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Original paper

The risk of renal function deterioration in abdominal aortic stent graft patients with and without previous kidney function failure – an analysis of risk factors

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Abstract

Purpose: Kidney failure influences the treatment outcomes of abdominal aortic aneurysm (AAA). A prospective study of renal function before and after aortic stent-graft treatment was performed. Special attention was paid to the influence of preoperative kidney function as well as the impact of the radiological follow-up.

Material and methods: A total of 214 endovascularly treated AAA patients were included. In all cases, pre- and postoperative estimated glomerular filtration rate (eGFR) and serum creatinine were noted. Patients were prospectively followed up for a minimum of two years.

Results: The baseline eGFR was 69.38 ± 16.29 ml/min/1.73 m^2. Chronic kidney disease at baseline was noted in 29% of patients. In the direct postoperative period, acute kidney injury was identified in 8.4% of cases. Additional endovascular procedures within two years of observation were performed in 5.6% of cases, and over the two years of follow-up, in the study group from one to six angio-computed tomographic scans (angio-CT) per patient were performed. The mean eGFR value after the 24-month follow-up was significantly lower than the preoperative value. Among the factors influencing kidney function, an angio-CT during the same hospital stay of the primary stent-graft procedures was identified. The type of stent-graft, contrast volume during the primary procedure, need for reintervention, concomitant disease presence, and statin use did not show statistical significance.

Conclusions: Angio-CT followed by stent-graft implantation over a short time interval (within the same hospitalisation) significantly worsened renal function in the late follow-up and should be avoided in elective AAA cases.

Key words: renal failure, abdominal aortic aneurysm, contrast induced nephropathy, aortic stent-graft.

Introduction

The risk of contrast-induced nephropathy, as well as renal function worsening, is an important consequence of intravenous or intra-arterial contrast administration during diagnostic and therapeutic procedures [1-3]. A growing number of minimally invasive endovascular procedures and contrast-enhanced computed tomography (CTs), together with the aging population and the increasing number of diabetic patients, has resulted in large numbers of patients being at risk of renal failure development as well as renal function deterioration [1,2,4-6].

Among this very special group, in the aspect of the renal function evaluation and follow-up, are patients with the abdominal aortic aneurysm (AAA), who are qualified to endovascular aneurysm treatment. In this clinical scenario,

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A Study design · **B** Data collection · **C** Statistical analysis · **D** Data interpretation · **E** Manuscript preparation · **F** Literature search · **G** Funds collection

proper renal function has a great influence on the clinical outcome and the long-term results [6-8]. Exposure of the vascular patient with renal function impairment to contrast medium during the aortic stent-graft implantation procedures potentially worsens final outcomes and increases the risk of renal function deterioration (in particular, if the postoperative follow-up is based on repeated angio-CT examinations).

However, renal function impairment is also important in open vascular reconstruction procedures; according to the literature, renal failure is a significant factor related to mortality and morbidity associated with open surgery for AAA [9-11]. Despite the lack of exposure to contrast medium, open AAA surgery seems to be related to a much higher acute renal failure rate than endovascular aneurysm repair [8-11]. Comparing the two methods of AAA treatment, Wald *et al.* analysed the clinical courses of a total of 6516 patients undergoing open or endovascular elective repairs. Endovascular aortic repair (EVAR) procedures were associated with lower odds of acute renal failure and acute renal failure requiring dialysis than in open surgery patients (in this study, all patients with initial end-stage renal disease were excluded, and the rate of the postoperative renal failure was 6.7% in the total population) [12]. Al Adas *et al.* suggested that open aneurysm repair was related to a 1.6 times greater likelihood of the development of immediate postoperative acute kidney injury, compared with EVAR. In another study, Tang *et al.* noted a 29% rate of acute renal failure after open surgery, Bang *et al.* suggested a rate of 18.8% of this complication, and Dariane *et al.* reported 24% [9,11,13].

