Role of a heart valve clinic programme in the management of patients with aortic stenosis

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Aims

We sought to assess the efficacy of a heart valve clinic (HVC) follow-up programme for patients with severe aortic stenosis (AS).

Methods and results

Three hundred and eighty-eight consecutive patients with AS (age 71 ± 10 years; aortic-jet velocity 5.1 ± 0.6 m/s) and an indication for aortic valve replacement (AVR) were included. Of these, 290 patients presented with an indication for surgery at their first visit at the HVC and 98 asymptomatic patients who had been enrolled in an HVC monitoring programme developed indications for surgery during follow-up. Time to symptom detection was significantly longer in patients that presented with symptoms at baseline (352 ± 471 days) than in patients followed in the HVC (76 ± 75 days, $P < 0.001$). Despite being educated to recognize and promptly report new symptoms, 77 of the 98 patients in the HVC programme waited until the next scheduled consultation to report them. Severe symptom onset (NYHA or CCS Class $\geq$ III) was present in 61% of patients being symptomatic at the initial visit and in 34% of patients in the HVC programme ($P < 0.001$).

Conclusion

Delays in referral and symptom reporting as well as symptom denial are common in patients with AS. These findings support the concept of risk stratification to identify patients who may benefit from elective surgery. A structured HVC programme results in the detection of symptoms at an earlier and less severe stage and thus in an optimized timing of surgery.

Keywords

aortic stenosis • heart valve clinic • aortic valve replacement

Introduction

Aortic stenosis (AS) is the most frequent heart valve disease requiring surgery and its incidence is further increasing.[1] The natural history of severe AS is characterized by an asymptomatic phase with increasing left ventricular outflow tract obstruction and left ventricular pressure overload. Asymptomatic patients with severe AS can be managed according to a 'watchful waiting strategy', although elective surgery can be considered in selected patients after risk stratification. After the onset of symptoms, the outcome of patients with severe AS is dismal with conservative management[2,3] and aortic valve replacement (AVR) should be performed without delay.[4,5] However, from 30 to 50% of patients with an established indication for AVR are denied such a procedure. Undertreatment of AS is in part due to delays in symptom recognition and also late referral for intervention. Although the potential role of heart valve clinics (HVCs) for the management of patients with valvular heart disease (VHD) is increasingly recognized,[6,7] their clinical impact has not yet been evaluated.

The present study sought to evaluate the role of an HVC follow-up programme for the management of patients with severe AS and to evaluate its potential to reduce delays in symptom recognition and reporting and on the severity of symptoms at presentation.

Methods

Patient population

Consecutive patients who were assessed in the outpatient clinic for VHD at Medical University of Vienna between 2000 and 2010 who had an indication for AVR based on current practice guidelines due to severe AS defined by a peak aortic jet velocity ≥ 4.0 m/s and an aortic

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valve area ≤ 1.0 cm^2 were prospectively included into the study when they had no additional haemodynamically significant valve lesions (moderate or severe). Patients with low-flow, low-gradient AS were excluded.

According to these criteria, 388 patients (age 71 ± 10 years; 198 female; average peak aortic velocity 5.1 ± 0.6 m/s) were included. The majority of these patients were referred from outpatient care specialist in internal medicine and general cardiologists. At their initial visit, 290 of these patients already had an indication for AVR, while 98 patients were previously asymptomatic and had been enrolled in an HVC follow-up programme comprising 6 monthly clinical and echocardiographic examinations until they reached criteria for surgery. These latter patients had been educated to promptly report symptoms after their onset.

According to the purely observational study design, written informed consent was not demanded. The study protocol was approved by the ethics committee of the Medical University of Vienna.

Clinical data

The following clinical data were collected at study entry: age, gender, history of hypercholesterolaemia (total cholesterol >200 mg/dL or patient under lipid-lowering therapy), diabetes mellitus, arterial hypertension (on the basis of the average of repeated measurements: blood pressure $>140/90$ mmHg) and coronary artery disease (history of myocardial infarction, angioplasty, coronary artery bypass grafting, or angiographically documented coronary artery stenosis).

Echocardiographic data

All patients underwent a comprehensive echocardiographic examination on the basis of a standardized examination protocol including M-Mode, 2D echocardiography, conventional, and colour Doppler by an experienced echocardiographer using commercially available ultrasound systems. Multiple transducer positions were used to record peak aortic jet velocities and aortic valve area was calculated using the continuity equation.[8]

The degree of aortic valve calcification was scored according to the following previously described criteria[9]: (i) no calcification, (ii) mild calcification (isolated, small spots), (iii) moderate calcification (multiple bigger spots), and (iv) heavy calcification (extensive thickening/calcification of all cusps).

