TAVR bei Patienten mit chronischer Niereninsuffizienz, Adipositas und einer Einschränkung der alltäglichen Fähigkeiten

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Abkürzungsverzeichnis

ADL: activities of daily life.

ARF: acute renal failure.

AV: aortic valve.

BI: Barthel Index.

BMI: body mass index.

CM: contrast medium.

CT: computer tomography.

CV: core valve.

ES: edwars sapien.

GFR: glomerular filtration rate.

HU: Hounsfield Units.

LAHB: left anterior hemiblock.

LBBB: left bundle branch block.

LVOT: left ventricular outflow track.

MRI: magnetic resonance imaging.

MS: membranous septum.

PPMI: permenant pacemaker implantation.

SAVR: surgical aortic valve replacement.

TA: trans apical.

TAVR: Transcatheter aortic valve replacement.

THV: trancatheter heart valve.

TEE: transesophageal echocardiography.

TF: trans femoral.

TEE: transesophageal echocardiography.

1. Zusammenfassung

Hintergrund und wissenschaftlicher Rahmen

Transcatheter aortic valve replacement (TAVR) has advanced the treatment of severe symptomatic aortic valve stenosis not only in high and intermediate risk patients, but also in low risk surgical patients (Thyregod et al. 2015, Mack et al. 2019). Fortunately, the incidence of TAVR-related complications has decreased significantly in recent years, mainly due to progressive improvements in interventional techniques and the additional experience of heart teams. Many studies have investigated TAVR in challenging patients, such as obese patients, patients with reduced functional capacity and patients with chronic renal insufficiency. In these prior studies, there have been contradictory results regarding the outcomes of TAVR in patients with overweight and obesity. Furthermore, the outcomes of patients with reduced functional capacity as assessed by the Barthel Index (BI) have yet to be examined. However, BI is a commonly used scale to assess the activities of daily life in the German health system (Stone et al. 1994) and obesity is a common comorbidity in TAVR patients. Additionally, the safety and technique of trans femoral (TF) TAVR without the use of contrast medium (CM) in patients with chronic renal insufficiency has been reported in small number of patients and should be further investigated.

Fragestellung und Ziele

In three separate analyses, we aimed to assess the outcomes of TAVR in patients with BMI ≥ 25, in patients with reduced functional capacity, and in patients with chronic renal failure who underwent TAVR without the use of contrast medium.

Methodik

For these analyses, we retrospectively evaluated data from TAVR patients at the Central Hospital Bad Berka, Germany. All decisions regarding the method of TAVR, the choice of prosthesis, and the access route were made by the institutional heart-team, which is comprised of cardiologists, cardiac surgeons, and anesthesiologists.

Ergebnisse und Diskussion

In the first study, we included 25 patients with glomerular filtration rate (GFR) <30 mL/min/1.73 m2 who underwent TF-TAVR procedure with the Edwards Sapien balloon-expandable bio prostheses but without the use of contrast between September 2017 and

September 2018. The results obtained were compared with data acquired from 73 matched patients (the control group), who underwent TF-TAVR with Edwards Sapien balloon-expandable bio prostheses with the standard technique using CM. We showed that TF-TAVR without the use of CM can be considered a safe and reproducible alternative technique. This study is the largest case series to describe the safety of TAVR without the use of CM. However, there are many additional points that should be further investigated, including the accuracy of other imaging modalities, such as magnet resonance tomography or 3 D transesophageal echocardiography, for determining the size of the aortic annulus or for predicting the implantation angel in computer tomography (CT) without CM. In the second study, we investigated the influence of BMI on the 1-year outcomes after TF-TAVR in 1609 high- and intermediate-risk TAVR patients who underwent the procedure between March 2014 and March 2018. BMI ≥ 25 kg/m2 was independently associated with lower 1 year mortality after TF-TAVR. These findings were consistent with the results of previous studies but we included a larger number of patients (Van Der Boon et al. 2013). The rate of vascular complications was higher in patients with BMI ≥ 25 kg/m2, which indicates the need for optimization of puncture technique and careful selection of closure devices in this group of patients. In the third study, we investigated the influence of functional impairment, as assessed by the BI, on outcomes 3-months after TF-TAVR. The procedures were performed, under general anesthesia, between January 2017 and January 2018 in 336 patients. . A BI < 80 was associated with increased mortality, risk of neurological events, and cardiac decompensation after TF TAVI. A BI < 80 is an independent predictor of failure in fast track TAVI. This result could help the hospital TAVR team plan post-procedural care.

Schlussfolgerungen

The procedural complications after TAVR are different according to patients' characteristics. Obesity was associated with more vascular complications. Patients with chronic renal failure had higher rate of acute kidney injury, which could be reduced by reducing the amount of used CM. Patients with physical disability had high mortality and neurological events.

2. Einleitung

TAVR is a well-established alternative to surgery for the treatment of patients with severe aortic stenosis. The increasing experience of the heart teams have translated into a reduction of the majority of periprocedural complications and death over the time (Rodés-Cabau, Ellenbogen et al. 2019). Renal insufficiency, obesity, and reduced functional capacity are common comorbidities in TAVR patients. We have investigated how these issues affect specific outcomes in our TAVR patients.

2.1. Complication of TAVR

2.1.1. Permanent pacemaker implantation (PPMI) after TAVR.

2.1.1.1. Rate of PPMI after TAVR.

The incidence of PPMI after surgical AVR is lower than after TAVR even in recent studies which included low risk patients (Popma et al., 2019). New PPMI after surgical AVR was 4.2% during the 30 days postoperatively and 14.4% over 10 years; in a large cohort of patients n= 111,674. (Leyva et al., 2017) The rate of new PPMI after TAVR ranged between 2.3% and 36.1%. (van Rosendael et al., 2018) (Kaneko et al., 2019) (Jilaihawi et al., 2019), (Maeno et al., 2017) (Fujita et al., 2016).

2.1.1.2. Predictors of PPMI.

ECG Predictors: RBBB was independent consistent predictor of new PPMI in all published studies, which could be anatomically explained. In a large cohort of patients after surgical AVR; left axis independently predict postoperative AVB. We suppose that a large portion of those patients with left axis deviation had LAHB. None of TAVR trials found that LAHB is a predictor of PPMI. However, Medeiros et al found that LAHB was tended to be significant predictor of PPMI, in this trial most patients received Lotus valve. The association between the presence of atrial fibrillation and PPMI after TAVR was reported in previous study (Husser, Pellegrini et al. 2016). The cause of pauses in patients with atrial fibrillation is difficult to be differentiated if it is due to sick sinus syndrome or due to atrioventricular block, therefore it is difficult to differentiate, especially in asymptomatic patients, if it is caused by conduction injury after TAVR or not. CT Predictors of the pacemaker implantation: Some studies proved the role of the length of (membranous septum) MS to predict the need of new PPMI (Guetta, Goldenberg et al. 2011; Jilaihawi, Zhao et al. 2019) Treater et al found that gross anatomical variations in CT including the MS, were not associated with the occurrence of either PPMI or new LBBB (Tretter, Mori et al. 2019). However, they found that the relation between the length

of MS and the depth of implantation was a significant predictor of PPMI, this finding supported the results of Tretter et al (Tretter, Mori et al. 2019). The methodology of measuring the septum was different between these studies and this should be standardised to avoid intra and interobeserver variability. The association between the severity valve calcification and its location was not consistent in the previous studies. In 162 patients treated with Sapien and Core valves; elevated LCC calcification was identified as an independent predictor for PPI (Fujita et al., 2016). In other study the amount and the asymmetry of cusp calcification (Kaneko, Hoelschermann et al. 2019) as well as the presence of calcium in device landing zone (Maeno, Abramowitz et al. 2017) were a predictor of PPMI. The used Housnfield threshold during the measurement of valve calcium may dramatically affect the measured calcium score and volume. The threshold for the optimal CT number in Hounsfield Units (HU) to quantify aortic valvular calcium on contrast-enhanced scans has not been standardized. The use of fixed threshold may lead to under- or over- estimation of the valve calcification. Bettinger et al supposed that the best thresh is by adding 100 HU to the luminal attenuation HU (Bettinger, Khalique et al. 2017). The adding of native scan to measure calcium score to the routine protocol will increase the level of radiation exposure (Hou, Tsujioka et al. 2020), but it may provide better assessment of calcium volume. Devices and implantation techniques: Many studies showed that TAVR without predilatation decreased the rate of new PPMI without increasing the risk of paravalvular leak, postimplantation valvuloplasty or other composite endpoints (Bagur, Kwok et al. 2016) (Banerjee, Kandregula et al. 2018). The PPMI rate is between 4.0% and 24.0% with the new-generation SAPIEN 3 device. For self-expandable prostheses, the PPMI remained relatively higher (14.7-26.7%) than with SAPIEN prothesis, despite a reduction in PPMI rates with the new Evolut R (van Rosendael, Delgado et al. 2018). This could be due to the stronger radial force (Dumonteil et al., 2017). Another explaination is the higher rate of valvuloplasty in patients underwent TAVR with selfexpaindable valve, which was associated with higher rate of PPMI. However, selfexpandable prothese (ACURATE neo) has the lowest reported rate of PPMI 9.9% (SAVI TF). Adding to the role of the radial force of the protheses for the development of conduction disturbance after TAVR, the oversizing and the technique of implantation may influence the risk of complete AVB after TAVR in CV (Petronio, Sinning et al. 2015). On the other hand the high implantation technique might increase the risk of device migration. A tailored technique of implantation according to the lenghth of MS by positioning the device at a depth of < MS length; MInimizing Depth According to the membranous Septum (MIDAS) approach; showed to reduce the rate of new PPMI 9.7% to 3.0%, and the rate of new left bundle branch block from 25.8% to 9%. Also in other valves as ES and Lotus valve careful

attention to valve sizing and implant depth may help to reduce the rate of PPM. (Dumonteil, Meredith et al. 2017) (Husser, Pellegrini et al. 2016) whereas Gonska er al supposed that implantation depth and oversizing did not have an impact on PPMI.(Gonska, Seeger et al. 2017).

2.1.1.3. Monitoring after TAVR and the incidence of late conduction disturbance. According to the current recommendations; TAVR patients without RBBB or new ECG changes should be monitored only for 24 hours (see figure 1).

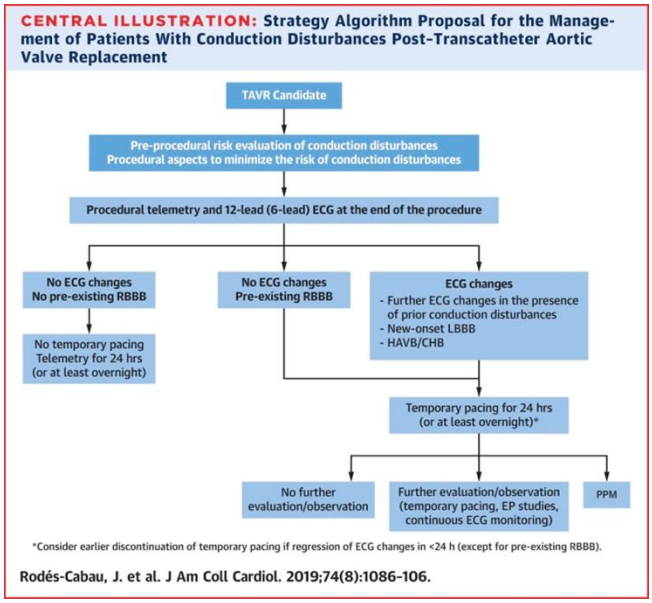


Figure 1: monitoring of TAVR-patients according to postoperative ECG changes (Rodés-Cabau et al. 2019).

2.1.1.4. Indication of PPMI after TAVR: the last european guideline for pacing was published in 2013, which should be updated to include the different scenarios of conduction disturbance after TAVR. The american heart association published in 2019 expert consensus document, which provides the best available guide for the management of conduction disturbances after TAVR (Rodés-Cabau, Ellenbogen et al. 2019) . In this recommendation, high degree AVB block or new bundle branch block with QRS > 150 millisecond and AVB > 24 millisecond were the indications to PPMI.The adherence to the guidelines (Petronio, Sinning et al. 2015) and the careful prolonged observation as well as the measurement of HV intervals in patients with new LBBB (Kostopoulou, Karyofillis et al. 2016) might reduce the incidence of new PPMI after TAVR.

2.1.1.5. The implication of PPMI after TAVR. The hospital stay after TAVR could be prolonged in patients with conductions disturbence, see the algorithm of the patients follow up after TAVR (see figure 1). This prolonged hospital stay can be avoided if the PPMI was done at the same day of TAVR, this concept showed to be safe and feasible(Sideris, Benetos et al. 2016), but it may increase the rate of new PPMI. Many studied showed that new PPMI after TAVR was not associated with adverse clinical outcomes (Urena, Webb et al. 2014) (Meduri, Kereiakes et al. 2019) . (Ueshima, Nai Fovino et al. 2018). However Partner trial showed that new PPM and chronic LBBB patients, had worsened clinical and echocardiographic outcomes relative to no PPM patients, and the presence of a PPM was independently associated with 1-year mortality. Ventricular dyssynchrony due to chronic RV pacing may be mechanistically responsible for these findings (Dizon, Nazif et al. 2015).

2.1.2. Coronary obstruction.

2.1.2.1. Diagnosis of coronary artery disease: The role of CT coronary angiography increase dramatically at the last years especially after publishing ischemia trial in 2018 (Maron, Hochman et al. 2018). However, the interpretation of the coronaries in TAVR patients is challenging because of high calcification burden and the lack of optimal preparations because of the aortic stenosis. Therefore, CTA has excellent performance in the setting of TAVR in terms of negative predictive value, at the cost of a relatively poor specificity (Faroux, Guimaraes et al. 2019).

2.1.2.2. The predictors of early coronary obstruction are: low coronary ostien < 10mm , narrow sinus of valsalva < 25, valve in valve, bulky calcified leaflet, THV with long frame and skirt.

2.1.2.3. The optimisation of implantation technique, especially in long frame valves, is necessary to improve the access of the coronaries after TAVR. In EvolutR: the valve should be introduced with the hub point to three o'clock, the hit marker should point to the outer curvature of the aorta, in two cusps view (where RCC and LCC overlapped) the hit marker should be in the middle or to the right. In Acurate neo: the valve should be rotated in ascending aorta to see the pins on both sides. Severe overlap of an Evolut valve commissure with the left main, right coronary, or one or both of these arteries was 33.1%, 20.3%, and 39.0%, respectively. During the initial deployment, when the black capsule "hat" marker on the valve catheter was positioned at the inner curve/center back of the aortic root, severe overlap of the neo-commissures with the left main and right coronary artery was much higher, 63.9% and 52.8%, respectively (see figure 2). In contrast, when the capsule hat marker was positioned on the outer curve/center front of the aortic root, the commissure of the Evolut valves overlapped

the left main and right coronary arteries in only 19.5% and 6.1% of cases, respectively (Tang, Zaid et al. 2019). Patients with a short distance between coronary ostia and annular plane, may benefit from the specific technology of the Symetis ACURATE neo. Its unique upper crown and X-Shaped design allow implant with the best coronary clearance by capping diseased native leaflets without any ostium occlusion.

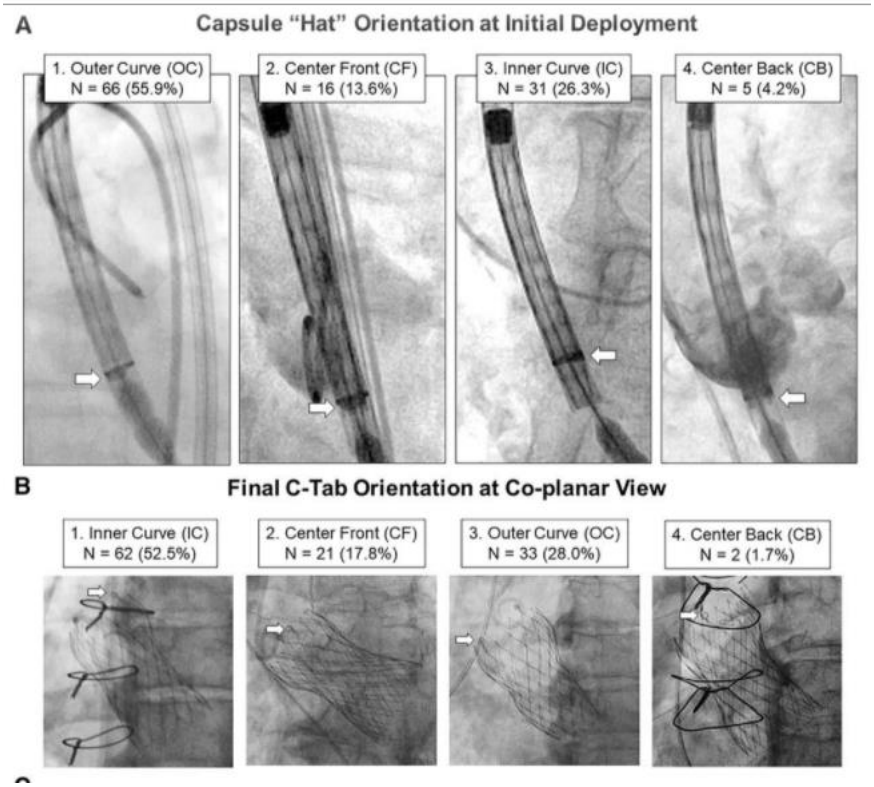


Figure 2: the different positions of „hat" marker before and after valve release (Tang et al. 2019).

