JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 71, NO. 15, 2018

PUBLISHED BY ELSEVIER

Implementation of Transcatheter Aortic Valve Replacement in France

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ABSTRACT

BACKGROUND Transcatheter aortic valve replacement (TAVR) has emerged as an alternative to surgical aortic valve replacement (SAVR), but unbiased data regarding evolution of the treatment of patients with aortic stenosis at the nationwide level are scarce.

OBJECTIVES This study sought to evaluate the number of aortic valve replacements (AVRs) performed in France, changes over time, and the effect of the adoption of TAVR.

METHODS Based on a French administrative hospital-discharge database, the study collected all consecutive AVRs performed in France between 2007 and 2015.

RESULTS A total of 131,251 interventions were performed: 109,317 (83%) SAVR and 21,934 (17%) TAVR. AVR linearly increased (from 10,892 to 18,704; p for trend $<$0.0001) mainly due to a marked increase in TAVR (from 244 to 6,722; p for trend = 0.0004), whereas SAVR remained stable (from 10,892 to 11,982; p for trend = 0.18). Parallel to a decrease in the Charlson index (p for trend $<$0.05), SAVR and TAVR in-hospital mortality rates significantly declined (both p for trend $<$0.01). The number of TAVRs significantly increased in all age categories ($<$75, 75 to 79, 80 to 84, and ≥85 years of age; all p for trend = 0.003), but reached or even exceeded SAVR in the 2 oldest categories. Although mortality rates declined for both isolated SAVR and TAVR, it became similar or slightly lower for TAVR than for isolated SAVR in 2015 in the 3 oldest age categories even if it did not reach statistical significance (p = 0.66, p = 0.47, and p = 0.06, respectively).

CONCLUSIONS The number of AVRs markedly increased in France between 2007 and 2015 due to the wide adoption of TAVR, which represented one-third of all AVRs in 2015. Patients' profile improved, suggesting that patients are referred earlier, and in-hospital mortality declined in all AVR subsets. Despite a worse clinical profile, the immediate outcome of TAVR compared favorably to isolated SAVR in patients $>$75 years of age. The results may have major implications for clinical practice and policymakers. (J Am Coll Cardiol 2018;71:1614–27) © 2018 by the American College of Cardiology Foundation.

Aortic stenosis (AS) is the most common valvular heart disease in Western countries and should be regarded as a major public health problem (1,2). AS prevalence increases with age and affects as many as 5% of the population after 75 years of age. AS is responsible for 300,000 surgical aortic valve replacements (SAVRs) worldwide annually, a number that is expected to double by 2050 with the aging of the population. Contrasting with the magnitude of the problem, there is no medical

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Manuscript received October 20, 2017; revised manuscript received December 30, 2017, accepted January 30, 2018.

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2018.01.079

therapy that can stop or prevent AS progression, and consequently there is currently no alternative to aortic valve replacement (AVR) (3).

AS is mainly observed in elderly patients with commonly associated comorbidities. The Euro Heart Survey suggested that up to one-third of patients were denied surgery merely because of age (4). The last decade has seen the development of an alternative to surgery, namely transcatheter aortic valve replacement (TAVR), for patients contraindicated or considered at high risk for surgery, and this technique has profoundly changed patients' management (5-11). However, since the first patient implanted in 2002 by Alain Cribier (12,13) and the Conformité Européenne approval in the mid-2000s in Europe, the technology has markedly improved along with the expertise of operators. Indications have been extended to lower-risk patients and data from countries such as Germany are suggesting that the number of TAVRs has caught up with the number of SAVRs (14). While recent randomized clinical trials have shown that TAVR performed at least as well (and possibly better) than SAVR for patients considered at intermediate surgical risk (15-17), uncertainties remain regarding extension of TAVR to lower-risk patients. Large unbiased registries are required to perform comparisons of both techniques in real life and to precisely and accurately analyze changes over time.

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The French Programme de Médicalisation des Systèmes d'Information (PMSI) (18), a mandatory administrative database, offers the unique opportunity to assess exhaustive and comprehensive data on all consecutive AVRs performed at the nationwide level and to evaluate how the treatment of AS patients has evolved in recent years. The present study aimed to: 1) evaluate the number of AVRs performed in France, changes over time, and effect of the adoption of TAVR in clinical practice; and 2) compare SAVR and TAVR outcomes and changes occurring with time.

METHODS

STUDY DESIGN AND POPULATION. Since the July 31, 1991 law on health care reform, all health care institutions are mandated to analyze their own activity and transfer the information to the state and to the national health insurance. To do so, the PMSI database was created to collect data on patients' diagnoses, procedures, and in-hospital outcomes (18). Each hospitalization is encoded in a standardized dataset, which includes information about the patient (age and sex), hospital, stay (date of admission, date of discharge and mode of discharge), pathologies, and procedures. Primary and secondary diagnoses are coded using the International Statistical Classification of Diseases-10th Revision (ICD-10). Procedures are coded using a French standardized classification (19).

Our study was based on 2007 to 2015 PMSI national data completed with the FRANCE (FRench Aortic National CoreValve and Edwards) study published data on TAVR performed in 2009 (20). We included all SAVRs and TAVRs performed in France both in public and in private hospitals. Our study population was identified using procedure codes for SAVR and TAVR along with the ICD-10 codes for aortic stenosis (I350, I352, I060, and I062). Patients who underwent associated cardiac surgery such as coronary bypass and mitral valve surgery were identified using their respective procedure codes. Exclusion criteria were age below 18 years and aortic regurgitation (ICD-10 codes I351 and I601, respectively). Ethical approval was not required, as all data were anonymized. The French Data Protection Authority granted access to the PMSI data.

CHARLSON COMORBIDITY INDEX. We used the Charlson Comorbidity Index (21) to assess patients' comorbidities. Each variable (acquired immune deficiency syndrome, metastatic solid tumor, moderate or severe liver disease, malignant lymphoma, leukemia, any nonmetastatic solid tumor, diabetes with end organ damage, moderate or severe renal disease, hemiplegia, diabetes without end organ damage, mild liver disease, ulcer disease, connective tissue disease, chronic pulmonary disease, dementia, cerebrovascular disease, peripheral vascular disease, congestive heart failure, and myocardial infarction) was identified using ICD-10 codes.

OUTCOME. In-hospital mortality was defined as death occurring between the intervention and hospital discharge during the same hospital stay. Complications were identified using their respective ICD-10 and procedures codes. Length of stay was calculated as the time duration between the admission and hospital discharge and expressed in days.

STATISTICAL ANALYSIS. Continuous variables were expressed as mean ± SD or median (95% confidence interval) and categorical variables as number of patients (percentage). Differences in baseline characteristics and complications between groups were

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVR = aortic valve replacement

CABG = coronary artery bypass grafting

ICD-10 = International Statistical Classification of Diseases-10th Revision

PMSI = French Programme de Médicalisation des Systèmes d'Information

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

JACC VOL. 71, NO. 15, 2018
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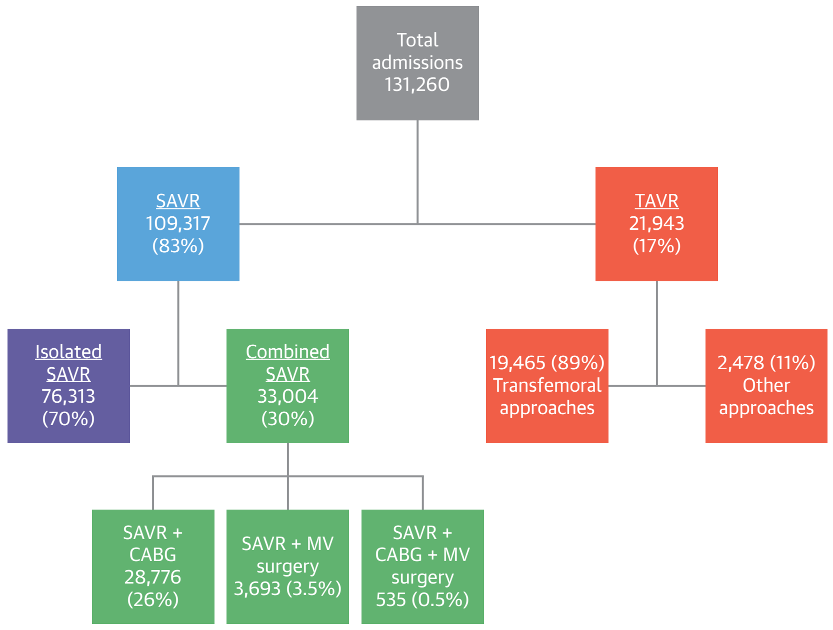
FIGURE 1 Flow Chart of the Population



