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ORIGINAL INVESTIGATIONS

Contemporary Management of Severe Symptomatic Aortic Stenosis

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ABSTRACT

BACKGROUND There were gaps between guidelines and practice when surgery was the only treatment for aortic stenosis (AS).

OBJECTIVES This study analyzed the decision to intervene in patients with severe AS in the EORP VHD (EURObservational Research Programme Valvular Heart Disease) II survey.

METHODS Among 2,152 patients with severe AS, 1,271 patients with high-gradient AS who were symptomatic fulfilled a Class I recommendation for intervention according to the 2012 European Society of Cardiology guidelines; the primary end point was the decision for intervention.

RESULTS A decision not to intervene was taken in 262 patients (20.6%). In multivariate analysis, the decision not to intervene was associated with older age (odds ratio [OR]: 1.34 per 10-year increase; 95% CI: 1.11 to 1.61; $P = 0.002$), New York Heart Association functional classes I and II versus III (OR: 1.63; 95% CI: 1.16 to 2.30; $P = 0.005$), higher age-adjusted Charlson comorbidity index (OR: 1.09 per 1-point increase; 95% CI: 1.01 to 1.17; $P = 0.03$), and a lower transaortic mean gradient (OR: 0.81 per 10-mm Hg decrease; 95% CI: 0.71 to 0.92; $P < 0.001$). During the study period, 346 patients (40.2%, median age 84 years, median EuroSCORE II [European System for Cardiac Operative Risk Evaluation II] 3.1%) underwent transcatheter intervention and 515 (59.8%, median age 69 years, median EuroSCORE II 1.5%) underwent surgery. A decision not to intervene versus intervention was associated with lower 6-month survival (87.4%; 95% CI: 82.0 to 91.3 vs 94.6%; 95% CI: 92.8 to 95.9; $P < 0.001$).

CONCLUSIONS A decision not to intervene was taken in 1 in 5 patients with severe symptomatic AS despite a Class I recommendation for intervention and the decision was particularly associated with older age and combined comorbidities. Transcatheter intervention was extensively used in octogenarians. (J Am Coll Cardiol 2021;78:2131-2143)

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

AHA = American Heart Association

AS = aortic stenosis

EACTS = European Association for Cardiothoracic Surgery

ESC = European Society of Cardiology

NYHA = New York Heart Association

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

VHD = valvular heart disease

Calcific aortic stenosis (AS) is the most frequent valvular heart disease (VHD) for which patients are referred to hospital in high-income countries, and its prevalence reaches 3%-5% after age 75 years (1). The poor prognosis of severe symptomatic AS and positive results of surgical and transcatheter intervention result in strong recommendations for aortic valve replacement. However, in the 2001 Euro Heart Survey, 33% of elderly patients with severe symptomatic AS did not undergo surgical aortic valve replacement (SAVR) (2), whereas other series report consistent underuse of SAVR (3,4). Since the 2000s, elaboration and/or update of the European Society of Cardiology (ESC) and American College of Cardiology (ACC)/American Heart Association (AHA) guidelines (5,6) combined with the emergence of transcatheter aortic valve replacement (TAVR) may have changed clinical decision making.

This study aimed to use data from the international EORP VHD (EURObservational Research Programme Valvular Heart Disease) II survey, designed by the ESC EURObservational Research Programme (7) to analyze the therapeutic decision and mode of intervention in patients with severe symptomatic AS, determine which objective characteristics were associated with a decision not to intervene (as compared with the 2001 Euro Heart Survey) (2), and assess the relationship between initial therapeutic decision and 6-month survival.

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METHODS

STUDY POPULATION. The VHD II survey was conducted between January 16, and August 28, 2017, in 222 centers across 28 countries and included 7,247 patients recruited over a 3-month period in each center, including 2,152 patients with severe AS of any etiology, with no restriction regarding associated aortic regurgitation, without concomitant moderate or severe mitral valve disease and without any previous valvular intervention (7). Patients were included in the VHD II survey if they were ≥18 years of age and had severe native VHD as defined by echocardiography using an integrative approach or if they had undergone any previous surgical or transcatheter valvular intervention. Exclusion criteria were acute infective endocarditis, enrolment in a valve intervention study impacting on management and VHD related to complex congenital heart disease (7). Heart failure was defined by the presence of clinical signs of congestive heart failure at the time of index hospitalization or outpatient clinic visit. The primary endpoint was the therapeutic decision taken by the responsible practitioner during the index hospitalization or outpatient visit. The VHD II survey was approved for the ESC by the Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé (October 5, 2016) and the Commission Nationale Informatique et Liberté (April 14, 2017). When required, the study was approved by each national or regional Ethical Committee or Institutional Review Board, according to local regulations. Written informed consent was obtained from all participants.