In both groups (open AAA surgery or EVAR), the presence of the preoperative renal function deterioration can significantly influence the treatment outcomes and represents an important factor related to a greater possibility of renal failure development in the post-operative period [11,14]. Another significant factor related to the risk of renal function worsening is further exposure to contrast medium, which is potentially important in the group of patients requiring follow-up studies based on contrast CT examinations (now an important component of the follow-up protocol in many medical centres) [11].

In this paper, a prospective assessment of renal function before and after endovascular treatment was performed. Special attention was paid to the influence of the preoperative kidney functional status, as well as of follow-up studies, on long-term proper renal function maintenance.

Material and methods

A group of 214 patients with AAA was evaluated. All of the patients were qualified for abdominal aortic stent-graft placement. There were 178 men and 36 women. The median age in the male population was 73 years (range 58-92) and 72 years in the female population (range 54-85). The size of the AAA ranged from 44 to 107 mm, and in the study, only non-ruptured AAA patients were evaluated. In 134 cases stent-grafts with suprarenal fixation (Zenith; COOK) were used, and in the other 80 cases an infrarenal fixation (Excluder, GORE) was applied; the choice of the aortic stent-graft was based on the vessel anatomy. In 70% of the patients, arterial hypertension was present, and in 61.6%, ischaemic heart disease was previously diagnosed (including 66 patients after previous heart infarction). In the study population, 10.2% suffered from atrial fibrillation, in 10.2% heart valve disease was noted, in 9.3% diabetes was recognised, and in 6.5% stroke in the past was reported. Of the patients, 10.2% suffered from chronic respiratory diseases, and in 2.3% gastroduodenal ulcer history was present. The median body mass index (BMI) in the female population was 27.14 (range 19.93-34.6), and in the male population it was 27.43 (range 14.53-40.74). Two patients died perioperatively and were excluded from the study; in both cases, no acute renal failure after surgery was observed, and the reasons for death were heart infarction and circulatory failure. In all of the patients, preoperative kidney function evaluation, based on estimated glomerular filtration rate (eGFR) and serum creatinine, was performed. Patients with renal artery stenosis, as well as end-stage renal disease, were excluded from the study. Another exclusion criterion was unilateral or bilateral kidney hypoplasia or aplasia. In all of the patients, during the evaluation and qualification process, angio-CT examination was performed preoperatively. Before stent graft implantation, in all patients of the study group, which fulfil AAA treatment criteria (symptomatic aneurysm, fast aneurysm growth, size > 5.5 cm), a CT angiogram examination was performed with an assessment of the abdominal aorta, iliac arteries, and access vessels. In the qualification process the anatomical criteria as well as the risk of surgery complications were taken into consideration, and all of the patients underwent cardiological consultation before the final decision. In the patients with severe renal function impairment a nephrological consultation was always requested. According to the renal protection protocol in our centre, in the patents with primary known renal function impairment, the special preparation before contrast administration during diagnostic (e.g. angio-CT) and therapeutic procedures were implemented. The protocol was based in the periprocedural hydration with crystalloids (1 ml/kg/h) 12 hours before and 12-24 hours after the procedure, the use of N-acetylcysteine, 1200 mg twice a day, and suspension of all potentially nephrotoxic drugs (including non-steroid anti-inflammatory drugs). The protocol was supported by daily creatinine and diuresis monitoring as well as periprocedural hypotension treatment and multiple procedure avoidance.

In 125 of the patients (58.5%), the CT angiogram was performed before hospitalisation (at least two weeks before) and in 89 patients (41.5%) during the same hospitalisation (after admission to the hospital) but before stent-graft implantation. Concerning the patients undergoing CT angiogram examination during the same hospitalisation (includ-

ing treatment procedure) the mean time interval between the CT and procedure was 3.6 days in the range from one to nine days. In all cases, the stent-graft implantations were performed under fluoroscopy with the contrast administration according to the standard protocol. Non-ionic contrast was used, and the volume of contrast used was recorded. All of the patients received dual antiplatelet therapy perioperatively and six weeks after, followed by lifelong aspirin administration. In 70% of the patients, statins were administered (because of concomitant disease presence): atorvastatin, simvastatin, and rosuvastatin were used. After the procedure (no perioperative deaths were reported), the presence of perioperative acute renal failure, defined as an increase of ≥ 50% and/or ≥ 0.3 mg/dl from preprocedural serum creatinine over 48 hours postoperatively, was reported [15,16].

