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Long- term clinical outcomes after Transcatheter Aortic Valve Implantation (TAVI) in Patients with chronic renal failure.

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Introduction

Anatomy of the aortic valve

Understanding the anatomy of the aortic root is particularly relevant in the current era of evolving management strategies including percutaneous and transcatheter therapeutic techniques for valve or device implantations (Carabello, 2013).

Walmsley (1921) stated 'at each of the arterial openings there is a short tubular zone formed of fibrous tissue, the proximal and distal borders of which, at its junctions with the ventricular muscle and with the typical arterial wall respectively, are uneven' (p 42–53). Later on he replaced the term 'arterial ring' with 'arterial root'. Mc Alpine in 1975 emphasized the lack of rings in all four cardiac valves. A footnote in his Atlas states: 'Annulus, in Latin, designates a ring, i.e. a circle. In this work, the word is applied only to the fibrous attachments of aortic and pulmonary leaflets. A search for a reasonable term has met with failure. The term annulus, used to designate four fibrous structures to which the four valves of the heart are attached, is ill-founded–no such structures are to be found'. In reviewing the aortic root, Berdajs insisted an annulus exists 'at the border between the superior and basal third of the aortic root wall' based both on macroscopic and microscopic examination (Berdajs, Lajos & Turina, 2002).

Aortic sinuses and sinutubular junction

The spaces between the luminal surface of the three bulges on the aortic root and their respective valvular leaflets are known as the aortic sinuses of Valsalva. Davies considered the wall of the aortic root the aortic

sleeve, distinguishing it from the aortic wall on account of its histological composition (Davies, 1980). The superior border of the sinuses is the sinutubular junction (also known as the supra-aortic ridge. On the outside, as Muriago et al (1997) described, the sinutubular junction is where the tubular portion of the aorta joins onto the sinusal portion. According to the authors there is usually a slightly raised ridge of thickened aortic wall, but the sinutubular junction is not perfectly circular. It takes on, stated the authors, the contour of the three sinuses, giving it a mildly trefoil or scalloped outline. The orifices of the coronary arteries are commonly found close to the level of the sinutubular junction.

Aortic stenosis

Aortic stenosis (AS) is the most often cause of sudden death among valvular heart diseases (Carabello, 2013). In a remarkable way, its natural history has changed over the past 50 years because its pathogenesis has changed and our management strategies, on the basis of better understanding of its pathophysiology, have altered its outcome (Carabello, 2013). Historically, the first aortic valve replacement procedures, done in the 1960s, carried a mortality rate of 25% to 50%, but over time the results have improved considerably, even for very complex procedures (Svensson, 2008).

Minor degrees of calcification involving the three-leaflet aortic valve are common in the elderly. Degenerative valvular stenosis caused by calcification is more commonly seen in patients over the age of 65 years. In such cases, commissural fusion is absent or minimal except where

there has been concomitant rheumatic valve disease (Sadée et al., 1994). Davies (1980) linked this to 'fusing the hinge of a door', rendering the leaflets immobile. In contrast, stenosis occurring in a tricuspid (trifoliate) aortic valve in infants and children is ofently due to dysplasia of the valvular leaflets (Siew, 2009). The unicuspid (unifoliate) and unicommissural aortic valve occurring in isolation is rare. The quadricuspid aortic valve is extremely rare and may become stenotic as calcification develops. However, according to Mc Alpine (1975) the quadricuspid valve with leaflets of equal size usually is regurgitant.

The incidence of bicuspid aortic valve is 1–2% or 0.9–2.5% in the normal population. The majority is not symptomatic and have no clinical signs. According to Siew (2009) this group of people tends to have a higher incidence of sclerosis or calcification on the leaflets leading to them presenting at a younger age with aortic stenosis compared to patients with a normal three-leaflet valve.

The so-called supravalvular stenosis is less frequent than valvular stenosis (Edwards, 1965). Conventionally, according to the author, three morphology forms are recognized: an hourglass deformity, a fibrous membrane with central orifice, and a diffusely hypoplastic ascending aorta. It involves the sinutubular junction as well as the aortic leaflets and sinuses and may be included as valvular stenosis (Stamm et al, 2001). The subaortic stenosis takes various forms but the form that approximates to the aortic root is the discrete form (Tamás & Nylander, 2007).

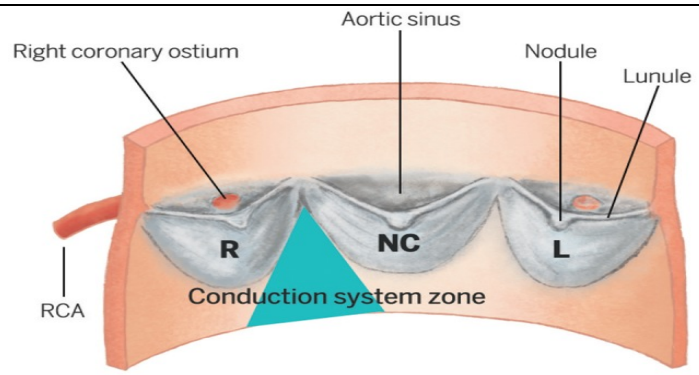

Figure 1: Spatial relationship between the three cusps of the aortic valve and the zone where the left bundle branch emerges beneath the membranous septum. L, Left cusp; NC, Non-Coronary cusp; RCA, Right Coronary Artery.

Pathogenesis of aortic stenosis

By 1970, rheumatic fever as a cause of aortic stenosis already had begun to wane in developed countries and was replaced pathogenetically by degenerative calcific disease (Stewart et al., 1997). The ambiguous term "degenerative" suggested that AS stemmed from wear and tear on the valve over time, perhaps explaining its greater incidence in older patients. Although calcification of the aortic valve is a disease of the elderly population, there is evidence that it is not simply a consequence of aging (Stewart et al., 1997). It is well- known that AS developed earlier in patients born with a bicuspid aortic valve, suggesting that hemodynamic stress might play a role. Recent evidence suggests active inflammatory processes (Rajamannan et al., 2007). Calcification of an aortic valve was thought to be a largely passive process, with serum calcium attaching to the surface of a valve leaflet, forming a nodule (Ross & Braunwald, 1968). Consistent with this understanding, surgical aortic valve replacement (AVR) has been considered to be the mainstay of treatment for calcific aortic stenosis with outflow obstruction and was

the primary treatment modality recommended for symptomatic severe calcific AS (ESC- Guidelines, 2007). However, emerging evidence indicates that calcification of an aortic valve is an active biological process (Rajamannan, 2008).

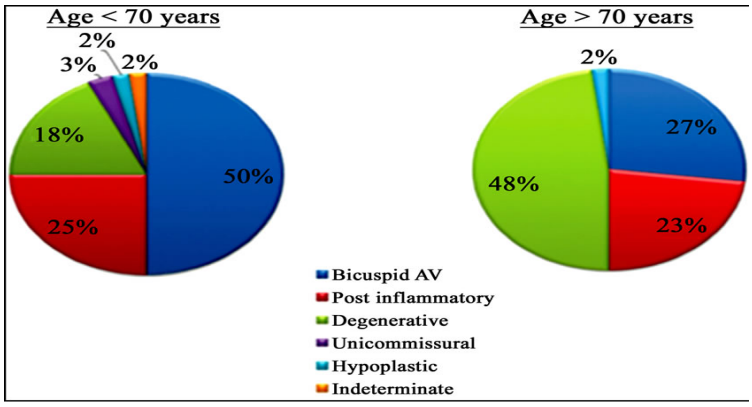

Figure 2: Differences in aetiology of aortic stenosis based on a cut-off age of 70 years.

Therapy of aortic stenosis

Untreated, severe, symptomatic aortic stenosis is associated with a dismal prognosis. The only treatment shown to improve survival is aortic valve replacement; however, before symptoms occur, aortic stenosis is preceded by a silent, latent phase characterized by a slow progression at the molecular, cellular, and tissue levels (Marquis et al., 2016). According to the authors, a specific medical therapy should halt aortic stenosis progression, reduce its hemodynamic repercussions on left ventricular function and remodeling, and improve clinical outcomes. Lipid-lowering therapy, antihypertensive drugs, and anticalcific therapy have been the main drug classes for a conservative medical therapy of aortic stenosis (Marquis et al., 2016).

Until 2002 the surgical approach was considered to be the only definitive therapy for symptomatic aortic stenosis. In 2002, Cribier reported the

first transcatheter aortic valve implant (TAVI) in a human subject for treatment of calcific aortic stenosis. Since then, another era has opened for patients with critical calcific aortic stenosis (AS) who are clinically deemed inoperable. Now, more than a decade later, there is good evidence that TAVI represents a true treatment-advance for this group of patients. Throughout its history, however, TAVI has been associated with the risk of five persistent major complications: high perioperative and late mortality, elevated early and late stroke rates; major vascular complications; patient prosthesis mismatch; and the occurrence of significant and progressive post-implant periprosthetic insufficiency (Sokoloff & Eltchaninoff, 2017). Compared with SAVR, TAVI may have similar or better early and midterm outcomes for adults with aortic stenosis, including those at low to intermediate risk (Gargiulo et al., 2016).

Objectives of the study

The aim of this study was to assess the influence of chronic kidney disease (CKD) on short- and long-term clinical outcomes in patients undergoing transcatheter aortic valve implantation (TAVI).

