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30 days and midterm outcomes of patients undergoing percutaneous replacement of aortic valve according to their renal function: A multicenter study

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ABSTRACT

Introduction: Chronic kidney disease (CKD) constitutes a predictor of adverse events for surgical aortic valve replacement. In patients undergoing TAVI no study was performed to evaluate outcomes according to renal clearance, which represents the most accurate instrument to assess kidney function.
Methods: From January 2007 to December 2011 all TAVI patients of our institutions were prospectively divided into 3 cohorts. Preserved renal function those with clearance more or equal to 60 ml/min/1.73 m2, moderate CKD those between 30 and 60, and severe CKD those between 15 and 30. Patients with a clearance less than 15 or in dyalysis were excluded. All outcomes were adjudicated according to VARC criterion.
Results: 72 patients with preserved renal function, 219 with moderate and 73 with severe CKD were included; those in the latter group were older and with lower ejection fraction. At 30 days, severe CKD was associated with a trend toward a higher risk of major events than preserved and moderate CKD: cardiovascular death (2.8% vs 6.7% vs 9%; $p = 0.256$) life threatening bleedings (10% vs 10% vs 16%; $p = 0.384$), major stroke (1.4% vs 2.3% vs 4.1%; $p = 0.763$). At a medium follow-up of 540 ± 250 days, cardiovascular death incidence was higher in patients with severe CKD (7% vs 8 vs 19%; $p < 0.0001$), however this difference was not consistently significant after multivariable adjustment ($p = 0.300$). Overall, 2% of patients developed kidney failure, whereas 47.1% of patients with severe CKD improved to moderate renal impairment.
Conclusions: Patients with severe chronic renal disease presented higher risk of adverse events, mainly driven by increased hazard of bleedings. TAVI procedures could offer kidney functional improvement in an important subset of patients.

1. Introduction

TAVI (transcatheter aortic valve implantation) underwent in these last years an impetuous development because of encouraging reports about medium term safety and efficacy [1,2].

This percutaneous strategy has been reserved to high risk patients burdened from important rates of comorbidities [3]. Renal function impairment constitutes one of the most significant factors, both for prognosis and clinical management. Because of increasing rates of mortality and morbidity after surgical valve replacement [4,5] it is evaluated in most of currently used risk scores like STS and Euroscore [6,7].

The impact of renal disease on outcomes of patients undergoing TAVI represents still a debated matter. To the best of our knowledge few studies are reported in literature: the work from Elhmidi et al [8] demonstrated that acute kidney injury (AKI) represented a risk factor for 30 days mortality, while the report from Sinning et al. obtained same results, also at one year [9].

Anyway, these studies were based mainly on creatinine assessment, which does not represent an accurate tool to correctly stratify such patients [10]. Both aging and severe cardiovascular disease, which represent typical features of TAVI patients, decrease serum creatinine, leading to potential misclassification of renal disease's severity [11]. Thus we prospectively evaluated patients undergoing TAVI at our institutions to appraise 30 days and midterm outcomes according to their renal clearance.

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2. Methods

2.1. Patients

From January 2007 to December 2011 all patients with severe symptomatic AS considered at prohibitive or high surgical risk, referred for TAVI at our Institutions (San Giovanni Battista Hospital, Torino; Ferrarotto Hospital, Catania; Istituto Clinico Sant'Ambrogio; Milano) were included in the present study.

Patients were divided into 3 groups according to their renal clearance, elaborated with Cockcroft–Gault formula [12–14] with last creatinine value before procedure: preserved renal function those with a clearance more or equal to 60 ml/min/1.73 m^2, moderate chronic kidney disease (CKD) those with clearance between 30 and 59 ml/min/1.73 m^2 and severe CKD those with clearance between 15 and 29 ml/min/1.73 m^2. Patients with a clearance less than 15 ml/min/1.73 m^2 or in dyalysis were excluded (established kidney failure). Their baseline, procedural and follow-up features and data were prospectively recorded in dedicated registries.

2.2. TAVI preparation and procedures

In each center, indication for TAVI was appraised after consensus by a team of cardiac surgeons, cardiologists and anesthetists. Coronary anatomy and hemodynamic status were assessed by coronary angiography, left and, when necessary, right heart catheterization. Valvular anatomy and annulus dimension were evaluated with transthoracic and transesophageal echocardiography (including 3-dimensional reconstruction), contrast angiography of the aortic root, and multislice computer tomography of the thoracic aorta. The vascular access site was assessed by color-Doppler sonography and multislice computer tomography with contrast angiography of the aorto-ilio-femoral system. Patients with pre-procedural chronic kidney disease were offered both intravenous hydration and N-acetylcysteine before and after TAVI and were prophylactically treated with intravenous bicarbonate to prevent contrast-induced nephropathy.

Transfemoral, transubclavian and transapical approach was performed according to single center experience, with implantation of Core valve (Medtronic Inc., MN, USA) and Edwards Sapien devices (Edwards Life science, Irvine CA).