Patients were followed up in the outpatient department; the follow-up was based on repeated US and angio-CT control. Angio-CT was routinely performed three months after the procedure, and the decision concerning the next follow-up CT was based on the three-month CT results, including aneurysm sack shrinking or expansion, as well as potential endoleak presence or suspicion (type II mostly). In some of the obese patients, the need for a CT-based approach was related to the lack of the proper aorta visibility on US examination during the subsequent follow-up examination. All of the patients were prospectively followed up for a minimum of two years, according to the standard protocol, and the number of contrast CT examinations and the number of patients requiring reintervention was recorded. In all of the patients, eGFR value after 24 months of follow-up was noted, and factor analysis influencing potential kidney function worsening was performed. During the last follow-up visit in the study (24 months after stent-graft implantation), US examination of both kidneys with kidney size measurements (B-mode) was performed.

In this analysis, preoperative kidney function was evaluated, including the preoperative presence of chronic renal failure. Other studied factors were the volume of contrast administered during the primary stent-graft procedure, the performance of angio CT during the same hospitalisation as the stent-graft procedure, the number of angio-CT procedures performed during the follow-up phase, the type of stent-graft fixation (suprarenal or subrenal), the need for reintervention, the presence of concomitant disease, the use of statins in the perioperative period, and the long-term treatment.

In the statistical analysis, the Statistica software, version 13.1, was used. The statistical tests were the *t*-test and Spearman's correlation, and for the evaluation of the importance of several risk factors to the final eGFR levels, ANOVA univariate analysis was performed. The results were considered significant with $p < 0.05$.

Results

In the analysed cohort, the baseline creatinine level was 1.05 ± 0.28 mg/dl. The baseline eGFR was 69.38 ± 16.29 ml/min/1.73 m^2. Chronic kidney disease, defined as eGFR ≤ 60 ml/min/1.73 m^2 at baseline, was noted in 29% of the patients. In the early postoperative period during the hospital stay, acute kidney injury was identified in 8.4% of cases, and all of the patients were treated conservatively without the need for dialysis during the hospital stay. In none of these patients was coverage of one or both renal arteries noted. In the follow-up period, one patient required dialysis due to renal function worsening in the late follow-up phase; this patient had already presented with chronic kidney failure before the primary procedure (without acute kidney injury during postoperative hospital stay). Over the 24-month follow-up period, from one to six angio-CT examinations were performed on each patient. The need for additional endovascular procedures within two years of follow-up was noted in 5.6% of cases. The mean eGFR value after 24 months of follow-up was 62.09 ± 18.5 ml/min/1.73 m^2 and was significantly lower than preoperatively (Figure 1). The worsening of the glomerular filtration rate involved not only the patients with primary present chronic kidney failure (eGFR ≤ 60 ml/min/1.73 m^2) but also patients with normal renal function preoperatively (Figure 2A-B).

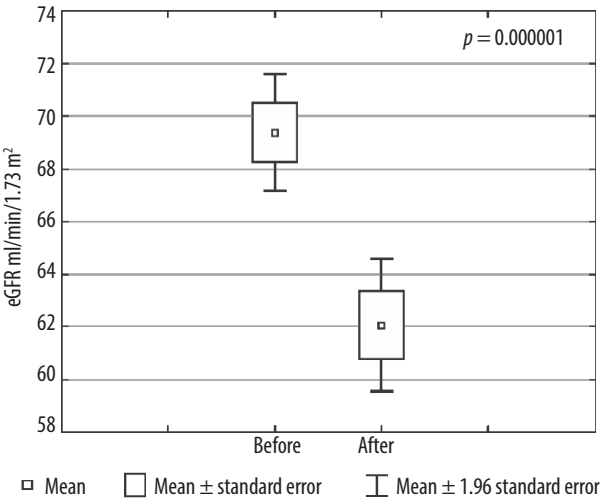

Figure 1. Estimated glomerular filtration before stent-graft implantation and after 2 years of follow-up in the whole group of abdominal aortic aneurysm patients ($p = 0.000001$, *t*-test)

