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par

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TITRE

EVALUATION PRONOSTIQUE DES PATIENTS BENEFICIANTS D'UN TAVI SELON LE TYPE DE RETRECISSEMENT AORTIQUE

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En présence des Maîtres de cette Faculté,

de mes chers condisciples

et selon la tradition d'Hippocrate,

je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent,

et n'exigerai jamais un salaire au-dessus de mon travail.

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RESUME

Introduction *:* Le rétrécissement aortique (RAo) serré est une pathologie fréquente chez les patients âgés de plus de 75 ans. Les dernières recommandations différencient quatre types de RAo selon : le volume d'éjection systolique indexé (VESi), le gradient moyen et la FEVG (fraction d'éjection du ventricule gauche). L'objectif de notre étude est d'évaluer le pronostic des patients ayant eu un remplacement valvulaire aortique percutané (TAVI), en termes de mortalité, selon le type de RAo.

Matériels et méthodes *:* Cette étude compare le pronostic des 620 patients ayant bénéficiés d'un TAVI au CHRU de Tours entre le 1er janvier 2015 et le 31 décembre 2018. Les patients étaient classés en 4 groupes selon le type de Rao : haut gradient ; bas gradient, bas débit, FEVG altérée ; bas gradient, bas débit, FEVG conservée ; bas gradient, débit conservé.

Résultats : *69* patients (11.1%) sont décédés dans les douze mois suivants la procédure : 49 dans le groupe à haut gradient (9.4%) ; 13 dans le groupe bas gradient, bas débit, FEVG altérée (47.1%) ; 1 dans le groupe bas gradient, bas débit, FEVG conservée (5%) ; 6 dans le groupe bas gradient, débit conservé, FEVG conservée (18.2%). La mortalité est plus élevée dans le groupe bas gradient, bas débit, FEVG altérée (p=0.0004) que pour les autres. Les patients de ce groupe étaient significativement plus souvent ré-hospitalisés pour insuffisance cardiaque que les patients du groupe haut gradient (p=0.009).

Conclusion : Une évaluation échographique complète est nécessaire pour évaluer les RAo, leur sévérité et leur type. Les patients du groupe bas gradient, bas débit, FEVG altérée ont un risque indépendant de mortalité à 12 mois plus élevée que les autres groupes et sont plus réhospitalisés que les patients du groupe haut gradient.

ABSTRACT

Introduction: Aortic Stenosis (AS) is a common condition in patients over 75 years. Latest ESC recommendations differentiate 4 types of AS according to: Indexed Stroke Volume (SVi), mean gradient and LVEF (left ventricular ejection fraction). The aim of our study is to evaluate prognosis of patients who have had a transcatheter aortic valve implantation (TAVI), in terms of mortality, according to the 4 types of RAo.

Methods: This study compares prognosis of the 620 patients who had TAVI at CHRU Tours between January 1, 2015 and December 31, 2018. Patients were classified into 4 groups according to AS type: high gradient; low gradient, low flow, low LVEF; low gradient, low flow, normal LVEF; low gradient, normal flow.

Results: 69 patients (11.1%) died within 12 months of the procedure: 49 in the high gradient group (9.4%); 13 in the low gradient, low flow, low LVEF group (47.1%); 1 in the low gradient, low flow, normal LVEF group (5%); 6 in the low gradient, normal flow, normal LVEF group (18.2%). All-cause mortality at one year follow-up is higher in low-gradient, low-flow, altered LVEF group (p=0.0004) than in other groups. Patients in this group were significantly more often admitted for heart failure than patients in high-gradient group (p=0.009).

Conclusion: A complete echocardiography evaluation is needed to evaluate AS, its severity and type. Patients in the low gradient, low flow, low LVEF group have an independent risk of mortality at 12 months higher than other groups and are more hospitalized than patients in the high gradient group.

Mots Clés: Cardiologie interventionnelle- TAVI- Remplacement valvulaire aortique- Rétrécissement Aortique- Volume d'Ejection Systolique- FEVG- Gradient Moyen Trans-valvulaire- Pronostique

Key Words : Interventional cardiology- TAVI- Aortic valve replacement- Aortic Stenosis- Stroke Volume- LVEF- Transvalvular Mean Gradient- Prognosis

ABREVIATIONS :

AR: Aortic Regurgitation

AS: Aortic Stenosis

AVA: Aortic Valve Area

ASA : Aortic Surface Area

EF: Ejection Fraction

ICM : Ischemic Cardiomyopathy

LVED: Left Ventricular End Diastolic

LVEF: Left Ventricular Ejection Fraction

LVOT: left ventricular outflow tract diameter

MG: Mean Transvalvular Gradient

MR: Mitral Regurgitation

MS: Mitral Stenosis

PASP: pulmonary artery systolic pressure

PTV: Peak Transvalvular Velocity

PVD: Peripheral Vascular Disease

SAVR: Surgical Aortic Valve Replacement

SVi: Stroke Volume Index

TAVI: Trans-catheter Aortic Valve Implantation

TVI : Time Velocity Interval

Introduction :

Commenté [b1]: Penser à justifier le texte au final

Severe aortic stenosis (AS) is the most common primary valve disease leading to surgery or catheter intervention in Europe and North America and degenerative calcific valvular aortic stenosis is the most common cause [1]. Due to aging of population, its prevalence is growing reaching more than 3.4% in those aged of 75 years old or more and 75.6% of them are symptomatic [1]. Severe AS carries a poor prognosis if left untreated [2].