Valve clinic programme and follow-up

Patients were followed prospectively. Patients that were initially asymptomatic had been followed at 6 monthly intervals in the HVC until surgical criteria according to the prevailing guidelines[4,5] at the moment were reached. At each visit a thorough medical history was taken by a physician experienced in the management of patients with VHD with a specific focus on inquiring the onset of AS-related symptoms and determining the duration of their onset. In addition to a comprehensive transthoracic echocardiogram, patients underwent a physical examination, blood testing, blood pressure measurement, and a 12-lead electrocardiogram. Exercise testing was performed in selected patients when doubts existed whether they were truly asymptomatic. Asymptomatic patients were instructed to recognize symptoms related to AS and to report any symptom onset without delay. In order to provide easy access to the HVC, symptomatic patients could schedule appointments via telephone every working day during office hours or present themselves directly at the HVC where they would be examined without delays.

Patients developing an indication for surgery were immediately referred to AVR and underwent a systematic preoperative work-up (including coronary angiography). Patients refusing surgery despite being informed about the unfavourable outcome of symptomatic severe AS were encouraged to reconsider their decision and were invited to further follow-up exams.

Patients who underwent surgery had a postoperative follow-up visit in the HVC to assess the surgical outcome. Further postoperative follow-up exams in the HVC were scheduled at extended intervals, depending on surgical and clinical outcomes. For the completion of postoperative follow-up information, additional follow-up information was obtained from interviews with the patients, their relatives and their physicians, and the review of medical records. Deaths were classified as non-cardiac or cardiac. The overall survival including perioperative and late deaths after AVR was assessed.

After each visit in the valve clinic patients were sent a comprehensive report including the findings obtained during that visit, recommendations given by the valve clinic based on these findings and dates for future appointments.

Statistical analysis

Quantitative variables are described as mean $\pm$ standard deviation. Survival data are summarized by means of Kaplan–Meier functions. Postoperative survival was analysed using the Kaplan–Meier method.

The effect of different variables (age, gender, hypercholesteraemia, diabetes mellitus, arterial hypertension, coronary artery disease, aortic valve jet velocity at entry, and severity of symptoms) on survival was analysed by means of a multiple Cox proportional hazard model and hazard ratios (HRs) as well as 95% confidence intervals (CIs) are reported. For *comparing* the *means* of two independent samples, Student's *t*-test was used. The χ^2 test was used to compare proportions between two independent samples. A *P*-value of <0.05 was considered to indicate statistical significance.

Results

Three hundred and eighty-eight patients were included in the study. Clinical and echocardiographic baseline characteristics of the patients in both groups were comparable and are depicted in *Table 1*.

Follow-up information was complete for all patients when the indication for surgery was established. Postoperative follow-up was complete for 377 patients (97.2%). After successful AVR, 10 patients were lost to follow-up. In addition, one patient who initially presented with symptoms but refused surgery was also lost to follow-up.

Patients that had been enrolled in the HVC follow-up programme

These 98 patients had been asymptomatic at their first visit at the HVC and had been enrolled in a regular follow-up programme with periodic visits to the HVC.

Delays in symptom reporting

The interval between the patient's perception of symptom onset and the reporting of these symptoms was 76 ± 75 days (*Figure 1A*). Although all patients in the HVC follow-up programme were educated to recognize symptoms related to AS and instructed to promptly report them, only 21 of these 98 patients reported the onset of symptoms on their own initiative before their next scheduled exam with a delay in symptom reporting of 21 ± 26 days. The remaining 77 patients waited for the next scheduled visit to report their symptoms with a delay in symptom reporting of 91 ± 77 days ($P < 0.001$; *Figure 1B*).

