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Original Article

Deep sedation vs femoral block anesthesia: beat-by-beat hemodynamic impact on TAVI procedure

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Abstract: Background: In spite of the increased use of Trans-catheter Aortic Valve Implantation (TAVI) due to the better patient selection, well-trained operators and improved technology, the choice of the best anesthesia regimen remains an open question. In particular, it remains to be clarified whether deep sedation (DS) in spontaneous breathing or femoral local anesthesia (LA) is best. Objective: This study compared the hemodynamic variations determined by deep sedation (DS) with spontaneous breathing and local femoral anesthesia (LA) in 2 groups of patients submitted to TAVI with two different kinds of anesthesia, using a beat-by-beat pulse contour method (MostCare®-UP). Methods: 82 patients with severe aortic stenosis and similar baseline characteristics and indications underwent trans-femoral TAVI: 50 with LA and 32 with DS. All patients were submitted to minimally invasive hemodynamic monitoring. The following parameters were measured: *pressure indexes*: systolic, diastolic, mean (SysP, DiaP, MAP) and dicrotic (DicP) pressures; *flow indexes*: cardiac output (CO), stroke volume (SV); *ventriculo-arterial coupling indexes* (VAC): peripheral arterial elastance (Ea_p), systemic vascular resistance (SVR); *cardiovascular system performance*: cardiac cycle efficiency (CCE), dP/dt_{max_rad}. Results: The TAVI procedure was successful in 89% of patients (VARC-2 criteria) with no difference between the 2 groups. Anesthesia induction determined a higher decrease of pressures in DS than in LA (P<0.01) with no differences in CO. The VAC parameters (Ea_p, SVR) decreased (P<0.01) in DS with an improvement in CCE (P<0.001); these parameters did not change in LA. The post-TAVI flow and VAC parameters, especially Ea, increased (P<0.05) more significantly in the LA group than in the DS group (P<0.001). Using logistic regression, the occurrence of the post-TAVI aortic regurgitation was correctly associated with the pressure gradient MAP-DicP in 63% of the study population (P=0.033). This association was more effectively detected in the LA group (78%, P=0.011) with a ROC AUC=0.779, than the DS group. Conclusion: The use of the pulse contour method to track the fast-hemodynamic changes during the TAVI procedure proved suitable for the aim. As expected, LA and DS induced different pre-TAVI hemodynamic conditions, which influenced the post-TAVI hemodynamic changes. The hemodynamic conditions induced by LA, enabled the occurrence of post-TAVI aortic regurgitation to be detected more effectively.

Keywords: Anesthesia and TAVI procedure, deep sedation or femoral block anesthesia, continuous hemodynamic monitoring, pulse contour analysis, evaluation of residual regurgitation

Introduction

Since 2010, the trans-catheter aortic valve implantation (TAVI) technique has become a feasible alternative to surgical aortic valve replacement for patients with severe aortic stenosis with increased surgical risk [1]. TAVI indications have been implemented in the more recent international guidelines for the treatment of valvular diseases [2, 3]. Improvements in pre-procedural planning, operators' training and valve technology have led to an impressive decrease in procedural complications such as vascular damage, bleeding, stroke, incorrect positioning, need for permanent pacemaker, and residual paravalvular regurgitation [1, 4]. Despite the advances in procedural technique and devices, the impact of the kind of anesthesia on the effects of TAVI remains poorly documented. Recently, data from the US registry comparing general anesthesia with conscious sedation in patients undergoing TAVI, have

shown that conscious sedation was safe and associated to a mortality rate reduction [5]. Therefore, the evaluation of different anesthesia techniques becomes essential. Until now, no randomized clinical trials comparing the benefits of one anesthetic technique to another have been published. Therefore, in clinical practice the choice between deep sedation in spontaneous breathing (DS) and local anesthesia (LA) mainly depends on anesthesiological team habits and training more than on clinical reasons. In the present study, we hypothesized that DS, when compared with LA, may change the hemodynamic context in which TAVI is performed. Little is known about the impact of pre-TAVI systemic hemodynamic modifications induced by the anesthetic regimen on the post-TAVI hemodynamic parameters. The aim of the present study was to compare the variations of hemodynamic parameters induced by DS and LA before, during and after the valve replacement using a minimally invasive hemodynamic monitoring system MostCare®-UP [6-8] based on the pulse contour method.