2.3. End-point and definitions

The primary end-point was the rate of death and of cardiovascular mortality, as defined in the Valve Academic Research Consortium (VARC) [15] at 30-days and at midterm follow-up. Secondary end-points were appraised both at 30 days (rates of peri-procedural myocardial infarction, spontaneous myocardial infarction, transient ischemic attack, major and minor stroke, bleedings, major and minor vascular complications) and at midterm follow up (rates of myocardial infarction, transient ischemic attack, stroke, bleedings, major and minor vascular complications, prosthesis dysfunction and of pace-maker implantation).

Renal clearance at follow up was elaborated with Cockcroft–Gault formula [11,12] with last creatinine reported from the patients, and compared with preintervention values, according to baseline kidney function.

In order to assess all procedural and in-hospital outcomes, our institutional electronic database and individual patient charts were consulted. Short and midterm outcomes with at least 6 months of follow up were recorded by phone, formal query to primary physicians and ambulatorial visits.

2.4. Statistical methods

Continuous variables are expressed as mean ± standard deviation and were compared with ANOVA. Categorical variables are presented as counts and percentage and were compared with the chi-squared test. Statistical significance was set at the two-tailed 0.05 level. According to number of events for variable appraised and for differences in follow up [13], propensity score and Cox proportional hazard analysis were performed for cardiovascular death at long term follow up, including age, ejection fraction, pulmonary hypertension, previous myocardial infarction, percutaneous or surgical coronary revascularization, peripheral artery disease and stroke as confounding variables. Calibration was tested with Hosmer–Lemeshow goodness of fit test with a nonsignificant p of 0.99, while the model showed a good discrimination, with an area under the curve of 0.79. Computations were performed with SPSS 11.0 (SPSS, Chicago, IL, USA).

3. Results

72 patients presented with a preserved renal function, 219 with moderate CKD and 73 with severe CKD were included. The three cohorts did not show statistically significant differences except for age (79 ± 5.7 vs 83 ± 4.8 vs 84 ± 5.1; p = 0.001), logistic EUROSCORE (17 ± 11 vs 23 ± 13 vs 30 ± 17; p<0.001) and STS score mortality (5 ± 4 vs 6 ± 3 vs 10 ± 7 p<0.001) (Table 1). Moreover ejection fraction was significantly lower in severe CKD disease (55 ± 10 vs 53 ± 11 vs 48 ± 15; p = 0.002): transfemoral approach was the most frequent in all groups (Table 2).

30 day outcomes were shown in Table 3. Patients with moderate and severe CKD demonstrated higher but not significant rates of death for any cause (2.8% vs 8.2% vs 9.6%, p = 0.227) and of cardiovascular death (2.8% vs 6.7% vs 9%, p = 0.256). About safety end-points, patients with severe CKD showed nonsignificantly higher rates of life-threatening (10% vs 10% vs 16%), major (9% vs 7% vs 10%) and minor (1% vs 5% vs 7%) bleedings (p = 0.384). Moreover they were exposed to higher stroke rates (1.4% vs 2.3% vs 4.1%, p = 0.763). Acute kidney injury was observed more frequently in patients with low clearance, considering AKI stage I (7% vs 13% vs 15%), AKI stage II (0% vs 1% vs 2%) and AKI stage III (1% vs 0% vs 1%) (p = 0.0475).

The median follow-up of our population was 540 ± 250 days. Cardiovascular death proved significantly higher in patients with severe CKD (7% vs 8% vs 19%, p = 0.041) at univariate analysis (Table 4). At multivariable adjustment, no significant difference was found for rates of cardiovascular death, both with Cox hazard analysis and with propensity score (p = 0.300).

Last creatinine value was obtained after 500 ± 270 days. Rates of ultrafiltration were 2% in all groups, while in patients with severe CKD 47% showed an improvement in renal function (Figs. 1, 2 and 3).

Table 1
Baseline features.

	Patients with preserved renal function N = 72	Patients with moderate CKD N = 219	Patients with severe CKD N = 73	p
Age (years)	79 ± 5.7	83 ± 4.8	84 ± 5.1	0.001
Male gender	44.4	42.9	38.4	0.728
Diabetes	39	27	36	0.098
Insulin dependent diabetes	7	3.4	8.2	0.391
Hypertension	89	84	92	0.207
Hyperlipidemia	55	54	52	0.977
Prior myocardial infarction	13	22	18	0.175
Surgical revascularization	9	13	14	0.550
Cerebrovascular disease[a]	13%	24%	30%	0.063
Peripheral artery disease[a]	17	24	29	0.222
Last creatinine value before intervention	0.86 ± 0.18	1.16 ± 0.29	1.89 ± 0.51	<0.001
Clearance[b]	79.50 ± 20.10	43 ± 8	24.0 ± 4.00	<0.001
NYHA	2.83 ± 0.605	2.84 ± 0.627	2.92 ± 0.662	0.625
Logistic euro score[c]	17 ± 11	23 ± 13	30 ± 17	<0.001
STS score mortality[a]	5 ± 4	6 ± 3	10 ± 7	<0.001

[a] According to STS (Society of Thoracic Surgeons) definition http://209.220.160.181/STSWebRiskCalc261/de.aspx.
[b] Cockcroft–Gault calculator http://nephron.com/cgi-bin/CGSIdefault.cgi.
[c] http://www.euroscore.org/calc.html.