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Table 1 Baseline patient characteristics according to whether they presented with symptoms at the first visit or were enrolled in a heart valve clinic follow-up programme

	All patients	Symptomatic at initial visit	Enrolled in HVC programme	P-value
n	388	290	98	
Gender (female), n (%)	198 (51)	156 (54)	42 (43)	0.06
Age (years)	71 ± 10	71 ± 10	70 ± 9	0.13
Peak aortic jet velocity (m/s)	5.1 ± 0.6	5.1 ± 0.6	5.1 ± 0.7	0.88
Aortic mean gradient (mmHg)	67.2 ± 7.5	67.3 ± 17.2	66.8 ± 18.5	0.79
Aortic valve area (cm^2)	0.6 ± 0.2	0.6 ± 0.2	0.7 ± 0.2	0.11
Indexed aortic valve area (cm^2/m^2)	0.33 ± 0.09	0.33 ± 0.01	0.35 ± 0.09	0.06
Coronary artery disease, n (%)	131 (34)	99 (34)	32 (33)	0.79
Hypertension, n (%)	290 (75)	211 (73)	79 (81)	0.11
Diabetes mellitus, n (%)	89 (23)	66 (23)	23 (23)	0.89
Hypercholesterolemia	156 (40)	117 (40)	39 (40)	0.92

HVC, heart valve clinic.
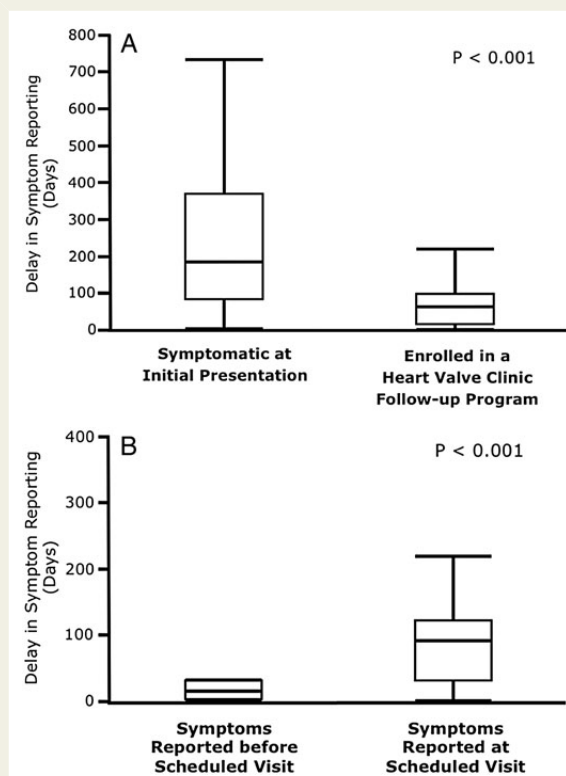
Figure 1 (A) Delay in symptom reporting. Time to symptom reporting in patients enrolled in a heart valve clinic follow-up programme when compared with patients being addressed with symptoms at their first visit to the heart valve clinic. (B) Delay in symptom reporting in patients enrolled in a heart valve clinic. Time to symptom reporting in patients enrolled in a heart valve clinic follow-up programme that reported their symptoms at the next scheduled follow-up exam only, when compared with patients enrolled in a heart valve clinic follow-up programme who reported their symptoms before the next scheduled visit.

Severity of symptoms at initial reporting

A severe onset of symptoms (defined as an NYHA or CCS Class ≥III) was observed in 34% of patients enrolled in the follow-up programme. No differences in age (69 ± 9 and 70 ± 9 years; $P = 0.75$) and gender (45 and 42%; $P = 0.71$) were observed among patients with severe or mild symptom onset (Table 2).

Indications for aortic valve replacement

Surgery was indicated for the following reasons: 85 developments of symptoms [dyspnoea or chest pain in all patients, additional syncope in 9 patients (9%)]; 8 significant aortic valve calcification and rapid hemodynamic progression; 2 reduced left ventricular systolic function; 2 prior to major non-cardiac surgery; and 1 positive exercise test.

Patients presenting with an indication for surgery at their initial visit

Two hundred and ninety patients presented with symptoms when they first presented at the HVC. All of these patients thus already had an indication for surgery at presentation. Most of these patients were referred from an outpatient care setting by specialists in internal medicine and general cardiologists.

Delays in symptom reporting

The interval between the onset of symptoms perceived by the patient and the reporting of these symptoms was 352 ± 471 days.

