RENAL REPLACEMENT THERAPIES AFTER ABDOMINAL AORTIC ANEURYSM REPAIR – A REVIEW

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SUMMARY – The objective of this review is to assess the incidence of postoperative acute renal failure that necessitates the application of hemofiltration and to determine the factors that influence the outcome in patients undergoing surgical repair of abdominal aortic aneurysm. In addition, the review aims to assess the outcomes of postoperative early hemofiltration as compared to late intensive hemofiltration. Different forms of renal replacement therapies for use in abdominal aortic aneurysm surgery patients are discussed. Electronic literature searches were performed using Pubmed, Medline, Embase, Sumsearch, Cinahil, The Cochrane Central Register of Controlled Trials and Excerpta Medica. The search identified 419 potentially eligible studies, of which 119 were excluded based on the title and abstract. Of the remaining 300 studies, full articles were collected and re-evaluated. Forty-five articles satisfied our inclusion criteria, of which only 12 were of the IA Level of evidence. The search results indicated that the underlying disease, its severity and stage, the etiology of acute renal failure, clinical and hemodynamic status of the patient, the resources available, and different costs of therapy might all influence the choice of the renal replacement therapy strategy. However, clear guidelines on renal replacement therapy duration are still lacking. Moreover, it is not known whether in acute renal failure patients undergoing abdominal aortic aneurysm surgery, renal replacement therapy modalities can eliminate significant amounts of clinically relevant inflammatory mediators. This review gives current information available in the literature on the possible mechanisms underlying acute renal failure and recent developments in continuous renal replacement treatment modalities.

Key words: *Renal replacement therapy; Acute renal failure; Oxidative stress; Abdominal aortic aneurysm*

Introduction

The objective of this review is three-fold: 1) to assess the incidence of postoperative acute renal failure (ARF) that necessitates the application of hemofiltration; 2) to determine the factors that influence the outcome in patients undergoing surgical repair of abdominal aortic aneurysm (AAA); and 3) to assess the outcomes of postoperative early hemofiltration as compared to late intensive hemofiltration. ARF occurs in approximately 2% of patients with normal preoperative renal function who undergo endovascular abdominal aortic aneurysm repair (EVAR), up to 10% after open surgical repair (OSR)[1]. For patients with preoperative renal impairment, the perioperative mortality rate is high, 27% following EVAR, to up to 66% after OSR[2]. To explore the differential application and outcomes of EVAR and open surgical AAA repair, we used data from the Nationwide Inpatient Sample (NIS), the largest all-payer inpatient care database in the United States, as well as electronic literature searches using Pubmed, Medline, Embase, Sumsearch, Cinahil, The Cochrane Central Register of Controlled Trials and

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Received July 14, 2010, accepted October 3, 2011

Excerpta Medica. Renal injury during cardiac surgery appears to be mechanistically related to the pre-existing renal dysfunction, diabetes mellitus, ventricular dysfunction, older age, hypertension, microembolic and macroembolic processes, inflammatory mediators, sensitivity to sympathetic stimulation, and perturbation in renovascular resistance and flow[3-5]. Although ARF incidence is relatively low, it is of major concern because, when it occurs, it is associated with high morbidity and mortality. Based on the outcome data on EVAR, renal implications of the procedure need to be scrutinized. Although patients receiving EVAR are spared from ischemic insult of the aortic cross-clamping and have less perioperative hemorrhage, the potential nephrotoxicity of intravenous contrast must be considered[6]. The establishment of continuous renal replacement therapy (CRRT) has been proposed as a means of reducing the in-hospital mortality in patients who develop postoperative ARF. In this review, we focus primarily on the literature dealing with renal complications occurring in the perioperative phase of abdominal aortic surgery. There is currently a unanimous agreement that renal complications have a severe impact upon the patient's management and outcome. Specifically, it has an impact on the method of renal replacement therapy (RRT), i.e. dialysis (based on the diffusion principle) or hemofiltration (based on convention), the dose of renal replacement therapy (urea KT/V for dialysis *vs* hemofiltration flow (mL/kg/h), and timing of RRT (early *vs* late). Here we discuss the mechanisms leading to the induction of ARF postoperatively and focus on the different modalities of CRRT available.

Methods

Database

Electronic database search was made through biomedicine databases, from 1977 to 2008, such as Pubmed, Medline, Embase, Sumsearch, Cinahil, The Cochrane Central Register of Controlled Trials and Excerpta Medica. To determine the clinical value of a study (Level of evidence) we utilized a method currently suggested in evidence-based medicine (Table 1).