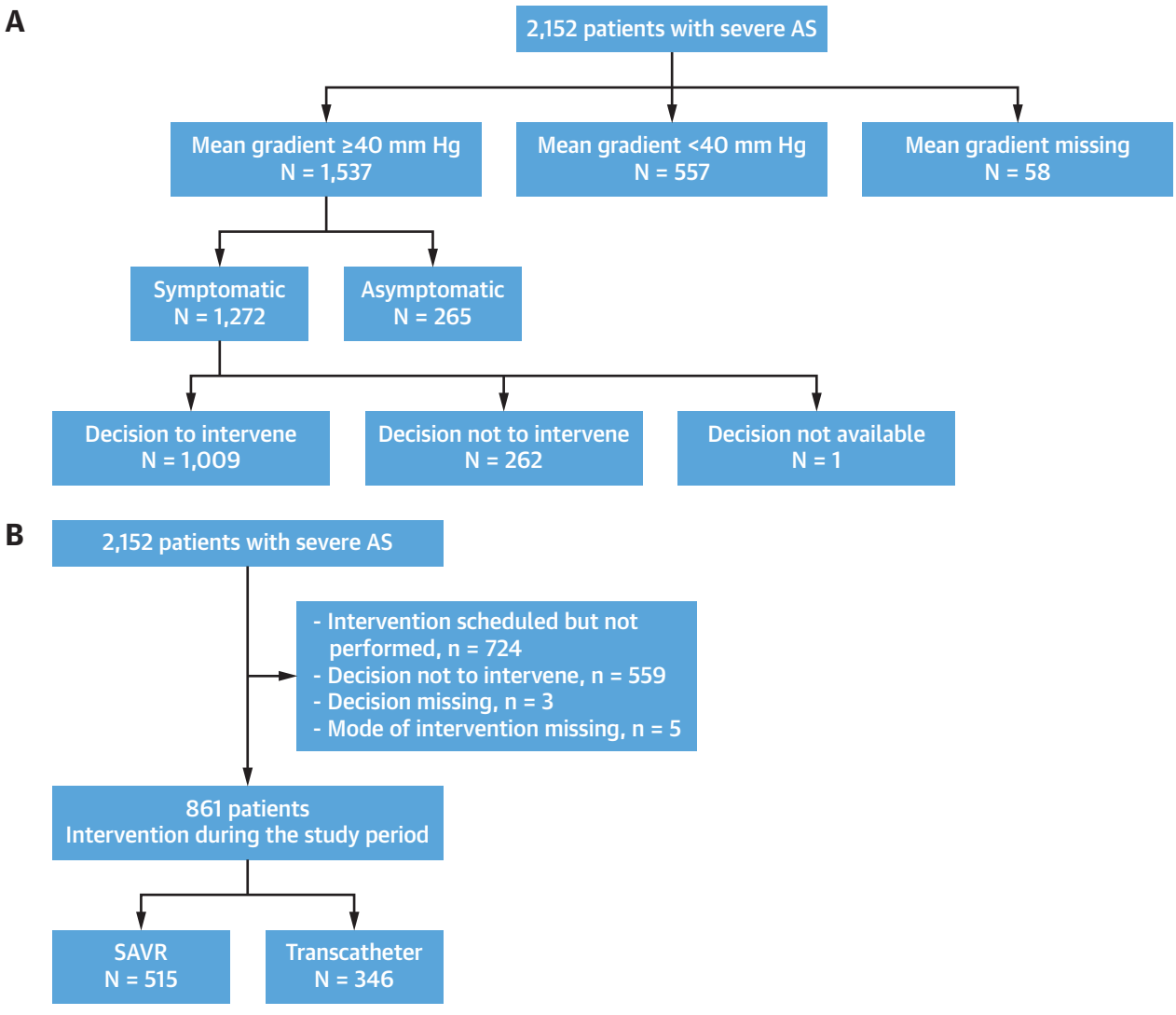
From the 2,152 patients with severe AS (**Figure 1, Supplemental Table 1**) who have been previously described (7), we specifically studied 2 topics: 1) the decision taken by the responsible practitioner to intervene (both SAVR and transcatheter) or not was analyzed among the subgroup of patients with high-gradient AS who were symptomatic (n = 1,271), which correspond to consistent Class I recommendations for intervention according to the 2012 ESC/European Association for Cardiothoracic Surgery (EACTS) VHD guidelines and the 2014 AHA/ACC guidelines, which were applicable at the time of the survey (8,9); and 2) the mode of intervention was analyzed among the population of patients with AS who actually underwent intervention during the study period.

DECISION FOR INTERVENTION. The primary endpoint of the VHD II survey was the final therapeutic decision for surgical or transcatheter intervention determined during the index hospitalization or outpatient visit. Factors associated with a decision not to intervene were analyzed in 1,271 patients who were symptomatic (New York Heart Association [NYHA] functional class ≥II or angina) with transaortic mean gradient ≥40 mm Hg, corresponding to conditions fulfilling Class I recommendations for intervention according to the 2012 ESC/EACTS guidelines and the 2014 AHA/ACC guidelines.

MODE OF INTERVENTION. During the study period, 866 of 2,152 patients with AS underwent aortic valve intervention. Five patients were excluded because of missing information concerning the mode of intervention.

6-MONTH FOLLOW-UP. Six-month follow-up was prespecified in the VHD II survey and was reported by the investigators. Among the 1,271 patients with a Class I indication for intervention, 6-month survival and events occurring during follow-up were analyzed according to the initial decision for intervention,

FIGURE 1 Distribution of Patients With AS According to the Presentation of AS



(A) The flow chart shows the categorization of the 2,152 patients with severe aortic stenosis (AS) into symptomatic high-gradient AS, asymptomatic high-gradient AS, low-gradient AS and patients with missing data for gradient. **(B)** The flow chart shows the distribution of the 2,152 patients with severe AS according to the type of intervention performed during the survey period whatever the indication. SAVR = surgical aortic valve replacement.

without taking into account subsequent interventions during follow-up.

STATISTICAL ANALYSIS. Continuous variables are reported as median (interquartile range), and categorical variables as percentages. Comparisons between groups were performed with a chi-square or Fisher exact test for categorical variables and a Kruskal-Wallis test for continuous variables. Six-month survival was analyzed using the Kaplan-Meier method and compared according to the decision to intervene using a log-rank test.

Variables associated with a decision not to intervene were identified in univariate analysis comparing the characteristics of patients with a decision to intervene or not, as listed in **Table 1**. Variables with $P < 0.10$ and the 5 geographic regions (Supplemental Table 2) were included in 2 different multivariate logistic regression models: multivariate model 1 included separate comorbidities, whereas multivariate model 2 combined these using the age-adjusted Charlson comorbidity index (10). EuroSCORE (European System for Cardiac Operative Risk Evaluation) II

TABLE 1 Factors Associated With a Decision Not to Intervene in Symptomatic Severe AS: Univariate Analysis

	Severe Symptomatic AS (n = 1,271, 100%)	Decision to Intervene (n = 1,009, 79.4%)	Decision Not to Intervene (n = 262, 20.6%)	*P* Value
Patient characteristics				
Age, y	76.0 (67.0-83.0)	74.0 (66.0-82.0)	79.0 (72.0-85.0)	<0.001
Female	577 (45.4)	453 (44.9)	124 (47.3)	0.48
Body mass index, kg/m^2	28.0 (25.0-31.3) [1,249]	28.0 (24.8-31.6) [995]	28.0 (25.2-31.2) [254]	0.86
Previous coronary intervention	174/1,269 (13.7)	137/1,008 (13.6)	37/261 (14.2)	0.81
Hospitalization for heart failure during the last year	227 (17.9)	173 (17.1)	54 (20.6)	0.19
NYHA functional class				0.002
I[a]	52 (4.1)	40 (4.0)	12 (4.6)	
II	675 (53.1)	521 (51.6)	154 (58.8)	
III	496 (39.0)	416 (41.2)	80 (30.5)	
IV	48 (3.8)	32 (3.2)	16 (6.1)	
Angina pectoris	290 (22.8)	222 (22.0)	68 (26.0)	0.17
Congestive heart failure	224 (17.6)	151 (15.0)	73 (27.9)	<0.001
Atrial fibrillation/flutter	152/1,270 (12.0)	122/1,008 (12.1)	30/262 (11.5)	0.77
Creatinine clearance, mL/min	65.8 (47.5-87.1) [1,218]	67.1 (48.7-89.2) [971]	61.0 (42.7-80.2) [247]	0.004
Risk factors				
Active smoking	116 (9.1)	91 (9.0)	25 (9.5)	0.79
Hypertension	992 (78.0)	781 (77.4)	211 (80.5)	0.28
Dyslipidemia	726 (57.1)	570 (56.5)	156 (59.5)	0.37
Diabetes mellitus	373 (29.3)	294 (29.1)	79 (30.2)	0.75
Family history of cardiovascular disease	152/1,065 (14.3)	119/866 (13.7)	33/199 (16.6)	0.30

