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ORIGINAL RESEARCH

Epidemiological Features of Aortic Stenosis in a French Nationwide Study: 10-Year Trends and New Challenges

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BACKGROUND: Aortic stenosis (AS) is one of the most common forms of valvular heart disease. Our aim was to estimate the burden of AS in the hospital in France, describe patient characteristics, and evaluate the mortality rate and temporal trends.

METHODS AND RESULTS: All patients hospitalized for AS in France between 2006 and 2016 were identified from the national hospital discharge database. Patients' sociodemographic, medical, and surgical characteristics and temporal trends were described. All AS-related deaths between 2000 and 2014 were identified using death certificates. In 2016, 26 071 patients were hospitalized for AS: 56.5% were men with an average age of 77 years. The all-cause mortality rate at 1 year postindex stay was 11%. The rate of patients hospitalized for AS increased by 59% between 2006 and 2016, reaching 38.7/100 000 person-years in 2016. This increase was most pronounced in patients aged >75 years. The number of transcatheter aortic valve implantations increased following their introduction in 2010. In 2016, 44% of patients were treated with aortic valve surgery during the index hospital stay or following year (mean age, 71.5 years), and 34% were treated with transcatheter aortic valve implantation (mean age, 83.0 years). In 2014, 6186 deaths caused by AS were identified in death certificates: 41.6% were men with an average age of 87 years. The age-standardized mortality rate increased by 5% between 2000 and 2014, reaching 8.5/100 000 person-years in 2014.

CONCLUSIONS: The rate of patients hospitalized for AS increased in recent years in line with the higher life expectancy and introduction of transcatheter aortic valve implantation. Mortality increased more moderately.

Key Words: aortic valve stenosis ■ epidemiology ■ heart valve diseases ■ incidence ■ mortality

Aortic stenosis (AS) is the most common form of valvular heart disease in Europe[1,2] and the second most common in the United States.[3] AS can remain asymptomatic for a long period of time, but its progression is rapid after the onset of symptoms. The natural history of AS is associated with excess mortality and major cardiovascular events, such as sudden death, atrial fibrillation, stroke, or congestive heart failure.[4–6] In Western countries, the main cause of AS is age-related degeneration by calcification of the valve.[1,7] Its prevalence increases exponentially with age and has been estimated at 0.2% of the US population before the age of 65 years and 2.8% after the age of 75 years,[3] and 9.8% after the age of 80 years in a Norwegian population.[8] The burden of AS is expected to increase in the coming years because of population aging.[9]

In Europe, results of epidemiological studies are inconsistent. In 2005, in Scotland, the incidence of patients hospitalized for AS was 36.5 per 100 000 person-years (PY), which has been increasing since 1997.[8,10] By contrast, a Swedish study suggested a decrease in the incidence of diagnosed AS between 1989 and 2009 in line with improved cardiovascular

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CLINICAL PERSPECTIVE

What Is New?

- This cohort study found an increase in the rate of patients hospitalized for aortic stenosis in France, with the latest estimates at 38.7/100 000 person-years.
- The proportion of patients receiving transcatheter aortic valve implantation has increased, and in 2016, one third of patients hospitalized for AS had a valve replacement by transcatheter aortic valve implantation and 44% by surgical aortic valve replacement.

What Are the Clinical Implications?

- The burden of aortic stenosis is increasing, probably related to a change in context, with a reduction in acute rheumatic fever and an aging population, but especially related to changes in the management of cardiovascular risk factors and aortic valve replacement procedures.
- These elements make it necessary to increase awareness about aortic stenosis and monitor trends in the coming years.

Nonstandard Abbreviations and Acronyms

AS	aortic stenosis
PD	principal diagnosis
PY	person-years
RD	related diagnosis
SAVR	surgical aortic valve replacement
TAVI	transcatheter aortic valve implantation

therapies.[11] Clinical risk factors for the development of calcified AS are similar to those for atherosclerosis and other cardiovascular diseases.[4,11,12] In France, limited data are available on epidemiological trends in valvular heart disease and AS.

AS treatment is by surgery or, in recent years, by transcatheter aortic valve implantation (TAVI). This new technique allows the management of a greater number of surgical high-risk patients with contraindications to surgical aortic valve replacement (SAVR), especially very elderly patients.[13] The guidelines in favor of TAVI have gradually broadened.[14,15] In 2017, the guidelines of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery recommended SAVR or TAVI, depending on symptoms, AS severity, comorbidities, and the clinical evaluation of the heart team.[16,17] Moreover, recent studies suggest the benefits of TAVI for intermediate-risk,[18,19] low-risk,[20,21] and asymptomatic patients,[22] despite an increase in some cardiovascular events, such as major vascular complications.[18,23–25] A Canadian study showed that TAVI is cost-effective in patients with severe AS at intermediate and high surgical risk.[26] Thus, these new perspectives increase the number of patients who can be managed with valve replacement, which, in turn, increases the number of patients hospitalized for AS[27] and reduces mortality by providing an alternative to SAVR.[18,23–25]

The aim of this study was to estimate the burden of AS in the hospital and among deaths in France, providing the temporal trends of the rate of patients hospitalized for AS each year, describing their characteristics and care management and estimating the mortality rate.

METHODS

Data Availability Statement

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be submitted to the Institut National des Données de Santé (indsante.fr/).

Data Sources and Populations

Hospitalized Patients

This study was conducted using the French national health data system (Système National des Données de Santé), which provides detailed information on the real-life management of the entire population living in France (≈65 000 000 individuals).[28–30] Système National des Données de Santé includes several databases linked by an anonymous number for each beneficiary identifier. Among these databases, the French health insurance claim database contains demographic data (age, sex, vital status, and place of residence), as well as exhaustive data on all reimbursements for outpatient medical care: treatments, diagnoses, and therapeutic procedures. Système National des Données de Santé also includes the national hospital discharge database (Programme de Médicalisation des Systèmes d'Information) in which all short-stay hospitalizations in both public and private hospitals are recorded.

For each hospital stay, the Programme de Médicalisation des Systèmes d'Information contains the principal diagnosis (PD), possibly related diagnosis (RD), and associated diagnosis, coded according to the *International Classification of Diseases, Tenth Revision* (*ICD-10*). The PD and RD identified the reason for the hospital stay. All patients hospitalized in France between 2006 and 2016 with a PD or RD of AS (*ICD-10* codes

I060, I062, I350, and I352) were selected. For each year of study, the first stay of the year in which the patient was hospitalized for AS (ie, with a PD or RD of AS) was selected and defined as the index stay. This index stay was recorded for the measurement of the annual rate of patients hospitalized for AS. Associated diagnoses were not used to identify patients hospitalized for AS because they reflect to patient comorbidities or complications and not the reason for the hospitalization.

The *ICD-10* classification differentiates AS cause between nonrheumatic AS (I350-I352) and rheumatic AS (I060-I062). Aortic valve procedures (ie, SAVR or TAVI), coded using the French classification of medical procedures (Classification Commune des Actes Médicaux), were searched during the index hospital stay as well as all hospital stays taking place in the following rolling year. The "following rolling year" corresponded to the 365 days following discharge from hospital. A procedure code for TAVIs was introduced into this classification in 2010.

Mortality

Mortality data were extracted from the death certificates of people residing in France (excluding Mayotte) found in the national database of the Epidemiological Center on the Medical Causes of Death (CépiDC-INSERM).[31] From 2000 to 2014, all patients with AS as the initial or associated cause of death (multiple causes of death) identified by *ICD-10* codes I060, I062, I350, and I352 were selected.