We performed search with mash technique using the following key words: renal replacement therapy, acute renal failure, abdominal aortic aneurysm, oxidative stress, inflammation. The dataset provides detailed information on patient demographics, outcomes (e.g., in-hospital mortality, length of stay), total

Table 1. Method utilized in evidenced based medicine to determine the clinical value of a study (Level of evidence)

Level of evidence	Description (type of study)
IA	Systematic Review (or Meta-analysis) (with homogeneity) of Randomized Controlled Trials (RCT)
IB	Individual RCT (with narrow Confidence Interval)
IIA	Evidence from at least one controlled study without randomization. Systematic Review (with homogeneity) of cohort studies
IIB	Evidence from at least one other type of quasi-experimental study. Individual cohort study (including low quality RCT; e.g., <80% follow-up)
III	Evidence from non-experimental descriptive studies such as comparative studies, correlation studies, and case-control studies. Systematic reviews (SR) (with homogeneity) of case-control studies. Individual Case-Control Study
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both. Case-series (and poor quality cohort and case-control studies). Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

charges, hospital characteristics, and insurance status. In addition, hospital and discharge weights are provided to extrapolate estimates to a national level and ensure that standard errors that are used for the analyses reflect the sampling scheme of the dataset. In the review, we included questions designed to address the extent to which the information on baseline characteristics and study design suggested treatment modalities were comparable using the Level of evidence method. A score ranging from 1-5 was generated where „1" indicated that the groups were „definitely different", „3" indicated „uncertainty", and „5" indicated that the groups were „definitely equal".

Patient population

In brief, we identified all discharges of patients >18 years of age with a primary diagnosis of an unruptured AAA (open repair, n=3936; endovascular repair, n=2678). Hospitalizations in which an aortorenal bypass was performed in addition to the AAA repair (n=42) were excluded to evaluate the specific impact of the aortic procedure on kidney function. Patients receiving maintenance dialysis (n=56) were excluded from the analysis by identifying codes associated with end-stage renal disease and removing all discharges in which there was a dialysis code but no concurrent diagnosis of ARF.

Exposure, outcome, and covariates

Procedure type

The type of the procedure, i.e. EVAR *vs* open AAA repair, was the key exposure of interest. The primary outcome was postprocedure ARF. ARF requiring hemodialysis was also considered. We evaluated patient demographic and clinical characteristics that might contribute to the risk of ARF. These included patient age, gender, and key comorbidities including chronic kidney disease, diabetes mellitus, chronic lung disease, congestive heart failure, and chronic liver disease[7-15].

We also adjusted for hospital type (rural, urban-teaching, urban-nonteaching) and procedure volume, the latter dichotomized as above and below the median number of AAA procedures performed in a given hospital.

Results

Database

The search identified 419 potentially eligible studies of which 119 were excluded based on title and abstract. Of the remaining 300 studies, full articles were collected and re-evaluated. Forty-five articles satisfied our inclusion criteria, of which only 12 were of the IA Level of evidence. The search results pointed out that the underlying disease, its severity and stage, the etiology of ARF, clinical and hemodynamic status of the patient, the resources available, and different costs of therapy may all influence the choice of the renal replacement therapy strategy. Exactly 6516 patients were included in the analysis of published reports. We were able to assess baseline severity of illness only in 12 studies (number of patients 1400; Level of evidence IA). The results and the overall quality and severity scores of the blinded review are presented in Table 2.

Patient population

With respect to non-acute kidney injury(non-AKI), there appeared to be a stepwise increase in the relative risk (RR) of death going from the risk (RR=2.40) through injury (RR=4.15) to failure (6.37, $P<0.0001$ all); however, the element of patient population heterogeneity was noted on interpreting the results. Among 6516 patients that met the inclusion criteria, 3865 (59.3%) were for open AAA repair and 2651 (40.7%) were for EVAR. Patients receiving EVAR were older, more likely to be male and to be diagnosed with diabetes mellitus, but were less likely to have pre-existing congestive heart failure or chronic lung disease. Both procedures were done across 412 hospitals. Both procedure types were performed at 222 of the hospitals encompassing 5573 of the admissions; 177 sites performed open AAA repair only (915 admissions), and 13 sites (28 admissions) performed only EVAR. The median number of procedures *per* hospital was eight.