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was not included as a covariate because of redundancy with comorbidities. Except for the 5 geographic regions that were forced in the model, variables were selected using a backward procedure with a threshold of $P = 0.05$.

The relationship between 6-month survival and the decision to intervene or not was analyzed using an unadjusted Cox proportional hazard model and 2 different Cox models adjusted according to EuroSCORE II or the Charlson comorbidity index. Proportional hazards assumption was assessed from the analysis of weighted Schoenfeld residuals.

A 2-sided *P* value of <0.05 was considered statistically significant. Analysis was performed with SAS statistical software version 9.4 (SAS Institute Inc).

RESULTS

DECISION FOR INTERVENTION. Among 1,271 patients who were symptomatic with a Class I indication for intervention, 1,009 (79.4%) were referred for SAVR or transcatheter intervention, whereas in 262 patients (20.6%) the decision was not to intervene. Intervention was performed during the recruitment period in 570 patients (56.5%) and scheduled in 439 (43.5%). A decision for intervention was taken in 259 of 331 patients (78.2%) aged ≥75 years and in NYHA functional classes III and IV.

In univariate analysis of these 1,271 patients, factors associated with a decision not to intervene were older age, NYHA functional class, congestive heart failure, lower creatinine clearance, presence of comorbidities, and lower mean gradient (**Table 1**). **Figure 2** shows the therapeutic decision according to age. A decision not to intervene was taken in 14.7% of patients aged <75 years, 27.4% of patients aged 75-79 years, and 27.3% of patients aged ≥80 years. Left ventricular ejection fraction was not associated with the decision for intervention (Supplemental Figure 1).

In the multivariate analysis including separate comorbidities, factors independently associated with a decision not to intervene were older age, NYHA functional classes I and II (vs III), congestive heart failure, limited mobility, lower limb atherosclerosis, and lower mean gradient (**Table 2**).

In the multivariate analysis including age-adjusted Charlson comorbidity index, factors independently associated with a decision not to intervene were older age, NYHA functional classes I and II (vs III), higher Charlson comorbidity index, and lower mean gradient (**Table 3**).

MODE OF INTERVENTION. Among 861 patients for whom data concerning the mode of intervention were available, SAVR was performed in 515 and transcatheter intervention in 346 (TAVR 333, balloon aortic valvuloplasty 13). Patients who underwent

TABLE 1 Continued

	Severe Symptomatic AS (n = 1,271, 100%)	Decision to Intervene (n = 1,009, 79.4%)	Decision Not to Intervene (n = 262, 20.6%)	*P* Value
Comorbidities				
Chronic dialysis	11 (0.9)	8 (0.8)	3 (1.1)	0.71
Chronic pulmonary disease	163/1,267 (12.9)	119/1,007 (11.8)	44/260 (16.9)	0.03
Liver dysfunction	19/1,264 (1.5)	15/1,008 (1.5)	4/256 (1.6)	1.0
Previous myocardial infarction	100/1,261 (7.9)	67/1,001 (6.7)	33/260 (12.7)	0.001
Lower limbs atherosclerosis	77/1,200 (6.4)	53/975 (5.4)	24/225 (10.7)	0.004
Limited mobility	95 (7.5)	57 (5.6)	38 (14.5)	<0.001
Cancer				0.55
Active	36 (2.8)	27 (2.7)	9 (3.4)	
Remission	94 (7.4)	78 (7.7)	16 (6.1)	
Dementia	15 (1.2)	8 (0.8)	7 (2.7)	0.02
Previous stroke/TIA	86 (6.8)	62 (6.1)	24 (9.2)	0.08
Charlson comorbidity index	4.0 (3.0-6.0) [1,174]	4.0 (3.0-5.0) [931]	5.0 (3.0-6.0) [243]	<0.001
EuroSCORE II	1.9 (1.1-3.2) [1,160]	1.8 (1.1-3.0) [943]	2.1 (1.3-4.1) [217]	0.001
Transthoracic echocardiography				
LV ejection fraction				0.29
<30%	19/1,256 (1.5)	13/997 (1.3)	6/259 (2.3)	
30%-40%	63/1,256 (5.0)	45/997 (4.5)	18/259 (6.9)	
40%-50%	108/1,256 (8.6)	86/997 (8.6)	22/259 (8.5)	
50%-60%	390/1,256 (31.1)	306/997 (30.7)	84/259 (32.4)	
≥60%	676/1,256 (53.8)	547/997 (54.9)	129/259 (49.8)	
Valve area, cm^2	0.7 (0.6-0.8) [1,094]	0.7 (0.6-0.8) [863]	0.7 (0.6-0.8) [231]	0.94
Mean gradient, mm Hg	53.0 (46.0-63.0)	54.0 (47.0-64.0)	50.0 (45.0-60.0)	<0.001
Aortic regurgitation ≥ moderate	153 (12.0)	120 (11.9)	33 (12.6)	0.76
Diameter of ascending aorta				
≥45 mm	65/1,036 (6.3)	54/817 (6.6)	11/219 (5.0)	0.39
≥55 mm	3/1,036 (0.3)	2/817 (0.2)	1/219 (0.5)	0.51
SPAP				0.34
<30 mm Hg	521/1,143 (45.6)	403/906 (44.5)	118/237 (49.8)	
30-55 mm Hg	531/1,143 (46.5)	430/906 (47.5)	101/237 (42.6)	
>55 mm Hg	91/1,143 (8.0)	73/906 (8.1)	18/237 (7.6)	
Geographical region				<0.001
Western Europe	409 (32.2)	364 (36.1)	45 (17.2)	
Northern Europe	82 (6.5)	73 (7.2)	9 (3.4)	
Eastern Europe	467 (36.7)	396 (39.2)	71 (27.1)	
Southern Europe	301 (23.7)	166 (16.5)	135 (51.5)	
North Africa	12 (0.9)	10 (1.0)	2 (0.8)	

