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Transcatheter aortic valve implantation in patients with pre-existing chronic kidney disease☆

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ABSTRACT

Background: We investigated the effect of chronic kidney disease (CKD) on morbidity and mortality following transcatheter aortic valve implantation (TAVI) including patients on haemodialysis, often excluded from randomised trials.

Methods and results: We performed a retrospective post hoc analysis of all patients undergoing TAVI at our centre between 2008 and 2012. 118 consecutive patients underwent TAVI; 63 were considered as having (CKD) and 55 not having (No-CKD) significant pre-existing CKD, (defined as estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2). Chronic haemodialysis patients (n = 4) were excluded from acute kidney injury (AKI) analysis. Following TAVI, in CKD and No-CKD patients respectively, AKI occurred in 23.7% and 14.5% (p = 0.455) and renal replacement therapy (RRT) was necessary in 8.5% and 3.6% (relative risk (RR) [95% CI] = 2.33 [0.47–11.5], p = 0.440); 30-day mortality rates were 6.3% and 1.8% (p = 0.370); and 1-year mortality rates were 17.5% and 18.2% (p = 0.919). Patients who developed AKI had a significantly increased risk of 30-day (12.5% vs. 1.1%, p = 0.029) mortality. We found the presence of diabetes (odds ratio (OR) [95% CI] = 4.58 [1.58–13.3], p = 0.005) and elevated baseline serum creatinine (OR [95% CI] = 1.02 [1.00–1.03], p = 0.026) to independently predict AKI to statistical significance by multivariate analysis.

Conclusion: TAVI is a safe, acceptable treatment for patients with pre-existing CKD, however caution must be exercised, particularly in patients with pre-existing diabetes mellitus and elevated pre-operative serum creatinine levels as this confers a greater risk of AKI development, which is associated with increased short-term post-operative mortality.

1. Introduction

Aortic stenosis (AS) is the commonest cause of valvular heart disease in the elderly with prevalence estimated up to 8.1% at 85 years [1]. In patients with severe symptomatic AS the prognosis is poor for those managed conservatively, with 1-year survival only 60% and 5-year survival 32% [1]. Previously, surgical aortic valve replacement (SAVR), with or without concomitant coronary artery bypass surgery (CABG) was the only treatment modality, however for patients declined SAVR on the grounds of prohibitively high surgical risk, medical therapy including balloon valvuloplasty offered little or no improvement on survival [2]. One in three patients with severe valvular heart disease does not have surgery due to comorbidities [3]. The development of percutaneous techniques for aortic valve replacement has offered new hope to this cohort of patients. Transcatheter aortic valve replacement (TAVI) is superior to medical therapy alone [2]. This older and potentially frailer cohort, with a greater burden of co-morbidity has provided an additional challenge in patient selection and management following valve replacement. More than 30,000 TAVI procedures have been performed over the last 10 years [4,5].

Acute kidney injury (AKI) is associated with adverse outcomes even when transient [6] and more so when associated with the need for renal replacement therapy (RRT) [7]. The presence of pre-existing chronic kidney disease (CKD) is known to be a factor predisposing patients to AKI following cardiothoracic surgery [8], has been shown to increase the risk of mortality following SAVR [9,10] and is correlated with worse outcome following TAVI [11]. AKI can occur in up to one in three patients undergoing cardiac surgery [3] with a significant proportion at risk of requiring long-term haemodialysis [12–14]. AKI following cardiac surgery is an independent predictor of in-hospital [15], mid- and long-term mortality in the setting of contrast-induced nephropathy

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[16–18] and minimally invasive cardiac surgery [19]. CKD is a known predictor of AKI [20,21] and exists in 10–25% of patients undergoing TAVI [15,19,22]. CKD represents other challenges, with the burden of aortic calcification being higher in this cohort of patients [23–25] and particularly in those undergoing chronic haemodialysis [26,27].

Recent studies vary in the frequency of AKI following TAVI, reported as low as 7% [28] and as high as 41% [29], however different definitions of AKI have been used in different studies with heterogeneous populations and varying study sizes. This rate may potentially still be lower than SAVR in patients with pre-existing CKD [15]. TAVI can involve the use of contrast media, episodes of hypotension and haemodynamic stress, ischaemia and possible perioperative volume depletion thereby putting patients at risk of developing AKI.

The Valve Academic Research Consortium (VARC) has published criteria defining standards for endpoints following valve TAVI [30], and recently updated these as The Valve Academic Research Consortium-2 (VARC-2) Consensus Document [31]. This updates the previous definition of AKI following TAVI with the use of the Acute Kidney Injury Network (AKIN) criteria (see Supplementary Table 1; all subsequent tables are in the 'Tables' document, all figures in the 'Figures' document and supplementary data in the 'Supplementary Data' document) in favour over the 'modified' RIFLE criteria [32] and extends the period through which AKI can be defined from 72 h to 7 days post-procedure. Studies have suggested that smaller changes in serum creatinine than those categorised by RIFLE may be important in predicting adverse outcome, supporting a shift towards the use of AKIN criteria [33–35].

