



ELSEVIER

A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease

Bernard lung^{a*}, Gabriel Baron^b, Eric G. Butchart^c, François Delahaye^d, Christa Gohlke-Bärwolf^e, Olaf W. Levang^f, Pilar Tornos^g, Jean-Louis Vanoverschelde^h, Frank Vermeerⁱ, Eric Boersma^j, Philippe Ravaud^b, Alec Vahanian^a

Received 9 January 2003; revised 7 March 2003; accepted 12 March 2003

KEYWORDS

Valvular heart disease; Echocardiography; Cardiac surgery Aims To identify the characteristics, treatment, and outcomes of contemporary patients with valvular heart disease (VHD) in Europe, and to examine adherence to guidelines. Methods and results The Euro Heart Survey on VHD was conducted from April to July 2001 in 92 centres from 25 countries; it included prospectively 5001 adults with moderate to severe native VHD, infective endocarditis, or previous valve intervention. VHD was native in 71.9% of patients and 28.1% had had a previous intervention. Mean age was 64±14 years. Degenerative aetiologies were the most frequent in aortic VHD and mitral regurgitation while most cases of mitral stenosis were of rheumatic origin.

Coronary angiography was used in 85.2% of patients before intervention. Of the 1269 patients who underwent intervention, prosthetic replacement was performed in 99.0% of aortic VHD, percutaneous dilatation in 33.9% of mitral stenosis, and valve repair in 46.5% of mitral regurgitation; 31.7% of patients had ≥1 associated procedure. Of patients with severe, symptomatic, single VHD, 31.8% did not undergo intervention, most frequently because of comorbidities. In asymptomatic patients, accordance with guidelines ranged between 66.0 and 78.5%. Operative mortality was <5% for single VHD. Conclusions This survey provides unique contemporary data on characteristics and management of patients with VHD. Adherence to guidelines is globally satisfying as regards investigations and interventions.

 $\ensuremath{\mathbb{G}}$ 2003 The European Society of Cardiology. Published by Elsevier Ltd. All rights reserved.

E-mail address: bernard.iung@bch.ap-hop-paris.fr (B. lung).

^aCardiology Department, Bichat Hospital, AP-HP, Paris, France

^bEpidemiology, Biostatistic, and Clinical Research Department, Bichat Hospital, AP-HP, Paris, France

^cCardiac Surgery Department, University Hospital, Wales, Cardiff, UK

^dCardiology Department, Hopital Cardiologique, Lyon, France

^eCardiology Department, Heart Centre, Bad Krozingen, Germany

^fCardiac Surgery Department, St. Elizabeth Hospital, Trondheim, Norway

^gCardiology Department, Vall d'Hebron Hospital, Barcelona, Spain

^hDivision of Cardiology, Catholic University of Louvain, Brussels, Belgium

¹Laurentius Ziekenhuis Roermond, Netherlands

^jThoraxcentre, Rotterdam, Netherlands

^{*} Corresponding author: Bernard lung, MD, Cardiology Department, Bichat Hospital, 46 rue Henri Huchard, 75018 Paris, France. Tel.: +33-1-40-25-67-60; fax. +33-1-40-25-67-32

Introduction

The Euro Heart Survey (EHS) programme has been initiated by the European Society of Cardiology in order to provide quantitative information on cardiovascular disease in Europe.¹ Previous surveys have been conducted in the field of prevention, heart failure and acute coronary syndromes.^{2,3}

Although valvular heart disease (VHD) is less frequent than coronary disease, heart failure, or hypertension, it is of interest for several reasons: firstly, VHD is still common and often requires intervention. Secondly, important changes have occurred as regards the presentation and treatment of the disease over recent years, and thirdly there are very few registers or trials in the field as compared with other heart diseases. In addition, no such survey exists in the field of VHD.

The same limitations exist with regard to guidelines. There is only one set of guidelines in the field of VHD in the USA⁴ and three national guidelines in Europe.^{5–7} Moreover, recent publications suggest that there is a real gap between the existing guidelines and their effective application.^{8–10}

Thus there is a need for contemporary information on VHD in Europe, and this was the purpose of this survey.

As was the case for other surveys in the EHS programme, the aims of EHS on VHD were to characterise frequency and outcomes of valve disease in Europe, to evaluate current practices in the management of the disease, and finally to compare them whenever possible with available guidelines.