Exposure, outcome, and covariates

ARF was diagnosed in 439 (6.7%) patients. Endovascular aortic repair was inversely associated with the development of ARF. Older age and female gender

Table 2. Summary of most important individual studies (Level of evidence IA – continuous renal replacement therapy (CRRT) after abdominal aortic aneurysm (AAA) repair)

Study	References	Year	Number of patients	Mortality (CRRT)	Quality score
Mauitz	29	1986	58	75%	3.11
Bartlett	10	1986	56	71.9%	2.63
Simpson	12	1987	32	50.0%	2.47
McDonald	9	1991	42	77.3%	2.40
Kierdorf	27	1991	146	78.1%	2.73
Bosworth	8	1991	320	82.1%	1.92
Bastien	25	1991	66	50.0%	2.20
Bellomo	11	1993	167	59.0%	2.98
Krucynski	28	1993	35	33.3%	2.81
Simpson	30	1993	123	70.8%	2.29
van Bommel	31	1995	94	56.7%	2.85
Mehta	32	1996	166	65.5%	3.24
Overall			1400	68.0%	2.62

were significantly associated with ARF, as were the presence of chronic kidney disease, congestive heart failure, and chronic lung disease. When adjusted for covariates, the association between EVAR and the risk of ARF remained significant. There were 173 (2.7%) postoperative deaths. Mortality was higher among patients who underwent open repair compared with EVAR (3.9% *vs* 1%). In-hospital mortality was markedly higher among patients who developed ARF compared with those who did not (18.9% *vs* 1.6%, $P<0.0001$). After adjustment for procedure type, demographic factors, comorbidity, and hospital related factors, ARF remained independently associated with mortality (OR, 11.3; 95% CI, 7.6 to 16.8). The association of ARF with mortality did not differ according to the type of procedure ($P=0.42$ for interaction term).

Discussion

The findings reported here may help clarify conflicting results from other observational studies and clinical trials. The Dutch Randomized Endovascular Aneurysm Management (DREAM) trial showed that postoperative changes in serum creatinine levels were similar in patients undergoing EVAR and open AAA repair. However, enrolment in this randomized trial was limited to centers that performed at least 30 open AAA repairs and 50 EVAR procedures annually. In addition, the patient population in the DREAM study was younger, included fewer women, and had a lower frequency of some comorbidities, including diabetes and chronic lung disease, compared with the cohort we have described.

Whether early initiation of RRT is associated with improved survival is unknown, and clear guidelines on RRT durations are still lacking. In particular, it remains unclear whether hemodynamically unstable patients who develop septic shock pre- and postoperatively can benefit from early RRT initiation. In addition, it is not known whether in AKI patients undergoing cardiac surgery, RRT modalities can eliminate significant amounts of clinically relevant inflammatory mediators. This review gives an update of information available in the literature on the possible mechanisms underlying AKI and recent developments in continuous RRT modalities.

Prevalence and incidences

Patients who develop ARF following AAA surgery have higher rates of mortality and their management requires significantly greater resource utilization, par-

ticularly for those patients on chronic dialysis[6]. Historically, the incidence of ARF is reported to be 5%, however, up to 2% of the patients who develop ARF would require CRRT[7], a mode of treatment that was introduced in the 1980s[8]. The development of mild to moderate ARF is also associated with a mortality rate of 10%-20%[9]. Considering the need for aortic surgery worldwide, it is of great surprise that to date little attention has been paid to the management of patients who develop ARF. ARF is the standard term for an abrupt and sustained decrease in renal function resulting in retention of nitrogenous (urea and creatinine) and non-nitrogenous waste products. Depending on the severity and duration of renal dysfunction, this accumulation is accompanied by metabolic disturbances such as metabolic acidosis and hyperkalemia, changes in body fluid balance, and effects on many other organ systems. In 2004, the Acute Dialysis Quality Initiative workgroup proposed a multilevel classification system for ARF identified by the acronym RIFLE (risk, injury, failure, loss of kidney function, and end-stage kidney disease)[10]. In the intensive medicine arena, several studies have used this consensual definition for assessing whether outcomes progressively worsened with the severity of AKI[11]. Ricci *et al.* recently conducted a literature search from August 2004 to June 2007 on 24 studies in which the RIFLE classification was used to define AKI[22]. The authors concluded that the RIFLE classification is a simple, readily available clinical tool to classify AKI in different populations and suggested that even mild degrees of kidney dysfunction may have a negative impact on outcome[12]. Furthermore, many of the patients undergoing urgent AAA surgery have been undergoing angiography prior to surgery and are exposed to the additional risk of contrast nephropathy. Contrast nephropathy has been associated with a high cardiovascular mortality of nearly 40% without the need for dialysis, and 45% when the patient has been on hemodialysis[12].

