CHAPTER 116

Renal Function During Cardiac Mechanical Support and Artificial Heart

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OBJECTIVES

This chapter will:
1. Introduce the types of mechanical cardiac support.
2. Evaluate the clinical evidence regarding the impact of mechanical cardiac devices on renal function in patients with severe congestive heart failure.
3. Examine renal and patient outcomes in recipients of mechanical heart devices.

Heart failure (HF) remains one of the leading causes of hospitalization and is associated with significant morbidity and mortality. According to NHANES 2009–2012 data, an estimated 5.7 million Americans 20 years or older of age had HF (Heart and Stroke Statistics 2016 per American Heart Association). In 2012 the total cost for HF was estimated to be $30.7 billion, and of this 68% was attributable to direct medical costs. Projections show that by 2030, the total cost of HF will increase almost 127% to $69.7 billion from 2012. Moreover, it also is estimated that the prevalence of HF will increase 46% from 2012 to 2030, resulting in more than 8 million people 18 years of age or older with HF.

HF is associated with increased mortality and morbidity with aggregate 5-year survival rate of patients with heart failure estimated to be 50%; for those with advanced heart failure the 1-year mortality rate can be as high as 50%.[1] Cardiac transplantation, as a successful treatment for end-stage CHF, was performed first in 1967. According to recent report of United Network for Organ Sharing (www.unos.org), 2804 heart transplants were performed in United States in the year 2015. Because a limited number of donor hearts are available in the United States each year for transplantation, the need for other approaches to cardiac replacement is now well established. Various short-term and long-term circulatory support devices have been used to treat intractable heart failure since the inception of the artificial heart program at the National Institutes of Health (NIH) in 1964. Several different types of mechanical devices since have been approved for either short-term usage, bridge to transplantation (BTT), or as destination therapy (DT) for heart failure.[5] For example, in 2014, 20.4% of heart recipients were aged 65 years or older, compared with 10.3% in 2004; and half of heart transplant recipients had a ventricular-assist device (VAD) in place at the time of transplant in 2014, compared with 23.7% a decade earlier.

INDICATIONS AND TYPES OF MECHANICAL CARDIAC SUPPORTS

Severe cardiogenic shock that is not responsive to medical therapy is a unified indication for considering mechanical cardiac support. Based on the cause of cardiac failure and whether the expected duration of support is short term or long term, various modalities may be used. Intraaortic balloon pump (IABP) counterpulsation is a temporary form of inotropic support. Insertion of IABP is used commonly in cardiogenic shock resulting from acute myocardial infarction, in association with cardiopulmonary bypass surgery, or high-risk coronary angioplasty. Influence of IABP on renal function can be divided into two major categories. First, procedure-related complications may occur, such as renal artery occlusion, dissection, or atheroembolic and thromboembolic complications. These anatomic and embolic events may lead to a spectrum of abnormalities, including mild temporary renal dysfunction, to a more catastrophic event such as renal infarction and cortical necrosis.[2] Second, preoperative IABP support has been demonstrated consistently to be an independent risk factor of severe postoperative acute renal failure (ARF).[3,4] Whether the effect is causal, via direct interference of renal blood flow/embolic phenomenon, or IABP is a surrogate for the severity of hemodynamic state during the preoperative period remains unclear. However, it can be used as one of the key predictors to identify patients who are at a higher risk of developing postoperative kidney injury.

Over the past few decades there have been tremendous advances in other types of mechanical cardiac support such as VAD. The discussion in the following sections focuses on types of devices, selection of patients, and renal and related patient outcomes in VAD recipients.

Ventricular assist devices are "blood pumps" and can be classified in multiple ways. One of the ways to classify these devices is indicated in Table 116.1. In terms of expected response, patients can be categorized broadly as follows: (1) BTT: patients actively listed for transplant who would not survive or would develop progressive end-organ dysfunction from low cardiac output before an organ becomes available; (2) bridge to candidacy (BTC): for patients not currently listed for transplant, but who do not have an absolute or permanent contraindication to solid-organ transplant; (3) DT: for patients who need long-term support but are not eligible for transplant because of one or more relative or absolute contraindications; (4) bridge to recovery (BTR): for patients who require temporary circulatory support, during which time the heart is expected to recover from an acute injury, and mechanical support then is removed without need for transplant; (5) bridge to bridge: many are receiving temporary percutaneous circulatory support, sometimes referred to as *bridge to bridge* (BTB), as a way to support circulation and triage the sickest patients for eventual durable LVAD.