We present herein the initial assessment and the 30-day results concentrating on patients characteristics, diagnostic procedures, and interventions.

Methods

Participating Clusters

The national co-ordinators for the EHS programme supplied a list of potential medical centres in each country that would be technically suitable to set up such a survey. For each country, the aim was to choose clusters of hospitals, composed of academic and non-academic hospitals and hospitals with and without cardiac catheterization laboratories and cardiac surgery facilities.

Duration of Survey

The survey was designed to include all consecutive consenting patients between 1st April to 31 July 2001 who meet the inclusion criteria. Follow-up

was to be made either personally or by telephone by the local investigator at 30 days. One-year follow-up is ongoing.

Patients

The screened population consisted of patients who were hospitalised in medical or surgical cardiology departments, and those who were seen in outpatient clinics (1 day per week, the day being chosen randomly each week) of medical departments included in the clusters.

The case report form was filled out only for patients fulfilling the inclusion criteria which were as follows.

Age ≥18 years and:

- primary and significant VHD as defined by echocardiography:
 - aortic stenosis (AS) with a maximal jet velocity
 ≥2.5 m/sec,
 - or mitral stenosis (MS) with a valve area
 ≤2 cm²,
 - or mitral regurgitation (MR) grade ≥2/4,
 - or a ortic regurgitation (AR) with a grade $\ge 2/4$,
- or diagnosis of suspected or definite endocarditis as assessed by Duke criteria,
- or patients who had undergone any operation on a cardiac valve (percutaneous balloon commissurotomy, valve repair, valve replacement).

The inclusion was performed by the cluster Data Collection Officer. The case report form included details regarding the demographic, clinical, and echocardiographic characteristics of the patient. For hospitalized patients, the case report form comprised also details on diagnostic and treatment modalities, in-hospital complications, and discharge status. In addition, the Data Collection Officer was asked to interview the attending physicians for decisions regarding the main reasons for the choice of management and therapy. The case report form contained 809 variables. Aetiologies of VHD were classified following surgical findings if applicable, echocardiographic findings, and clinical context. Severe VHD was defined as AS with a valve area ≤0.6 cm²/m² body surface area, MS with a valve area ≤1.5 cm², AR grade ≥3/4, or MR grade $\geq 3/4.^{11}$

Data Collection

In each hospital, data were collected using the Macro™ software (InferMed, UK) on portable computers and sent to the central database in the

Table 1 Reasons for Inclusion						
	Outpatient Clinic <i>n</i> =1934	Medical Department <i>n</i> =2138	Surgical Department <i>n</i> =939			
Routine follow-up (%)	72.9	2.9	3.1			
Diagnostic (%)	17.1	27.3	7.9			
Worsening clinical condition (%)	8.0	53.5	63.1			
Complication (%)	0.9	10.7	8.7			
Extra-cardiac intervention (%)	0.5	0.9	3.3			
Other (%)	0.6	4.7	13.9			

	Total popula	ation <i>n</i> =5001		Patients v	vith intervention	n <i>n</i> =1269
Native valve disease (%)	71.9			87.0		
Aortic (% native)		44.3			57.4	
Aortic stenosis (%)			33.9			46.6
Aortic regurgitation (%)			10.4			10.8
Mitral (% native)		34.3			24.3	
Mitral stenosis (%)			9.5			10.2
Mitral regurgitation (%)			24.8			14.1
Multiple (% native)		20.2			16.8	
Right (% native)		1.2			1.5	
Previous intervention (%)	28.1			13.0		
Conservative surgery (%)		18.4			28.7	
Valve replacement (%)		81.6			71.3	

European Heart House via the Internet. Initial internal edit checks for missing or contradictory entries or for values excessively out of the normal range were implemented by the software. Additional edit checks were implemented by the data management staff at the European Heart House and the EHS VHD data analysis centre at Bichat Hospital. Patient identification was not entered on the local computer or transferred to the central database.

Site audits for source document verification versus data collected in the central database, were randomly performed by the EHS staff in sample sites. Site audits were not intended to validate the accuracy of the discharge diagnosis by the attending physicians.

Analysis was performed with SAS statistical software (SAS Institute Inc, release 8.2). Results are presented as mean±standard deviation or percentages.