Materials and Methods

Patient Selection

Data from 320 consecutive patients who underwent transapical TAVI between December 2007 and March 2015 with the Edwards-Sapien valve (Edwards Lifesciences, Inc. Irvine, Calif), or Symetis valve (ACCURATE Symetis, Ecublens, Switzerland) for treatment of severe symptomatic aortic stenosis were analyzed. All included patients were high- risk patients (STS- Score and EuroSCORE II> 4%). The cohort of the present study was divided in two groups: Group I included Patients without chronic kidney disease (CKD). Group II included those Patients who had chronic kidney disease according to the Kidney Disease Outcomes Quality Initiative (KDOQI, 2002).

Evaluation before TAVI was conducted by a multidisciplinary Heart-team encompassing the expertise of interventional cardiologists, imaging cardiologists, cardiac surgeons, and cardiac anesthetists. Because TAVI remains a relatively new procedure, it is currently only recommended for patients who are functionally limited as a result of severe AS, with a life expectancy of >1 year, and in whom surgery is considered to be high risk or contraindicated (ESC- Guidelines, 2007).

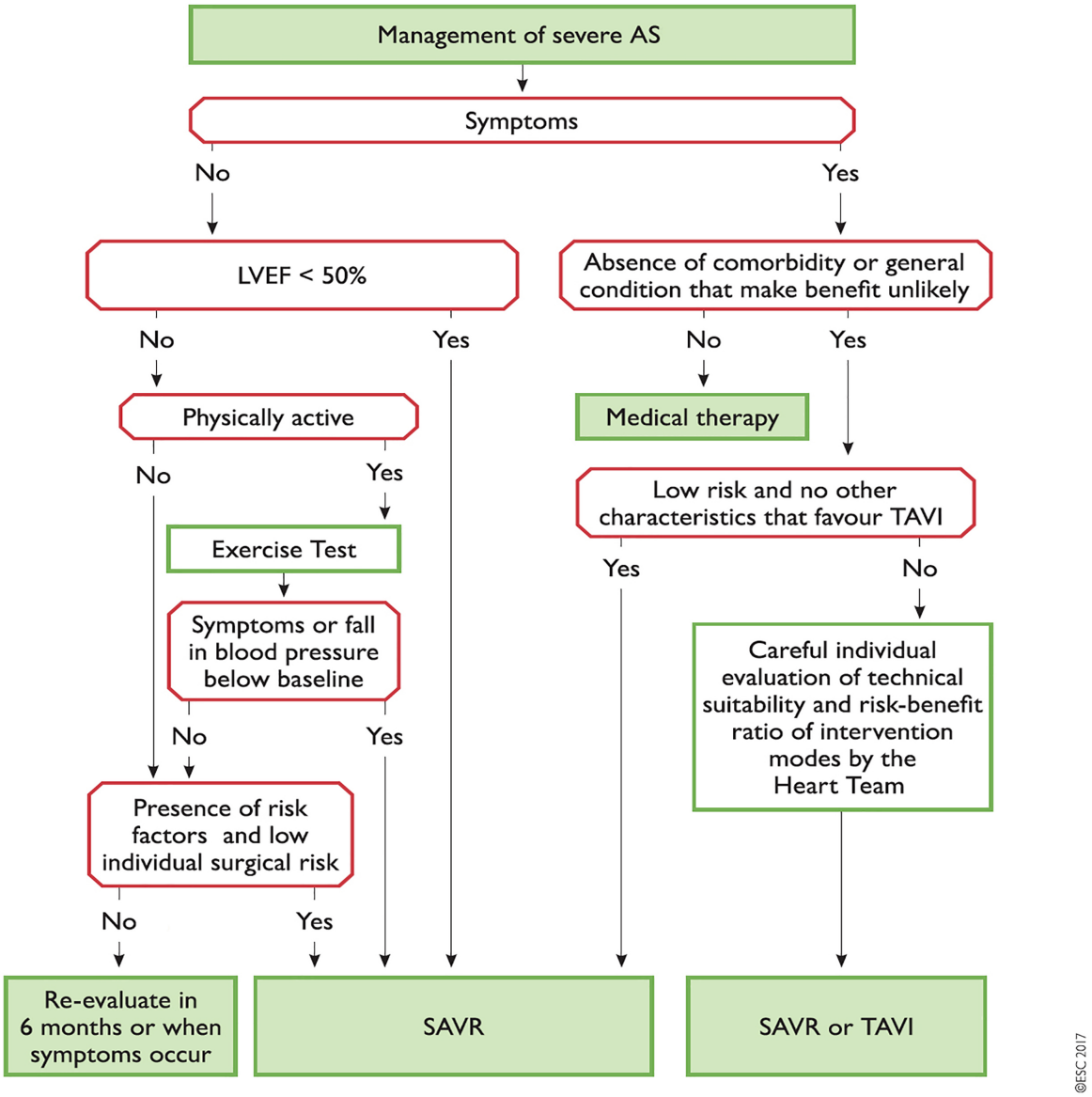

Figure 3: Management of severe aortic valve stenosis. European Society of Cardiology 2017**.**

Inclusion criteria for TAVI

Our patient selection criteria for transcatheter aortic valve replacement (TAVI) based on the indications formulated by the American College of Cardiology (ACC) published in year 2012:

1. Calcific aortic valve stenosis with the following echocardiographic criteria: mean transvalvular gradient >40 mm Hg or jet velocity >4.0m/s, severely calcified valve leaflets with reduced systolic motion AND / OR

Aortic valve area of <1.0 cm^2. Or indexed effective orifice area <0.6 cm^2/m^2.

2. In the setting of LV systolic dysfunction, severe AS is present when the leaflets are calcified, with reduced systolic motion, and dobutamin stress echocardiography shows an aortic velocity of >4.0m/s, or mean gradient >40 mm Hg with a valve area <1.0 cm^2. Or aortic valve index <0.6 cm^2/m^2 at any flow rate.

3. Patients are symptomatic (New York Heart Association [NYHA] functional class II or greater) from aortic valve stenosis, rather than from symptoms related to comorbid conditions.

A cardiac interventionalist and an experienced cardiothoracic surgeon agreed that surgical aortic valve replacement is either precluded or at high- risk, based on a conclusion that the probability of death or serious irreversible morbidity exceeds the probability of meaningful improvement. The surgeon's consult notes should specify the medical or anatomic factors leading to this conclusion and should include a printout of the calculation of at least one of the well- established risk scores.

The most recent ESC- guidelines for management of aortic stenosis are shown in Table 2. The preoperative chronic kidney disease was defined in reference to the KDOQI- 2002 classification (Kidney Disease Outcomes Quality Initiative) based on five categories of estimated glomerular filtration rate (eGFR).

Table 1: KDOQI- 2002 classification of chronic kidney disease Findings should be present for at least 3 months preoperatively.					
	eGFR (ml/min/1.73 m²)				
	≥90	60–89	30–59	15–29	<15
Normoalbuminuria	No CKD	No CKD	Stage 3	Stage 4	Stage 5
Microalbuminuria/macroalbuminuria	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5

The level of eGFR is accepted as the best measure of overall kidney function in health and disease. In principle, the level of GFR is the product of the number of nephrons and the single nephron GFR. Therefore, GFR can be affected by chronic kidney disease, which reduces the number of nephrons, or by hemodynamic factors that affect single nephron GFR. In chronic kidney disease, as in normal individuals, GFR is modulated by hemodynamic factors.

Table 2: Aspects to be considered by the Heart Team for the decision between sAVR and TAVI in patients with severe aortic stenosis and increased surgical risk. The European Society of Cardiology 2017. All rights reserved).		
	Favors TAVI	**Favors sAVR**
Clinical characteristics		
STS- Score/EuroScore II< 4% (Logistic EuroScore I < 10%)		+
STS- Score/EuroScore II> 4% (Logistic EuroScore I > 10%)	+	
Presence of severe morbidity not adequately	+	

reflected by scores		
Age < 75		+
Age < 75	+	
Previous cardiac surgery	+	
Frailty	+	
Restricted mobility that may affect the postoperative rehabilitation process	+	
Anatomical and technical aspects		
Favorable access for transfemoral TAVI	+	
Unfavorable access (Any) for TAVI		+
Sequlae of chest radiation	+	
Porcelain aorta	+	
Presence of intact coronary bypass graft at risk when sternotomy is performed	+	
Expected Patient- prothesis mismatch	+	
Severe chest deformation or scoliosis	+	
Short distance between coronary ostia and aortic valve annulus		+
Size of aortic valve annulus out of range for TAVI		+
Aortic root morphology unfavorable for TAVI		+
Valve morphology (Bicuspid, degree of calcification, calcification pattern) unfavorable for TAVI		+
Presence of Thrombi in aorta or LV		+
Cardiac conditions in addition to aortic stenosis that require consideration for concomitant intervention		
Severe CAD requiring revascularization by CABG		+
Severe primary mitral valve disease which can be treated surgically		+
Severe tricuspid valve disease		+
Aneurysm of the ascending aorta		+
Septal hypertrophy requiring myectomy		+

Exclusion criteria for TAVI according to experts' consensus (ACC, 2012)

- Bicuspid or unicuspid or noncalcified aortic valve
- Severe aortic regurgitation (>3+)
- Native aortic annulus size as measured by echocardiography <18 mm or >the largest annulus size for which a transcatheter aortic valve implantation (TAVI) device is available. Of note, this criterion is subject to change as the range of available device sizes changes.

