Original Article

Mid-term survival after transcatheter aortic valve implantation: Results with respect to the anesthetic management and to the access route (transfemoral versus transapical)

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ABSTRACT

Context: Several studies have analyzed the long-term survival after transcatheter aortic valve implantation (TAVI). However, no previous studies have looked at survival beyond 1-year with respect to the type of anesthesia. **Aims:** The aim was to evaluate the mid-term survival after TAVI with respect to the type of anesthesia (general anesthesia [GA] vs. local anesthesia ± sedation [LASedation]) or the type of procedure (transfemoral [transfem] vs. transapical TAVI) performed. **Settings and Design:** Retrospective cohort study. **Subjects and Methods:** This retrospective study included TAVI's between January 2009 and June 2013. Patients were divided into three groups: transfem TAVI under GA, transfem TAVI under LASedation and transapical TAVI. A total of 176 patients were eligible. The following clinical outcomes were evaluated: (1) Mortality, (2) Major cardiovascular complications, (3) Conduction abnormalities and arrhythmias, (4) Acute kidney injury, (5) Aortic regurgitation, (6) Neurologic events, (7) Vascular complications, (8) Pulmonary complications, (9) Bleeding, (10) Infectious complications, (11) Delirium. **Statistical Analysis Used:** A Kruskal–Wallis test was performed to test significance between the three groups for quantitative variables. Categorical variables were compared using a Chi-square test. Survival was estimated using Kaplan–Meier method. **Results:** There was no statistically significant difference between the survival of both transfem TAVI's ($P = 0.46$). The short-term outcome of the transfem TAVI groups was better than the transapical arm, but their mid-term survival did not show any significant difference ($P = 0.69$ transapical vs. transfem GA; $P = 0.07$ transapical vs. transfem LASedation). **Conclusions:** Our results demonstrate that the type of anesthesia and the access route do not influence mid-term survival after TAVI.

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INTRODUCTION

Since the initial introduction of transcatheter aortic valve implantation (TAVI) in Europe and after Food and Drug Administration approval in 2011 in the United States, there has been an exponential increase of the number of patients who have undergone a TAVI. The procedure is performed in high elderly patients with severe aortic stenosis who are not suitable for conventional aortic valve replacement under cardiopulmonary bypass. Currently, there are no prospective randomized trials comparing general anesthesia (GA) versus sedation for

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these patients.[1] There is as such no consensus, which technique is superior with respect to the outcome of these patients. Until date, an increasing number of studies have analyzed the survival after TAVI beyond 1 year.[2-8] Hence, no previous studies have looked at survival beyond 1 year considering the type of anesthesia applied at the moment of the procedure. The aim of this retrospective study was to evaluate the mid-term survival (survival beyond 1 year) after TAVI with respect to the type of anesthesia (GA vs. local anesthesia ± sedation [LASedation]) performed. The mid-term survival with respect to the type of procedure (transfemoral [transfem] vs. transapical TAVI) was analyzed as well.

SUBJECTS AND METHODS

This study has been approved by Le Comité d'Ethique Hospitalo-Facultaire Saint-Luc-UCL on December 23, 2013 (2013/544).

The records of all patients who had undergone a TAVI between January 2009 and June 2013 were retrospectively reviewed. Follow-up (FU) was completed in November 2013. In total 176 patients were eligible. Patients were divided into three groups: Transfem TAVI under GA (transfem GA), transfem TAVI under LASedation (transfem LASedation) and transapical TAVI. This study includes patients who underwent TAVI soon after the initiation of the implantation program up to June 2013. The very first patients after the start of the TAVI program were not included to exclude an eventual impact of a learning curve. All the patients were truly inoperable with severe aortic stenosis. They all had very high logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE). Although the EuroSCORE II has been launched in 2011, it was possible to calculate it from our dataset. The decision to perform a TAVI was taken by a multidisciplinary team composed of cardiologists and cardiac surgeons. A preprocedure agreement on an emergency plan was available in all cases. All procedures were performed in a hybrid operating room. A perfusionist and a cardiac surgeon were available in case it was deemed to start cardiopulmonary bypass. Experienced cardiac anesthesiologists only were in charge of the patient. The type of approach was decided by the interventional cardiologists and the cardiac surgeons and was mainly based on the permeability and the degree of calcification of the iliofemoral arteries on one hand and on the size of the aortic annulus on the other hand.

