Send Orders for Reprints to reprints@benthamscience.ae

Current Vascular Pharmacology, **2018,** *16,* **000-000**

REVIEW ARTICLE

Renal Dysfunction Following Elective Endovascular Aortic Aneurysm Repair

Dj Radak[1], M Neskovic[1], P Otasevic[1] and ER Isenovic[2,*]

[1]*Department of Vascular Surgery, Dedinje Cardiovascular Institute, Belgrade University School of Medicine, 11040 Belgrade, Serbia;* [2]*Laboratory of Radiobiology and Molecular Genetics, Institute of Nuclear Sciences Vinca, University of Belgrade, Mike Petrovica Alasa 12-14, 11000 Belgrade, Serbia*

ARTICLE HISTORY

Received: October 17, 2017
Revised: October 31, 2017
Accepted: October 31, 2017

DOI:
10.2174/1570161115666171116163203

Abstract: Abdominal aortic aneurysm (AAA) is a degenerative disease of the aortic wall with potentially fatal complications. Open repair (OR) was considered the gold standard, until the emergence of endovascular aneurysm repair (EVAR), which is less invasive and equally (if not more) effective. As the popularity of endovascular procedures grows, related complications become more evident, with kidney damage being one of them. Although acute kidney injury (AKI) following EVAR is relatively common, its true incidence is still uncertain. Also, there is insufficient data concerning long-term renal outcomes after EVAR, especially with repeated contrast agent exposure. Despite the lack of firm evidence on the effectiveness of individual strategies, it is evident that prevention of AKI following EVAR requires a multifactorial approach. This review focuses on recent findings based on human studies regarding the current evidence of renal impairment after EVAR, its quantification and strategies for its prevention.

Keywords: Endovascular aneurysm repair, acute kidney injury, contrast-induced nephropathy.

1. INTRODUCTION

Abdominal aortic aneurysm (AAA) is a degenerative disease of the aortic wall with a prevalence of 2.2% in the elderly population [1]. The treatment of AAA is offered to prevent AAA rupture, which is often a fatal complication. Open repair (OR) was considered the gold standard until the emergence of endovascular aneurysm repair (EVAR), which is less invasive and equally (if not more) effective [2-4]. The number of AAAs treated with EVAR is rising each year, especially in Western countries [5, 6].

As the popularity of endovascular procedures grows, related complications become more evident, with kidney damage being one of them. Aside from nephrotoxicity of contrast media used during the procedure [7], other factors could also compromise both short- and long-term kidney function after EVAR, such as microembolization induced by endograft manipulation, accessory renal artery coverage, lower extremity ischemia-reperfusion reaction and a systemic inflammatory response [8]. Post-procedural acute kidney injury (AKI) may result in prolonged hospital stay and new-onset haemodialysis requirement in some patients and has a strong impact on long-term survival after major surgery [9, 10]. The additional use of contrast media for post-EVAR surveillance may also contribute to late outcomes.

This review focuses on recent findings based on human studies regarding the evidence of renal impairment after EVAR, its quantification and strategies for its prevention.

2. ASSESSMENT OF KIDNEY FUNCTION

The initial studies used serum creatinine (SCr) levels and creatinine clearance (CrCl), predominantly calculated by the Cockcroft-Gault equation, to assess renal function after AAA treatment. As SCr showed unsatisfactory sensitivity, different formulas were introduced for estimation of glomerular filtration rate (eGFR), which included other patient characteristics [21-22]. Both the Modification of Diet in Renal Disease (MDRD) study equation and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulas include age, race, gender, and SCr levels, but the latter proved superior in determining (eGFR), especially in patients with better kidney function [23].

Novel biomarkers have been developed for the detection of early kidney injury [24]. A prospective observational study analyzed changes of SCr, urinary neutrophil gelatinase-associated lipocalin (NGAL), blood NGAL, N-acetyl-β-D-glucosaminidase (NAG), albumin (Alb) and liver fatty acid binding protein (L-FABP) in 47 patients after elec-

*Address correspondence to this author at the Institute of Nuclear Sciences Vinca, University of Belgrade, Laboratory of Radiobiology and Molecular Genetics, P.O. Box 522, 11000 Belgrade, Serbia; Tel/Fax: +38111-3408147; E-mail: isenovic@yahoo.com

1570-1611/18 $58.00+.00

tive EVAR. Renal injury before AKI was detected by increased SCr levels, while NGAL corrected by urinary creatinine values demonstrated the best predictive value [25]. Obata *et al.* demonstrated that urinary L-FABP level significantly increased 4 h after EVAR and 2h after aortic cross-clamping during surgery [26], while another small prospective study showed that urinary NGAL and interleukin 18 (IL-18) concentrations peaked at 12 h after EVAR [27].

Another prospective study reported that urinary cystatin C was superior to SCr in the early detection of AKI after OR and EVAR [28]. In addition, Abdelhamid *et al.* noted a significant rise in cystatin C levels at 1, 6 and 12 months during EVAR follow-up, which was not followed by a rise in sCr levels and a decrease in eGFR, both in patients with normal and decreased preprocedural kidney function [29]. Novel early biomarkers of kidney injury show promising diagnostic value, but their cost-effectiveness remains to be determined in larger prospective studies.

A small retrospective study compared renal outcomes between OR and EVAR, by applying the MDRD equation and measuring renal volume using semiautomatic post-processing algorithm based on computerized tomography (CT) angiography [30]. The decrease in renal volume correlated with deterioration of kidney function over time, thus suggesting that it could be a good marker of postoperative renal impairment. More advanced CT image processing software has been developed but is yet to be implemented in routine practice [31].