Indications for ventricular assist devices include post-cardiotomy shock, cardiogenic shock as a consequence of myocardial ischemia, decompensated heart failure regardless of transplant eligibility, myocarditis, and ventricular arrhythmias refractory to treatment.

TABLE 116.1

Summary of Types of Ventricular-Assist Devices

Pulsatile VAD	Pneumatic	Abiomed BVS 5000 Thoratec VAD
	Electric	Thoratec-HeartMate Novacor
Nonpulsatile VAD	Axial flow	MicroMed DeBakey HeartMate II Jarvik 2000
	Centrifugal flow	HeartMate III
Total Artificial Heart (TAH)	Biventricular, orthotopic, pneumatic, pulsatile blood pump	CardioWest
	Biventricular, orthotopic, nonpulsatile, centrifugal flow pump	AbioCor

The actual devices are meant to be representative examples in each category and may not include all available devices that are currently in use.
VAD, Ventricular-assist device.

PATTERNS OF USE OF VENTRICULAR-ASSIST DEVICE

The contemporary knowledge regarding the use of VAD is derived from a registry (INTERMACS: A global International Society for Heart and Lung Transplantation Registry for Mechanical Circulatory Support).[5] Based on this data source, between 2006 and 2014, 15,745 patients who received a US Food and Drug Administration (FDA)–approved MCS device were entered into the INTERMACS database. The registry includes more than 15,000 patients from 158 participating hospitals. The predominant use of continuous flow (CF) technology is evident, with more than 90% of patients receiving an intracorporeal CF pump. During 2014, approximately twice the number of axial-flow CF pumps, as compared with centrifugal-flow CF pumps, was entered into the registry. The progressive increase in VADs implanted for destination therapy (DT) has plateaued (46% DT implants in 2014). Thirty percent of patients were listed for heart transplantation at the time of device implant (BTT), and an additional 23% were implanted with an anticipated possibility of listing (BTC).

Pathophysiologic Considerations

The normal renal blood flow averages about 1.2 L per minute (normal cardiac output = 6 L per minute) such that it receives 20% of the total cardiac output in physiologic state. This translates into a blood flow of approximately 400 mL/min per 100 g of kidney tissue, whereby it has the highest oxygen delivery of all major vital organs (84 mL/min/100 g). In addition, the renal outer medulla has the highest ratio of oxygen consumption to oxygen delivery (79%).[6] With progressive heart failure, various compensatory changes in the sympathetic activity, renin-angiotensin system, and vasopressin axis can have a spectrum of effects on renal circulation and renal function. Regional blood flow, especially to the kidney, can be affected independent of central venous pressures in the setting of congestive heart failure. The vascular resistance of regional vascular beds, such as renal or hepatic blood flow, is better correlated with systemic vascular resistance than the recorded mean arterial pressure.[7] Mechanical support devices may influence the renal blood flow depending upon the type of devices – as indicated by experimental models. Intrarenal distribution of renal blood flow can be influenced by pulsatile versus nonpulsatile blood flow; pulsatile-assisted devices may have a better intrarenal vascular redistribution.[8,9] In addition, early institution of right ventricular support with its associated changes in filling pressures also has been implicated in preservation of renal function.[10] Whether data from experimental models translate to the clinical setting of heart failure remains less clear.

For instance, there has not been a satisfactory consensus definition of what constitutes pulsatile flow. Although modified roller pumps are proposed to generate so-called pulsatile flow, this bears little resemblance to the pulsatile flow generated by the natural heart. One of the problems in comparing the different perfusion modes or different types of pulsatile flow is the lack of precise quantification of pressure-flow waveforms. Without a common definition or a precise quantification of pulsatility, it is difficult to make meaningful comparisons between different perfusion systems as they relate to vital organ flow/function. In CF devices, on the other hand, although the pump flow is nonpulsatile, arterial waveforms have some degree of pulsations because the natural heart is also pumping. Moreover, if the patient's heart recovers well, then it is possible to achieve near physiologic arterial pressure waveforms with these devices in place. Additional challenges occur in monitoring patients with respect to various hemodynamic parameters when using these devices.