Statistical Analysis

Sociodemographic (age, sex, and geographic social deprivation) and medical data (Charlson comorbidity index, hospitalization between 2006 and 2015 for AS, number of hospital stays, length of stay, management of AS, and mortality) of patients hospitalized for AS were described for the more recent available year (2016). The Charlson comorbidity index was calculated using the method of Quan et al.[32] The level of social deprivation was estimated using the French deprivation index developed by Rey et al.[33] This ecological indicator defines population quintiles according to the level of social deprivation in their municipality of residence (smallest administrative unit in France). For our analyses, we used the French deprivation index, dividing the general population into quintiles and calculated over the latest year available (2013). The index uses a scale based on the place of residence according to 4 factors: mean household income, percentage of high school graduates among the inhabitants aged ≥15 years, percentage of manual workers in the working population, and unemployment rate. The first quintile group represents the least disadvantaged group in France.[33]

Crude and age-standardized rates (standardized to 2010 European population data) of patients hospitalized for AS and mortality were computed for the overall population and then by AS cause. The rate of patients hospitalized for AS was defined as the number of patients hospitalized for AS at least once during the year divided by the number of French people during this year. They are expressed per 100 000 PY. National average population data for 2000 to 2016 are taken from the National Institute of Statistics and Economic Studies. Poisson regression was used to analyze the average annual percentage change by age group and sex, with the log of the populations as an offset variable.

Statistical analyses were performed with SAS software (version 7.11; SAS Institute Inc, Cary, NC). The French National Public Health Agency has permanent access to the Système National des Données de Santé database, approved by decree, and the national data protection authority.

Ethics Approval

This study was approved by the French data protection agency (Commission Nationale de l'Informatique et des Libertés) (regulatory decision DE-2011-078).

RESULTS

Hospitalized Patients

In 2016, 26 071 patients were hospitalized with a PD or RD of AS: 1.5% for rheumatic AS and 98.5% for nonrheumatic AS. The average age of the patients hospitalized for AS was 77 years, younger for patients with rheumatic AS (73 years). The proportion of women was 43% among patients with nonrheumatic AS and 56% among patients with rheumatic AS. A socioeconomic gradient was observed in the distribution of patients hospitalized for AS: 23% of patients were in the most socially disadvantaged quintile (quintile 5) compared with 17% in the least disadvantaged quintile (quintile 1) (Table 1). Approximately 12% of patients hospitalized in 2016 for AS had already been hospitalized for this reason between 2006 and 2015. The mean length of index was 7 days regardless of cause. The median number of all-cause hospital stays during the year following the index stay (including the hospital stay) was 2, corresponding to a median of 15 days of annual hospitalization. More than 40% of patients hospitalized for AS were readmitted for AS in the year following the index hospital stay. The all-cause mortality rate at 1 year postindex stay was 11% (Table 1). The description limited to patients who had never been hospitalized for AS before 2016 did not show a difference in population distribution (Table S1).

Table 1. Characteristics of Patients Hospitalized for AS, According to Cause (2016, France)

Characteristic	AS		
	Total (n=26 071)	Rheumatic (n=395)	Nonrheumatic (n=25 676)
Age, y			
Mean (SD)	769 (10.7)	727 (13.7)	769 (10.6)
Sex, n (%)			
Men	14 733 (56.5)	175 (44.3)	14 558 (56.7)
Women	11 338 (43.5)	220 (55.7)	11 118 (43.3)
FDep, n (%)*			
Quintile 1 (least disadvantaged)	4233 (16.6)	61 (16.4)	4172 (16.6)
Quintile 2	4505 (17.7)	79 (21.2)	4426 (17.7)
Quintile 3	5246 (20.6)	63 (16.9)	5183 (20.7)
Quintile 4	5714 (22.5)	90 (24.2)	5624 (22.4)
Quintile 5 (most disadvantaged)	5746 (22.6)	79 (21.2)	5667 (22.6)
Rate of patients hospitalized for AS (/100 000 PY)			
Crude rates	39.2	0.59	38.6
Standardized rates	38.7	0.60	38.2
History of hospitalization for AS (2006–2015), n (%)			
Hospitalization for AS between 2006 and 2015	3295 (12.6)	49 (12.4)	3246 (12.6)
Charlson comorbidity index			
Mean (SD)	0.89 (1.29)	0.94 (1.32)	0.89 (1.29)
Hospitalizations in the year following the index hospital stay (including the index hospital stay), median (quintile 1–quintile 3)			
No. of hospital stays	2 (1–3)	2 (1–3)	2 (1–3)
No. of hospitalization days	15 (10–25)	15 (10–25)	15 (10–25)
No. of hospital stays for AS	1 (1–2)	1 (1–2)	1 (1–2)
No. of hospitalization days for AS	10 (7–15)	11 (7–15)	10 (7–15)
Hospital readmission in the year following the index hospital stay			
Proportion of patients readmitted for AS, n (%)	11 206 (43.0)	162 (41.0)	11 044 (43.0)
Length of index stay (d)			
Median (quintile1–quintile 3)	5 (2–10)	5 (2–11)	5 (2–10)
Mean (SD)	7.3 (7.8)	7.5 (7.5)	7.3 (7.8)
Aortic valve management during the index hospital stay or the following year, n (%)			
Surgical aortic valve replacement	11 523 (44.2)	188 (47.6)	11 335 (44.1)
During index stay	5860 (22.5)	93 (23.5)	5767 (22.5)
During the following year	5663 (21.7)	95 (24.1)	*5568 (21.7)*
Transcatheter aortic valve implantation	8944 (34.3)	94 (23.8)	8850 (34.5)
During index stay	3876 (14.9)	30 (7.6)	3846 (15.0)
During the following year	5068 (19.4)	64 (16.2)	5004 (19.5)
No aortic procedure	5604 (21.5)	113 (28.6)	5491 (21.4)
All-cause mortality, n (%)			
At 30 d	820 (3.1)	19 (4.8)	801 (3.1)
At 1 y	2935 (11.3)	52 (13.2)	2883 (11.2)

AS indicates aortic stenosis; FDep, French deprivation index; and PY, person-years.
*FDep, only available for metropolitan France (missing data=627).

Temporal Trends

In 2016, the age-standardized rates for patients hospitalized for AS reached 38.7 per 100 000 PY for all AS, 38.2 for nonrheumatic AS, and 0.6 for rheumatic AS (Table 1). The age-standardized rate for patients hospitalized for AS (all causes) was higher among men than women, reaching 53.4 for men and 27.9 for women in 2016 (per 100 000 PY). Between 2006 and 2016, these rates increased by 59.0% (men, 56%; women,

66%) (Figure 1). The average annual percentage change in rates of patients hospitalized for AS was the most significant among older age groups and women. Among those aged >85 years, the average annual of rate increased by 12.4% for men and 11.2% for women (Figure 2). Temporal trends limited to patients who had not been hospitalized for AS in the previous 2 years showed increases but smaller increases (Figure S1). Between 2006 and 2016, the age-standardized rate of patients hospitalized for rheumatic AS decreased by 54.9%, whereas the rate of nonrheumatic AS increased by 65.5% (Figure S2).