Procedure and devices

For the transfemoral approach, vascular sheaths were inserted into the femoral artery and vein after administration of unfractioned heparin. After the placement of temporary transvenous pacemaker, and testing of capture, a guidewire was placed retrogradely across the aortic valve. Rapid right ventricular pacing was initiated to ensure stable device positioning. Once the valve was deployed, and after angiographic control of its position and function, vascular sheaths were removed and closure was performed either surgically or by the use of a vascular closure device (Prostar XL, Abbott, IL, USA). Unfractioned heparin was antagonized by protamine sulfate (Leo Pharma, Dublin, Ireland).

For the transapical approach, an anterolateral mini-thoracotomy was performed. After placing apical purse-string sutures, an introducer was placed. Heparin was administered. A guidewire was positioned through the aortic valve under continuous fluoroscopy. Rapid ventricular pacing was realized through epicardial pacemaker electrodes to ensure stability during deployment. After fluoroscopic and transesophageal echocardiographic valve control, the introducer was removed, and the apical purse-string sutures were secured. Protamine sulfate was injected to achieve normalized activated coagulation time.

The devices used were Edwards-Sapien valve (Edwards Life-Sciences Inc., Irvine, CA, USA), the CoreValve System (Medtronic, Inc., Minneapolis, MN, USA) or Portico THV (St. Jude Medical, Minneapolis, MN, USA).

Anesthetic management

At the initiation of the TAVI program in this center, all the transfem procedures were performed under GA. Subsequently, with the gained experience and the use of newer vascular devices, we opted to perform all the transfem implantations under LASedation.

General anesthesia

Monitoring consisted of a peripheral intravenous cannula, a 5-lead electrocardiogram and a radial artery catheter for invasive blood pressure monitoring. External adhesive defibrillator pads were used in all the patients. Cerebral monitoring was performed by the use of bilateral cerebral oximetry (INVOS 5100, Somanetics Corporation, Troy, MI, USA) and NeuroSENSE® (NeuroWave Systems, Inc., Cleveland, OH, USA). The choice of anesthetic agents used was left at the discretion of the anesthesiologist. Induction was performed with the use of midazolam, ketamine,

sufentanil and etomidate, or propofol. Rocuronium or atracurium were used to facilitate tracheal intubation. The maintenance of anesthesia was achieved with either a target-controlled infusion of propofol or inhaled sevoflurane. A three lumen central venous catheter was inserted. Epinephrine and norepinephrine drips were prepared and ready for an eventual urgent administration. A bladder catheter was inserted. All the injected fluids were warmed up. For a small number of patients in the transfem group, a laryngeal mask was used. For every intubated patient, a transoesophageal echocardiography was performed in addition to the fluoroscopic control.

Local anesthesia ± sedation

In contrast to patients who underwent GA, no central venous line, and no bladder catheter were inserted. Instead, two large bore peripheral venous catheters were put. One of them was used for volume administration. The other was exclusively used for eventual administration of vasopressors and/or inotropes via a three lumen valve. Oxygen was administered with a partial rebreathing face-mask. Capnography was measured by positioning the distal part of the capnography lumen under the face-mask. Sedation was only performed if deemed necessary by the anesthesiologist in charge and consisted of target-controlled infusion of propofol. LA was performed by the interventional cardiologist. In all cases, access to the patient was as such that the airway could be secured easily.

Statistical analysis

All data are expressed as median (percentile 25–75) or numbers and percentages as appropriate. Normal distribution was tested by a Kolmogorov–Smirnov test. A Kruskal–Wallis test was performed to test significance between the three groups for quantitative variables. An adjusted *post-hoc* Bonferonni test was used with significance accepted as $P < 0.0166$. A Mann–Whitney U-test was then performed to analyze the significant difference between paired groups. Categorical variables were compared using a Chi-square test. An adjusted *post-hoc* Bonferonni test was also applied. A Fisher exact test was used to compare paired data when appropriate. Survival was estimated using Kaplan–Meier method. A log-rank test was used to compare survival between different groups. All *P* values are two-tailed. Statistical analysis was performed using SPSS version 21 (SPSS Inc., Chicago, IL, USA).