Results

Population

Five thousand and one patients were included in 92 clusters from 25 countries; 76 centres (82.6%) were volunteers. The database was locked on 15 December 2001. The type of VHD was detailed in 4910 patients (98.2%). Thirty-day follow-up was complete in 4952 patients (99.0%). Participating centres are detailed in the Appendix A. The division between countries was well balanced between Western (1407 patients), Mediterranean (1444 patients), and Eastern Europe (1750 patients), but a more limited number of patients were included from Northern Europe (400 patients).

The sites of inclusion were medical departments in 2128 patients (42.5%), out-patient clinics in 1934 (38.7%), and surgical departments in 939 (18.8%). The reasons for inclusion are summarised in Table 1. Of the 5001 patients, 1269 underwent a valvular intervention during the survey period.

The type of VHD is shown on Table 2. Among the single native left-sided valve diseases, AS was the most frequent (1197 patients, 43.1%) followed by MR (877 patients, 31.5%), AR (369 patients, 13.3%), and MS (336 patients, 12.1%). Single native valve disease was severe in 809 patients with AS, 546 with MR, 230 with AR, and 232 with MS. Multiple valve disease represented a significant sub-group while right sided lesions were infrequent. As much as 28.1% of patients had had previous cardiac intervention.

The aetiology of the major native VHD is shown in Table 3. In AS the aetiology was mostly degenerative. In AR degenerative aetiology was also

	Aortic stenosis <i>n</i> =1197	Aortic regurgitation <i>n</i> =369	Mitral stenosis <i>n</i> =336	Mitral regurgitation n=877
Degenerative (%)	81.9	50.3	12.5	61.3
Rheumatic (%)	11.2	15.2	85.4	14.2
Endocarditis (%)	0.8	7.5	0.6	3.5
Inflammatory (%)	0.1	4.1	0	0.8
Congenital (%)	5.4	15.2	0.6	4.8
Ischaemic (%)	0	0	0	7.3
Other (%)	0.6	7.7	0.9	8.1

	Total population <i>n</i> =5001	Patients with intervention <i>n</i> =1269
Risk Factors		
Smoking (current or former) (%)	38.7	37.2
Hypertension (%)	49.2	47.6
Hyperlipidemia (%)	35.5	39.7
Diabetes (%)	15.3	14.1
Family history (%)	25.7	26.3
Comorbidities		
Previous myocardial infarction (%)	13.0	9.8
Carotid artery disease (%)	4.3	4.0
Lower limbs atherosclerosis (%)	5.0	4.7
Chronic obstructive pulmonary disease (%)	14.8	14.3
Serum ceratinine ≥200 µM/l. (%)	3.3	2.4
Dialysis (%)	0.5	0.4
Neurological dysfunction (%)	7.2	4.8

predominant, but rheumatic origin was present in 15.2% and endocarditis accounted for 7.5%. In MR degenerative aetiology was also most common followed by rheumatic disease, then ischaemic; endocarditis was present in 3.5%. Most cases of MS were rheumatic in origin.

As regards the main clinical characteristics, mean age was 65±14 years (range: 19–101); 16.8% were aged <50 years, 44.9% between 50 and 70, 30.0% between 70 and 80, and 8.3% ≥80 (0.5% being ≥ 90); 49.5% of the patients were females. At inclusion 30.2% of patients were in NYHA class I, 28.5% in class II, 32.9% in class III, and 8.4% in class IV. Major cardiovascular risk factors and comorbidities are detailed in Table 4.

Investigations

The investigations performed are detailed in Table 5. Transoaesophageal echocardiography was performed in 18.6% of the total population and 28.8% in those undergoing a further intervention.

The reasons advocated for its performance, either singly or in combination, were: assessment of valve morphology if transthoracic examination

was inconclusive (75.3%), search for left atrial thrombus (16.6%), to detect prosthetic dysfunction (13.1%), during endocarditis (21.6%), after embolism (5.2%), and finally as a systematic examination (overall 21.3%, as a sole reason 2.0%).

Stress tests were performed in 7.9% of the total and 7.4% of the operated patients. It was exercise electrocardiography in 70.0% of cases. The reasons for performing the tests were: assessment of functional capacity in patients with no or equivocal symptoms (49.1%), before allowing the performance of strenuous exercise (13.1%), for prognosis evaluation in presence of left ventricular dysfunction (12.1%), to detect coronary disease (61.0%), and systematic (22.9%, as a sole reason in 1.0%). In severe AS an exercise test was performed in only 5.7% of patients with no symptoms. On the other hand it was still performed in 3.2% of patients in NYHA class III or IV.