Risk factors for post-aortic surgery acute renal failure

The causes of renal hypoperfusion and subsequent ARF are variable and include pre-existing chronic renal insufficiency, older age, previous cardiovascular surgery, tissue edema, microembolism, endothelial dysfunction, length of aortic cross-clamp time, perioperative hypotension, duration of surgery, increased generation of reactive oxygen species, pre-existing reduction in renal blood flow, pre-existing anemia, coexisting morbidities such as hypovolemia, congestive heart failure, requirement of vasopressure support, and exposure to nephrotoxic agents/drugs (aminoglycosides, vancomycin, contrast dye) in the immediate preoperative period[13-18]. Although numerous variables were identified as predictors of AKI, information is still lacking regarding the specific risk factors associated with the level of preoperative renal function[19,20].

The possible mechanisms of post-aortic surgery acute renal failure

The development of AKI as the result of renal ischemia depends on the degree and duration of the ischemic event and functionality of the countervailing mechanism. Prolonged renal arteriolar vasoconstriction is perpetuated by hypovolemia, dehydration, increased levels of vasoconstrictors (adenosine, angiotensin, aldosterone, endothelin, catecholamines, and thromboxanes) as well as a decrease in atrial natriuretic peptide (ANP) and nitric oxide-dependent renal vasorelaxation[13,14,20]. For example, endothelial dysfunction of diabetic renal vasculature is characterized by an impaired nitric oxide-dependent and prostaglandin-dependent vasorelaxation[14,15]. Hence, adenosine-induced vasoconstriction of the afferent arterioles, which occurs as the result of mitochondrial ATP hydrolysis during renal ischemia, is markedly exacerbated in diabetic renal vasculature and causes a much more profound ischemia-induced reduction of renal blood flow when compared with non-diabetic conditions. This apparent increase in the risk of developing AKI in the diabetic milieu is linked to a higher sensitivity of the renal vasculature to adenosine-induced renal vasoconstriction *via* adenosine A1 receptors, as the result of a diminished renal prostaglandin- and nitric oxide-dependent vasodilatory capacity[16-18,20].

Continuous renal replacement (CRRT) therapy for postoperative acute renal failure

CRRT is subdivided into venovenous and arteriovenous categories; it offers continuous and steady fluid removal and uremic toxin clearance. Previously published studies have revealed that hemofiltration improves heart and lung functions in patients with ARF and cardiac shock after cardiovascular surgery[21,22].

This can reduce the need of inotropic support, which contributes to patient survival[22,23]. This method provides better control of fluid status, improves uremia, and also ultrafiltrates toxic proteins such as myocardial depressant factors. CRRT also helps in improving the ventricular function by restoring the myocardial water content (MWC) within the normal limits[23].

Continuous venovenous hemofiltration

Continuous hemofiltration with the aid of a blood pump provides solute removal by convection. It offers high volume ultrafiltration using replacement fluid, which can be administered pre-filter or post-filter. The pump guarantees adequate blood flow to maintain required ultrafiltration rates. Venous blood access is usually femoral, jugular or subclavian using a double lumen cannula. This mode is used for removal of fluid and middle-sized molecules (Fig. 1).

Continuous venovenous hemodialysis (CVVH)

These are new modifications of continuous replacement therapy, most useful in patients who are hemodynamically compromised. This technique uses an infusion pump, hemodialysis membrane and dialysate solution as well as the same blood access circuitry as the CVVH technique. The use of a pump-driven venovenous circuit in this technique permits blood flows that are both higher and more constant than those provided by an arteriovenous circuit. In addition, the elimination of the need for a large bore arterial catheter eliminates the associated risks of arterial thrombosis and arterial bleeding (Fig. 2).

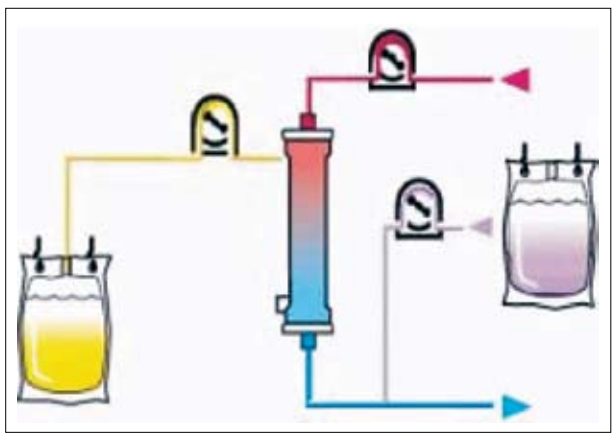

Fig. 1. Continuous venovenous hemofiltration. Continuous hemofiltration with the aid of a blood pump provides solute removal by convection. It offers high volume ultrafiltration using replacement fluid, which can be administered pre-filter or post-filter. The pump guarantees adequate blood flow to maintain required ultrafiltration rates. Venous blood access is usually femoral, jugular or subclavian using a double lumen cannula.