In the statistical analysis, we did not find a relationship between the presence of concomitant diseases, including arterial hypertension, ischaemic heart disease, and diabetes, and worsening of renal function (ANOVA univariate). Additionally, the type of implanted stent-graft (infra-renal or supra-renal fixation) did not influence renal function worsening. The use of statin treatment perioperatively, as well as during long-term follow-up, did not significantly influence GFR changes between the statin and no-statin groups. There were also no correlations between the initial procedure (stent-graft placement), contrast medium volume, and final eGFR value. Concerning other exposures to contrast medium, the performance of the angio-CT examination followed by stent-graft placement during the

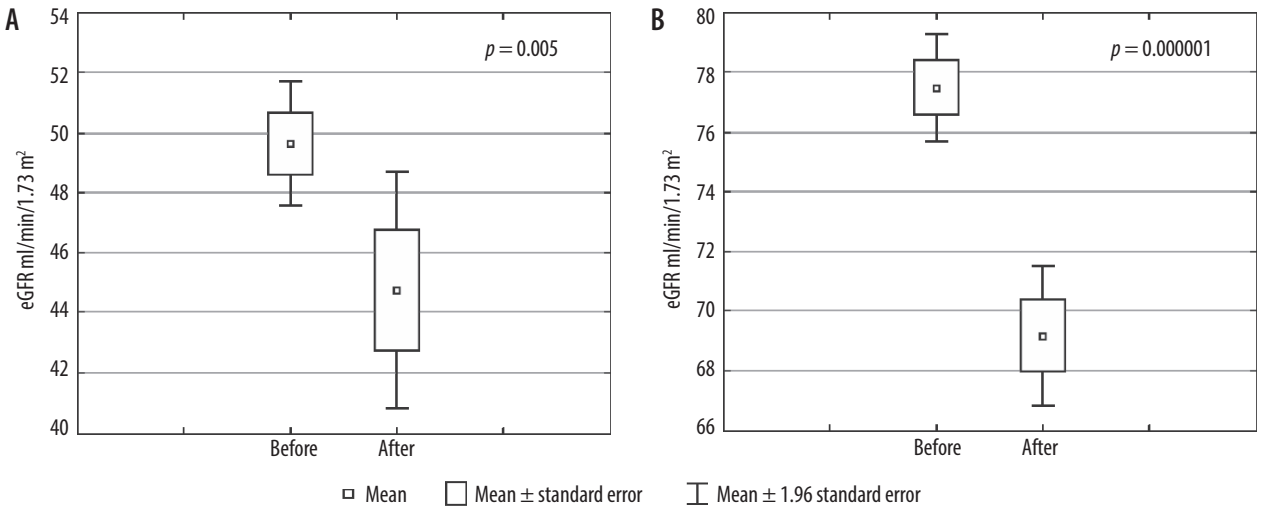

Figure 2. Estimated glomerular filtration (eGFR) before stent-graft implantation and after 2 years of follow-up in patients with chronic renal failure **(A)** (GFR ≤ 60 ml/min/1.73 m²) preoperatively ($p < 0.005$) or without chronic renal failure **(B)** (GFR > 60 ml/min/1.73 m²) ($p = 0.000001$), *t*-test evaluation