Total population treated between 2007 and 2015 and the numbers and type of procedures performed. CABG = coronary artery bypass grafting; MV = mitral valve; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

calculated with the use of the chi-square test for categorical variables and the Student's *t*-test or Wilcoxon/Kruskal-Wallis tests for continuous variables as appropriate. Trends in patients' characteristics and outcome over time were estimated by the Mann-Kendall trend test. All tests were 2-sided and performed using SAS version 9.3 (SAS Institute, Cary, North Carolina), JMP version 9.0 (SAS Institute), or XLSTAT (Microsoft, Redmond, Washington). A p value <0.05 was considered statistically significant.

RESULTS

BASELINE CHARACTERISTICS OF THE POPULATION. Between 2007 and 2015, 131,251 AVRs were performed in France (mean 74 ± 11 years of age; median age 76 years [95% CI: 49 to 90 years]; 79,123 [60%] men); 109,317 (83%) were SAVRs and 21,934 (17%) were TAVRs (Figure 1). SAVR was performed in isolation in 76,313 patients (70% of all SAVRs), whereas combined coronary artery bypass grafting (CABG) was

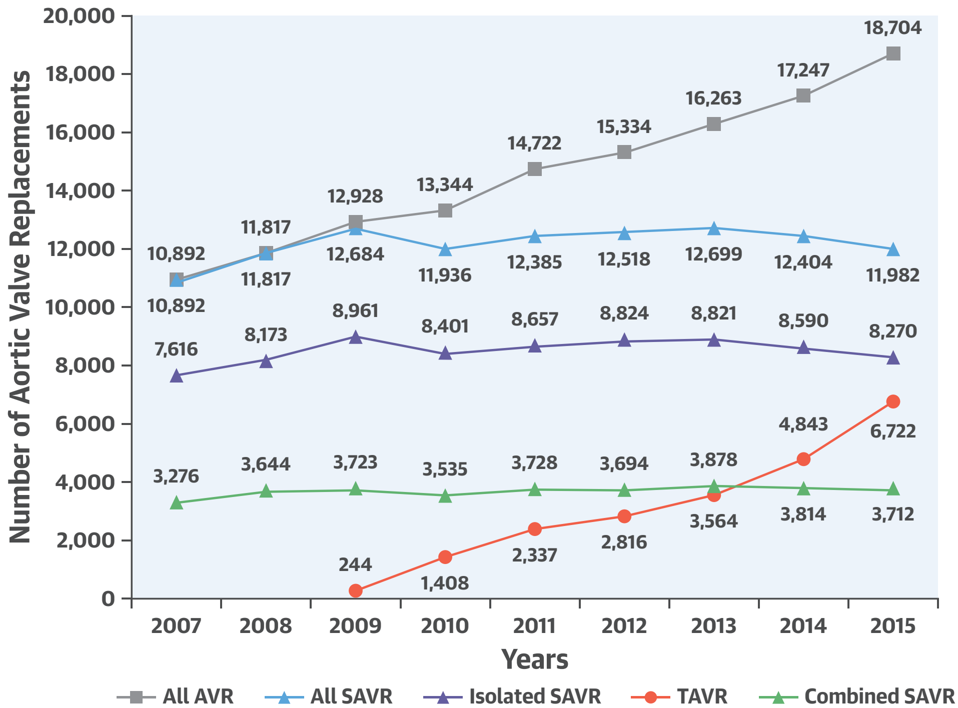
TABLE 1 Baseline Characteristics of the Overall Population According to the Type of Procedure

	Overall Population (N = 131,251)	SAVR (n = 109,317)	TAVR (n = 21,934)	Isolated SAVR (n = 76,313)	Combined SAVR (n = 33,004)
Age, yrs	74 ± 11	72 ± 10	83 ± 7	72 ± 11	74 ± 9
Male	79,123 (60)	68,350 (63)	10,773 (49)	44,929 (59)	23,421 (71)
Charlson score	0.97 ± 1.35	0.94 ± 1.34	1.10 ± 1.38	0.84 ± 1.26	1.16 ± 1.15
Charlson score ≥2	31,821 (24)	25,575 (23)	6,246 (29)	15,955 (21)	9,620 (29)
In-hospital mortality	5,417 (4.1)	4,259 (3.9)	1,158 (5.3)	2,283 (3.0)	1,576 (6.0)
Length of stay, days	13.9 ± 10.4	14.4 ± 10.7	11.1 ± 8.6	13.8 ± 9.6	15.9 ± 12.8
Pacemaker implantation	7,823 (6.0)	4,775 (4.4)	3,048 (14.0)	3,420 (4.5)	1,355 (4.1)
Stroke	2,244 (1.7)	1,725 (1.6)	519 (2.4)	1,142 (1.5)	583 (1.8)
Acute renal failure	13,415 (10.2)	11,919 (10.9)	1,496 (6.9)	6,861 (9.0)	5,058 (15.3)

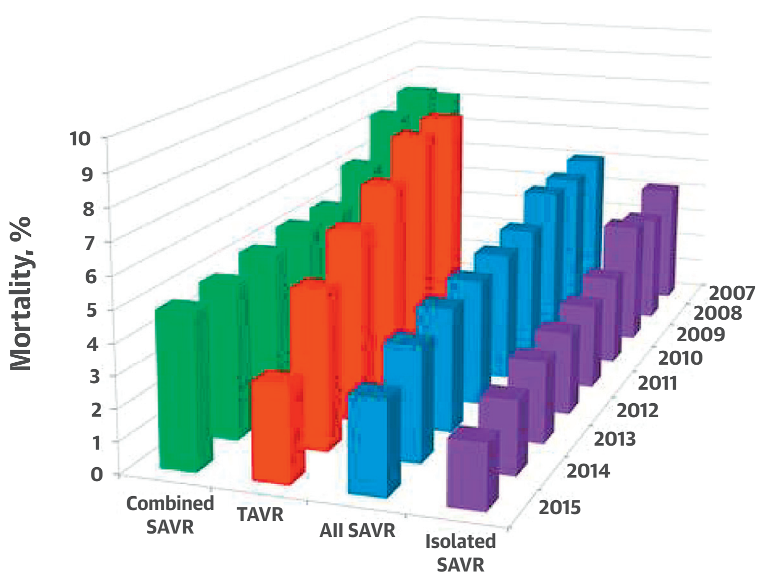
Values are mean ± SD or n (%). All p values for surgical aortic valve replacement (SAVR) (total, isolated, or combined) vs. transcatheter aortic valve replacement (TAVR) were highly significant, except for the rate of Charlson score ≥2 in combined SAVR (p = 0.38).