Other exclusion criteria may include the following:

- Evidence (CK plus CK-MB elevation and/or troponin elevation) of an acute myocardial infarction within one month before the intended treatment.
- Hemodynamic or respiratory instability requiring inotropic support, mechanical ventilation, or mechanical heart assistance within 30 days of screening evaluation.
- Need for emergency surgery.
- Hypertrophic cardiomyopathy with or without obstruction.
- Left ventricular ejection fraction <20 percent.
- Severe pulmonary hypertension and right ventricular dysfunction.
- A known contraindication or hypersensitivity to all anticoagulation regimens or inability to be anticoagulated for the study procedure.
- Echocardiographic evidence of intracardiac mass, thrombus, or vegetation.
- MRI confirmed CVA or TIA within six months (180 days) of the procedure.
- Severe incapacitating dementia.

- Estimated life expectancy <12 months due to noncardiac comorbid conditions.

Significant aortic disease including the following abnormalities may preclude a transfemoral approach:

- Thoracic or abdominal aortic aneurysm (luminal diameter ≥5 cm), marked tortuosity (hyperacute bend)
- Aortic arch atheroma (especially if >5 mm thick, protruding, or ulcerated)
- Narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta
- Marked tortuosity (hyperacute bend) of the aorta or severe "unfolding" of the thoracic aorta
- Intermediate surgical risk patients—as expertise with TAVI grows, technology matures, and data on long-term valve durability become available, patient selection criteria are likely to expand to include additional patients who are not deemed inoperable or high risk surgical candidates.

Risk assessment for transcatheter aortic valve replacement

According to the American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) guidelines for the management of valvular heart disease, a central component for considering treatment for severe symptomatic aortic valve stenosis with TAVI is assessing the underlying risk, partly guided by Society of Thoracic Surgeons (STS) score or European System for Cardiac Operative Risk Evaluation (EuroSCORE) II. The STS scores

are conveniently categorized as low (< 4%), intermediate (4%–8%), or high (> 8%) surgical risk in the ACC/AHA guidelines, whereas the ESC/EACTS guidelines use low (STS score or EuroSCORE II < 4%) or increased (STS score or EuroSCORE II > 4%) surgical risk.

Preoperative echocardiography

With calcification of the aortic valve, the severity of valve calcification can be graded semi-quantitatively, as mild, moderate, or severe according to the visual assessment of the valve thickening and echogenicity.

Table 3: Recommendations for classification of AS severity

	Aortic sclerosis	Mild	Moderate	Severe
Aortic jet velocity (m/s)	≤2.5 m/s	2.6–2.9	3.0–4.0	>4.0
Mean gradient (mmHg)	–	<20 (<30[a])	20–40[b] (30–50[a])	>40[b] (>50[a])
AVA (cm^2)	–	>1.5	1.0–1.5	<1.0
Indexed AVA (cm^2/m^2)		>0.85	0.60–0.85	<0.6
Velocity ratio		>0.50	0.25–0.50	<0.25

[a]ESC Guidelines.

[b]AHA/ACC Guidelines.

Assessment of the left ventricular Functions

Our transthoracic echocardiographic assessment of the left ventricle included the following Parameter: Doppler, and M- mode Echo to rule out any regional wall motion abnormality (RWMA) due to any disease that might have affected the myocardium (e.g. ischemic heart disease).

The antegrade systolic velocity across the narrowed aortic valve, or aortic jet velocity, is measured using continuous-wave (CW) Doppler (CWD) ultrasound (Burwash et al., 1993; Currie et al., 1985). The difference in pressure between the left ventricular (LV) and aorta in systole, or transvalvular aortic gradient, is another standard measure of stenosis severity (Burwash et al., 1993; Currie et al., 1985; Smith, 1986). Gradients are calculated from velocity information. The transaortic pressure gradient was calculated from velocity (v) using the Bernoulli equation as: $P = 4xV^2$. The mean gradient was calculated by averaging the instantaneous gradients over the ejection period. The aortic valve area was calculated based on the continuity-equation concept that the stroke volume (SV) ejected through the LV outflow tract (LVOT) all passes through the stenotic orifice (AVA) and thus SV is equal at both sites: $SV_{AV} = SV_{LVOT}$.

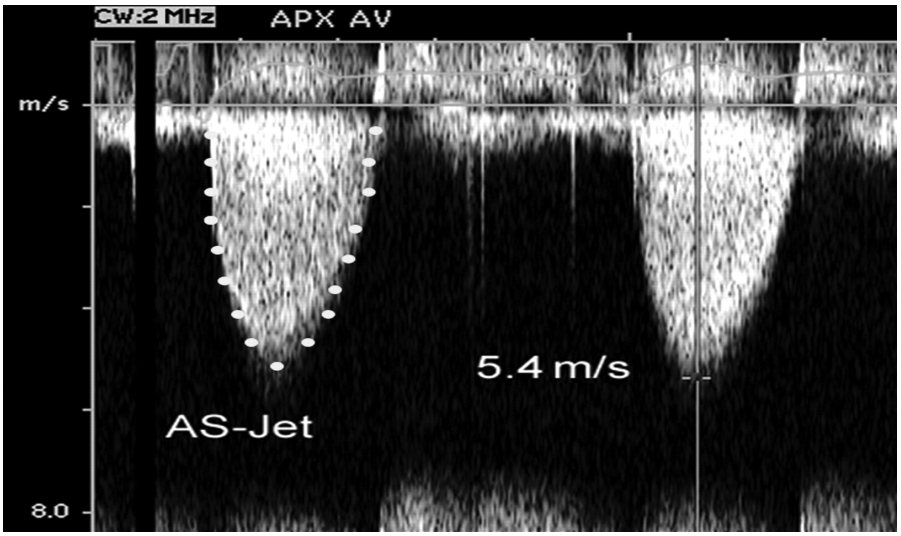

Figure 4: Continuous-wave Doppler of severe aortic stenosis jet showing measurement of maximum velocity and tracing of the velocity curve to calculate mean pressure gradient.

Assessment of the right ventricular Functions

The following echocardiography parameter were transthoracically assessed: right ventricular enddiastolic diameter (RVEDD), right ventricular endsystolic diameter (RVESD), right ventricular ejection fraction (RVEF) using fractinal area change (FAC) and Simpson's method, pulmonary artery systolic pressure (PAPs) from the peak tricuspid regurgitation (TR) velocity using the simplified Bernoulli equation ($P = 4x\ V^2$, added to an estimated RA pressure of 10 mmHg), septal wall motion, RV wall thickness, and proximal PA diameter using the parasternal short axis view at the level of the aortic valve.

TEE Imaging

Pre- and intraoperative TEE was performed in all patients using a TEE transducer and ultrasound system (X7-2t Live 3D TEE transducer, iE33, Philips Medical Systems). Measurements of the 2D TEE aortic root dimensions were performed during early systole as recommended by the American Society of Echocardiography for quantification of stroke volume and aortic stenosis severity (Baumgartner, 2009). Determinations of 2D TEE aortic annular and LVOT diameters were performed in the 3-chamber long-axis view at approximately the 120° angle. The aortic annular diameter was measured from the junction of the aortic leaflet with the septal endocardium to the junction of the leaflet with the mitral valve posteriorly, using the inner edge to inner edge. The LVOT diameter was obtained 5 mm into the LVOT from the level of the annulus. During the 2D TEE image acquisition, every attempt was made to ensure the largest annulus diameter was obtained.

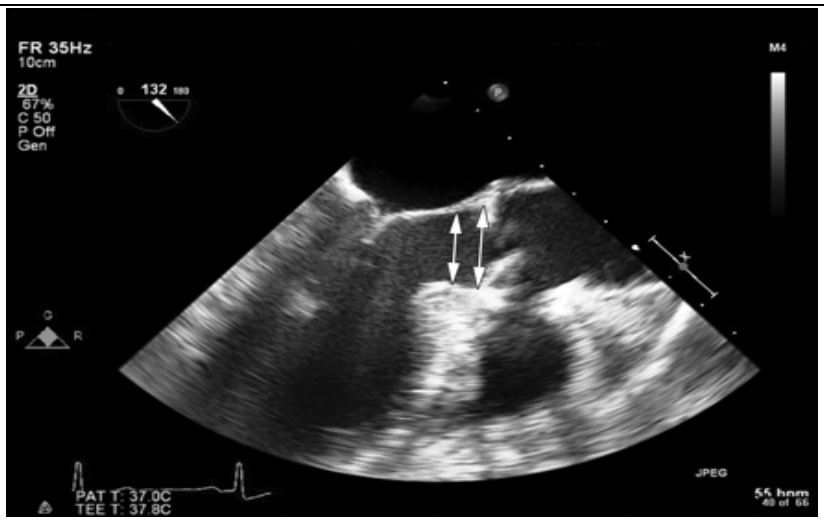

Figure 5: Two-dimensional TEE image of the aortic root, long-axis view. The aortic annular and LVOT diameters were obtained as the largest possible diameter during systole using the inner edge to inner edge. The LVOT diameter was obtained exactly 5 mm below the level of the aortic annulus.

Multi- Slice CT Imaging

All patients clinically underwent preoperative and postoperative evaluations of the aortic root and transcatheter aortic valve deployment by MSCT using either a 64-slice or 320-slice MSCT scanner (Siemens, Erlangen, Germany). The patient's heart rate and blood pressure were monitored before each scan. All scans were performed during mid-inspiratory breath-hold, and 80 to 90 mL of contrast medium was injected. Subsequently, data sets were reconstructed and off-line processed. Early systolic images of the aortic root at 30% to 35% of R-R interval were selected and using the 3 multiplanar reformations (MPR) planes, a long-axis image analogous to the 120° long-axis view of the aortic annulus/LVOT on TEE were obtained. In a manner similar to the 3D TEE image analysis, 2 orthogonal MPR planes bisect the long axis of the LVOT in parallel, and a third transverse plane bisects the aortic annulus directly beneath the lowest insertion points of all 3 aortic cusps to obtain the short-axis aortic annular view. The transverse MPR plane

was then moved 5 mm into the LVOT to obtain a representative short-axis LVOT view. Planimetered areas for both the aortic annulus and LVOT were obtained from the various MSCT short-axis MPR views and represent the "gold standard" cross-sectional aortic annular/LVOT areas.