It is no surprise, however, that in disorders of progressive cardiac failure (or institution of cardiac support) kidney function remains a direct "downstream target." Epidemiologic data increasingly recognize that abnormal kidney function has a striking impact on morbidity and mortality associated with cardiac failure.[11] Worsening kidney function, as an end organ failure, carries a poor prognosis in severe heart failure, and more importantly, it influences the decisions regarding medical treatment, mechanical support strategies, and cardiac transplantation. Of course, this is an introductory and simplistic view of interrelationship between the heart and the kidney, and the pathophysiology of the types of cardiorenal syndromes is discussed in much greater detail in other sections of this textbook.

Preoperative Assessment

There has been significant expansion in the pool of patients considered to be eligible for VAD placement. Before insertion of VAD, several aspects unrelated to patient characteristics play a role in patient or device selection. These include institutional expertise, availability of sophisticated postoperative care, and a functioning transplant program. The devices and techniques continue to improve over time, and the selection criteria will change concurrently with it. Insertion of VAD is contraindicated absolutely in patients with active infections or sepsis. In addition, irreversible neurologic injury is accepted widely as a contraindication to provide mechanical support. Other end-organ failure, particularly renal failure, has been associated with poor postoperative outcomes. However, with early initiation of renal replacement therapy and improved strategies of ultrafiltration, presence of renal failure as a contraindication for mechanical support must be evaluated on a case-by-case basis. The present

evidence limits us in making robust predictive assessments, in terms of patient outcomes, after instituting support.

Hemodynamic criteria considered for eligibility have been those traditionally representative of cardiogenic shock, including cardiac index less than 2.0 L/min/m^2, systolic blood pressure of less than 90 mm Hg, left or right atrial pressures greater than 20 mm Hg, and a systemic vascular resistance greater than 2100 dyne-sec.cm.[12,13] Additional criteria to screen patients for VAD use are based primarily on the estimate of postoperative success. Oz et al. published a single-center experience proposed a scoring system to predict immediate postoperative mortality after VAD insertion.[14] Urine output less than 30 mL/hr (3 points), central venous pressure greater than 16 mm Hg (2 points), mechanical ventilation (2 points), prothrombin time greater than 16 (2 points), and prior surgery (1 point) were selected as independent predictors of mortality. At a score of more than 5, the operative mortality was 38% as compared with 13% in patients with a score of 5 or less, with a Receiver Operating Characteristic curve (ROC) value of 0.73. Urine output during the immediate preoperative period, and not serum creatinine level, was a better predictor of postoperative survival. This score was validated a decade later in a separate cohort of patients, albeit at the same institution, when neither creatinine nor urine output predicted postoperative survival.[15] It was postulated that patients may have received aggressive therapy aimed at improving urine output, or volume status in general, which may have been related to the change in the association between urine output and post-VAD survival.

In another study from European cardiothoracic registry, Friedel et al. evaluated organ recovery during mechanical assistance, for respiratory, hepatic, and renal function parameters in patients who underwent BTT procedures.[16] The study found that preimplant data such as serum creatinine, liver enzymes, and pulmonary gas exchange did not provide predictive indicators of irreversible organ damage. More than 85% of patients experienced functional recovery of preexisting respiratory, hepatic, and renal dysfunction after VAD insertion. Subsequent transplantation, however, was affected by the number of failing organs before mechanical support. Of 17 patients with isolated organ failure before assist, 14 (82%) were transplanted. In contrast, only 9 out of 12 (75%) with combined failure of two organs and only 6 out of 11 (54%) patients with three failing organ systems received transplants. In all patients who underwent successful transplantation, however, transplantation was associated with rapid organ recovery within 10 to 15 days after initiating mechanical assistance.