Methods

This monocentric retrospective study analyzed data routinely collected during TAVI procedures performed by 2 different groups of interventional cardiologists of the same hospital: Careggi Hospital of Florence. The study enrolled consecutive severe aortic stenosis patients receiving indication to TAVI according to the Institutional multidisciplinary meeting (Heart Team). Patients not suitable for transfemoral TAVI were excluded from the study. Two patients died during the procedure and were excluded from the analysis. Each patient gave their written consent before the procedure to authorize data collection, in agreement with the protocol previously approved by the local ethical committee (Azienda Ospedaliero-Universitaria Careggi, Firenze, Area Vasta Centro, Italia; ref. number Cineca 11574). From March 2016 and May 2017, the 2 groups performed the TAVI procedures in patients with severe aortic stenosis following the same guidelines for indications and using the same TAVI devices. The surgical risk was individually assessed by the currently used risk scores (EuroSCORE II [9], STS-PROM [10]) and the decision to perform TAVI was made for the whole cohort after a multidisciplinary meeting (Heart Team) evaluating the clinical history and comorbidities. A thoraco-abdominal angio-CT scan was performed before the TAVI procedure to select the best access route and the type and size of the TAVI prosthesis based on aortic annulus dimension and valve characteristics. The two groups of interventional cardiologists used two different anesthesia protocols based on their different expertise and usual practice. The adoption of 2 different anesthesiological methods gave the opportunity to investigate the hemodynamic changes induced in DS and in LA. The two teams authorized the study investigators to independently collect the data during TAVI procedures with no communication of the values, except those useful for the patients' security. In the DS group (32 patients) hemodynamic parameters were collected before, during and after sedation obtained with propofol® (initial bolus followed by infusion at (1-2 mg/kg/h) associated with remifentanil (0.1 mcg/kg/min). In the LA group (50 patients), data were collected before and after a femoral block and post valve implantation. The femoral block was performed under echographic guide and without sedation: after 0.5-1 mcg/kg of iv fentanyl, a local injection around the femoral artery of 1:1 lidocaine 1% and ropivacain 0.5% (10-12 ml in total). If the patient did not collaborate or asked for sedation, sedation guided by the BIS level technique could be performed. Baseline demographics, clinical and echocardiographic data are reported in **Table 1**.

A radial catheter (Leadercath Arterial polyethylene catheter 20 gauge, 0.6 mm internal diameter; Vygon, Ecouen, France) was inserted before starting the procedure and was linked to a pressure transducer (TruWave system; Edwards Lifesciences, Irvine, CA, USA). The hemodynamic values were collected before and after DS and LA, during and after the TAVI procedure using the pulse contour system MostCare®-UP (Vygon, Padova, Italy). The electronic data storage started after radial artery cannulation when the pressure signal was suitable for the analysis. It was stopped when the patients left the catheterization laboratory [11, 12]. All peri-procedural events were noted and adverse clinical events were reported in accordance with VARC-2 criteria [13].

TAVI procedure

The TAVI procedure has been previously described in detail [14]. The technique used in the present study did not differ from the recommendations. The transfemoral route was used

Table 1. Baseline clinical and echocardiographic characteristics of study population

	Local anaesthesia (n=50)	Deep sedation (n=32)	Comparison between groups
Age (years)	85.3 ± 4.9 (70.5-94.7)	84.2 ± 5.7 (67-96)	P=0.355 (*)
Male	23 (46%)	13 (41%)	P=0.802
BSA (m^2)	1.73 ± 0.19	1.77 ± 0.16	P=0.326 (*)
EuroSCORE II	4.4 ± 4.5 (0.9-22.4)	4.5 ± 4.2 (0.9-17.2)	P=0.920 (*)
STS score	6 ± 4.5 (1-22.9)	5.3 ± 5.2 (1-26.3)	P=0.520 (*)
Hypertension	36 (72%)	27 (84%)	P=0.304
Diabetes	14 (28%)	8 (25%)	P=0.965
Atrial fibrillation	13 (26%)	4 (13%)	P=0.216
Chronic lung disease	6 (12%)	4 (13%)	P=0.781
Renal failure (eGFR <60 ml/min)	23 (46%)	9 (28%)	P=0.166
Peripheral vascular disease	4 (8%)	5 (16%)	P=0.474
Cerebrovascular disease	1 (2%)	1 (3%)	P=0.681
Previous CABG	5 (10%)	6 (18%)	P=0.423
Previous PCI	20 (40%)	12 (38%)	P=0.995
NYHA class II	20 (40%)	11 (34%)	P=0.780
NYHA class III	26 (52%)	20 (63%)	P=0.480
NYHA class IV	4 (8%)	1 (3%)	P=0.669
LVEF (%)	52.8 ± 10 (29-68)	51.7 ± 10.3 (28-70)	P=0.632 (*)
Mean pressure gradient (mmHg)	46.4 ± 15.2 (20-84)	51.5 ± 13.9 (26-78)	P=0.130 (*)