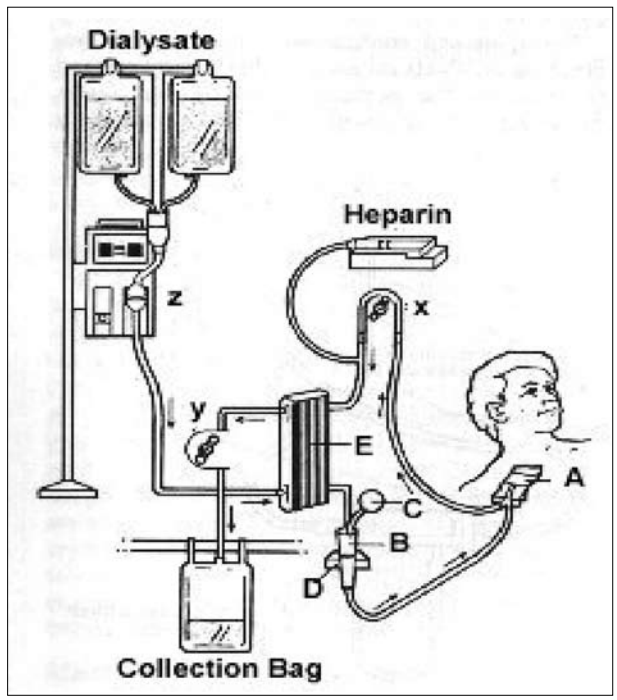

Fig. 2. Continuous venovenous hemodialysis. This technique uses an infusion pump, hemodialysis membrane and dialysate solution. As with the continuous arteriovenous hemodialysis system, adding the dialysis membrane and the dialysate solution increases the efficiency of the procedure. The process of continuous diffusion dialysis in continuous venovenous hemodialysis is less effective than continuous arteriovenous hemodialysis because the lower pressure venous system does not filter as much blood per unit of time. The use of a pump-driven venovenous circuit in continuous venovenous hemodialysis permits blood flows that are both higher and more constant than provided by an arteriovenous circuit. In addition, the elimination of the need for a large bore arterial catheter eliminates the associated risks of arterial thrombosis and arterial bleeding. A = double-lumen subclavian vein access; B = venous air trap; C = venous pressure monitor; D = air detector; E = dialyzer; x,y,z = blood and dialysate pumps.

Continuous venovenous hemodialfiltration

This approach utilizes a blood pump and venous access site for removal of solutes by diffusion and convection simultaneously. It offers high volume ultrafiltration using replacement fluid, which can be administered pre-filter or post-filter. Simultaneously, dialysate is pumped in counter flow to blood. This mode is used where large amounts of fluid are removed and replaced *per* hour, as a means of 'cleaning' the plasma, for example to remove inflammatory cytokines (Fig. 3).

Continuous arteriovenous hemodialysis (CAVHD)

This is a continuous diffusion process of removing uremic toxins from blood into a sterile dialysate fluid. Blood flows spontaneously through an AV shunt or femoral cannulation of an artery and vein. Blood and dialysis fluid flows are counter-current to maximize diffusion. This technique was developed to augment the solute clearances obtainable with continuous arteriovenous hemofiltration. This modality is similar to continuous venovenous hemodialysis, with one exception: the addition of the continuous perfusion of dialysate through the hemofilter counter-current to the direction of blood flow, most commonly at a rate of 1–2 L/h. As a result, technical requirements for satisfactory performance of CAVHD are similar to those of continuous venovenous hemodialysis (Fig. 4).

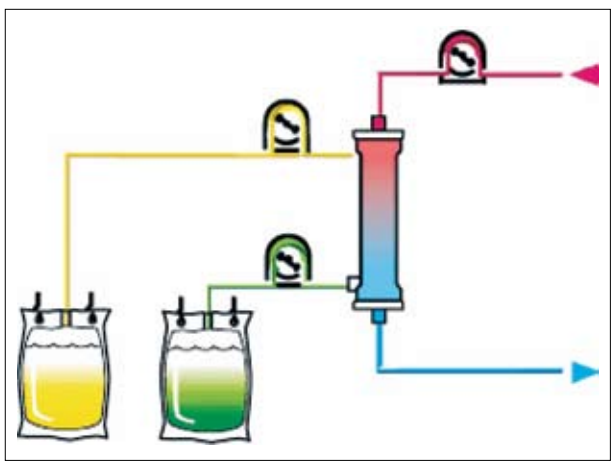

Fig. 3. Continuous venovenous hemodialfiltration. Continuous hemodialfiltration with the aid of a blood pump provides solute removal by diffusion and convection simultaneously. It offers high volume ultrafiltration using replacement fluid, which can be administered pre-filter or post-filter. Simultaneously, dialysate is pumped in counter flow to blood.