Evaluation of a patient suspected of severe aortic stenosis is crucial in order to decide an optimal care because mortality rises very fast as soon as first symptoms appear [3]. Echocardiography is the key diagnosis tool. Doppler echocardiography is the preferred technique for assessing the severity of aortic stenosis with mean gradient measurement and aortic valve area calculation with continuity equation. It's now admitted that AS is not a unique entity but that different AS profiles are observed. According to last European Society of Cardiology guidelines for the management of valvular heart disease [4], 4 categories of AS are defined using 3 echocardiographic parameters (Figure 1): mean transvalvular gradient (MG), left ventricular ejection fraction (LVEF) and stroke volume index (SVi).

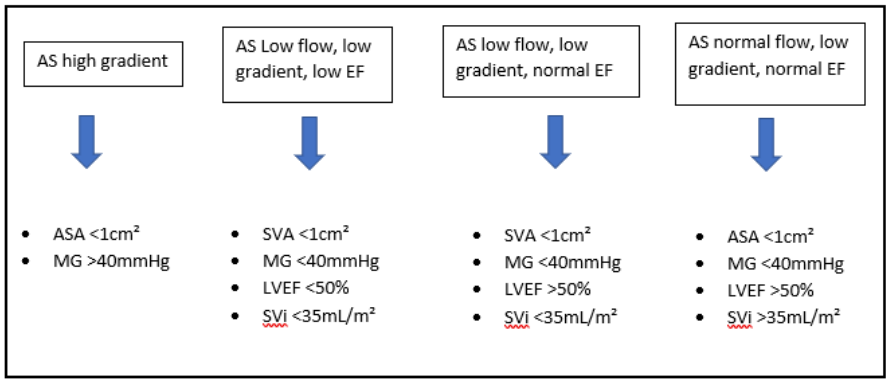

Figure 1 : 4 categories of AS

Patients with depressed LVEF, low flow, low gradient AS represent 5 to 10% of AS population [5]. In case of low gradient AS, other parameters allow to increase probability of severe AS especially increase of gradient with dobutamine [5; 6] , calcic score calculation by multislice computed tomography [7], and SVi calculation by other imaging methods (transoesophagial echocardiography, tomography, MRI).

In case of a severe and symptomatic AS, two interventional strategies are currently recommended [4] : surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI). TAVI is a therapeutic strategy whose use keep increasing, indicated for high and intermediate-surgical risk patients [8], meaning with an Euroscore II >4%. In France, between January 2010 and December 2015, 16 969 patients benefited from this procedure in 48 centers [9].

TAVI benefit in terms of mortality and functional improvement is well established for patients with a severe AS with a high gradient, but it seems that mortality is higher in patients with SVi <35mL/m² according to some recently published studies [10; 11].

The aim of the present study was to analyze population of patients having had a TAVI according to the 4 types of AS and to assess prognosis in terms of mortality, functional improvement and hospitalization for heart failure depending on AS' type.

Methods

Study population

We retrospectively analyzed all patients who have had an aortic valve replacement by TAVI at CHRU Tours between January 1, 2015 and December 31, 2018.

Data were collected thanks to hospitalization's records, echocardiography's reports and loops (stocked on institutional medical imaging server), TAVI's procedure records and medical consultation's records allowing patient's follow up. We excluded patients having had a TAVI on aortic regurgitation without severe aortic stenosis and patients for whom echocardiographic data were incomplete and didn't allow to classify the aortic stenosis in one of the 4 defined categories. Figure 2 shows the flow chart of the study.

Ischemic cardiomyopathy (ICM) background was defined by superior or equal to 50% coronary stenosis, and a history of coronary stenting or coronary artery bypass. History of respiratory pathology is defined by: an obstructive ventilatory disorder reversible or not, a restrictive ventilatory disorder or a respiratory failure whatever the origin defined by home oxygen therapy needing. History of peripheral vascular disease (PVD), stroke, transient ischemic attack, and liver failure were also collected.