CENTRAL ILLUSTRATION Changes in Number, Type, and Mortality Rates of AVRs in France From 2007 to 2015

A Changes in Number of Aortic Valve Replacements From 2007 to 2015



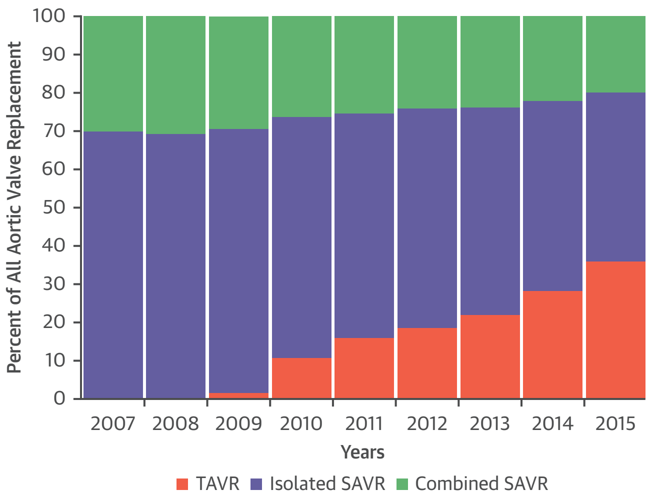
B Mortality Rates of Aortic Valve Replacements From 2007 to 2015



Nguyen, V. et al. J Am Coll Cardiol. 2018;71(15):1614–27.

(A) Number of aortic valve replacements (AVRs) performed yearly between 2007 and 2015 according to the type of AVR and associated procedure. **(B)** Changes in in-hospital mortality from 2007 to 2015. All AVR are presented in **gray**, all surgical aortic valve replacements (SAVR) in **blue**, isolated SAVR in **purple**, combined SAVR in **green**, and transcatheter aortic valve replacements (TAVR) in **orange**.

FIGURE 2 Changes in the Respective Part of SAVR and TAVR



Evolution of the proportion of surgical aortic valve replacement (SAVR) either isolated or combined and transcatheter aortic valve replacement (TAVR) between 2007 and 2015. TAVR in **orange**, isolated SAVR in **purple**, combined SAVR in **green**.

performed in 28,776 (26%) and a combined mitral valve surgery in 3,693 (3.5%). A total of 535 CABG and mitral valve surgeries were performed combined with SAVR. TAVR was mainly performed through the transfemoral approach (n = 19,456 [89%]). A comparison of patients' characteristics between SAVR and TAVR is presented in Table 1. TAVR patients were older, more frequently women, and presented with a higher Charlson score (1.10 ± 1.38 vs. 0.94 ± 1.34; $p < 0.0001$).

NUMBER AND TYPE OF PROCEDURES. As shown in the Central Illustration, total number of AVRs significantly and linearly increased by 72% from 2007 (10,892 replacements) to 2015 (18,704 replacements; p for trend <0.0001). The increase in AVRs was mainly due to a marked increase in the number of TAVRs (+2,557%, from 244 in 2009 to 6,722 in 2015; p for trend = 0.0004), whereas the number of SAVRs remained stable (+10%, from 10,892 in 2007 to 11,982 in 2015; p for trend = 0.18). Interestingly, both the number of isolated SAVRs (from 7,616 in 2007 to 8,270 in 2015; p for trend = 0.61) and combined SAVRs, with either CABG or mitral valve surgery (from 3,276 in 2007 to 3,712 in 2015; p for trend = 0.08) also remained stable. However, the proportion of TAVR of all AVRs significantly increased (from 2% in 2009 to 36% in 2015), whereas the proportion of isolated SAVR and combined SAVR markedly decreased (from 70% in 2007 to 44% in 2015, and from 30% in 2007 to 20% in 2015, respectively; $p < 0.0001$) (Figure 2).

CHANGES IN BASELINE CHARACTERISTICS AND RISK PROFILES. Although age remained unchanged both in the SAVR and TAVR groups all along the study period, there was a marked decrease in the patients' risk profile, as illustrated by the significant decrease of the Charlson index (Table 2). Thus, the Charlson index decreased by 35%, from 1.13 ± 1.46 in 2007 to 0.74 ± 1.14 in 2015, in the SAVR group (p for trend = 0.004), and by 31%, from 1.43 ± 1.53 to 0.98 ± 1.32 (p for trend = 0.017), in the TAVR group. In addition, the absolute number and percentage of patients who underwent a SAVR or a TAVR with a Charlson index ≥2 decreased over time (all p for trend <0.003). In the subsets of isolated and combined SAVR, Charlson index and the proportion of patients with a Charlson index ≥2 also decreased over time (all p for trend <0.006). Of note, whatever the year, the Charlson score remained higher in the TAVR group than in all SAVR groups (total, isolated, or combined) ($p < 0.0001$, $p < 0.0001$, and $p < 0.05$, respectively).

IN-HOSPITAL MORTALITY AND COMPLICATION RATES OVER TIME. Crude in-hospital mortality and complication rates according to the type of intervention are reported in Table 1 and change over time in Table 2. Overall, SAVR was associated with a lower in-hospital mortality rate (3.9% vs. 5.3%; $p < 0.0001$), a lower rate of pacemaker implantation (4.4% vs. 14.0%; $p < 0.0001$), and a lower rate of stroke (1.6% vs. 2.4%; $p < 0.0001$), but a higher rate of acute renal failure (10.9% vs. 6.9%; $p < 0.0001$), than TAVR. Length of stay was also significantly longer in the SAVR group than in the TAVR group (14.4 ± 10.7 days vs. 11.1 ± 8.6 days; $p < 0.0001$).

In the SAVR group, although rates of combined procedure remained unchanged over time, parallel to the decrease in the Charlson score, the in-hospital mortality rate significantly declined up to 2011 and then remained relatively stable (from 5.0% in 2007 to 2.9% in 2015; p for trend <0.0001) (Table 2, Central Illustration). Stroke and acute renal failure rates remained stable (from 1.5% in 2007 to 1.4% in 2015; p for trend = 0.92; and from 10.0% in 2007 to 11.2% in 2015; p for trend = 0.36, respectively), whereas the pacemaker rate slightly increased (from 4.0% in 2007 to 5.3% in 2015; p for trend = 0.006). Similar changes in mortality and complication rates were observed in the subsets of isolated and combined SAVR (Table 2). Length of stay significantly decreased overall (from 15.3 ± 11.9 days in 2007 to 13.8 ± 10.3 days in 2015;

TABLE 2 Changes in Baseline Characteristics and Outcome From 2007 to 2015 According to the Type of Intervention, SAVR or TAVR