Aortic Valve Procedures

In 2016, 44% of patients had SAVR during the index hospital stay or in the following year, 34% had a TAVI, and 21.5% had no aortic procedure. Among patients hospitalized for AS, the proportion treated by TAVI increased by 27.0%, whereas the rates of patients treated by SAVR or without any aortic procedure decreased by 20.2% (Figure 3). These trends were particularly important in older patients: in 2016, 47.6% of patients hospitalized for AS aged ≥75 years were receiving TAVI surgery (data not shown). Patients receiving TAVI were older, were more often women, and had more comorbidities than those receiving SAVR or without any aortic procedure. The mean length of hospital stay was longer for SAVR (13.1 days) than for TAVI (8.7 days) and longer than for the index stay (7.3 days).

More than half of the patients who had surgery (51%) and 43% of those who had TAVI received it during the index stay. For 40% of the patients hospitalized for AS and not having a procedure during the index stay but having one within the following year, we found that the main reason for hospitalization was a preoperative check-up (43% for the SAVR group and 35% for the TAVI group). Moreover, 20% of patients who did not have any aortic procedure within the following year had been hospitalized for a preoperative check-up.

The all-cause mortality rate at 1 year postindex stay was 4.8% for patients undergoing SAVR, 10.4% for patients undergoing TAVI, and 25.8% for patients without any aortic procedure (Table 2 and Figure S3). The crude all-cause mortality rate at 1 year after aortic valve replacement was 5.2% and 11.3% for patients undergoing SAVR and TAVI, respectively, decreasing since 2010 (6.4% and 18.6%, respectively) (Figure S4).

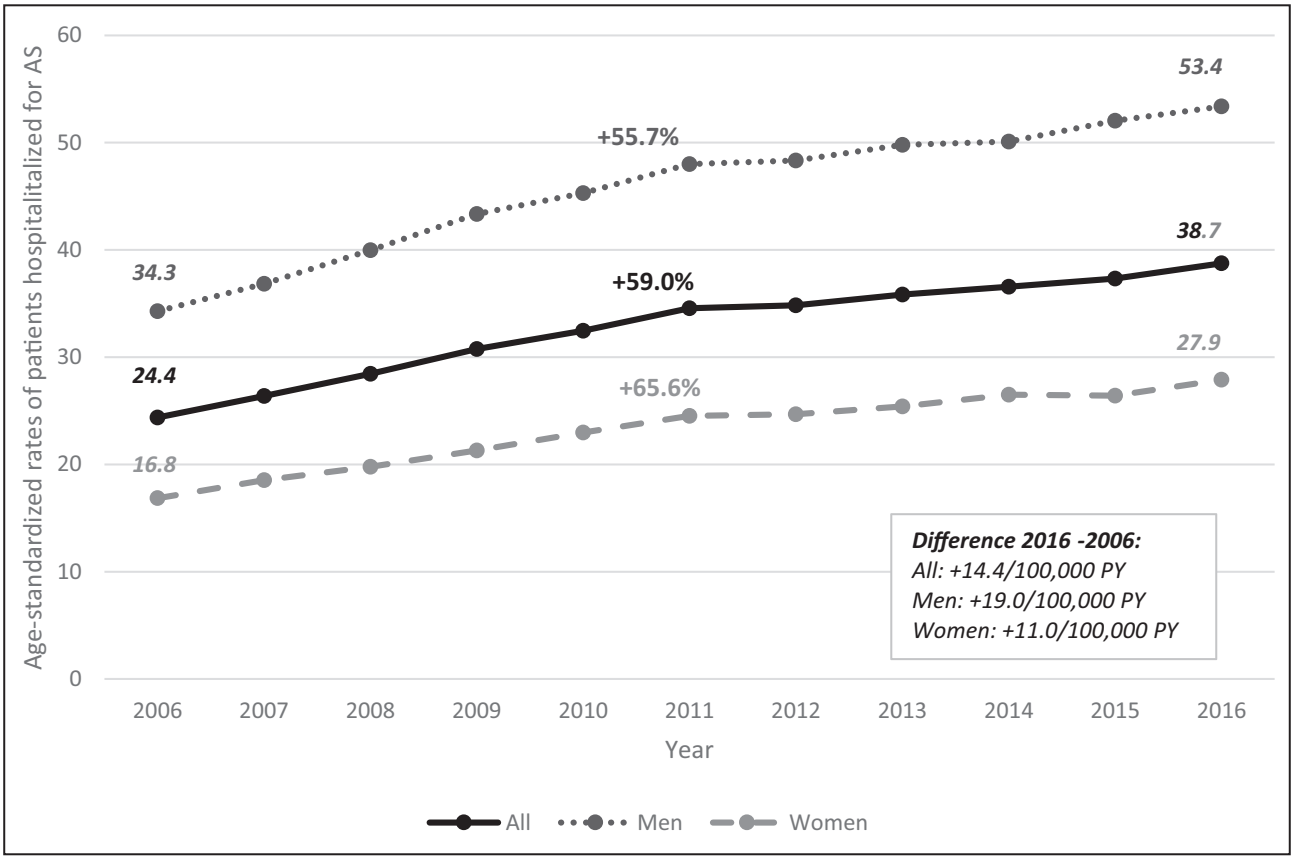

Figure 1. Trends in age-standardized rates of patients hospitalized for aortic stenosis (AS) in person-years (PY), according to sex (2006–2016, France).