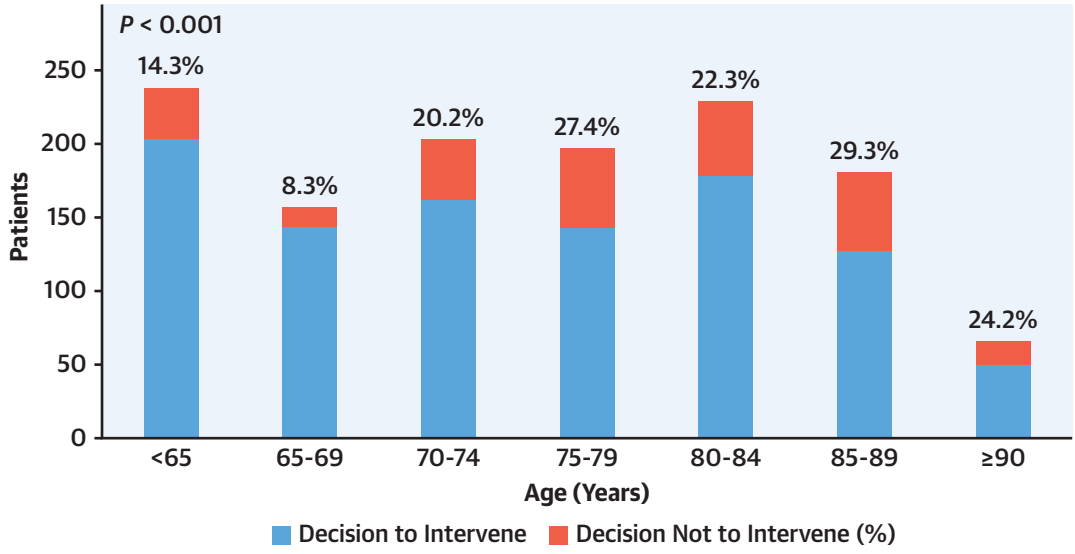
Values are median (interquartile range) or n/N (%). Denominator or [number of patients] is specified in case of missing data. All patients had a Class I indication for intervention. [a]Patients in NYHA functional class I were considered symptomatic because they all had angina pectoris.

AS = aortic stenosis; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LV = left ventricular; NYHA = New York Heart Association; SPAP = systolic pulmonary artery pressure; TIA = transient ischemic attack.

transcatheter intervention were on average 15 years older, more frequently female, had more comorbidities, and had more advanced heart disease (more severe symptoms, more frequent atrial fibrillation, and higher systolic pulmonary artery pressure) (**Table 4**). EuroSCORE II was 2-fold higher than in patients who underwent SAVR. Transcatheter intervention was performed in 9.1% of patients aged <75 years, 35.3% of patients aged 75-79 years, and 84.1% of patients aged ≥80 years. The mode of intervention according to age is detailed in **Figure 3**. There was no association between the mode of intervention and left ventricular ejection fraction (Supplemental Figure 2).

Of the 515 patients who underwent SAVR, 178 (34.6%) received a mechanical prosthesis, 322 (62.5%) a bioprosthesis, 10 (1.9%) a autograft, 2 (0.4%) a homograft, and 3 (0.6%) had valve repair. Associated procedures were coronary artery bypass graft in 133 patients (25.8%) and surgery on ascending aorta in 39 (7.6%); percutaneous coronary intervention was performed in 11 patients (2.1%). Of the 333 patients who underwent TAVR, 178 (53.5%) received a self-expandable prosthesis, 152 (45.6%) a balloon-

FIGURE 2 Decision to Intervene According to Age



The decision to intervene was analyzed in the 1,271 patients with severe aortic stenosis and Class I indications for intervention. The decision to intervene decreased significantly but moderately with increasing age. The decrease in indications after the age of 80 years was less pronounced than in the 2001 Euro Heart Survey (2).

expandable prosthesis, and 3 (0.9%) another type of prosthesis. The approach was transfemoral in 308 patients (92.5%), transapical in 12 (3.6%), subclavian in 5 (1.5%), and another approach was used in 8 (2.4%). Percutaneous coronary intervention was performed in 35 patients (10.5%).

In-hospital outcomes according to the type of intervention are detailed in Supplemental Table 3.

There were considerable regional differences in the use of transcatheter intervention, varying from 9.2%-69.7% across European regions and North Africa—patients were older in regions where TAVR was more widely used (**Table 5,** Supplemental Figure 3).

6-MONTH FOLLOW-UP. Among 1,271 patients who were symptomatic with a Class I indication for intervention, 6-month vital status was known in 900 patients (89.2%) with a decision to intervene and 225 patients (85.9%) with a decision not to intervene. Median follow-up was 180 days (interquartile range: 159-180 days). Six-month survival rates were 94.6% (95% CI: 92.8-95.9) and 87.4% (95% CI: 82.0-91.3), respectively ($P < 0.001$) (**Central Illustration**). The decision not to intervene was significantly associated with higher 6-month mortality, even after adjustment for EuroSCORE II or Charlson comorbidity index (**Table 6**).

Events occurring during follow-up are represented in Supplemental Table 4. The percentage of patients who underwent valvular intervention within 6 months after index hospitalization or outpatient visit was 50.3% when the initial decision was to intervene and intervention was scheduled but not performed and 20.1% when the initial decision was not to intervene.

DISCUSSION

In this international survey involving a wide range of public and private centers, a decision not to intervene was taken in 20.6% of patients included during a 3-month period in 2017 with severe symptomatic AS, despite a Class I indication according to ESC/EACTS and AHA/ACC guidelines. Older age, mild symptoms, congestive heart failure, and combined comorbidities were the main patient characteristics associated with a decision not to intervene. Despite important geographical discrepancies, TAVR represented almost 40% of interventions and was performed in more than 80% of octogenarians and nonagenarians. The decision not to intervene was associated with higher 6-month mortality.

INTERVENTIONAL DECISION MAKING. We chose to analyze the adherence to guidelines for

interventions in patients with severe high-gradient AS who were symptomatic because this corresponds to Class I indications in both ESC/EACTS and AHA/ACC guidelines (8,9), which were applicable at the time of the survey and remained unchanged in 2017 (5,11).