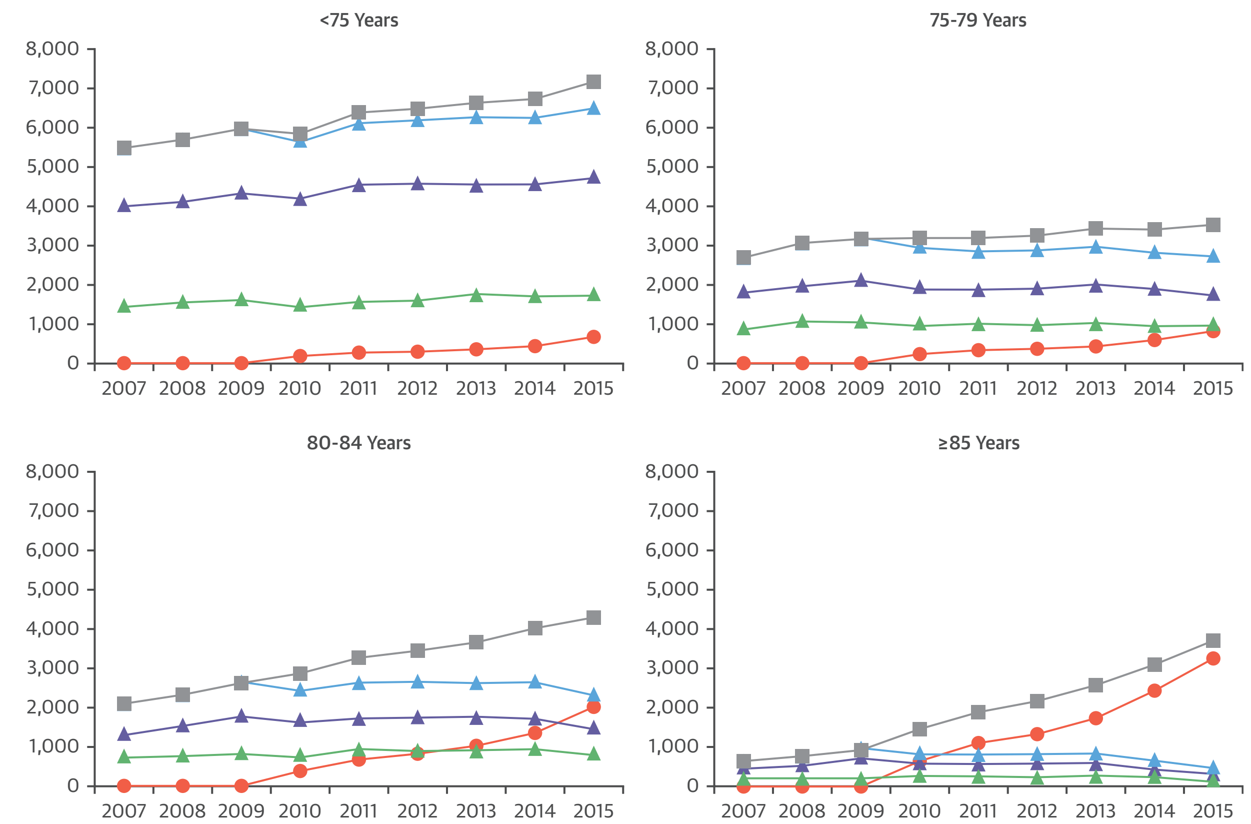
	2007	2008	2009	2010	2011	2012	2013	2014	2015	p Value for Trend
Surgical AVR	10,892	11,817	12,684	11,936	12,385	12,518	12,699	12,404	11,982	0.61
Age, yrs	72 ± 10	73 ± 10	73 ± 10	73 ± 10	72 ± 10	72 ± 10	72 ± 10	72 ± 11	72 ± 11	0.16
Male	6,638 (61.0)	7,266 (61.0)	7,867 (62.0)	7,346 (62.0)	7,709 (62.0)	7,823 (62.0)	8,027 (63.0)	7,822 (63.0)	7,852 (66.0)	0.003
Charlson score	1.13 ± 1.46	1.19 ± 1.51	1.21 ± 1.57	1.13 ± 1.47	0.82 ± 1.22	0.77 ± 1.19	0.76 ± 1.18	0.74 ± 1.14	0.74 ± 1.14	0.004
Charlson score ≥2	3,134 (29.0)	3,584 (30.0)	3,852 (30.0)	3,414 (29.0)	2,558 (21.0)	2,354 (19.0)	2,315 (18.0)	2,219 (18.0)	2,145 (18.0)	0.002
Combined AVR	3,442 (30.0)	3,780 (31.0)	3,840 (29.0)	3,620 (30.0)	3,808 (30.0)	3,752 (29.0)	3,907 (31.0)	3,848 (31.0)	3,712 (31.0)	0.36
In-hospital mortality	549 (5.0)	582 (4.9)	638 (5.0)	463 (3.9)	433 (3.5)	429 (3.4)	428 (3.4)	388 (3.1)	349 (2.9)	<0.0001
Length of stay, days	15.3 ± 11.9	14.9 ± 11.2	14.8 ± 11.8	14.4 ± 10.4	14.3 ± 10.1	14.3 ± 10.3	14.1 ± 10.0	13.8 ± 10.1	13.8 ± 10.3	<0.0001
Pacemaker implantation	439 (4.0)	479 (4.1)	532 (4.2)	466 (3.9)	506 (4.1)	512 (4.1)	577 (4.5)	627 (5.1)	637 (5.3)	0.006
Stroke	162 (1.5)	182 (1.5)	216 (1.7)	206 (1.7)	190 (1.5)	207 (1.7)	211 (1.7)	185 (1.5)	166 (1.4)	0.92
Acute renal failure	1,096 (10.1)	1,299 (11.0)	1,588 (12.5)	1,257 (10.5)	1,288 (10.4)	1,346 (10.8)	1,351 (10.6)	1,349 (10.9)	1,345 (11.2)	0.36
TAVR			244	1,408	2,337	2,816	3,564	4,843	6,722	0.0004
Age, yrs			82 ± 7	82 ± 7	83 ± 7	83 ± 7	83 ± 7	83 ± 7	83 ± 7	0.24
Male			138 (57.0)	711 (51.0)	1,168 (50.0)	1,393 (49.0)	1,733 (49.0)	2,304 (48.0)	3,321 (49.0)	0.64
Charlson score				1.43 ± 1.53	1.22 ± 1.45	1.12 ± 1.38	1.14 ± 1.41	1.07 ± 1.34	0.98 ± 1.32	0.017
Charlson score ≥2				522 (37.0)	759 (32.0)	814 (29.0)	1,055 (30.0)	1,360 (28.0)	1,736 (26.0)	0.002
In-hospital mortality			31 (12.7)	113 (8.0)	186 (8.0)	195 (6.9)	218 (6.1)	244 (5.0)	202 (3.0)	0.03
Length of stay, days				13.3 ± 10.1	12.6 ± 9.2	12.3 ± 9.7	11.2 ± 8.4	10.7 ± 8.3	9.9 ± 7.7	0.003
Transfemoral approach			173 (71.0)	1,162 (83.0)	1,915 (82.0)	2,329 (83.0)	3,150 (88.0)	4,439 (92.0)	6,303 (94.0)	0.0004
Pacemaker implantation			29 (11.8)	200 (14.0)	274 (11.7)	377 (13.4)	504 (14.1)	770 (15.9)	1,073 (16.0)	0.01
Stroke			9 (3.6)	29 (2.1)	55 (2.4)	77 (2.7)	84 (2.4)	126 (2.6)	148 (2.2)	0.77
Acute renal failure				161 (11.4)	216 (9.2)	233 (8.3)	307 (8.6)	278 (5.7)	301 (4.5)	0.02
Isolated SAVR	7,616	8,173	8,961	8,401	8,657	8,824	8,821	8,590	8,270	0.61
Age, yrs	71 ± 11	72 ± 11	72 ± 11	72 ± 11	72 ± 11	72 ± 11	71 ± 11	72 ± 11	71 ± 11	0.70
Male	4,390 (58.0)	4,724 (58.0)	5,256 (59.0)	4,862 (58.0)	5,111 (59.0)	5,181 (59.0)	5,231 (59.0)	5,053 (59.0)	5,121 (62.0)	0.02
Charlson score	1.02 ± 1.39	1.06 ± 1.43	1.10 ± 1.49	1.02 ± 1.37	0.74 ± 1.14	0.69 ± 1.12	0.68 ± 1.01	0.66 ± 1.06	0.66 ± 1.07	0.004
Charlson score ≥2	1,967 (26.0)	2,218 (27.0)	2,465 (28.0)	2,161 (26.0)	1,596 (18.0)	1,463 (17.0)	1,443 (16.0)	1,339 (16.0)	1,303 (16.0)	0.002
In-hospital mortality	314 (4.3)	296 (3.8)	361 (4.2)	245 (3.0)	236 (2.8)	234 (2.7)	229 (2.7)	200 (2.4)	168 (2.1)	<0.0001
Length of stay, days	14.60 ± 10.38	14.30 ± 9.73	14.25 ± 11.33	13.87 ± 9.68	13.56 ± 8.53	13.60 ± 9.28	13.44 ± 8.86	13.10 ± 8.56	13.14 ± 9.35	0.0002
Pacemaker implantation	322 (4.2)	352 (4.3)	389 (4.3)	358 (4.3)	378 (4.4)	360 (4.1)	388 (4.4)	435 (5.1)	438 (5.3)	0.006
Stroke	100 (1.3)	121 (1.5)	146 (1.6)	145 (1.7)	138 (1.6)	127 (1.4)	136 (1.5)	121 (1.4)	108 (1.3)	0.61
Acute renal failure	632 (8.0)	721 (9.0)	980 (1.01)	747 (9.0)	737 (9.0)	796 (9.0)	766 (9.0)	749 (9.0)	733 (9.0)	0.36
Combined SAVR	3,276	3,644	3,723	3,535	3,728	3,694	3,878	3,814	3,712	0.08
Age, yrs	74 ± 8	74 ± 9	74 ± 9	74 ± 9	74 ± 9	74 ± 9	74 ± 9	74 ± 8	73 ± 9	0.18
Male	2,248 (69.0)	2,542 (70.0)	2,611 (70.0)	2,484 (70.0)	2,598 (70.0)	2,642 (72.0)	2,796 (72.0)	2,769 (73.0)	2,731 (74.0)	0.002
Charlson score	1.39 ± 1.59	1.46 ± 1.65	1.48 ± 1.71	1.40 ± 1.65	1.01 ± 1.37	0.96 ± 1.33	0.93 ± 1.33	0.92 ± 1.28	0.90 ± 1.27	0.002
Charlson score ≥2	1,167 (36.0)	1,366 (37.0)	1,387 (37.0)	1,253 (35.0)	962 (26.0)	891 (24.0)	872 (22.0)	880 (23.0)	842 (22.0)	0.006
In-hospital mortality	235 (7.2)	286 (7.8)	277 (7.4)	218 (6.2)	197 (5.3)	195 (5.3)	199 (5.1)	188 (4.9)	181 (4.9)	0.001
Length of stay, days	16.82 ± 14.83	16.28 ± 13.85	16.20 ± 12.63	15.74 ± 11.83	15.99 ± 12.80	15.98 ± 12.37	15.64 ± 12.09	15.32 ± 12.70	15.14 ± 11.96	0.0002
Pacemaker implantation	117 (3.6)	127 (3.5)	143 (3.8)	108 (3.1)	128 (3.4)	152 (4.1)	189 (4.9)	192 (5.0)	199 (5.4)	0.01
Stroke	62 (1.9)	61 (1.7)	70 (1.9)	61 (1.7)	52 (1.4)	80 (2.2)	75 (1.9)	64 (1.7)	58 (1.6)	0.76
Acute renal failure	464 (14)	578 (16)	608 (16)	510 (14)	551 (15)	550 (15)	585 (15)	600 (16)	612 (16)	0.08