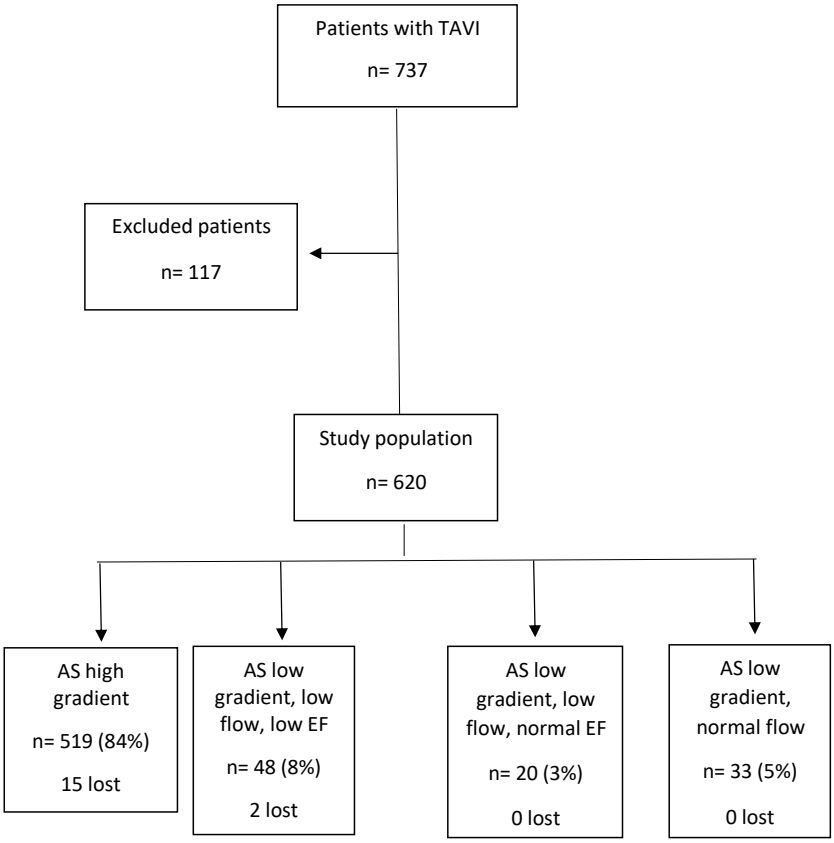

Figure 2: Flowchart of the study

Echocardiographic data

AS evaluation with transthoracic echocardiography was realized following current guidelines[12]. Following general data were collected: left ventricle end-diastolic (LVED) diameter, LVEF , Indexed Stroke Volume (SVi) pulmonary artery systolic pressure (PASP), existence of another concomitant valve disease and its severity.

For AS severity, have been collected: left ventricular outflow tract diameter (LVOT), peak transvalvular velocity (PTV), mean transvalvular pressure gradient, LVOT time-

velocity interval (TVI). Aortic surface area has been calculated according to continuity equation with the following formula:

$$ASA = \frac{\frac{LVOT^2}{4} \times \pi \times lvotTVI}{aorticTVI}$$

SV was calculated with doppler method using the formula:

$$SV = \frac{LVOT^2 \times \pi \times LVOT\ TVI}{4}$$

SV was then indexed to body surface.

Patients were classified into 4 groups according to echographic data[4]: (Figure 1)

- Group 1: AS high gradient: ASA <1cm^2 and mean gradient >40mmHg regardless LVEF;
- Group 2: AS low gradient, low flow with LVEF <50%, ASA <1cm², MG <40mmHg, LVEF <50% and SVi<35mL/m²
- Group 3: AS with low gradient, low flow with LVEF >50%[12]; ASA<1cm², MG<40mmHg, LVEF >50%, SVi<35mL/m²
- Group 4: AS low gradient and normal flow; ASA <1cm², MG <40mmHg, LVEF >50%, SVi >35mL/m².

Interventional procedure

3 types of aortic valve have been implanted during that period: Corevalve EvolutR 3 (Medtronic), Edwards SAPIEN 3 (Edwards lifescience), EnVeo MCR (Medtronic).

Four approaches have been used: transfemoral approach, trans-carotid approach, subclavian approach and trans-aortic approach.

Outcomes and patients follow up

First outcome was all-cause mortality at 1 year. Second outcomes was functional improvement and hospitalization for heart failure. During the month following valve implantation, procedure complications were collected: device implantation and embolic event (peripheric emboly or stroke).

Every patient benefited of a medical consultation at one month with an echocardiography systematically performed. At one month after procedure, consultation allowed the dyspnea quotation on the NYHA scale. It also allowed to quote post TAVI aortic regurgitation with echocardiography defined this way: ¼ : small; 2/4 = moderate; ¾ : middle; 4/4 : severe. At one year after procedure, patients were reviewed in consultation or contacted by phone. If no response, the general practicionner was contacted. All-cause mortality was collected. Cardio-vascular mortality was defined by mortality due to heart failure, endocarditis, acute coronary syndrome, sudden death. Occurrence of hospitalization for heart failure during the first year after procedure was collected.

Statistical analysis

Continuous variables were presented in mean +/- standard deviation, nominal data in numeric values and percentages. Group comparisons were made by ANOVA analysis for quantitative data and by Fischer exact test for qualitative data.