The decision not to intervene in patients aged ≥75 years and in NYHA functional classes III and IV fell from 33.3% in the 2001 Euro Heart Survey to 21.8% in VHD II (2). This marked improvement in adherence to guidelines may relate to publication of ESC guidelines on VHD in 2007 and 2012 and their consistency with AHA/ACC guidelines. In addition, the availability of TAVR led to intervention in more patients with AS during the last decade (12,13).

The strong influence of age on interventional decision making has already been observed in the 2001 Euro Heart Survey and other studies (2-4). However, the association with age now seems less important because a decision not to intervene was made for <30% of octogenarians and nonagenarians (compared with almost 50% in the 2001 Euro Heart Survey). Mortality in octogenarians is acceptable after SAVR in selected patients (14,15), and TAVR is safe and effective if the risk of SAVR is high or prohibitive (16-18). Evidence supporting TAVR appears to be a strong incentive for clinicians to screen a wider range of patients for intervention.

In contrast with the 2001 Euro Heart Survey, combined comorbidities (defined by a higher Charlson comorbidity index) were associated with a decision not to intervene. Increased awareness of the contribution of overall comorbidity assessment to clinical decision making may be explained by development of the heart team concept in the 2010s (8,9). Suboptimal performance of risk scores has also led to a greater appreciation of the benefits of multidisciplinary assessment (19,20). Lower limb atherosclerosis was the only individual comorbidity associated with a decision not to intervene. Limited mobility, which is a component of frailty, was also associated with a decision not to intervene.

Patients who are symptomatic have a dismal prognosis compared with those who are asymptomatic; however, a decision not to intervene was more frequently taken in patients with mild symptoms (NYHA functional class II) despite a Class I indication in guidelines (5,6,9,11). This suggests subjectivity of symptom interpretation and that practitioners may be reluctant to intervene early after symptom onset, although intervention is recommended as soon as patients become symptomatic (5,6). Conversely, a decision not to intervene was more frequently taken in patients with congestive heart failure, despite their high risk of early death and the clear benefits of intervention (5,6).

TABLE 2 Factors Associated With a Decision Not to Intervene in Symptomatic Severe AS: Multivariate Model 1

	Odds Ratio	95% CI	*P* Value
Age per 10-y increase	1.46	1.22-1.75	<0.001
NYHA functional class[a]			
I-II vs III	1.86	1.30-2.68	<0.001
I-II vs IV	0.87	0.40-1.93	0.74
Congestive heart failure at the time of examination	1.68	1.11-2.54	0.015
Lower limbs atherosclerosis	1.90	1.07-3.35	0.028
Limited mobility	1.79	1.04-3.07	0.036
Aortic mean gradient (per 10–mm Hg decrease)	0.81	0.71-0.92	0.001

All patients had a Class I indication for intervention. Multivariate model 1 includes separate comorbidities. [a]Overall $P = 0.002$ for NYHA functional class.
Abbreviations as in Table 1.

Lower left ventricular ejection fraction was no longer associated with a decision not to intervene in the present survey, whereas an ejection fraction <50% was significantly associated with a decision not to operate in the 2001 Euro Heart Survey (2), suggesting more appropriate analysis of the risk-benefit ratio of interventions in the VHD II survey than in the Euro Heart Survey. Relief of AS in patients with severe AS and low left ventricular ejection fraction (particularly those with high gradient) is associated with improved long-term survival compared with outcomes associated with medical therapy (21-23).

The objective patient characteristics associated with a decision not to intervene in multivariate analysis (particularly older age, comorbidities, and limited mobility) may correspond to procedures that were considered futile. A decision not to intervene may therefore be justified in certain patients in whom the benefit on survival and functional improvement may be questionable or hardly predictable (24,25). The appropriateness of the decision to intervene cannot be assessed for an individual

TABLE 3 Factors Associated With a Decision Not to Intervene in Symptomatic Severe AS: Multivariate Model 2

	Odds Ratio	95% CI	*P* Value
Age per 10-y increase	1.34	1.11-1.61	0.002
NYHA functional class[a]			
I-II vs III	1.63	1.16-2.30	0.005
I-II vs IV	1.06	0.45-2.48	0.90
Charlson comorbidity index per 1-point increase	1.09	1.01-1.17	0.03
Aortic mean gradient per 10-mm Hg decrease	0.81	0.71-0.92	<0.001

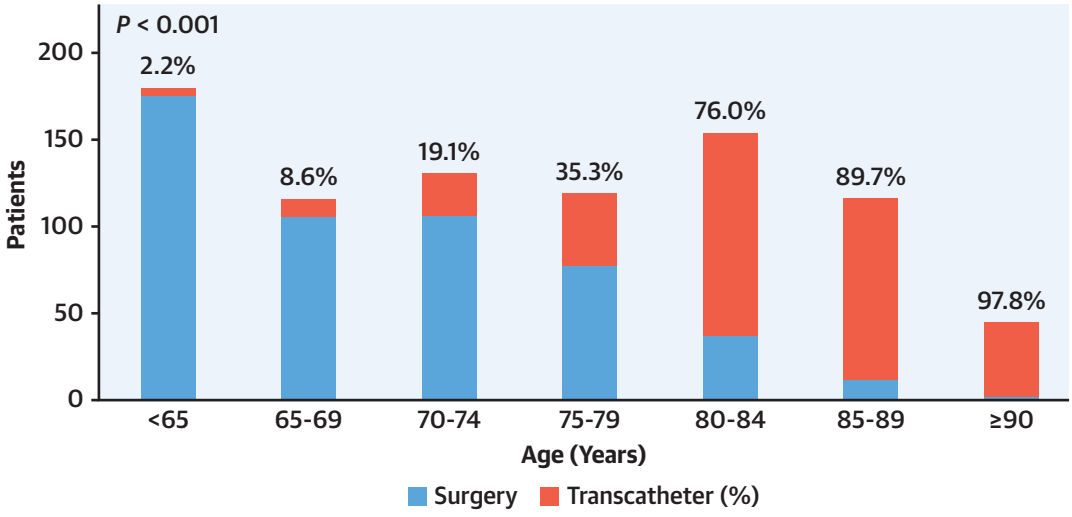
All patients had a Class I indication for intervention. Multivariate model 2 includes comorbidities combined in the Charlson comorbidity index. [a]Overall $P = 0.02$ for NYHA functional class.
Abbreviations as in Table 1.