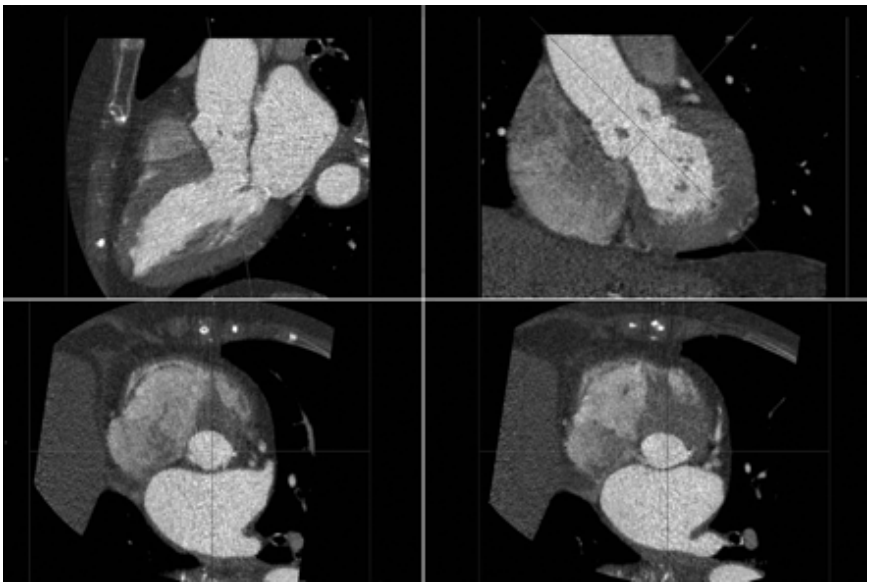

Figure 6: MSCT multiplanar reformations of the aortic root. MSCT planimetered areas were obtained at the level of aortic annulus (bottom left panel) and LVOT (bottom right panel).

Preoperative stress- echocardiography

In the ESC- guidelines it was stated 'When stenosis is severe and cardiac output is normal, the mean transvalvular pressure gradient is generally greater than 40 mmHg'. The more pronounced concentric LV remodelling and smaller LV cavity size found in PLF (preserved low flow) patients is akin to a restrictive physiology where there was lower than expected transvalvular pressure gradient (Dumesnil et al., 2010). Indeed, the decrease in stroke volume is primarily due to deficient ventricular filling in relation with the smaller cavity size rather than

deficient ventricular emptying Low-flow, low-gradient (LF-LG) aortic stenosis (AS) may occur with depressed or preserved left ventricular ejection fraction (LVEF). In both cases, the decrease in gradient relative to AS severity is due to a reduction in transvalvular flow (Orsinelli, 1993; Pai et al., 2008). Paradoxical low- flow low- gradient (LF-LG) severe AS despite a normal LVEF is a recently described entity that is characterized by pronounced LV concentric remodeling, small LV cavity size, and a restrictive physiology leading to impaired LV filling, altered myocardial function, and worse prognosis (Das et al., 2005; Lancellotti et al.,2005; Pibarot & Dumesnil, 2012;).

In some cases, where there was a remarkable discrepancy between the planimetric and Doppler assessment of the severity of the aortic stenosis, as well as for further assessment of the functional class in asymptomatic severe aortic stenosis, a dobutamine stress echocardiography was applied and the contractile reserve and stenosis severity were reassessed (Jean et al., 2010). The following parameters were reassessed under pharmacological stress: the valve opening area, EF, longitudinal myocardial contractility (MAPSE, TDIs), peak transvalvular velocity, peak and mean transvalvular pressure gradient. The changes in haemodynamics during exercise study provide a better index of stenosis severity than a single resting value (AHA/ACC, 2006). Exercise testing has become accepted for risk stratification and assessment of functional class in asymptomatic severe AS (AHA/ACC, 2006). The increase in mean pressure gradient with exercise predicts the clinical outcome and provides information beyond a regular exercise test (Lancellotti et al., 2005). Failure of the stroke volume or ejection fraction to increase by at

least 20% with dobutamine administration indicates an absence of LV contractile reserve and a high risk for aortic valve intervention (Tribouilloy et al., 2009).

Results

Between December 2007 and March 2015 a total number of 320 Patients with severe aortic stenosis who underwent transapical TAVI with Edwards-Sapien valve (Edwards Lifesciences, Inc. Irvine, CA, USA) or Symetis valve (ACCURATE Symetis, Ecublens, Switzerland) were collected (P=0.89). Of these 219 patients (Group I) did not have chronic renal failure, and 101 (Group II) were known to have chronic renal failure. Baseline characteristics and the clinical outcomes were recorded. Chronic renal failure was defined according to the KDOQI classification, and our study population was divided into two parallel groups according to the pre- operatively estimated glomerular flow rate (eGFR) level. We determined the cut- off point for separating the two groups by eGFR 60 ml/ml.

All patients were deemed non- operable or had a high risk for a conventional aortic valve replacement. The mean EuroSCORE- II for Group I was 8.6 ± 7.5%, and for Group II 12.7 ± 9% (P<0.001). The mean logistic EuroSCORE-I was 29±11.5% for Group I, and 37±16% for Group II (P<0.002). The STS- Score for Group I was 8.1± 5.2% and for Group II was 12.7 ± 7.4% (P<0.001). The mean transvalvular pressure gradient for Group I was 45.4 ± 19 and for Group II was 45.4± 18 mmHg (P=0.9).

As table 4a reveals, the mean age of Group I was 80±5.5 years, and the mean age of Group II was 79±6.8 (P<0.5). There was no significant difference in age, BMI, Pmean and effective orifice area between the two study groups (P=0.46, 0.46, 0.1, und 0.9 respectively). The preoperative ejection fraction (EF) was not significantly different between Group I and Group II (P=0.8). The mean length of hospital stay was 12.0±15.3 in

Group I, and 13.2 ± 10.4 in Group II without a significant difference (P=0.129).

Table 4a: baseline characteristics

Variable	Chronic renal failure	Mean	SD	Min.	25 %-Perc.	Median	75 %-Perc.	Max	p[1)]
Age at OP [in years]	no	79.8	5.5	65	77	80	84	94	0.466
	yes	78.9	6.8	55	74	80	85	96	
BMI [kg/m²]	no	27.15	5.01	16.0	23.7	26.6	29.5	43.8	0.465
	yes	28.37	8.14	17.8	23.8	26.5	30.3	70.5	
BSA [m²]	no	1.817	0.202	1.42	1.65	1.81	1.96	2.40	0.180
	yes	1.871	0.240	1.43	1.72	1.82	1.97	2.82	
STS Score	no	8.140	5.228	2.50	4.50	6.30	9.90	29.20	<0.001
	yes	12.454	7.426	2.20	6.72	10.30	16.10	34.70	
EuroSCORE- II	no	8.586	7.586	1.60	4.05	6.55	9.90	60.38	<0.001
	yes	12.705	9.840	1.44	6.30	9.52	16.70	45.76	
EuroSCORE- I	no	29	11,5	49.5	14.7	24,51	33,14	43,51	<0.002
	yes	37	16	53	17.7	34,36	41,11	63,52	
EF [%]	no	50.5	9.8	20	45	50	56	75	0.841
	yes	50.2	10.1	21	45	53	57	74	
P mean [mmHg]	no	45.42	19.46	4.1	33.0	43.7	55.2	107.0	0.913
	yes	44.40	18.51	2.0	30.0	45.0	54.0	112.0	
Effective orifice area [cm²]	no	0.723	0.291	0.30	0.53	0.70	0.80	2.00	0.110
	yes	0.756	0.294	0.30	0.60	0.74	0.89	2.20	
Pre-op. Creat. [ml/min]	no	1.321	0.806	0.73	1.01	1.17	1.40	8.30	<0.001
	yes	2.176	1.522	0.90	1.33	1.70	2.24	8.80	
Pre- op. eGFR [ml/min]	no	54.0	15.3	7	44	55	65	92	<0.001
	yes	36.8	15.4	6	28	37	46	84	

[1)] p value of Mann-Whitney-U test

Table 4b: Baseline data of the study population: frequencies of categorical variables			
		Chronic renal failure	

Variable	Value	No (n=219)		Yes (n=101)		p value[1)]
		N	%	N	%	
Gender	Male	96	43.8	56	55.4	0.055
	Female	123	56.2	45	44.6	
aHTN	No	15	6.8	8	7.9	0.816
	Yes	204	93.2	93	92.1	
pHTN	No	183	83.6	75	74.3	0.067
	Yes	36	16.4	26	25.7	
Hypercholesterinimia	Missing	1				
	No	112	51.1	43	42.6	0.186
	Yes	107	48.9	58	57.4	
COPD	No	148	67.6	59	58.4	0.131
	Yes	71	32.4	42	41.6	
DM	No	158	72.1	55	54.5	0.002
	Yes	61	27.9	46	45.5	
IHD	Missing	1				
	0	121	55.3	33	32.7	<0.001
	1	68	31.1	46	45.5	
	2	8	3.7	14	13.9	
	3	22	10.0	8	7.9	
AF	Missing	1				
	No	158	72.5	65	64.4	0.151
	Yes	60	27.5	36	35.6	
PVD	No	146	66.7	50	49.5	0.004
	Yes	73	33.3	51	50.5	
Previous CABG	Missing	27		1		
	0	155	80.7	77	77.0	0.430
	1	36	18.8	22	22.0	
	2			1	1.0	
	3	1	0.5			

[1)] p value of Fisher's exact test

Table 4b shows that systemic hypertension, pulmonary hypertension and chronic obstructive lung disease (COPD) were not significantly

different between the two groups (P=0.8, 0.06, and 0.13 respectively). However Diabetes mellitus and ischemic heart disease (IHD) were significantly different (P=0.002, 0.001 respectively).