3. DEFINITIONS OF AKI AND CHRONIC KIDNEY DISEASE (CKD)

AKI is usually defined as the abrupt decline in renal function. However, a precise definition is not consistently used, limiting comparisons between studies. In 2002, the Acute Dialysis Quality Initiative (ADQI) group formed the Risk of renal dysfunction; Injury to the kidney; Failure of kidney function; Loss of kidney function; End-stage kidney disease (RIFLE) criteria, which included the first uniform AKI definition (Table **1**) [32]. Next, the Acute Kidney Injury Network (AKIN) incorporated a wider spectrum of renal injury under the term AKI put in the timeframe of 48h (Table **2**) [33]. By comparing the 2 criteria, Bang *et al.* showed that AKIN had a better predictive value in terms of overall mortality in patients undergoing OR of infrarenal AAA [34]. In Kidney Disease Improving Global Outcomes (KDIGO) clinical guidelines, released in 2012, the 2 former definitions were merged to define AKI as: increase in SCr by ≥0.3 mg/dL (26 μmol/l) within 48 h, increase in SCr to ≥1.5 times baseline within the last 7 days, or urine output <0.5 mL/kg/h for 6 h (Table **3**) [35]. A recent paper highlighted the need for a uniform definition of AKI after EVAR and proposed a new scoring system (ARISe - Aneurysm Renal Injury Score), that has yet to be validated [36].

CKD was initially defined and classified by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) [37]. Subsequently, the definition of CKD was updated in KDIGO guidelines, where it represents a decreased eGFR of <60 ml/min/1.73/m^2 for at least 3 months [35].

4. INCIDENCE OF AKI FOLLOWING EVAR

Initial reports of AKI after EVAR consisted of papers comparing either EVAR with OR or different stent-graft fixation methods [11-15]. The design varied considerably across the studies, predominantly being retrospective, with the absence of uniform perioperative patient care protocol and procedure information, such as quantity of contrast media used, procedure time and coverage of accessory renal arteries. In addition, the inconsistency in defining AKI throughout the studies was the main limiting factor.

The first cohort study which defined AKI according to KDIGO criteria and explored its incidence after elective EVAR [18] used renoprotective fluid therapy preoperatively and a single device with infrarenal fixation in all patients.

Table 1. RIFLE criteria for acute renal failure.

Stage	GFR Criteria	Urine Output Criteria
Risk	Increased sCr x1.5 or GFR decrease >25%	UO < 0.5 ml/kg/h for 6 h
Injury	Increased sCr x2 or GFR decrease >50%	UO < 0.5 ml/kg/h for 12 h
Failure	Increased sCr x3 or GFR decrease >75% or sCr ≥ 4 mg/dL (353.6 μmol/l) with an acute rise of ≥ 0.5 mg/dL (44.2 μmol/l)	UO < 0.3 ml/kg/h for 24 h or anuria for 12 h
Loss	Persistent ARF = complete loss of kidney function >4 weeks	
ESKD	Need for dialysis for >3 months	

The classification system includes separate criteria for sCr and urine output, which can be fulfilled either independently or simultaneously. RIFLE - Risk of renal dysfunction; Injury to the kidney; Failure of kidney function; Loss of kidney function; End-stage kidney disease; GFR - glomerular filtration rate; sCr - serum creatinine levels; UO - urine output; ARF - acute renal failure; ESKD - End-stage kidney disease. Modified from [30].

Table 2. AKIN criteria for AKI.

Stage	sCr Criteria	Urine Output Criteria
1	Increase in sCr of ≥0.3 mg/dL (26.5 μmol/l) or increase in sCr ≥150-200% from baseline	UO <0.5 ml/kg/h for 6 h
2	Increase in sCr ≥200-300% from baseline	UO <0.5 ml/kg/h for 12 h
3	Increase in sCr >300% from baseline or sCr ≥4 mg/dL (353.6 μmol/l) with an acute rise of ≥0.5 mg/dL (44.2 μmol/l)	UO <0.3 ml/kg/h for 24 h or anuria for 12 h

Only one criterion has to be fulfilled to qualify for a stage. Patients on renal replacement therapy are considered to have met the criteria for stage 3. AKIN - Acute Kidney Injury Network; AKI - acute kidney injury; sCr - serum creatinine levels; UO - urine output. Modified from [31].

Table 3. KDIGO criteria for AKI.

Stage	sCr criteria	Urine Output Criteria
1	sCr x1.4-1.9 baseline or sCr ≥0.3 mg/dL (26.5 μmol/l) increase	UO <0.5 ml/kg/h for 6-12 h
2	sCr 2.0-2.9 times baseline	UO <0.5 ml/kg/h for ≥12 h
3	sCr 3.0 times baseline or Increase in sCr of ≥4.0 mg/dL (353.6 μmol/l) or Initiation of renal replacement therapy or In patients <18 years, decrease in eGFR <35 mL/min/1.73m^2	UO <0.5 ml/kg/h for ≥24 h or Anuria for ≥12 h

These criteria were developed from RIFLE and AKIN criteria. KDIGO - Kidney Disease Improving Global Outcomes; AKI - acute kidney injury; RIFLE - Risk of renal dysfunction; Injury to the kidney; Failure of kidney function; Loss of kidney function; End-stage kidney disease; AKIN - Acute Kidney Injury Network; sCr - serum creatinine levels; UO - urine output. Modified from [32].

