Editorial

Renal function after implantation of the total artificial heart

Keyur B. Shah

The Pauley Heart Center, Virginia Commonwealth University, Richmond, VA, USA

Correspondence to: Keyur B. Shah, MD. David E. Tolman Professor in Heart Failure, The Pauley Heart Center, Virginia Commonwealth University Health, 1200 E. Broad Street, Richmond, VA 23298-0036, USA. Email: keyur.shah@vcuhealth.org.

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The total artificial heart (TAH) remains a viable and effective option for the treatment for end-stage heart failure as a bridge to heart transplantation. The device is often reserved for the most critically ill patients failing medical therapy, who may not be candidates for immediate transplantation or a left ventricular assist device (LVAD). Expectedly, complications related to bleeding, thrombosis, neurological injury and infection are frequent (1).

An enigma concerning TAH complications, however, is the very high rate of dialysis-dependent renal failure after device implantation, with reported incidence ranging from 19–62% in various reports (2,3). Even when selecting for patients who are not hemodialysis-dependent prior to device implantation, Arabía *et al.* reported from the INTERMACS registry that 29% of patients required *de-novo* hemodialysis (1). At our center, renal failure after TAH implantation is associated with a six-fold increase of death on device (4).

The high incidence of renal dysfunction may be attributable to the extraordinary acuity of illness prior to TAH implantation. Patients are often in cardiogenic shock refractory to intravenous therapies, suffering from acute end-organ dysfunction and requiring devices such as intra-aortic balloon pumps, temporary ventricular assist devices or extracorporeal membrane oxygenation. These portentous clinical characteristics are associated with hypotension and hypoperfusion, anemia, inflammation, oxidative stress, increased venous congestion, and device-related hemolysis, which may predispose one to intra- and post-operative renal injury. However, a clear clinical characterization of the TAH population at risk of renal failure, is lacking.

Irrespective of the acuity of illness, removal of both ventricles results in the abrupt withdrawal of B-type natriuretic peptide (BNP), which may also contribute to additional renal dysfunction. BNP is a cardiac hormone primarily secreted from ventricular cardiomyocytes in response to cardiac stretch and volume overload. Circulating BNP has several renal modulating effects, including cyclic guanosine monophosphate-mediated arterial vasodilation and suppressive effects on angiotensin II, aldosterone and renin secretion (5). In healthy patients, infusion of nesiritide (synthetic BNP) has been shown to increase renal blood flow and promote diuresis and natriuresis via direct tubular effects (6).

Several small, non-comparative studies have suggested a renal protective effect of exogenous BNP infusion after implantation of a TAH. Delgado first reported on three patients implanted with the AbioCor TAH (AbioMed, Danvers, MA, USA), who exhibited fluctuations in renal function related to dosing of nesiritide (7). In this case series, initiation of BNP infusion at various points after device implantation, even days after surgery, resulted in increased urine output and improved estimated glomerular filtration rate (eGFR) in patients exhibiting diuretic-refractory renal failure. In a 5-patient prospective study, we showed that all patients, after TAH implantation, developed renal dysfunction (≥50% decrease in the eGFR or urine output ≤30 mL/h), and infusion of nesiritide increased urine output 3–4 fold without worsening of renal function (8). Spiliopoulos *et al.* demonstrated in consecutive TAH patients that early routine nesiritide infusion initiated in the operating room, and continued for 3–7 days duration, was effective for avoiding post-operative hemodialysis-dependent renal failure in 9 out of 10 patients (9).

On closer examination of the TAH experience at our institution, even with routine infusion of nesiritide after device implantation, the rate of renal failure remained high. Nearly two-thirds of patients required hemodialysis after TAH implantation and one-half of

those experienced delayed recovery. Predictors of post-operative renal failure included pre-operative support with extracorporeal membrane oxygenation, ischemic etiology of heart failure, and low pre-operative eGFR (especially ≤30 mL/min/1.73m^2) (4). In other words, supplementation with exogenous BNP alone does not seem sufficiently protective in the setting of overwhelming risk factors related to poor renal reserve, systemic ischemic disease or profound shock.

An adequately powered, comparative study of BNP supplementation for patients after TAH implantation has unfortunately never been conducted. Nesiritide, which was initially indicated for the management of acute decompensated heart failure, was heavily criticized in the cardiovascular medical community and eventually, production of the drug was discontinued. Anecdotally, off-label use of low dose angiotensin receptor-neprilysin inhibitors (sacubitril/valsartan) in ambulatory TAH patient has been effective in controlling blood pressure and improving renal function. Neprilysin is an endopeptidase that is responsible for degrading natriuretic peptides, and its inhibition increases circulating BNP concentrations. Currently, there are no clinically available forms of synthetic BNP, however, opportunities exist to further explore the value of endopeptidase inhibition to increase concentration of endogenous circulating BNP.

Preventing renal failure in patients with the TAH will first require a better understanding of who is at risk. Multicenter registries or retrospective analyses that are focused on complications may influence clinical care and guide future study. Moreover, research deepening our understanding of ventriculectomy-related interruption of neuronal and hormonal pathways may help develop mitigating strategies and will be crucial to the successful development and use of any mechanical circulatory support platform that replaces the heart.

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Footnote

Conflicts of Interest: The author is on the Medical Advisory Board for SynCardia Systems.

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