Survival data, namely death occurrence in the first year of follow up and re-hospitalization for heart failure occurrence in the first year, were analyzed using Kaplan-Meier curves. To compare group mortality, a log rank test was realized. Predictive factor of mortality were analyzed according to the Cox proportional hazards of regression model. Statistics were realized thanks to Graph Prism 6

software and statview. Differences were judged significant when $p<0.05$.

Results

Characteristics of patients and echocardiographic parameters

620 patients were included in the study: 519 in group 1 (84%), 48 in group 2 (8%), 20 in group 3 (3%), 33 in group 4 (5%) (Table 1). Significant differences between 4 groups were observed concerning: gender, number of patients with functional class NYHA I or IV, hospitalization during the year before for acute pulmonary edema or heart failure, bypass history, angioplasty history, ischemic cardiomyopathy, atrial fibrillation history, peripheral arterial disease, diabetes history, and previous pacemaker implantation. Groups were significantly different about creatinine and Euroscore, with patients in Group 2 having the highest Euroscore.

There were more women and less ischemic cardiomyopathy in Group 1 and 3 than in Group 2 and 4. There were in Group 2 more patients with angioplasty history, atrial fibrillation history, pacemaker history than in Group 1 and 4, and more hospitalizations for heart failure or acute pulmonary edema and peripheral arterial disease than in Group 1 and more diabetes than in Group 1 and 3. Creatinine was significantly higher and there were more bypass history in Group 2 and 4 than in Group 1. Finally, there were more respiratory diseases in Group 4 than in Group 3.

There were more patients with NYHA IV class of dyspnea in Group 2 than in other groups and asymptomatic patients having a TAVI were patients needing another surgery under general anesthesia.

Table 1: Patients's characteristics

	Group 1 High gradient N= 519	Group 2 Low gradient, low flow, low EF N= 48	Group 3 Low gradient, low flow, normal EF N=20	Group 4 Low gradient, normal flow N=33	*p*
Age (years)	84 +/- 6,1	83 +/- 5,4	85 +/- 5	84+/- 5	0,6
Women (%)	256 (49,3)	15 (31,3)*	12 (60)#	11 (33,3)∞	<0,05
Syncope (%)	46 (8,8)	1 (2,1)	3 (15)	3 (9,1)	0,3
Angor (%)	63 (12,1)	2 (4,2)	2 (10)	5 (15,2)	0,36
Dyspnea NYHA I (%) NYHA II (%) NYHA III (%) NYHA IV (%)	 64 (12,7) 173 (,4,3) 240 (47,6) 27 (5,4)	 0 (0)* 13 (27,1) 26 (54,2) 9 (18,8)*	 4 (21,1)# 3 (15,8) 12 (63,2) 0 (0)#	 2 (6,5) 10 (32,3) 18 (58,1) 1 (3,2)#	 <0,05 0,3 0,38 <0,01
Heart failure/ acute pulmonary edema (%)	94 (18,1)	19 (39,6)*	5 (25)	10 (30,3)	<0,01
Bypass history (%)	19 (3,7)	11 (22,9)*	2 (10)	7 (21,2)*	<0,01
Angioplasty history (%)	174 (33,5)	29 (60,4)*	8 (40)	12 (36,4)#	<0,01
Ischemic cardiomyopathy (%)	233 (44,9)	39 (81,3)*	11 (55)#	21 (63,6)*	<0,01
Surgical aortic valve replacement history (%)	18 (3,5)	0 (0)	1 (5)	1 (3)	0,15
Other valve replacement history (%)	4 (0,8)	1 (2,1)	0 (0)	1 (3)	0,48
Atrial fibrillation (%)	157 (30,3)	25 (52,1)*	8 (40)	9 (27,3)#	<0,05
Respiratory disease (%)	71 (13,7)	6 (12,5)	0 (0)	7 (21,2)∞	0,18
Créatinine (µmol/L)	104 +/- 64,7	141 +/- 74,3*	107 +/- 49	136 +/- 106,4*	<0,01
dialysis history (%)	12 (2,3)	2 (4,2)	1 (5)	3 (9,1)	0,13
Peripheral vascular disease (%)	63 (12,1)	15 (31,3)*	2 (10)	4 (12,1)	<0,01
Stroke history (%)	49 (9,4)	7 (14,6)	2 (10)	4 (12,1)	0,69
Liver failure (%)	15 (2,9	0 (0)	0 (0)	0 (0)	0,39
High blood pressure (%)	382 (73,6)	38 (79,2)	13 (65)	28 (84,8)	0,31
Diabetes (%)	159 (29,7)	22 (45,8)*	1 (5)*#	8 (24,2)	<0,01
Pacemaker (%)	66 (12,7)	16 (33,3)*	3 (15)	3 (9,1)#	<0,01
Euroscore (%)	4,4 +/- 3,7	10,1 +/- 7,1*	5,4 +/- 4,2#	5,6 +/- 4,7#	<0,01

** p <0.05 vs Group 1*

 # p<0.05 vs Group 2

∞p<0.05 vs Group 3

Echocardiographic parameters at inclusion and procedures data are presented in Table 2.