2.1.3. Paravalvular leak.

2.1.3.1. Predictors. Eccentricity, severity and asymmetry of annular calcification and LVOT calcification as well as the type of THV predicts the rate of PVL. Figure 3 showed the impact of the type of the TAVR prosthesis on the PVL.

2.1.3.2. Evaluation. The best method to evaluate the severity and mechanism of PVL is the TEE. However, the use of intraprocedural transesophageal echocardiography is currently uncommon. In most of centers, the evaluation of acute PVL mainly on TTE and the aortogram. The evaluation of PVL in TTE is not easy due to artefact and should be done in the short axis. Therefore, may studies tried to classify the PVL objectively with aortic regurge index or with viedo densitometry. (Modolo, Chang et al. 2020).

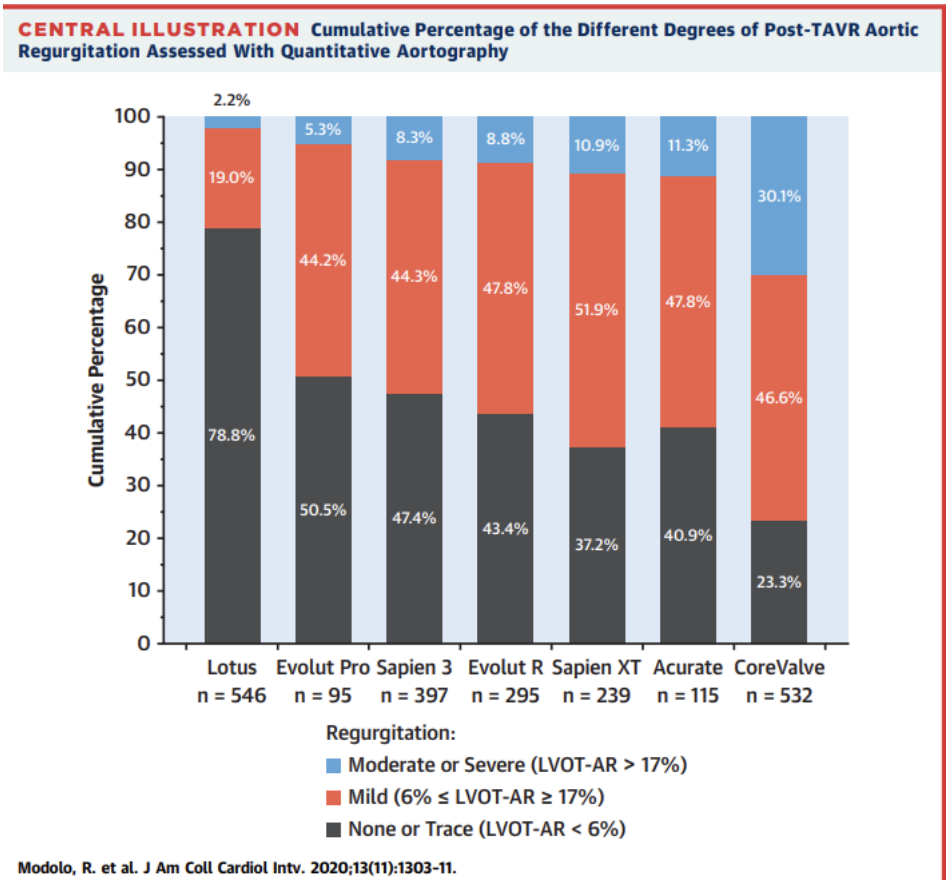


Figure 3: the incidence of PVL in different TAVR prosthesis (Modolo et al. 2021)

2.1.3.3. How to treat. Moderate to severe PVL increased mortality and should be treated. The first step to treat PVL is to understand the mechanism of PVL. If the position and sizing of the THV is correct, so the post dilatation and closure with dedicated devices are the commonly used therapy. The last line therapy is either valve in valve or conventional surgery.

2.1.4. Vascular complication.

2.1.4.1. Predictors: sheath to vessel ratio, tortouisity (> two more than 90° bends), female gender and amount of calcification especially on the anterior wall of common femoral artery (Blakeslee-Carter, Dexter et al. 2018).

2.1.4.2. Prevention: ultrasound – or road map- guided puncture of the common femoral artery as well as safety wire from ipsilateral or contralateral are effective measures to reduce major vascular complications (Sanghvi, Swarup et al. 2020; Witberg, Tzalamouras et al. 2020).

2.1.4.3. Treatment: in most of cases the VCs could be treated interventionally. However, the involvement of vascular surgeon in the decision making is crucial especially in comlex cases as the presence of large pseoudoaneurysm. However, there is a case report showed us how we can treat a large pseudoaneurysm through an angioseal closure device.

2.1.5. Neurological complication

2.1.5.1. Predictors: the inciedence of ischemic and hemorrhagic strokes were 2.4% and 0.2% in a recent retrospective analysis of 36,220 patients who underwent TAVR . In these analysis the factors independently associated with post-TAVR ischemic stroke included a history of carotid artery disease, peripheral artery disease, atrial fibrillation or flutter, older age, bicuspid aortic valve, and female sex were predictors of neurological complications after TAVR.

2.1.5.2. Preventions: use of the cerebral protection devices was associated with a lower risk for in-hospital mortality and ischemic stroke but a higher cost of the index hospitalization. (Megaly, Sorajja et al. 2020)

2.1.5.3. Cerebral protection devices: the available CP devices are showed in table 2. The most commonly used device until now is sentinel device, which implanted through righ radial artery and based on two filters technique , one should be implanted on left carotid artery and the second on the common brachiocephalic trunk (Cubero-Gallego, Pascual et al. 2019).

2.1.6. LV perforation. LV perforation is serious life-threatening complication requiring immediate emergency surgery. The incidence of this complication decreased significantly over the years from 10% to 1.4% in other series (Eggebrecht, Vaquerizo et al. 2018). The resulting cardiac tamponade is lethal, recording average mortality of 75% (Seiffert, Conradi et al. 2013). Small left ventricular cavity with hypercontractile state and narrow aortomitral angle are potential predictors of left ventricular perforation (Rezq, Basavarajaiah et al. 2012; Owais, El Garhy et al. 2017). The use of dedicated wires and pacing over the LV wire may be helpful to avoid ventricle perforation (Faurie, Abdellaoui et al. 2016).

2.1.7. Annular rupture.The site and the extent of LVOT rupture influence the clinical presentation (see figure4), the outcomes and the way to treat this perforation (see diagram). Therefore, the mortality of subannular LVOt injury varies between 49 and 67 % (Coughlan, Kiernan et al. 2018). Subannular calcification in close proximity of the anatomically unprotected muscular LVOT (Girdauskas, Owais et al. 2017) are the main risk factor for the “non-contained” rupture. Other risk factors for LVOT rupture are ballon expandable valve, valvulplasty and oversizing >20% (Pasic, Unbehaun et al. 2012; Hansson, Nørgaard et al. 2015). Contained LVOT rupture can be conservatively treated and had low mortality (~25%)

(Coughlan, Kiernan et al. 2018). Nonetheless; it is a catastrophic complication and should be treated promptly. Even with early surgical intervention the mortality still very high up to 100% in high risk patients (Girdauskas, Owais et al. 2017).

2.1.8. Valve degeneration. Subclinicalleaflet thrombosis, characterized by hypoattenuatedleaflet thickening (HALT) and reducedleaflet motion (RLM) represent a form of bioprosthetic valve dysfunction (Makkar, Blanke et al. 2020). HALT with RLM was not rare but usually subclinical. Valve hemodynamics and mid-term outcomes were uneventful even without additional anticoagulant therapy in our limited number of cases. Male sex, larger sinus and bioprosthesis size, and elevated D-dimer levels during follow up were associated with this phenomenon (Yanagisawa, Hayashida et al. 2017). On MDCT, 12.5% of patients showed HALT or reduced leaflet motion, whereas only one of these patients had abnormal valve haemodynamics on echocardiography. Neither HALT nor increased transvalvular gradient were associated with stroke/TIA (Vollema, Kong et al. 2017). The frequency of HALT and RLM was similar between TAVR with EvolutR and surgical AVR (about 30% in 1 year). Aortic valve hemodynamic status was not influenced by the presence or severity of HALT or RLM at either time point (see figure 5). The rates of HALT and RLM were similar after the implantation of supra-annular, self-expanding transcatheter, or surgical bioprostheses.

Figure 4: the consequence of annular complication according to the site of calcification (Girdauskas et al. 2017).

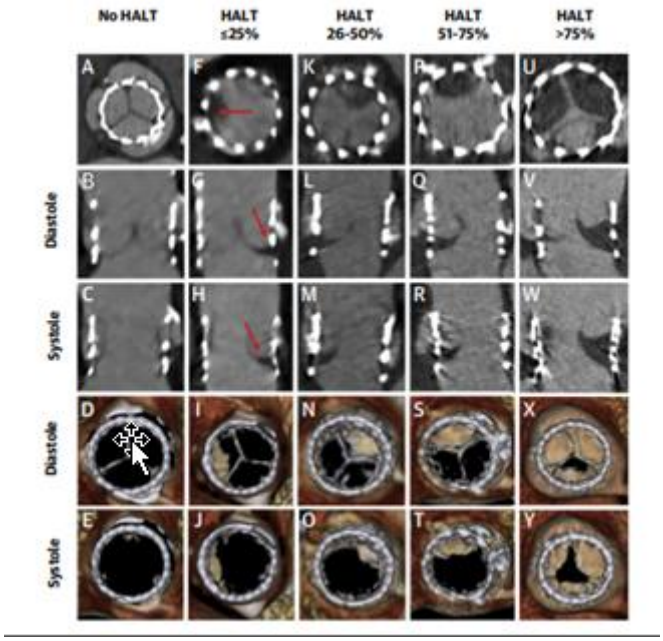


Figure 5: different types and grades of valve thrombosis, characterized by hypoattenuatedleaflet thickening (HALT) and reducedleaflet motion (RLM) (Makkar et al. 2020).

2.2. TAVR in patients with renal insufficiency

2.2.1. Acute renal failure (ARF) after TAVR The incidence of TAVR-related complications has decreased significantly over recent years, mainly due to progressive improvements in interventional skills, additional experience of the heart team and advancements in catheter-based equipment. The risk of ARF is less common in TAVR compared to in surgical aortic valve replacement (SAVR) (Bagur et al. 2016). However, ARF remains one of the most relevant complications after TAVR and , despite being rare, is associated with increased post procedural morbidity and mortality (Yamamoto et al. 2013b). ARF is most likely a multifactorial event that is not only related to the use of contrast solution but also to the presence of preexisting renal disease, congestive heart failure, age, anemia, diabetes and profound hypotension (Perrin et al. 2018). Notably, CM-induced renal failure is the third most common cause of in-hospital acquired renal failure. The prevalence of contrast medium-induced renal failure peaks at 48 hours postoperatively and then gradually declines until normalizing during the second post procedural week(Briguori et al. 2007). Thus, using previously published case reports (Latib et al. 2014, Bruschi et al. 2016, Arrigo et al. 2015), we developed our protocol for performing TAVR procedures without contrast solution. This strategy has significant potential for decreasing the incidence of contrast induced-ARF following TAVI.

2.2.2. How to reduce the use of CM in the setting of TAVR The risk of ARF after TAVR could be reduced by limiting the exposure to CM. Preoperative, the measuring of aortic annulus could be done with 3 D transesophageal echocardiography (TEE) instead of contrast enhanced CT. However, additionally native CT scan should be done to assess the calcification of aortic valve and left ventricular outflow track (LVOT), to assess the height of coronary ostium and the annulus angel projection. Chaturvedi et al. reported that magnetic resonance imaging (MRI)-based AV annular measurements were superior to the CT-based measurements (Chaturvedi et al. 2016). In the future, MRI could be a useful diagnostic tool for contrast-free TAVI programs if this modality can successfully replace multislice CT measurements(Chaturvedi et al. 2016). Another alternative approach to reducing the contrast medium burden during coronary angiography with iodine is the use of gadolinium; because of their different chemical structures, gadolinium and iodine CM have no cross-reactivity in patients with iodine allergies, and gadolinium has a lower nephrotoxicity at the recommended doses than iodine CM (Chaturvedi et al. 2016). Intraoperatively, the use of TEE is mandatory to reduce the amount of used CM during the valve implantation.

2.2.3. Reported cases of TAVR without the use of contrast medium A TAVR without the use of CM was initially described by Ferrari et al. in 2010 (Ferrari et al. 2010) using a balloon-expandable Sapien valve via trans apical approach. However, there are only a very limited number of case series that report the same “contrast-free” trans femoral TAVR implantation technique. For instance, Bruschi et al. and Arigo et al. published a case report on a contrast-free TAVI with Core Valve (Bruschi et al. 2016, Arrigo et al. 2015); Latib et al. published a series of 3 patients who underwent Direct Flow valve implantation and the use of single contrast shot to only check the femoral closure site [10] (Latib et al. 2014); and Leroux et al. published one TAVR case with a balloon-expandable Sapien valve without the use of contrast solution (Leroux et al. 2013).

2.3. TAVR in obese patients

2.3.1. Obesity paradox Obesity is considered to be a morbidity- and mortality-dependent cardiovascular factor(Poirier et al. 2006). Nevertheless, several studies have reported that obese patients undergoing aortic valve replacement have better outcomes than no obese patients (Vaduganathan et al. 2012, Thourani et al. 2011) and this was also found for percutaneous coronary intervention(Gruberg et al. 2002). We would explain this finding by the fact that overweight patients might have more metabolic reserve and are usually intensively treated with optimum medical therapy for the associated risk factors and consequently contributing to better outcomes(Konigstein et al. 2015).

2.3.2. Obesity paradox in TAVR patient The impact of obesity is still being debated in the current literature with respect to TAVR. Tokarek et al. showed that increased BMI was independently associated with 1-year survival benefit after TAVR. However, there was no difference between the groups in terms of 30-day all-cause mortality(Tokarek et al. 2019). Van der Boon et al showed that obesity was associated with a decrease in 30-days mortality, but had no effect on long-term outcomes(Van Der Boon et al. 2013). In an analysis from the FRANCE2 (French Aortic National Core Valve and Edwards 2), overweight and obesity were associated with improved 1- year survival(Yamamoto et al. 2013a). BMI remained an independent predictor of improved survival in multivariate analysis.

2.3.3. Vascular complication in obese patients undergoing TAVR Major vascular complications in the setting of TAVR were associated with markedly increased mortality. Sheath to femoral artery ratio (van Kesteren et al. 2018), Pelvic vessel tortuosity (at least 2 bends ≥90°) and coronary artery disease (Batchelor et al. 2020) were independent predictors of major vascular complications. In these studies, neither obesity nor the depth of femoral artery in CT were an independent predictor of major vascular complication in TAR (van Kesteren et al. 2018, Batchelor et al. 2020), this may be due to the improvement of puncture techniques and closure devices. Notably, these two studies included only patients treated with Sapien Valve. Perhaps the flexibility of the e Sheath decreased the rate of vascular complication compared with the use of the ratio with a stiffer sheath. Also in patients treated with ACURATE neo prosthesis, the use of only the expandable mesh component of the trans Glide introducer system (Mesh only) instead of the use of introducer sheath was feasible in all patients and decreased the major vascular complication (Kim et al. 2019). However, this technique is not the standard and is not popular.

