implantation kidney dysfunction in some patients. Despite these macrocirculatory improvements, LVADs often do not cause substantial sustained kidney function improvement. Group-average eGFR changes in LVAD recipients shows early
increase in eGFR, peak eGFR ~1 month after implantation, followed by decline.\textsuperscript{25,54} Relationships between changes in kidney function and outcomes are non-linear.\textsuperscript{25}

**Mechanisms and pathophysiology**

Numerous potential mechanisms have been proposed (Figure 2) for adverse kidney outcomes with prolonged MCS. A long-standing concern is over lack of pulsatility. For a time, continuous flow was thought to induce periarteritis in the kidneys, based on an animal study;\textsuperscript{57} however, this periarteritis has not been found in humans.\textsuperscript{58} Evidence is stronger for continuous flow causing endothelial dysfunction from reduced endothelial release of nitric oxide, increased secretion of endothelin-1, and other factors.\textsuperscript{59-62} Continuous flow may activate the sympathetic nervous system and renin angiotensin system (RAS) systemically and in the kidneys.\textsuperscript{63-66} Intravascular hemolysis resulting in free hemoglobin in the plasma can harm the kidneys through vasoconstriction from nitric oxide sequestration, tubular casts, and proximal tubular heme toxicity.\textsuperscript{67,68} Although hemolysis appears very limited with newer devices, this is a possible mechanism for chronic and acute kidney damage in some cases.\textsuperscript{69} Chronic RV impairment following LVAD implantation is another potential factor driving long-term kidney dysfunction.\textsuperscript{70}

**Clinical considerations**

Interventions to improve kidney health with long-term LVAD support are unknown, and limitations of endogenous filtration marker-based kidney function estimates make it difficult to accurately assess kidney health in this setting.\textsuperscript{71} Nevertheless, large changes in serum creatinine or cystatin C levels or eGFR, or clear
trajectories, may allow inferences about health and prognosis. Given the apparent RAS activation with continuous flow, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use is attractive for kidney preservation; however, the risks and benefits in this setting are uncertain. These medications are often continued following LVAD implantation.72

Special management is necessary for maintenance dialysis in persons with LVADs. Earlier devices were quite sensitive to reductions in preload, complicating ultrafiltration.73 Modern devices, however, have limited preload sensitivity, facilitating volume removal.74 Several case series of outpatient hemodialysis have been published, as well as case reports of outpatient peritoneal dialysis.75-78 A theme of these reports is close cooperation between the dialysis providers and MCS teams, including initial education about interpreting LVAD device information (pump speed, flow rate, and pulsatility index) and availability of immediate communication. Blood pressure measurement is important, and depends on whether the aortic valve continues to open during the cardiac cycle causing a detectable pulse pressure. Aortic valve opening is influenced by native heart contractility and pump flow. If the aortic valve opens, systolic and diastolic blood pressure may be measureable with usual techniques.79 If the aortic valve does not open, blood pressure can be measured using a Doppler ultrasound device and manual sphygmomanometer, and the mean arterial pressure (MAP) is obtained from the pressure at which flow is detected. Goal MAP is generally 70-80 mmHg; MAP greater than 90 mmHg is avoided given increased risk of stroke.80-82 Vascular access for maintenance hemodialysis is an important consideration. Arteriovenous access placement, and avoidance of long-term tunneled catheter use, is
desirable given the elevated risk of blood stream infections with dialysis catheters. Several cases of successful arteriovenous fistula placement, maturation, and use have been reported. Concerns remain, however, about arteriovenous fistula maturation in the setting of low pulsatile blood flow, and others have advocated for arteriovenous grafts as the preferred access. Peritoneal dialysis is an option as modern LVADs do not compromise the peritoneal space. As either KFRT treated with dialysis or LVAD use alone have high complication rates related to underlying disease factors and treatment factors, patients with both are at very high risk.

**Future investigations**

The growing availability of techniques discussed in prior sections may enable important insights into the effects of prolonged MCS on kidney health. Longitudinal assessments of biomarker panels and multi-omics data and accurate, comprehensive assessments of clinical characteristics in large cohorts would be needed to accurately assess the multiple dimensions of kidney health in LVAD recipients and to draw inferences about mechanistic effects of durable LVAD support on the kidneys. It seems clear now that the idea of a single, predominant salutary effect on kidney function with macrocirculatory parameter improvement with LVAD support does not capture most patients’ experiences, and that molecular mechanisms rather than macrocirculatory mechanisms underlie much of cardiac-LVAD-kidney interactions.

