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# Determinants of Acute Kidney Injury and Renal Function Decline After Endovascular Abdominal Aortic Aneurysm Repair

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**WHAT THIS PAPER ADDS**

This study analysed risk factors for the occurrence of acute kidney injury (AKI) and long-term renal function deterioration following endovascular aneurysm repair. Besides peri-operative complications this study identified the use of angiotensin II receptor blockers as a risk factor for AKI and the presence of renal artery stenosis as a risk factor for long-term renal function deterioration. Better understanding of these pathophysiological mechanisms could help to implement preventive strategies.

**Objective/Background:** Endovascular aneurysm repair (EVAR) may be associated with renal injury and more insight is needed into potential risk factors. The aim was to identify clinical, anatomical, and peri-procedural parameters as potential risk factors for the occurrence of acute kidney injury (AKI) and to evaluate chronic kidney disease (CKD) after EVAR.

**Methods:** A cohort of 212 consecutive patients who underwent elective EVAR for abdominal aortic aneurysm from January 2009 to October 2016 was included. A subgroup of 149 patients with 2 years follow-up was compared with a set of 135 non-operated aneurysm patients with smaller aneurysms (similar cardiovascular risk profile) to assess CKD. Primary outcomes were AKI (Acute Kidney Injury Network criteria) and CKD measured by estimated glomerular filtration rate (Kidney Disease Improving Global Outcomes guidelines). For AKI, candidate risk factors were identified by univariate and multivariate logistic regression analysis; for chronic renal function decline, risk factors were identified using Cox regression analysis.

**Results:** AKI occurred in 30 patients (15%). On multivariate analysis, the use of angiotensin II blocker (odds ratio [OR] 4.08, 95% confidence interval [CI] 1.38–12.07) and peri-operative complications (OR 3.12, 95% CI 1.20–8.10) were independent risk factors for AKI, whereas statin use was a protective factor (OR 0.19, 95% CI 0.07–0.52). EVAR resulted in a significant increase (23.5%) in the occurrence of CKD compared with the control group (6.7%; $p < .001$). On univariate and multivariate Cox regression the risk factors: aortic neck diameter (per mm increase) (hazard ratio [HR] 1.13, 95% CI 1.02–1.25), renal artery stenosis >50% (HR 2.24, 95% CI 1.05–4.79), and the occurrence of AKI (HR 2.19, 95% CI 0.99–4.85) were significant predictors of CKD.

**Conclusion:** This study identified use of angiotensin II blockers and peri-operative complications as risk factors for AKI. In addition, the problem of renal function decline after EVAR is highlighted, which indicates that prolonged protective measures (e.g., in those patients at high risk) over time are needed to improve patient outcomes.



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## INTRODUCTION

The occurrence of acute kidney injury (AKI) is associated with increased morbidity and mortality after vascular interventions. It has been demonstrated that after percutaneous coronary intervention and elective coronary bypass grafting, patients with AKI have a 20 fold increased risk of post-procedure mortality.[1,2]

In open abdominal infrarenal aortic surgery, post-operative renal dysfunction is also associated with increased in hospital mortality.[3] Furthermore, other studies have documented increased long-term mortality associated with the occurrence of AKI after cardiovascular procedures.[4,5] In aneurysm treatment, studies have focused on the differences in occurrence

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of renal dysfunction between open surgery and endovascular aneurysm repair (EVAR) and it is clear that both treatment approaches carry a risk of AKI.[3,6,7] After EVAR, a wide range of AKI incidences have been reported (3–19%), depending on the criteria used. However, more recent data using the Kidney Disease Improving Global Outcomes (KDIGO) guidelines suggested that about 15% to 20% of all EVAR patients develop AKI.[6,8,9] With a shift towards more endovascular procedures and, consequently, more re-interventions in aneurysm treatment, extra attention is being paid to the problem of EVAR related long-term renal function decline. A recent systematic review and meta-analysis on renal function after EVAR indicated that there is a significant deterioration in renal function in the follow-up period.[10] However, it is not clear whether the EVAR procedure itself or the cardiovascular risk profile of the patient and/or re-interventions is affecting long-term renal function. Compared with open aneurysm repair, EVAR is associated with fewer operative haemodynamic changes that have an impact on renal function. However, EVAR is accompanied by other potential insults to the kidneys, such as contrast material and microemboli.[11] Recent studies have described reduced renal function and poor cardiovascular reserve as significant risk factors for AKI after EVAR.[12,13] Other studies showed contradictory results with regard to whether suprarenal graft fixation might be associated with renal function decline.[9,14] In order to reduce the occurrence of AKI in endovascular aneurysm treatment more studies are needed to unravel its mechanism and elucidate specific risk factors. Moreover, additional knowledge is needed on potential decline in renal function during follow-up. Therefore, this study examined the occurrence of post-operative AKI after EVAR and evaluated risk factors associated with AKI. In addition, by using a control group of non-operated aneurysm patients, this study examined clinically relevant renal function decline during follow-up.