Definitions of clinical outcomes

For detailed definitions of the clinical outcomes we analyzed [Appendix 1].

RESULTS

Baseline patient characteristics are shown in Table 1. There was no significant difference between both transfemoral groups with regards to the preoperative data. Patients in the transapical group had a significantly higher EuroSCORE II compared with the transfem population. However, there was no significant difference between the logistic EuroSCORE values of the three studied populations ($P = 0.22$). Operative and postoperative patient data are illustrated in Table 2. Patients undergoing a transapical TAVI procedure stayed significantly longer in the Intensive Care Unit and in the hospital compared with the transfem TAVI's. When comparing both transfem groups, patients in the transfem LASedation arm had a statistically significant shorter hospital stay compared with the transfem GA group. GA was necessary in four patients in the transfem LASedation group. Two subjects were not cooperative and in other two vascular complications required surgical repair at the end of the procedure. These patients have been considered in the transfem LASedation arm.

One patient in the transfem LASedation arm required a TAVI-in-TAVI. In one patient in the transapical arm embolization of the TAVI resulted in placement of a second TAVI. In another patient in the transapical group, emergency cardiopulmonary bypass was initiated for severe hemodynamic instability.

None of the patients died in the operating room. No endocarditis was observed throughout the study period.

Clinical outcome

Intrahospital and 30 day mortality were statistically significantly higher in the transapical TAVI group. Thirty-day mortality was 17% in the transapical TAVI, 2% in the transfem GA group and 5% in the transfem LASedation group. Major cardiac complications occurred more frequently in the transapical TAVI group compared with both transfem TAVI arms. Table 3 illustrates the clinical outcome data of the three groups. The number of vascular complications was statistically significantly higher in the transfem GA group when compared with the other two groups. Although there was no significant difference between the three groups regarding the occurrence of conduction abnormalities and arrhythmias, the number of permanent pacemakers was significantly higher in the transfem LASedation arm. Interestingly, no patient in the transfem LASedation group showed infectious complications. This is in

Table 1: Baseline patient characteristics

	Transfem GA (*n*=51)	Transfem LASedation (*n*=66)	Transapical (*n*=59)
Age (years)	86 (82-88)	86 (83-88)	84 (81-87)
BMI (kg/m^2)	25 (22-29)	26 (22-27)	27 (23-31)
Male sex (%)	31 (61)	26 (39)	34 (58)
Creatinine (mg/dL)	1.24 (1.03-1.55)	1.14 (0.89-1.53)	1.29 (1.02-1.85)
GFR (ml/min)	51 (41-67)	55 (41-66)	42 (30-65)
BNP (ng/L)	396 (216-539)	430 (169-1277)	310 (197-623)
Hb (g/dL)	12.6 (11.1-13.8)	12.7 (10.8-13.4)	12.1 (10.5-13.0)
EuroSCORE II (%)	5.5 (3.7-10.6)	4.9 (2.7-8.5)	8.6 (4.6-13.3)*
Logistic EuroSCORE (%)	25.28 (16.30-38.90)	27.14 (14.55-39.96)	31.80 (21.32-46.75)
FS (%)	29 (20-36)	27 (18-40)	33 (24-42)
PG aortic valve (mmHg)	74 (52-86)	70 (55-94)	78 (55-87)
Aortic surface (cm^2)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.6 (0.5-0.7)
Ischemic cardiomyopathy (%)	39 (76)	40 (61)	47 (80)
History of CVA or TIA (%)	12 (24)	12 (18)	11 (19)
History of arrhythmias (%)	24 (47)	23 (35)	24 (41)
Diabetes (%)	15 (29)	13 (20)	7 (12)
COPD (%)	12 (24)	25 (38)	16 (27)
Redo surgery (%)	13 (25)	11 (17)	25 (42)**
Pulmonary hypertension (%)	10 (20)	9 (14)	9 (15)
NYHA II (%)	17 (33)	23 (35)	19 (32)
NYHA III (%)	32 (63)	35 (53)	36 (61)
NYHA IV (%)	2 (4)	8 (12)	4 (7)