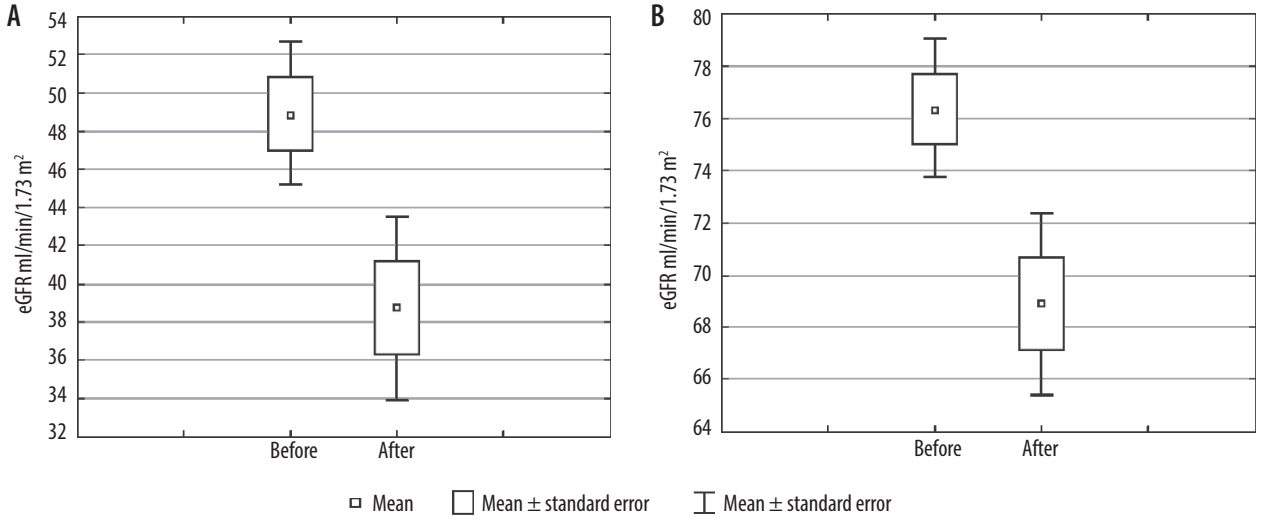

Figure 3. Estimated glomerular filtration (eGFR) before stent-graft implantation and after 2 years of follow-up in the patients with renal failure **(A)** (GFR ≤ 60 ml/min/1.73 m²) and angio-computed tomography (CT) performed before stent-graft placement during the same hospitalisation ($p = 0.000012$, *t*-test); **B)** eGFR before stent-graft implantation and after 2 years of follow-up in the patients with no renal failure (GFR > 60 ml/min/1.73 m²) and CT angiogram performed before stent-graft placement during the same hospitalisation ($p = 0.0002$, *t*-test)

same hospitalisation turned out to be a factor of statistical importance in both the chronic renal failure (Figure 3A) and no chronic renal failure (Figure 3B) groups.

As previously mentioned, in all of the patients, CT angiography was performed at least once postoperatively (three months after the procedure). The number of the CT angiograms ranged from one to six. Looking for the correlation between the number of CT angiogram procedures performed and the differences between the initial and 24-month follow-up eGFR, no statistically significant relationship was observed (Figure 4). One important explanation for this fact could be an observation concerning the reduced number of CT examinations in patients with initial renal failure (Figure 5); in this patient group, in the later phase of the follow-up, the CTs were supplemented by ultrasound examination (if no clinical need for a CT-based approach was noted). In the patients without initial renal failure, there was no correlation between the number of CTs and the eGFR value.

The performance of an additional endovascular procedure over the two-year follow-up period (12 patients required reintervention – 5.6%) did not influence the final eGFR value after 24 months of follow-up.

When analysing the kidney morphological criteria (assessed at the 24-month follow-up visit), the correlation between the kidney length and 24-month follow-up eGFR was observed only in patients with initially normal renal function (Figure 6). In patients with chronic renal failure, such observations were not confirmed at the last follow-up visit – the size of the kidney did not correlate with the eGFR value in the patients with impairment of renal function at the beginning of the study.

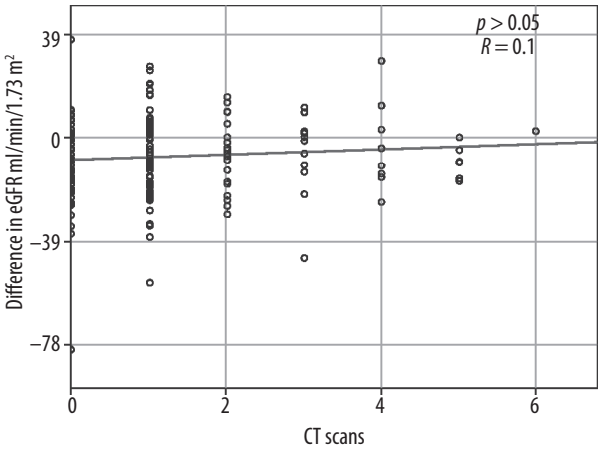

Figure 4. Estimated glomerular filtration rate (eGFR) difference between preoperative eGFR value and 24-month follow-up eGFR assessment in relationship to the number of angio-computed tomography procedures performed in the follow-up phase ($p > 0.05$)