AKI developed in 28 out of 149 (18.8%; 26 classified as stage 1, 2 as stage 2) patients; none of the patients needed dialysis postoperatively. A subsequent paper by these authors analyzed potential risk factors for AKI after elective EVAR with both supra- and infrarenal fixation [19]. The incidence of AKI was 17.6%, which was in accordance with previous results. This study identified baseline eGFR (OR: 1.02 per unit decrease; 95% CI: 1.003-1.041; p = 0.025) and CKD stage >2 at baseline (OR: 1.28; 95% CI 1.269-2.531; p = 0.001) being the main predictive factors, along with cardiovascular comorbidities. Also, an interesting finding was that contrast media volume did not have an impact on AKI development (p = 0.12). The study did not differentiate renal outcomes between the fixation methods used.

A retrospective review of the Vascular Quality Initiative (VQI) database found that 470 out of 14,475 (3.2%) patients suffered from renal dysfunction after elective EVAR (2.9% with AKI, and an additional 0.4% with new haemodialysis requirement) [20]. Postoperative renal dysfunction was defined as a rise in SCr of 0.5 mg/dL (44 μmol/l) or new-onset haemodialysis. Strong independent predicting factors were new-onset heart failure and a return to the operating room, while a preoperative eGFR >60 mL/min/1.73m^2 was a protective factor. The low incidence of AKI as compared with previous reports could be attributed to its restricted definition and irregular follow-up, with 15% of patients having only 1 day of follow-up.

Castagno *et al.* compared the incidence of AKI among 146 patients undergoing EVAR and 285 undergoing OR, using the ARISe scoring system in a retrospective single-center study [38]. The development of AKI was more common after OR (26.3 *vs* 5.5%) and in patients with pre-existing decreased kidney function. Interestingly, a high percentage of patients (77.5% in OR, 62.5% in EVAR) restored their baseline sCr levels during the hospital stay, which implies that AKI could be a transient condition. Also, since the ARISe criteria are stricter in defining AKI compared with the RIFLE criteria, its clinical usefulness was questioned. The authors concluded that consensus in defining and staging AKI is urgently needed.

In another retrospective study analyzing AKI after EVAR (9% were snorkel-EVARs with renal artery stenting), the authors stratified 134 patients in 5 CKD classes according to the KDOQI guidelines before the intervention, with 88% of the patients in CKD class 2 and 3 [39]. The staging was recalculated 7 days after the intervention and AKI was defined as increased CKD stage after EVAR. Twenty-five (19%) patients developed AKI, but on the other hand, another 17 (13%) had improved their kidney function. CKD progression could have been predicted by a presence of the shaggy aorta, absence of oral beta-blocker administration and a higher preoperative sCr level (>1.4 mg/dL). Freedom from aneurysm-related death was significantly lower in patients with CKD progression during the median follow-up of 14.1 (range 1-36) months.

Surprisingly, a large systematic review and meta-analysis that included 4369 patients showed no significant rise in SCr or drop in CrCl in the first 30 days after EVAR, while further staging of renal dysfunction was not applied [40]. However, the authors pointed out the considerable heterogeneity in the definition of renal failure and the evident paucity of data reporting postoperative haemodialysis requirement.

The emerging of the chimney and fenestrated EVAR procedures revolutionized the treatment of pararenal AAAs. Although, these endovascular interventions showed superior renal outcomes compared with OR, [41, 42] they still bare a slightly higher risk of postoperative AKI compared with classic EVAR [43]. This could be attributed to a higher degree of juxtarenal endograft manipulation, conjunctive stenting of renal arteries and increased contrast media load. In a small study of 43 patients undergoing chimney EVAR, 14 (32.6%) patients experienced some form of AKI defined by the RIFLE criteria, with 10 (23.3%) classified as mild [44]. Another study reported a 28% AKI incidence after fenestrated EVAR, defined by AKIN criteria, with long procedure time and occlusion of accessory renal arteries being independent risk factors [45]. Oderich *et al.* evaluated the results of fenestrated and branched EVAR in patients with pararenal and thoracoabdominal aortic aneurysms in a prospective nonrandomized study, and noted a 9% AKI incidence, with 4/240 (1.6%) target renal artery occlusions [46]. Finally, a systematic review with pooled data analysis, consisting of 123 patients treated with chimney EVAR (group 1) and 631 patients treated with fenestrated EVAR (group 2), reported 9.7% and 12.4% postoperative renal impairment rate, in the 2 groups respectively, which was not statistically significant. [47]

Another question that stands out is if worse outcomes after EVAR should be expected in the subset of patients with preoperatively impaired kidney function. While some of the studies recognized increased baseline levels of sCr as a risk factor for developing postoperative AKI and worse outcomes in general, the answer remains unclear [18-20, 39]. Mehta *et al.*, retrospectively assigned 200 patients that underwent EVAR into 3 groups based on their preoperative sCr: group 1 (108 patients) < 1.5 mg/dL; group 2 (65 patients) 1.5-2.0 mg/dL; group 3 2.1-3.5 mg/dL [48]. There was no statistically significant difference in the incidence of postoperative renal complications between the groups. The authors also marked perioperative hypotension (OR 9.1, $p<0.001$) and the amount of contrast agent used (OR 1.6, $p<0.001$) as the 2 main risk factors for worsening kidney function. Even though these 2 risk factors might have had a stronger impact on patients with decreased kidney function, further investigation between the subgroups of patients was not conducted. An analysis of American College of Surgeons National Surgical Quality Improvement Program (NISQP) database, included 3886 EVAR patients and 1256 OR patients with moderate (eGFR 30-60 mL/min/1.73m^2) or severe (eGFR < 30 mL/min/1.73m^2) preoperative kidney dysfunction [49]. EVAR patients showed significantly lower renal complication (1.9 *vs* 7.8%; $p < 0.0001$) and 30-day mortality rate (1.6 *vs* 5.9%; $p < 0.0001$) in patients with moderate kidney dysfunction, while the same superiority was not present in patients with severe kidney dysfunction. However, the authors suggested that there is a strong possibility that most of the OR patients had juxtarenal AAA, which needed suprarenal clamping and thus produced unfavorable renal outcomes.