Benefits of continuous renal replacement therapy in maintaining post-surgery hemodynamic stability

While scientific criteria for the initiation of renal replacement therapy in ARF patients have not yet been defined, most renal physicians believe it is reasonable to prefer modalities that prevent physiological derangements as opposed to that of post-hoc correction. Although recommended for ARF, peritoneal dialysis (PD) is not suitable for adult critically ill patients because of the high rates of associated peritoneal infections and poor to inadequate solute clearance leading to less than optimal uremic controls[21]. PD also impedes diaphragmatic movements and is associated with pulmonary and cardiac dysfunction. Overall, intermittent hemodialysis is associated with hemodynamic instability and therefore hemofiltration is considered a safer modality for treatment of ARF patients[22,23]. Compared with other forms of uremic therapies, volume control is continuous and adaptable to the changing circumstances during CRRT. CRRT avoids swings in the intravascular volumes, maintains

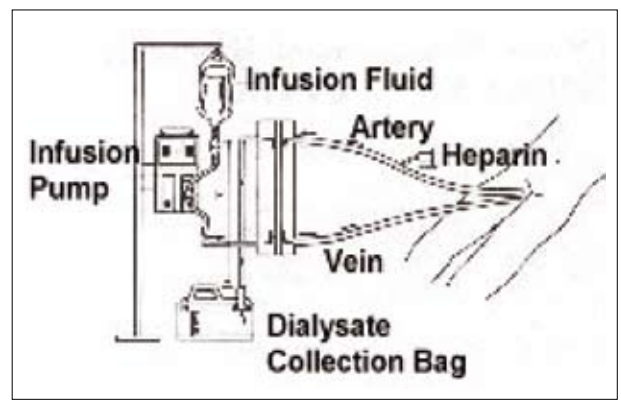

Fig. 4. Continuous arteriovenous hemodialysis. This technique uses an infusion pump, hemodialysis membrane and dialysate solution as well as the same blood access circuitry. An infusion pump pushes a continuous trickle of sterile dialysis fluid into the dialysate compartment of the hemodialyser membrane. The blood/dialysate interface is the hemodialysis membrane. This method uses the process of continuous diffusion dialysis to rid the body of fluid, electrolytes, and nitrogenous wastes. The preferred arterial access site is the common femoral artery.

blood pressure and prevents treatment-associated renal injury. Thus, CRRT achieves a much superior uremic control when compared with other forms of treatment for renal impairment[24]. CRRT also allows a greater metabolic control to be achieved and thus provides a platform for an aggressive, protein rich nutritional policy to improve daily nitrogen balance, thus having possible favorable effects on the immune function and overall outcome[22-24].

Elimination of inflammatory cytokines and anaphylatoxins by continuous renal replacement therapy

CRRT has added pumps to increase the filtration rates and sometimes combines primarily convective compound transport (by hemofiltration) with diffusive transport (with an additional dialysis cycle) across a hydrophobic membrane. Hydrophobic membranes have an asymmetric structure, allowing solutes of a wide range of molecular weights (cut-off 30 kDa) to be eliminated by convection. TNF-alpha (MW 52 kDa), a key mediator of sepsis, is unlikely to pass the commonly used filters owing to the size. Clinical studies have given conflicting evidence of its removal, with some studies suggesting no changes in the plasma TNF-alpha level and others showing substantial to minimal clearance[25-28]. Some studies have shown an increase in the plasma levels due to the passage through the hemofilter[29]. The plasma levels of TNF-alpha change during the course of illness and therefore depend on the time of CRRT initiation as well as on the amount eliminated by hemofiltration. Similarly, contradictory results exist for interleukin-6 (IL-6), MW 26 kDa, with some studies showing its presence in dialysis effluents[30], while others showing no IL-6[31]. Recent prospective studies have shown that CRRT does not have a significant impact on serum IL-6 levels despite significant transfer of IL-6 from blood into dialysate[32]. Other studies demonstrated that CRRT with high-volume hemofiltration (8 L/h) improved the cardiac index, which was related to improved survival[32].