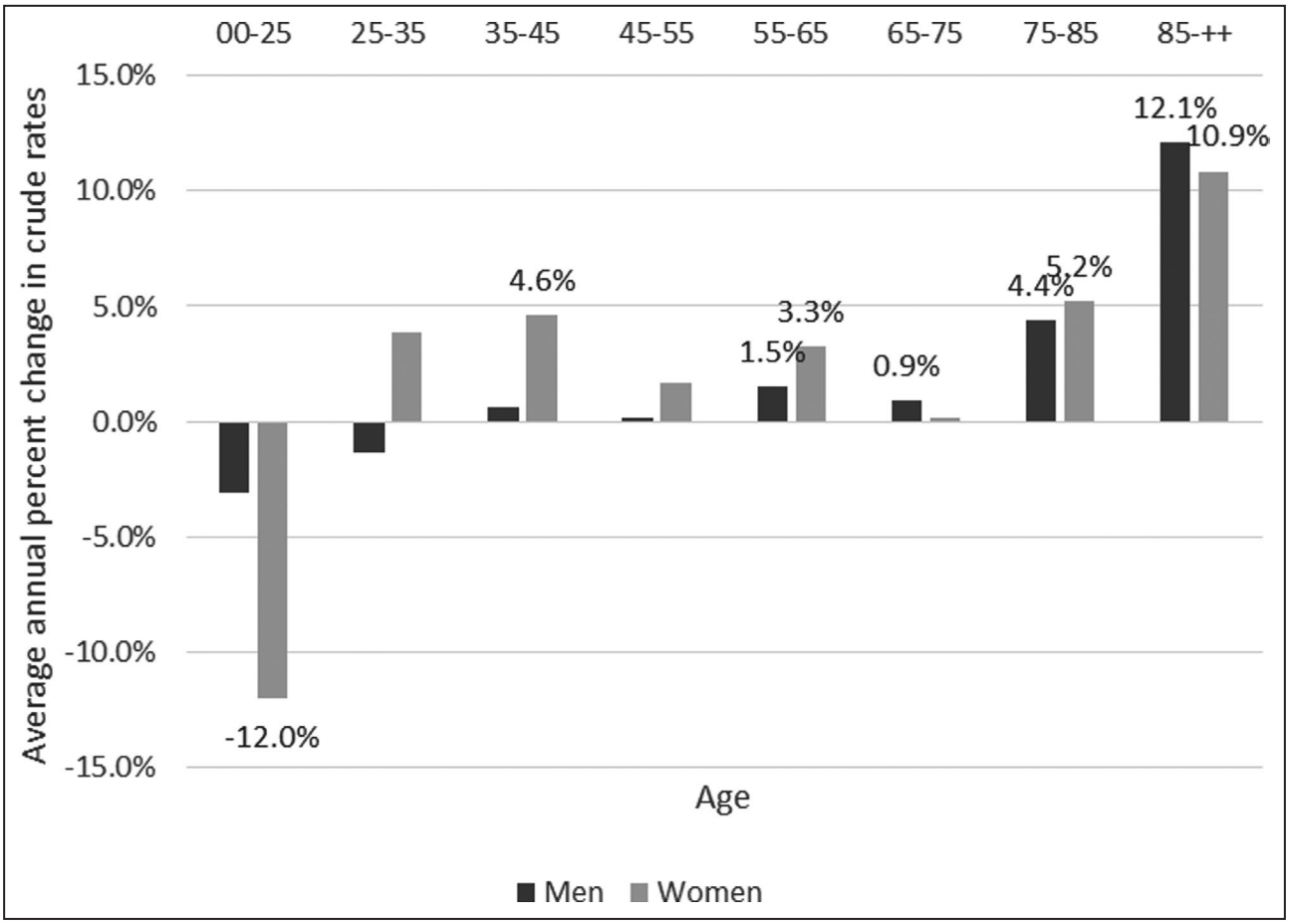

Figure 2. Average annual percentage change in crude rates of patients hospitalized for aortic stenosis, according to sex (2006–2016, France).
Only values significantly different from 0% are presented (α risk = 5%).

Mortality

In 2014, 6186 deaths caused by AS were identified in death certificates (CépiDC-INSERM). The mean age at death was 86.7 years (SD, 7.5 years), and the proportion of women was 58%. In 2014, the age-standardized mortality rate caused by AS was 8.5/100 000 PY. This rate increased by 5% between 2000 and 2014 and was higher for men (10.3) than for women (7.4). More precisely, the age-standardized mortality rate increased to a maximum of 8.98/100 000 PY before decreasing between 2012 and 2014 (Figure 4). The average annual percentage change in mortality rates decreased among patients aged <75 years and increased among those aged >85 years (men, 3.1% per year; women, 1.6% per year) (Figure 5).

DISCUSSION

In France, AS caused the hospitalization of 26 071 patients in 2016 and 6186 deaths in 2014. The standardized rate for hospitalized patients was 38.7/100 000 PY, and the standardized mortality rate was 8.5/100 000 PY. These rates have increased since 2006 and 2000, respectively, but a decrease in AS mortality began in 2012. Since the introduction of TAVI in 2010, the proportion of patients receiving TAVI has increased. In 2016, one third of patients hospitalized for AS had a valve replacement by TAVI and 44% by SAVR, whereas 21% had no aortic procedure. This study highlights that AS remains a pathological condition with a significant weight in France as in developed countries and that the increase in the prevalence of its risk factors and the development of management procedures (TAVI) has an effect on the number of patients hospitalized for the management of this pathological condition but also on the mortality caused by this valvular heart disease.

For patients hospitalized for AS, our data were in line to those found in European studies. A Swedish study found incidence rates for hospitalized patients of 37.8 for men and 24.2 for women over the period 2003 to 2010.[34] Our data complete these estimates in European countries after 2010.

In 2005, a Scottish study[10] on the incidence of patients with a first hospital admission for aortic valve disease found an incidence of 36.5/100 000 PY for isolated AS and 2.4/100 000 PY for AS with insufficiency.

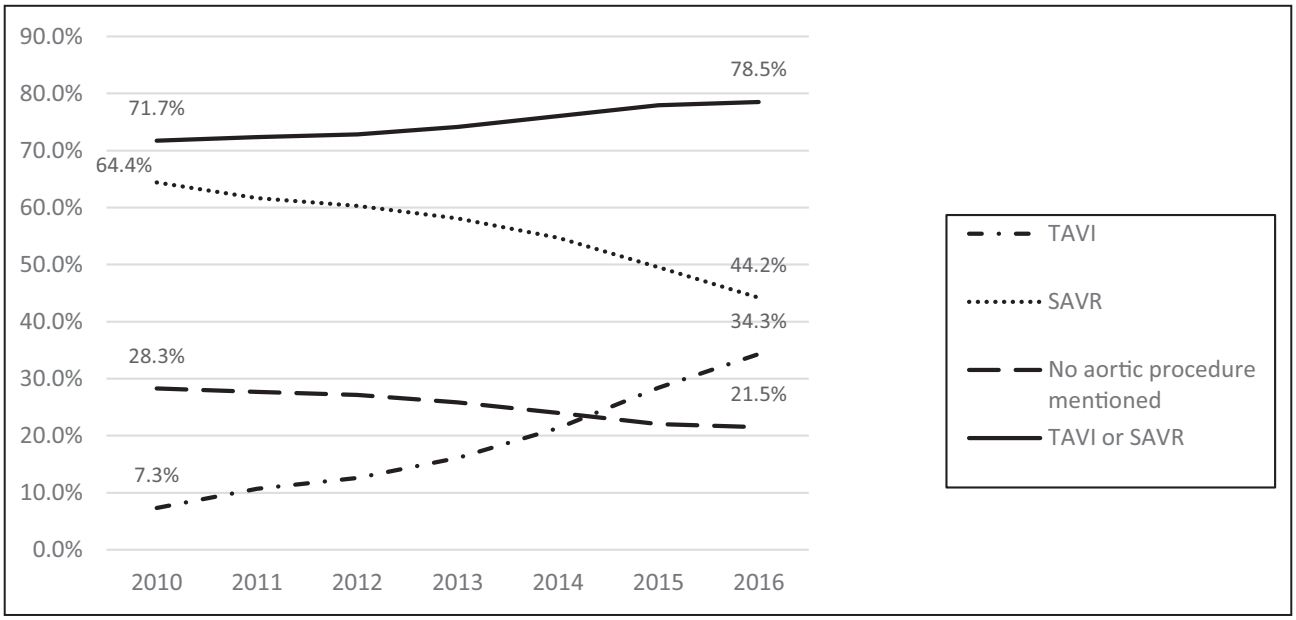

Figure 3. Trends in the proportion of patients undergoing surgical aortic valve replacement (SAVR), transcatheter aortic valve implantation (TAVI), or no aortic procedure during the index stay or the following year (2010–2016, France).

This study showed that the incidence of patients with a first hospital admission for AS nearly doubled from 1997 to 2005. Similarly, US data showed an increase in the in-hospital prevalence of AS between 2002 and 2012.[35]

Our 2016 results on sociodemographic characteristics were in accordance with previous studies.[3,5,11,13,34,35] The higher incidence of AS in men was likewise observed in other studies. Hypotheses about more fibrotic remodeling in women have been put forward,[36] but the pathophysiological features of AS remain unexplained and are the subject of research.