Values are means ± SD's or frequencies. Percentage values and (min/max) ranges are reported in parenthesis. All comparisons were computed with Unpaired Student's t-test (*) or χ^2. BSA, Body Surface Area; EuroSCORE, European System for Cardiac Operative Risk Evaluation; STS, Society of Thoracic Surgeons; CABG, Coronary Artery By-pass Graft; PCI, Percutaneous Coronary Intervention; NYHA, New York Heart Association; LVEF, Left Ventricular Ejection Fraction.

for all patients to implant a balloon-expandable (Sapien 3, Edwards Lifescience, Irvine, CA, USA) or self-expanding (CoreValve Evolut R, Medtronic, Minneapolis, MN, USA) valve, in relation with echocardiographic and CT data analysis. The balloon valvuloplasty was performed before valve implantation when appropriate, on the basis of the calcification pattern and chosen prosthesis. When the valve was positioned, the presence and severity of aortic regurgitation was checked by an angiography with 25 mL of contrast medium. If a moderate or severe residual aortic regurgitation was observed or the prosthesis expansion was incomplete, the valve was post-dilated during a ventricular pacing at 180 b/min.

Pulse contour analysis (MostCare®-UP)

The pulse contour method used of the hemodynamic analysis in the MostCare®-UP device is a Pressure Recording Analytical Method (PRAM) [7]. Briefly, MostCare®-UP is a minimally invasive monitoring system that does not require calibration or introduction of patients' characteristics [7, 8]. Multiple variables are obtained from beat-to-beat analysis of the arterial waveform recorded at 1000 Hz and stored electronically. The anthropometric data (height and weight) are only required for the calculation of indexed hemodynamic parameters (Stroke Volume index (SVI); cardiac index (CI). Using the radial pressure signal instead of central aortic pressure seems a reasonable approach without the use of a transfer function [15]. The "resonance points" between the incident wave and the reflected waves allows the computation of a function describing the ventricular-arterial coupling (VAC), which may change for each vessel as a function of equilibrium between incident and reflective waves [7, 16].

If the radial pressure is taken as a surrogate of central aortic pressure, it might be a source of error [6], but in our study we continuously monitored both the aortic and radial pressure recorded by Most-Care, these are strongly correlate both as SysP and DiaP, as recently reported [15].

In addition to pulse rate (PR bpm), the variables obtained can be clustered in "pressure indexes" such as systolic arterial pressure (SysP,

Table 2. Procedural aspects and complications rate

	All patients n=82	Local anaesthesia n=50	Deep sedation n=32	χ^2 test (*p*-value)
Balloon-expandable prosthesis	38 (46.3%)	26 (52%)	12 (37%)	(0.290)
Self-expanding prosthesis	44 (53.7%)	23 (46%)	21 (66%)	(0.131)
Balloon valvuloplasty	57 (69.5%)	37 (74%)	20 (62%)	(0.391)
Procedural Success (VARC-2 criteria)	73 (89%)	45 (90%)	28 (87%)	(0.993)
Lieve/Moderate AR	23/15 (28%/18%)	15/8 (30%/16%)	8/7 (25%/22%)	(0.811/×0.705)
Major vascular complications (VARC-2 criteria)	1 (1.2%)	0 (0%)	1 (3%)	(NA)
Minor vascular complications (VARC-2 criteria)	17 (20.7%)	10 (20%)	7 (22%)	(0.940)
Cerebrovascular complications	1 (1.2%)	0 (0%)	1 (3%)	(NA)
Permanent pacemaker implantation	12 (14.6%)	7 (14%)	5 (16%)	(0.907)

All comparisons are computed with χ^2. NA, not applicable; AR, aortic regurgitation; VARC, valve academic research consortium.

mmHg), diastolic arterial pressure (DiaP, mmHg), dicrotic arterial pressure (DicP, mmHg), mean arterial pressure (MAP, mmHg), gradient MAP-DicP (Mean arterial pressure-dicrotic arterial pressure) [16]; "flow indexes" such as cardiac output (CO, L/min) and stroke volume (SV, mL); "ventriculo-arterial coupling indexes" such as systemic vascular resistance (SVR in Dyn*s*cm^{-5}), peripheral arterial elastance (EaP = Pdic/SV in mmHg/mL) [17], and "cardiovascular performance indexes such as cardiac cycle efficiency (CCE, units) [16, 18], dP/dt_{max_rad} (mmHg/ms) [19, 20].