2.3.4. Assessment of central obesity using CT Fat analyses could be performed from CT data using a predefined image display setting [window with, − 150 to − 50 HU] to identify voxels that correspond to adipose tissue. The total abdominal fat composed of visceral abdominal fat (VAF) area and subcutaneous abdominal fat (SAF). This analyses could be helpful when evaluating the relationship between prognosis and obesity. In retrograde analysis of the CT data of 1,372 patients, the obesity paradox was approved in TAVR patients. Larger VAF and SAF were associated with better prognosis. In contrast, the clinical outcomes of patients with high density of adipose tissue were independently associated with increased risk of mortality(Shibata et al. 2020).

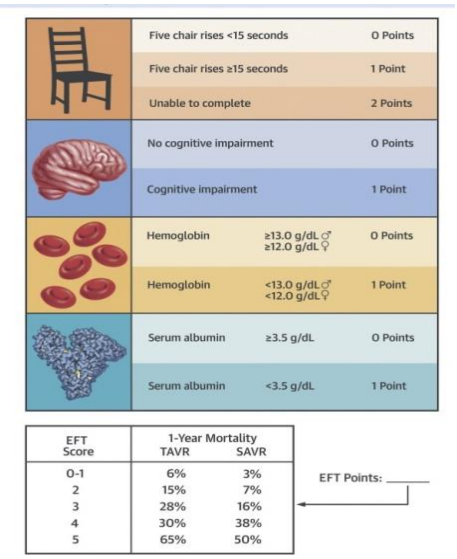
2.4. *2.3. TAVR in patients with functional and physical disability.*

2.4.1. TAVR in Patients with physical disability Preoperatively, physical disability is more prevalent among patients undergoing TAVR than in patients undergoing conventional aortic valve replacement (Genta et al. 2017). The consensus has been that functional impairment, as assessed by scales such as the Katz Index, Elderly Mobility Scale, Canadian Study of Health and Aging Scale, and Erasmus Scale, worsened the mid- and long-term outcomes after TAVR (see figure 4) (Goudzwaard et al. 2019, Kleczynski et al. 2017, Puls et al. 2014, Rogers et al. 2018). In the context of rehabilitation, the BI is a commonly used scale to assess the performance in activities of daily life (ADL) in the German health system(Wade und Collin 1988, Stone et al. 1994). However, prior research did not investigate the impact of functional impairment measured by the by BI on outcomes after TAVR. Pulls et al. showed that functional status measured by the Katz Index represents a powerful predictor of adverse early and late outcome after TAVI but not on of the success of early discharge(Puls et al. 2014). In the study by Puls et al., the rate of early discharge was very low 5%, as the concept of fast track TAVI was not yet well established in 2014 and 53% of study patients were operated through trans apical approach. Nevertheless, the incidence of prolonged hospital stay >14 days was more common in patients with Katz index <6. According to our experience, the success of fast track protocol improved patient's, families' and team's satisfaction and reduced the overall health care costs. But this needs a precise patient's selection to exclude patients who had negative predictors of the success of fast track protocol(Owais et al. 2018). In patients with impaired functional capacity there are two common comorbidities; delirium and frailty; which could influence the outcomes after TAVR.

2.4.2. TAVR in Patients with delirium The assessment of cognitive function using validated tools is mandatory. There are many avilable tests to screen for dementia e.g. Mini Mental State Examination or Nu-DESC test. Nu-DESC test are one of the commonly used delirium test in Germany. Several studies agreed that postoperative delirium was a predictor of long-term mortality (Eide et al. 2015, Bagienski et al. 2017, Goudzwaard et al. 2019).

2.4.3. TAVR in frail patients There is growing evidence that frailty is an independent predictor of mortality after TAVR (Rodés-Cabau und Mok 2012, Afilalo et al. 2017), see figure 6 and 7. The assessment of frailty could be done with different methods; subjectively based on "eyeballing," or objectively used different parameters as walk test, grip test, etc, see figure 5. In the study of Kleczynski et al., the percentage of frail patients ranged between 6.9% and 52% according to the used index(Kleczynski et al. 2017). Green et al. showed that frailty was not associated with increased procedural complications (Green et al. 2012). On the other hand , Rodes-Cabau et al. identified frailty assessed by eyeballing as an independent

predictor of mortality after TAVI (Rodés-Cabau und Mok 2012). In two recent studies, psoas muscle area and volume correlated to frailty indexes and predicted long term mortality after



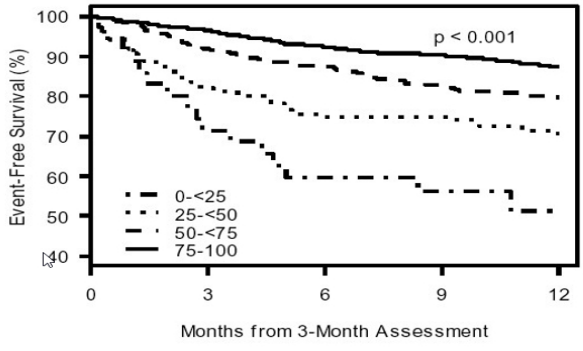
TAVI (Kleczynski et al. 2017, Saji et al. 2016).

Figure 6: different parameters of essential frailty tool test and its implication on the 1 year mortality (Afilalo et al. 2017) .

Figure 7: 1-year event free survival after TAVR stratified by Canadian Study of Health and Aging Scale (Kleczynski et al. 2017).

3. Ziele der Arbeit

In the first study, we aimed to compare the outcomes of TF-TAVR with and without the use of CM in patients with GFR <30 mL/min/1.73 m2.



In the second study, we evaluated the association between BMI and TAVR outcomes, particularly focusing on procedure-related complications and mortality.

In the third study, we investigated the influence of functional impairment as measured by the BI on 3-month outcomes after TF-TAVI performed under general anesthesia.

Transcatheter Aortic Valve Replacement Without the Use of Contrast Medium: An Alternative Safe Implantation Technique

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ABSTRACT: Background. New transcatheter equipment and accumulated experience have stimulated further refinements in implantation techniques. We aimed to compare the outcomes of transfemoral transcatheter aortic valve replacement (TF-TAVR) with and without the use of contrast medium (CM) in patients with glomerular filtration rate (GFR) <30 mL/min/1.73 m^2. **Methods.** This single-center, retrospective study included all patients who underwent TF-TAVR procedure with Edwards Sapien balloon-expandable bioprostheses between September 2017 and September 2018 at the Zentralklinik Bad Berka Germany, and compared outcomes of TF-TAVR with and without the use of CM. **Results.** A total of 98 consecutive patients were included in this study; 25 patients underwent TF-TAVR without the use of CM and 73 patients underwent TF-TAVR with the use of CM. Acute kidney injury was significantly higher in patients who received CM (15 patients [20.5%] in the control group vs 1 patient [4%] in the study group; *P*=.04). Other procedure-related complications were equally distributed between both groups. **Conclusion.** TF-TAVR without the use of CM can be considered a safe and reproducible alternative technique. Furthermore, it reduced the incidence of postoperative acute kidney injury in patients with GFR <30 mL/min/1.73 m^2.

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KEY WORDS: acute renal injury, contrast solution, kidney disease, nephropathy, TAVI

Recently, transcatheter aortic valve implantation (TAVI) has advanced in the treatment of severe symptomatic aortic valve stenosis in not only high-risk, but also intermediate surgical risk patients.[1] Fortunately, the incidence of TAVI-related complications has decreased significantly over recent years, mainly due to progressive improvements in interventional skills, additional experience with the heart team, and advancements in catheter-based equipment. However, acute renal failure (ARF) remains one of the most relevant complications and, despite being rare, is associated with increased postprocedural morbidity and mortality.[2,3] The risk of ARF is less common in TAVI patients than in those who undergo surgical aortic valve replacement (SAVR).[4] However, ARF is most likely a multifactorial event that is not only related to the use of contrast solution but also to the presence of pre-existing renal disease, congestive heart failure, age, anemia, diabetes, and profound hypotension.[5] Notably, contrast-medium induced renal failure is the third most common cause of in-hospital acquired renal failure. The prevalence of contrast-medium induced renal failure peaks at 48 hours post operation and then gradually declines until normalizing during the second postprocedural week.[6] Herein, we describe our new protocol for performing TAVI procedures without contrast solution. This strategy has significant potential for decreasing the incidence of contrast-induced ARF following TAVI.

Methods

Study population and data collection. The decisions regarding the method of aortic valve replacement (SAVR vs TAVI), the choice of TAVI prosthesis (balloon expandable vs self expandable), and the access route (transfemoral vs transapical) were made by the institutional heart team, which comprised cardiologists, cardiac surgeons, and anesthesiologists. The specific decision to use a contrast-free procedure was made following a multidisciplinary discussion within the institutional heart team. A total of 25 patients with pre-existing severe nephropathy were included in the study group. During the same study period (September 2017 to September 2018), a total of 187 patients underwent a TAVI procedure with Sapien balloon-expandable bioprostheses (Edwards Lifesciences) at our hospital. From those patients, we identified 73 matched patients with glomerular filtration rates <30 mL/min/1.73 m^2. All data were collected retrospectively from our institutional records. Preoperative parameters were obtained from the following: heart catheterization, to perform coronary and iliofemoral angiography; femoral duplex, to exclude femoral atherosclerosis and pseudoaneurysm; three-dimensional (3D) transesophageal echocardiography (TEE), to describe the size and morphology of the valve together with coronary ostia distances; and native computed tomography (CT), to roughly illustrate the valve annular size, coronary ostia distances, and iliofemoral tree gross anatomy.

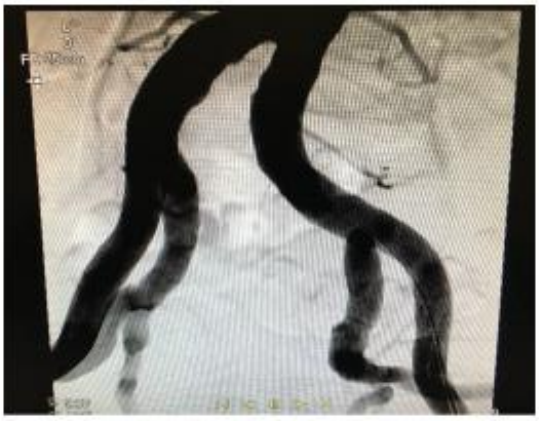

FIGURE 1. Iliofemoral angiography to assess the femoral artery anatomy.

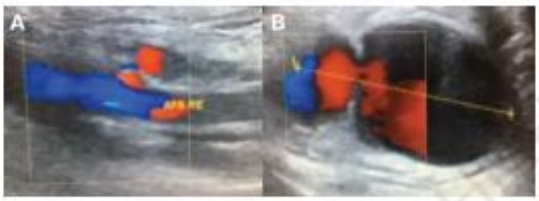

FIGURE 2. (A, B) Preoperative two-dimensional color Doppler ultrasound to assess femoral artery access.

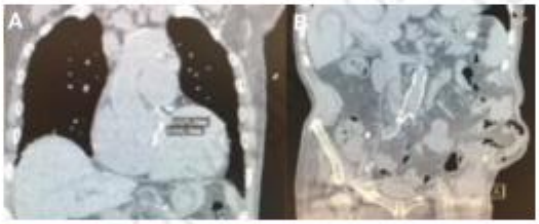

FIGURE 3. (A) Preoperative native computed tomography (CT) scan to measure aortic valve annular size, coronary ostia distances, and left ventricular outflow tract morphology. (B) CT scan of iliofemoral vessel anatomy.

Statistical analysis. Continuous variables are expressed as means and standard deviations. Categorical data are expressed as percentages. All analyses were done using SPSS statistical software (2013, IBM Corporation; IBM SPSS Statistics for Windows, version 22.0).

Technical aspects of the intervention. The primary goal of the preoperative and intraoperative protocol was to avoid intraoperative complications, such as annular rupture or valve migration, and to implant the transcatheter valve

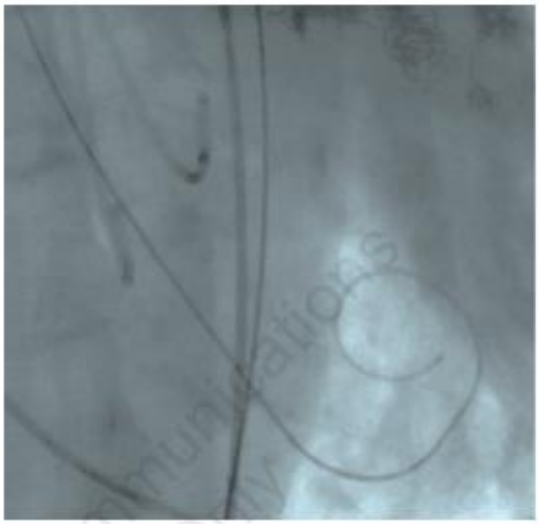

FIGURE 4. Intraoperative chest x-ray image demonstrating the presence of a preshaped stiff wire in the left ventricle and two pigtail catheters in the left coronary sinus and the non-coronary sinus.

in the most appropriate position without any compromises. Our aim was to implement a precise, complete, investigatory protocol for these patients. The major research question during the preoperative work-up was "how can we gain the same information that contrast-enhanced multislice CT scans preoperatively provide by other investigations, without using contrast solution?" For this purpose, we performed preoperative heart catheterization to perform coronary and iliofemoral angiography (Figure 1) and femoral duplex sonography to exclude femoral atherosclerosis and pseudoaneurysm (Figure 2). Coronary angiography was mandatory as a preoperative investigation. We simultaneously performed iliofemoral angiography with only 10 mL contrast medium, which is a smaller volume than would be used during CT.

Additionally, we used preoperative 3D-TEE to obtain aortic valve (AV) annular size measurements and to obtain a detailed description of the valve morphology as well as the coronary ostia distances. A native CT scan was performed to measure the AV annular size, coronary ostia distances, left ventricular outflow tract morphology, and iliofemoral vessel anatomy (Figure 3).

Intraoperatively, we aimed to puncture a well-palpable femoral artery after the anesthesiologist administered a minimal bolus of catecholamines. We performed all of the procedures through the transfemoral approach using two pigtail catheters. One pigtail catheter was positioned in the deepest point of the non-coronary cusp, and the second catheter was positioned in the left coronary cusp through

Table 1. Baseline characteristics of study patients.

	Group 1 (n = 25)	Group 2 (n = 73)	*P*-Value
Age (years)	82 ± 9.5	81.6 ± 8.6	.30
Men	14 (56%)	37 (50.6%)	.40
COPD	6 (24%)	14 (19.1%)	.30
CRF >II	25 (100%)	73 (100%)	NA
NYHA III-IV	23 (92%)	60 (82%)	.20
Previous myocardial infarction	8 (32%)	25 (34%)	.50
Pulmonary HTN	9 (36%)	22 (30%)	.30
BMI >30 kg/m²	7 (28%)	19 (26%)	.50
Preoperative creatinine (mg/dL)	2.4 ± 0.5	2.3 ± 0.4	.09
Log EuroScore	35.4 ± 13.3	36 ± 12	.10
STS score (%)	8.3 ± 2.1	8.5 ± 2.6	.30

Data presented as mean ± standard deviation or number (percentage). BMI = body mass index; COPD = chronic obstructive pulmonary disease; CRF = chronic renal failure; HTN = hypertension; NA = non-applicable; NYHA = New York Heart Association.

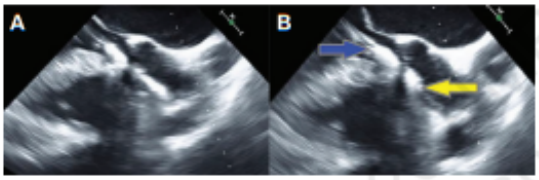

FIGURE 5. Implantation of balloon-expandable valve in a systematic two-step approach that included: (A) the positioning step; and (B) the full deployment step under transesophageal echocardiography and radiographic guidance. Arrows indicate the working length of the Sapien 3 balloon, which was inflated at 4 atm.

the right radial approach and the contralateral femoral artery (Figure 4).