We found a small number of rheumatic AS, which is consistent with the epidemiological features of acute rheumatic fever,[10,37] which is decreasing in industrialized countries following improvements in the management of streptococcal A angina, which more commonly has mitral valve lesions.[38,39]

The British OxVALVE Population Cohort Study demonstrated an association between socioeconomic status and valvular heart disease, with a higher prevalence of valvular heart disease in the most disadvantaged groups.[9] These results and our own are consistent with the pathophysiological hypotheses. Indeed, after age adjustment, a higher prevalence and incidence can be expected among the most disadvantaged patients, because they are more exposed to certain cardiovascular risk factors typically associated with AS (tobacco, dyslipidemia, and hypertension). We can also highlight the poorer screening and delayed management of the most disadvantaged patients, which would lead to more severe cases of AS requiring hospitalization. These inequalities in the rates of AS hospitalization may reflect disparities in access to care, which could lead to delays in diagnosis. This should be further explored, especially because it is well attested that mortality and hospitalization relating to certain cardiovascular diseases increase with social deprivation.[33,40–43]

Part of the increase in the rate of patients hospitalized for AS between 2006 and 2016 probably related to the increase in the number of patients managed for aortic valve replacement attributable to the development of TAVI. As we have observed, the proportion of patients receiving TAVI has increased sharply from the introduction of the TAVI code in 2010 (7% of patients) to 2016 (34%). In contrast, the proportion of patients receiving SAVR has decreased, but to a lesser extent than TAVI, and thus the overall proportion of nonoperated (neither TAVI nor SAVR) patients has decreased. In accordance with recent guidelines,[14,15,44] we can clearly assume that some inoperable patients with comorbidities were only treated medically (out of hospital) before the introduction of TAVI, whereas now they are hospitalized. This can partly explain the increase in hospitalized patients in our study. The development of TAVI means that a wider range of patients can benefit from interventions, and that a greater number of professionals and healthcare structures are able to perform the procedure. In the EURObservational Research Programme Valvular Heart Disease II Survey,[1] 80% of patients with class I indications for an intervention, as recommended by the 2012 European Society of Cardiology/European Association of Cardio-Thoracic Surgery and 2014 American Heart Association/American College of Cardiology guidelines,[14,44] were considered for or underwent a planned intervention.

Table 2. Characteristics of Patients Hospitalized for AS, According to Management, France, 2016

Characteristics	AS			
	Total (n=26 071)	SAVR (n=11 523)	TAVI (n=8944)	No Aortic Procedure (n=5604)
Age, y				
Mean (SD)	76.9 (10.7)	71.5 (9.7)	83.0 (6.6)	78.3 (12.2)
Sex, n (%)				
Men	14 733 (56.5)	7327 (63.6)	4378 (48.9)	3028 (54)
Women	11 338 (43.5)	4196 (36.4)	4566 (51.1)	2576 (46)
FDep, n (%)*				
Quintile 1 (the least disadvantaged)	4233 (16.6)	1706 (14.8)	1624 (18.2)	903 (16.1)
Quintile 2	4505 (17.7)	2054 (17.8)	1543 (17.3)	908 (16.2)
Quintile 3	5246 (20.6)	2363 (20.5)	1787 (20.0)	1096 (19.6)
Quintile 4	5714 (22.5)	2545 (22.1)	1938 (21.7)	1231 (22.0)
Quintile 5 (the most disadvantaged)	5746 (22.6)	2570 (22.3)	1897 (21.2)	1279 (22.8)
History of hospitalization for AS (2006–2015), n (%)				
Between 2006 and 2015	3295 (12.6)	1378 (12.0)	1431 (16.0)	486 (8.7)
Charlson comorbidity index				
Mean (SD)	0.89 (1.29)	0.71 (1.14)	1.01 (1.34)	1.08 (1.45)
Length of index stay (d)				
Median (quintile 1–quintile 3)	5 (2–10)	8 (2–11)	5 (2–8)	4 (2–9)
Mean (SD)	7.3 (7.8)	8.3 (8.8)	6.6 (6.6)	6.3 (7.0)
Mortality, all causes (index stay), n (%)				
During the index hospital stay	438 (1.7)	144 (1.2)	92 (1)	202 (3.6)
At 30 d	820 (3.1)	198 (1.7)	178 (2)	444 (7.9)
At 1 y	2935 (11.3)	558 (4.8)	933 (10.4)	1444 (25.8)
After TAVI or SAVR				
Stay with SAVR or TAVI				
Length of stay, d				
Median (quintile–quintile 3)		11 (9–14)	7 (5–10)	…
Mean (SD)		13.1 (8.5)	8.7 (6.7)	…
Minimum-maximum		1–197	0–149	…
Time interval between index stay and aortic act (among individuals not operated on in the index stay) (d)				
Median (quintile 1–quintile 3)		43 (20–75)	49 (24–91)	
Mean (SD)		55.9 (52.0)	68.2 (65.1)	
Mortality after SAVR or TAVI, n (%)				
At 30 d		315 (2.7)	304 (3.4)	…
At 1 y		594 (5.2)	1009 (11.3)	…

AS indicates aortic stenosis; FDep, French deprivation index; SAVR, surgical aortic valve replacement; and TAVR, transcatheter aortic valve implantation.
*FDep, only available for metropolitan France.

This rate has increased since 2001 and reflects the increase in the number of patients undergoing surgery. Moreover, the demographic and medical characteristics of patients receiving TAVI (older and higher comorbidities), as observed in our study and the literature, were consistent with this hypothesis.[13,45–47] In addition, patients' medical characteristics partly explained the higher crude all-cause mortality rate for patients with TAVI or without aortic procedures compared with patients with SAVR, although this was not found in randomized trials.[18]

Only 51% of patients of the SAVR group and 43% of the TAVI group had their aortic valve procedure during the index stay. For 40% of the patients hospitalized for AS who did not have a procedure in index stay but who had one within the year following discharge, we found the accuracy of a hospitalization for preoperative assessment (43% for the SAVR group and 35% for the