All data are expressed in median (percentile 25-75) or numbers (%). *P<0.05: Compared with other two groups, **P<0.05: Transapical versus Transfem LASedation. Transfem GA: Transfemoral general anesthesia, Transfem LASedation: Transfemoral local anesthesia±sedation, BMI: Body mass index, GFR: Glomerular filtration rate, BNP: Brain natriuretic peptide, Hb: Hemoglobin, EuroSCORE II: European System for Cardiac Operative Risk Evaluation II, FS: Fractional shortening, PG: Peak gradient, CVA: Cerebrovascular accident, TIA: Transient ischemic attack, COPD: Chronic obstructive pulmonary disease, NYHA: New York Heart Association

Table 2: Operative and postoperative patient characteristics

	Transfem GA (*n*=51)	Transfem LASedation (*n*=66)	Transapical (*n*=59)
ICU stay (days)	1 (1-1)	1 (1-1)	1 (1-2)*
Hospital stay (days)	9 (7-13)	7 (5-9)***	14 (10-17)*
Procedure time (min)	100 (85-125)	91 (75-111)	90 (70-99)
Total Intravenous anesthesia (%)	4 (8)	1 (6)	10 (17)
Sevoflurane anesthesia (%)	47 (92)	3 (4)	49 (83)
Edwards-Sapien (%)	50 (98)	55 (83)*	59
CoreValve (%)	1 (2)	5 (8)	0
Portico (%)	0	6 (9)*	0
RBC transfusion (%)	20 (39)	11 (17)*	23 (39)
Total RBC transfusion; units	2 (1-3)	0 (0-1)*	2 (1-3)
Peak troponin-I (ng/mL)	0.69 (0.49-1.44)	0.84 (0.45-1.53)	5.93 (4.36-9.13)*
Peak CRP (mg/dL)	10.2 (5.0-14.0)	2.4 (1.0-4.7)***	22.7 (18.7-26.7)*
Postoperative BNP (ng/mL)	342 (189-659)	308 (141-872)	468 (300-843)
Discharge Hb (g/dL)	10.4 (9.6-11.5)	10.8 (9.6-11.8)	10.1 (9.5-11.1)
Discharge creatinine (mg/dL)	1.05 (0.91-1.40)	1.03 (0.78-1.35)	1.22 (0.92-1.98)
Discharge GFR (ml/min)	55 (41-79)	60 (42-76)	49 (29-65)

All data are expressed in median (percentile 25-75) or numbers (%). *P<0.05: Compared with other two groups, ***P<0.05: In-between transfemoral groups. Transfem GA: Transfemoral general anesthesia, Transfem LASedation: Transfemoral local anesthesia±sedation, ICU: Intensive Care Unit, RBC: Red blood cells, CRP: C- reactive protein, BNP: Brain natriuretic peptide, Hb: Hemoglobin, GFR: Glomerular filtration rate

accordance with the significantly lower postoperative peak C-reactive protein concentrations in this group, as illustrated in Table 2.

Mid-term outcome

FU was available for the entire study cohort. All causes cumulative mortality was cardiovascular in

Table 3: Clinical outcomes

	Transfem GA (*n*=51) (%)	Transfem LASedation (*n*=66) (%)	Transapical (*n*=59) (%)
Major cardiovascular complications	2 (4)	4 (6)	17 (29)*
Renal replacement therapy	0	0	5 (8)**
Acute kidney injury	8 (16)	7 (11)	16 (27)
CVA and or TIA	2 (4)	2 (3)	7 (12)
Bleeding complications	5 (10)	2 (3)	6 (10)
Moderate AR	9 (18)	9 (14)	6 (10)
Vascular complications	15 (29)*	5 (7)	5 (8)
Infectious complications	11 (22)	0*	18 (31)
Permanent pacemaker	0	10 (15)***	3 (5)
Pulmonary complications	4 (8)	1 (2)	10 (17)**
Delirium	16 (31)	16 (24)	14 (24)
Conduction abnormalities	14 (27)	21 (32)	19 (32)
In-hospital mortality	1 (2)	2 (3)	9 (15)*
30 day mortality	1 (2)	3 (5)	10 (17)*

