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Contrast Induced Nephropathy and Long-term Renal Decline After Percutaneous Transluminal Angioplasty for Symptomatic Peripheral Arterial Disease

T.A. Sigterman [a,*], **A.G. Krasznai** [a], **M.G. Snoeijs** [a], **R. Heijboer** [a], **G.W.H. Schurink** [b], **L.H. Bouwman** [a]

[a] Atrium Medical Center Parkstad Heerlen, Heerlen, The Netherlands
[b] Maastricht University Medical Centre, Department of Surgery, Maastricht, The Netherlands

WHAT THIS PAPER ADDS

This prospective cohort study demonstrates for the first time that endovascular procedures for symptomatic peripheral arterial disease are frequently complicated by contrast induced nephropathy (CIN). Patients developing CIN experience significantly more cardiovascular events and death. The authors trust the current report leads to more awareness and increased research for potential alternatives that completely abolish contrast administration during endovascular interventions.

Objective/background: Administration of iodinated contrast media during endovascular procedures for peripheral arterial disease (PAD) may cause contrast induced nephropathy (CIN). The aim of the present study was to establish the incidence of CIN after these procedures and to study its association with long-term loss of kidney function, cardiovascular events, and death.

Methods: Consecutive patients first presenting with symptomatic PAD (Rutherford classification II–VI) who were treated with an endovascular procedure were included in this prospective observational cohort study. CIN was defined as >25% increase of serum creatinine concentration from baseline at 5 days after the intervention.

Results: Some 337 patients were included with a mean estimated glomerular filtration rate (eGFR) of 67 mL/minute. Thirteen percent (95% confidence interval [CI] 9–16) of these patients developed CIN after endovascular interventions for PAD. One year after treatment, eGFR was reduced by 12.4 mL/minute (95% CI 8.6–16.2) in patients with CIN compared with 6.2 mL/minute (95% CI 4.9–7.0) in patients without acute kidney injury ($p < .01$). After correction for potential confounders, CIN was associated with a 7.8 mL/minute (95% CI 4.5–11.0) reduction of eGFR at 1 year after endovascular intervention ($p < .01$). Furthermore, patients with CIN were at increased risk of long-term cardiovascular events and mortality.

Conclusion: Exposure to iodinated contrast media during endovascular procedures for symptomatic PAD frequently results in CIN. Patients with CIN are at increased risk of long-term loss of renal function, cardiovascular events, and death.

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INTRODUCTION

Worldwide, >200 million patients are affected by peripheral arterial disease (PAD). Patients may present without symptoms, with intermittent claudication and with rest pain or tissue loss due to critical limb ischemia (CLI). Since the 1980s, endovascular interventions have emerged as the first-choice treatment in symptomatic PAD. As a result, increased use of contrast media in diagnostic and interventional procedures is observed. In particular, patients with more complex problems or more severe stages of PAD are likely to undergo several angiograms and endovascular interventions in their lifetime.

Contrast induced nephropathy (CIN) is defined as an increase in serum creatinine by >25% or 44 μmol/L within the first 3 days of the procedure.[1,2] CIN characteristically manifests 3 days after administration of the contrast medium, with a peak in renal function decline 3–5 days after contrast exposure.[3] Besides surgery and hypotension, administration of radiocontrast is the third most common cause of acute kidney injury.[4] Many studies show that patients developing CIN have a greater risk of prolonged

* Corresponding author.
E-mail address: timsigterman@gmail.com (T.A. Sigterman).

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hospitalization, cardiovascular events, and death.[5] Furthermore, when patients with acute kidney injury require dialysis, mortality is higher compared with those not requiring dialysis. Owing to an increasingly elderly patient population the incidence of CIN is likely to increase rapidly.

Comprehensive literature is available regarding CIN following coronary intervention, with an incidence ranging from 11.3% to 14.5%.[6] However, limited data are available regarding CIN after endovascular interventions in patients with symptomatic PAD. Only one small retrospective study investigated the incidence of acute kidney injury in patients treated with balloon angioplasty for femoropopliteal PAD.[7] In the latter study patients with renal failure were treated with 10 hours of hydration and forced diuresis with furosemide medication. This medication has been proven to be nephrotoxic; nowadays, international guidelines discourage its administration on the day of the intervention. Finally, owing to the wide range of definitions available for acute kidney injury following contrast exposure, comparison of the data from published studies is difficult.