TABLE 4 Comparison Between Patients With Severe AS Who Underwent Surgery or Transcatheter Intervention During the Study Period

	AS (n = 861, 100.0%)	Surgery (n = 515, 59.8%)	Transcatheter (n = 346, 40.2%)	*P* Value
Patient characteristics				
Age, y	75.0 (66.0-83.0)	69.0 (61.0-74.0)	84.0 (80.0-87.0)	<0.001
Female	381 (44.3)	209 (40.6)	172 (49.7)	0.008
Body mass index, kg/m^2	28.0 (25.0-31.3) [853]	28.7 (25.9-32.1) [507]	27.0 (24.0-30.5) [346]	<0.001
Previous coronary intervention	150/859 (17.5)	50/514 (9.7)	100/345 (29.0)	<0.001
Hospitalization for heart failure during the last year	139 (16.1)	77 (15.0)	62 (17.9)	0.25
NYHA functional class				<0.001
I	89 (10.3)	68 (13.2)	21 (6.1)	
II	364 (42.3)	242 (47.0)	122 (35.3)	
III	379 (44.0)	192 (37.3)	187 (54.0)	
IV	29 (3.4)	13 (2.5)	16 (4.6)	
Angina pectoris	158 (18.4)	117 (22.7)	41 (11.8)	<0.001
Congestive heart failure	102 (11.8)	57 (11.1)	45 (13.0)	0.39
Atrial fibrillation/flutter	112 (13.0)	42 (8.2)	70 (20.2)	<0.001
Creatinine clearance, mL/min	66.3 (49.1-90.2) [846]	78.1 (60.4-100.3) [501]	51.5 (38.7-66.7) [345]	<0.001
Risk factors				
Active smoking	96 (11.1)	74 (14.4)	22 (6.4)	<0.001
Hypertension	678 (78.7)	396 (76.9)	282 (81.5)	0.11
Dyslipidemia	460 (53.4)	257 (49.9)	203 (58.7)	0.01
Diabetes mellitus	232 (26.9)	140 (27.2)	92 (26.6)	0.85
Family history of cardiovascular disease	82/719 (11.4)	68/431 (15.8)	14/288 (4.9)	<0.001
Comorbidities				
Chronic dialysis	6 (0.7)	3 (0.6)	3 (0.9)	0.69
Chronic pulmonary disease	106/856 (12.4)	45/514 (8.8)	61/342 (17.8)	<0.001
Liver dysfunction	13/859 (1.5)	8/514 (1.6)	5/345 (1.4)	0.90
Previous myocardial infarction	66/855 (7.7)	29/511 (5.7)	37/344 (10.8)	0.006
Coronary artery disease[a]	282/653 (43.2)	160/388 (41.2%)	122/265 (46.0)	0.22
Lower limbs atherosclerosis	55/826 (6.7)	18/493 (3.7)	37/333 (11.1)	<0.001
Limited mobility	47 (5.5)	11 (2.1)	36 (10.4)	<0.001
Previous or active cancer	97 (11.3)	40 (7.8)	57 (16.5)	<0.001
Dementia	8 (0.9)	1 (0.2)	7 (2.0)	0.009
Previous stroke/TIA	62 (7.2)	27 (5.2)	35 (10.1)	0.007
Porcelain aorta	13/847 (1.5)	1/510 (0.2)	12/337 (3.6)	<0.001
Chest deformation	3/860 (0.3)	0 (0.0)	3/345 (0.9)	0.06
Previous thoracic radiation	15 (1.7)	7 (1.4)	8 (2.3)	0.30
Charlson comorbidity index	4.0 (3.0-6.0) [762]	3.0 (2.0-4.0) [482]	5.0 (4.0-7.0) [280]	<0.001
EuroSCORE II	2.0 (1.2-3.6) [790]	1.5 (0.9-2.6) [485]	3.1 (2.0-5.1) [305]	<0.001
Transthoracic echocardiography				
LV ejection fraction				0.75
<30%	14/845 (1.7)	10/514 (1.9)	4/331 (1.2)	
30%-40%	52/845 (6.2)	34/514 (6.6)	18/331 (5.4)	
40%-50%	88/845 (10.4)	54/514 (10.5)	34/331 (10.3)	
50%-60%	239/845 (28.3)	149/514 (29.0)	90/331 (27.2)	
≥60%	452/845 (53.5)	267/514 (51.9)	185/331 (55.9)	
Valve area, cm^2	0.8 (0.6-0.9) [716]	0.8 (0.6-0.9) [402]	0.7 (0.6-0.9) [314]	0.29
Mean gradient, mm Hg	49.0 (41.0-61.0) [830]	50.0 (42.0-63.0) [497]	47.0 (40.0-57.0) [333]	<0.001
Aortic regurgitation ≥moderate	101 (11.7)	70 (13.6)	31 (9.0)	0.04
SPAP				<0.001
<30 mm Hg	291/737 (39.5)	240/457 (44.6)	87/280 (31.1)	
30-55 mm Hg	388/737 (52.6)	225/457 (49.2)	163/280 (58.2)	
>55 mm Hg	58/737 (7.9)	28/457 (6.1)	30/280 (10.7)	

Values are median (interquartile range) or n/N (%). Denominator or [number of patients] is specified in case of missing data. [a]At least 1 stenosis >50% of vessel diameter.
Abbreviations as in Table 1.

FIGURE 3 Mode of Intervention According to Age



The mode of intervention was analyzed in the 861 patients with severe aortic stenosis. There was a steep increase in the performance of transcatheter interventions after the age of 80 years, suggesting that age played a major role in the choice between surgery and transcatheter interventions, even in patients deemed at low risk.

patient in the present survey. However, analysis of the relationship between the therapeutic decision and a wide range of prespecified cardiac and noncardiac characteristics allows capture of the most striking characteristics underpinning the decision-making process.

The main differences with the Euro Heart Survey on VHD and the VHD II survey are summarized in Supplemental Table 5.

MODE OF INTERVENTION. We observed a progressive increase in the proportion of transcatheter interventions according to age from 65 years onward, and a marked shift from SAVR to TAVR after the age of 80 years, where TAVR accounted for more than 80% of interventions. The growing importance of TAVR in octogenarians shown in a recent nationwide study is confirmed here in a wide range of countries (12). In the VHD II survey, patients who underwent transcatheter interventions were at higher risk for SAVR. However, their median EuroSCORE II was only 3.1%. Therefore, not all patients were at high or prohibitive risk for SAVR as recommended in the 2012 ESC VHD guidelines, which were applicable at the time of the survey. Since 2012, randomized trials have shown noninferiority of TAVR in patients at lower risk for surgery and subsequent ESC/EACTS and ACC/AHA VHD guidelines further expanded the potential indications for TAVR (5,6). The more frequent use of TAVR versus SAVR in Western Europe suggests, as in the United States, anticipation in the extension of indications for TAVR in patients who are at low risk before guidelines are updated (26).