To position and implant the balloon-expandable valve prostheses, we used TEE combined with radiological images of two pigtail catheters in the aortic root as intraoperative guidance. Valve implantation was systematically performed in a two-step approach. During step 1, the balloon-expandable valve was positioned in the landing zone of the AV annulus under fluoroscopic and echocardiographic guidance and was slowly inflated under fast pacing (130 beats/minute) until we were able to see the inflated balloon under TEE. The position of the valve was re-evaluated by TEE, which presented an opportunity to reposition the valve using the fine-tuning knob on the Edwards Sapien 3 delivery system. The repositioning process was guided by TEE in the long-axis view, which ensured full visualization of the left ventricular outflow tract (LVOT)–aortic annulus–ascending aorta axis, as well as by radiological images of the two pigtail catheters in the aortic root. Step 2 was a rapid pacing phase, which was followed by the full balloon inflation and complete deployment of the valve prosthesis in the selected position (Figure 5).

Intraoperatively, coronary malperfusion was ruled out if the TEE showed no new regional wall-motion abnormalities and if the electrocardiogram was free of any new ischemic changes. Notably, intraoperative TEE was performed by the same anesthesiologist who performed the procedure preoperatively. Femoral access-site complications were ruled out if the clinical examination of the groin was unremarkable and no femoral bruit was heard on auscultation.

Results

The demographic and preoperative data of the entire study cohort are displayed in Table 1. The logistic EuroScore I was 35.4 ± 13.3% in the study group vs 36 ± 12 in the control group, while the Society of Thoracic Surgeons (STS) score was 8.3 ± 2.1% in the study group vs 8.5 ± 2.6% in the control group. All preoperative characteristics were equally distributed in both groups.

Table 2 displays all relevant intraoperative parameters. Most patients in both groups received a 26 mm Edwards Sapien 3 valve. The TEE measurements were the cornerstone of the valve size decision. All implantation procedures were uneventful, without major complications including valve embolization, severe paravalvular leakage, pericardial effusion, and aortic annulus rupture. Intraoperative and early postoperative TEE was extensively used to rule out these complications. Notably, the implantation times recorded in this series ranged between 35–60 minutes, which are very comparable to the standard contrast-guided transcatheter aortic valve replacement (TAVR) procedure.

Post operation, 1 patient (4%) required a pacemaker in the study group due to a total atrioventricular block vs 3 patients (4.1%) in the control group. There was no in-hospital mortality; however, 3 patients died during the 30-day follow-up period (1 patient [4%] in the study group vs 2 patients [2.7%] in the control group; *P*=.50). The patient in the study group was a multimorbid 83-year-old male with recurrent episodes of cardiac decompensation and pneumonia in addition to aortic stenosis. Furthermore, his surgery was postponed by 3 weeks until he reached a better compensatory state without pneumonia. There were no periprocedural strokes or major vascular complications. All postoperative results are summarized in Table 2.

Discussion

In the present study, we analyzed the procedural outcomes of 25 consecutive transfemoral (TF)-TAVI patients who underwent the procedure without receiving a single dose of contrast medium. All TF-TAVI procedures were performed by the same experienced and institutional TAVI team. Furthermore, we compared the outcomes in the study

Table 2. Operative results and postoperative endpoints.

	Group 1 (n = 25)	Group 2 (n = 73)	*P*-Value
Edwards Sapien 3	25 (100%)	73 (100%)	.70
23 mm	7 (28%)	15 (20.5%)	
26 mm	14 (56%)	47 (64.4%)	
29 mm	4 (16%)	11 (15.1%)	
Implantation success	25 (100%)	73 (100%)	NA
Valve embolization	0 (0%)	0 (0%)	NA
Conversion to sternotomy	0 (0%)	0 (0%)	NA
Perioperative myocardial infarction	0 (0%)	0 (0%)	NA
Annular rupture	0 (0%)	0 (0%)	NA
Pericardial tamponade	0 (0%)	0 (0%)	NA
Intra-aortic balloon pump	0 (0%)	0 (0%)	NA
Emergency cardiopulmonary bypass	0 (0%)	0 (0%)	NA
Extubation in OR	25 (100%)	73 (100%)	NA
30-day mortality	1 (4%)	2 (2.7%)	.50
Postoperative PI	1 (4%)	3 (4.1%)	.70
Acute kidney injury	1 (4%)	15 (20.5%)	.04
Major vascular complication	0 (0%)	0 (0%)	NA
Postoperative mean transvalvular gradient >20 mm Hg	0 (0%)	0 (0%)	NA
Postoperative mean transvalvular gradient (mm Hg)	9 ± 5	8 ± 3	.10
Moderate to severe PVL	0 (0%)	0 (0%)	NA
Stroke	0 (0%)	0 (0%)	NA

Data presented as number (percentage) or mean ± standard deviation. NA = not applicable; OR = operating room; PI = pacemaker implantation; PVL = paravalvular leak.

patients with those of matched patients who underwent TAVI with the use of contrast media.

This study is limited to balloon-expandable TAVR valves because of the opportunity to visualize balloon inflation under TEE guidance. A similar procedure was initially described by Ferrari et al[7] in 2010. However, there is a very limited number of case series that report the same "contrast-free" TAVR implantation technique. For instance, Bruschi et al[8] and Arigo et al[9] published case reports on a contrast-free TAVI with the CoreValve (Medtronic); Latib et al[10] published a series of 3 patients who underwent implantation of a Direct Flow valve (Direct Flow Medical) and the use of a single contrast shot to check the femoral closure site; and Leroux et al[11] published 1 TAVR case with a balloon-expandable Sapien valve without the use of contrast medium. To the best of our knowledge, the present series represents the largest cohort to date with the TAVR procedure performed without any use of contrast media.

The major difference between our cohort and the study by Ferrari et al[7] is the implantation approach; all implantations in our study were performed using the TF approach, whereas the Ferrari study established transapical access. Ferrari et al[7] published a series of 30 TAVR patients who underwent the procedure without the use of contrast media in 2010, but all of the procedures were performed with a transapical approach.

During the preoperative work-up, we tried to minimize the amount of contrast medium employed during coronary and iliofemoral angiography before TAVI (mean amount 25 mL, ranging from 23-36 mL) by performing coronary angiogram in a biplane C-arm setting. Another alternative approach to reducing the burden from iodinated contrast medium during coronary angiography is the use of gadolinium; because of their different chemical structures, gadolinium and iodinated contrast have no cross-reactivity in patients with iodine allergies, and gadolinium has a lower nephrotoxicity at the recommended doses than iodinated contrast media.[12]

At 30-day follow-up, the composite endpoint of death from any cause, valve embolization, vascular complications, cerebrovascular complications, pacemaker implantation, and postoperative myocardial infarction was equally distributed between both groups, and was comparable with previous studies.[1-3] Our initial focus was to monitor renal function during the postoperative follow-up period. One patient in the study group developed a postoperative acute kidney injury, which could potentially be explained by the use of general anesthesia and the hemodynamic effect of the implantation procedure in very high-risk patients. However, contrast-induced nephropathy was significantly higher in patients who received contrast media (15 patients [20.5%] in control group vs 1 patient [4%] in the study group; *P*=.04).

The 30-day mortality rate of this high-risk study cohort that underwent TF-TAVI without CM was 4.0%, which compares well with other contemporary studies on TAVI patients.[1-3]

In our study protocol, accurately performing annular sizing was another challenge. For this purpose, our anesthesiology team was specifically trained to obtain the TEE measurements needed to follow the method of Bleakely et al.[13] An additional native CT scan was used as a second imaging tool for reference. Furthermore, before starting this program, we performed an internal validation of our AV

annular measurements by comparing the TEE measurements with those obtained with "contrast-enhanced" CT scans in a retrospective cohort from our institution. Based on this retrospective analysis, we decided to completely abandon the contrast-enhanced CT examination in this specific patient cohort and performed only TEE-based annular measurements.

Chaturvedi et al reported that magnetic resonance imaging (MRI)-based AV annular measurements were superior to the CT-based measurements.[12] In the future, MRI could be a useful diagnostic tool for contrast-free TAVI programs if this modality can successfully replace multislice CT measurements.[12]

In the contrast-free TAVI technique, the use of TEE is mandatory, which limits the TAVR procedure to being performed under general anesthesia and, unfortunately, completely precludes the possibility of adapting TAVI to being performed under local anesthesia.

Future prospects. Admittedly, a valuable piece of information was always missing when performing this implantation technique. The angulation of the TAVR implantation plane could only be obtained through contrast CT, which this study aimed to avoid. For this purpose, we reviewed all relevant published literature and consulted radiology experts to learn how to obtain the angulation of the implantation plane from the native multislice CTs. According to the protocol published by Bruschi et al in 2015,[9] this measurement could be obtained from native electrocardiography-gated multislice CT. From the double-oblique transverse images, three points are positioned at the most inferior aspects of the severely calcified valve cusps. The implantation projection was determined when the triangle that connected all three points was not evident and was replaced by a single line, with the point of the right cusp equidistant from the left and non-coronary cusps. Carbon dioxide and digital subtraction angiography can be safely used in patients with nephropathy to assess the femoral artery anatomy; in this technique, carbon dioxide is used instead of the iodinated contrast material. Ultrasound-guided femoral artery puncture could be used to reduce access-related complications.[14]

Conclusion

Our initial experience demonstrates the safety and reproducibility of contrast-free TAVR procedures using balloon-expandable valves. In addition, it significantly reduced the incidence of postoperative acute kidney injury in patients with severe nephropathy.

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Research Article

Contemporary Results of Transcatheter Aortic Valve Replacement in Obese Patients

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Background. Little research has been conducted to explore the postoperative outcomes of obese patients after transfemoral transcatheter aortic valve replacement (TF-TAVR). *Objective.* We investigated the influence of body mass index (BMI) on 1-year outcomes after TF-TAVR. *Methods.* We included retrospectively 1609 high- and intermediate-risk TAVR patients (mean EuroSCORE II 21 ± 11) operated under general anesthesia between March 2014 and March 2018 in central hospital, Bad Berka, Germany. We stratified the patients according to BMI. *Results.* Our demographic data analysis showed 41% of patients were male and the mean age was 78 (range, 61–92 years). According to the WHO classification, 33% patients had normal weight, 42% were defined as overweight, and 22% were obese. Obese patients showed statistically significant difference in their clinical parameters as having higher incidence of hypertension, diabetes mellitus, pulmonary hypertension, and chronic obstructive pulmonary disease; on the contrary, obese patients were found to be younger than others. We found no differences in valve types and sizes among the different BMI categories. Our mortality rate during the 1-year follow-up period was 17.8% (287 patients). Mortality was significantly higher in patients with BMI < 25 kg/m^2 (1 year mortality 149 patients 28.2% in patients with BMI < 25 kg/m^2 vs. 138 patients 12.6% in patients with BMI ≥ 25 kg/m^2; $P = 0.0001$). Even after considering the confounding risk factors, BMI ≥ 25 kg/m^2 was independently associated with reduced 1 year mortality (odds ratio (OR): 0.36, 95% confidence interval (CI): 0.21–0.6; $P = 0.01$) in multivariate logistic regression analysis. The rate of vascular complication was higher in patients with BMI ≥ 25 kg/m^2. However, the rate of blood transfusion was higher in patients with BMI < 25 kg/m^2. All other serious complications occurred with equal distribution in both groups. *Conclusion.* In our single-center study, BMI ≥ 25 kg/m^2 was independently associated with lower 1 year mortality after TF-TAVR.

1. Introduction

Obesity is considered to be a morbidity- and mortality-dependent cardiovascular factor [1]. However, this clinical factor is still under investigation in the literature in the domain of transcatheter aortic valve replacement (TAVR). Nevertheless, several studies expressed obese patients as having better outcomes when compared with nonobese patients in aortic valve replacement procedures [2, 3] and in percutaneous coronary intervention [4]. Tokarek et al. showed that increased BMI was independently associated with 1-year survival benefit after TAVR. However, there was no difference between the groups in terms of 30-day all-cause mortality [5].

As for the progressively increasing population and awareness to medical consequences, it would be logical to expect greater number of obese patients with aortic valve stenosis referred for TAVR. In this study, we evaluated how influential is the body mass index (BMI) on TAVR outcomes concerning procedure-related complications and mortality.

1.1. Study Population and Data Collection

1.1.1. Methods

(1) Study Design and Follow-Up. In this study, we retrospectively collected data of TAVR patients in our institute (Zentralklinik Bad Berka, Germany) in the period between March 2014 and March 2018. All patients signed routinely an informed consent preoperatively. Clinical, echocardiographic, and hemodynamic criteria were our diagnostic tools. Computerised tomography was our preparatory tool. Eligibility for TAVR was determined by our heart team. We collected 1609 patients in this period who underwent transfemoral TAVR. After hospital discharge, all patients were subjected to follow-up schedule at 3 months and 1 year. Mortality data were collected by contacting the patients and the referring physicians.

(2) TAVR Procedure. TAVR was performed under general anesthesia. Three types of aortic valve prostheses were used: the Evolut aortic valve prosthesis (Medtronic, Inc., Minneapolis, MN) (23, 26, 29, or 34 mm), the Edwards SAPIEN 3 prosthesis (Edwards Lifesciences Corp, Irvine, CA) (23, 26, and 29 mm), and the Symetis aortic valve prosthesis (Boston Scientific) (small, medium, and large). Two senior TAVR operators (a cardiac surgeon and an interventional cardiologist) were in charge of the whole procedure. Valve type and size were decided preoperatively according to CT and echocardiography. All intraoperative and postoperative special findings or complications were always recorded and documented.

(3) End Points. Periprocedural complications and mortality rates were evaluated according to VARC-2 definitions [6]. End points of the study were all-cause mortality at 1 year, major and life-threatening bleeding complications, major vascular complications, blood transfusions, cerebrovascular events, and need for permanent pacemakers following the procedure.

(4) BMI (Body Mass Index). This parameter was obtained from patients' files by dividing the weight in kilograms by the square of the height in meters. We classified the patients into three groups: normal weight, BMI from 18.5 to 24.9 kg/m^2; overweight, BMI from 25.0 to 29.9 kg/m^2; and obese, BMI $\geq$ 30 kg/m^2. In our cohort, only 1% of the patients were classified as underweight and being statistically non-influential. This group was excluded from our study.

Before 01/2018, all TAVR patients were treated postoperatively with dual antiplatelet therapy (aspirin and clopidogrel) for 6 weeks and then monotherapy lifelong. Since 01/2018, all TAVI patients were treated postoperatively with monotherapy either aspirin or clopidogrel in the absence of indication to anticoagulation or anticoagulants.

(5) Statistical Analysis. All data were displayed as mean (standard deviation) for continuous variables and as the number (percentage) of patients in each group for categorical variables. Student's *t*-test or the analysis of variance test was used to evaluate the statistical significance between continuous variables, whereas the χ^2 test was used in case of categorical variables, respectively. Odds ratios were calculated with a confidence interval of 95%. The analysis was done for BMI as continuous as well as categorical variables (BMI < or 25 kg/m^2). Furthermore, multivariate analysis is performed to explore the association between BMI $\geq$ 25 kg/m^2 and 1 year mortality. All of the analyses were considered significant at a 2-tailed P value of <0.05. All analyses were done using SPSS statistical software (IBM Corp. released 2013, IBM SPSS Statistics for Windows, version 22.0, Armonk, NY).

2. Results

Our total study cohort included 1609 patients (41% males) with a mean age of 78 (range, 61–92 years). Our demographic data analysis showed that the mean logistic EuroSCORE of the study patients was 21%, 88% of patients suffering from hypertension, 19% from COPD, 12% from PH, 57% from carotid stenosis, and 34% from diabetes. 28% of patients were classified as New York Heart Association class IV. Edwards SAPIEN 3 was implanted in 60% of patients, while the Evolut prosthesis was used in 31% of patients and Symetis prosthesis in 9% of patients. The clinical characteristics of patients according to their BMI classification are presented in Table 1. According to the WHO classification, 1% of patients were defined as underweight, 33% had normal weight, 42% were defined as overweight, and 22% were obese. As shown in Table 1, the obese patients showed statistically significant difference in their clinical parameters as having higher incidence of hypertension, diabetes mellitus, pulmonary hypertension, and chronic obstructive pulmonary disease; on the contrary, obese patients were found to be younger than others and consequently have lower logistic EuroSCORE. We found no differences in valve types and sizes among the different BMI categories.