Statistical methods

Statistical analysis was performed with SPSS 20.0 package (IBM-SPSS, Chicago, USA). Continuous and categorical variables were reported as mean ± standard deviation or frequencies and percentages, respectively. The normality of the data was verified by the Kolmogorov-Smirnov test. The Student's t-test (for unpaired data) and the χ^2 test, were used to compare differences between study groups. The protocol steps were analyzed by ANOVA for repetitive measurements testing the interactions between groups and protocol steps. This analysis was adjusted for different confounding factors as part of the patients' baseline characteristics (age, gender, EuroSCORE II, hypertension, diabetes, atrial fibrillation, pulmonary disease, estimated Glomerular Filtration Rate, vasculopathy, ischemic heart disease, NYHA class and ejection fraction). The best predictor item(s) for aortic regurgitation were determined in whole cohort by multivariable logistic regression analysis with backward selection method. The validity of the logistic models was tested by analysis of Receiver Operating Characteristic (ROC) curves, and areas under the curves (AUC). Statistical significance threshold was set for $P<0.05$.

Results

Baseline characteristics and TAVI outcomes

As shown in **Table 1**, no differences in baseline characteristics between the 2 groups were observed. The balloon valvuloplasty before the implantation of the prosthetic valve was performed in 57 out of 82 patients (69.5%). According to VARC-2 criteria, 73 patients (89%) had a successful TAVI procedure. **Table 2** shows the procedural aspects and the type and rate of complications in the whole cohort. Forty-four patients (53.7%) were treated with a self-expanding valve (CoreValve Evolut R or EvolutPRO, Medtronic, Minneapolis, MN, USA), 38 patients (46.4%) with a balloon-expandable one (Edwards Sapien 3, Edwards Lifescience, Irvine, CA, USA). The percentage of patients treated with the two types of valves were similar in both groups. The rate of periprocedural complications did not differ between the two groups (**Table 2**). A persisting moderate aortic regurgitation despite post-dilatation was observed in 15 patients (18%). In one patient a second prosthesis implantation was necessary due to the migration of the first implanted valve. Two patients' peri-procedural deaths were not included in the group of 82 patients analyzed (**Table 2**).

Comparison between groups at the different steps of the procedure

Table 3 shows the comparison of hemodynamic variables at the different steps of the moni-

Table 3. Hemodynamic results for the two groups patients. The groups treatment with peripheral block (patients n=50) and with sedation (patients n=32) at Baseline (base), Anesthesia (treat) and End procedure (end)

	baseline n=50 (n=32)	anesthesia n=50 (n=32)	end n=50 (n=32)	t-test paired base/treat	t-test paired base/end	t-test paired treat/end
PR (beats/min)	70.1 ± 10.5 (71.4 ± 13.7)	68.8 ± 13.3 (67.9 ± 12.4)	66.3 ± 10.6 (66.7 ± 10.7)	0.162 (0.010)	0.001 (0.054)	0.034 (0.553)
DiaP (mmHg)	64. ± 12.0 (61±12.4)	61 ± 10.9** (49 ± 7.0)	61 ± 10.7** (53 ± 9.1)	0.017 (<0.001)	0.129 (0.004)	0.795 (0.059)
SysP (mmHg)	148 ± 29 (147 ± 27.4)	138 ± 25.7** (114 ± 19.7)	148 ± 25.5** (131 ± 22.2)	<0.001 (<0.001)	0.978 (0.019)	0.009 (0.001)
DicP (mmHg)	94 ± 16 (92 ± 16.2)	89 ± 13.9** (71 ± 9.7)	91 ± 16.5** (78 ± 13.7)	0.004 (<0.001)	0.126 (0.001)	0.471 (0.014)
MAP (mmHg)	92 ± 15.5 (90 ± 14.5)	87 ± 13.8* (70 ± 8.9)	90 ± 13.4** (79 ± 12.1)	0.001 (<0.001)	0.386 (0.005)	0.104 (0.002)
MAP-DicP (mmHg)	-1.88 ± 6.09 (-1.86 ± 5.19)	-1.84 ± 5.43 (-0.41 ± 4.53)	-0.27 ± 7.52 (0.81 ± 6.81)	0.920 (0.025)	0.091 (0.041)	0.081 (0.787)
dP/dt_{max_rad} (mmHg/ms)	0.96 ± 0.36 (0.97 ± 0.33)	0.85 ± 0.33* (0.68 ± 0.25)	1.14 ± 0.34 (1.04 ± 0.28)	<0.001 (<0.001)	<0.001 (0.347)	<0.001 (<0.001)
SVR (dyn s cm^{-5})	1660 ± 224 (1660 ± 224)	1634 ± 215** (1412 ± 212)	1491 ± 212 (1418 ± 218)	0.297 (<0.001)	<0.001 (<0.001)	0.894 (<0.001)
CCE (number)	-0.325 ± 0.338 (-0.270 ± 0.393)	-0.309 ± 0.348* (-0.148 ± 0.368)	0.050 ± 0.193* (0.149 ± 0.211)	0.642 (0.001)	<0.001 (<0.001)	<0.001 (<0.001)
CO (L/min)	4.45 ± 0.59 (4.30 ± 0.66)	4.26 ± 0.58 (4.03 ± 0.53)	4.89 ± 0.71* (4.48 ± 0.65)	<0.001 (0.006)	<0.001 (0.197)	<0.001 (0.002)
SV (mL)	67 ± 14.2 (63 ± 18.3)	66 ± 14.9 (63 ± 15.9)	79 ± 17.7* (70 ± 17.3)	0.530 (0.625)	<0.001 (0.031)	<0.001 (0.010)
Ea_p (mmHg/ml)	1.461 ± 0.328 (1.592 ± 0.540)	1.401 ± 0.306* (1.233 ± 0.371)	1.216 ± 0.262 (1.211 ± 0.476)	0.084 (<0.001)	<0.001 (0.001)	<0.001 (0.304)