Major geographical variations were observed, with high use of TAVR in Western Europe (69.7% of patients) and much more marginal use in Eastern Europe (9.2% of patients). Disparities in the implementation of TAVR (Supplemental Figure 4) (27) are partly related to local availability and health care resources, as well as also to major differences in the proportion of octogenarians (62.7% in Western Europe, 9.2% in Eastern Europe).

FOLLOW-UP. Six-month survival was higher if a decision was taken to intervene, and this difference remained highly significant after adjustment for risk scores. Six-month survival was poor after initial decision not to intervene and consistent with the natural history of severe symptomatic AS.

Among patients with a decision to intervene but who had an intervention scheduled but not performed during the recruitment period, only 50.3% actually underwent intervention within 6 months. Deferring intervention is associated with a risk of mortality during waiting time. In addition, intervention at a later stage may increase early mortality and compromise the quality of late results.

CLINICAL IMPLICATIONS. The findings from the VHD II survey highlight the need for increased awareness toward patients with severe AS as soon as

TABLE 5 Characteristics and Type of Intervention Performed in Patients With Severe AS According to the 5 Regions

	Northern Europe (n = 75)	Western Europe (n = 346)	Eastern Europe (n = 315)	Southern Europe (n = 119)	North Africa (n = 6)	*P* Value
Patient characteristics						
Age, y	76.0 (68.0-81.0)	82.0 (75.0-86.0)	68.0 (60.0-73.0)	74.0 (68.0-82.0)	69.0 (49.0-80.0)	<0.001
≥80 y	27 (36.0)	217 (62.7)	29 (9.2)	40 (33.6)	2 (33.3)	<0.001
Female	31 (41.3)	165 (47.7)	147 (46.7)	36 (30.3)	2 (33.3)	0.015
NYHA functional classes III-IV	46 (61.3)	169 (48.8)	149 (47.3)	41 (34.5)	3 (50.0)	0.007
Charlson comorbidity index	4.5 (3.0-6.0) [70]	5.0 (4.0-6.0) [269]	3.0 (2.0-4.0) [313]	4.0 (3.0-6.0) [109]	4.0 (4.0-4.0) [1]	<0.001
EuroSCORE II	2.4 (1.4-3.5) [70]	2.6 (1.6-4.3) [294]	1.5 (0.9-2.6) [314]	2.0 (1.3-4.2) [108]	4.0 (3.2-5.8) [4]	<0.001
LVEF <50%	12 (16.0)	49 (14.2)	57 (18.1)	34 (28.6)	2 (33.3)	0.008
Type of intervention						
Surgery	43 (57.3)	105 (30.3)	286 (90.8)	78 (65.5)	3 (50.0)	<0.001
Mechanical prosthesis	11 (25.6)	15 (14.3)	116 (40.6)	36 (46.2)	0	
Bioprosthesis	32 (74.4)	88 (83.8)	157 (54.9)	42 (53.8)	3 (100.0)	
Valve repair	0	0	3 (1.0)	0	0	
Autograft	0	2 (1.9)	8 (2.8)	0	0	
Homograft	0	0	2 (0.7)	0	0	
Associated CABG	16 (37.2)	30 (28.6)	66 (23.1)	21 (26.9)	0	
Associated surgery of the aorta	5 (11.6)	9 (8.6)	21 (7.3)	4 (5.1)	0	
Transcatheter	32 (42.7)	241 (69.7)	29 (9.2)	41 (34.5)	3 (50.0)	<0.001
TAVR	31 (96.9)	235 (97.5)	25 (86.2)	39 (95.1)	3 (100.0)	
Percutaneous balloon aortic valvuloplasty	1 (3.1)	6 (2.5)	4 (13.8)	2 (4.9)	0	

Values are median (interquartile range) or n/N (%). Denominator or [number of patients] is specified in case of missing data.
CABG = coronary artery bypass graft; LVEF = left ventricular ejection fraction; TAVR = transcatheter aortic valve replacement; other abbreviations as in Table 1.

they develop mild symptoms (NYHA functional class II dyspnea) because they derive the greatest benefit from valvular intervention. The timing of surgery should also be improved because only one-half of the patients who had intervention scheduled actually underwent intervention within 6 months. When intervention is scheduled, it should be performed rapidly because of the risk of death during prolonged waiting times (28),

STUDY LIMITATIONS. This voluntary survey was not population-based, and there may be legitimate concerns concerning its ability to represent wider practice because of potential selection, referral, and treatment bias. However, the design of the present survey allows for a detailed analysis of the relationship between patient characteristics and therapeutic decision in the light of ESC guidelines in a wide spectrum of health care structures and countries.

Analysis of decision making was limited to patients with severe symptomatic AS and transaortic mean gradient ≥40 mm Hg who fulfilled Class I recommendation for intervention according to the 2012 ESC/EACTS VHD guidelines. This Class I recommendation is unchanged in more recent guidelines (5,6,8). The results cannot therefore be expanded to patients who are asymptomatic or those with low-flow low-gradient AS.

Echocardiographic data were reported by the investigators and no quality control was performed. Left ventricular volumes, right ventricular function, and natriuretic peptides were not collected. Missing data and concerns on data accuracy are inherent to large surveys performed in a wide range of centers. In particular, the lack of standardized assessment of frailty precluded an objective assessment in across a large number of centers (29).