Our mortality rate during the 1-year follow-up period was 17.8% (287 patients). Mortality was significantly higher in patients with BMI < 25 kg/m^2 (The 1-year mortality in patients with BMI < 25 kg/m^2 was 28.2% (149 patients) vs 12.6% (138 patients) in patients with BMI $\geq$ 25 kg/m^2; $P = 0.0001$), see Figure 1. Even after considering the confounding risk factors, BMI $\geq$ 25 kg/m^2 was independently associated with reduced 1 year mortality (odds ratio (OR): 0.36, 95% confidence interval (CI): 0.21–0.6; $P = 0.01$) in multivariate logistic regression analysis, as shown in Table 2 und Figure 2. The rate of vascular complication was lower in patients with BMI $\geq$ 25 kg/m^2. However, the rate of blood transfusion was higher in patients with BMI < 25 kg/m^2. All other serious complications occurred with equal distribution in both groups, as shown in Table 3.

3. Discussion

In this retrospective observational study, we targeted to focus on the influence of BMI on TAVR outcomes. The principle conclusion was patients with BMI $\geq$ 25 kg/m^2 had lower long-term mortality rates and, on the other hand, higher rate of procedure-related complications. As reported

Table 1: Baseline clinical characteristics of patients according to BMI classification.

Variables	Entire cohort, 1609 patients	18.5 < BMI ≤ 24.9, normal weight, 528 patients	25 ≤ BMI ≤ 29.9, overweight, 676 patients	BMI ≥ 30, obese, 405 patients	P value
Age (years), mean ± SD	78 ± 6.2	86 ± 6	81 ± 5	78 ± 6	0.01
Gender (male), n (%)	692 (41)	216 (41)	332 (50)	124 (30)	0.01
Diabetes mellitus, n (%)	562 (34)	136 (26)	232 (34)	188 (46)	0.005
Hypertension, n (%)	1436 (88)	436 (81)	608 (90)	380 (93)	0.012
Dyslipidemia, n (%)	1280 (77)	400 (75)	528 (78)	336 (82)	0.41
Smoking, ever, n (%)	421 (27)	128 (24)	160 (24)	124 (30)	0.42
PVD, n (%)	152 (6)	56 (12)	44 (6)	16 (4)	0.137
CAD, n (%)	951 (57)	316 (59)	408 (60)	236 (56)	0.73
GFR (MDRD) (mL/min/1.73 m^2), mean ± SD	58 ± 15	62 ± 19	65 ± 20	56 ± 17	<0.01
Albumin (g/l)	42 ± 2.8	42 ± 3.7	42 ± 2.6	43 ± 3.5	0.09
Atrial fibrillation, n (%)	484 (31)	184 (35)	168 (25)	128 (30)	0.17
Prior stroke, n (%)	159 (9)	52 (10)	64 (10)	40 (10)	0.99
COPD, n (%)	316 (19)	84 (16)	112 (17)	120 (29)	0.015
Previous PCI, n (%)	704 (42)	236 (45)	300 (45)	164 (41)	0.65
Previous MI, n (%)	272 (16)	116 (22)	92 (14)	60 (15)	0.12
CABG, n (%)	251 (16)	92 (17)	144 (21)	44 (11)	0.08
NYHA class, n (%)					
III	1084 (68)	288 (54.5)	520 (48)	264 (65)	
IV	471 (28)	220 (42)	116 (17)	124 (31)	<0.01
Barthel index < 80	209 (13%)	61 (11.5%)	86 (12.7%)	62 (15.3%)	*0.08*
EuroSCORE, mean ± SD	21 ± 17	24 ± 12	24 ± 11	21 ± 9	0.01
Aortic valve area (cm^2), mean ± SD	0.6 ± 0.3	0.6 ± 0.2	0.6 ± 0.1	0.7 ± 0.2	0.073
Ejection fraction (%), mean ± SD	59 ± 6.9	56.1 ± 8.9	52.8 ± 6.1	61.4 ± 7.5	0.058
Valve type (Evolut), n (%)	499 (31)	221 (41)	161 (23)	117 (28)	0.08

BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; GFR (MDRD), glomerular filtration rate (modification of diet in renal disease); MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SD, standard deviation.

by the Nutrition Council of the American Heart Association, obesity is considered a risk factor for cardiovascular morbidity and mortality [1]. Obesity rates are progressively rising due to the sedentary life style and still associated with higher morbidity and mortality [7, 8]. On the contrary, Batty et al. and Lancefield et al. reported a better survival rates among obese patients [9, 10].

TAVR is known to be indicated in high and intermediate surgical risk candidates for aortic valve replacement [11]. However, to our knowledge, the BMI is an absent parameter in logistic EuroSCORE, and consequently, its influence on the TAVR outcomes has not been directly investigated in detail. Van der Boon et al. showed that obesity was associated with a decrease in 30-day mortality, but had no effect on long-term outcomes [12]. This conclusion point differs from our results in the following aspects: our cohort group is bigger in comparison with his as they retrospectively investigated 944 patients vs 1609 patients in our study. However, on the contrary, they reported no increase in procedure-related complications among the obese group which is opposite to what we found out in our study. Despite an increase in our periprocedural complications, we found lower 1-year mortality in patients with BMI ≥ 25 kg/m^2. We would explain this finding by the fact that overweight patients might have more metabolic reserves [13]. Another explanation might be the fact that we were introducing a new closure device in our institute during the phase where this study was conducted. Our results go on line with the recent analysis from the FRANCE2 (French Aortic National CoreValve and Edwards 2) registry, according to which, among the TAVR population, overweight and obesity were associated with improved 1-year survival [14]. BMI remained an independent predictor of improved survival in multivariate analysis. This might be explained by the fact that overweight and obese patients are usually intensively treated with optimum medical therapy for the associated risk factors and consequently contributing to better outcomes [13].

Blood transfusion was found to be less frequent in the obese cohort in our study group. Despite the fact that hemoglobin level was similar among all groups on admission and the increased number of procedure-related complications in the obese group, we would interpret this as those patients were seen as less frail and less fragile and hence blood transfusion in this group was restricted only to patients suffering from progressive anemia and active bleeding; therefore, overall, patients defined as obese were treated with blood transfusion less frequently. Several studies support our results [15–17].

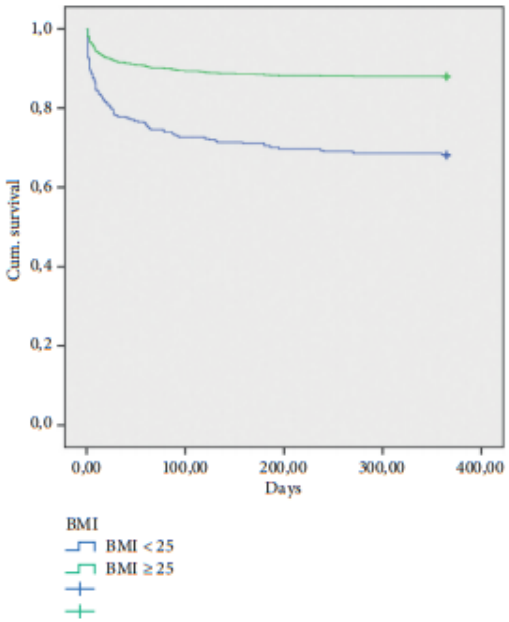

Figure 1: Kaplan–Meier curve showing the survival curve of patients with BMI < 25 compared with patients with BMI ≥ 25.

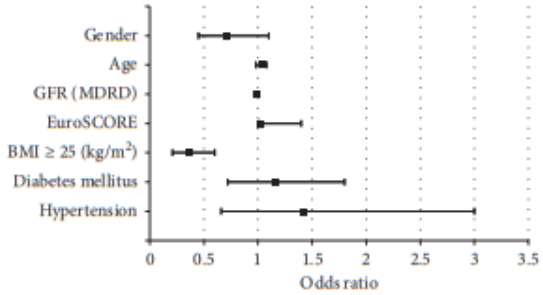

Figure 2: Odds ratio for 1-year mortality in study patients.

Table 2: Multivariate Cox proportional hazard model.

Variables	Hazard ratio	Confidence interval	*P* value
Gender	0.71	0.45–1.14	0.16
Age	1.03	0.98–1.08	0.15
Diabetes mellitus	1.16	0.72–1.87	0.53
Hypertension	1.41	0.66–3.00	0.36
COPD	1.63	0.96–2.78	0.07
GFR (MDRD)	0.99	0.97–1.00	0.13
EuroSCORE	1.02	1.01–1.4	<0.001
BMI ≥ 25 kg/m^2	0.36	0.21–0.6	0.01

BMI, body mass index; COPD, chronic obstructive pulmonary disease; GFR (MDRD), glomerular filtration rate (modification of diet in renal disease); NYHA, New York Heart Association.

3.1. Study Limitations. The main limitation of this study is being a retrospective observational study and there may have residual confounders (as the indicators of central obesity, CT measurements of visceral fat, and medications) that we did not account for. Another limitation of the current study is that the clinical follow-up for more than one year was not available, which might decrease the influence of important predictors such as age on mortality.

Table 3: Clinical outcomes according to BMI classification.

	Entire cohort, 1609 patients	BMI ≤ 24.9, normal weight, 528 patients	25 ≤ BMI ≤ 29.9, overweight, 676 patients	BMI ≥ 30, obese, 405 patients	*P* value
Vascular complications, *n* (%)	140 (9)	36 (5)	40 (7)	64 (18)	0.015
Major/life-threatening bleeding, *n* (%)	212 (15)	48 (11)	84 (13)	80 (22)	0.055
Blood transfusions, *n* (%)	532 (38)	220 (49)	192 (31)	120 (35)	0.01
New atrial fibrillation, *n* (%)	112 (7)	40 (7.5)	40 (6)	32 (8)	0.78
New pacemaker, *n* (%)	344 (21)	96 (17.5)	128 (18)	120 (30)	0.067
Acute kidney injury, *n* (%)	196 (12)	64 (12)	80 (12)	52 (13)	0.96
Cerebral ischemic event, *n* (%)	88 (5.4)	24 (4)	44 (6)	20 (5)	0.71

BMI, body mass index.

4. Conclusion

In our single-center study, BMI ≥ 25 kg/m^2 was independently associated with lower 1-year mortality after transfemoral TAVR.

Data Availability

The data used to support the findings of this study have not been made available because of the absence of hospital agreement.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Owais T and El Garhy M contributed equally to this work.

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Functional impairment assessed by the Barthel Index influenced outcomes after transcatheter aortic valve implantation

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ORIGINAL ARTICLE

Functional impairment assessed by the Barthel Index influenced outcomes after transcatheter aortic valve implantation

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ABSTRACT

Objective. We investigated the influence of functional impairment assessed by the Barthel index (BI) on the three-month outcomes after transfemoral-transcatheter aortic valve intervention (TF-TAVI) under general anesthesia. *Design*. We included retrospectively analyzed 336 patients undergoing TAVI between January 2017 and January 2018 in central hospital, Bad Berka, Germany. All patients were followed up at three-month in our center's outpatient clinic. We stratified the patients according to the BI. *Results*. At baseline, 76 patients had a BI <80. Patients with a BI <80 were characterized by advanced age (80.6 ± 5.6 vs. 83 ± 4.1 years. $p = .027$), diabetes mellitus on insulin and higher surgical risk scores. A prior cerebral ischemic event was recorded more in patients with a BI ≥80. Regarding intermediate outcomes, three-month mortality was significantly higher in patients with a BI <80. Patients with a BI <80 developed significantly more postoperative cardiac decompensation, delirium and strokes. Patients with BI <80 had lower hemoglobin level preoperative and needed more blood transfusion postoperative. Other valve academic research consortiums (VARCs) complications were equally distributed in both groups. A BI <80 was associated with prolonged postoperative hospital stay and was an independent predictor of FT protocol failure (OR 4; CI 95% 1.3–11. p .02). *Conclusions*. A BI <80 is associated with increased mortality and risk of neurological events and cardiac decompensations after TF TAVI. A BI <80 is an independent predictor of failure in fast track TAVI.

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TAVI; fast track; Barthel index; functional impairment; frailty

Introduction

Transcatheter aortic valve intervention (TAVI) has become the standard-of-care for high and intermediate risk patients [1]. Many risk scores are developed to predict patients' outcomes after TAVI. The lack of functional as well as frailty parameters in these risk scores might reduce its predictive power [2]. Preoperatively, physical disability is more prevalent among patients undergoing TAVI than in patients undergoing conventional aortic valve replacement [3]. The consensus has been that functional impairment, assessed by scales as Katz index, elderly mobility scale, Canadian Study of Health and Aging scale and Ersamus scale, worsened the mid- and long-term outcomes after TAVI [4–7]. In the context of rehabilitation, the Barthel index (BI) is a commonly used scale to assess the performance in activities of daily life (ADL) in the health system [8,9]. However, prior research did not investigate the impact of functional impairment assessed with BI on the outcomes after TAVI. We aimed to explore whether the functional impairment assessed by the BI at hospital admission has an impact on three-month mortality and length of hospital stay after TF-TAVI.

Methods

A retrospective observational study was conducted in our institution for patients undergoing TAVR between January 2017 and January 2018. Three hundred thirty-six consecutive high-risk patients with mean age of 80.6 ± 5.6 years and median (interquartile range; IQR) and EuroSCORE II 14 (10–14), were included in this study. All patients were followed up at three-month in our center's outpatient clinic.

In our institution, we routinely measure the original BI [8,9] in all patients undergoing TAVI for the purpose of rehabilitation [10]. We collected the BI scores from patient records. This assessment takes about 15 min and is done by the treating physician preoperatively. Walk test was done during the preoperative assessment, the patient was asked to walk until he feels too breathless to continue. The assessment of frailty was routinely obtained in all patients from the TAVI protocol, depending on the answer of operator on a simple question; if the patient is frail or not?

We studied the three-month outcomes in patients with BI <80 comparing to patients with BI ≥80. Multivariate analysis was performed to explore if BI <80 is an

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independent predictor of patient outcome. Periprocedural complications and mortality rates were evaluated according to valve academic research consortium (VARC-2) definitions, which provided standardization of endpoint definitions for studies evaluating the use of TAVI [11]. The procedural endpoints according to VARC-2 definition included mortality, myocardial infarction, stroke, bleeding, acute kidney injury, pacemaker implantation and vascular complications. Delirium was diagnosed when nursing delirium screening scale (NU-DESC) scale ≥2 [12], the assessment was performed by an experienced nurse at intensive care about three hours post-op. The Nu-DESC is based on patient behavior (disorientation, inappropriate behavior, inappropriate communication, hallucination and psychomotor retardation).

The study was approve by the local ethics committee and was performed in agreement with the declaration of Helsinki. All patents gave written informed consent. The study was not funded by any company or research institute.

Statistical analysis

Continuous variables were tested for normal distribution using the Kolmogorov–Smirnov test. Non-normally distributed variables are expressed as median and IQR and were compared between groups using the Mann–Whitney *U*-test. Normally distributed variables are expressed as mean ± SD and were compared between groups using Student's *t*-test. Categorical data are expressed as percentages. Univariable analyses using Fisher exact or t test were used to identify differences between both groups. In order to determine if BI < 80 is associated with mortality morbidities and failed fast track protocol, logistic regression model was generated. All analysis was done using SPSS statistical software (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

Results

Our retrospective results showed that patients with a BI <80 were characterized by advanced age (80.6 ± 5.6 vs. 83 ± 4.1 years. $p = 0.027$), diabetes mellitus on insulin (26.3% vs 12.3%. $p = 0.006$) and a high measure for common surgical risk scores (EuroScore II, $p = .001$) (Table 1). Prior cerebral ischemic events were recorded more in patients with a BI ≥80 (17.9% vs. 6.7%. $p = .002$) other factors were equally distributed in both groups (Table 1).

The mean BI in all study patients was 76.6 ± 15.4. Baseline echocardiographic parameters (ejection fraction, transvalvular gradients, aortic valve area, pulmonary artery systolic pressure, prevalence and degree of aortic regurgitation) did not differ between both groups. From 336 patients, 260 patients had BI ≥80 (77.6%), whereas 76 patients had BI <80 (22.4%).