Table 2: Echocardiography and procedures group's characteristics

	Group 1 High gradient N= 519	Group 2 Low gradient, low flow, low EF N= 48	Group 3 Low gradient, low flow, normal EF N=20	Group 4 Low gradient, normal flow N=33	*p*
LVED diameter (mm)	45 +/- 7,8#	52,6 +/- 7	44 +/- 6,2#	46,8 +/- 8,2#	<0,01
LVEF (%)	58 +/- 11	35 +/- 9,7	59 +/- 7,7	54 +/- 12,2	<0,01
Peak velocity (m/sec)	4,5 +/- 0,5	3,3 +/- 0,5	3,5 +/- 0,5	3,6 +/- 0,3	<0,01
Mean Gradient (mmHg)	55 +/- 13	28,4 +/- 8,4	32,2 +/- 6,7	33,4 +/- 4,7	<0,01
SVi (mL/m²)	42 +/- 12,6	26,8 +/- 9,3	31,7 +/- 7,1	45,7 +/- 8,2	<0,01
ASA (cm²)	0,7 +/- 0,2	0,7 +/- 0,2	0,7 +/- 0,2	0,9 +/- 1,7	<0,01
PASP (mmHg)	40 +/- 12,6#	46 +/- 13,6	32,6 +/-16,9	38 +/- 11,7#	0,03
AR middle or severe (%)	20 (3,9)	2 (4,2)	3 (15)*	0 (0)∞	0,054
MR middle or severe (%)	13 (2,5)	8 (16,7)*	4 (20)*	0 (0)#∞	<0,01
MS middle or severe (%)	18 (3,5)	0 (0)	1 (5)	3 (9)	0,18
Approach: femoral (%); transcarotidian (%) transaortic (%) subclavian (%)	 496 (95,6) 6 (1,2) 14 (2,7) 2 (0,39)	 45 (93,8) 1 (2,1) 1(2,1) 1(2,1)	 17 (85) 1 (5) 2 (10) 0 (0)	 30 (91) 1 (3) 2(6) 0(0)	 0,13 0,43 0,2 0,4
Valve: Corevalve (%) Edward Sapiens (%) EVOR (%)	 296 (57,4) 213 (41,3) 2 (0,39)	 20 (41,7)* 28 (58,3)* 0(0)	 14 (70) 6 (30) 0 (0)	 14 (42,4) 19 (57,6) 0(0)	 <0,05 <0,05 0,94
Prothese diameter (mm)	26 +/- 2,5#	27,4 +/- 2,2	26,8 +/- 2,1	26 +/- 2,5#	0,01

** p <0.05 vs Group 1*

 # p<0.05 vs Group 2

∞p<0.05 vs Group 3

Outcomes

All-cause mortality and cardiovascular mortality

83 patients (13.4%) died within 12 months of the procedure: 61 in Group 1 (12.1%); 14 in Group 2 (30.4%); 2 in Group 3 (10%); 6 in Group 4 (18.2%). 22 patients (3.5%) died of cardiac cause within 12 months of the procedure: 16 in group 1 (13.2%); 5 in group 2 (11.1%) ; 1 in Group 3 (5%) and 0 in Group 4.

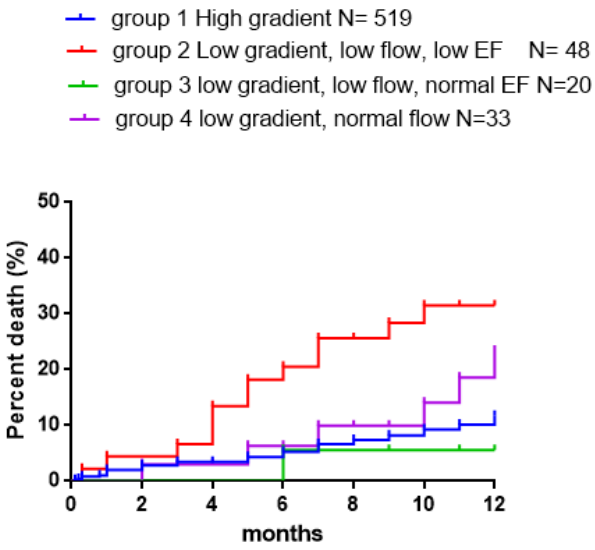

Figure 3: Analyzis of all-causes mortality between the 4 groups

p< 0.0001 between Group 2 and 1

(HR = 7.011; IC 95% 2.718-18.09)

p = 0.0417 between Group 2 and 3

(HR= 3.235; IC 95% 1.045-10.02)

