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Combined Impact of Chronic Kidney Disease and Contrast Induced Acute Kidney Injury on Long-term Outcomes in Patients with Acute Lower Limb Ischaemia

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WHAT THIS PAPER ADDS

The findings emphasise the importance of the interaction between chronic kidney disease (CKD) and contrast induced acute kidney injury (CI-AKI) in early risk stratification. Any amount of peri-procedural CI-AKI in this highly susceptible subgroup with more extensive comorbidities predisposes them to long-term adverse events, including major adverse limb event (MALE) and death. In efforts to identify ways of decreasing the incidence of peri-operative CI-AKI, targeting the high risk group with CKD is becoming more important. Also the identification of CI-AKI survivors with CKD represents an important opportunity to improve care and outcomes in this population.

Introduction: Acute lower limb ischaemia (ALI) is the sudden onset of decreased arterial perfusion with imminent threat to limb viability. Contrast induced acute kidney injury (CI-AKI) is one of the complications that increases mortality in patients who undergo contrast imaging in coronary procedures. The goal of this study is to evaluate the impact of chronic kidney disease (CKD) and CI-AKI on long-term clinical outcomes in patients with ALI undergoing lower limb revascularisation.

Methods: A total 1017 consecutive patients with acute lower limb ischaemia who were admitted between July 1, 2006, and January 1, 2017, were retrospectively reviewed. Patients who had end stage renal disease, those who had end stage heart and malignant disease and died within 7 days of limb revascularisation, and those who did not undergo angiography were excluded. Thus 546 patients were included in the final analysis. Patients were classified as with or without CKD and were then subdivided according to the presence or absence of the development of CI-AKI, defined as an increase in serum creatinine of $\geq$0.5 mg/dL or by $\geq$25% from the baseline value within the first 72 h after contrast exposure. The primary end point was all cause mortality and secondary major adverse limb event (MALE).

Results: Both CKD and CI-AKI were associated with the highest rate of all cause mortality (chi square = 55.77, d.f. = 1, $p < .01$, log rank test) and MALE (chi square = 79.07, d.f. = 1, $p < .01$, log rank test). The presence of CKD and CI-AKI were significant risk factors associated with long-term all cause mortality (HR = 2.61, $p < .01$) and MALE (HR = 2.87, $p < .01$).

Conclusion: In patients with ALI undergoing lower limb revascularisation, both CKD and CI-AKI were significantly associated with poor long-term outcomes compared with either CKD or CI-AKI alone. Further studies are required to assess this association and to confirm the combined effect of CKD and CI-AKI on long-term clinical outcomes.

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INTRODUCTION

Acute lower limb ischaemia (ALI) is the sudden onset of decreased arterial perfusion with an imminent threat to limb viability.[1] Patients with ALI represent a high risk cohort[2] in need of complex revascularisation procedures that are often associated with a significant rate of complications.

Chronic kidney disease (CKD) has been associated with increased morbidity and mortality after coronary revascularisation.[3] In contrast there are only limited data regarding

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the influence of CKD in patients undergoing limb revascularisation.[4,5] Contrast induced acute kidney injury (CI-AKI) is one of the complications in patients who are undergoing angiography prior to lower limb revascularisation. This group of patients is at higher risk for CI-AKI than those who undergo elective procedures, because of the inability to provide adequate renal protective therapy. Indeed, small changes in serum creatinine (sCr) after surgery or interventional procedures are recognised as strong independent predictors for short and long-term mortality.[6]

Several studies have shown that AKI is associated with a higher incidence of long-term morbidity such as progression to CKD and development of end stage renal disease (ESRD).[7,8] In addition, long-term survival in patients with AKI is significantly decreased.[9,10] Increasing evidence has shown that CKD and AKI are associated with poor outcomes in patients with limb ischaemia.[11] Although there is evidence about the occurrence of AKI and poor outcome in patients after lower extremity revascularisation,[11,12] the clinical significance of CI-AKI episodes with respect to clinically relevant long-term outcomes has not been yet well studied. Furthermore studies assessing the impact of renal dysfunction on outcomes in patients with ALI, and the combined effect of CKD and CI-AKI on outcomes has not been well defined.

The goal of this study is to evaluate the impact of CKD and CI-AKI on long-term clinical outcomes in patients with ALI undergoing lower limb revascularisation.