Although these observational data provide some guidelines for physicians in screening patients, the studies include relatively small numbers of patients, and the predictive accuracy of the scoring models approaches ROC values of 0.75. Larger prospective validation across multiple centers, which includes a comparison of the devices used, is necessary before such criteria can be accepted widely as a standard of care. At present, the selection process takes into account a very conservative approach, which may overlook patients who otherwise may benefit from support versus too liberal criteria that may include patients with very high risk of postoperative mortality.

Preimplant Renal Function

Relationships between preimplant renal function and patient outcomes after VAD insertion have been reported as observational studies. The majority of such studies emanate from registries of clinical trials in which subsequent nested analyses were performed. In one such study involving Novacor LVAD placement, 220 patients who underwent surgeries between 1996 and 2003 were examined.[17] Overall, 38% patients died on LVAD support. Preoperative creatinine clearance significantly influenced post-LVAD survival. Patients with clearance greater than 95 mL/min had a 30-, 180-, and 365-day survival of 90%, 78%, and 66%, respectively, compared with 74%, 41%, and 26% survival, respectively, in patients with preoperative clearance of less than 45 mL/min. The relationship between level of baseline renal function and survival after LVAD placement was directly proportional. The association between preoperative renal function and post-LVAD survival was independent of transplant status. A similar relationship existed when patients who received transplants were assessed separately for survival to transplant or 30 days posttransplant. In addition, the investigators examined the effect of change in renal function after LVAD support as a predictor of survival. Patients were stratified at a preoperative creatinine clearance level of 50 mL/min and followed postoperatively to study the changes in renal function. For those patients who started out at lower than 50 mL/min but increased to more than 50 mL/min post-LVAD the 30-day survival was 84% compared with 66% in those whose renal function did not improve post-LVAD placement. The difference in survival was not statistically significant.

In another observational study that specifically addressed the question of impact of preoperative renal dysfunction, 18 patients with pre-VAD creatinine levels of more than 3.0 mg/dL were observed for their postoperative outcomes.[18] Seven patients required post-LVAD hemodialysis for further worsening of renal function. Seven patients died before transplant, of which three were on hemodialysis at the time of death, whereas the remaining four patients had demonstrated improvement in renal function and died of other causes. Overall, 11 patients were bridged successfully to transplantation, which included 4 patients who had required postoperative dialysis. None of the 11 patients were on dialysis at the time of transplant, and the mean creatinine level had improved significantly as compared with the time of LVAD placement (1.6 mg/dL vs. 4.1 mg/dL, respectively).

Two more recent (representative) studies examined effect of pre-VAD level of renal function on survival.[19,20] In the first study, Yoshioka et al. analyzed 84 LVAD patients over a 5-year period and categorized patients based on INTERMACS levels. Preoperative serum creatinine was noted to be an independent predictor of 90-day mortality among INTERMACS level 1 group data. The actuarial survival rates were 96.2% at 30 days, 88.0% at 90 days, and 77.5% at 1 year in patients with Cr levels of 1.96 mg/dL or less and 60.0% at 30 days, 46.7% at 90 days, and 31.1% at 1 year in patients with Cr levels exceeding 1.96 mg/dL ($p = .0011$). In another study that examined 86 patients (1998–2007) undergoing CF-LVAD implants as BTT, Sandner et al. retrospectively analyzed the effect of estimated glomerular filtration rate (eGFR) on outcomes. Post-VAD survival at 1, 3, and 6 months was 91.3%, 79.9%, and 72.6%, respectively, in patients with MDRD eGFR exceeding 60 mL/min, whereas survival was 92.5%, 66.5%, and 47.9% in GFR less than 60 mL/min ($p = .038$). BTT rate was lower for patients with eGFR less than 60 than for those with greater than or equal to 60 (40% vs. 63% $p = .033$).

These studies represent three different ways of estimating renal function as well as different ways of treating categories of renal function; all of which indicate that there is a graded relationship between level of renal function before VAD and

clinical outcomes. One area of concern is that creatinine and estimates of eGFR may not be accurate in assessing functional/reversible components of renal dysfunction because of cardiorenal physiology. Butler et al. highlighted the tendency of patients with the maximum increase in eGFR to experience the biggest benefit. This may suggest that, independent of the level of eGFR, the reversibility of renal function may be equally important in determining long-term outcomes.