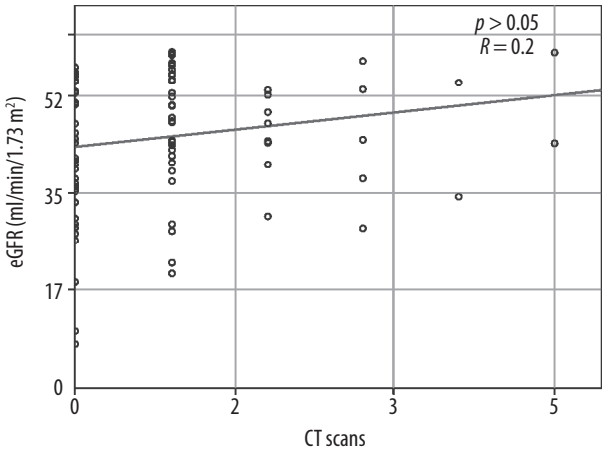

Figure 5. The number of computed tomography scans performed after stent-graft implantation in patients with initial renal failure and estimated glomerular filtration after 24 months of follow-up ($p > 0.05$, $r = 0.2$, Spearman's correlation)

Discussion

Development of minimally invasive procedures in vascular surgery, as well as common use of diagnostic procedures with contrast medium, has made renal function maintenance a significant problem in contemporary medicine. In the analysed cohort, according to the initial pre-procedural assessment, the rate of impaired renal function was 29%, and in the majority of the patients, significant comorbidities were present. Over the two-year follow-up period, a decrease in eGFR was observed in the renal failure group, as well as in the normal renal function group. This outcome suggests the risk of renal function deterioration also in patients without previous renal function deterioration.

Looking at the peri- and postoperative renal function worsening in vascular patients, acute kidney injury, as well as chronic renal failure, should be mentioned. The literature has described the rate of acute renal failure related to contrast administration as 1-13%, depending on the treated population [1-4]. Despite development of new contrast media, the number of kidney complications remains relatively high, and deterioration of renal function after contrast-based radiological or endovascular procedures must be considered. Another problem related to contrast administration is CT angiogram follow-up studies, as well as re-performance of procedures. Although acute renal injury is less likely to occur after endovascular aneurysm treatment, the EVAR procedure and postoperative follow-up of stent-graft patients can lead to significant, often delayed worsening of renal function [11]. In terms of the postoperative mortality and morbidity, in the long-term follow-up, not only potential endoleak presence but also renal function should be monitored.

Among the known risk factors for acute renal failure in patients undergoing contrast administration are dehydration, diabetes, concomitant medical treatment with metformin, ACE inhibitors, non-steroidal anti-inflammatory drugs, and certain antibiotics [17-21]. In AAA patients treated endovascularly, haemodynamic instability, blood transfusions, poor cardiac reserve, duration of the procedure, as well as the contrast volume used, and previous renal failure should also be mentioned [9,11,12,23].

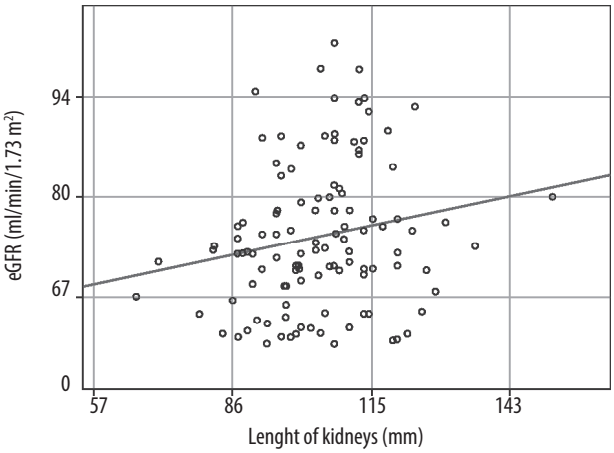

Figure 6. Estimated glomerular filtration after 24 months of follow-up and length of kidneys in patients without initial renal failure ($p = 0.03$, $r = 0.19$, Spearman's correlation)