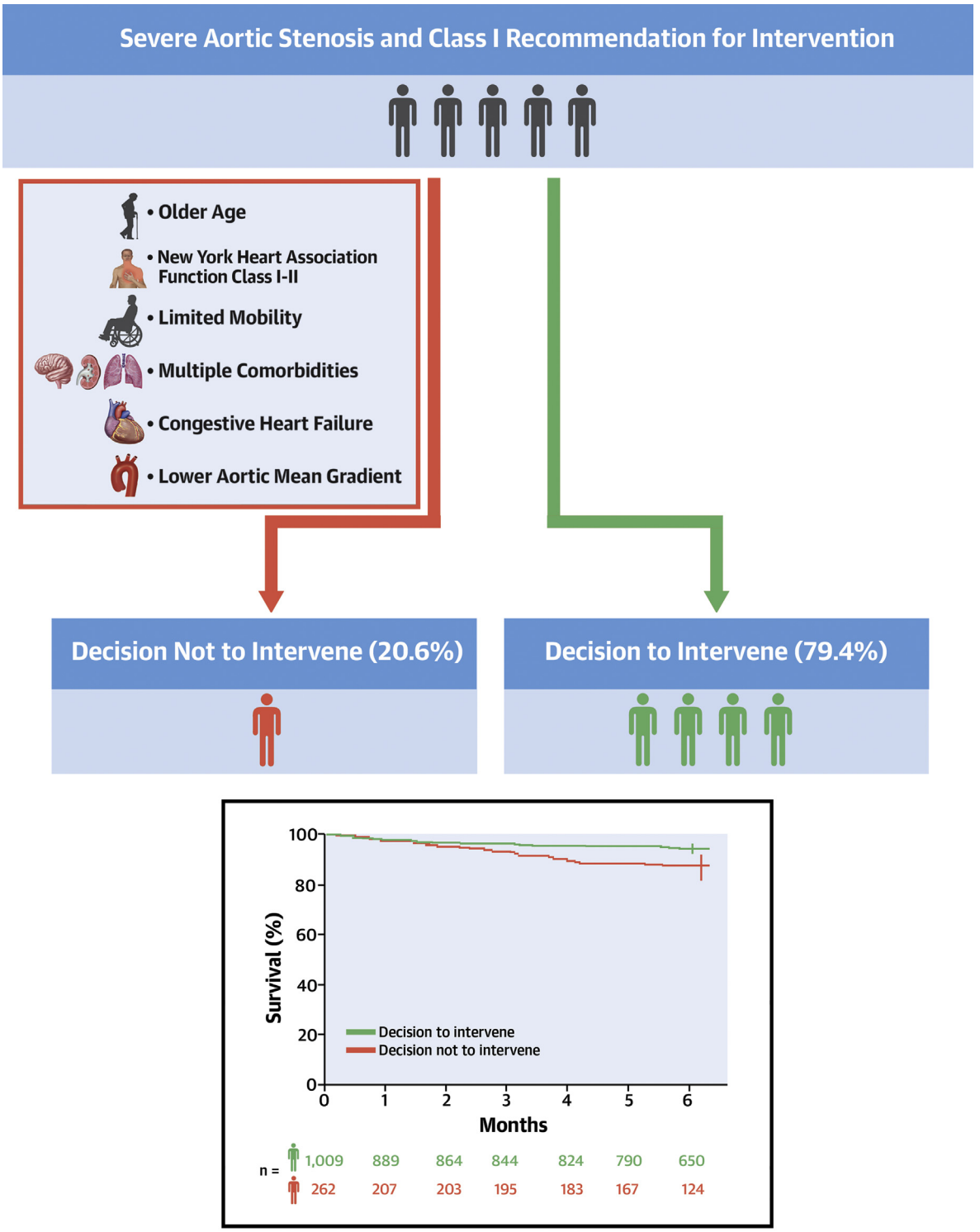
Follow-up was limited to 6 months in the VHD II protocol. Despite relatively short follow-up there was, however, a significant relationship between initial therapeutic decision and mortality.

Survey findings concerning the mode of intervention correspond to 2017 and are subject to changes with the extension of indications for TAVR to patients at lower risk for surgery.

CONCLUSIONS

In the time interval between the 2001 Euro Heart Survey and 2017 VHD II surveys (both specifically designed to analyze clinical decision making in VHD), the proportion of patients with severe symptomatic AS and a decision not to intervene fell from one-third to one-fifth. This is the first time that 2 surveys following the same methodology showed a marked

CENTRAL ILLUSTRATION **Survival at 6 Months According to the Decision for Intervention**



Eugène, M. et al. J Am Coll Cardiol. 2021;78(22):2131–2143.

Six-month survival is represented in the 1,271 patients with severe aortic stenosis and Class I indications for intervention. A decision not to intervene was taken by the responsible practitioner for 1 in 5 patients with severe symptomatic AS and a Class I recommendation for intervention. The decision not to intervene was particularly associated with older age and combined comorbidities. A decision not to intervene was associated with lower 6-month survival. Factors associated with a decision not to intervene are represented without taking into account their respective strengths. NYHA = New York Heart Association.

TABLE 6 HRs for Death at 6 Months According to the Decision to Intervene or Not

	HR	95% CI	*P* Value	*P* Schoenfeld Residuals[a]
Unadjusted				<0.05
Decision not to intervene	2.37	1.53-3.69	<0.001	
Adjusted on EuroSCORE II				<0.05
Decision not to intervene	2.36	1.46-3.80	<0.001	
EuroSCORE II per 1% increase	1.12	1.08-1.16	<0.001	
Adjusted on Charlson comorbidity index				>0.05
Decision not to intervene	2.03	1.28-3.23	0.003	
Charlson comorbidity index per 1-point increase	1.28	1.20-1.35	<0.001	

[a]Global correlation test based of the weighted Schoenfeld residuals.
EuroSCORE = European System for Cardiac Operative Risk Evaluation.

improvement in adherence to guidelines in a large number of centers in diverse countries. Besides improved implementation of guidelines with regard to indications for intervention, the advent of TAVR enabled the consideration of intervention in a wider range of patients with AS. Older age and combined comorbidities were linked with the decision not to intervene, whereas there was no longer any relationship with left ventricular ejection fraction, suggesting more appropriate risk-benefit analysis for decision making in the 2017 VHD II survey than in the 2001 Euro Heart Survey. However, another novel finding is that patients are still referred at an advanced stage of disease because a decision to intervene was less frequently taken in patients with mild symptoms. The choice between transcatheter interventions and SAVR pays important attention to age, whereas surgical risk scores attest that the use of TAVR is not restricted to patients at increased risk of SAVR. This is particularly illustrated by the extensive use of TAVR in octogenarians. The present findings support guideline-based educational initiatives aimed at practitioners and patients to improve early referral and health care policies that homogenize access to TAVR across different regions.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with severe AS who are symptomatic, adherence to guidelines for interventions improved between 2001 and 2017, but patients are still frequently referred with severe symptoms.

TRANSLATIONAL OUTLOOK: Repeated surveys that assess guideline implementation are necessary to improve outcomes for patients with AS because the evolution of transcatheter techniques will continue to change management.

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KEY WORDS aortic stenosis, decision making, guidelines, surgical aortic valve replacement, transcatheter aortic valve replacement

APPENDIX For the list of EORP VHD II Registry investigators and the supplemental figures and tables, please see the online version of this paper.