This interval was significantly longer than in patients that were enrolled in the HVC follow-up programme ($P < 0.001$; Figure 1A).
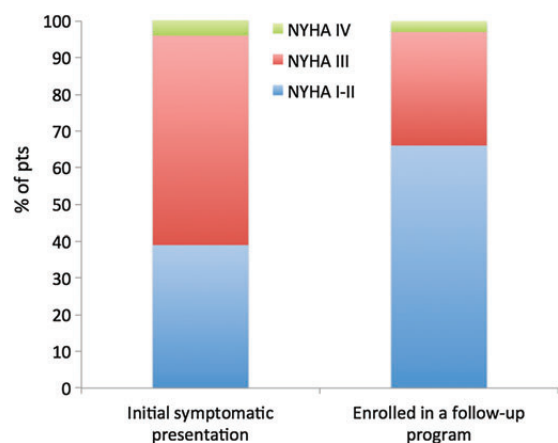
Severity of symptoms at initial reporting

Severe symptom onset (defined as an NYHA or CCS Class ≥III) was observed in 61% of the patients. Patients presenting with severe symptoms (NYHA Class ≥III) were older (73 ± 9 vs. 69 ± 10 years; $P = 0.006$) and more likely to be women (64 vs. 38%; $P < 0.0001$) than those presenting with mild symptoms (Table 2).

In comparison, patients enrolled in an HVC programme were referred to surgery with significantly less advanced symptoms when

Table 2   Baseline patient characteristics according to severity of symptom onset

Variable	Symptomatic at initial visit			Enrolled in an HVC follow-up program		
	NYHA ≤II	NYHA ≥III	*P*-value	NYHA ≤II	NYHA ≥III	*P*-value
Gender (female), *n* (%)	42 (38)	114 (64)	<0.001	27 (42)	15 (45)	0.71
Age (years)	69 ± 10	73 ± 9	0.006	70 ± 9	69 ± 9	0.75
Peak aortic jet velocity (m/s)	5.1 ± 0.6	5.1 ± 0.6	0.69	5.1 ± 0.6	5.0 ± 0.7	0.69
Aortic mean gradient (mmHg)	66.3 ± 16.5	67.9 ± 17.6	0.44	68.1 ± 18.2	64.2 ± 19.1	0.34
Aortic valve area (cm^2)	0.7 ± 0.2	0.6 ± 0.2	0.05	0.6 ± 0.2	0.7 ± 0.2	0.39
Indexed aortic valve area (cm^2/m^2)	0.34 ± 0.08	0.32 ± 0.08	0.08	0.35 ± 0.09	0.35 ± 0.09	0.76
Coronary artery disease, *n* (%)	46 (41)	53 (30)	0.05	18 (28)	14 (42)	0.15
Hypertension, *n* (%)	74 (66)	137 (77)	0.04	49 (75)	30 (91)	0.05
Diabetes mellitus, *n* (%)	20 (18)	46 (26)	0.11	14 (22)	9 (27)	0.53
Hypercholesterolaemia, *n* (%)	49 (44)	68 (38)	0.35	25 (38)	14 (42)	0.71

HVC, heart valve clinic; NYHA, New York Heart Association Class.

Figure 2 Severity of symptom onset. Severity of symptom onset in patients enrolled in a heart valve clinic follow-up programme when compared with patients that presented with symptoms at their initial visit at the heart valve clinic.

compared with patients presenting with symptoms at their first visit (*P* < 0.0001) (*Figure* 2).

Indications for aortic valve replacement

The indication for AVR was due to manifest symptoms in all but two patients [dyspnoea or chest pain in 245 patients (84%), dyspnoea or chest pain and syncope in 34 patients (12%), syncope only in 9 patients (3%)]. In one patient, the symptomatic status was unclear (the patient had previously experienced syncope; however, during medical work-up, a meningioma was detected as well) and an exercise test unmasked dyspnoea at low-level exercise. In another patient that was scheduled for major orthopaedic surgery, AS was detected in the preoperative workup and a decrease in the physical capacity was noted despite a reduced mobility of the patient.

Patients refusing surgery

Surgery was refused by 27 of the 388 patients. Six of these had been enrolled in the HVC follow-up programme. Fifteen of the 27 (55%) patients changed their mind after initially refusing surgery and agreed to have surgery with a mean delay of 412 days and after having been invited for a mean of 1.5 additional follow-up exams. Three of the 15 patients contacted the HVC on their own initiative without the need for additional follow-up exams. One patient eventually decided to undergo surgery after eight additional follow-up exams.

In addition, two patients who were found not to be suitable candidates for surgery in the pre-transcatheter aortic valve implantation (TAVI) era died from heart failure within 2 years of symptom onset.

Mortality on the waiting list and in patients refusing surgery

Three deaths occurred in patients awaiting surgery (all acute heart failure, preserved left ventricular function at the last echocardiographic exam). One patient who had a moderately reduced left ventricular function needed in-hospital cardiopulmonary resuscitation for bradyasystole during the stay in which AVR was scheduled and also took place. All four of these patients were symptomatic at their first visit in our HVC (two in NYHA Class II and two in NYHA Class III). In addition, eight patients who had refused surgery despite the development of progressive symptoms died of acute heart failure (4), myocardial infarction (3), or sudden death (1). Seven of these patients presented with an indication for surgery at their first visit in the HVC.