Mortality was significantly higher in patients with a BI <80 (0% vs. 5.3%. $p = .03$ for 90-day mortality; and 0% vs. 2%. $p = .04$ for procedural mortality). The success of fast track protocol, discharge from hospital in the fifth postoperative day, was more in patients with a BI ≥80; 70.8% vs. 31.6% ($p = .0001$). Furthermore, patients with a BI <80 developed significantly more postoperative cardiac decompensation (6.2% vs. 31.6%. $p = .0001$), postoperative delirium (11.1% vs. 3.1%, $p = .005$), strokes (0% vs. 15.8%. $p = .0001$). Patients with a BI <80 had lower hemoglobin level preoperative and needed more blood transfusion postoperative (4.7% vs. 36.8%. $p = .0001$) (Figure 1) adding to our published independent predictors of fast-track protocol failure.

A BI <80 (OR 4; CI 95% 1.3–11. $p = .02$) was also independent predictor of fast track protocol failure (Figure 2).

Table 1. Preoperative patients' characteristics.

	Barthel index ≤ 80 260 (77.6%)	Barthel index < 80 76 (22.4)	Total 336 (100%)	*p* Value
Male *n* (%)	68 (43%)	80 (44%)	(44%)	.912
Age mean ± SD	80 ± 5.7	83 ± 4.1	80.6 ± 5.6	.027
EUROII median (IQR)	18 (9–29)	22.5 (14–34)	21 (19–23)	.0001
STS median (IQR)	11 (9–14)	14 (10–15)	14 (10–14)	.1
Frailty %	70.0%	60.0%	66.7%	.3
BMI *n* (%)	28.9 ± 3	25.6 ± 2.9	27.4 ± 2.8	.764
CS uni *n* (%)	8 (5.1%)	12 (6.7%)	20 (6.0%)	.6
CS bi *n* (%)	12 (7.7%)	8 (4.4%)	20 (6.0%)	.2
Stroke *n* (%)	28 (17.9%)	12 (6.7%)	40 (11.9%)	.002
Redo *n* (%)	28 (17.9%)	20 (11.1%)	48 (14.3%)	.08
PCI *n* (%)	52 (33.3%)	60 (33.3%)	112 (33.3%)	1.0
CRF ≥ stage 3 *n* (%)	104 (40.0%)	32 (42.1%)	136 (40.5%)	.7
NYHA IV *n* (%)	168 (64.6%)	44 (57.9%)	212 (63.1%)	.3
LVEF < 30% *n* (%)	24 (9.4%	12 (15.8%	36 (10.8%	.1
pHTN *n* (%)	124 (48.4%)	40 (52.6%)	164 (49.4%)	.6
IDDM *n* (%)	32 (12.3%)	20 (26.3%)	52 (15.5%)	.006
RBBB *n* (%)	8 (3.1%)	0 (0%)	8 (2.4%)	.3
proBNP median (IQR) pg/ml	1352 (630–2075)	1920 (1814–2204)	1902 (630–2204)	.6
Albumin median (IQR) g/l	45 (38–47)	42 (36–45)	43 (39–46)	.04
GFR median (IQR) ml/min/1.73 m^2	60 (45–60)	60 (56–60)	60 (46–60)	.4
Hb mean ± SD	8.1 ± 1 mmol/l	7.4 ± 0.8 mmol/l	8 ± 0.9 mmol/l	.016

BMI: Body mass index; BNP: brain natrutic peptide; COPD: chronic obstructive lung disease; CRF: chronic renal failure; CS: carotid artery; stenosis; GFR: glomerular filtration rate; Hb: hemoglobin; IDDM: insulin dependent diabetes mellitus; IQR: interquartile range; LVEF: left ventricular ejection fraction; *N*: Number; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; pHTN: pulmonary hypertension; RBBB: right bundle branch block; SD: standard deviation; STS: society of thoracic surgery score.

Furthermore, this failure increased successively with lower BI score (Figure 3). All other VARC2 complications occurred with equal distribution in both groups. Table 2 showed the odds ratio for the BI to different clinical end points.

Seventy percent of patients with a BI ≥80 were assessed as frail vs. 60% in patients with a BI <80, $p = .3$. Frailty was associated with increased risk of vascular complications; OR (CI at 95%) was 9 (3.1–25). Other end points were similar between frail and nonfrail patients (Table 2).

Discussion

There are two main findings of this study: first, a BI <80 is associated with increased mortality and risk of neurological events and cardiac decompensations after TF TAVI and second, a BI <80 is an independent predictor of failure of fast track TAVI.

In our institution, we routinely use the original BI to assess ADL because it showed to be the best tool to rate patient independence [13]. On the other hand, it is the most widely used tool [8,9]. To the best of our knowledge, it is the first time to study the influence of functional impairment assessed with a BI on the postoperative outcomes after TF-TAVI. In this study, mean BI was 76.6 ± 15.4, which is higher than what reported by Tarro et al. [3] 67 ± 24, this could be due to the inclusion of intermediate risk patients in the last years. However, the rate of independent patients in our study was higher than the incidence reported with Plus et al. (67% vs. 77.6%) taking in account the different used scores in both studies. Tarro et al. demonstrated a significant improvement of the BI after TAVI at discharge, 85 ±17 vs. 67 ± 24; $p = .001$ [3]. We did not routinely compare the BI pre- and postop.

In our previous study [8], we missed to assess the role of functional impairment in the failure of the fast track protocol [8]. In the current study, a BI <80 was an independent predictor of the failure of fast track protocol, which mainly caused by decompensated heart failure, postoperative strokes, delirium and anemia. These complications are expected in this group of patients with advanced age and insulin dependent diabetes mellitus. Puls et al. [4] showed that functional status measured by the Katz Index represents

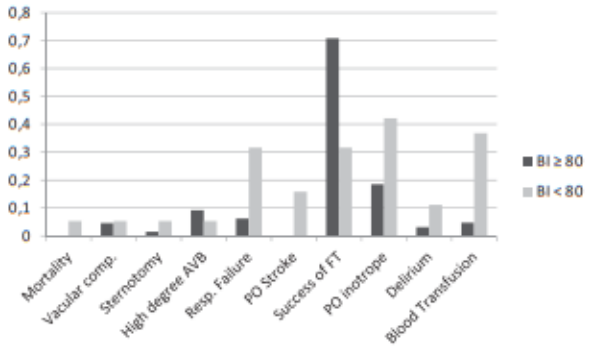

Figure 1. Comparison between both groups as regard three-month outcomes. AVB: atrioventricular block; BI: Barthel index; BT: blood transfusion; comp.: complications; PO: postoperative; resp.: respiratory; FT: fast track.

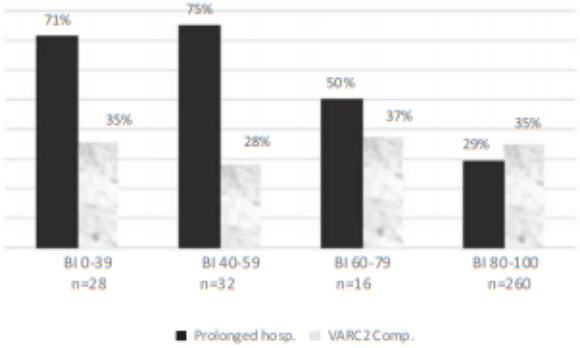

Figure 3. Incidence of prolonged hospital stay after TF-TAVI according to BI. BI: Barthel index; *n*: number.

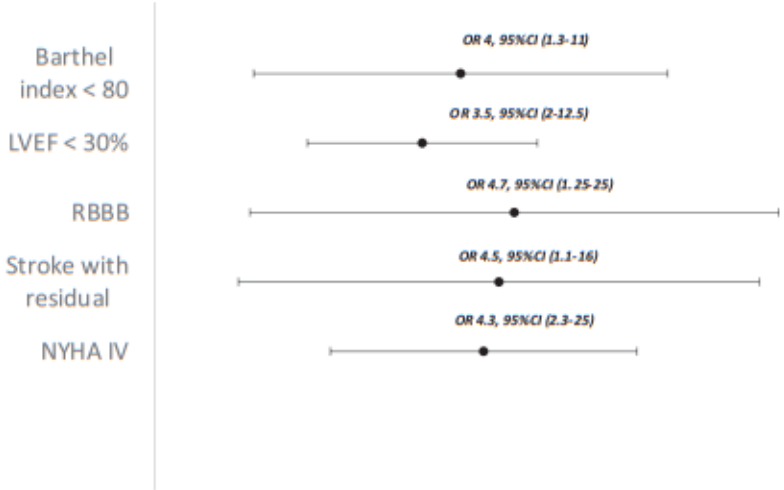

Figure 2. Odds ratios of variables that were identified as independent predictors of prolonged hospital stay after TF-TAVI. LVEF: left ventricular ejection fraction; RBBB: right bundle branch block; NYHA: New York Heart Association; OR: odds ratio; CI: confidence interval.

Table 2. Odds ratio values for Barthel index to end points.

	Barthel index < 80		Frailty	
	OR (CI at 95%)	p Value	OR (CI at 95%)	p Value
Mortality	6 (2–13)	.0001	3.8 (0.6–12)	.1
Major vascular comp.	0.8 (0.6–1.3)	.2	9 (3.1–25)	.0001
Myocardial infarction	1.2 (0.58–2.6)	.7	0.8 (0.2–1.3)	1
Stroke	1.9 (1.3–3)	.001	0.9 (0.8–1.2)	.3
Bleeding	0.7 (0.4–1.3)	.3	0.5 (0.1–1.6)	.3
Acute kidney injury	0.8 (0.4–1.7)	.4	0.9 (0.6–1.8)	.2
Pacemaker implantation	1.1 (0.5–2.5)	.8	1.2 (0.4–3.8)	.7
Prolonged hospital admission	2.3 (1.4–1.6)	.0001	0.9 (0.4–1.7)	.8
Emergency operation	0.8 (0.2–3.5)	1.0	0.8 (0.7–1.1)	.6

OR: odds ratio; CI: confidence interval.

a powerful predictor of adverse early and late outcome after TAVI but not on of the success of early discharge. In the study by Puls et al., the rate of early discharge was very low 5%, as the concept of fast track TAVI was not yet well established in 2014 and 53% of study patients were operated through transapical approach [4]. Nevertheless, the incidence of prolonged hospital stay >14 days was more common in patients with Katz index <6 (32% vs. 22%, $p = .047$). According to our experience, the success of fast track protocol improved patient's, families' and team's satisfaction and reduced the overall health care costs. But this needs a precise patient's selection to exclude patients who had negative predictors of the success of fast track protocol.

This study demonstrated that a BI <80 was associated with increased risk of neurological events and cardiac decompensation. Nevertheless, other VARC-2 listed complications were equally distributed between different subgroups (Table 2 and Figure 3). Patients with a BI <80 had more postoperative strokes, albeit the rate of preoperative ischemic strokes was higher in patients with a BI ≥80. This may be due to exclusion bias of patients with previous stroke, because of expected TAVI futility. In our study, we used Nu-DESC test for the assessment of delirium. Several studies agreed that postoperative delirium was a predictor of long-term mortality [7,14,15], which may explain the higher mortality in patients with a BI <80.

There is growing evidence that frailty is an independent predictor of mortality after TAVI [16,17]. This study showed that frailty was not an independent predictor for mortality. Frailty was associated with higher vascular complications; otherwise other complications were similar between frail and nonfrail patients. The assessment of frailty was subjective based on "eyeballing," which might influence our results. Unfortunately, the walk test was not done according to specific protocol and was not documented. Green et al. [18] showed that frailty was not associated with increased procedural complications. In contradictory to our results, Rodes-Cabau et al. [16] identified frailty assessed by eyeballing as an independent predictor of mortality after TAVI. In the study of Kleczynski et al. [5], the percentage of frail patients ranged between 6.9% and 52% according to the used index. Our results could be influenced by the subjective assessment of frailty. In two recent studies, psoas muscle area and volume correlated to frailty indexes and predicted long term mortality after TAVI [19,20].

Study limitations

The limitations of our study are: first being a retrospective observational single center study and there may have residual confounders that we did not account for. Second: short follow up period. We cannot consider our study as a conclusive study. However, it could be used to generate hypothesis. Moreover, we could not exclude the role of confounding factors in patients with a BI <80, which lead to worse outcomes. We believe that there is a necessity of more prospective studies in this domain.

In conclusion, a BI <80 is associated with increased mortality and risk of neurological events and cardiac decompensations after TF TAVI. BI <80 is an independent predictor of failure in fast track TAVI.

Disclosure statement

No potential conflict of interest was reported by the authors.

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5. Diskussion

A total of 98 consecutive patients were included in the first study; 25 patients underwent TF-TAVR without the use of CM and 73 patients underwent TF-TAVR with the use of CM. All patients had GFR <30 mL/min/1.73 m2. Acute kidney injury was significantly higher in patients who received CM (15 patients [20.5%] in the control group vs 1 patient [4%] in the study group; P=.04. In previous studies, the incidence of AKI after intervention was 13.7-50%(Yamamoto et al. 2013b).

The other predictors of AKI was out of the scope of our study as we compared between two matched groups and all patients had GFR <30 mL/min/1.73 m2. In previous studies, other predictors of AKI were reduced left ventricular ejection fraction and blood transfusion (Yamamoto et al. 2013b). In contradictory to our results, Rodriguez et al. found no association between the amount of CM and periprocedural intravenous hydration with AKI in TAVR patients (Rodriguez et al. 2020). The use of low osmolar CM and the hemodynamic improvement after TAVR may mask the effect of CM on the kidney function. Rodriguez et al. 2020 supposed that other factors such as procedural hypotension and embolization of cholesterol crystals are more important in the development of AKI in TAVR patients (Rodriguez et al. 2020). In the study of Rodriguez et al. non-tans femoral approach was associated with more AKI, this could be explained that those patients had severe peripheral vascular disease and more embolization of cholesterol crystals during TAVR (Rodriguez et al. 2020). A significant increase in plasma levels of pro-inflammatory cytokines (hsCRP, interleukin 6, tumor necrosis factor alpha receptors) and markers of oxidative stress (MPO) after TAVR was observed especially in trans-apical (TA) TAVR. This was associated with a higher incidence of AKI in the TA cohort compared to TF (Navaratnarajah et al. 2020).

Based on PCI trials Solomon et al developed a risk calculator to predict the AKI after CM , this score depends on eight identified variables (hypotension, intra-aortic balloon pump, congestive heart failure, chronic kidney disease, diabetes, age >75 years, anemia, and volume of contrast) (Solomon 2014). If this risk score is also applicable in TAVR patients has not yet been studied.

We depends for the diagnosis of AKI on the GFR (MDRD) using creatinine level and on the urine output volume, this is the most commonly used methodology but might be not the best one because of following:

1. Creatinine is a break-down product of creatinine phosphate in muscle tissue and is eliminated both by filtration and tubular excretion. Only in a steady state of body muscle serum creatinine concentrations reflects underlying GFR (Rihal und Kashani 2015)

2. The lag between AKI and the increase of creatinine may take up to 72 hours.

3. The increase of creatinine is neither specific nor sensitive for AKI (Solomon 2014).

Even with other injury markers such as NGAL, IL-18, and KIM-1, there is no specificity for contrast-induced injury(Solomon 2014). The increase of cystatin c after AKI occurred earlier than the increase of creatinine. However, it was not more predictive for AKI if compared with an absolute increase of creatinine ≥ 0.3mg/dl (Solomon et al. 2009). Moreover, the increase of creatinine was a better predictor for major adverse events. In most of the previous studies, the contrast volume (CV) to glomerular filtration rate (GFR) ratio was the most important predictor of AKI after cardiovascular interventions. (Sedaghat et al. 2019, Yamamoto et al. 2013b).

After identifying the patient with high risk for developing AKI, the prevention of AKI is very important in TAVR patients as it was associated with increased short term and long term mortality (Sedaghat et al. 2019, Yamamoto et al. 2013b). The TAVR population is also different from PCI patients because they are all in various degrees of decompensated heart failure and may, in fact, need diuresis and left ventricular unloading rather than volume expansion. In our patients the hydration of was done with Delta jonin isotonic infusion at the dose of 1ml/kg/h 12 hours before and after the procedure. In patients with heart failure and severely reduced ejection fraction we reduced the infusion volume to 0.5ml/kg/h. The Renal Guard system (Renal Guard Solutions Inc., Milford, Massachusetts) causes renal flushing by carefully matching intravenous infusion of isotonic saline solution to furosemide-forced diuresis according to urine output (see figure8).