Values are means ± SD's unless otherwise specified. All comparisons are computed with unpaired Student's t-test: * =*p*-value <0.05, ** =*p*-value <0.01. PR, Pulse rate; DiaP, Diastolic pressure; SysP, Systolic pressure; DicP, Dicrotic pressure; MAP, Mean Arterial Pressure; SVR, Systemic vascular resistance; CCE, Cardiac cycle efficiency; CO, Cardiac Output; SV, Stroke volume; Ea_p, Peripheral Arterial Elastance; MAP-DIC, Mean arterial pressure-dicrotic pressure; dP/dt_{max_rad}, Δ (systolic-diastolic)/Δt peripheral evaluation.

toring protocol. Before anesthesia, the 2 groups did not show any significant difference. After anesthesia we observed the following variations: *Pressure indexes*: the DS induced a more pronounced reduction in SysP, DiaP and DicP than the LA (P<0.01). This difference between the two groups also persisted after the end of the TAVI procedure, with the LA group showing pressure indexes superimposable on the baseline values (**Table 3**). *Flow indexes* the type of anesthesia did not induce any significant differences in CO and SV in comparison with the baseline values in both groups. After the TAVI procedure, CO increased significantly only in the LA group compared to baseline values; on the contrary SV increased significantly in both groups (**Table 3**). *VAC variables*: SVR decreased significantly in all steps in DS group (P<0.001); in the LA group we observed a significant reduction between baseline and the end of the procedure. Ea_p did not decrease significantly from baseline to anesthesia in the LA group, and significantly during the other steps. In the DS group Ea_p did not decrease significantly between anesthesia induction and the end of the procedure but deceased significantly in the other steps (**Table 3**). The $dP/dt_{max.rad}$ decreased after anesthesia in both groups but more deeply after DS than after LA (P<0.05). After the TAVI procedure, the $dP/dt_{max.rad}$ increased in both groups but the increase was statistically significant only in the LA group (**Table 3**). The global cardiovascular performance evaluated by CCE improved significantly (P<0.05) after anesthesia in the DS group but not in the LA group with a significant difference of values between the two groups (P<0.05). After TAVI, the CCE level in LA had significantly improved compared to DS (P<0.05).

Baseline characteristics-weighted comparison of hemodynamic measures

In **Table 4** we reported results obtained by ANOVA analysis for repeated measures weight-

Table 4. Comparing the procedural trends between the 2 groups while controlling for the pre-procedure anthropometric and clinical values