Despite the fact that AKI following EVAR seems to be transient in most cases, some studies highlighted its importance as a predictive factor for decreased overall survival and increased long-term cardiovascular morbidity [18, 20, 45].

5. IMPACT OF EVAR ON LONG-TERM KIDNEY FUNCTION

The early survival advantage of EVAR compared with OR gradually fades over time [50, 51]. Although the increased mortality in long-term follow-up is mostly attributed to aneurysm-related complications, the progressive impairment of renal function should not be disregarded. The nature of the disease prevents the formation of an adequate control group, which would consist of patients with large AAAs that had not previously undergone repair. On the other hand, population-based studies, which could be used for comparison, detected either the absence of or minor deterioration in renal function over time in elderly patients [52, 53].

Post hoc analyses of large randomized trials comparing EVAR with OR reported limited information on long-term renal dysfunction after EVAR [54-56]. In the initial report of the Open Versus Endovascular Repair (OVER) trial, the incidence of new-onset dialysis after EVAR was 1.1% within 1 year of the procedure [55]. The 5 year follow-up study of the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial showed a mean decline in eGFR, calculated by CKD-EPI equation, of 4.2 mL/min/1.73m^2 (95% CI: 3.2-5.3) [56].

Mohammed *et al.* included 212 patients in a retrospective single-center study of long-term renal outcomes after EVAR [57]. Patients were classified in 5 CKD stages according to KDOQI guidelines and were followed for up to 20 months. Estimated freedom from progression to CKD stage 3 was 80%, 76%, and 63% at 6, 12, and 18 months, while freedom from progression to CKD stage 4 was 97%, 96%, and 93% at the same time points, thus showing a more rapid progression to CKD stage 3 than to CKD stage 4 during mid-term follow-up. Although intraoperative contrast volume was not associated with CKD stage progression, the notable fact is that postoperative surveillance consisted of multi-detector CT angiography at 1, 6, 12 months and annually thereafter.

A systematic review and a subsequent meta-analysis of studies exploring renal outcomes after EVAR estimated an average 18% of patients with clinically relevant deterioration in kidney function 1 year after the procedure [40]. Saratzis *et al.* conducted a nested case-control study, with three groups of patients undergoing AAA repair matched by demographic and preoperative angiographic parameters: OR (45 patients), EVAR with suprarenal and EVAR with infrarenal fixation (90 patients each) [17]. During the 2 year follow-up, there was a significant progressive drop in eGFR in the OR and suprarenal fixation EVAR group, with different time patterns of eGFR decline between the groups, suggesting diverse aetiology. Also, this was the first study to evaluate the correlation between neck length and diameter with eGFR drop, which was not significant. Although, some other studies proposed that suprarenal endograft fixation

bares a higher risk of AKI compared with infrarenal fixation, which can be attributed to unfavourable neck anatomy and subsequent increased risk of microembolization in the renal arteries, meta-analyses on the subject failed to confirm this hypothesis [58, 59].

The impact of additional contrast media exposure on kidney function during follow-up is a highly neglected matter. Firstly, CT angiography is still a frequently utilized method in 10 year post-EVAR surveillance, despite strong evidence of other imaging modalities having equal or similar diagnostic value [60, 61]. A prospective study of 278 patients showed that contrast-enhanced ultrasonography (CEUS) was diagnostically equivalent to CT angiography in the detection of endoleaks in the first-year follow-up, with the sensitivity of 85% and specificity of 95% [62]. In a systematic review and meta-analysis including 25 studies, the authors concluded that both duplex ultrasonography (DUS) and CEUS have sufficient accuracy in detection of type I and type III endoleaks. [63] Another meta-analysis analyzed the diagnostic value of magnetic resonance imaging (MRI) in addition to DUS and CEUS while using CT angiography as the gold standard. [64] Again the accuracy of CEUS, along with the MRI was more than acceptable in the detection of endoleaks, while DUS showed worse results. As a result, it is safe to assume that ultrasonography can be used for post-EVAR surveillance, at least in uncomplicated cases. Thus, further nephrotoxicity of contrast media can be avoided and the true impact of EVAR on long-term kidney function can be evaluated.

Some of the EVAR complications, such as different types of endoleaks, require elective endovascular reintervention in the postoperative period. The reported reintervention rate across the major studies ranges from 5.1-8.5% [51], which can have a significant impact on kidney function during EVAR follow-up. In addition to contrast media administration, the manipulation in the juxtarenal segment of the aorta could lead to further degradation of kidney function. However, there is still a lack of studies exploring this problem.

The most recent systematic review included 6 papers, which compared EVAR and OR renal outcomes during mid- and long-term follow-up [65]. The high heterogeneity between the studies, in terms of perioperative treatment, the definition of renal dysfunction, postoperative surveillance, and follow-up, limited the subsequent meta-analysis. The authors defined kidney function impairment as a decrease of eGFR >20% compared with the preoperative level. Pooled data analysis showed that there was 5.3% incidence of postoperative kidney dysfunction among 1096 EVAR patients and 5.2% in 1006 OR patients; these values did not differ significantly.