**Temporary MCS**

Several temporary MCS devices are available for use in high-risk percutaneous coronary interventions, acute decompensated HF, cardiogenic shock, and cardiac arrest
resuscitation (Table 1). The evidence basis to guide usage decisions is limited, and decisions rely on expert opinion and experience, pathophysiological considerations, and observational studies. A recent analysis of administrative data found increased use of temporary MCS for post-cardiac surgery cardiogenic shock. Temporary MCS use prior to durable MCS has also increased. ST-elevation myocardial infarction (STEMI) was complicated by cardiogenic shock in 8.7% of cases in an analysis of data from 2003-2012, and temporary MCS was used in over half of these cases.

Nephrology considerations and kidney pathophysiology

Temporary MCS devices improve macrocirculatory parameters that may affect kidney function, and clinical experience of marked kidney function improvement in some individuals is clear. However, there is limited published data on kidney outcomes. A case series of 5 patients who underwent placement of a left atrial-to-femoral artery bypass pump found no change in serum creatinine, although urine output more than doubled following device placement. Observational studies suggest that impeller-driven axial flow pumps are associated with lower risk of AKI during high-risk PCI. A small study of 15 patients with cardiogenic shock found that increasing axial flow pump rate decreased renal resistive index without changing blood pressure, suggesting kidney perfusion may have increased. The effects of venoarterial ECMO on kidney function are challenging to assess, given it is reserved for situations involving respiratory failure or cardiac arrest where numerous processes affecting kidney health/function are at play. Studies of long-term kidney outcomes are not available.

There are several explanations for why kidney function improvement is often not observed with temporary MCS. The limits of routine kidney assessments mean that
pre-existing subclinical kidney damage with loss of reserve capacity and sensitivity to insults may be underestimated. This, combined with the perturbations of the acute process necessitating temporary MCS, puts these patients at high risk for damage regardless of macrocirculatory improvement, and assessment of kidney microcirculation and parenchymal markers may improve understanding.

The inflammatory environment in temporary MCS may be damaging to the kidneys. Systemic inflammation is well documented in settings that can lead to temporary MCS use—such as acute MI or acute HF decompensation—in clinical and experimental settings. While systemic and cardiac inflammatory environments have been most studied, it is likely that the kidneys are affected by systemic and intrarenal inflammation as well. Temporary MCS may exacerbate inflammation, through procedural factors and exposure of the blood to artificial material. This has been most noticeable with ECMO, where a systemic inflammatory response syndrome (SIRS) often develops, attributed to activation of the innate immune system with extensive blood exposure to artificial material, in addition to a pro-inflammatory effect of non-pulsatile blood flow. Experimental studies have demonstrated ECMO in healthy animals causes SIRS with mobilization of cellular stores of inflammatory cytokines. In contrast to ECMO, IABP use has been reported to reduce inflammation in some settings, perhaps due to pulsatility.

**Nephrology Clinical Management Considerations**

Nephrology evaluation of acutely ill persons on temporary MCS includes assessing their pre-episode kidney health/function, their recent exposures to kidney insults, and their current status, with particular attention to urine output, electrolytes, and
likely trajectory (Figure 1). Routine nephrology critical care assessments, including consideration of a wide differential diagnosis for causes and contributors to kidney injury, in addition to clinical judgment on how the acute cardiac process is driving the presentation, is appropriate. Frequent monitoring of urine output, electrolytes, and acid-base status is crucial as well to enable optimal supportive care and assess need for dialysis, with close communication with the cardiovascular and intensivist teams.

Patients requiring temporary MCS who develop severe AKI may require dialysis. Given the hemodynamic instability and risk for severe acid-base, electrolyte, and volume disturbances, continuous renal replacement therapy (CRRT) is usually the modality of choice. Management considerations are similar to other situations, with volume management paramount. Catheter placement location may be influenced by the temporary MCS method if venous access is used for MCS, such as with venoarterial ECMO or percutaneous RV support devices. With venoarterial ECMO, attachment of the CRRT machine to the ECMO circuit is often possible, making an additional catheter unnecessary. In all forms of temporary MCS, systemic anticoagulation is used, and thus regional or systemic anticoagulation specifically for dialysis is not necessary.