	baseline	treatment	end	Comparisons, *p* and F value	
				Within groups	Between groups§
PR					
Group 1 (n=50)	70.1 ± 10.5	68.8 ± 13.3	66.3 ± 10.6	F=1.861; 0.186	F<0.001; 0.987
Group 2 (n=32)	71.4 ± 13.7	67.9 ± 12.4	66.7 ± 10.7	F=2.254; 0.144	
Pdia					
Group 1 (n=50)	64.0 ± 12.0	61.1 ± 10.9	61.5 ± 10.7	F=0.769; 0.377	**F=16.399; <0.001**
Group 2 (n=32)	61.4 ± 12.4	48.6 ± 7.0	52.6 ± 9.1	**F=15.53; <0.001**	
PSys					
Group 1 (n=50)	148.0 ± 29.0	137.7 ± 25.7	148.1 ± 25.5	F=2.920; 0.087	**F=7.518; 0.008**
Group 2 (n=32)	147.4 ± 27.4	113.9 ± 19.7	131.0 ± 22.2	**F=19.90; <0.001**	
PDic					
Group 1 (n=50)	94.0 ± 16.4	88.6 ± 13.9	90.5 ± 16.5	F=1.600; 0.219	**F=14.643; <0.001**
Group 2 (n=32)	92.1 ± 16.2	70.8 ± 9.7	77.9 ± 13.7	**F=23.98; <0.001**	
MAP					
Group 1 (n=50)	92.1 ± 15.5	86.6 ± 13.8	90.3 ± 13.4	F=2.213; 0.148	**F=16.477; <0.001**
Group 2 (n=32)	90.0 ± 14.5	70.4 ± 8.9	78.8 ± 12.1	**F=22.06; <0.001**	
MAP-Dic					
Group 1 (n=50)	-1.88 ± 6.09	-1.83 ± 5.43	-0.27 ± 7.52	F=0.821; 0.363	F=0.160; 0.690
Group 2 (n=32)	-1.86 ± 5.19	-0.41 ± 4.53	0.81 ± 6.81	**F=3.499; 0.047**	
dp/dt_{max_rad}					
Group 1 (n=50)	0.96 ± 0.36	0.85 ± 0.33	1.14 ± 0.34	**F=26.72; <0.001**	F=1.111; 0.296
Group 2 (n=32)	0.97 ± 0.33	0.68 ± 0.25	1.04 ± 0.28	**F=23.23; <0.001**	
SVR					
Group 1 (n=50)	1660 ± 224	1634 ± 215	1491 ± 212	**F=16.38; <0.001**	**F=4.142; 0.046**
Group 2 (n=32)	1693 ± 266	1412 ± 212	1418 ± 218	**F=27.23; <0.001**	
CCE					
Group 1 (n=50)	-0.33 ±0.34	-0.31 ± 0.35	0.05 ± 0.19	**F=61.85; <0.001**	F=2.893; 0.094
Group 2 (n=32)	-0.27 ± 0.39	-0.15 ± 0.37	0.15 ± 0.21	**F=36.54; <0.001**	
CO					
Group 1 (n=50)	4.45 ± 0.59	4.26 ± 0.58	4.89 ± 0.71	**F=33.09; <0.001**	**F=5.552; 0.021**
Group 2 (n=32)	4.30 ± 0.66	4.03 ± 0.53	4.48 ± 0.65	**F=6.597; 0.002**	
SV					
Group 1 (n=50)	67.0 ± 14.2	66.2 ± 14.9	79.4 ± 17.7	**F=26.88; <0.001**	F=1.501; 0.225
Group 2 (n=32)	63.2 ± 18.3	63.3 ± 15.9	70.3 ± 17.3	F=3.437; 0.051	
Ea					
Group 1 (n=50)	1.46 ± 0.33	1.40 ± 0.31	1.22 ± 0.26	**F=19.75; <0.001**	F=0.596; 0.443
Group 2 (n=32)	1.59 ± 0.54	1.23 ± 0.37	1.21 ± 0.48	**F=19.46; <0.001**	

Values are means ± SD's unless otherwise specified. All comparisons are computed by analysis of covariance: bold =*p*-value <0.05. PR, Pulse rate; DiaP, Diastolic pressure; SysP, Systolic pressure; DicP, Dicrotic pressure; MAP, Mean Arterial Pressure; MAP-DIC, Mean arterial pressure-dicrotic pressure; dp/dt_{max_rad}, Δ (systolic-diastolic)/Δt peripheral evaluation; SVR, Systemic vascular resistance; CCE, Cardiac cycle efficiency; CO, Cardiac Output; SV, Stroke volume; Ea_p, Peripheral Arterial Elastancel; § This analysis was weighted for the baseline characteristics of patients (that is, age, gender, EuroSCORE II, hypertension, diabetes, atrial fibrillation, pulmonary disease, estimated Glomerular Filtration Rate, vasculopathy, ischemic heart disease, NYHA class and ejection fraction).