METHODS

Patient population

This is retrospective single centre cohort study, with patients from the registry who were followed prospectively. Between July 1, 2006, and January 1, 2017, a total of 1017 consecutive patients with acute lower limb ischaemia who were admitted to the hospital were recruited to the study. Lower extremity ALI was defined as the sudden onset or deterioration of arterial perfusion of one or both lower extremities causing a threat to limb viability from an arterial thromboembolism, in situ thrombosis of the native vessels, or thrombosis of a previous bypass graft or stent. The severity of ALI was determined based on the Rutherford classification.[1] At the clinic there is a clear protocol for treating ALI. Patients with ALI and no previous signs and symptoms of lower extremity atherosclerotic disease and in the presence of cardiac disease that might cause thromboembolism undergo an emergency surgical procedure without preceding angiography. Patients who have clinical findings of thrombosis and previous signs of chronic limb ischaemia, thrombosed graft, or stent undergo angiography. The type of intervention was selected by the vascular surgeon based on the angiographic (multislice computed tomography (MSCT) or conventional) and intra-operative finding of the affected lower limb.

Twenty-six patients who had end stage renal disease (eGFR$<$15 mL/min/1.73 m^2) on admission were excluded; those who had end stage heart and malignant disease and died within 7 days of limb revascularisation (n = 38) and those who did not undergo angiography (n = 407) were also excluded. Thus, 546 patients were included in the final analysis (Fig. 1). All patients did not receive the pretreatment and renovascular protection strategies before angiography such as *N*-acetylcysteine, intravenous hydration with 0.9% saline or discontinuation of nephrotoxic medication because of the other comorbid conditions.

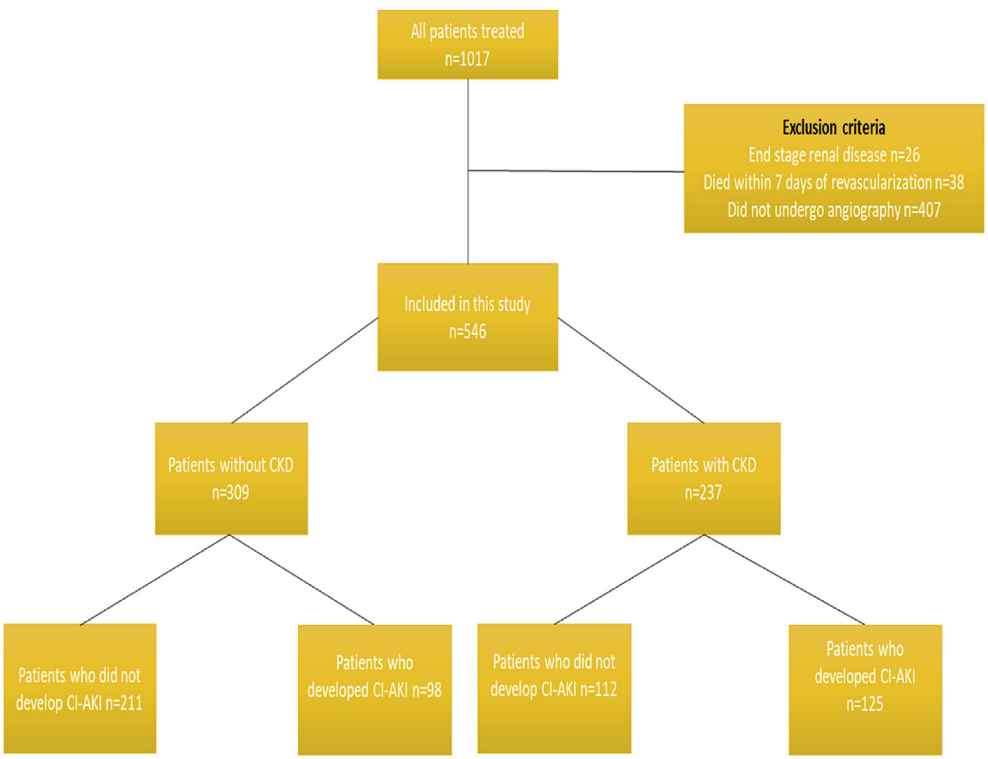

Figure 1. Flow diagram.

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