Values are n, mean ± SD, or n (%).
Abbreviations as in Table 1.

p for trend <0.0001) and both in isolated and combined AVR subsets (both p for trend = 0.002).

In the TAVR group, in-hospital mortality markedly declined (from 12.7% in 2009 to 3.0% in 2015; p for trend = 0.003), as did the acute renal failure rate (from 11.4% in 2010 to 4.5% in 2015; p for trend = 0.02), whereas the stroke rate remained unchanged (from 3.6% in 2009 to 2.2% in 2015; p for trend = 0.77) and the pacemaker implantation rate increased (from 11.8% in 2009 to 16.0% in 2015; p for trend = 0.01). Interestingly, the mortality rate of TAVR was similar to the overall SAVR mortality rate

FIGURE 3 Changes in Number of AVRs According to Age



The number of AVRs performed yearly between 2007 and 2015 according to the type of AVR and associated procedure in 4 age categories (<75, 75 to 79, 80 to 84, and ≥85 years of age). All AVR are presented in **gray**, all SAVR in **blue**, isolated SAVR in **purple**, combined SAVR in **green**, and TAVR in **orange**. Abbreviations as in Figure 1.

in 2015 (3.0% vs. 2.9%; $p = 0.72$), but not when only isolated SAVRs were considered (3.0% vs. 2.0%; $p < 0.0001$) (Central Illustration). Length of stay also significantly decreased from 13.3 ± 10.1 days in 2010 to 9.9 ± 7.7 days in 2015 (p for trend = 0.003).

TAVR IMPLEMENTATION ACCORDING TO AGE. **Number of procedures.** We then divided our population into 4 age categories: <75 years of age (n = 56,328, 43%), 75 to 79 years of age (n = 28,903, 22%), 80 to 84 years of age (n = 28,609, 22%), and ≥85 years of age (n = 17,157, 13%). As shown in Figure 3, the number of SAVRs increased in the youngest age category (p for trend = 0.001) but remained stable in the other 3 age categories (p for trend = 0.14, 0.36, and 0.61, respectively). In contrast, the number of TAVRs significantly increased in all age subsets (all p for trend = 0.003) and caught up and even exceeded the number of SAVRs in the 2 oldest subsets. In the 2 youngest subsets, TAVR was more marginally performed.

Overall risk profile and mortality rates. Mortality by age category is presented in Table 3 and Figure 4. The mortality rate in the TAVR group was not significantly different in all age categories (approximately 5%; $p = 0.63$), whereas they markedly increased with age in both isolated and combined SAVR groups (from 1.8% to 6.4% and from 4.3% to 10.8%, respectively; both $p < 0.0001$). Importantly, in each age category, the mortality rate was significantly different among isolated SAVR, combined SAVR, and TAVR (all $p < 0.0001$), but ranking changed as age increased. Thus, TAVR was associated with a higher mortality rate in the 2 youngest age categories (both $p < 0.0001$), but was not different between 80 and 85 years of age ($p = 0.15$) and was lower after 85 years of age ($p = 0.03$), although the Charlson index was always higher in the TAVR group.

Change in mortality rates over time. Mortality rates over time in all 4 age categories and for all 3 treatment groups (isolated SAVR, combined SAVR, and TAVR) are illustrated in Figure 5. The mortality rate in the isolated SAVR declined from 2007 to 2015, although the decrease was mainly observed in the first years (2007 to 2010; all p for trend <0.05). In contrast, the mortality rate of combined SAVR remained overall stable in all categories, except in the 80 to 85 years of age category (p for trend $= 0.002$). On the other hand, the TAVR mortality rate in the youngest category remained unchanged (p for trend $= 0.72$), but declined in the other 3 age categories (p for trend $= 0.003$, 0.06, and 0.003, respectively). Importantly, in 2015, the TAVR mortality rate remained higher than the mortality rate of isolated SAVR in patients <75 years of age, but became similar or slightly lower in the 75 to 80, 80 to 84, and ≥85 years of age groups even if it did not reach the statistical significance ($p = 0.66$, $p = 0.47$, and $p = 0.06$, respectively). It is also worth noting that the Charlson score in the isolated SAVR group was significantly lower than in the TAVR group in all 3 age categories (all $p < 0.0001$), and was similar above 85 years of age ($p = 0.82$) (Table 3).

DISCUSSION

In the present study, we report contemporary, exhaustive, nationwide data on trends in numbers, type, and outcomes of AVR in France from 2007 to 2015. Main results can be summarized as follows. First, there was a linear increase in the number of AVR performed in France (+70%; +8% per year). This increase was mainly related to the marked development and widespread diffusion of TAVR, which represented approximately one-third of all AVRs performed in 2015, whereas SAVR remained relatively stable. Second, the overall profile of patients who underwent an AVR improved over time, and we observed a parallel in-hospital mortality decrease overall and in all AVR subsets (isolated SAVR, combined SAVR, and TAVR). Third, in 2015, among patients 75 years of age or older, the in-hospital mortality rate of TAVR was similar or slightly lower than the mortality rate of isolated SAVR despite an overall worse clinical profile.