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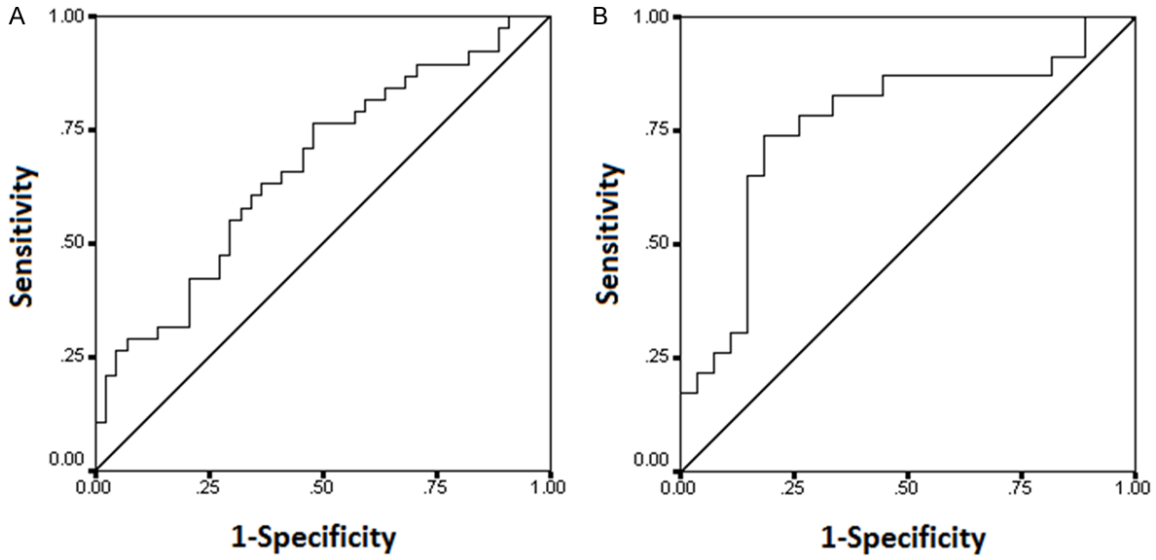

Figure 1. Receiver Operating Characteristic (ROC) curves: (A) For MAP-DicP gradient and its correlation with residual aortic regurgitation after TAVI implantation in the 82 patients group (63% of patients correctly classified; AUC=0.62, P=0.106); (B) For MAP-DicP gradient and diastolic pressure (DiaP) and its correlation with residual aortic regurgitation after TAVI implantation in the 50 patients Local Anethesia group (78% of patients correctly classified; AUC=0.779, P=0.001). Mean Arterial Pressure (MAP); Dicrotic Pressure (DicP); Diatolic Pressure (DiaP).

Residual aortic regurgitation evaluation

In 38 of 82 patients, a residual aortic regurgitation of any grade was identified by echocardiography: 23 patients in the LA group and 15 patients in the DS group.

In the whole cohort, the only hemodynamic parameters found by the logistic regression associated with the post-procedure residual aortic regurgitation, was the MAP-DicP gradient (P=0.033). 63% of patients were correctly classified (31/44=70.5% and 21/38=55.2% correctly classified without and with residual aortic regurgitation respectively) with an area under ROC curve=0.62, P = 0.106 (**Figure 1A**). When the residual aortic regurgitation parameter was tested separately in the 2 groups, the MAP-DicP gradient and DiaP resulted significative (P=0.011 and P=0.048 respectively) for the LA group (n=50), with 78% of patients correctly classified (22/27=81.5% and 17/23= 79.3% correctly classified without and with residual aortic regurgitation respectively) and with an area under ROC curve (**Figure 1B**). In the DS group (n=32), no parameters were statistically associated with residual aortic regurgitation.

Discussion

The main findings of our study are the following: 1) during anesthesia treatment the pressure indexes (SysP, DiaP, DicP) decreased significantly in the DS group but not in the LA group due to the well-known effects of propofol. These differences also persisted at the end of the procedure; 2) after anesthesia treatment, but before the valve implantation, the flow indexes (CO, SV) did not change significantly in comparison with the baseline in both groups. However, the LA group maintained higher pressure values and consequently, a better perfusion of the organs. After valve implantation all pressure and flow indexes increased in both groups; 3) during anesthesia treatment VAC indexes (SVR, Ea_p) decreased significantly in comparison with the baseline in both groups but in the DS group the decrease was more pronounced due to the pressure reduction observed in this group; 4) due to the greater decrease in SVR and Ea observed in the DS group, it was not possible to evaluate the presence of aortic regurgitation after valve implantation by means of MAP-DicP gradient and DiaP.