All data are expressed in numbers (%). **P*<0.05: Compared with other two groups, ***P*<0.05: Transapical versus transfem LASedation, ****P*<0.05: In-between transfemoral groups. Transfem GA: Transfemoral general anesthesia, Transfem LASedation: Transfemoral local anesthesia±sedation, CVA: Cerebrovascular accident, TIA: Transient ischemic attack, AR: Aortic regurgitation

63% and noncardiovascular in 23% of the patients. In the remaining 14% of the patients the cause of death was unknown. One year mortality was calculated as percentage of mortality after 30 days postprocedure. One year mortality was 24%, 11% and 16% in respectively the transfem GA, transfem LASedation and transapical group. The maximum FU was 46 months, 29 months and 55 months for respectively the transfem GA, transfem LASedation and transapical group. The overall estimated survival at maximum FU was 26% for the transfem GA group, 63% for the transfem LASedation group and 0% for the transapical population. The estimated survival rate at 12 months and 24 months was 72% and 57% for the transfem GA group, 76% and 63% for the transfem LASedation group and 67% and 51% for the transapical group. Figure 1 shows the Kaplan–Meier survival curve of the three TAVI groups. There was no statistically significant difference between the mid-term survival of both transfem TAVI's ($P = 0.46$). The mid-term survival of the transapical group did not show any statistically significant difference when compared with the transfem TAVI population ($P = 0.69$ when compared with the transfem GA group, $P = 0.07$ when compared with the transfem LASedation).

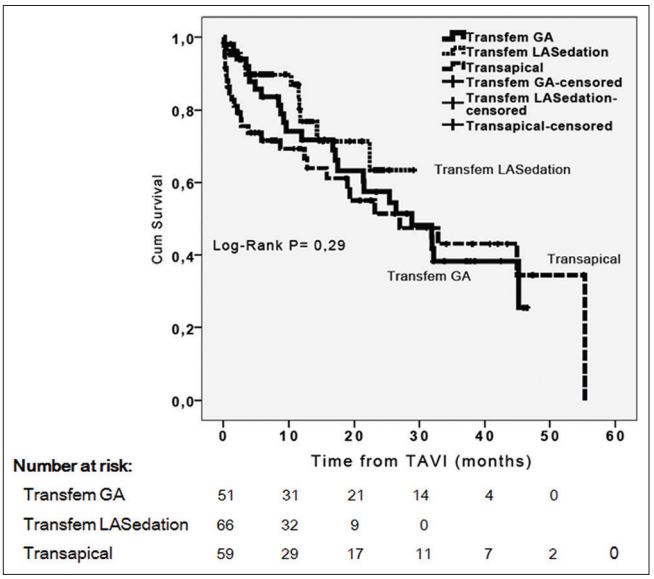

Figure 1: Kaplan–Meier survival curve of 3 transcatheter aortic valve implantation groups

DISCUSSION

In this retrospective analysis we analyzed the mid-term survival of patients undergoing TAVI with respect to the type of anesthesia and with respect to the type of procedure performed. Despite its small sample size, this study is to the best of our knowledge the first to analyze the mid-term survival rate of patients undergoing transfem TAVI depending on the type of anesthesia performed.[9] A very recent large study has compared the transfem TAVI under GA versus LA, but their maximum FU was 1 year.[10] The maximum FU in the current study was 47 months in the transfem GA group and 29 months in the transfem LASedation group. There was statistically no significant difference in the mid-term survival between both groups ($P = 0.46$), despite some differences in their short-term clinical outcome. Indeed, the transfem LASedation group had a significantly shorter hospital stay, which is in accordance with previous publications.[11,12] They also presented significantly less vascular complications