6. PREVENTION OF AKI FOLLOWING EVAR

A number of different strategies are used for the prevention of AKI after endovascular procedures, with most of them focusing on the reduction of contrast-induced nephropathy (CIN) incidence following coronary interventions. Firstly, there should be a tendency to administer as low a volume of contrast media as possible, with the use of isoosmolar contrast in high-risk patients [66]. After an extensive investigation, it seems that the only proven preventive treatment is the expansion of intravascular volume with consequent stimulation of renal contrast elimination through urine output, which is achieved by administration of isotonic crystalloid solutions [66, 67]. However, a newly published result of AMACING trial countered this standard of care, by showing that no prophylaxis is non-inferior and more cost-effective to prophylactic intravenous fluid administration in preventing CIN. Additionally, the authors reported a non-negligible complication rate associated with volume expansion [68]. A recent large meta-analysis reported evidence of the protective effect of N-acetylcysteine against CIN after coronary interventions; however, this was challenged by other large randomized controlled trials (RCTs) [69, 70]. As for chronic therapy, a systematic review and meta-analysis of studies concerning coronary interventions showed a significant risk reduction of CIN in patients who received preprocedural high-dose statin therapy compared with controls (3.7 *vs* 8.3%; relative risk, RR, 0.46; $p < 0.00001$) [71].

Evidence regarding methods for prevention of renal dysfunction after EVAR mostly consists of pilot studies with small numbers of patients [72-74]. Moore *et al.* conducted a small study; 20 patients undergoing EVAR were randomized either to standard hydration therapy or to standard hydration therapy with N-acetylcysteine [72]. None of the patients developed AKI, and there was no significant difference in postoperative levels of renal function markers between the groups. Another trial with 86 patients undergoing elective EVAR showed a small but significant benefit from intraoperative mannitol administration for renal function in the first 24 h after the procedure, but not in the long-term follow-up [73]. Moulakakis *et al.* examined the impact of statin use on the incidence of renal dysfunction following EVAR in 127 patients [74]. Their study showed the absence of early deterioration of kidney function in patients undergoing EVAR with suprarenal fixation, who were taking statins for at least 3 months preoperatively, whereas a deterioration was present in patients that were not using statins. However, a similar protective effect of statins was not observed in other recent studies investigating AKI following EVAR, though specific information about therapeutic regimen was not reported [18-20]. Also, it should be noted that some papers suggest that the true renoprotective effect of statins emerges after more than a year of its regular administration [75]. The data on the benefit of preoperative statin therapy for patients undergoing coronary interventions support its initiation in all patients planned for EVAR [71, 76, 77].

Despite the lack of firm evidence on the effectiveness of individual strategies, it is evident that prevention of AKI following EVAR requires a multifactorial approach [61]. Also, future studies should focus on identifying high-risk patients by considering parameters, such as aortic stiffness, full blood count and a shaggy aorta [78-80].

CONCLUSIONS

AKI is a relatively common complication following EVAR, which is associated with prolonged hospital stay and long-term morbidity and mortality. Its true incidence is still uncertain, due to lack of uniform definitions of kidney dysfunction and consolidated perioperative protocols. Also, there is a lack of published studies concerning renal out-

comes after EVAR during long-term follow-up, especially evaluating the impact of repeated contrast exposure. Despite the extensive evidence on different preventive strategies against CIN after percutaneous coronary interventions, the data on the such strategies in the prevention of AKI following EVAR is still insufficient. While preoperative intravenous hydration treatment with isotonic crystalloid solutions is the current standard of care, it is clear that multifactorial approach is needed. A similar argument has been raised regarding the use of contrast media for carotid artery stenting (CAS) [81], a procedure which is used for patients with carotid artery stenosis. Compared with carotid endarterectomy, CAS is a less invasive but this procedure requires the use of contrast material and this can result in the development of CIN.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

This work is supported by the grants III41028 (to DjR) and No.173033 (to ERI) from the Ministry of Science, Republic of Serbia.

REFERENCES

[1] Sampson UK, Norman PE, Fowkes FG, *et al*. Estimation of global and regional incidence and prevalence of abdominal aortic aneurysms 1990 to 2010. Glob Heart 2014;9:159-70.

[2] United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ. Endovascular versus open repair of the abdominal aortic aneurysm. N Engl J Med 2010;362:1863-71.

[3] De Bruin JL, Baas AF, Buth J, *et al.*; DREAM Study Group. Long-term outcome of open or endovascular repair of the abdominal aortic aneurysm. N Engl J Med 2010;362:1881-9.

[4] Lederle FA, Freischlag JA, Kyriakides TC, *et al.*; OVER Veterans Affairs Cooperative Study Group. Long-term comparison of endovascular and open repair of the abdominal aortic aneurysm. N Engl J Med 2012;367:1988-97.

[5] Ultee KH, Hurks R, Buck DB, *et al.* The impact of endovascular repair on specialties performing abdominal aortic aneurysm repair. J Vasc Surg 2015;62:562-8.e3.

[6] Dua A, Kuy S, Lee CJ, Upchurch GR Jr, Desai SS. Epidemiology of aortic aneurysm repair in the United States from 2000 to 2010. J Vasc Surg 2014;59:1512-7.

[7] Fähling M, Seeliger E, Patzak A, Persson PB. Understanding and preventing contrast-induced acute kidney injury. Nat Rev Nephrol 2017;13:169-80.

[8] Saratzis A, Nduwayo S, Sarafidis P, Sayers RD, Bown MJ. Renal Function is the Main Predictor of Acute Kidney Injury after Endovascular Abdominal Aortic Aneurysm Repair. Ann Vasc Surg 2016;31:52-9.