Table 5a: Intra-operative data of the study population: descriptive measures of metric variables

Variable	Chronic renal failure	N	Mean	SD	Min	25 %-Perc.	Median	75 %-Perc.	Max	p[1)]
Amount of injected contrast medium [ml]	no	211	148.9	65.3	20	103	139	180	500	0.117
	yes	97	162.8	73.3	50	113	148	200	380	
X-Ray Exposure time [min]	no	209	5.822	2.967	2.00	3.83	5.23	7.00	22.00	0.369
	yes	94	6.257	3.489	2.08	4.13	5.62	7.10	25.00	
Prosthesis size [mm]	no	166	25.7	2.2	23	23	26	27	29	0.322
	yes	93	26.1	2.3	23	23	26	29	29	

[1)] p value of Mann-Whitney-U test

Table 5b: Intra-operative data of the study population: frequencies of categorical variables

Variable	Value	chronic renal failure				p value[1)]
		no (n=219)		yes (n=101)		
		n	%	n	%	
pre-Op valvuloplasty	Missing	59		12		
	No	156	97.5	83	93.3	0.174
	Yes	4	2.5	6	6.7	
Prosthesis	Missing	49		4		
	Edwards	120	70.6	67	69.1	0.890
	Symetis	50	29.4	30	30.9	

[1)] p value of Fisher's exact test

Table 6a: Post-operative data of the study population: Incidence of postoperative complications (VARC2- Complications) in both study groups

		Chronic renal failure	

Variable	Value	No (n=219)		Yes (n=101)		p value[1)]
		n	%	N	%	
post-operative: MI	Missing	6		1		
	No	206	96.7	97	97.0	1
	Yes	7	3.3	3	3.0	
post-operative: Heart Failure	Missing	2				
	No	202	93.1	82	81.2	0.003
	Yes	15	6.9	19	18.8	
post-operative: Stroke	Missing	5				
	No	211	98.6	99	98.0	0.657
	Yes	3	1.4	2	2.0	
post-operative: Dialysis	Missing	2				
	No	199	91.7	68	67.3	<0.001
	Yes	18	8.3	33	32.7	
post-operative: Bleeding	Missing	1				
	No	213	97.7	96	95.0	0.298
	Yes	5	2.3	5	5.0	
post-operative: acute kidney injury	Missing	13				
	No	186	90.3	71	70.3	<0.001
	Yes	20	9.7	30	29.7	
post-operative: pace maker implantation	Missing	1				
	No	209	95.9	90	89.1	0.026
	Yes	9	4.1	11	10.9	
All- cause mortality in 30 - days	No	212	96.8	88	87.1	0.002
	Yes	7	3.2	13	12.9	
All- cause mortality in 1- year	No	203	92.7	77	76.2	<0.001
	Yes	16	7.3	24	23.8	
CV mortality in 30- days	Missing			2		
	No	219	100	94	94.9	0.003
	Yes	0	0	5	5.1	
CV Death in 1- year	Missing			3		
	No	215	98.2	90	91.8	0.010
	Yes	4	1.8	8	8.2	

p value of Fisher's exact test (1

Table 6b: Post-operative data of the study population: descriptive measures of Hospital Stay

Variable	Chronic renal failure	N	Mean	SD	Min	25 %-Perc.	Median	75 %-Perc.	Max	p[1)]
Length of hospital [days]	No	219	12.0	15.3	0	7	8	13	162	0.129
	Yes	101	13.2	10.4	1	7	9	16	62	

[1)] p value of Mann-Whitney-U test

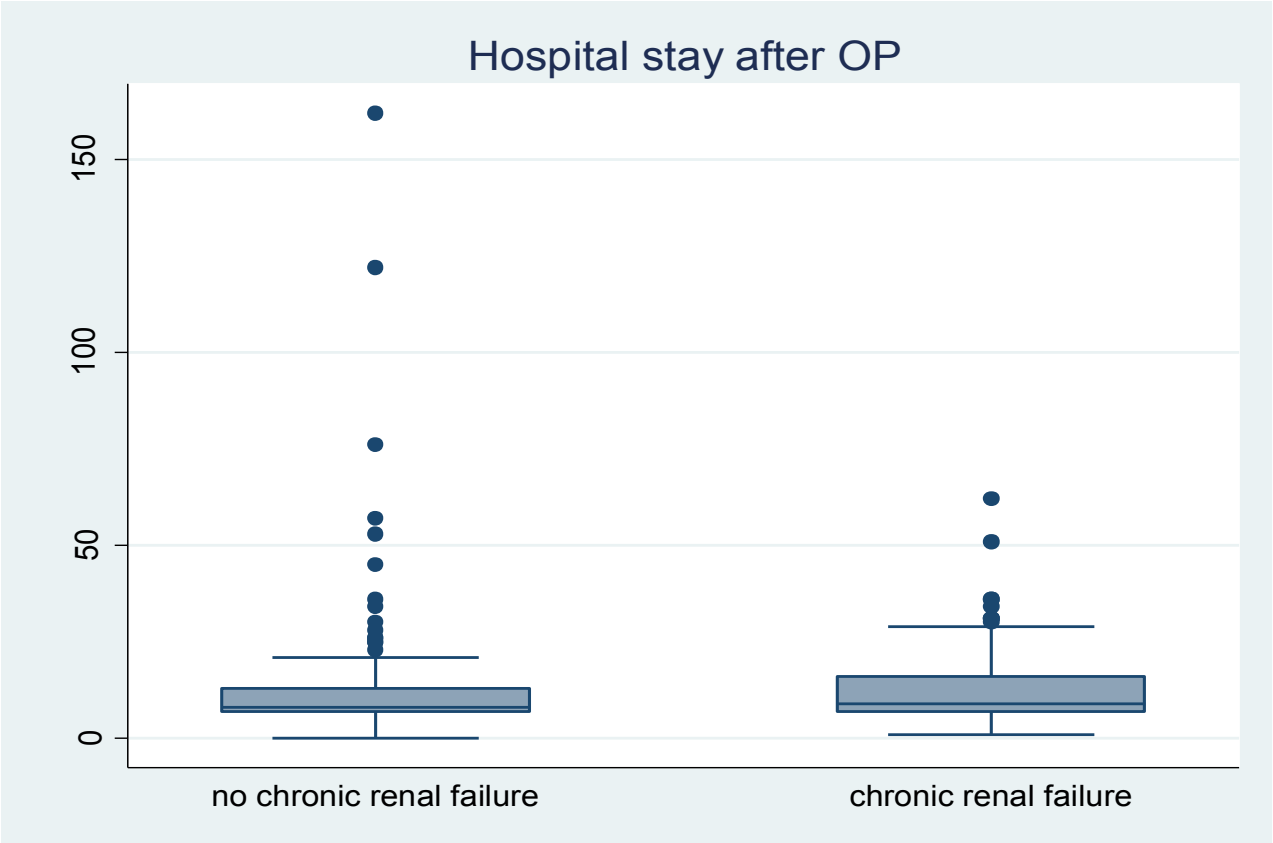

Figure 7: Length of hospital stay in the two groups.

Short-, mid- und long-term survival in both study groups

We observed that the baseline chronic kidney disease, irrespective of the degree of renal failure, was significantly associated with increased all-cause mortality (30- days mortality, 1- year mortality) in comparison to those patients without a pre-existing renal dysfunction (P=0.002, and P=0.003 respectively). The Kaplan-Meier survival curve showed a significant difference in the long- term survival (132 Months) between the two study groups (P=0.002). Table 5 shows a significant difference between the two groups in term of postoperative 30- days-cardiovascular mortality (P=0.003).