compared with the GA group. This point should however be interpreted with caution. The increasing learning curve and the improvement of the vascular devices used, could have biased the results in favor of the transfem LASedation cohort. Interestingly, we observed significantly less infectious complications in the transfem LASedation arm. This point is in accordance with the significantly shorter hospital stay in this group compared with the GA group. The lower incidence of infectious complications may be explained by the following points: The lack of bladder catheterization, no central venous catheter insertion and no intubation, less access-site related complications and less transfusion. This lower incidence of infectious complications explains the significantly lower postoperative peak C-reactive protein concentrations in the transfem LASedation arm. Significantly more patients in the transfem LASedation arm needed a permanent pacemaker. The type and the positioning of the implanted valve probably explain this number. The number of Portico and Edwards-Sapien valves (but not CoreValve) was significantly different in the transfem LASedation group compared with the two other groups. To be noted, information about the exact positioning of the implanted valve (magnetic resonance imaging) was not available to evaluate if a lower implantation technique has increased the risk for conduction disturbances.

In this cohort of patients undergoing transfem TAVI, 30 day mortality was 2% in the GA arm and 5% in the LASedation group. This rate is lower than most studies,[13-15] and is an encouraging finding with respect to the initial learning curve and the rather low sample size.

In general the mid-term survival rate of our patients undergoing a transfem TAVI procedure is consistent with previous publications. The 1 year mortality rate of most studies is between 20% and 30%. The 2 years mortality rate is between 22% and 38%. Table 4 illustrates a summary of these studies. The difference in survival rate at the maximum FU between the transfem GA and the LASedation group is not unexpected considering the natural history of death in this high elderly population. As a matter of fact death was from a noncardiac origin in 23% of the entire study cohort.

In this study we also evaluated the survival rate of patients undergoing transapical TAVI compared with the transfem approach. Estimated survivals at 12 months and 24 months were respectively 67% and 51%. At maximum FU (55 months) the survival rate was 0%. However, there was no statistically significant difference when the mid-term survival of the transapical group was compared with the transfem cohort. This lack of difference in the mid-term survival is in contrast with the worse short-term clinical outcome of the transapical group.

The mid-term survival of our transapical population seems to be in accordance with previous publications.[8,18] However, it should be noted that very few studies have focused on survival of transapical TAVI's beyond 3 years.[2,5] The lack of difference in the mid-term survival in our study is in accordance with the large Canadian multicenter trial published by Rodés-Cabau *et al*.[5] Our results are however in contrast with a recent multicenter study comparing transapical versus transfem TAVI's.[19] Although the median FU of the latter was only 1 year, estimated survival including hospital stay and FU period was 83% in the transfem group versus 68% in the transapical arm ($P = 0.01$). The only explanation for this discrepancy would be the low number of subjects in their transapical arm ($n = 89$) compared with the transfem group ($n = 793$) which is in favor of a better and faster learning curve on their transfem population.

Study limitations

As mentioned earlier, patients in the transfem GA group were the very first patients to participate in a TAVI program. Any bias considering their short- and mid-term outcome should be taken into account. This study was assessed over a period of at least 4 years. The use of smaller sheaths and different devices may have resulted in different complications. Moreover, the effect of the learning curve was not accounted for in the data analysis. Although we looked for all eventual clinical complications, we did not apply the Valve Academic Research Consortium definitions[20] as clinical endpoints. Furthermore, mortality stratified according to Society of Thoracic Surgeons Risk Scores could not be calculated from our dataset.