Table 3: Multivariate analysis of mortality predictive factors

	Univariate analysis		
	HR	95% TI	p value
Age, by year	0,989	0.946-1.034	0.63
Male sex	1,632	0.916-2.908	0.10
NYHA class, by class	**1,49**	**1.027-2.162**	**0.04**
Acute pulmonary oedema history/ cardiac decompensation	0,811	0.428-1.539	0.52
High Blood Pressure	0,892	0.497-1.599	0.70
Diabete	0,821	0.449-1.499	0.52
Atrial fibrillation	0,707	0.397-1.258	0.24
Respiratory failure	0,569	0.241-1.343	0.20
Chronic kidney disease	1,136	0.627-2.059	0.68
Creatinine by 10µmol/L	1,003	0.999-1.007	0.11
Peripheral vascular disease	1,779	0.908-3.488	0.09
Ischemic cardiomyopathy	1,291	0.573-2.906	0.54
Angioplasty history	0,995	0.458-2.164	0.99
Bypass history	1,153	0.447-2.969	0.77
Aortic valve replacement history	0,673	0.134-3.387	0.63
Atroke	1,431	0.669-3.062	0.36
Mean gradient >40mmHg	0,672	0.344-1.312	0.24
SVi >35mL/m²	1,099	0.620-1.947	0.75
LVEF >50%	1,27	0.630-2.560	0.51
AR middle or severe	1,088	0.323-3.672	0.89
MR middle or severe	0,736	0.191-2.840	0.66

In multivariate analyses, NYHA class before procedure was the only predictive factor of mortality.

Heart Failure

Within 12 months after the procedure, 36 patients (5.8%) were hospitalized for heart failure: 27 in Group 1 (5.4%); 6 in Group 2 (13%); 1 in Group 3 (5%); 2 in Group 4 (6.1%). There was no significant difference between the four groups (p= 0.08) but only a difference between group 2 and 1 with more rehospitalization in group 2 (p = 0.0094) (Figure 4)

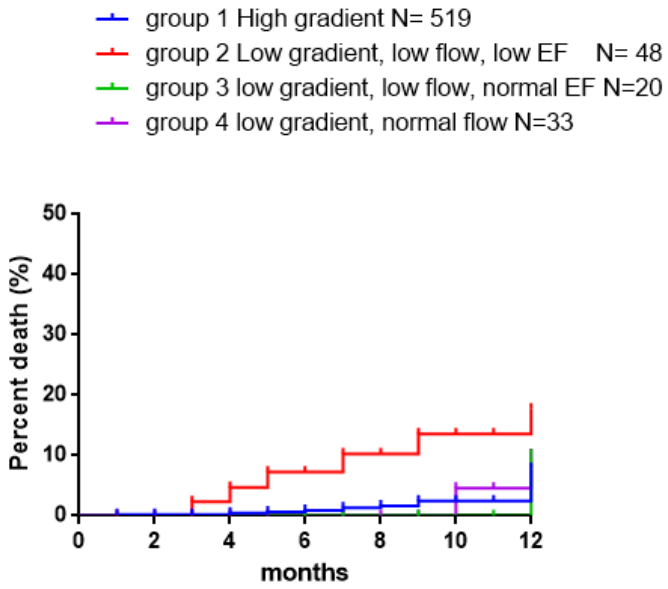

Figure 4: Rehospitalization for heart failure between the 4 groups

p = 0.0094 between Group 2 and 1

(HR = 6.132 ; IC 95% 1.562 – 24.08)

Acute pulmonary oedema history, cardiac decompensation and LVEF <50% were predictive factors of rehospitalization during the year following procedure.

Functional status and procedure's complications

Table 4 presents patient's outcome after procedure. One month after procedure, there were significantly more patients in class I NYHA I in Group 1 and 3 than in Group 4. There were significantly more peripheric emboly complicating procedure in Group 2 than in the other groups.

There was no significant difference between each group for periprosthetic aortic regurgitation degree after procedure. Finally, patients in Group 4 had a longer hospital stay than patients in Group 1.

Table 4: Patient's becoming after procedure

	Group 1 High gradient N= 519	Group 2 Low gradient, low flow, low EF N= 48	Group 3 low gradient, low flow, normal EF N=20	Group 4 low gradient, normal flow N=33	*p*
NYHA Class (%)					
I	274 (59,8)	20 (41,7)	12 (60)	10 (30,3)*∞	<0,05
II	140 (30,6)	14 (29,2)	3 (15)	14 (42,4)	0,15
III	36 (7,9)	3 (6,3)	2(10)	2 (6,1)	0,95
IV	8 (1,7)	3 (6,3)	0 (0)	1 (3)	0,13
Aortic regurgitation at 1 month					
0	194 (40)	23 (47,9)	11 (55)	10 (30,3)	0,15
1	140 (28,9)	8 (16,7)	3 (15)	12 (36,4)	0,14
2	124 (25,6)	11 (22,9)	5 (25)	6 (18,2)	0,9
3	24 (4,9)	2 (4,2)	0 (0)	3 (9,1)	0,48
4	3 (0,6)	0 (0)	0 (0)	1 (3)	0,33
Embolic complications (%)					
Stroke (%)	107 (20,6)	10 (20,8)	4 (20)	5 (15,2)	0,9
Peripheric emboly (%)	15 (2,9)	1 (2,1)	1 (5)	1 (3)	0,93
	6 (1,2)	3 (6,3)*	0 (0)	0 (0)	<0,05
Pacemaker (%)	123 (23,7)	6 (12,5)	5 (25)	12 (36,4)#	0,1
Duration of the hospital stay (days)	6,3 +/- 3,4	6,8 +/- 4	7,6 +/- 4	7,8 +/- 4,7*	<0,05