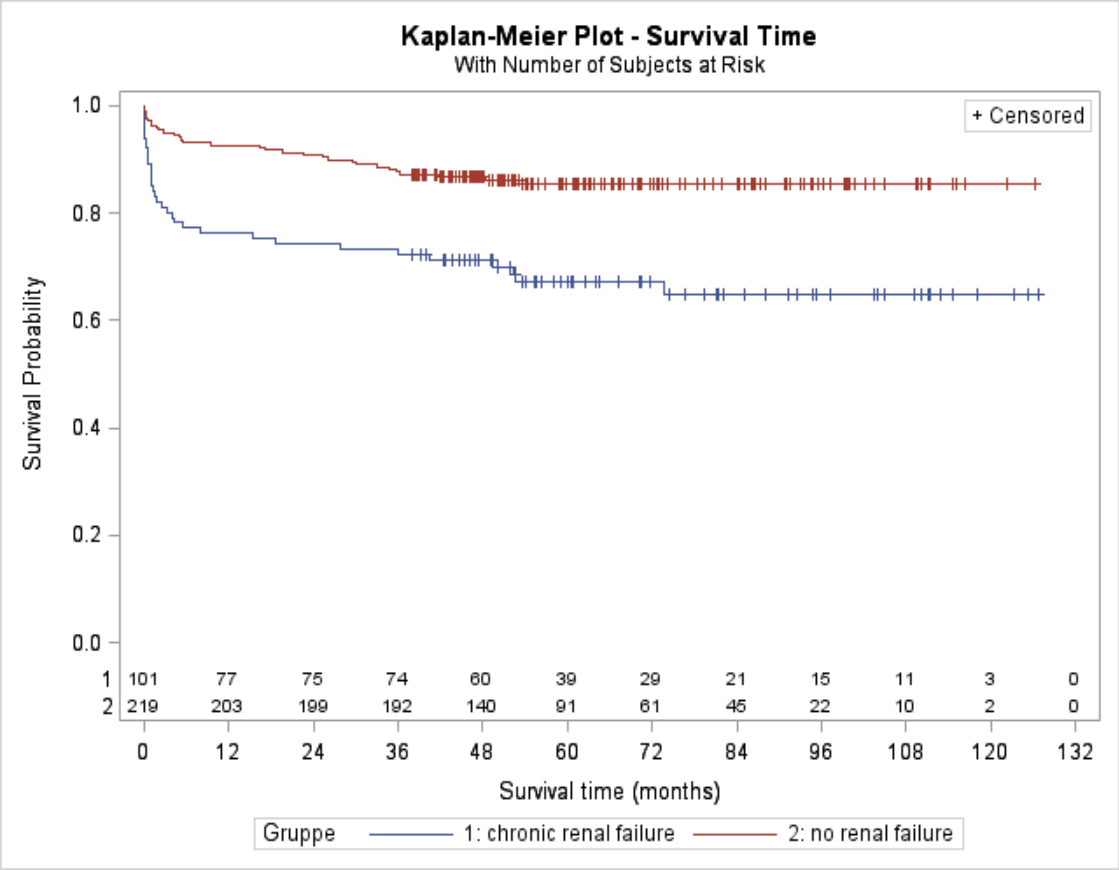

Figure 8: Kaplan- Meier presentation of long-term survival in months (> 120 months, **P=0.002**) between the two study groups. Red color depicts survival in months in patients without renal failure. Blue color depicts survival in years in patients with chronic renal failure.

Cardiovascular death in the two study groups

In our work we found that the incidence of the 30- day cardiovascular mortality was significantly high in Patients with chronic renal failure in comparison to those with a normal pre-operative baseline kidney function (P=0.003). Furthermore our work revealed a statistically significant difference in the 1- year cardiovascular mortality between the two study groups (P=0.010)

Table 7: Frequencies of post-operative complications

	chronic renal failure			
	no (n=219)		yes (n=101)	
Variable	n	%	N	%
CV death in 1 year	4	1,8	8	8,2
CV death in 30 days			5	5,1
Pace maker implantation	9	4,1	11	10,9
Acute Kidney injury	20	9,7	30	29,7
Bleeding	5	2,3	5	5,0
Postoperative Dialysis	18	8,3	33	32,7
Stroke	3	1,4	2	2,0
Heart Failure	15	6,9	19	18,8
MI	7	3,3	3	3,0
Shock	18	8,3	27	26,7

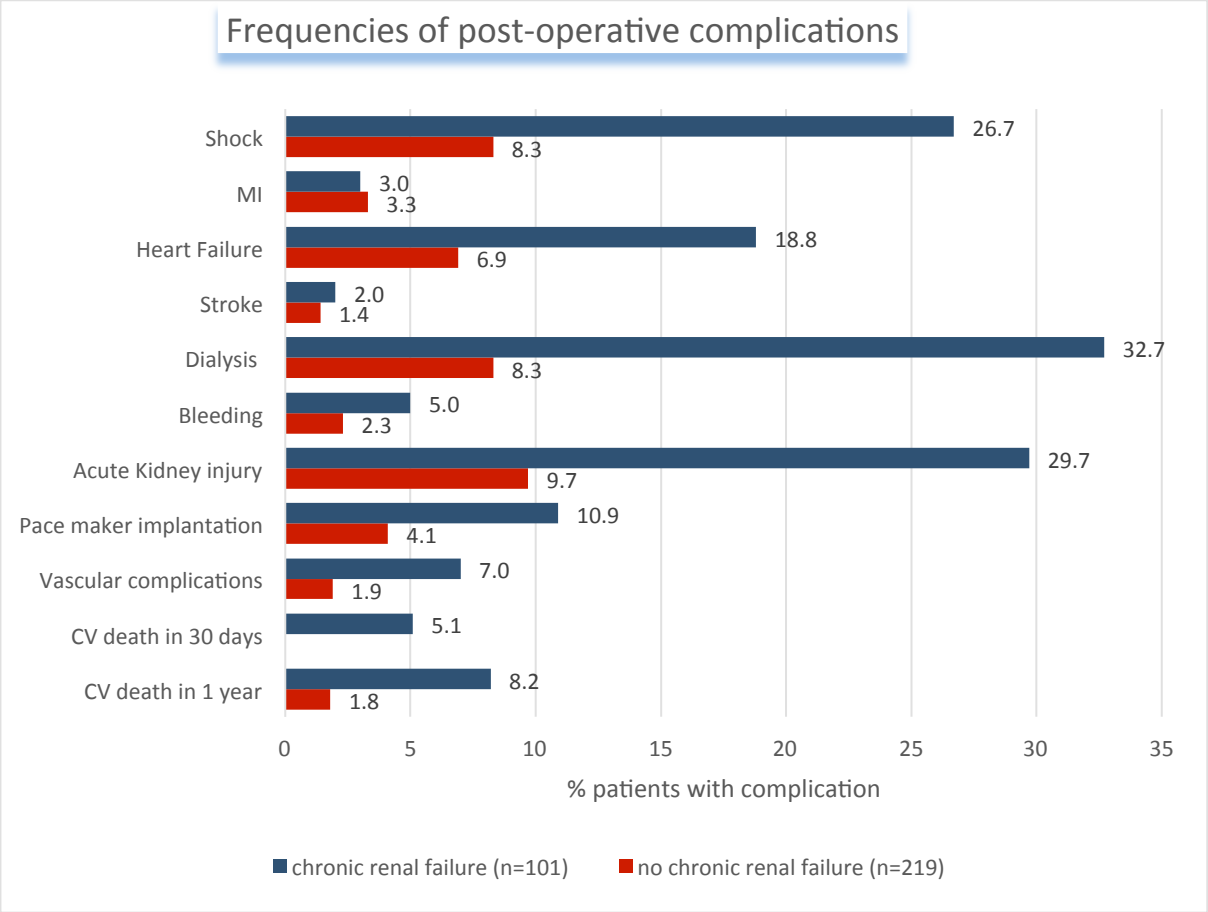

Figure 9: Incidence of postoperative complications in the two study groups.

Postoperative incidence of VARC-2 complications (Vascular Academic Research Consortium)

Our work showed a significant difference between the two groups in the incidence of the following complications: post- operative acute renal failure (P=0.001), incidence of postoperative dialysis (P=0.001), incidence of acute heart failure (P=0.003), the post- operative permanent pacemaker implantation (P=0.02), and the incidence of postoperative cardiogenic shock (P=0.001). However we did not notice any significant difference between the two study groups in terms of postoperative stroke (P=0.65), acute myocardial infarction (P=1.0), the occurrence of a

severe postoperative bleeding (P=0.29), and in the length of postoperative hospital stay (0.13).

Degree of renal dysfunction and long-term survival

Our work revealed a strong association between the pre-procedural renal dysfunction and long- term survival in patients undergoing TAVI. We furthermore divided the group of Patients (Group II) known to have CKD (101 patients) into two subgroups according to the level of eGFR. There were 71 patients with eGFR between 30 und 59 ml/min (70.3%), and 30 patients with eGFR under 30 ml/min (29.7%). Within 30 days died 8 patients (12.7%) with eGFR > 30 ml/min, and 3 Patients (10%) with eGFR < 30 ml/min (P=1). The 1-year mortality between the two subgroups was not significant (P=1). As it is shown in the Kaplan- Meier survival curve our work did not reveal a graded fashion impact of the CKD on short- and long-term mortality (P=1).