In summary, these studies could be interpreted to suggest that the level of preoperative renal function affects short-term and long-term survival (30 days to 1 year) after VAD placement. As expected, the key to long-term survival is the successful replacement of cardiac function by transplantation. Once bridged to transplantation, the pretransplant renal function does not seem to influence long-term survival after transplant. The analyses do not establish an independent relationship between preoperative renal dysfunction and postoperative survival. The data suggest, however, that VAD insertion leads to improvement in renal function. Thus level of renal function should not preclude patients from receiving mechanical support, especially if they are considered suitable for transplant candidacy. In addition, our ability to accurately predict reversibility of renal function after VAD insertion remains limited.

Postimplant Renal and Patient Outcomes

Patient outcomes and renal outcomes after VAD insertion must be assessed in the context of whether the indication for VAD use was for BTT or as a DT. Most of the data regarding renal outcomes are derived from clinical trials conducted with various devices in these two categories of patient population. Both of these groups can be distinctly different with respect to certain comorbidities that determine the eligibility for transplantation.

In patients with VAD used as a destination therapy, a randomized controlled trial, Randomized Evaluation of Mechanical Assistance for Treatment of Congestive Heart Failure (REMATCH), enrolled 129 patients that were not candidates for transplantation. Patients were randomized to either medical therapy or VAD insertion as a destination therapy.[21] Sixty-eight patients underwent VAD placement. The study found that there was a 48% risk reduction in death rate from any cause in the VAD group as compared with the medical management group over a 2-year period. One-year survival estimates were 52% in the device group versus 25% in the medical management group and at 2 years, the survival in device group was 23% as opposed to 8% in medically managed patients. Median survival was 408 days in device-placed patients, whereas it was 150 days in the other group. The study also reported quality of life, as assessed by physical function, emotional well-being, and Living with Heart Failure score, which were significantly better in the device group, at 1- and 2-year follow-up. Patients with device placement were at a greater risk of adverse events. Within 3 months after implantation the likelihood of infection of VAD was 28%, including fatal sepsis. The frequency of bleeding as an adverse event was 42% within 6 months of implantation. There was no device failure within 1 year of follow-up, but the probability of failure of device was 35% at 24 months.

Based on the survival advantage in this randomized controlled trial, it is estimated that for every 1000 patients with end-stage heart failure, 270 deaths could be prevented, as indicated by a 27% absolute risk reduction in mortality. Although these estimates are far superior to improved survival resulting from advances in drug treatment, the results must be considered in the context of the complexity and the costs of care involved in treating patients with VAD. Nevertheless, there is little doubt that, in suitable patients, the option of VAD can contribute to meaningful improvement in survival and quality of life in an otherwise fatal end-organ failure. A true comparison of improved survival weighed against costs and complexity of care is difficult because the technology of artificial cardiac support continues to evolve over time. In addition, ethical considerations as well as dynamics of the healthcare system and healthcare delivery must be accounted for before generalizing the "protocols" for use of these therapies. The randomized controlled trials of device placement tend to "select" patients who may be destined to have some short-term success, and the therapies naturally are not instituted with severely ill patients with a high predicted mortality. As is evident from the data, the baseline renal function of patients randomized to VAD insertion was approximately 1.7 mg/dL. Thus, based on existing observational evidence of perioperative renal function, these patients were in the "lower risk" category in terms of the influence of renal function on postoperative outcomes. None of the reported adverse events in the 2-year period included severe ARF.

The data regarding renal outcomes associated with VAD placement, when used as bridge to transplantation, indicate a slightly different observation. In a prospective multicenter trial conducted at 24 centers in the United States, 280 transplant candidates were treated with HeartMate (vented electric left ventricular system).[22] Post-VAD renal dysfunction was defined as a serum creatinine of more than 2.2 mg/dL or a blood urea nitrogen value of more than 50 mg/dL. Mean baseline serum creatinine in the 280 patients was 1.72 mg/dL. In this cohort, 158 patients (56%) experienced postoperative renal dysfunction. The renal function had improved significantly, however, at the time of transplantation or death, relative to baseline. Median waiting time from VAD placement to transplantation was 105 days. Of the 280 patients, 67% (n, 188) successfully bridged to transplantation, 4% elected to remove the device, and 29% (n, 82) died before transplantation. Four major risk factors associated with poor survival included level of baseline creatinine, age, prior cardiac surgery, and elevated total bilirubin level. Probability of survival to transplantation was approximately 60% at 1 year; in contrast, once the patients received a transplant, the 1-year survival was 84%.