The reduction in pressure parameters in the DS group with the propofol administration was expected due to the well-known effects of this drug. Propofol induced an average decrease of 22% in blood pressure components, resulting mainly from SVR decrease associated with a reduction in Ea, a major component of arterial load [21]. The reduction of these parameters,

in the DS group, determined a remarkable reduction in arterial load but without any improvement in left ventricle output due to the limitation represented by the aortic stenosis [22]. The absence in both groups of modifications for flow parameters (SV, CO) after anesthesia and before prosthesis implantation, was mainly ascribed to the fixed obstacle to left ventricle output represented by the valve stenosis. However, the LA group maintained higher pressure values and consequently a more pronounced hemodynamic stability and better perfusion of the organs. After valve implantation all pressure and flow indexes increased in both groups. These results were confirmed by ANOVA analysis for repeated measures comparing the trend between the two groups weighted by different confounding factors as part of the patients' baseline characteristics. In the LA group MAP-DicP, DiaP and DicP did not show any significant variations during all steps of the procedure. This observation suggested that the LA group at the end of TAVI was heterogeneous in relation to these parameters. The LA group was composed, in relation to the presence or not of residual aortic regurgitation, by two subgroups of patients: 27 without and 23 with residual aortic regurgitation. During the TAVI procedure the above specified variables (MAP-DicP, DiaP and DicP) changed in opposite directions. For this reason, when the fifty patients treated with LA were considered as a single group, it was impossible to demonstrate any significant variations.

Analyzing the Valve implantation phase, we observed important hemodynamic changes in both groups, obtained however, by different mechanisms. In the DS group the pressure and flow indexes (SV, CO) increased without changing the V-A coupling parameters such as Ea_P and SVR.

In the LA group, the blood pressure values, unchanged by the anesthesia, were superimposable on baseline values and not affected by the valve implantation, despite a large increase in flow parameters (CO and SV) and a reduction in left ventricle arterial load suggested by the decrease in Ea_P.

The changes in SV and CO determined by valve implantation were significantly greater in the LA group than in the DS group for two reasons: a) in the LA group there was a reduction in the left ventricle post-load not observed in the DS group, b) the LA group showed a more pronounced improvement in left ventricle performance because of the absence of the depressing effect of propofol on cardiac systolic performance [23]. The integrative parameter CCE similarly improved in both groups, but in relation to the different mechanisms explained above.

Moreover, the more stable hemodynamic status obtained by LA can facilitate the detection of some complications related to the procedure. The online monitoring of pressure, flow, A-V coupling indexes, integrated by the CCE parameter, may help to rapidly recognize the mechanisms of an acute impairment of cardiac performance.

The incidence of post-TAVI aortic regurgitation in our study population was concordant with previously published reports [24]. After valve implantation, the occurrence of post-procedural aortic regurgitation is usually suspected due to pressure component changes as evaluated with the Aortic Regurgitation Index (ARI) [25].

However, in the DS group of our population, due to the reduction determined by propofol, all pressure indexes seemed less reliable to detect residual aortic regurgitation, as suggested also by the logistic regression model. On the contrary, in the LA group, in the logistic regression model, the MAP-DicP gradient and DiaP were both associated with the presence of aortic regurgitation. The ability of LA to better detect the occurrence of post-TAVI regurgitation than DS is an important advantage in favor of this technique of anesthesia.

Limitation

There are several limitations in our study: first of all, the sample size was small and we need further studies to establish the normal range of the residual aortic regurgitation. Secondly, this is a retrospective single-center study. Finally, the post-TAVI outcome of the two groups of treatment was not investigated.

Conclusions

The predominant hemodynamic benefit of a successful TAVI was an increase in flow index values that could be easily monitored beat-by-

beat with the pulse contour method. The well-known risk of residual aortic regurgitation after valve implantation or other complications that suddenly determine an impairment of cardiovascular performance should be rapidly detected by the interventional cardiologist as well as the anesthesiologist in the catheterization laboratory. The identification of a remarkable residual aortic regurgitation or other major complications may drive the team to modify the standard protocol of the TAVI procedure and this hemodynamic monitoring system is useful for this aim. Although deep sedation limits the stressful conditions around the TAVI procedure, the marked reduction in blood pressure components and the potential negative inotropic effect of propofol jeopardize the cardiovascular reserve to maintain or improve the tissue perfusion. In selected patients the local femoral block may be preferred to deep sedation because it induces pressure stability, allows a more accurate assessment of hemodynamic changes induced by TAVI and seems to facilitate the detection of a residual aortic regurgitation. Further larger studies are necessary to select the most suitable anesthesia for the single patient.

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Disclosure of conflict of interest

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