To the best of the authors' knowledge limited literature is available on CIN in patients with symptomatic PAD treated by endovascular interventions. The aim of the present study was to establish the incidence of CIN after peripheral endovascular interventions and to study its association with long-term loss of kidney function, cardiovascular events, and death. The hypothesis of the present study is that patients with CIN have greater renal decline following endovascular interventions than patients without CIN.

METHODS

Study design

A prospective observational cohort study design was used including all patients with intermittent claudication or CLI who were treated by endovascular interventions for PAD. Inclusion was at a large teaching hospital in the south of the Netherlands from 1 May 2013 to 15 February 2014. The study was approved by the local institutional review board and registered with the following code (TC = 4921). Patients with end stage renal disease (estimated glomerular filtration rate [eGFR] < 15 mL/minute), without pre-operative serum creatinine measurements, patients receiving computed tomography angiography for diagnostic work up, and patients who received additional iodinated contrast media during the first year of follow up were excluded from analysis. Serum creatinine concentration was measured before the intervention, on the fifth day after the intervention, at 1 month (±2 days) and 1 year (±1 month) after the intervention. GFRs were estimated according to the chronic kidney disease epidemiology collaboration (CKD-EPI) formula. CIN was defined as a >25% increase of serum creatinine concentration 5 days after the intervention when compared with baseline value. Patients with and without CIN were prospectively observed for changes in GFR, cardiovascular events, and death.

Variables

Vital sign data closest in time before (but within 12 months of) the index date were used for analyses. Major adverse cardiovascular events were considered to include cardiovascular mortality, myocardial infarction, stroke, and congestive heart failure. Congestive heart failure was defined as an ejection fraction <40%.[8] Arterial hypertension was assumed when measurement of arterial blood pressure exceeded 140 mmHg (systolic) and/or 90 mmHg (diastolic) on at least two different time points, or if the patient was on antihypertensive medication.[9] Hyperlipidemia was defined by a total serum cholesterol level >5 mmol/L, serum high density lipoprotein cholesterol level <1 mmol/L, or serum triglyceride level >2 mmol/L.[9] Diabetes mellitus was defined by fasting blood sugar levels >120 mg/dL or HbA1c level >6%. In addition, the presence of diabetes mellitus was assumed if the patient received any hypoglycemic drugs.[9] Current smoking habits were divided into either smoking or non-smoking.[9] Anemia was defined as a hemoglobin concentration <8.1 mmol/L in men and <7.5 mmol/L in women.[10] Hereditary cardiovascular disease was defined as a positive family history of cardiovascular disease for first-degree relatives.

Pre-operative workup

All patients underwent ankle brachial pressure index (ABPI) measurement, duplex arterial mapping, and contrast enhanced magnetic resonance angiography. All patients were evaluated in a multidisciplinary setting (vascular surgeons, interventional radiologists, and vascular technicians). All patients received statin and antiplatelet therapy. Patients included in the present study were treated according to national and international guidelines on cessation of nephrotoxic medication and pre-procedural hydration indication.[11] Nephrotoxic drugs included non-steroidal anti-inflammatory drugs, diuretics, angiotensin converting enzyme inhibitors, metformin, digoxin, sotalol, lithium, and colchicine. Pre-procedural hydration was used for patients with eGFR <45 mL/minute/1.73 m^2 or eGFR <60 mL/minute/1.73 m^2 with additional risk factors (diabetes mellitus, hypotension, congestive heart failure, age >75 years, anemia). The study population was routinely seen in the outpatient clinic for evaluation of symptoms, ABPI, and duplex examination 4 weeks after the endovascular procedure.

Endovascular procedures

All endovascular procedures were performed by experienced physicians in an endovascular suite equipped with a Philips Allure Xper FD20 (Philips, Eindhoven, the Netherlands) on a carbon fiber movable interventional table. During these endovascular interventions, two types of contrast agents were used: Xenetix 300 (Geurbet, Gorinchem, the Netherlands) in patients requiring nephroprotection or with a known allergy for contrast, and Omnipaque 240 mg for all other patients (GE Healthcare, Pittsburgh, PA, USA).