Randomized controlled trials, although critical, enroll selected patient populations and are usually performed in high-volume valve centers, and thus generalizability to real life may be questioned. Propensity matching of real-world cohorts such as the recent study based on the Society of Thoracic Surgeons National Database/American College of Cardiology TVT (Transcatheter Valve Therapy) registry are important, but are also subject to selection bias and precludes evaluation of changes over time (22). National TAVR registries have been implemented in France (8,20) as well as abroad (23-26), but only provide information of transcatheter therapies. Furthermore, participation in the FRANCE TAVI registry, which has succeeded the FRANCE 2 registry, is now only on a volunteer basis and is not anymore exhaustive, and thus it is potentially biased, as has recently been shown (27). In contrast, the PMSI database is exhaustive, consecutive, and thus includes all AVRs performed in France, as it is mandatory for all French health care institutions. The PMSI database therefore offers a unique opportunity to evaluate real-life outcomes and changes in TAVR comparatively to surgery at the nationwide level in France.

In the present study, we clearly demonstrate the dramatic increase of AVR performed in France in the last decade. Similar trends at the German nationwide level have also been reported, although for a shorter period of evaluation (28). Aortic valve stenosis is a degenerative disease whose prevalence increases with age. However, it is unlikely that the observed AVR increase was only related to the aging of the population in such a limited period of time. In addition, age-adjusted trends showed similar results (data not presented). These results raise 2 important questions: first, whether these changes can be attributed to a substitutive or complementary use of TAVR (availability and increased awareness of this novel technology); and second, whether this linear trend will continue and for how long.

As illustrated in Figure 3, the number of surgeries decreased as age increased. Thus, surgery was only marginally performed after 85 years of age and represented only 6% of all AVRs in 2007. With availability of TAVR, a dramatic increase of AVR was observed in this age category (+583%). In 2015, AVR performed after 85 years of age represented 20% of all AVRs, and the immense majority were TAVR. Thus, TAVR has addressed an unmet medical need in this elderly population and usefully complemented SAVR. As age decreased, the use of TAVR was less prominent. This is fully in line with clinical practice guidelines at that time, which restricted TAVR use to patients contraindicated for surgery or at high surgical risk. As evidence regarding TAVR efficacy has accumulated in intermediate-risk patients, a substitutive effect in the youngest age categories (especially 75 to 85 years of age) has also possibly occurred. It is worth noting

TABLE 3 Changes in Charlson Index and Mortality From 2007 to 2015 According to the Type of Intervention and Age

	Overall			2007		
	Total	Mortality	Charlson	Total	Mortality	Charlson
<75 yrs of age						
TAVR	2,233	119 (5.3)	1.61 ± 1.78			
Isolated SAVR	39,627	723 (1.8)	0.79 ± 1.25	4,020	101 (2.5)	0.93 ± 1.35
Combined SAVR	14,468	616 (4.3)	1.14 ± 1.51	1,449	88 (6.1)	1.35 ± 1.58
Total	56,328	1,548 (2.6)	0.91 ± 1.36	5,469	189 (35)	1.04 ± 1.43
75–80 yrs of age						
TAVR	2,790	141 (5.1)	1.30 ± 1.51			
Isolated SAVR	17,175	563 (33)	0.91 ± 1.29	1,806	85 (4.7)	1.13 ± 1.46
Combined SAVR	8,938	568 (6.4)	1.19 ± 1.50	891	64 (7.2)	1.45 ± 1.61
Total	28,903	1,272 (4.4)	1.03 ± 1.39	2,697	149 (5.5)	1.24 ± 1.52
80–85 yrs of age						
TAVR	6,229	320 (5.1)	1.10 ± 1.38			
Isolated SAVR	14,737	668 (4.7)	0.90 ± 1.27	1331	96 (7.2)	1.09 ± 1.37
Combined SAVR	7,643	581 (7.6)	1.14 ± 1.44	760	65 (8.6)	1.41 ± 1.60
Total	28,609	1,589 (5.6)	1.01 ± 1.35	2,091	161 (7.7)	1.20 ± 1.47
≥85 yrs of age						
TAVR	10,438	578 (5.5)	0.94 ± 1.20			
Isolated SAVR	4,767	307 (6.4)	0.92 ± 1.27	459	32 (7.0)	1.15 ± 1.45
Combined SAVR	1,952	211 (10.8)	1.16 ± 1.45	176	18 (10.2)	1.35 ± 1.57
Total	17,157	1,096 (6.4)	0.96 ± 1.25	635	50 (7.9)	1.21 ± 1.49

	2011			2012		
	Total	Mortality	Charlson	Total	Mortality	Charlson
<75 yrs of age						
TAVR	274	18 (6.6)	1.57 ± 1.36	301	20 (6.6)	1.75 ± 1.96
Isolated SAVR	4,536	81 (1.8)	0.69 ± 1.15	4,579	71 (1.6)	0.67 ± 1.14
Combined SAVR	1,562	53 (3.4)	0.97 ± 1.39	1,596	52 (3.3)	0.96 ± 1.35
Total	6,372	152 (2.4)	0.80 ± 1.25	6,476	143 (2.2)	0.80 ± 1.28
75–80 yrs of age						
TAVR	328	24 (7.3)	1.35 ± 1.50	380	25 (6.6)	1.38 ± 1.51
Isolated SAVR	1,861	60 (3.2)	0.74 ± 1.12	1,904	68 (3.6)	0.70 ± 1.08
Combined SAVR	992	52 (5.2)	1.02 ± 1.32	969	52 (5.4)	0.96 ± 1.33
Total	3,181	136 (4.3)	0.89 ± 1.25	3,253	145 (4.5)	0.85 ± 1.23
80–85 yrs of age						
TAVR	651	53 (8.1)	1.19 ± 1.48	802	51 (6.4)	1.11 ± 1.29
Isolated SAVR	1,699	64 (3.8)	0.84 ± 1.16	1,755	67 (3.8)	0.75 ± 1.14
Combined SAVR	930	68 (7.3)	1.06 ± 1.34	889	72 (8.1)	0.98 ± 1.29
Total	3,280	185 (5.6)	0.97 ± 1.29	3,446	190 (5.5)	0.89 ± 1.22
≥85 yrs of age						
TAVR	1,084	91 (8.4)	1.11 ± 1.35	1,333	99 (7.4)	0.92 ± 1.16
Isolated SAVR	560	31 (5.5)	0.82 ± 1.06	585	27 (4.6)	0.64 ± 1.02
Combined SAVR	244	24 (9.8)	1.04 ± 1.48	240	19 (7.9)	0.99 ± 1.27
Total	1,888	146 (7.7)	1.01 ± 1.30	2,158	145 (6.7)	0.85 ± 1.15

Values are n, n (%), or mean ± SD.
Abbreviations as in Table 1.

Continued on the next page

that TAVR adoption seemed to have occurred earlier and faster in several countries such as Germany, possibly due to a faster shift from high- to lower-risk patients. In 2014, the number of TAVRs already exceeded the number of isolated SAVR in Germany (14).