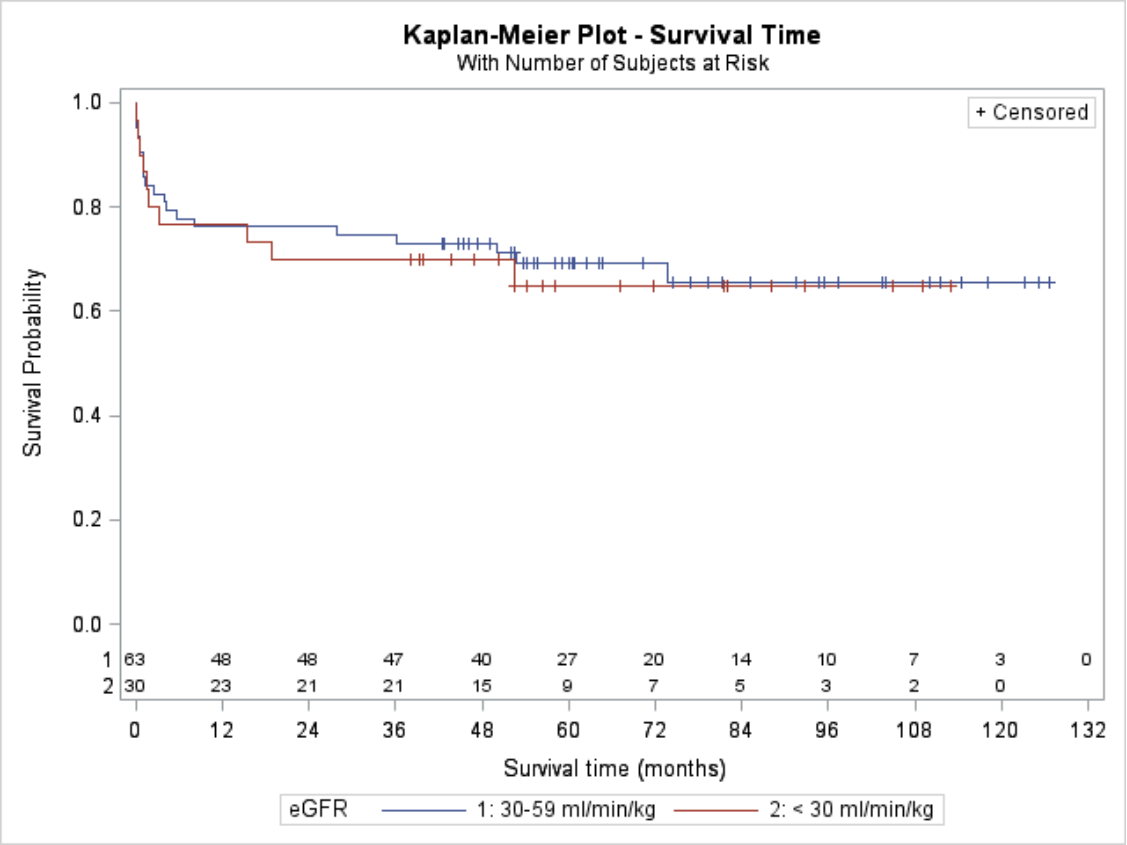

Figure 10: Kaplan- Meier presentation of long-term survival in Patients with CKD according to the level of pre-operative eGFR **(P=1).**

Discussion

Chronic kidney disease (CKD) is recognized as a major public health problem affecting 13–16% of the adult population (Levy et al., 2007) and it is associated with increased risk of all-cause mortality (Tonelli et al., 2006). Life expectancy at different ages is a measure commonly used to estimate health status and impact of disease burden at a population level. A large population- based registry from Canada showed that life expectancy falls by approximately 20 % with an eGFR of 45–59 ml/min, by approximately 50 % with an eGFR of 30–44 ml/min and by approximately 65 % with an eGFR of 15–29 ml/min when compared with those with an eGFR of ≥60 ml/min (Neild, 2017).

The adverse impact of chronic kidney disease on life expectancy was seen to be more obvious in patients with cardiovascular diseases, and influences the postoperative clinical outcomes in almost every cardiac surgery. A plethora of clinical studies evaluated the clinical outcomes after valve surgery in patients with CKD. Glaser et al. (2016) evaluated the influence of CKD on late survival after surgical aortic valve replacement (sAVR) and noticed a graded- fashion increase in mortality according to the degree of CKD. A recent work by Kumar et al. (2017) revealed that surgical aortic valve replacement (sAVR) was associated with higher intra-hospital mortality ($P<0.001$) compared to TAVI in patients with chronic kidney disease. Kumar and his team concluded that TAVI could be a preferable therapy approach in patients with severe aortic stenosis in the setting of CKD. D'Errigo and his team, however, evaluated the impact of renal failure on outcomes after TAVI and SAVR

and found that SAVR was associated with somehow better early and late survival (D'Errigo et al., 2016).

A recent analysis by Gaede et al. (2018) showed that the in-hospital mortality after transvascular transcatheter aortic valve implantation (TV-TAVI) decreased over the last few years. Moreover this analysis claimed that the post- TAVI intrahospital mortality was for the first time lower than the respective mortality rate after isolated surgical aortic valve replacement (iSAVR) in 2016.

Prospective randomized data from the PARTNER B cohort has demonstrated that transcatheter aortic valve implantation (TAVI) is superior to medical therapy in inoperable patients up to five years after valve implantation (Kapadia et al., 2015). A number of randomized trials compared the outcome of TAVI versus surgical aortic valve replacement (sAVR) in patients at high risk for sAVR (mean STS score 7-11%, mean logistic EuroSCORE 18-29%). Results up to five years showed that TAVI is non-inferior to sAVR (Reardon et al., 2015). Those patients who are suitable candidates for transfemoral access had an additional benefit from TAVI. New data from randomized intermediate-risk patients (mean STS Score 4-8%) again demonstrated no difference in one-year mortality between TAVI and sAVR, with the lowest mortality observed in transfemoral TAVI patients (Leon et al., 2016).

Our current study included a total number of 320 Patients with severe aortic stenosis who underwent transapical TAVI with Edwards-Sapien valve (Edwards Lifesciences, Inc. Irvine, CA, USA) or Symetis valve (ACCURATE Symetis, Ecublens, Switzerland). Of these 219 patients

(Group I) did not have chronic renal failure, and 101 (Group II) were known to have chronic renal failure. Baseline characteristics and the clinical outcomes were recorded. Chronic renal failure was defined according to the KDOQI classification, and our study population was divided into two parallel groups according to the pre- operatively estimated glomerular flow rate (eGFR) level. The cut- off point for separating the two groups was: eGFR 60 ml/ml.

Baseline characteristics and the clinical outcomes were recorded. Chronic kidney disease was defined according to the KDOQI classification. All individuals with GFR <60 mL/min/1.73 m^2 for more than 3 months preoperatively were classified as having chronic kidney disease, irrespective of the presence or absence of structural kidney damage. All patients met the criteria for transcatheter aortic valve implantations as we thoroughly detailed in the chapter of Methodology.

Through our current work we aimed to assess the short- and long –term clinical outcomes after (TAVI). A relatively large control group was parallel compared and thoroughly followed up. Our primary end points were determined: postoperative all- cause and cardiovascular mortality (30- day, 1- Year, and long-term mortality). Furthermore we compared the incidence of VARC2- complications (Valve Academic Research Consortium-2 consensus) between the two observation groups. The first Valve Academic Research Consortium (VARC) consensus manuscript was published in January 2011 with the goal of achieving consensus for selecting appropriate clinical endpoints, and standardizing definitions for single and composite clinical endpoints for transcatheter aortic valve implantation clinical trials (Leon et al., 2011). This was thoroughly

reevaluated and updated into VARC2 in 2012. This newly updated evaluation system focused on the following postoperative complications: mortality (all- cause, cardiovascular, non- cardiovascular death), stroke, permanent pace maker implantation, bleeding, vascular complications, acute kidney injury, and myocardial infarction. As our patients received exclusively transapical implantations we neglected the incidence of postoperative vascular complications, which were primarily defined in the VARC- 2 initiative in terms of dissection, perforation, hematoma and pseudoaneurysm.

All –cause mortality

It is well- known that chronic kidney disease leads to increased cardiovascular mortality through an accelerated progression of coronary artery disease and coronary events, exacerbation of congestive heart failure and an increased risk of sudden death (Shamseddin & Parfrey, 2011; Smith et al., 2013;). Patients with aortic stenosis undergoing TAVI exhibit a high prevalence of coronary artery disease, systolic and diastolic heart failure and atrioventricular conduction disturbances (Rodés-Cabau, 2011). The presence of chronic kidney disease may therefore worsen clinical outcomes by further affecting all these cardiovascular abnormalities.

Chronic kidney disease (CKD) has long been identified as a risk factor for patients undergoing surgical aortic valve replacement (sAVR). This is relevant not only to the perioperative period, for which it predicts 30-day mortality, but also to the longer-term prognosis. Data from the Society of Thoracic Surgeons database included more than 145,000 patients who underwent sAVR with or without concomitant coronary bypass grafting,

demonstrated that patients with chronic kidney disease had a ≥50% reduction in median survival over a period of 15 years (Brennan et al., 2012).

On the other side, the adverse impact of CKD on life expectancy after TAVI was revealed in a work by Yamamoto et al. (2013). In their work 642 consecutive patients treated with TAVI were divided into 4 groups according to the degree of chronic kidney disease (CKD), determined using their estimated glomerular filtration rate (eGFR) before TAVI. The investigators found that patients with chronic kidney disease (CKD) grade 4 (eGFR <30 ml/min) had higher 30-days mortality. High degrees of chronic kidney disease, in addition to the logistic European System for Cardiac Operative Risk Evaluation score, were found to be the only independent predictors of 1-year mortality after TAVI. In the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry it was demonstrated that chronic kidney disease is among the strongest independent predictors of 1-year survival (Thomas et al., 2011).

In our work we found that the baseline chronic renal failure, in a non-graded fashion, was associated with significantly increased all-cause mortality (30- day, 1- year mortality, and long- term mortality) in comparison to those patients without a known renal failure (P=0.002, P=0.003, P=0.002 respectively). Furthermore our study demonstrated that the incidence of 30- day and the 1- year cardiovascular mortality was significantly high in Patients with pre- operative chronic renal failure in comparison to those with a normal pre-operative baseline kidney function (P=0.003, 0.01, respectively).

In a multicenter study including a total of 2075 consecutive patients who had undergone TAVI the researchers evaluated the clinical outcomes at 30-days and within the follow-up time (median of 15 months) according to the VARC- 2 criteria. Advanced chronic kidney disease was shown to be an independent predictor of 30-day major/life-threatening bleeding (P=0.001) mortality (P=0.027), and late cardiovascular and non-cardiovascular mortality (P<0.01 for all) (Allende et al., 2015). A recent meta-analysis by Ifedili et al. (2017) revealed that a pre-existing chronic kidney disease (defined as eGFR < 60 ml/min) is a strong predictor of worse short- and long-term clinical outcomes after TAVI.