[9] Zakkar M, Bruno VD, Guida G, *et al.* Postoperative acute kidney injury defined by RIFLE criteria predicts early health outcome and long-term survival in patients undergoing redo coronary artery bypass graft surgery. J Thorac Cardiovasc Surg 2016;152:235-42.

[10] Bell S, Dekker FW, Vadiveloo T, *et al.* Risk of postoperative acute kidney injury in patients undergoing orthopaedic surgery--development and validation of a risk score and effect of acute kidney injury on survival: observational cohort study. BMJ 2015;351:h5639.

[11] Greenberg RK, Chuter TA, Lawrence-Brown M, Haulon S, Nolte L; Zenith Investigators. Analysis of renal function after aneurysm repair with a device using suprarenal fixation (Zenith AAA Endovascular Graft) in contrast to open surgical repair. J Vasc Surg 2004;39:1219-28.

[12] Parmer SS, Carpenter JP; Endologix Investigators. Endovascular aneurysm repair with suprarenal vs infrarenal fixation: a study of renal effects. J Vasc Surg 2006;43:19-25.

[13] Wald R, Waikar SS, Liangos O, Pereira BJ, Chertow GM, Jaber BL. Acute renal failure after endovascular vs open repair of the abdominal aortic aneurysm. J Vasc Surg 2006;43:460-6; discussion 466.

[14] Waasdorp E, van't Hullenaar C, van Herwaarden J, *et al.* Renal function after endovascular aortic aneurysm repair: a single-center experience with transrenal versus infrarenal fixation. J Endovasc Ther 2007;14:130-7.

[15] Gawenda M, Brunkwall J. Renal response to open and endovascular repair of abdominal aortic aneurysm: a prospective study. Ann Vasc Surg 2008;22:1-4.

[16] de Bruin JL, Vervloet MG, Buimer MG, Baas AF, Prinssen M, Blankensteijn JD; DREAM Study Group. Renal function 5 years after open and endovascular aortic aneurysm repair from a randomized trial. Br J Surg 2013;100:1465-70.

[17] Saratzis A, Sarafidis P, Melas N, Khaira H. Comparison of the impact of open and endovascular abdominal aortic aneurysm repair on renal function. J Vasc Surg 2014;60:597-603.

[18] Saratzis A, Melas N, Mahmood A, Sarafidis P. Incidence of Acute Kidney Injury (AKI) after Endovascular Abdominal Aortic Aneurysm Repair (EVAR) and Impact on Outcome. Eur J Vasc Endovasc Surg 2015;49:534-40.

[19] Saratzis A, Nduwayo S, Sarafidis P, Sayers RD, Bown MJ. Renal Function is the Main Predictor of Acute Kidney Injury after Endovascular Abdominal Aortic Aneurysm Repair. Ann Vasc Surg 2016;31:52-9.

[20] Zarkowsky DS, Hicks CW, Bostock IC, Stone DH, Eslami M, Goodney PP. Renal dysfunction and the associated decrease in survival after elective endovascular aneurysm repair. J Vasc Surg 2016;64:1278-85.e1.

[21] Levey AS, Coresh J, Greene T, *et al.*; Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006;145:247-54.

[22] Levey AS, Stevens LA, Schmid CH, *et al.*; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.

[23] Delanaye P, Cavalier E, Cristol JP, Delanghe JR. Calibration and precision of serum creatinine and plasma cystatin C measurement: impact on the estimation of glomerular filtration rate. J Nephrol 2014;27:467-75.

[24] Andreucci M, Faga T, Riccio E, Sabbatini M, Pisani A, Michael A. The potential use of biomarkers in predicting contrast-induced acute kidney injury. Int J Nephrol Renovasc Dis 2016;9:205-21.

[25] Ueta K, Watanabe M, Iguchi N, *et al.* Early prediction of acute kidney injury biomarkers after endovascular stent graft repair of aortic aneurysm: a prospective observational study. J Intensive Care 2014;2:45.

[26] Obata Y, Kamijo-Ikemori A, Ichikawa D, *et al.* Clinical usefulness of urinary liver-type fatty-acid-binding protein as a perioperative marker of acute kidney injury in patients undergoing endovascular or open-abdominal aortic aneurysm repair. J Anesth 2016;30:89-99.

[27] Noorani A, Sadat U, Rollins KE, *et al.* Assessment of renal injury in patients undergoing elective EVAR using urinary neutrophil gelatin-associated lipocalin, Interleukin 18, and retinol-binding protein. Angiology 2017;68:547-22.

[28] Pirgakis KM, Makris K, Dalainas I, Lazaris AM, Maltezos CK, Liapis CD. Urinary cystatin C as an early biomarker of acute kidney injury after open and endovascular abdominal aortic aneurysm repair. Ann Vasc Surg 2014;28:1649-58.

[29] Abdelhamid MF, Davies RS, Vohra RK, Adam DJ, Bradbury AW. Assessment of renal function by means of cystatin C following standard and fenestrated endovascular repair. Ann Vasc Surg 2013;27:708-13.

[30] Martin-Gonzalez T, Pinçon C, Hertault A, *et al*. Renal outcomes analysis after endovascular and open aortic aneurysm repair. J Vasc Surg 2015;62:569-77.

[31] Khalifa F, Soliman A, Elmaghraby A, Gimelfarb G, El-Baz A. 3D Kidney Segmentation from Abdominal Images Using Spatial-Appearance Models. Comput Math Methods Med 2017:9818506.

[32] Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004;8:R204-12.