Perioperative and late mortality

A total of 371 patients underwent AVR. Three hundred seventeen patients received a biological prosthesis (including 4 TAVI), and 53 patients received a mechanical valve prosthesis. A Ross procedure was performed in one patient. Ninety-two patients required concomitant aortocoronary bypass surgery. In total, 95 of the operated

patients died during follow-up. There were 15 perioperative (within 30 days of surgery) deaths (12 in patients with an initial indication for surgery). Eight deaths (six in patients with an initial indication for surgery) occurred in the early postoperative period (1−3 months after surgery) for the following reasons: one aspiration pneumonia after tracheostomy; one acute respiratory distress syndrome; one systemic inflammatory response syndrome (SIRS); two sepsis; two sepsis after sternal infection; and one cardiac decompensation. Seventy-two deaths were observed during late follow-up (32 cardiac deaths, 37 non-cardiac deaths, and 3 unknown).

The actuarial probability of survival (including perioperative and late deaths after AVR) was 92% at 1 year, 88% at 2 years, 86% at 3 years, and 75% at 4 years.

Prognostic factors associated with postoperative survival

The severity of preoperative symptoms was associated with postoperative survival. Survival rates for patients with mild symptoms (NYHA or CCS ≤II) were 94 ± 2, 90 ± 3, 87 ± 3, and $74 \pm 5\%$ at 1, 2, 3, and 6 years, whereas survival rates for patients with severe symptoms (NYHA or CCS ≥III) were 90 ± 2, 86 ± 3, 84 ± 3, and $62 \pm 5\%$ at 1, 2, 3, and 6 years, respectively ($P = 0.008$) (*Figure 3*). Postoperative all-cause mortality was not different between the two groups ($P = 0.95$).

By multivariable analysis, male sex [$P = 0.03$, HR 1.68 (CI 1.03−2.72)], age at baseline [$P < 0.0001$, HR 1.08 (CI 1.05−1.12)], severe preoperative symptoms [$P = 0.04$, HR 1.60 (CI 1.00−2.61)], and diabetes [$P = 0.008$, HR 2.0 (CI 1.20−3.26)] were associated with a higher postoperative mortality.
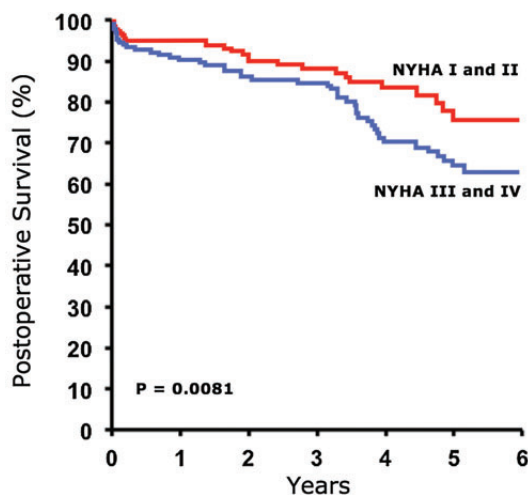
Figure 3 Postoperative survival according to severity of symptoms. Kaplan−Meier postoperative survival for patients in NYHA Classes I and II (red line) when compared with patients in NYHA Classes III and IV (blue line).

Discussion

Importance of specialized care for patients with VHD

The potential benefits of HVCs are being increasingly recognized.[6,7] In particular, patients with severe AS can be safely managed according to a watchful waiting strategy[9] even in the presence of associated aortic regurgitation.[10] Nevertheless, patients with VHD are not always managed in an appropriate setting. Information and education of these patients are often suboptimal and many do not receive a timely diagnosis and optimal care according to current best practice guidelines,[11] resulting in a delayed referral for surgery. An analysis of the STS database confirmed that 38 and 10% of patients undergoing AVR in 2006 presented in NYHA Classes III and IV, respectively.[12] However, an improvement was achieved in comparison with 1997 when 46 and 19% of patients presented in NYHA Classes III and IV, respectively.[12] Data from the Euro Heart Survey show that 216 of 284 patients with AS presented with severe symptoms and that surgery was denied in 33% of symptomatic elderly patients with severe AS.[13] Therefore, without appropriate care, patients with VHD are likely to have a poor outcome characterized by high morbidity and mortality caused in part by late referral but also by denial of surgery. With optimized timing of intervention, surgery is an effective treatment that improves both symptoms and survival.[9,14] Furthermore, the threshold to refer a high-risk patient to treatment has recently been lowered by the advent of TAVI.