CONCLUSIONS

The results of this retrospective study show no significant difference in the mid-term survival of patients undergoing transfem TAVI whether or not GA was performed. The short-term outcome of the transfem LASedation group was however better. When

Table 4: Summary of published studies reporting 1-3 years outcome after transcatheter aortic valve implantation

Publication	Route	*n*	1 year outcome	2 years outcome	3 years outcome
Moat *et al*.[7]	Transfemoral	599	18.5% mortality	22.5% mortality	NA
	Other routes	271	27.7% mortality	36.7% mortality	NA
Rodés-Cabau *et al*.[4]	Transfemoral	162	75% survival	65% survival	NA
	Transapical	177	78% survival	64% survival	NA
Walther *et al*.[18]	Transapical	299	73% survival	68% survival	58% survival
Ussia *et al*.[16]	Transfemoral and transsubclavian	181	23.6% mortality	30.3% mortality	34.8% mortality
Bleiziffer *et al*.[17]	Transfemoral and other routes	227	74.5% survival	64.4% survival	NA
Kodali *et al*.[3]	Transfemoral and transapical	348	24.3% mortality	33.9% mortality	NA
D'Onofrio *et al*.[8]	Transapical	774	81.7% survival	76.1% survival	67.6% survival

NA: Not available

considering the access route for TAVI no significant difference could be found in the mid-term survival of patients whether transapical or transfem TAVI was performed. This finding was in contrast with the worse short-term outcome of the transapical cohort.

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Conflict of interest

There are no conflict of interest.

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APPENDIX 1: DEFINITIONS OF CLINICAL OUTCOMES

Mortality

All deaths were reported at the last follow-up. Mortality was divided into cardiovascular and noncardiovascular. Cardiovascular death was defined as death due to any cardiac or vascular cause or death due to the procedure and its complications. Any sudden death was considered as cardiovascular death. Noncardiovascular death was any death related to a clear condition which was not cardiovascular (cancer, pneumonia,…).

Major cardiovascular complications

Major cardiovascular complications were defined as the presence of one or several following conditions:

- Signs and symptoms of myocardial infarction during the procedure and during the hospital stay postprocedure
- Any cardiac arrest or malignant arrhythmia resulting in severe hemodynamic instability
- New signs and symptoms of heart failure or multiple organ failure due to heart failure
- Evidence of new pericardial effusion resulting in hemodynamic instability and necessitating drainage
- Unplanned use of cardiopulmonary bypass or conversion to open surgery due to severe hemodynamic instability.

Conduction abnormalities and arrhythmias

- Any new onset atrial fibrillation or atrial flutter
- Any new or worsened cardiac conduction abnormality
- Any new arrhythmia requiring electrical conversion and/or medical therapy
- New permanent pacemaker implantation.

Acute kidney injury

For the definition of acute kidney injury, the first three categories (risk, injury, failure) of the RIFLE criteria have been adopted.[8,9] Patients who required renal replacement therapy and as such were in the last categories of the RIFLE criteria (loss, end-stage kidney disease) were considered as a separate group because of the risks associated with this condition.

Aortic regurgitation

Aortic regurgitation was assessed by transthoracic echocardiography before discharge. Both central and paravalvular components were considered to measure the total regurgitant volume.

Neurologic events

Neurologic events include stroke and transient ischemic attacks. Stroke was defined as neurologic deficit lasting more than 24 h or lasting <24 h but with positive brain imaging study. Transient ischemic attack was defined as transient neurologic dysfunction and absence of tissue damage on imaging studies.

Vascular complications

- Any peripheral vascular injury leading to upper or lower limb ischemia and/or to endovascular stenting and/or unplanned surgical intervention
- Any access site vascular bleeding, hematoma, or pseudoaneurysm requiring other treatment than manual compression.

Pulmonary complications

- Any pleural effusion and/or pleural hematoma requiring active drainage
- Any hypoxemia and/or hypercapnia necessitating invasive and/or noninvasive ventilation
- Any bronchospasm requiring medical treatment.

Bleeding

- Any access-related bleeding that necessitates surgical intervention

- Any bleeding that results in hypovolemic shock
- Any transfusion of red blood cells or other blood products due to procedure related active bleeding.

Infectious complications

- Any access-related local infection necessitating local antiseptic treatment
- Any urinary or catheter infection requiring antibiotics and/or removal of the catheter
- Any positive hemoculture with clinical and biological signs of infection
- Any documented valvular endocarditis.

Delirium

- Any acute disturbances of consciousness with decreased attention
- Any agitation, visual or auditory hallucinations, disorientation to place time and person were considered as delirium. No objective tests were used to document delirium.