Quiani et al. examined the VAD experience from European registry between 1986 and 1993, during which 258 patients underwent surgeries from VAD placement.[23] In 69% of patients the placement was intended as a BTT, whereas the remaining patients constituted various other indications, including cardiogenic shock, postcardiotomy, graft failure, or rejection. Of the total number of patients, 56% received pneumatic devices, 30% received total artificial heart (TAH), and 14% received nonpulsatile devices. Postoperative acute renal failure occurred in 25% of cases. When defined as a need for dialysis, the incidence of ARF was 13%. The overall mortality rate during support was 38%, whereas 62% received an organ transplant. Risk factors of mortality during support included renal failure, infection, and neurologic complications. One hundred and sixty patients were transplanted, of which 105 patients were discharged from the hospital (40% of the VAD recipients).

The study also analyzed predictors of mortality in all VAD recipients who were not able to be discharged from the hospital, including transplant recipients. Graft failure and renal failure were the two most important determinants of mortality in this subgroup. Another single-center experience

from the United States examined the experience with different devices on VAD outcomes.[24] In 243 patients Thoratec HeartMate was placed as a BTT between 1990 thru 2003. The study included 174 (72%) patients with single-lead vented electric devices (SLVED), 17 (7%) patients with dual-lead vented electric devices (DLVED), and the remaining 21% with pneumatic VAD. Overall, 70% of 243 patients received a transplant, and the rate of transplantation was the highest in SLVED (72%). The 1-, 3-, 5- and 10-year survival after transplant was not influenced by pretransplant placement of VAD. Overall actuarial survival posttransplant was 90% at 1 year and 40% at 10 years.

Although several studies report the incidence of postoperative renal dysfunction, detailed analyses of predictors of postoperative ARF remain unclear. In one study, 201 patients undergoing VAD placement between 1996 and 2004 were examined.[25] As many as 65 patients (32%) required postoperative continuous renal replacement therapy (CRRT). Advanced age, preoperative use of IABP, lower albumin, and higher LVAD score were associated with postoperative CRRT in an unadjusted analysis, but only LVAD score was the independent predictor of postoperative CRRT. Baseline creatinine levels at the time of VAD implant were similar in ARF and no-ARF groups. Although long-term postoperative survival was lower in those patients who require CRRT, the majority of deaths in CRRT group occurred during either during the hospitalization or with the first few months after surgery. When survival was examined based on transplant status, for those who received cardiac transplant, the long-term survival was not influenced by postoperative requirement of CRRT. These findings could be interpreted to suggest that postoperative ARF requiring CRRT is a marker of overall poor outcome of the patients during the postoperative period, as predicted by the LVAD score. It is not clear whether postoperative ARF adds discriminatory function to the existing LVAD score used to predict postoperative mortality. If the patients were bridged successfully to transplant, however, their long-term outcomes were not influenced by pretransplant need for CRRT. In contrast to the US data, data from the German group indicated much poorer outcomes associated with postoperative ARF. Kaltenmaier et al. examined 227 LVAD recipients (Berlin Heart System, Novacor or HeartMate 2000) between 1988 and 1995.[26] The VAD was used as a BTT in 72% of the patients. Fifty-five patients (24%) developed postoperative ARF requiring dialysis. Thirty-day survival was 61% in the non-ARF group as compared with 38% in the ARF group. At 6 months, the survival in non-ARF group was 40% as opposed to a meager 7% in ARF group. The authors conclude that post-LVAD ARF portends an extremely poor short-term or long-term outcome regardless of the indication of VAD placement, particularly including BTT patients.