Indeed, an appropriate setting is essential for a watchful waiting approach,[9,15,16] which is recommended by current guidelines in asymptomatic patients with severe VHD in the absence of specific risk factors that may warrant earlier intervention.[4,5]

Severity of symptom onset

The severity of preoperative symptoms is a marker of increased operative risk.[14] Ideally, patients should be referred for surgery with the onset of mild symptoms. Severe symptom onset, defined as an NYHA or CCS Class ≥III, was observed in 34% of patients that had regular follow-up exams in the HVC programme and in 61% of patients presenting with symptoms at the first visit. Patients being operated with severe symptoms had significantly worse survival rates when compared with patients being operated with mild symptoms.

Women and elderly patients were at particular risk to present with severe symptoms at their first visit in the HVC, indicating that these patient groups are at an even more accentuated risk of referral delays. However, in patients enrolled in the HVC follow-up programme, no differences in age or gender were observed between patients with mild or severe symptom onset, indicating that state-of-the-art management avoids the potential discrimination of these populations.

Delays in symptom reporting

Considering an annual mortality rate of ~30% for patients with severe symptomatic AS,[3,17] an individual patient's risk can effectively be lowered by early recognition of symptoms and consequently a timely referral to valve intervention. This is the first study to specifically assess the benefits of an HVC—based follow-up programme

for the management of patients with AS. Patients being included in a follow-up programme had a significantly shorter duration of symptoms and presented in an advanced symptomatic stage. In contrast, patients being addressed with symptoms at their first visit to the HVC presented with long delays between symptom onset and referral, amounting to 1 year on average.

In addition, a mortality risk on the waiting list for surgery of ~15% per year can be assumed.[18] This risk is illustrated by the fact that in the present study, three patients died while waiting for surgery and another patient received successful cardiopulmonary resuscitation while being admitted for surgery—all of these four patients presented with an indication for surgery at baseline. In this regard, enrolment in an HVC programme in a specialized cardiovascular centre might avert the risk of unnecessary delays in referral for surgery once that an indication is present.

Importance of risk stratification

Only 21% of the patients enrolled in the HVC follow-up programme reported an onset of symptoms before the next scheduled visit. The fact that 79% of the patients waited for the next visit to report their symptoms might be explained by denial of symptoms, the attribution of mild symptoms to 'aging' or 'lack of exercise' rather than AS as well as lacking perception of early symptoms by individuals with more sedentary lifestyles. The reason for a relatively short interval between symptom onset and reporting in these latter patients is only explained by the tightly scheduled follow-up exams. Although it is important to educate the patients to recognize the possible symptoms that may occur, such a measure alone remains insufficient and close monitoring is warranted. Even when enrolled in a follow-up programme, 34% of the patients presented with severe symptoms (NYHA $\geq$III). These findings highlight the importance of risk stratification,[19] to identify patients who are likely to develop symptoms in the near future and in whom elective surgery should be considered.[9,20,21]

Importance of follow-up visits after patient refusal of surgery

After being invited to additional follow-up exams, 15 (55%) of the 27 patients who initially refused surgery would later accept an AVR. While most of the patients reconsidered their decision after one to three additional follow-up exams, one patient changed her mind after as many as eight follow-up exams. A strategy of repetitive follow-up exams and continuous patient education is thus beneficial even in patients who initially refuse surgery despite a clear indication for surgery and should be offered systematically.

Study limitations

The present study was not specifically designed and powered to detect differences in postoperative survival between the two groups. It is therefore limited in this regard by the number of patients undergoing surgery in each of the groups.

Exercise testing was performed according to clinical judgment and not systematically.

The assessment of early symptoms in AS and the precise evaluation of symptom duration might be clinically challenging and subject to interobserver variability.

Until recently, no standards for the organization and structure of HVCs had been defined and the results reported in this study were obtained in one single centre.

Conclusion

Delays in referral and symptom reporting as well as symptom denial are common in patients with AS. These findings support the concept of risk stratification to identify patients who may benefit from elective surgery. A structured HVC programme results in the detection of symptoms at an earlier and less severe stage and thus in an optimized timing of surgery. The dissemination of such centres of excellence should therefore be promoted. **Q4**

Conflict of interest: none declared. **Q5**

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