*Future investigations*

To understand the effects of temporary MCS on the kidneys, the improved non-invasive assessments of kidney function discussed in the context of durable MCS will be crucial. Temporary MCS devices differ greatly in function, uses, and potential risks, leading to great heterogeneity in potential kidney effects, heterogeneity that will require detailed non-invasive molecular techniques to understand and characterize. This will
enable individualized diagnosis and prognosis and development of targeted therapeutic and management strategies to improve kidney and overall outcomes

Conclusions

The high burden of cardiovascular disease in the US, improving MCS technologies, and changing use patterns, combined with the common coexistence of kidney and cardiovascular disease, means that need for nephrology care for patients receiving MCS will continue to increase. Nephrologists play an important role in ensuring patient safety and improving outcomes in this setting. Although current kidney-related management strategies in MCS are mostly opinion and experience-based, the rapid development of tools and techniques for granular, individualized kidney assessment hold the promise of improved diagnostic tools and development of targeted management strategies and therapies in the future.

Disclosures

A. Civitello reports the following: Consultancy Agreements: Medtronic; Honoraria: Medtronic, Abbott; Scientific Advisor or Membership: Medtronic Titan Medical Advisory Board.

S. Navaneethan reports the following: Consultancy Agreements: Bayer, Boehringer Ingelheim, Vifor and Tricida; Research Funding: Keryx; Honoraria: Bayer, Boehringer Ingelheim, Vifor and Tricida; Scientific Advisor or Membership: AJKD, CJASN, CardioRenal Medicine, Current Opinion in Nephrology and Hypertension, American Journal of Nephrology and KDIGO: Guideline writing committee member. The remaining authors have nothing to disclose.
**Funding**

Dr. Walther is supported by the National Institute of Diabetes and Digestive and Kidney Diseases, (Grant / Award Number: 'K23DK122131').

**Acknowledgments**

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or Veterans Administration.

**Author Contributions**

Carl Walther: Conceptualization; Visualization; Writing - original draft; Writing - review and editing. Andrew Civitello: Writing - review and editing. Kenneth Liao: Writing - review and editing. Sankar Navaneethan: Conceptualization; Supervision; Writing - review and editing.
Table 1. Mechanical circulatory support (MCS) uses, device types, and considerations.

<table>
<thead>
<tr>
<th>Durable MCS</th>
<th>Use categories</th>
<th>Uses</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular support (LVAD)</td>
<td>• Can be for bridge to transplantation, bridge to candidacy, or as destination therapy</td>
<td>• Most common durable MCS category by far</td>
<td></td>
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<tr>
<td>Biventricular support (BiVAD)</td>
<td>• Used in severe BiV failure</td>
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<tr>
<td>Biventricular replacement device (TAH)</td>
<td>• Used primarily for bridge to transplantation or bridge to candidacy⁴</td>
<td>• Replaces the native ventricles and the 4 valves</td>
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<td>Right ventricular support (RVAD)</td>
<td>• Used for isolated RV failure</td>
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<tr>
<th>Device types</th>
<th>Considerations</th>
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<tr>
<td>Axial flow devices</td>
<td>• The most used devices for many years¹</td>
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<tr>
<td>Centrifugal flow devices</td>
<td>• Designed for improved durability, smaller size, and improved blood flow compared to axial flow pumps</td>
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<tr>
<td>Pneumatic displacement pump devices</td>
<td>• Require larger drivelines than axial or centrifugal flow devices</td>
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<th>Temporary MCS</th>
<th>Use categories</th>
<th>Uses</th>
<th>Considerations</th>
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<tr>
<td>Intra-aortic balloon pump</td>
<td>• High risk PCI</td>
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<td>Axial flow pumps</td>
<td>• Acute decompressed heart failure</td>
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<td>Centrifugal flow pumps</td>
<td>• Cardiogenic shock</td>
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<td></td>
<td></td>
<td>• Widely available</td>
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<td>• Easily inserted and maintained</td>
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<td>• Limited hemodynamic support</td>
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<td>• Placed percutaneously or surgically</td>
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<td>• Some devices can supply high levels of hemodynamic support</td>
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<td>• Placed percutaneously or surgically</td>
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<td>• Can be used for prolonged periods</td>
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<tr>
<td>Implantation</td>
<td>Applicable Conditions</td>
<td>Method of Placement</td>
<td>Additional Information</td>
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| Venoarterial ECMO | • Cardiogenic shock  
• Cardiac arrest | • Placed percutaneously  
• Placed surgically | • Can provide respiratory support |