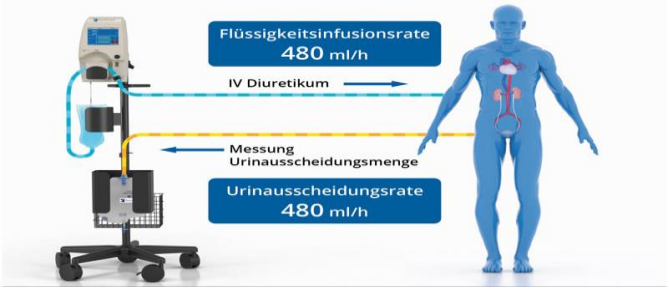


Figure 8: Renal Guard system (Renal Guard Solutions Inc., Milford, Massachusetts).

Many studies showed that the Renal Guard system reduced the incidence of AKI in patients undergoing TAVR (Barbanti et al. 2018, Rihal und Kashani 2015). Moreover, Putuzu et al showed in metyanalysis included 699 patients that Renal Guard system reduced that rate of renal replacement therapy. Although at first glance it appears impressive that the Renal Guard system appear to lower post-procedural creatinine increases, we are not sure if it does actually prevent renal dysfunction or merely flush serum creatinine? (Rihal und Kashani 2015). The Renal Guard system should be furtherly evaluated in larger multicenter trials to investigate its efficacy to reduce the clinical end points in TAVR patients. the use of nacetylcysteine (NAC) peri-procedurally has been associated with lower acute renal injury(Bugani et al. 2021).

A similar procedure (TAVR without CM) has been previously described with the trans apical approach (Ferrari et al. 2010). However, there are only a limited number of case series describing this "contrast-free" TAVR implantation technique by the TF approach. For instance, Bruschi, et al. and Arrigo, et al. published case reports on a contrast-free TAVI with the Core Valve (Medtronic); Latib, et al. published a series of 3 patients who underwent implantation of a Direct Flow valve (Direct Flow Medical) and the use of a single contrast shot to check the femoral closure site; and Leroux, et al published 1 TAVR case with a balloon-expandable Sapien valve without the use of contrast medium (Bruschi et al. 2016, Arrigo et al. 2015, Latib et al. 2014, Leroux et al. 2013). To the best of our knowledge, the present series represents the largest cohort to date in which the TAVR procedure was performed without the use of any contrast media.

Ferrari et al1 published a series of 30 TAVR patients who underwent the procedure without the use of contrast media in 2010, but all of the procedures were performed with a trans apical approach(Ferrari et al. 2010). During the preoperative work-up, we minimized the amount of CM used during coronary and iliofemoral angiography before TAVI (mean 25 mL, range 23-36 mL) by performing coronary angiogram with a biplane C-arm setting. Another alternative approach to reducing the burden of iodinated CM during coronary angiography is the use of gadolinium. Due to their different chemical structures, gadolinium and iodinated contrast have no cross-reactivity in patients with iodine allergies, and gadolinium has a lower nephrotoxicity at the recommended doses than iodinated CM (Chaturvedi et al. 2016).

At 30-day follow-up, the composite endpoint of death from any cause, valve embolization, vascular complications, cerebrovascular complications, pacemaker implantation, and postoperative myocardial infarction was equally distributed between both groups, and was comparable with previous studies. Our initial focus was to monitor renal function during the

postoperative follow-up period. One patient in the study group developed a postoperative acute kidney injury, which could potentially be explained by the use of general anesthesia and the hemodynamic effect of the implantation procedure in a very high-risk patient. However, contrast-induced nephropathy was significantly higher in patients who received contrast media (15 patients [20.5%] in control group vs 1 patient [4%] in the study group; P=.04).

The 30-day mortality rate of this high-risk study cohort that underwent TF-TAVI without CM was 4.0%, which compares well with other contemporary studies on TAVI patients (Thyregod et al. 2015, Sinning et al. 2010).

In our study protocol, accurately performing annular sizing was another challenge. For this purpose, our anesthesiology team was specifically trained to obtain transesophageal echocardiography (TEE) measurements according to the method of Bleakely, et al (Bleakley et al. 2017).

The steps of the analysis are as following:

Open the 3D analysis software package. The displayed image will be seen in four sections (sagittal, coronal, transverse and a full volume render). Select the mid-systolic frame (Table 2). 2. Align the sagittal and coronal planes to bisect the long axis of the aortic valve (Table 2). 3. It is then necessary to align the transverse plane at the level of the annulus, at the most caudal attachment of the three cusps (the hinge point). In this case, the red line representing the transverse view is moved such that it crosses the hinge point of the right coronary cusp in the sagittal view (red arrow) and left (blue arrow) and non-coronary cusp (yellow arrow) in coronal view (Table 2). By rotating the orthogonal plane of the transverse view, it is important to ensure that the annulus to be measured falls below the hinge points and does not include any caudal aspect of the cusps as this may interfere with accurate measurements. Table 2 demonstrates how rotating the blue plane will help in assuring that the transverse view is bisecting the hinge point at the level of the non- and left-coronary cusps. 4. Select the transverse plane image from this dataset (Table 2). 5. Trace the circumference and area of the annulus by pointing and clicking in an iterative manner around it. This is done in a similar manner to CT, using the inner edge of the annulus, ignoring any soft low-intensity echoes and irregular bright (calcium) indentations, which are traced through. 6. Once the annulus has been measured, it is possible to identify the ostium of the left main coronary artery and measure the distance between this and the base of the left-coronary cusp (any measurement below 11mm is considered too small to accommodate valve expansion without significant risk of coronary ostial occlusion). The figures below outline this process (Table 2). Firstly, align the sagittal and coronal planes to

bisect the long-axis of the aortic valve. The red marker line on the sagittal plane is then advanced cranially along the aortic root until the origin of the left main stem (LMS) is identified as an indentation at roughly the 10 O'clock position of the transverse image. The green marker of the transvers image is then rotated anticlockwise until it is aligned with the LMS ostium. The distance from the base of the left coronary cusp to the ostium can then be measured as shown by the yellow marker.

An additional native CT scan was used as a second imaging tool for reference. Furthermore, before starting this protocol, we performed an internal validation of our AV annular measurements by comparing the TEE measurements with those obtained by "contrast-enhanced" CT scans in a retrospective cohort from our institution. Based upon the results of this retrospective analysis, we completely abandoned the contrast-enhanced CT examination in this specific patient cohort and performed only TEE-based annular measurements.

Chaturvedi et al reported that magnetic resonance imaging (MRI)-based AV annular measurements were superior to the CT-based measurements.12 In the future; MRI could be a useful diagnostic tool for contrast-free TAVI procedures if this modality can successfully replace multislice CT measurements (Chaturvedi et al. 2016).

A limitation of this contrast-free TAVR technique is that the use of TEE is mandatory during the procedure; therefore, the TAVR procedure needs to be performed under general anesthesia. Unfortunately, this completely precludes the possibility of performing "contrast-free" TAVR under local anesthesia. An alternative reasonable approach to CM free TAVR is the restricted use of CM according to GFR. This approach might be not applicable in TAVR centers, where there still nor experience with TAVR without the use of CM and in case of difficulty to measure the annulus with 3D TEE. The use of isoosmolar CM was supposed to reduce the rate of AKI than the commonly used low osmolar CM(Solomon 2014, Solomon et al. 2009), as Ultravist 370 in this study. However, Per Liss et al found that the use of isoosmolar CM increased the incidence of acute kidney injury in a large observational study based on the data of the Swedish system(Liss et al. 2006).

Protocol to reduce the acute kidney injury post TAVR

Protocol A in patients after complete bypass revascularisation or patients without a history of CAD :

1. MSCT with low dose contrast (50ml), detection of contrast at lower Hounsfield 80-100, rate of injection 4ml/s, 100 kv.

2. Coronary angiography in biplane cath only if there is a severe stenosis in the proximal vessels.

3. Puncture of the femoral artery ultrasound guided.

4. Use TEE intraprocedural to assess the competence of the valve instead of aortography.

5. Duplex evaluation of the vessels after procedure on table.

Protocol B in patients with history of PCI > 6 months:

1. Coronary angiography in biplane cath.

2. 3D TEE to evaluate the annular size

3. Native MSCT of heart and femoral and iliac arteries to evaluate:

- The amount and location of calcification of annulus, LVOT and femoral arteries (see figure 9).

- Angulation of implantation (see figure 10)

- The height of coronary ostia (see figure 11)

4. MR angiography to evaluate the course of aorta and the diameter of femoral arteries.

5. Duplex evaluation of femoral arteries.

6. Puncture of the femoral artery ultrasound guided.

7. Use TEE intraprocedural (see figure 12) to evaluate the size of the annulus and two pigtail catheters to alligne the three cusps (see figure 13). TEE guiding of the level of implantation (see figure 14).

8. Duplex evaluation of the vessels after the procedure.

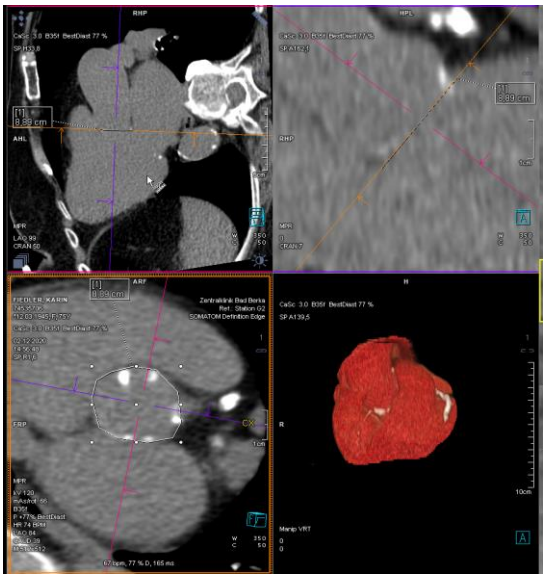


Figure 9: the measurement of annulus area in native CT.

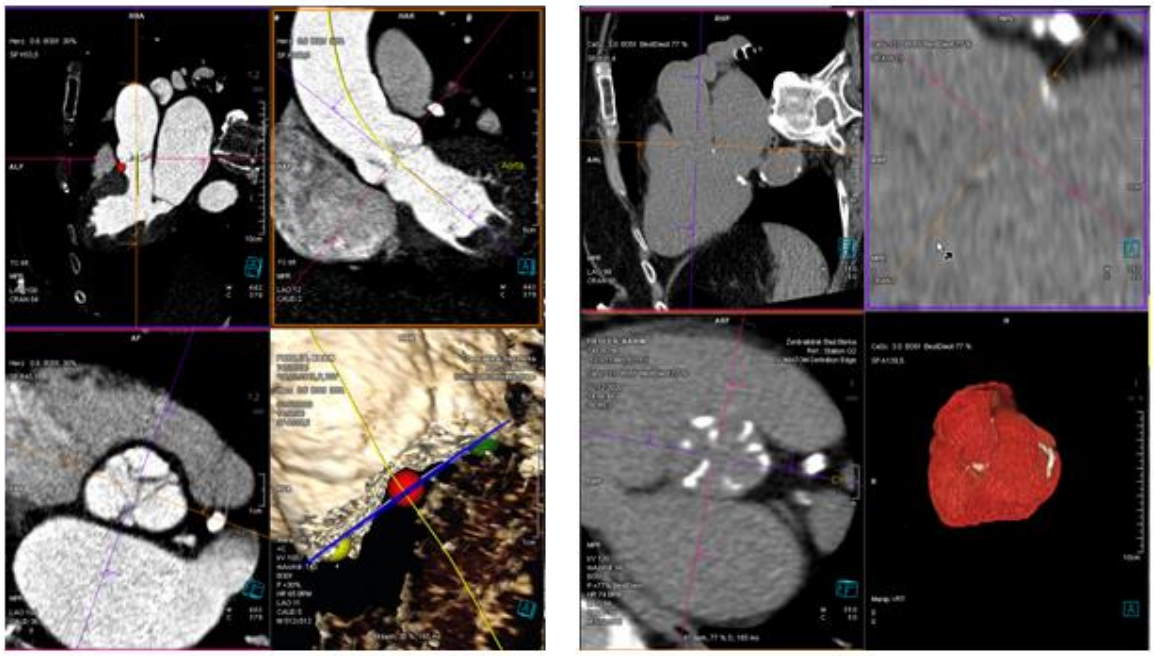


Figure 10: the difference between the estimations of 3-cusps view in CT with and without contrast medium.

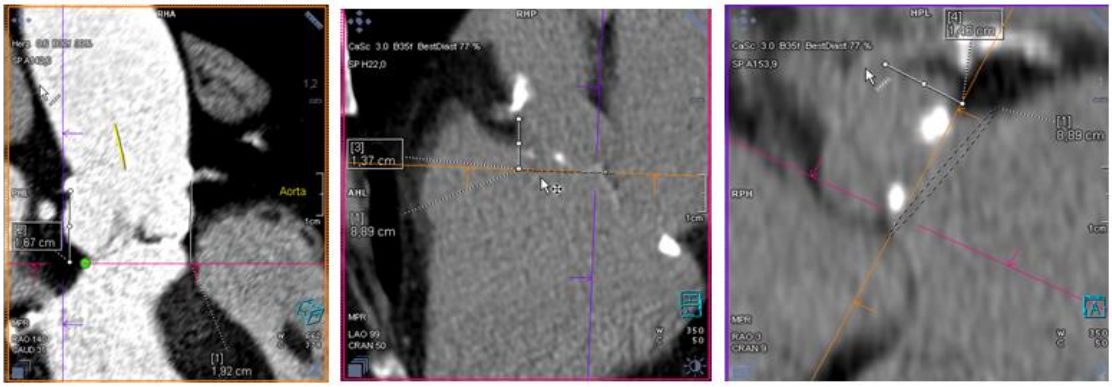


Figure 11: the difference between the estimation of the height of coronary ostiae in CT with and without contrast medium.

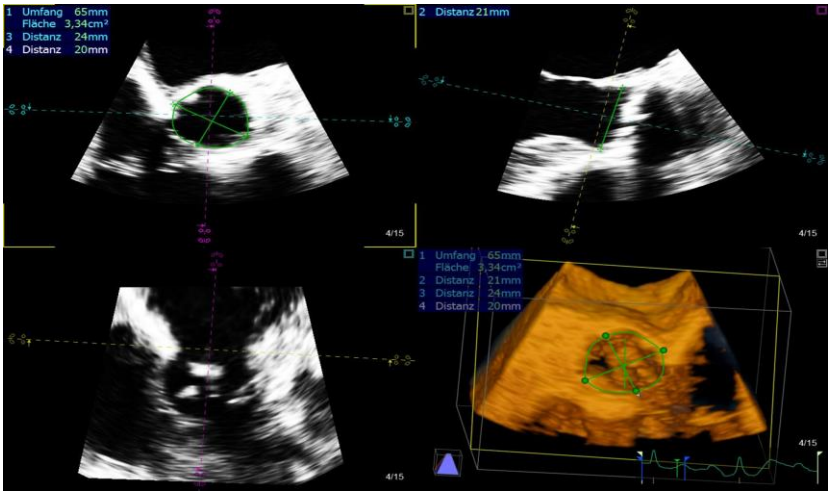


Figure 12: the assessment of annulus size using 3D TEE.

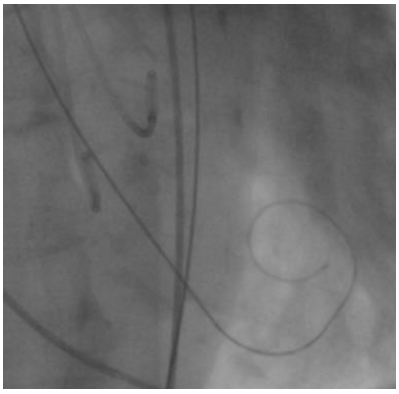


Figure 13: Intraoperative chest x-ray image demonstrating a pre-shaped stiff wire in the left ventricle and two pigtail catheters in the left coronary sinus and in the non-coronary sinus.