Brisco et al. recently detailed comprehensive information on prevalence and prognostic importance of changes in renal function after mechanical cardiac support.[27] The primary goals of this analysis were to describe serial post-VAD changes in estimated eGFR and determine their association with all-cause mortality. The study included adult patients enrolled in the INTERMACS with serial creatinine levels available (n = 3363). Early post-VAD, eGFR improved substantially (median improvement, 48.9%; $p < .001$), with 22% of the population improving their eGFR by more than 100% within the first few weeks. However, in the majority of patients, this improvement was transient, and by 1 year, eGFR settled to be on average 6.7% above the pre-VAD value ($p < .001$). This pattern of early improvement followed by deterioration in eGFR was observed with pulsatile and CF devices. Interestingly, there was a J-shaped relationship between post-VAD renal function response and survival, with poor survival associated with marked improvement (adjusted hazard ratio [HR], 1.64; 95% confidence interval [CI], 1.19–2.26; $p = .002$) and worsening in eGFR (adjusted HR, 1.63; 95% CI, 1.15–2.13; $p = .004$).

The study highlights that at both extremes, improvement and worsening of eGFR post-VAD may represent either marked cardiorenal dysfunction before surgery or irreversible parenchymal kidney damage. Thus studies with use of tissue specific biomarkers could add value in risk-stratifying this patient population.

COMPLICATIONS

The complications associated with VAD are related to the device or the surgical procedure involved. The rate of device failure has continued to decline as the technology advances. In recent randomized studies, the reported rates of failure are less than 5% at 1 year but increase to above 30% at 24 months. Depending on the device surface, anticoagulation can be necessary to prevent thrombosis and embolic complications. Improvements in the biocompatibility of the materials used to construct these devices have reduced the risk of thromboembolic or inflammatory complications. Use of short-term or long-term anticoagulation is associated with perioperative bleeding, one of the most frequent complications associated with VAD insertion. For various reasons, there is an increase in the need for blood transfusions in these patients, including platelet transfusions resulting from consumptive coagulopathy. The need for frequent transfusions can sensitize these patients, further complicating their transplant recipient status. No clinical studies have examined this risk factor in an analytical way, however. Infection and sepsis after VAD are associated with poor patient outcome. Infection of the pocket or the parts of the device can be difficult to treat and may result in explantation. Sepsis leading to multiorgan system failure is the most frequently reported cause of death. Insertion of LVAD can lead to increased load on the right ventricle and to right ventricular failure. Central venous pressure monitoring, before and soon after LVAD insertion, may allow determination of early indications for Right Ventricular Assist Device (RVAD).

Ventricular-Assist Device and Dialysis

Although many VAD recipients experience improvement in renal function after implantation, some develop the need for chronic hemodialysis. Estimates of end-stage renal disease in VAD recipients are not accurate. However, recent studies suggest that as many as 6% of VAD recipients have stage IV chronic kidney disease (CKD) equivalent eGFR or require dialysis before VAD placement. Another estimate suggests that 3% of VAD recipients may require chronic dialysis.[28]

Despite a lack of definitive evidence, peritoneal dialysis (PD) may have several significant advantages for patients with a VAD. Most importantly, infections secondary to a peritoneal catheter seldom lead to bacteremia. Peritonitis is a significant infection, but the risk can be minimized with connectivity training and close patient monitoring. In addition, a PD catheter can be placed with conscious sedation and local anesthetic in the acute setting; it can

be used soon after placement; and it allows the patient to perform dialysis at home. This last point is critical, because patients with significant cardiac impairment or a VAD may not be candidates for outpatient management in a dialysis facility because of their tenuous hemodynamics. Moreover, patients with a VAD do not have a pulsatile blood pressure that can be recorded by standard devices, complicating the safety of monitoring a patient during outpatient dialysis.

There are other potential benefits to PD in VAD patients, including the ability to provide continuous and sustained daily ultrafiltration and preservation of residual renal function, along with a lower risk of bloodstream infection. Conversely, barriers to PD include requirement for a caregiver, social support, and some basic functional abilities in a patient.

Other challenges in VAD patients on dialysis include hemodynamic monitoring and anemia. Blood pressure (BP) monitoring in dialysis patients with VAD is difficult. The standard measures of obtaining BP using automated BP devices, auscultation of Korotkoff sounds, and palpation are usually not feasible unless there is a significant PP present from residual left ventricle function. In one study, the success rates for obtaining BP by these methods were 53%, 14%, and 3%, respectively.