Another striking observation of the present study was the overall decrease in the Charlson index in all AVR subsets and across all age categories. A possible interpretation of this observation is that interventions (either TAVR or SAVR) were considered at an earlier stage in the course of the disease. Elderly patients or those with comorbidities, who were often neglected and rarely considered for surgery a few years ago, are now more frequently referred to centers with surgical or transcatheter programs earlier

TABLE 3 Continued

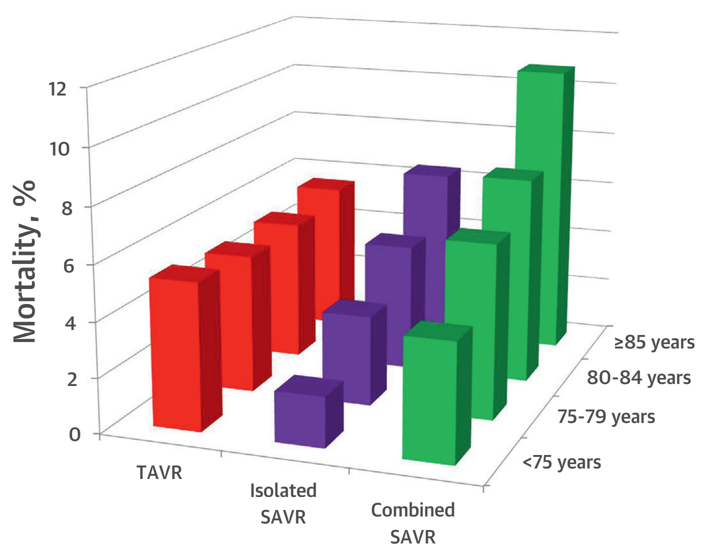
2008			2009			2010		
Total	Mortality	Charlson	Total	Mortality	Charlson	Total	Mortality	Charlson
			NA			178	11 (6.2)	1.88 ± 1.72
4,127	93 (2.3)	0.99 ± 1.40	4,337	110 (2.5)	1.00 ± 1.47	4,194	75 (1.8)	0.93 ± 1.33
1,567	97 (6.2)	1.52 ± 1.71	1,631	78 (4.8)	1.47 ± 1.74	1,469	50 (3.4)	1.41 ± 1.65
5,694	190 (3.3)	1.14 ± 1.51	5,968	188 (3.2)	1.31 ± 1.60	5,841	136 (2.3)	1.08 ± 1.45
			NA			236	20 (8.5)	1.76 ± 1.80
1,965	78 (4.0)	1.14 ± 1.48	2,112	75 (3.6)	1.15 ± 1.44	1,943	53 (2.7)	1.17 ± 1.46
1,091	79 (7.2)	1.43 ± 1.61	1,059	91 (8.6)	1.53 ± 1.73	1,009	80 (7.9)	1.53 ± 1.78
3,056	157 (5.1)	1.24 ± 1.54	3,171	166 (5.2)	1.28 ± 1.55	3,188	153 (4.8)	1.33 ± 1.61
			NA			378	24 (6.3)	1.43 ± 1.50
1,542	85 (5.5)	1.14 ± 1.45	1,787	110 (6.2)	1.20 ± 1.56	1,684	79 (4.7)	1.04 ± 1.35
782	76 (9.7)	1.45 ± 1.63	836	80 (9.6)	1.42 ± 1.61	797	66 (8.3)	1.26 ± 1.55
2,324	161 (6.9)	1.26 ± 1.52	2,623	190 (7.2)	1.27 ± 1.58	2,859	169 (5.9)	1.15 ± 1.44
			NA			616	58 (9.4)	1.17 ± 1.30
539	40 (7.4)	1.11 ± 1.43	723	65 (9.0)	1.24 ± 1.54	578	38 (6.6)	1.04 ± 1.28
204	34 (16.7)	1.15 ± 1.40	196	28 (14.3)	1.58 ± 1.78	260	22 (8.5)	1.31 ± 1.37
743	74 (10.0)	1.12 ± 1.42	919	93 (10.1)	1.31 ± 1.60	1,454	118 (8.1)	1.14 ± 1.31

2013			2014			2015		
Total	Mortality	Charlson	Total	Mortality	Charlson	Total	Mortality	Charlson
355	31 (8.7)	1.83 ± 1.99	453	17 (3.8)	1.52 ± 1.70	672	22 (3.3)	1.43 ± 1.68
4,543	73 (1.6)	0.66 ± 1.15	4,552	65 (1.4)	0.65 ± 1.10	4,739	54 (1.1)	0.61 ± 1.04
1,729	64 (3.7)	0.92 ± 1.36	1,709	65 (3.9)	0.93 ± 1.33	1,756	69 (3.9)	0.86 ± 1.28
6,627	168 (2.5)	0.79 ± 1.29	6,714	147 (2.2)	0.78 ± 1.23	7,167	145 (2.0)	0.75 ± 1.20
449	28 (6.2)	1.39 ± 1.50	590	26 (4.4)	1.24 ± 1.42	807	18 (2.2)	1.09 ± 1.47
1,965	52 (2.6)	0.68 ± 1.06	1,870	48 (2.6)	0.71 ± 1.06	1,749	44 (2.5)	0.70 ± 1.09
1,002	50 (5.0)	0.89 ± 1.25	948	49 (5.2)	0.90 ± 1.23	977	51 (5.2)	0.94 ± 1.27
3,416	130 (3.8)	0.84 ± 1.21	3,408	123 (3.6)	0.85 ± 1.20	3,533	113 (3.2)	0.86 ± 1.24
1,032	57 (5.5)	1.14 ± 1.39	1,367	70 (5.1)	1.13 ± 1.41	1,999	65 (3.3)	0.98 ± 1.33
1,730	72 (4.2)	0.72 ± 1.05	1,726	60 (3.5)	0.64 ± 0.99	1,483	55 (3.7)	0.75 ± 1.10
893	56 (6.3)	0.96 ± 1.34	936	51 (5.4)	0.90 ± 1.20	820	47 (5.7)	0.92 ± 1.23
3,655	185 (5.1)	0.90 ± 1.24	4,029	181 (4.5)	0.86 ± 1.21	4,302	167 (3.9)	0.89 ± 1.24
1,728	102 (5.9)	0.94 ± 1.19	2,433	131 (5.4)	0.92 ± 1.17	3,244	97 (3.0)	0.85 ± 1.16
583	32 (5.5)	0.65 ± 1.02	441	27 (6.1)	0.64 ± 0.97	299	15 (5.0)	0.87 ± 1.17
253	29 (11.5)	1.06 ± 1.33	220	23 (10.5)	1.08 ± 1.40	159	14 (8.8)	0.93 ± 1.35
2,564	163 (6.4)	0.89 ± 1.18	3,094	181 (5.9)	0.89 ± 1.17	3,702	126 (3.4)	0.86 ± 1.17

and not so unduly conservatively managed anymore. This point also illustrates the complementary use of TAVR and SAVR. Although we could not exclude that less futile intervention may have been performed with time, it remains marginal in our opinion (29).

Parallel to the better patient profiles, outcomes improved in all AVR subsets (isolated SAVR, combined SAVR, and TAVR). In the surgical group, improvement is probably related, at least partially, to a shift from SAVR to TAVR in high-risk patients, as suggested by the decline in mortality rates that mainly occurred in the early days of TAVR (2010 to 2011). With technological improvement, experience and expertise of the operators, and better selection of patients, TAVR has reached maturity. Overall, in 2015, in-hospital