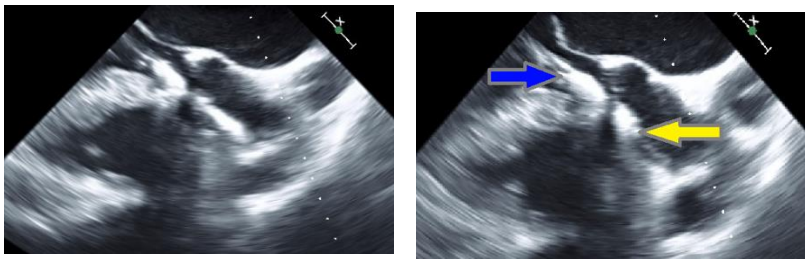


Figure 14: implantation of balloon expandable TAVR in a systematic two-steps approach; (a) positioning step and (b) full deployment step under TEE and radiographic guidance

In the second study, we focused on the role of BMI on TAVR outcomes. The principle conclusion was patients with BMI ≥ 25 kg/m2 had a lower long-term mortality rate; however, they also had a higher rate of procedure-related complications. The Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association, has designated obesity a risk factor for cardiovascular morbidity and mortality(Poirier et al. 2006). Furthermore, obesity rates are progressively rising due to sedentary lifestyles, even though obesity is known to be associated with higher morbidity and mortality(Adams et al. 2006). Nevertheless, an "obesity paradox" has previously been noted. For example, Batty et al. and Lancefield et al. reported better survival rates among obese patients with cardiovascular disease (Batty et al. 2006, Lancefield et al. 2010).

TAVR is indicated in patients considered to have high or intermediate risk for surgical aortic valve replacement(Leon et al. 2016). However, BMI is not a parameter in Euro SCORE II, and consequently, its influence on the TAVR outcomes has not been directly investigated in detail. Van der Boon et al. and the "PRAGMATIC-Plus" researchers found that obesity was associated with a decrease in 30-day mortality, but had no effect on long-term outcomes. They also reported no increase in procedure-related complications among the obese group (Van Der Boon et al. 2013). Our cohort was larger than that reported by PRAGMATIC-Plus. They retrospectively investigated 944 patients, whereas we retrospectively analyzed data from 1609 patients... Although we found lower 1-year mortality in patients with BMI ≥ 25 kg/m2, we did note an increase in periprocedural complications, which differs from the results of Van der Boon and colleagues. The lower mortality maybe partly due to overweight patients having have more metabolic reserves(Konigstein et al. 2015). Our results are consistent with the recent analysis from the FRANCE2 (French Aortic National Core Valve and Edwards 2) registry, according to which, among the TAVR population, overweight and obesity were associated with improved 1-year survival(Yamamoto et al. 2013a). BMI remained an independent predictor of improved survival in multivariate analysis. This might also be explained by the fact that overweight and obese patients are usually intensively treated with optimum medical therapy for the associated risk factors and consequently contributing to better outcomes(Konigstein et al. 2015).

We found more major vascular complications in obese patients, the explanation might be the fact that we were introducing a new closure device in our institute during the phase where this study was conducted and secondly we treated 31% of the study patients with ACURATE neo prosthesis using the standard technique with 20 F sheaths. Kim et al showed that the use of only the expandable mesh component of the transGlide introducer system (Mesh only) instead of the use of introducer sheath decreased the major vascular complication (Kim et al. 2019). However, the authors showed that this technique was feasible in all patients this could be due to selection bias of patients with favorable anatomy. Blood transfusions were found to be less frequent in the obese cohort in our study group. Despite the fact that hemoglobin levels were similar among all groups on admission and despite the increased number of procedure-related complications in the obese group, we would interpret this as those patients were seen as less frail and less fragile. Thus, blood transfusions in this group were restricted only to patients suffering from progressive anemia and active bleeding; therefore, overall, patients defined as obese were treated with blood transfusions less frequently. Several studies support our results (Nuis et al. 2012, Nuis et al. 2011, Tchetche et al. 2012).

There are two main findings of the third study. First, a BI < 80 is associated with increased mortality and risk of neurological events and cardiac decompensations after TF TAVR. Second, a BI < 80 is an independent predictor of failure in fast track TAVR.

There are different modalities for the objective assessment of frailty as well as mental and physical function, which is essential to determine procedural risk and to avoid TAVR futility (Arnold et al. 2016).

1. Assessment of physical function: 5 meter walk test ≥ 6 seconds, 6 minutes walk test < 100, Grip test, psoas muscle area in CT.
2. Assessment of nutritional status: albumin < 40 mg/dl, hemoglobin < 7mmol/dl, BMI < 18.5 and non-intended loss of weight.
3. Assessment of ADL and quality of life: Katz index > 3, Barthel index <80, the Kansas City Cardiomyopathy Questionnaire < 50.
4. Assessment of mental function: Mini-mental-status test < 19.

In our institution, we routinely use the original BI to assess ADL because it has been found to be the best tool to rate patient's independence(Mayoral et al. 2019). It is also the most widely used tool in German health system (Stone et al. 1994, Wade und Collin 1988). To the best of our knowledge, we are the first to study the influence of functional impairment measured

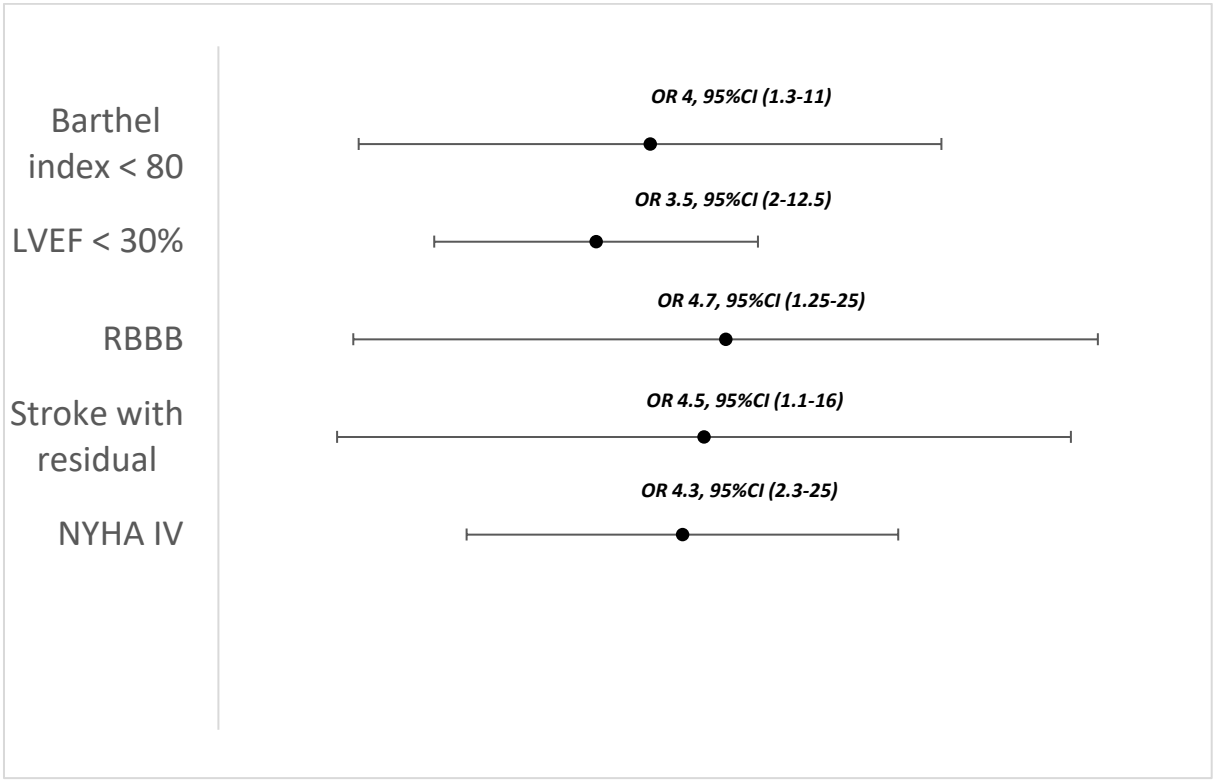
by the BI on postoperative outcomes after TF-TAVR. In this study, the mean BI was 76.6±15.4, which is higher than what reported by Tarro Genta et al 67±24 (Genta et al. 2017), which could be secondary to the inclusion of intermediate risk patients in the last years. However, the rate of independent patients in our study was higher than the incidence reported with Puls et al. (67% vs 77.6%), even after taking in account the different used indices used(Puls et al. 2014). Genta et al demonstrated a significant improvement in BI after TAVI at discharge, 85±17 vs. 67±24; P=0.001(Genta et al. 2017). We did not routinely compare the BI pre- and post-op.

In the current study, a BI < 80 was an independent predictor of the failure of the fast track protocol. Puls, et al. showed that functional status measured by the Katz Index represents a powerful predictor of adverse early and late outcome after TAVI, but not of the success of early discharge (Puls et al. 2014). In Puls et al work, the rate of early discharge was very low 5%, as the concept of fast track TAVI was not yet well established in 2014 and 53% of study patients were operated through trans apical approach (Puls et al. 2014). Nevertheless, the incidence of prolonged hospital stay > 14 days was more common in patients with Katz index < 6 (32% vs 22%, p value=0.047), see figure 15. According to our experience, the success of the fast track protocol improved patient's, families' and team's satisfaction and reduced the overall health care costs; however, this requires precise patient selection so as to exclude patients who have negative predictors of success with the fast- track protocol. Patients with BI < 80 had more decompensated heart failure, postoperative strokes, delirium, and procedural futility. These complications are expected in this group of patients with advanced age and insulin dependent diabetes mellitus. The prediction of improvement of symptom and complications before such a complex intervention as TAVR in these particular high risk patients is very important, as this was the priority most of our patients rather than prolongation of life span. Other predictors should be studied to select the patients who will gain a real clinical benefit from TAVR. It seems that one factor alone cannot predict the improvement of functional classification after TAVR combining TAVR scores along with frailty parameters, echocardiographic parameters and the presence of specific organ failure may be more accurate to predict TAVR-related futility (Puri et al. 2016).

This study also demonstrated that a BI < 80 was associated with increased risk of neurological events and cardiac decompensation. Nevertheless, other VARC-2 listed complications were equally distributed between different subgroups (figure 15). Patients with a BI < 80 had more postoperative strokes, albeit the rate of preoperative ischemic strokes was higher in patients with a BI ≥ 80. This may be due to exclusion bias of patients with previous stroke due to

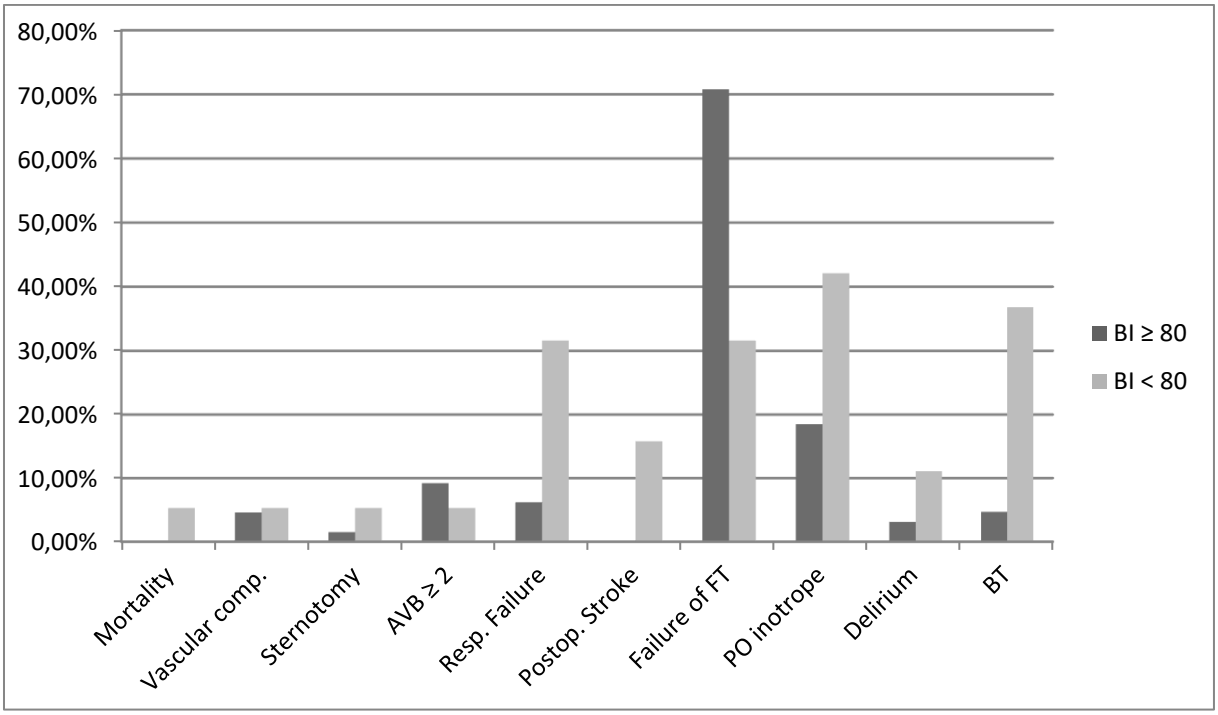
expected TAVR futility. Assessment of the neurological status before and after TAVR is essential as postoperative delirium is a predictor of long-term mortality (Goudzwaard et al. 2019), which may explain the higher mortality in patients with a BI < 80. Instenes et al. found that post-TAVR delirium associated with strong and distressing memories such as "Like dreaming while awake", "Disturbed experiences of time", "Existing in a twilight zone", "Trapped in medical tubes", "Moving between different surroundings" and "Meeting with death and the deceased". These memories can persist for up to 12 months later (Instenes et al. 2018). In our practice we do routinely the assessment of delirium using RASS and CAM-ICU scores postoperative. These two scores asses mainly the confusion postoperatively (Cieplinska-Legge) and did not provide a complete neurological assessment. Although postoperative cognitive dysfunction is a relevant complication after surgery, assessment for the condition is not routine in clinical practice (Pérez-Belmonte et al. 2019).

Figure 15: Odds ratios of variables that were identified as independent predictors of prolonged hospital stay after TF-TAVI.



LVEF: left ventricular ejection fraction; RBBB: right bundle branch block; NYHA: new York heart association; OR: odds ratio; CI: confidence interval.

Figure 16: Comparison between both groups as regard 3-month outcomes.



AVB: atrioventricular block; BI: Barthel index; BT: blood transfusion; comp.: complications; PO: postoperative; resp.: respiratory; FT: fast track.

6. Schlussfolgerungen:

1. TF-TAVR without the use of CM can be considered a safe and reproducible alternative technique. Furthermore, it reduced the incidence of postoperative acute kidney injury in patients with GFR <30 mL/min/1.73 m2. The angulation of the implantation plane could be obtained from the native multislice CTs.
2. BMI ≥25 kg/m2 was independently associated with lower 1 year mortality after trans femoral TAVR. However, the incidence of major vascular complications was more in patients with BMI ≥25 kg/m2. The improvement of puncture and implantation techniques as well as the use of flexible sheath could decrease the incidence of vascular complication in those patients.
3. A BI < 80 is associated with increased mortality and risk of neurological events and cardiac decompensations after TF-TAVR. BI < 80 is an independent predictor of failure in fast track TAVR. The limitations of our study are: first being a retrospective observational single center study and there may have residual confounders that we did not account for. Second: short follow up period. We cannot consider our study as a conclusive study. However, it could be used to generate hypothesis. Moreover, we could not exclude the role of confounding factors in patients with a BI <80, which lead to worse outcomes. We believe that there is a necessity of more prospective studies in this domain.

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Wissenschaftliche Arbeit:

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Ehrenwörtliche Erklärung

Hiermit erkläre ich, dass mir die Promotionsordnung der Medizinischen Fakultät der Friedrich-Schiller-Universität bekannt ist,

ich die Dissertation selbst angefertigt habe und alle von mir benutzten Hilfsmittel, persönlichen Mitteilungen und Quellen in meiner Arbeit angegeben sind,

mich folgende Personen bei der Auswahl und Auswertung des Materials sowie bei der Herstellung des Manuskripts unterstützt haben: Ass. Professor (Kairo) Tamer Owais, Elizabeth Costello, MD, PhD (USA),

die Hilfe eines Promotionsberaters nicht in Anspruch genommen wurde und dass Dritte weder unmittelbar noch mittelbar geldwerte Leistungen von mir für Arbeiten erhalten haben, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertation stehen,

dass ich die Dissertation noch nicht als Prüfungsarbeit für eine staatliche oder andere wissenschaftliche Prüfung eingereicht habe und dass ich die gleiche, eine in wesentlichen Teilen ähnliche oder eine andere Abhandlung nicht bei einer anderen Hochschule als Dissertation eingereicht habe.

Bad Berka, den 20.01.2022 Mohammad El Garhy