Catheterization was performed in 31.1% of the total population and 63.0% among the operated patients. In the global population, the type of catheterization were: isolated right heart catheterization in 2.8% of the cases, left heart catheterization in 11.6%, and right and left heart

	Aortic stenosis n=1197	Aortic regurgitation n=369	Mitral stenosis n=336	Mitral regurgitation n=877	Multiple valve disease n=712	Previous intervention n=1454
Transoesophageal echocardiography (%)	8.3	22.8	27.4	23.0	21.9	18.8
Stress test (%)	6.7	12.2	7.4	11.3	8.6	5.7
Catheterization (%)	44.4	30.4	32.7	31.9	30.3	20.3
Coronary angiography (%)	69.3	42.5	39.0	43.9	38.9	24.3

catheterization in 16.7%. The most frequent indications were: to assess severity of valve lesion (50.6%) or left ventricular function (23.3%) in case of inconclusive non-invasive testing. Catheterization was said to be systematically combined with coronary angiography in 62.9% of cases and this was the sole reason for performance in 29.1%.

Coronary angiography was the most frequently performed investigation: 43.0% of cases in total and 84.9% in operated patients. In the global population, it showed the presence of coronary artery disease in 39.4% of cases: 1-vessel disease in 13.9%, 2-vessel disease in 11.5%, 3-vessel disease in 12.8%, and left main disease in 1.2%. The reasons for performing coronary angiography in the global population were: presence of ≥1 risk factor before surgery (72.1%), suspicion of ischaemia (32.9%), presence of ischaemia in a patient with moderate valve lesion (24.3%), ischaemia suspected as an aetiology (16.6%). Finally coronary angiography was claimed to be systematically combined with catheterization in 44.7% (as the sole reason in 7.6%).

Among the 188 patients (14.8%) who did not undergo coronary angiography before surgery, the reasons advocated for not performing the investigation were: absence of cardio vascular risk factor (31.3%), acute endocarditis (14.9%), aortic dissection (2.7%), emergency operation (11.7%), poor haemodynamic condition (14.4%), no catheterization facility available (2.1%), and the absence of evidence of ischaemia (72.8%) (as the sole reason in 31.3%, i.e. in 4.6% of all patients who underwent intervention).

Interventions performed

Population

An intervention was planned in 1740 patients during the survey period. In 471 patients (27.1%) intervention was scheduled but not yet performed during the study period, 85.6% of them were on a waiting list with a mean duration of 8±4 weeks, up to 24 weeks.

The other 1269 patients underwent intervention during the survey. Interventions were performed on an elective basis in 73.0% of patients, urgently in 25.0% (performed during the same hospital stay), and as an emergency in 2.0% (within 24 h after admission).

As shown in Table 2, interventions were performed for native VHD in 87.0% of patients, mostly for AS, and were re-do operations in 13.0%.

The demographics of the patients who underwent an intervention are comparable to the total population: their mean age was 64 ± 13 years [range: 20-92], 16.1% were aged <50 years, 46.4% between 50 and 70, 32.1% between 70 and 80, and $5.4\% \ge 80$ (0.1% being ≥ 90); 46.7% were females. The distribution of preoperative symptoms was as follows: 13.9% in NYHA class I, 29.5% in class II, 43.1% in class III, and 13.5% in class IV. Congestive heart failure was present at the time of intervention in 21.3% of the patients. The detailed preoperative characteristics of the largest groups of patients are given in Table 6.

Indications for intervention

The reasons for not performing an intervention in the 31.8% of patients with severe single-valve disease who did not undergo intervention, while in NYHA class III or IV, were: regression of symptoms under medical treatment (overall 39.9%, 1.8% as the sole reason), end-stage disease (18.4%), symptoms attributed to coronary artery disease (14.9%), and recent myocardial infarction (7.9%). Besides cardiac causes, the presence of at least one extracardiac cause was considered to contraindicate surgery in 55.3% of cases. The most frequent reasons stated were: old age (27.6%, as a sole reason in 1.3%), chronic obstructive pulmonary disease (13.6%), renal failure (6.1%), and short life expectancy (19.3%).