## MATERIAL AND METHODS

### *Study population*

This study was based on a retrospective analysis of a cohort of 212 consecutive patients who underwent elective EVAR for infrarenal aortic or iliac aneurysm from January 2009 to October 2016 at the HAGA Teaching Hospital, The Hague, The Netherlands. This retrospective study was approved by the local ethical committee of HAGA Hospital which issued a waiver for informed consent. Data were derived from electronic patient records, which included clinical data, imaging studies from the PACS image storage system, and laboratory values (collected as part of routine patient care). Patients treated for a ruptured abdominal aortic aneurysm, those treated with fenestrated/ branched or chimney stent grafts, and patients who were on pre-operative dialysis were excluded (Fig. 1).

### *Study outcomes*

The primary outcome of this study was occurrence of AKI in the post-operative period. Secondary outcome was details of clinically relevant renal function decline 2 years after the procedure. AKI was defined using Acute Kidney Injury Network criteria (KDIGO; www.kdigo.org). AKI (stage 1) is present when an abrupt (in 48 hours) reduction in kidney function results in an absolute increase in serum creatinine of $\geq$ 0.3 mg/dL (26 μmol/L) or serum creatinine rise of $>$ 1.5 fold from the reference value, known to have occurred within 1week. The highest level of creatinine within this period after EVAR was used to evaluate the presence of AKI.[15,16] Increase in serum creatinine of $>$ 2–3 fold compared with baseline is classified as stage 2 and more than threefold as stage 3 AKI. The evaluation of renal function during follow-up was based on estimated glomerular filtration rate (eGFR; mL/minute/1.73 $m^2$). eGFR was determined using the abbreviated Modification of Diet in Renal Disease study equation.[17] Clinically relevant renal function decline was defined using the KDIGO clinical practice guideline for the evaluation and management of chronic kidney disease (CKD); renal function is categorized in several grades, based on eGFR ($>$ 90 [G1], 60–89 [G2], 45–59 [G3a], 30–44 [G3b], 15–29 [G4], $<$ 15 [G5]). A significant decrease in eGFR is defined as a drop in GFR category accompanied by a $\geq$ 25% drop in eGFR from baseline.[18]

### *Study outcome assessment*

Before patients underwent EVAR, eGFR was determined pre-operatively (routinely performed and in most patients prior to contrast imaging studies). Thereafter, renal function was measured several times during hospital stay (data used for AKI outcome). After hospital discharge, patients visited the clinic at regular, protocolled time intervals for follow-up. To evaluate clinically relevant renal function decline eGFR values were compared in the follow-up period (at 2 years) to pre-operative eGFR. eGFR values were also collected in a control cohort consisting of patients with a small aneurysm. This control group of patients had an aortic diameter $>$ 3 cm and was periodically examined by ultrasound at the vascular outpatient clinic. For both EVAR and control patients, serial measurements of eGFR and follow-up for at least 2 years were required to be included in these analyses (comparing clinically relevant renal function decline). Patients and controls were identified during the same period.

The EVAR procedure using stent grafts with suprarenal fixation was performed in the operating theatre, usually under general anaesthesia. All EVAR procedures were performed percutaneously with minimal blood loss and only patients with a neck length $>$ 1 cm were considered for EVAR in this series. The details of the procedure have been described previously.[19] Patients with a pre-operative eGFR $<$ 45 were routinely pre-hydrated with 1 L 0.9% NaCl over 4 hours pre-operatively. All patients received 2 L lactated Ringer's solution in the first 24 hours post-operatively.

### *Risk factors*

Candidate risk factors for the development of AKI and clinically relevant renal function decline included patient

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