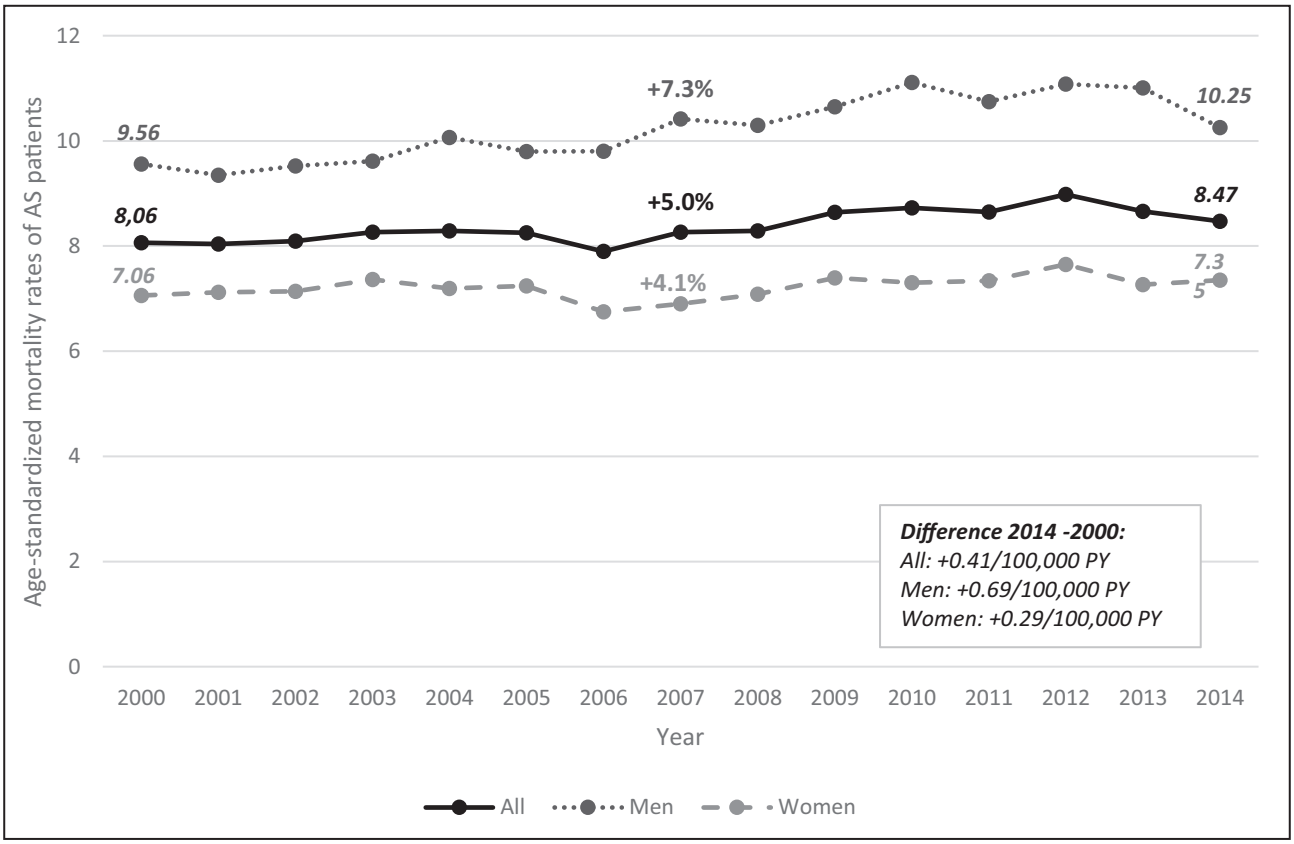

Figure 4. Trends in age-standardized mortality rates of patients with aortic stenosis (AS) in person-years (PY), according to sex (2000–2014, France).

TAVI group). For the remaining 60%, this may not be coded and can be assumed that this index stay, without an aortic valve act, was intended to pose the indication for aortic valve replacement and/or to perform the preoperative assessment.

For patients without any aortic valve procedure (neither during index stay nor the year following), the all-cause mortality at 30 days, after index stay, was ≈8%. However, the mean time interval between index stay and aortic act of patients operated in the following year was 56 days (SAVR) to 68 days (TAVI). Thus, we can assume that a proportion of these patients did not have aortic procedures because they had died before their management or because they had too severe AS. Indeed, among these no-aortic valve procedures patients, at least 20% were nevertheless hospitalized for preoperative assessment. This group is therefore probably made up of patients with many comorbidities that make them inoperable or who die before their aortic valve procedures. We can also assume that another part of this group had mild AS.

Nearly half of patients hospitalized for AS were readmitted for AS in the year following the index hospital stay. This rate may seem high, but it could correspond to patients hospitalized for the preoperative check-up during the index stay and then readmitted for the procedure. However, more and more preoperative check-ups are done on an outpatient basis. It could also correspond to patients managed during the index stay but who have a complication/relapse in the year, needing to be readmitted to hospital.

In accordance with Bevan et al,[48] deaths caused by AS were selected on the basis of the initial or associated cause of death. We could not claim a direct causal link between death and AS with this method of selection. However, the coding of this AS as the initial or associated cause of death showed that AS directly or indirectly, through the patient's frailty, contributed to the disease process. Our results agree with the US data reported by Bevan et al.[48] The age-adjusted mortality rate in the United States was slightly higher than ours in 2016 (10.9/100 000 PY), although the temporal trends were similar, with a trend toward higher mortality rates until 2013 and a decrease in recent years. The increased mortality rate could be explained by an increase in diagnoses and coding on death certificates. The decrease in mortality was concomitant with the management shift for patients with AS. Our data showed that mortality decreased in the youngest patients and increased in the oldest, which may reflect a better survival of patients with AS.

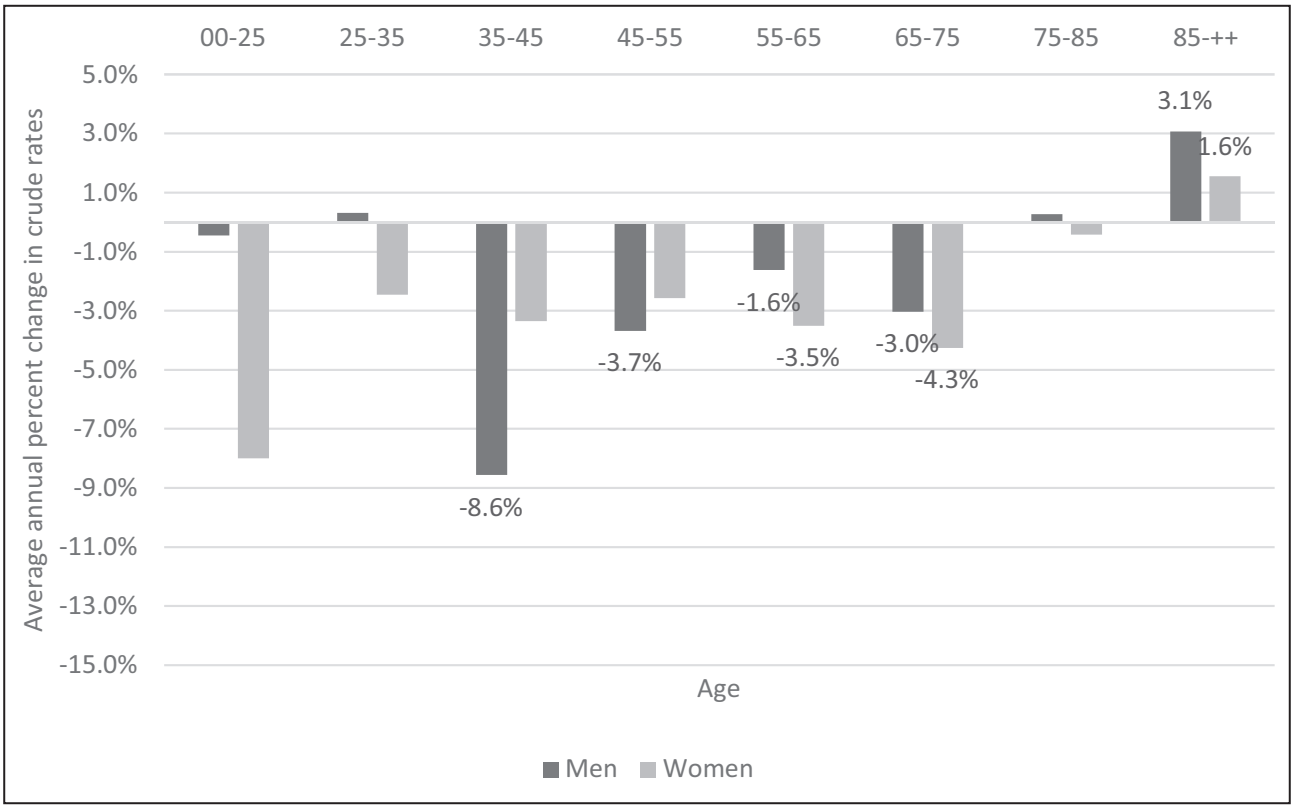

Figure 5. Average annual percentage change in crude mortality rates of patients with aortic stenosis, according to sex (2000–2014, France).
Only values significantly different from 0% are presented (α risk = 5%).