The comparison between the reasons given for intervention in asymptomatic patients (NYHA class I and no angina) with severe single valve disease and

	Aortic stenosis n=512	Aortic regurgitation <i>n</i> =119	Mitral stenosis n=112	Mitral regurgitation <i>n</i> =155	Multiple valve disease n=185	Previous interventior <i>n</i> =164
Age ≥ 70 years (%)	54.3	19.3	17.9	31.6	25.4	33.5
Symptoms						
NYHA Class (%)						
Class I	15.8	20.7	5.4	15.0	7.2	14.1
Class II	37.1	31.9	31.3	27.5	18.2	18.4
Class III	38.8	36.2	58.9	42.5	48.6	44.8
Class IV	8.3	11.2	4.4	15.0	26.0	22.7
Left ventricular						
Ejection fraction (%)						
<30%	2.9	2.7	0	3.5	0.6	2.7
30-50%	16.4	21.8	8.7	16.2	21.6	15.4
50-60%	24.2	36.4	32.7	17.6	40.1	25.5
≥60%	56.5	39.1	58.6	62.7	37.7	56.4

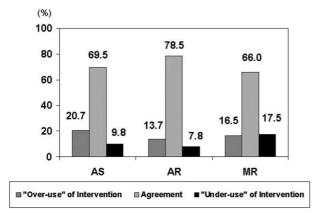


Fig. 1 Comparison between the indications retained for intervention in asymptomatic patients with severe single-valve disease and the recommendations from Working Group on Valvular Heart Disease of the European Society of Cardiology. 11 'Over-use of intervention' refers to patients who underwent interventions without having an indication according to the guidelines. 'Under-use of intervention' refers to patients who had no intervention but for whom there was an indication according to the guidelines. AS: aortic stenosis; AR: Aortic regurgitation; MR: mitral regurgitation

the recent recommendations is shown in Fig. 1.¹¹ The actual management was in accordance with these recommendations in 66.0 to 78.5% of cases among the different single native valve disease. The feasibility of repair was considered as a factor in 23.3% of cases, in particular in mitral valve disease where it was mentioned in 48.4% of cases.

Type of intervention

The type of intervention, either surgical or percutaneous, in patients with single valve disease is shown in Table 7. Nearly all patients with aortic

valve disease (99.0%) underwent prosthetic valve replacement. Valve repair was performed in 46.5% of patients with MR. In MS, percutaneous balloon commissurotomy was used in 33.9% of cases.

Associated procedures were often performed. Overall 31.7% of patients had one or more associated procedures, mostly coronary bypass grafting (22.8%).

Reasons for the choice of the type of intervention

The reasons for choosing valve replacement over valve repair in patients with MR were: unfavourable anatomy (77.1%), or failure of conservative surgery (10.2%). Valve replacement was also the only option in the absence of local availability of conservative surgery (32.5%). Finally cardiologist's or surgeon's preference (40.9%, 4.8% as the sole reason) was more frequently a factor than patient's preference (7.7%).

Another question concerned the choice of the type of prosthesis to implant in patients with AS. The reasons for choosing a mechanical prosthesis were: young age (84.6%), a mechanical valve in another position (1.6%), renal failure (0.8%), anticoagulation for other purpose (7.3%), physician's or surgeon's preference (70.5%, 4.9% as the sole reason), or patient's preference (19.0%). In patients operated on for AS, the distribution between mechanical prosthesis and bioprosthesis according to age is shown in Fig. 2.

Operative mortality and morbidity

Thirty-day follow-up was complete in the 1269 patients (99.2%) who underwent intervention. Operative (30-day) mortality according to the type of VHD is shown in Table 8. Operative mortality

	Aortic stenosis n=512	Aortic regurgitation $n=119$	Mitral stenosis n=112	Mitral regurgitation n=155
Mechanical prosthesis (%)	49.0	76.5	58.0	43.2
Bioprosthesis (%)	50.0	17.6	4.5	10.3
Homograft (%)	0.6	2.5	0	0
Autograft (%)	0.4	1.7	0	0
Valve repair (%)	0	1.7	3.6	46.5
Percutaneous intervention (%) Associated procedures	0	0	33.9	0
- CABG (%)	33.0	15.1	7.1	31.6
 Total aorta replacement (%) 	0.6	19.3	0	0
 Anti-arrhythmic surgery (%) 	0.2	0.8	4.5	1.9

100% 80% 60% 40% 20% 0% <60 60-65 65-70 70-75 75-80 80-85 85-90 Age (years) ■ Mechanical Prosthesis Bioprosthesis

Fig. 2 Distribution between mechanical prosthesis and bioprosthesis according to age in patients operated on for aortic stenosis

according to the type of intervention is shown in Table 9.