Abbreviations: MCS, mechanical circulatory support; LVAD, left ventricular assist device; BiVAD, biventricular assist device; TAH, total artificial heart; RVAD, right ventricular assist device; RV, right ventricular; BiV, biventricular; PCI, percutaneous coronary intervention; ECMO, extracorporeal membrane oxygenation.
Figure 1. Kidney considerations throughout the timeline of mechanical circulatory support (MCS). The focus is on durable MCS, but many considerations will apply to temporary MCS as well.

**Preprocedural**

- Assess acute kidney health/function and complications
  - Effects of acute and subacute cardiovascular processes
    - CO, CVP, SBP, DBP
    - Kidney and other organ perfusion
      - Urine output, cystatin C, creatinine, BUN
    - Mental status, skin and extremity perfusion, lactate, liver enzymes
    - Integrate data into anticipated trajectory
  - Kidney health/function effects
    - Volume overload (intra- and extravascular)
    - Electrolytes
    - Acid-base status
    - Assess if KRT needed
  - Consider non-cardiovascular contributors to kidney dysfunction
    - Urinalysis, physical exam, history, and clinical reasoning may in rare cases suggest acute non-cardiovascular processes

**Early post-operative**

- Reassess kidney parameters/functional changes
  - Potential for improvement or deterioration
  - Assess if KRT needed
  - Assess changes in kidney function
    - Urine output gives some immediate information
  - Evaluate for subtle signs of kidney damage that may influence recovery course
    - Review operative/procedural details
    - Presence of granular casts on urine microscopy suggests significant tubular injury
    - Consider [TIMP2]*[IGFBP7] biomarker score measurement

**Follow-up considerations**

- Cystatin C has theoretical benefits over creatinine (e.g., less dependent on muscle mass)
- Urinalysis and albuminuria measurement give additional information
- Further targeted kidney evaluations as needed dictated by kidney and clinical course
  - If substantial kidney function decline consider obstruction, hemolysis, RV dysfunction, ischemia
  - Consider rare causes unrelated to MCS
- Blood pressure management is driven by stroke risk
  - Goal MAP 70-80 mmHg
- RAS inhibition often continued, based on theoretical cardiac benefit
  - Theoretical kidney benefit as well

**History and baseline**

- Kidney health history assessment
  - Clinically evident CKD
    - Prior records
    - Filtration markers
      - Cystatin C, creatinine, BUN, estimated GFR
    - Albuminuria
  - Detailed kidney history may yield information
    - Diabetes history
    - Hypertensive history
    - Prior AKI episodes and causes
    - Toxic exposures (e.g., chemotherapy)
    - Procedures on the kidneys (e.g., lithotripsy)
    - Review of kidney imaging

**Up to 6 months post-operative**

- New steady state may become apparent
  - Evaluations at least monthly
  - Filtration markers may be approaching long-term stability
    - Normally early decrease, with nadir about 1 month post-op (suggesting improved kidney function) followed by later increase

**Long term**

- Periodic evaluations of kidney health/function
  - Consider at least every 3 months
  - Filtration marker trajectory may (in context of overall clinical course) provide information about future kidney health/function

**Kidney replacement therapy (KRT) considerations**

- Indications and techniques in the acute setting are similar to other critical care situations, and continuous KRT is most often used.
- Intermittent hemodialysis can be performed in stable inpatients, and in outpatients with close cooperation with dialysis units. Maturation of AV fistulas has been reported with durable MCS, as has peritoneal dialysis.
Abbreviations: CKD, chronic kidney disease; AKI, acute kidney injury; CO, cardiac output; CVP, central venous pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; BUN, blood urea nitrogen; KRT, kidney replacement therapy; RV, right ventricle; MAP, mean arterial pressure; MCS, mechanical circulatory support.
Figure 2. Potential mechanisms for LVAD effects (beneficial and harmful) on the kidneys.

Abbreviations: RAS, renin angiotensin system; CVP, central venous pressure; RV, right ventricle
References