FIGURE 4 Mortality Rates of AVR According to Age



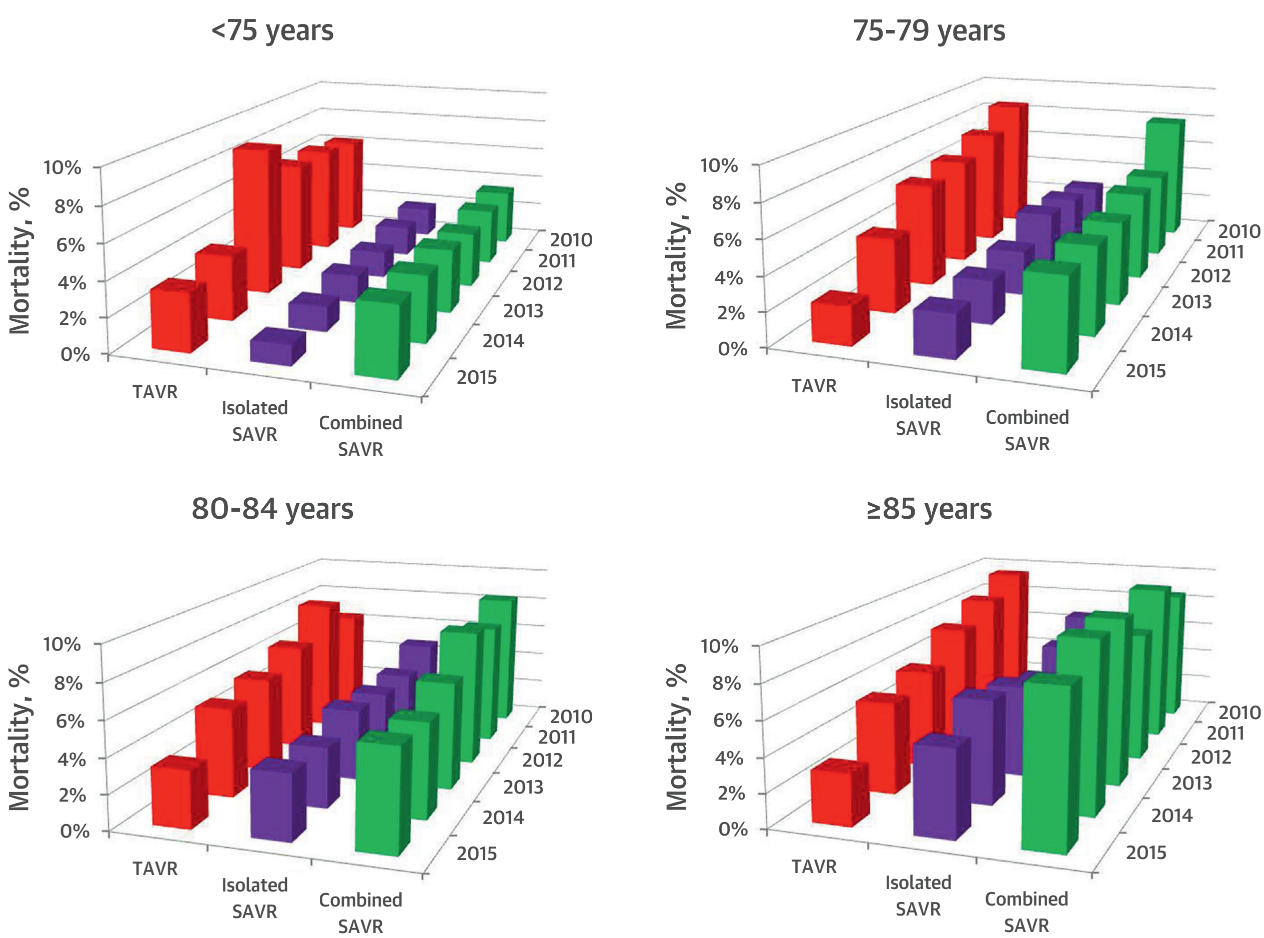
In-hospital mortality according to the type of AVR (isolated SAVR in **purple**, combined SAVR in **green**, and TAVR in **orange**) and age category (<75, 75 to 79, 80 to 84, and ≥85 years of age). Abbreviations as in Figure 1.

mortality was only 3% compared with 2% for isolated SAVR irrespective of age and comorbidities. More specifically, when TAVR and isolated SAVR outcome were analyzed according to age categories, TAVR compared favorably to isolated SAVR in patients 75 years of age or older. On the other side, comparison of TAVR and SAVR results in patients younger than 75 years of age should take into account the fact that patients referred to TAVR in this subset are probably the sickest, with the greater comorbidity explaining the worse outcomes. Complication rates after TAVR also declined except the need for pacemaker and compared well with SAVR and length of stay was significantly shorter. The good TAVR outcomes are further reinforced by the fact that we did not individualize patients who underwent a TAVR through a transfemoral or another approach. One may argue that TAVR and SAVR populations are not comparable, but this should have played in the other direction, as the Charlson score index was consistently higher or equal in TAVR patients than in isolated SAVR patients. However, we could not exclude that patients with the worst associated conditions (either clinical or anatomical) were finally referred to surgery. Although ultimate TAVR durability remains uncertain, while waiting for the ongoing randomized trials comparing TAVR to SAVR in low-risk patients, the heart team should take into account age, anatomical, and technical aspects, as recently proposed in the latest clinical practice guidelines on valvular heart disease, when determining the best therapeutic option between TAVR and SAVR (30,31).

STUDY LIMITATIONS. First, the present study was based on administrative data, with limitations inherent to such methodology. However, the scale of the database minimizes coding errors, and as coding of complications is linked to reimbursement, it is expected to be of good quality. Furthermore, age, type of AVR (SAVR or TAVR), and in-hospital mortality, the 3 major key items of the present study, are easy to collect and ascertain. Second, we were limited in our analysis to the variables present in the database, which meant that precise patient characteristics including left ventricular ejection fraction, anatomical considerations, type of surgical prosthesis, and prevalence and degree of paravalvular regurgitation (a major source of post-operative mortality and morbidity) could not be obtained. We were also not able to calculate surgical risk scores such as the EuroSCORE or the Society of Thoracic Surgeons score. However, similar declines in surgical risk scores have been reported in several TAVR and SAVR registries (23,27,28). The Charlson index was used as a surrogate, but we acknowledge that it is far from perfect, as it disregards important comorbidities or characteristics such as ejection fraction or previous cardiac surgery and is based off of coding at hospital discharge by physicians with varied expertise in this area. Third, the PMSI database is not currently linked to any death record database, and we were unfortunately not able to provide mid- or long-term survival. Finally, although the adoption timescales of TAVR may vary across countries depending on the structure of their health care system and reimbursement schemes, similar trends are expected to occur in all Western countries, as shown in Germany.

SOCIETAL AND ECONOMIC IMPLICATIONS. With the aging of the population, the number of AVRs is expected to continue to grow in France as well as in all Western countries. One major issue will be at which speed this growth will occur, as it portends major implications for health system organization and budget impact. Modeling studies based on the aging of the population, and prevalence of severe AS may be helpful, but this is outside the scope of the present study. Our results could also be helpful for updating evaluation of the cost effectiveness of TAVR technology compared with SAVR (assuming a similar mid- and long-term outcome after hospital discharge) (32). Indeed, in addition to in-hospital mortality, main complication rates and length of stay were collected. Another major policy implication is to raise

FIGURE 5 **Changes in Mortality Rates of AVR According to Age**



Changes in in-hospital mortality rates from 2007 to 2015 according to the type of AVR (isolated surgical AVR [SAVR] in **purple**, combined SAVR in **green** and transcatheter AVR [TAVR] in **orange**) and age category (<75, 75 to 79, 80 to 84, and ≥85 years of age). Abbreviations as in Figure 1.

awareness on the major AS social and economic burden and strongly incentivize government bodies and policymakers to support research programs aimed at tackling the occurrence and progression of AS (33).

CONCLUSIONS

Based on an administrative database, we were able to report the changes in number, type, and outcomes of all AVRs performed in France between 2007 and 2015. We show that the number of AVRs has markedly increased due to the wide availability and adoption of TAVR, especially in elderly patients. The overall increase was associated with an improvement in patient profile, suggesting that patients are now referred earlier in the course of disease, and we observed a marked in-hospital mortality decline in all AVR subsets (isolated SAVR, combined SAVR, and TAVR). Finally, despite a worse clinical profile, the TAVR in-hospital mortality rate compared favorably with isolated SAVR in patients 75 years of age or older. Our results may have major implications for clinical practice and policymakers.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: In France, TAVR has transformed the management of patients with symptomatic severe AS, and maturation of the technology has been associated with a marked decline in procedural mortality and complications. Ongoing randomized trials in lower-risk patients and long-term surveillance of patients with implanted valves seem likely to make TAVR the first-line therapy for patients with symptomatic AS irrespective of age or surgical risk.

TRANSLATIONAL OUTLOOK: Data from comprehensive nationwide databases of consecutive patients undergoing AVR, despite inherent limitations, should complement ongoing randomized trials to provide insight into long-term outcomes, including the longevity of prosthetic materials and the consequences and management of their degeneration over time.

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KEY WORDS aortic stenosis, aortic valve replacement, outcome, transcatheter therapies