Among the other major perioperative complications the most frequent were bleedings followed by thromboembolic complications. Perioperative myocardial infarction and local septic complications were rare. Overall mortality and morbidity were higher in patients with multiple valve disease and those with redo surgery.

Discussion

The data from EHS on VHD allow a contemporary insight into the different aspects of the disease. It is unique since the only registries available in the field come from surgical registries which include only a limited amount of detailed information, ^{12–14} and series from large specialised centres do not always reflect 'the real world'. This survey was pan-European, since most European countries participated and included more than a hundred

patients. The extension of the different sites of inclusion from medical departments to surgical ones and outpatient clinics allowed for the capture of a wide scope of management of these patients including routine follow-up, investigations and management of complications.

Patient characteristics

As regards the distribution of VHD, AS was the most frequent native valve disease followed by MR, while AR and MS were observed with equivalent frequency. In this survey, patients with previous valve interventions represented a significant sub-group for which we unfortunately have very little data available and very few guidelines.

Rheumatic disease used to be the most frequent etiology of valve disease in previous decades, but this survey, like other contemporary series from Europe and the USA, ^{15–18} shows that degenerative origin is by far the most frequent in AS, MR, and AR, with the associated implications related to patient characteristics and treatment. Endocarditis is still a serious concern in AR and MR. Finally an ischemic origin is present in 7.3% of MR.

Overall the patients with VHD are often elderly with a high frequency of cardiovascular risk factors and comorbidities.¹⁹ These changes in aetiology and clinical characteristics have important implications for management.

Investigations

Besides transthoracic echocardiography, which was required for inclusion in the survey, the work-up of patients participating in the survey included few other non-invasive investigations. The reasons given for the use of transoesophageal echocardiography in the survey were in good agreement with

Table 8 Operative mortality and morbidity of interventions according to the underlying valve disease							
	Aortic stenosis n=512	Aortic regurgitation <i>n</i> =119	Mitral stenosis n=112	Mitral regurgitation <i>n</i> =155	Multiple valve disease n=185	Previous conservative intervention <i>n</i> =47	Previous prosthetic replacement <i>n</i> =117
Mortality (%)	3.1	3.4	0.9	3.9	6.5	2.1	6.2
Major Bleeding (%)	7.7	2.5	2.7	7.7	10.8	4.3	12.0
Tamponade (%)	2.9	1.7	0.9	2.6	4.3	0	1.7
Embolisma (%)	3.1	2.5	2.7	7.1	2.2	2.1	3.4
Prosthetic thrombosis ^b (%)	0.2	0	0.9	0.6	0	0	0
Myocardial infarction (%)	1.0	0	0	0.6	0.5	0	1.7
Mediastinitis (%)	0.6	0.8	0	1.3	2.2	0	0

The 16 patients operated on for right-sided valve disease are not detailed. Major bleeding is defined by bleeding leading to death, surgery, or transfusion.

Table 9 Operative mortality in the Euro Heart Survey for valvular heart disease compared with surgical registers according to the type of surgical procedure

	STS 2001 ^a	UKCSR ^b 1999–2000	EHS 2001
Aortic valve replacement no CABG ^c	3.7	3.1	2.7
Aortic valve replacement+CABG	6.3	7	4.3
Mitral valve repair no CABG	2.2	2.8	0
Mitral valve replacement no CABG	5.8	6.2	1.7
Mitral valve repair or replacement+CABG	10.1	8.6	8.2
Multiple valve replacement (with or without CABG)	7.2	11.4	6.5

^a STS: Society of Thoracic Surgeons (USA). Mortality for STS includes first and redo interventions.

the current recommendations, 20,21 even if the overall use of the technique was rather low.