Timing of continuous renal replacement therapy on operative outcomes

Although there is continuing debate on the underlying mechanisms by which CRRT improves survival, there is also no international consensus on important issues such as the indication for and timing of initiation of CRRT due to the absence of relevant guidelines and an international consensus on the definition of ARF[33]. Until recently, it was not known whether small subtle changes in renal function could have an impact on operative outcomes. To address this, Mangos *et al.* studied the association between small serum creatinine changes after surgery and mortality, independently of other established perioperative risk indicators[10]. The authors suggested that even a mild change in the renal function may have an effect on the operative outcomes and then concluded that elevated creatinine may be an independent indicator for the risk of death. In another study, Schiffl *et al.* report on the effect of daily intermittent hemodialysis as compared with conventional (alternate-day) intermittent hemodialysis, on survival among patients with acute renal failure[34]. It was found that less frequent hemodialysis (on alternate days as opposed to daily) was an independent risk factor for death. In contrast, Sander *et al.* studied the effects of the initiation time of continuous venovenous hemofiltration and of the ultrafiltrate rate in patients with circulatory and respiratory insufficiency developing early oliguric ARF[35]. The authors concluded that survival and recovery of renal function were not improved by using high ultrafiltrate volumes or early therapy initiation. Other recent studies, however, have shown that the introduction of CRRT early in the course of treatment may improve survival[15,17]. Not many studies have looked at the outcome of postoperative renal dysfunction with or without the need of CRRT and the long-term outcome. A recent study by Sanchez Izquierdo *et al.* investigated in-hospital and long-term prognosis of patients with postoperative renal deterioration[36]. None of the survivors in their study developed end-stage renal disease, however, details on the timing of CRRT initiation and levels of long-term renal function were not provided, making it difficult to ascertain whether the episodes of ARF were associated with a progressive decline in renal function and also whether early initiation of CRRT had any beneficial effects on patient survival.

Effect of duration and intensity of continuous renal replacement therapy

Some recently published randomized studies have failed to demonstrate outcome improvement with more

intense RRT[37,38]. Bellomo *et al.* studied critically ill patients with acute kidney injury requiring intensive renal support in terms of mortality, improvement in recovery of kidney function, or reduction in the rate of non-renal organ failure as compared with less-intensive therapy involving a defined dose of intermittent hemodialysis three times *per* week and continuous RRT at 20 mL/kg/h[37]. The results appear to suggest the possibility that the duration of applying intense *versus* less-intense RRT did not affect the outcomes. Tonnesen *et al.* studied the effect of the CVVHDF dosage on survival in ARF patients[39]. The observations in these studies raise concerns as to the issues surrounding the definition of ARF, whether inappropriate patient selection criteria were used, whether results from different treatment modalities are comparable in different patient groups, and whether the studies were adequately powered.

Limitations of the study

As electronic databases are administrative data sources, we could not adjust for confounding by aneurysm location or structure[40]. Information bias is an important limitation of this study. The ascertainment of ARF is particularly susceptible to misclassification. Central to this problem is the absence of a universally accepted definition of ARF. The lack of clear criteria for the assignment of an ARF diagnosis (and a subsequent diagnostic code for ARF) leads to a situation where coding practices, rather than clinical reality, may guide the inclusion of ARF in a discharge summary. This source of information bias is likely to be nondifferential because there is no reason to expect that the accuracy of ARF coding should differ between the procedure types. Nondifferential misclassification would bias the association toward the null. It is also reassuring that the rate of ARF in patients undergoing open AAA repair was similar to that reported in previous series[1-3]. Finally, since the administration of hemodialysis for ARF is unlikely to be coded inaccurately, it is notable that the protective effect of EVAR on the outcome of ARF requiring hemodialysis paralleled the impact of procedure type on the development of ARF overall.

A further source of differential information bias is rooted in the differing lengths of stay in the two groups. Given a markedly shorter length of stay in the EVAR group, it is conceivable that clinical evidence of AKI developed after discharge in some EVAR patients, which would not be captured in this database. As contrast nephropathy usually becomes apparent within 24 to 48 hours of the procedure[42,43], under-ascertainment of ARF among EVAR recipients whose length of stay was ≤2 days may have occurred. Unfortunately, the NIS does not permit the assessment of post-discharge data and because each discharge – rather than the actual patient – it is assigned a specific identifier, information on readmissions for ARF would be unobtainable. However, we estimated that among EVAR patients discharged within 2 days, ARF incidence would have to surpass 5% for EVAR to lose its relative protective effect. Because this figure exceeds reported rates for post-EVAR ARF, it is unlikely that this form of misclassification would be substantial enough for the inverse association between EVAR and ARF to be lost.