We aimed to identify whether the presence of pre-existing renal impairment influenced the development of AKI. In addition, we assessed whether there was an association between the presence of pre-existing renal impairment and outcome in terms of morbidity and mortality and whether the development of AKI influenced morbidity and mortality.

2. Methods

2.1. Study population and definitions

We present our experience of TAVI in consecutive patients with and without pre-existing CKD performed between December 2007 and June 2012. We performed a post hoc analysis of our prospectively collected registry data and defined the presence of CKD according to the estimated glomerular filtration rate (eGFR) calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation [36]. Patients were divided into those with established CKD Stage 3 or above ("CKD" group, estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2) and those in CKD Stage 2 or below ("No-CKD" group, eGFR > 60 mL/min/1.73 m^2), as defined by the Renal Association (UK) [37]. Mortality and morbidity data were obtained from the on-going registry entries, hospital records and telephone calls to patients' General Practitioners. AKI was defined according to the AKIN classification (Supplementary Table 1) as outlined by VARC-2 [31]. Importantly, this defines patients who required RRT following TAVI as suffering Stage 3 AKI irrespective of changes in serum creatinine or urine output. The 'baseline serum creatinine' reading was taken as the first reading obtained upon admission, usually the day before the TAVI procedure, so as to avoid any confounding factors that may influence this (e.g. pre-operative hydration). The 'peak serum creatinine' was selected as the peak value following a rise that began within the first 48 h, peaking within 7 days post-TAVI, as per VARC-2. The 'discharge creatinine' was the final serum creatinine recorded prior to discharge, which was always 1–2 days prior to discharge and 'follow-up creatinine' the reading recorded during a follow-up visit either at our or at the patient's local centre between 1 and 6 months following the index procedure. Post-operative urine output was not used to define AKI due to the different factors influencing this such as the use of diuretics and post-operative volume status.

2.2. Procedural details

All patients were recruited following referral to our centre with symptomatic severe AS. Following initial assessment, all patients were discussed at a multidisciplinary team meeting attended by Cardiologists, Cardiothoracic Surgeons and Cardiac Anaesthetists. TAVI was agreed upon following formal discussion including at least two cardiac surgeons. All patients underwent pre-operative assessment using echocardiographic assessment of left and right heart function, left heart catheterisation in order to assess coronary anatomy and calibre of the aortic root, ascending aortic, iliac and femoral arteries. In patients who were found to suffer from significant coronary artery disease (defined as a stenosis of >70% of a major epicardial vessel), pre-TAVI percutaneous coronary intervention (PCI) was performed at least 1 week prior to the TAVI procedure. From 2011 all patients had comprehensive assessment by CT angiography. Lung function and carotid Doppler assessment were also performed where indicated. All procedures were performed in the same hospital, under general anaesthetic by experienced TAVI operators. Access routes included femoral (percutaneous and surgical cut-down), axillary, subclavian, transapical and transaortic. Patients received either Medtronic CoreValve or Edwards LifeSciences Sapien valves. All patients provided written informed consent prior to the procedures undertaken. Routine blood testing including renal function tests (serum urea, creatinine and electrolytes) was performed on all patients prior to TAVI and following TAVI on a daily basis for the first 72 h then up to 7 days following the procedure if the serum creatinine continued to rise. Where indicated, a final pre-discharge blood test was also recorded in all patients.

2.3. Statistical methods

Statistical analyses were performed using IBM SPSS Statistics Version 21 and GraphPad Prism version 6.00 (GraphPad Software, La Jolla California USA) using standard statistical methods with groups defined as described above. Continuous variables for each group were assessed for normality using histogram analysis, normality plots and where relevant the Shapiro–Wilk test and where normally distributed populations were found, parametric tests such as the Student's t test was used to compare means, or in the case of non-normally distributed groups, the Mann–Whitney U or Wilcoxon matched-pairs signed rank test was used as deemed appropriate. For categorical data, the Chi-square test or Fisher's exact test was used as deemed appropriate.

Predictors of AKI were identified through univariate and multivariate logistic regression analysis with data presented as odds ratio (OR), confidence intervals (CI) and p-values. Promising variables for the multivariate model were selected based upon those cited in the literature and/or where $p < 0.05$ following univariate analysis.

Predictors of mortality at 1-year were identified using Cox proportional hazards regression was performed, again modelling promising variables ($p < 0.05$ by univariate analysis) and/or those cited in the literature. For the purposes of this analysis and to ensure all patients were included in the mortality analysis, patients already established on haemodialysis were considered as not having developed AKI to increase robustness of the multivariate model.

3. Results

3.1. Population characteristics

Full baseline characteristics are displayed in Table 1. One hundred and eighteen patients underwent 120 TAVI procedures between December 2007 and June 2012 and all were included in this analysis. Two patients had repeat TAVI procedures several months apart. For the purposes of this analysis, data relating to the procedure references the first TAVI procedure. Overall, patients were aged 81.3 ± 7.7 years (presented as mean ± standard deviation, for all