[33] Mehta RL, Kellum JA, Shah SV, *et al.* Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.

[34] Bang JY, Lee JB, Yoon Y, Seo HS, Song JG, Hwang GS. Acute kidney injury after infrarenal abdominal aortic aneurysm surgery: a comparison of AKIN and RIFLE criteria for risk prediction. Br J Anaesth 2014;113:993-1000.

[35] Acute Kidney Injury Work Group. Kidney Disease: Improving Global Outcomes (KDIGO) - Clinical Practice Guideline for Acute Kidney Injury. Kidney Int 2012; 2:1-138.

[36] Twine CP, Boyle JR. Renal dysfunction after EVAR: time for a standard definition. J Endovasc Ther 2013;20:331-3.

[37] Levey AS, Coresh J, Balk E, *et al*. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139:137-47.

[38] Castagno C, Varetto G, Quaglino S, *et al*. Acute kidney injury after open and endovascular elective repair for infrarenal abdominal aortic aneurysms. J Vasc Surg 2016;64:928-933.

[39] Toya N, Ohki T, Momokawa Y, *et al*. Risk factors for early renal dysfunction following endovascular aortic aneurysm repair and its effect on the postoperative outcome. Surg Today 2016; 46:1362-69.

[40] Karthikesalingam A, Bahia SS, Patel SR, *et al*. A systematic review and meta-analysis indicates underreporting of renal dysfunction following endovascular aneurysm repair. Kidney Int 2015;87:442-51.

[41] Katsargyris A, Oikonomou K, Klonaris C, Töpel I, Verhoeven EL. Comparison of outcomes with open, fenestrated, and chimney graft repair of juxtarenal aneurysms: are we ready for a paradigm shift? J Endovasc Ther 2013;20:159-69.

[42] Shahverdyan R, Majd MP, Thul R, Braun N, Gawenda M, Brunkwall J. F-EVAR does not Impair Renal Function more than Open Surgery for Juxtarenal Aortic Aneurysms: Single Centre Results. Eur J Vasc Endovasc Surg 2015;50:432-41.

[43] Linsen MA, Jongkind V, Nio D, Hoksbergen AW, Wisselink W. Pararenal aortic aneurysm repair using fenestrated endografts. J Vasc Surg 2012;56:238-46.

[44] Lee JT, Varu VN, Tran K, Dalman RL. Renal function changes after snorkel/chimney repair of juxtarenal aneurysms. J Vasc Surg 2014;60:563-70.

[45] Sailer AM, Nelemans PJ, van Berlo C, *et al.* Endovascular treatment of complex aortic aneurysms: prevalence of acute kidney injury and effect on long-term renal function. Eur Radiol 2016;26:1613-9.

[46] Oderich GS, Ribeiro M, Hofer J, *et al*. Prospective, nonrandomized study to evaluate endovascular repair of pararenal and thoracoabdominal aortic aneurysms using fenestrated-branched endografts on supraceliac sealing zones. J Vasc Surg 2017;65:1249-59.e10.

[47] Donas KP, Torsello G, Bisdas T, Osada N, Schonenfeld E, Pitoulias GA. Early outcomes for fenestrated and chimney endografts in the treatment of pararenal aortic pathologies are not significantly different: a systematic review with pooled data analysis. J Endovasc Ther 2012;19:723-8.

[48] Mehta M, Veith FJ, Lipsitz EC, *et al.* Is elevated creatinine level a contraindication to endovascular repair? J Vasc Surg 2004;39:118-23.

[49] Nguyen BN, Neville RF, Rahbar R, Amdur R, Sidawy AN. Comparison of outcomes for open abdominal aortic aneurysm repair and endovascular repair in patients with chronic renal insufficiency. Ann Surg 2013;258:394-9.

[50] Patel R, Sweeting MJ, Powell JT, Greenhalgh RM; EVAR trial investigators.. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. Lancet 2016;388:2366-74.

[51] Powell JT, Sweeting MJ, Ulug P, *et al*.; EVAR-1, DREAM, OVER and ACE Trialists. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. Br J Surg 2017;104:166-78.

[52] Hemmelgarn BR, Zhang J, Manns BJ, *et al*. Progression of kidney dysfunction in the community-dwelling elderly. Kidney Int 2006;69:2155-61.

[53] Glassock RJ, Winearls C. Ageing and the glomerular filtration rate: truths and consequences. Trans Am Clin Climatol Assoc 2009;120:419-28.

[54] Brown LC, Brown EA, Greenhalgh RM, Powell JT, Thompson SG; UK EVAR Trial Participants. Renal function and abdominal aortic aneurysm (AAA): the impact of different management strategies on long-term renal function in the UK EndoVascular Aneurysm Repair (EVAR) Trials. Ann Surg 2010;251:966-75.

[55] Lederle FA, Freischlag JA, Kyriakides TC, *et al.*; Open Versus Endovascular Repair (OVER) Veterans Affairs Cooperative Study Group. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA 2009;302:1535-42.

[56] de Bruin JL, Vervloet MG, Buimer MG, Baas AF, Prinssen M, Blankensteijn JD; DREAM Study Group.. Renal function 5 years after open and endovascular aortic aneurysm repair from a randomized trial. Br J Surg 2013;100:1465-70.

[57] Mohammed S, Kougias P, Mandviwala TM, Barshes NR, Pisimisis GT. Progression to stage 3 and 4 chronic kidney disease and risk factor stratification following endovascular aortic aneurysm repair. Vascular 2016;24:598-603.

[58] Sun Z, Stevenson G. Transrenal fixation of aortic stent-grafts: short- to midterm effects on renal function--a systematic review. Radiology 2006;240:65-72.