However a small Japanese study observed the clinical outcomes after TAVI in a group of 17 dialysis patients, and found 0% 1-year mortality (Maeda, 2015).

In our present study the chronic kidney disease (eGFR<60 mL/min or dialysis) was associated with an increased risk of death at 30-days and in the long-term follow-up of more than 7 years following TAVI operation. We found an increased risk of both cardiovascular and non-cardiovascular death.

Long-term survival

Chronic kidney disease is an independent predictor of mortality in patients undergoing transcatheter aortic valve implantation (TAVI). A recent multicenter study included 1204 Patients from 10 centers in Europe, Japan, and Israel, of them had 464 advanced chronic renal disease. The study revealed that advanced chronic kidney disease was associated with a 2-fold increase in the adjusted risk of 1-year all-cause death ($P<0.001$), and a 1.9-fold increase in cardiovascular death (Levi et al., 2017). Another recent study by Escárcega et al. (2015) evaluated the long-term survival following transcatheter aortic valve implantation in a maximum follow-up duration of 5 years and showed that the overall long-term survival is strongly affected by certain clinical factors, e.g. atrial fibrillation and intrahospital stroke. The effect of preoperative chronic renal failure on the long-term survival after transcatheter aortic valve implantation remained until the last couple of years unexplored (Levi et al., 2017). However, there are many data revealing the short- and mid-term clinical outcomes after TAVI in patients with chronic renal failure.

In the UK- TAVI registry the outcomes on all TAVI procedures performed within the UK were reported. Data were collected prospectively from 1. January 2007 until 31. December 2012. According to the registry- data the pre-procedural renal dysfunction was associated, in a graded fashion independently of dialysis status, with worse outcomes, including mortality in patients undergoing TAVI (Ferro et al., 2014).

However, our current work did not reach the same results the UK-registry did. We did not notice a graded- fashion impact of renal dysfunction upon the short- and long-term survival in patients underwent TAVI- procedure (P=1).

A Chinese meta-analysis found an increased mid-term mortality after TAVI in patients with a preexisting chronic renal disease. In accordance with the results of the UK- TAVI registry this was seen to be significant in a graded fashion being most significant in Patients with chronic kidney disease stage IV (Chen et al., 2015).

Our results do confirm a strong independent effect of the chronic kidney disease on long-term survival. Over more than 7 years our patients were followed up. The all- cause long-term mortality was seen to be significantly high in the group of patients with a preexisting chronic renal failure (P=0.002).

Incidence of postoperative complications (VARC-2)

Pre-procedural chronic kidney disease (CKD) is one of the most frequent comorbidities of TAVI patients and has been found to significantly worsen patients' prognosis at short and long-term follow-up as it has been revealed in multiple studies. Post-procedural acute kidney injury (AKI) is a frequent and relevant complication associated with increased mortality (Barbanti et al., 2016). In a recent work by Koifman et al. (2016) a group of 207 patients, who underwent TAVI, were evaluated for the development of postoperative acute kidney injury. The researchers observed that the occurrence of acute kidney injury (AKI) after TAVI adversely affects the clinical outcomes with increased long-term mortality. The results our work revealed correlate strongly with these

findings. We noticed a significantly higher incidence rate of post-procedural acute kidney injury (AKI) in patients with preexisting chronic kidney disease (CKD) in comparison to those with normal preoperative kidney functions (P=0.001). This group of patients showed to be strongly correlated with increased long-term mortality (P=0.002). Furthermore, a significant number of our patients with a preexisting renal disease received postoperative dialysis in comparison to those without renal dysfunction (P=0.001).

Most strikingly our study did not notice a significant difference in the postoperative length of hospital stay between the two groups (P=0.13). A previous study (Awad et al., 2014) compared the postoperative resource consumption following TAVI and conventional valve surgery. The study concluded that despite the fact that TAVI is being performed in a high risk group of patients; the length of hospital stay was similar to the conventional valve replacement. To the best of our knowledge, the length of hospital stay after TAVI according to the pre- procedural renal function was not studied.

Post- procedural pace maker implantation

Furthermore the permanent pace maker implantation after TAVI is a well-known postoperative complication. A previous study showed that different degrees of AV- Block occur in approximately 90% of patients in the first week after TAVI and recommended a strong intrahospital follow up (Erkapic, 2012). According to this multi-institutional study the overall requirement of permanent pacemaker implantation after TAVI is said to be 17% compared to 5% in conventional sAVR. A relatively recent anatomical study by Kawashima and Sato (2014) reported that the AV-

node and left bundle branch are located more anteriorly, distally, and cranially and closer to the aortic root than previously believed. The authors thought that patients with pre-existing right bundle branch block or first-degree AV-block would be at greater risk for heart block with device manipulation in the left ventricular outflow. Aortic stenosis is pathologically a degenerative process, a process which underlies the development of the conduction abnormalities. Kawashima assumed a high prevalence of pre-existing conduction abnormalities in the patients who are candidates for TAVI. There was fairly a few available data about the incidence of conduction abnormalities in patients with pre-existing chronic renal failure undergoing TAVI.

In our work we noticed, comparatively, a significantly high requirement for permanent pacemaker implantation in patients with preexisting chronic renal disease (P=0.026).

Post- procedural stroke

In a previous meta- analysis by Levi et al. (2017) it was revealed that perioperative stroke after TAVI was associated with >6 times greater risk of 30-day stroke-related mortality. A relatively recent study carried out by Muralidharan et al. (2016) analyzed data gathered from 1.413 TAVIs and showed that the overall incidence of cerebrovascular events complicating TAVI was 3.2%. 40% of all cerebrovascular events were classified as transient ischemic attacks (TIA) with symptoms lasting <24 hours, and 60% were classified as stroke with symptoms persisting>24 hours. Our work revealed a minimal increase (P=0.657) in the incidence of stroke in patients with preexisting renal failure (2%) compared to those without renal failure (1.2%). We concluded, according to our

results, that a preoperative renal dysfunction does not significantly affect the incidence of perioperative stroke.

Post- procedural myocardial infarction

Our study defined a postoperative myocardial infarction as a post-procedural increase of CK-MB and/or Troponin level >5 times the upper reference limit. A previous study claimed to have found an incidence of myocardial injury in 17% of patients subjected to TAVI (Werner et al., 2016). Our intra-hospital follow up and observations did not reveal a significant difference in the incidence of myocardial injury between the two study groups (P=1). However, we noticed a 3% overall incidence of perioperative myocardial injury.

Conclusion

Several works investigated the collective clinical outcomes after transcatheter aortic valve implantation (TAVI) in different clinical contexts. Our work aimed at observing the short- and long-term postoperative clinical outcomes after TAVI- Operations in Patients with preexisting chronic renal failure. The long- term mortality, over 7 years, was our primary objective, and showed to be significantly higher in the group of patients with chronic renal failure in a non- graded fashion. Other adverse complications (atrioventricular conduction disturbance, cardiogenic shock, requirement of postoperative dialysis, and acute kidney injury) were shown to be significantly higher in patients with renal failure in comparison to those with normal preoperative renal functions. We found that chronic kidney disease correlates with poor clinical outcomes and could be considered as a significant independent risk for TAVI. Active measures should be taken to mitigate the post-procedural risk in this group of patients.

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List of abbreviations

AS	Aortic valve stenosis
AVR	Aortic valve replacement
TAVI	Trans-catheter aortic valve implantation
LA	Left atrium
LV	Left ventricle
RA	Right atrium
RV	Right ventricle
IVST	Interventricular septal thickness
PWT	Posterior wall thickness
EF	Ejection fraction
FS	Fractional shortening
SV	Stroke volume
CO	Cardiac output
LVEDV	Left ventricular end-diastolic volume
LVESV	Left ventricular end-systolic volume
LVH	Left ventricular hypertrophy
LVOT	Left ventricular outflow tract
MAPSE	Mitral annulus peak systolic excursion
TAPSE	Tricuspid annulus peak systolic excursion
E	Peak velocity in early diastole
A	Peak velocity during atrial systole
E/A	Ratio of E and A velocity
EDT	E-wave deceleration time
Sm	Myocardial peak systolic velocity
Em	Myocardial peak early diastolic velocity
E/Em	Ratio of E and Em velocity
FT	Filling time
ET	Ejection time
t-IVT	Total isovolumic time

VTI	Velocity time integral
CSA	cross-sectional area
SR	Strain rate
PLF	Paradoxical low flow
KDOQI	Kidney Disease Outcomes Quality Initiative
eGFR	Estimated glomerular filtration rate
AVA	Aortic valve area
IHD	Ischemic heart disease
HR	Heart rate
BSA	Body surface area
NYHA	New York Heart Association class
BNP	Brain natriuretic peptide
pVO2	Peak oxygen consumption
CABG	Coronary artery bypass grafting
STS score	Society of Thoracic Surgeons scoring system
EuroSCORE	European system for cardiac operative risk evaluation
ROI	Region of interest
ECG	Electrocardiogram
TDI	Tissue Doppler imaging
TIA	Transitory ischemic attack
CVA	Cerebrovascular accidents
AVC	Aortic valve closure time
MRI	Magnetic resonance imaging
CT	Computed tomography
AF	Atiral fibrillation
CAD	Coronary artery disease
LDL	Low density lipoprotein
ACE-inhibitor	Angiotensin-converting enzyme inhibitor
BAV	Balloon aortic valvuloplasty
RVP	Rapid ventricular pacing
CKD	Chronic kidney injury

VARC- 2	Postoperative incidence of VARC-2 complications
iSAVR	isolated surgical aortic valve replacement
MPR	multiplanar reformation
MSCT	Multislice Computer Tomography

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