Looking for factors responsible for acute renal failure defined in our population as creatinine level increase of 0.3 mg/dl or 50% creatinine increase from the initial value within 48 hours of the procedure, we did not find any significant ones except for 65% of these cases occurring in patients with previous renal function impairment. The type of implanted stent graft, contrast volume used, concomitant disease presence, and medication used did not influence AKI frequency in our study; however, as mentioned in the material description, patients with end-stage renal disease were excluded from the study. None of the treated patients required dialysis due to AKI during hospitalisation.

Chronic renal failure progression seems to be even more difficult to avoid in patients exposed to contrast me-

dium if repeated procedures are needed [11]. In our cohort, in both groups with and without previous renal function impairment, continuous eGFR decrease was noted. Seeking the most significant factor, angio-CT examinations followed by stent-graft placement during the same (initial) hospitalisation were critical. This important observation concerned both groups with and without renal failure. In light of this finding, in patients qualified for AAA elective endovascular treatment, preoperative angio-CT should be planned before the admission dedicated to stent-graft implantation. The time interval between the CT angiogram examination and procedure performance in both groups (with and without renal failure) should be planned.

The presence of concomitant diseases, including diabetes (present in our cohort only in 10.2%), statin use, reperformance of procedures, the type of stent-graft (infra- or suprarenal fixation), and primary procedure contrast volume, did not show statistical significance in terms of chronic renal failure development. In the follow-up period, at least one CT angiogram was performed in each patient (the number of CT studies within 24 months of follow-up ranged from one to six). Repeated CT examinations did not influence renal failure occurrence if proper renal function was initially observed. According to the observation protocol, the time interval between CT studies was 6-12 months and was shortened if endoleaks or aneurysm sack expansion was present. In the patients with primary injured kidneys, attention was paid to the need for US-based follow-up, which significantly decreased the number of the CT examinations performed in this group after the initial three-month follow-up examination.

De Bruin, in post hoc analysis of data from the DREAM trial (Dutch Randomised Endovascular Aneurysm Management) found that renal function five years after open aneurysm repair and EVAR for AAA did not differ between the two groups, and the surgical procedure did not accelerate the loss of renal function [24]. Brown *et al.* observed similar results in a study based on the UK EndoVascular Aneurysm trial with a 3.6-year follow-up period. In both groups (open and endovascular AAA repair), the renal function deterioration was slow with little evidence to suggest any long-term difference between treatment with EVAR or open surgery [25]. Other investigators did not agree with this statement. Al Adas, in a study based on more than 700 AAA patients, suggested that renal function decline in late follow-up is more common in patients treated with aortic stent-graft implantation [11]. Milis *et al.*, comparing the effects of open and endovascular AAA repair on long-term renal function, confirmed that renal function decline was significantly more common in the endovascular arm than after open surgery [26].

An interesting observation also comes from morphological kidney assessment. In the reported material, there was no correlation between the size of the kidneys and 24-month eGFR value in patients with initial renal failure, suggesting the limited value of the kidney morphology evaluation (and its changes) in patients with renal function impairment according to laboratory assessment. In contrast to this observation, the reduction in the kidney size of the patients with primary proper renal function was a potential marker for renal function impairment and should be monitored during follow-up studies because it has the potential to select patients at risk of chronic renal failure if repeated contrast studies are performed.

Conclusions

In patients qualified for abdominal aortic endovascular treatment, especially those with chronic renal failure, precise renal function assessment, as well as renal function protection, should always be considered. Angio-CT followed by stent-graft implantation in a short time interval (within the same hospitalisation) significantly decreased renal function in late follow-up and should be avoided in elective AAA cases.

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Conflict of interest

The authors report no conflict of interest.

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