[59] Walsh SR, Boyle JR, Lynch AG, *et al*. Suprarenal endograft fixation and medium-term renal function: systematic review and meta-analysis. J Vasc Surg 2008;47:1364-70.

[60] Mell MW, Garg T, Baker LC. Under-Utilization of Routine Ultrasound Surveillance after Endovascular Aortic Aneurysm Repair. Ann Vasc Surg 2017;44:54-8.

[61] Schaeffer JS, Shakhnovich I, Sieck KN, Kallies KJ, Davis CA, Cogbill TH. Duplex Ultrasound Surveillance After Uncomplicated Endovascular Abdominal Aortic Aneurysm Repair. Vasc Endovascular Surg 2017;51:295-300.

[62] Bredahl KK, Taudorf M, Lönn L, Vogt KC, Sillesen H, Eiberg JP. Contrast Enhanced Ultrasound can Replace Computed Tomography Angiography for Surveillance After Endovascular Aortic Aneurysm Repair. Eur J Vasc Endovasc Surg 2016;52:729-34.

[63] Karthikesalingam A, Al-Jundi W, Jackson D, *et al.* Systematic review and meta-analysis of duplex ultrasonography, contrast-enhanced ultrasonography or computed tomography for surveillance after endovascular aneurysm repair. Br J Surg 2012;99:1514-23.

[64] Guo Q, Zhao J, Huang B, *et al*. A Systematic Review of Ultrasound or Magnetic Resonance Imaging Compared With Computed Tomography for Endoleak Detection and Aneurysm Diameter Measurement After Endovascular Aneurysm Repair. J Endovasc Ther 2016;23:936-43.

[65] Spanos K, Karathanos C, Athanasoulas A, *et al.* Renal function impairment in patients undergoing elective EVAR vs. elective ope repair during follow up period: a systematic review of the literature. Curr Vasc Pharmacol 2017;15:103-11.

[66] McCullough PA, Choi JP, Feghali GA, *et al*. Contrast-Induced Acute Kidney Injury. J Am Coll Cardiol 2016;68:1465-73.

[67] Briguori C, Donnarumma E, Quintavalle C, Fiore D, Condorelli G. Contrast-induced acute kidney injury: potential new strategies. Curr Opin Nephrol Hypertens 2015;24:145-53.

[68] Nijssen EC, Rennenberg RJ, Nelemans PJ, *et al.* Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomized, phase 3, controlled, open-label, non-inferiority trial. Lancet 2017;389:1312-22.

[69] Wang N, Qian P, Kumar S, Yan TD, Phan K. The effect of N-acetylcysteine on the incidence of contrast-induced kidney injury: A systematic review and trial sequential analysis. Int J Cardiol 2016;209:319-27.

[70] ACT Investigators. Acetylcysteine for prevention of renal outcomes in patients undergoing coronary and peripheral vascular an-

giography: main results from the randomized Acetylcysteine for Contrast-induced nephropathy Trial (ACT). Circulation 2011;124:1250-9.

[71] Wang N, Qian P, Yan TD, Phan K. Periprocedural effects of statins on the incidence of contrast-induced acute kidney injury: A systematic review and trial sequential analysis. Int J Cardiol 2016;206:143-52.

[72] Moore NN, Lapsley M, Norden AG, *et al.* Does N-acetylcysteine prevent contrast-induced nephropathy during endovascular AAA repair? A randomized controlled pilot study. J Endovasc Ther 2006;13:660-6.

[73] Kalimeris K, Nikolakopoulos N, Riga M, *et al.* Mannitol and renal dysfunction after endovascular aortic aneurysm repair procedures: a randomized trial. J Cardiothorac Vasc Anesth 2014;28:954-9.

[74] Moulakakis KG, Matoussevitch V, Borgonio A, Gawenda M, Brunkwall J. Evidence that statins protect renal function during endovascular repair of AAAs. Eur J Vasc Endovasc Surg 2010;40:608-15.

[75] Nikolic D, Banach M, Nikfar S, *et al.*; Lipid and Blood Pressure Meta-Analysis Collaboration Group. A meta-analysis of the role of statins on renal outcomes in patients with chronic kidney disease. Is the duration of therapy important? Int J Cardiol 2013;168:5437-47.

[76] Katsiki N, Athyros VG, Karagiannis A, Mikhailidis DP. Contrast-Induced Nephropathy: An "All or None" Phenomenon? Angiology 2015;66:508-13.

[77] Paraskevas KI, Giannoukas AD, Kotsikoris I, Mikhailidis DP. Contrast-induced nephropathy and the vascular patient. Angiology 2010;61:721-3.

[78] Uçar H, Gür M, Yildirim A, *et al.* Increased aortic stiffness predicts contrast-induced nephropathy in patients with stable coronary artery disease undergoing percutaneous coronary intervention. Angiology 2014;65:806-11.

[79] Spanos K, Matsagkas M, Giannoukas AD. Full Blood Count as a Potential Predicting Factor of Contrast-Induced Nephropathy After Endovascular Aortic Aneurysm Repair. Angiology 2016;67:882.

[80] Hosaka A, Kato M, Motoki M, Sugai H, Okubo N. Quantified aortic luminal irregularity as a predictor of complications and prognosis after endovascular aneurysm repair. Medicine (Baltimore) 2016;95:e2863.

[81] Paraskevas KI, Mikhailidis DP. Contrast-Induced Acute Kidney Injury in Patients Undergoing Carotid Artery Stenting: An Underestimated Issue. Angiology 2017;68:752-6.