For mortality by management, these descriptive data should be interpreted with caution. Indeed, the all-cause mortality rate is higher in patients receiving TAVI than in those receiving surgery, but patients receiving TAVI are older (difference of 11.5 years for mean age) and have more comorbidities (difference of 0.3 Charlson comorbidity index points).

Strength and Limitations

The main strength of this study is its inclusion of the entire French population, because it was conducted using the national health data system and the national death certificate database, which are exhaustive databases. In the national hospital discharge database, all patients hospitalized for AS (cases diagnosed and managed in hospital) can be selected to describe managed patients, estimate rates of patients hospitalized for AS, and monitor temporal trends using the same method over several years. These estimates, based on exhaustive data, confirmed and updated the trends observed in Europe and Western countries. Moreover, to our knowledge, this is the first study based on exhaustive and real-life data to describe patients hospitalized for AS and those undergoing TAVI or SAVR, in real clinical practice.

These indicators should be extrapolated with caution because the rate of patients hospitalized for AS depends on the incidence of AS, their diagnosis, their severity, and their hospital management. The AS managed at the hospital was probably the most symptomatic and severe AS. Nevertheless, these indicators are useful for monitoring the burden of AS and to anticipate hospital healthcare needs.

In our database, we do not have comprehensive information on patient history, because information on hospitalizations is only available from 2006 onward and diagnoses made outside the hospital are not available. Also, we could not accurately date the diagnosis of AS. In fact, this diagnosis is most often made outside the hospital and hospitalization occurs only late, when AS is severe or when the aortic valve needs to be replaced. Of the 2016 study population, 12% of patients had been hospitalized for AS between 2006 and 2015. Furthermore, a large proportion of the patients not hospitalized between 2006 and 2015 were likely to have had their AS for several years. Despite this limitation, which prevents us from accurately estimating the incidence of pathological features, we observe that the burden of AS in the hospital is increasing. We can reasonably assume that this is the case regardless of the history of AS because the study of the subpopulation of patients with no AS hospitalization in the previous 2 years also

shows an increase in the rate of patients hospitalized for AS and the patients hospitalized in 2016 had similar sociodemographic and medical characteristics. The higher increase in the overall rate of patients compared with those without a history of hospitalization for AS may be caused by more frequent valve replacement for patients with severe AS (with a history of hospitalization) since the development of surgical techniques and TAVI.

A misclassification bias related to the coding of AS diagnoses in hospital cannot be excluded. The quality of the coding was not evaluated, but the observed rates are in line with the scientific literature.[10,34] In addition, d'Arcy et al showed that undiagnosed AS is mainly of mild severity and not clinically significant.[9]

Second, certain information not included in the national hospital discharge database, such as AS severity, echocardiographic elements, or quality of life, was not available in this study. Moreover, information on hospitalizations was not available before 2006.

These data have updated the scientific literature on the epidemiological features of AS in a European country from exhaustive data. The study of causes showed 2 groups of patients and the benefit effect of the improvement in the management of streptococcal A angina. The study of management by TAVI or surgery has made it possible to estimate the current place of TAVI in real life. These epidemiological trends can be monitored over time.

CONCLUSIONS

This study presented the first French estimations on the rates of patients hospitalized for AS and AS-related mortality rates. The higher rates observed over the past 10 years are probably related to a change in context, with a reduction in acute rheumatic fever and an aging population, but especially to changes in the management of cardiovascular risk factors and new aortic valve replacement procedures. These elements are only now starting to translate into a decrease in AS mortality, thus making it necessary to increase awareness about AS and monitor trends in the coming years.

ARTICLE INFORMATION

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Disclosures

Y. Juillière has participated on the boards of the following companies: Abbott Vascular, Air Liquide Sante International, Bayer, Boston Scientific, St. Jude Medical, and Novartis. He has participated in sponsored investigational trials and/or meetings as speaker or chairperson for Abbott Vascular, Amgen, Bayer, Bristol-Myers Squibb, Boston Scientific, GSK, The Medicines Company, MSD/Schering-Plough, Novartis, Roche Diagnostics, Sanofi-Aventis, Servier, and St. Jude Medical. These are without any link to the present research. C. Tribouilloy has participated in meetings as speaker or chairperson for Bristol-Myers Squibb, Novartis, MSD, Actelion, and Astra Zenaca, and he was invited to a congress organized by Edwards, Bayer, and LIVA NOVA. These are without any link to the present research. The remaining authors have no disclosures to report.

Supplementary Material

Table S1
Figures S1-S4

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SUPPLEMENTAL MATERIAL

Table S1. Characteristics of patients hospitalized for aortic stenosis, who had no prior history of hospitalisation for AS (2016, France).

	No previous hospitalization history for AS (2006-2015) (n=22,776)	
Age, mean (SD)	76.7	(10.8)
Women, n (%)	9,872	43.3%
Fdep		
Quintile 1	3,753	16.9%
Quintile 2	3,961	17.8%
Quintile 3	4,562	20.5%
Quintile 4	4,964	22.3%
Quintile 5	4,987	22.4%
Aetiology		
Rhumatic	346	1.5%
No rhumatic	22,43	98.5%
Charlson comorbidity index, mean (SD)	0,88	(1.3)
Proportion of patients readmitted for AS, n %	10,400	45.7%
Length of index stay		
Median (Q1-Q3)	4	[2-10]
Mean (SD)	7.1	(7.7)
Aortic valve management during index stay or the following year		
SAVR	10,145	44.5%
TAVI	7,513	33.0%
No aortic procedure	5,118	22.5%
All-cause mortality, n (%)		
At 30 days	556	2.4%
At 1 year	2,510	11.0%

Figure S1. Trends in age-standardized rates of patients hospitalized for aortic stenosis in person-years, according to sex, among patients without history of hospitalisation for AS in the past two years (2006-2016, France).

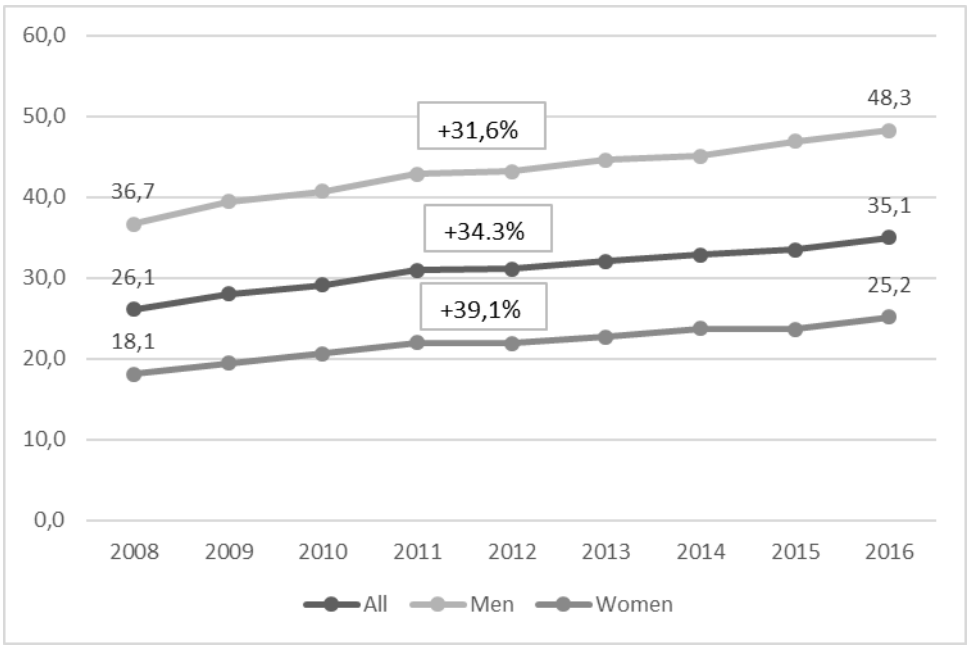

Figure S2. Trends in age-standardized rates of patients hospitalized for aortic stenosis (AS) in person-years (PY), according to aetiology, France, 2006-2016, France).