As for risk factors and treatment of anemia in these patients, these patients are at a higher risk of bleeding. In one series it was reported that as many as 30% of VAD patients are at a higher risk of gastrointestinal bleeding. This could be related to need for anticoagulation, acquired von Willebrand disease, and development of arteriovenous malformations in the bowel. In addition, hemolytic anemia is also not uncommon in VAD patients and can complicate management in those receiving chronic dialysis.

Total Artificial Hearts

The use of TAH is still very limited, and currently there are two approved devices in the United States, for either BTT (CarioWest TAH) or as DT (AbioCor). The Jarvik-7 TAH was implanted first in 1982 and was used previously in United States and France as BTT support.[29] A slightly modified version, now available in the United States as CardioWest TAH, has been approved for use by the FDA as a BTT. Between 1993 and 2002, 62 consecutive recipients of TAH were studied[30]; 23% of the patients died before receiving cardiac transplant; 48 patients (77%) received a transplant, of which 42 patients survived to be discharged from the hospital. Average preimplantation creatinine was 1.7 (range 0.4–5.2). Postimplant renal dysfunction was defined as a more than 0.5 mg/dL increase in serum creatinine or new requirement for dialysis. Twelve patients developed postimplant ARF, of which five patients showed improvement in renal function. In the seven remaining patients, ARF was associated with death. Another device, AbioCor (ABIOMED) TAH has been placed as a DT in a small group of patients. The device recently was approved by the FDA for use. In the initial published experience, seven patients, with an expected 30-day mortality of more than 70%, received this device, of whom one died intraoperatively and four patients died between postoperative days 51 to 151.[31] Two patients were able to be discharged from the hospital.

Based on the numbers of patients, there are insufficient data to comment on the impact of renal function on patient outcomes; however, descriptive data suggest that acute renal dysfunction continues to represent a marker of poor outcomes. Whether it will be a modifiable risk factor still remains to be answered. In consideration of the very high mortality in an end-stage organ failure, these supportive therapies represent a significant advance in medical technology and techniques to prolong survival. As these therapies become more prevalent, an assessment of costs of care and benefits in terms of survival and/or quality of life will have to be addressed further.

In a field that continues to evolve and has seen rapid advances, it is difficult to examine past evidence and be confident about practice guidelines in future. Outcomes in VAD recipients represent a perfect example of such a scenario. Preoperative care of the patient has seen changes in terms of use of IABP support, early selection of patients for VAD insertion, difference in approaches to optimize fluid status, and use of broad-spectrum antibiotic prophylaxis. In addition to the development of newer generation of devices and techniques, certain intraoperative practices such as use of inotropes, vasodilators, or antibiotics also have changed over many years. Improvements in postoperative intensive unit care, timing of institution of CRRT, and aggressive use of RVAD to prevent pulmonary hypertension and right-heart failure are some of the postoperative practices that have changed over time. These factors are important when examining epidemiologic data related to outcomes in critically ill patients. There is evidence to suggest that trends in incidence of survival change over time independent of the characteristics of the patient population. However, it is extremely difficult to quantify these changes to examine them as study variables.

BOX 116.1

Complications of VAD

Complications of VAD:
- Bleeding
- Infection/sepsis
- Device failure
- Multiorgan system failure
- Right ventricular failure
- Thromboembolic events

Key Points

1. Level of preoperative renal function influences short-term and long-term outcomes after placement of ventricular-assist devices (VADs). At the present time, the level of preoperative renal function does not seem to be a contraindication for instituting mechanical cardiac support.
2. Postoperative improvement or decline in renal function is of prognostic importance after left ventricular-assist device insertion.
3. Once successfully bridged to transplantation, neither pre-VAD renal function nor post-VAD renal failure influences posttransplant outcomes. Thus, if the patient is deemed suitable for transplantation, the degree of renal insufficiency should not preclude patients from receiving VAD support.
4. With destination LVAD therapy, managing patients with VAD and chronic dialysis poses a significant challenge.

Key References

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