** p <0.05 vs Group 1*

 # p<0.05 vs Group 2

∞p<0.05 vs Group 3

Discussion

The present study showed that prognosis of patients with low flow, low gradient, low EF AS at one year after TAVI was worse than in other AS groups. Mortality rate was high, and these patients were more often admitted for cardiac decompensation after TAVI than patients with high gradient AS. On the other hand, there was no significant difference in functional improvement a month after TAVI between the four groups. We did not observe any difference in mortality between other groups, particularly prognosis of patients with low flow, low gradient, normal EF did not differ from patients with high gradient AS. High class NYHA of dyspnea before procedure was a predictive factor of mortality. Depressed LVEF, cardiac decompensation and acute pulmonary oedema were predictive factors of rehospitalization during the year following procedure.

TAVI's benefit in terms of survival and quality of life is well established in patient with AS with high gradient. In France TAVI registery[13], 9.6% of population died one year after TAVI compared with 13.4% in our population. Interest of contractile reserve assessment that had been previously demonstrated for surgical aortic valve replacement does not appear to apply to patients receiving percutaneous aortic valve replacement[14].

A Japanese study published in 2018 from Kataoka[15] et al compared prognosis of patients undergoing TAVI regarding the new AS classification[4]. Patients with low gradient, low flow and normal EF represented 13% of patients against 3% in our study. In literature those patients represent 10 to 25% of severe AS[16; 17; 18]. This difference can be explained with the difficulty to evaluate those patients. For example, an underestimation of LVOT can classify them in severe AS whereas they are not. Moreover, stroke volume is sometimes difficult to evaluate, particularly when

there is an obstruction. It's possible then that difference between low gradient, low flow, normal EF group and low gradient, normal flow is not so precise. In that case, combination of those two groups in our study represented 8% of our population.

Low gradient, normal flow AS group was difficult to assess because it is often considered that those patients do not have a severe AS. It's above all important, especially in this group, to make sure that there is no measurement mistake that could lead to the wrong assessment. In Minners's study[19] , on the basis of AVA, a higher proportion of patients was classified as having severe aortic valve stenosis (69%) compared with mean pressure gradient (40%) and peak flow velocity (45%). A mean gradient of 40mmHg corresponds most often to an AVA <0.8cm², which explains why in group 4, the AVA is <1cm² while the gradient is <40mmHg. In this group, aortic valve replacement's benefice in term of survival whether surgical or percutaneous was demonstrated in Zusman's study[20]. They tested observation vs intervention in symptomatic patients with normal flow, low gradient severe aortic stenosis. They showed that TAVI was associated with improved survival versus conservative treatment (hazard ratio [HR]: 0.49; 95% confidence interval [CI]: 0.26 to 0.93; p= 0.03), and lower cardiac mortality (HR: 0.3; 95% CI: 0.10 to 0.74; p= 0.007) with no significant difference for SAVR versus TAVI.

In august 2019, the "US food and drunk administration" approved TAVR for low-risk patients based on PARTNER 3 trial for Sapien 3 valve and on Evolut low risk trial for Corevalve[21] creating a paradigm shift in severe aortic stenosis care and making the correct assessment of the type of AS even more important regarding the prognosis impact.

Low Flow

Stroke volume is a major determinant of the transaortic gradient since the greater the blood flow through the stenotic orifice is (i.e. the SV), the higher the gradient will be[22]. Stroke volume is also a determinant of ASA because aortic surface area depends on it according to the following equation: ASA (cm^2) = SV / aortic VTI. It's nowadays essential to carry out a complete evaluation of aortic stenosis by measuring the following parameters according to current recommendations[16]: LVOT diameter, sub valvular aortic flow and aortic flow. Low flow defined by a SV <35mL/m^2 is associated with a survival decrease in patients with AS. Left ventricular ejection fraction may underestimate the extent of myocardial systolic dysfunction in presence of concentric remodeling such as generally observed in patients with severe AS, whereas SVi is a direct measure of the efficiency of cardiac pump function and its ability to meet tissue perfusion and metabolic demand [10].