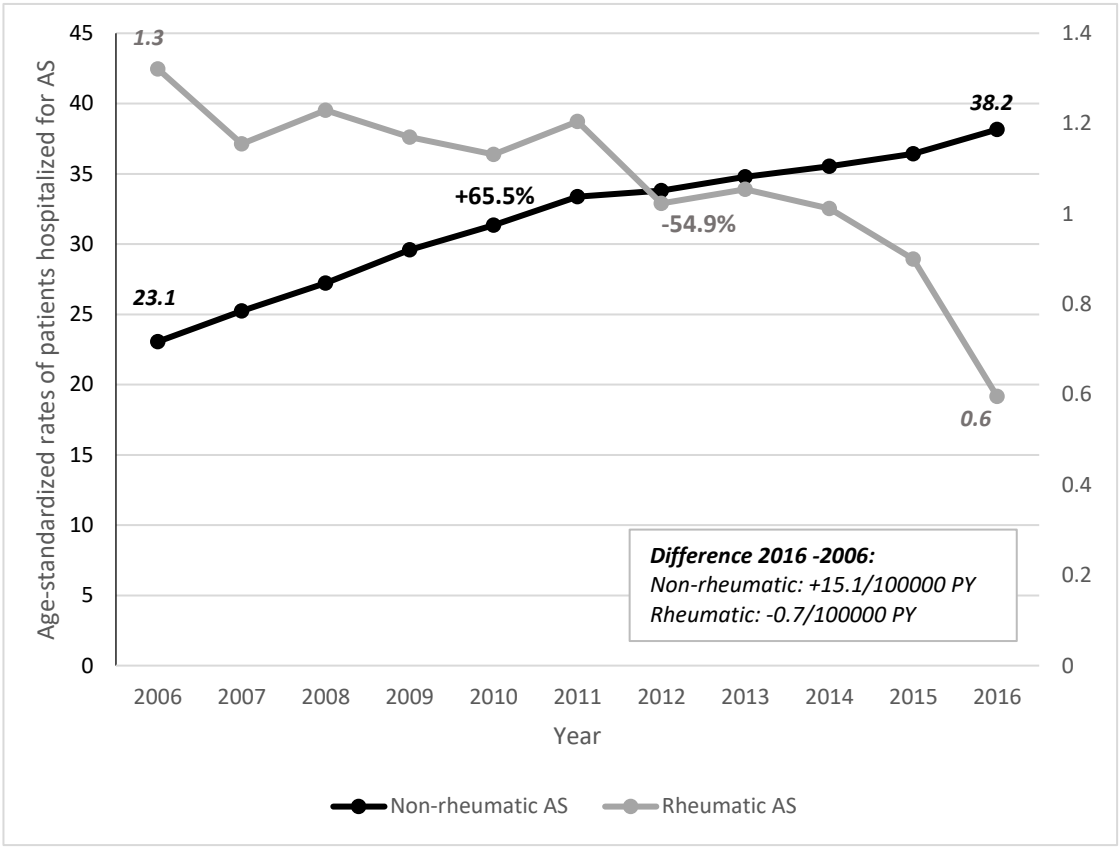

Figure S3. Survival curve after index stay, of patients hospitalized in 2016 for AS, by management, France.

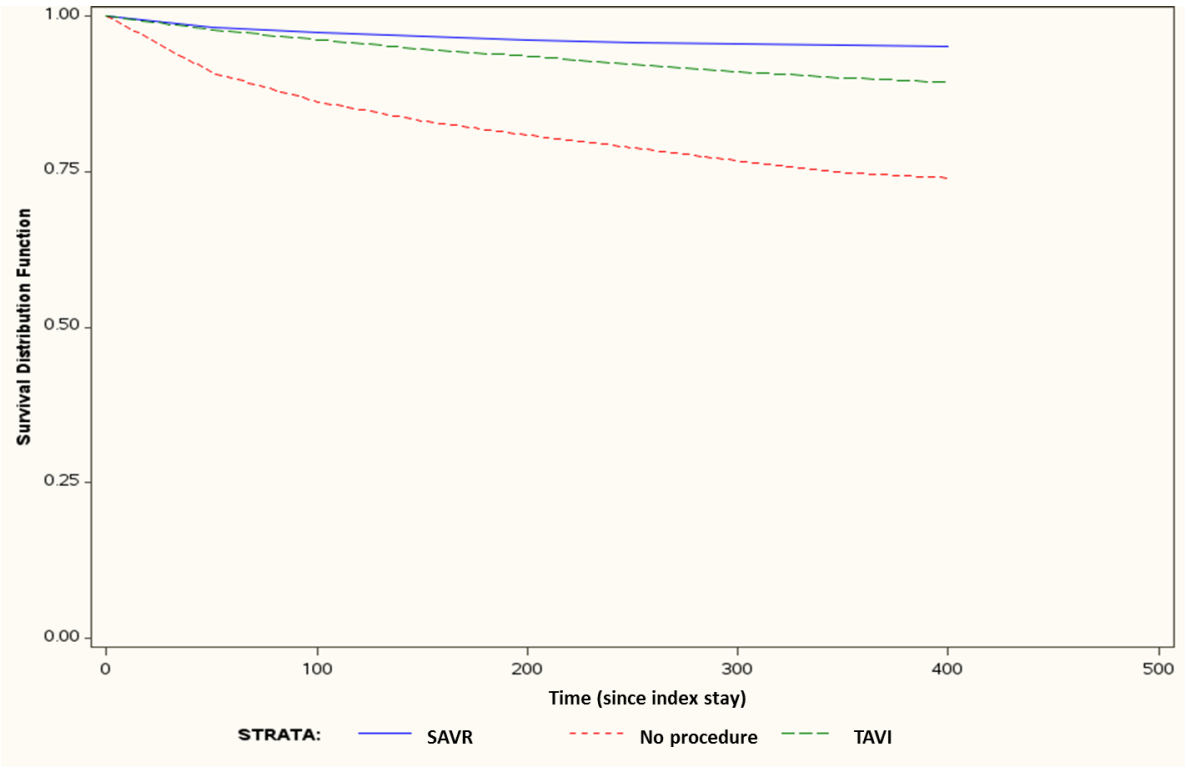

Figure S4. Trends in crude all causes mortality after TAVI or SAVR, 20010-2016, France).