Further studies

It is disappointing that CRRT has been a therapeutic option in critical care practice for over 20 years without definitive evaluation of its benefits. While recent clinical trials have shown reduced all-cause mortality with changes in other forms of supportive care such as mechanical ventilation[43], it is possible that changing dialysis modality will also reduce mortality. Our analysis suggests that a definitive CRRT to AAA surgery trial would require roughly more than 1000 patients for beneficial results. Such a trial should control for factors such as membrane and co-interventions and, based on recent evidence[43-47], should consider treatment dose, perhaps in factorial design with treatment modality. Efforts should be made to limit crossovers between treatment modalities. Finally, it would seem to be important to stratify randomization on the presence or absence of hemodynamic instability because this is the major determining variable for who receives CRRT in practice. Nevertheless, we suggest that such a trial is necessary and, in the meanwhile, CRRT should be made available to at least some patients with ARF. To develop a predictive score for ARF following abdominal aortic surgery, we need to improve individualized patient care focuses on the identification of early predictive biomarkers such as urine neutrophils, gelatinase-associated lipocalin, urinary IL-8, and liver

fatty acid-binding protein[38,39,48,49]. Future studies could be designed to identify high-risk individuals based on standardized score. This could lead to initiation of timely interventions that might prevent or ameliorate renal injury and improve operative outcomes. A key element is dissemination of information across the continuum of care. This calls for multidisciplinary collaboration among cardiovascular surgeons, nephrologists, and allied personnel involved in patient care who may not be aware of study findings published in selective society journals[50-53]. This has thus far limited the adaptation of study findings into clinical practice. We conclude that future progress in this area will depend primarily on the choices we make now.

Conclusion

This study provides important information on the renal safety of a novel approach to the repair of AAAs. Compared with open AAA repair, our findings suggest that EVAR is associated with a lower risk of post-procedure ARF. These results reflect the outcomes of actual practice in a heterogeneous and unselected patient population that received care in a wide spectrum of renal therapies.

Observations from the presented studies reinforce the notion that there are many unresolved issues related to postoperative ARF. The time has come for the implementation of a consensus on the standard definition of ARF that is sensitive and specifically defines this complication. This will permit an accurate assessment of the impact of ARF on outcomes, and allow comparison of patients across centers worldwide. The preoperative risk assessment scores will need to be re-validated prospectively using the standardized definitions and should incorporate emerging knowledge of patient characteristics and care elements. In this regard, a prognostic score system for AKI would help anticipate patient treatment. As EVAR becomes a more widely practiced procedure, strategies to further reduce procedure-related kidney injury should be diligently investigated.

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Sažetak

ZAMJENSKE BUBREŽNE TERAPIJE NAKON KIRURŠKOG LIJEČENJA ANEURIZME ABDOMINALNE AORTE – PREGLEDNI ČLANAK

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Danas postoje brojni oblici zamjenske terapije u svrhu liječenja akutne bubrežne bolesti poslije kirurškog liječenja aneurizme abdominalne aorte. Cilj ovoga preglednog članka je utvrditi učestalost poslijeoperacijskog akutnog zatajenja bubrega koje iziskuje uporabu hemofiltracijskih postupaka te utvrditi čimbenike koji utječu na ishod liječenja bolesnika poslije kirurškog liječenja aneurizme abdominalne aorte. Stupanj težine združenih bolesti, etiologija akutne bubrežne bolesti, klinički i hemodinamski čimbenici bolesnika, veličina raspoloživih materijalnih sredstava, te troškovi terapije imaju izravan utjecaj na odabir i vrstu zamjenske terapije za liječenje akutne bubrežne bolesti. Postoje različita mišljenja o svrsishodnosti uporabe zamjenske terapije za liječenje akutne bubrežne bolesti. Nadalje, do danas su nedostatno opisane smjernice o potrebnom trajanju zamjenske terapije za liječenje akutne bubrežne bolesti. Nedostatno je razjašnjeno kakva je učinkovitost zamjenske bubrežne terapije kod hemodinamski nestabilnih bolesnika kod kojih nastaje akutna bubrežna bolest neposredno prije i poslije operacijskog zahvata. Također, nedostatno je poznavanje učinkovitosti mehanizama djelovanja zamjenskih bubrežnih terapija u smislu odstranjenja štetnih proizvoda metabolizma bubrega. U ovom preglednom članku opisuju se najnovija saznanja o mehanizmima i djelovanju te vrstama zamjenskih bubrežnih terapija koje su danas u uporabi kod bolesnika kod kojih se razvija akutna bubrežna bolest poslije kirurškog liječenja aneurizmatske bolesti abdominalne aorte.

Ključne riječi: *Bubreg, transplantacija; Akutno bubrežno zatajenje; Oksidacijski stres; Aneurizma abdominalne aorte*