Kataoka's study [15] showed that all cause mortality was significantly higher in low gradient, low flow, normal EF AS group compared to the high gradient, normal flow AS group. SVi's calculation then seems essential since beyond AS's type evaluation, it allows a prognosis evaluation

Patients with low flow, low gradient, low EF represented 8% of our patients. It matches with data from the literature which reports 5 to 10% [17; 23] of this group in patients with severe AS. In our study they had a larger LVED diameter than other patients and more significant mitral regurgitation.

Low flow is now also recognized as a poor prognosis factor in patients having a TAVI regardless of LVEF[24; 25; 26]. In Le Ven's study, all-cause mortality during a 12 months follow up was higher in patients with low flow than patients with normal flow. Low flow

but not low LVEF or low gradient was determined to be an independent predictor of early and late mortality following TAVI in high risk patients with severe AS. They conclude that SVi should be integrated in risk stratification process of these patients. Unlike our study, this study didn't show any significant difference between low flow, low gradient, low EF and low flow, low gradient, normal EF's groups. In our study, not all patients with a SVi<35mL/m² had a poor prognosis but those with a low EF associated with the low flow. However, there was only a limited number of patients in the low flow, low gradient, normal EF group. It is therefore hard to draw strong conclusions.

Patients in the low gradient, low flow, LVEF <50% group have, for the most part, another cause of heart disease in addition to their valvular heart disease. There was a significant difference in term of ischemic cardiomyopathy between Group 2 and Group 1 and 3 (39/48 (81.3%) against 233/519 (44.9%) and 11/21 (55%)). In some patients, cardiac amyloidosis can be associated to the low flow, low gradient, low LVEF AS and this associated pathology establish a bad prognosis [27; 28; 29].

Study limitations

First of all, this is a retrospective study. Some patients were excluded because of a lack of echocardiographic datas. Calculations performed in order to classify patients in the 4 groups were done using reporting data. It did not prevent from measurement errors. Finally, the group low flow, low gradient, normal EF only counted 20 patients which doesn't allow to make strong conclusions.

CONCLUSION

Echographic evaluation of aortic stenosis should be complete systematically reporting all parameters. This evaluation following clinical examination is primordial because it allows to assess AS severity and to determine when an aortic valve replacement is necessary. It allows to distinguish the 4 types of aortic stenosis and so the different prognosis especially in term of one-year survival after TAVI. This is all the more important now that the indication of TAVI is to be extended to low and intermediate risks. Patients of low gradient, low flow, low LVEF have a poorest prognosis than other patients with a higher mortality at one year than other groups and more re-hospitalization for heart decompensation than high gradient AS group.

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Vu, le Directeur de Thèse

Vu, le Doyen

De la Faculté de Médecine de Tours

Tours, le

Lacout Marion

39 pages – 4 tableaux – 4 figures

Résumé : Introduction : Le rétrécissement aortique (RAo) serré est une pathologie fréquente chez les patients âgés de plus de 75 ans. Les dernières recommandations différencient quatre types de RAo selon : le volume d'éjection systolique indexé (VESi), le gradient moyen et la FEVG (fraction d'éjection du ventricule gauche). L'objectif de notre étude est d'évaluer le pronostic des patients ayant eu un remplacement valvulaire aortique percutané (TAVI), en termes de mortalité, selon le type de RAo.
Matériels et méthodes : Cette étude compare le pronostic des 620 patients ayant bénéficiés d'un TAVI au CHRU de Tours entre le 1er janvier 2015 et le 31 décembre 2018. Les patients étaient classés en 4 groupes selon le type de Rao : haut gradient ; bas gradient, bas débit, FEVG altérée ; bas gradient, bas débit, FEVG conservée ; bas gradient, débit conservé.
Résultats : 69 patients (11.1%) sont décédés dans les douze mois suivants la procédure : 49 dans le groupe à haut gradient (9.4%) ; 13 dans le groupe bas gradient, bas débit, FEVG altérée (47.1%) ; 1 dans le groupe bas gradient, bas débit, FEVG conservée (5%) ; 6 dans le groupe bas gradient, débit conservé, FEVG conservée (18.2%). La mortalité est plus élevée dans le groupe bas gradient, bas débit, FEVG altérée (p=0.0004) que pour les autres. Les patients de ce groupe étaient significativement plus souvent ré-hospitalisés pour insuffisance cardiaque que les patients du groupe haut gradient (p=0.009).
Conclusion : Une évaluation échographique complète est nécessaire pour évaluer les RAo, leur sévérité et leur type. Les patients du groupe bas gradient, bas débit, FEVG altérée ont un risque indépendant de mortalité à 12 mois plus élevée que les autres groupes et sont plus réhospitalisés que les patients du groupe haut gradient.

Mots clés : Cardiologie interventionnelle- TAVI- Remplacement valvulaire aortique- Rétrécissement Aortique- Volume d'Ejection Systolique- FEVG- Gradient Moyen Trans-valvulaire- Pronostique

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