The use of stress testing was low and essentially aimed at identifying coronary artery disease, which it does poorly in the setting of valve disease. Exercise testing is too seldom used in asymptomatic patients with valve disease. This is particularly true for AS, despite the fact that the performance of the test is strongly advocated in the recent European recommendations and is a grade IIa recommendation in the ACC/AHA guidelines. 4,11,22 This under-use may be explained by an insufficient implementation of the current guidelines and fear of complications or inexperience in exercise testing.

Catheterisation was the second most frequently performed investigation. In most of the cases it was performed to assess the severity of valve lesions, however in as much as 28.7% of the cases it was performed in a systematic fashion in combination with coronary angiography. This high figure is surprising at a time when there is a large amount of data showing the accuracy of echocardiography in

assessing the severity of valve disease. The performance of catheterization in the absence of discordant clinical findings and echocardiography is either grade IIb or grade III according to the type of valve disease. This over-use may be due to the fact that clinicians want further reassurance before advising operation. However the over-use of catheterization is not without risks, in particular in AS, and increases costs. ²³

As expected, because of the characteristics of the patients in the survey, coronary angiography was the most frequently performed investigation. This was particularly true in patients undergoing surgery. In this setting, the reasons for performing or not performing the investigation were sought. Overall the agreement between practice and guidelines was good.⁴

Interventions performed

The demographics of the patients operated on in this survey are similar to those of other series, for

^a including transient ischaemic attacks.

^boclusive or non-occlusive thrombosis.

^bUKCSR: United Kingdom Cardiac Surgical Register. Mortality for UKCSR corresponds to first interventions only.

^cCABG: coronary artery bypass grafting.

example in severe AS over half of the patients were operated on after the age of 70 years. 24,25 In keeping with the patient characteristics and the predominance of degenerative aetiologies, intervention is often necessary in elderly patients with coronary disease and comordidities. 12 In addition intervention is a re-do operation in more than 10% of the cases. Besides these characteristics which increase the operative risk, another important finding is that intervention is often performed at an early stage of the disease, since almost half of the patients were in NYHA Class I or II at the time of operation, with 13.9% being operated on at an asymptomatic stage. This trend towards early intervention is confirmed by the fact that the majority of patients with AS and AR and even more importantly MR are operated on with preserved left ventricular function. The overall correspondence between the recent recommendations and the practice in 66 to 78.5% of cases in the survey is encouraging in this respect. 11 The feasibility of valve repair has been often considered as an incentive for early intervention in particular in mitral valve disease where conservative surgery and percutaneous intervention are available. These encouraging findings should not, however, lead us to forget that a tenth of the patients are still being operated on at a far too advanced stage of the disease.

The reasons for not advising intervention in patients with severe valve disease were either cardiac, extracardiac, or both.

Among the cardiac reasons, as in another study, decrease of symptoms under medical treatment is often wrongly cited as justification for procrastination. ⁹ The other reasons are debatable and more controversial. For example, severe depression of left ventricular function should seldom be used as a contraindication even if it increases the operative risk. Recent myocardial infarction may delay surgery but will not contraindicate it in most cases. Finally, severe coronary disease is seldom not bypassable unless diffuse and distal. As a general comment, these reasons can be criticised individually but certainly not rejected especially if they are combined.9 The role of comorbidities is crucial since they are present in over one half of the cases. Among these comorbidities, age is the most frequently cited but, in accordance with what is stated in the guidelines, it is very rarely the sole contraindication for intervention. The predictive value of the other parameters is insufficiently studied in the field of valve intervention and their value remains largely debatable. There are no precise recommendations on the contraindications for surgery in the field of VHD and the decision requires a careful individual weighing of each of these parameters after a multidisciplinary consultation. The multi-factorial nature of the decision process and the absence of clear guidance explains the wide variability of advice given. It is clearly a domain were it is difficult to make a meaningful comparison with guidelines. The way forward is probably to perform studies with more precise assessment of the risk using available risk scores. ^{26,27}

As regards the type of interventions performed, valve replacement remains the standard in aortic valve disease. There is an almost equal split between bioprostheses and mechanical valves in patients with AS. The higher proportion of mechanical prostheses in AR as compared to AS is the consequence of the greater proportion of younger patients in AR. The age threshold for choosing a bioprosthesis or a mechanical prosthesis remains a matter of debate.²⁸ In the current guidelines the threshold for choosing a mechanical valve over a bioprosthesis is 65.4 In the survey there is a shift from 65 to 70 or 75. This trend is consistent with what was observed in the UK heart valve registry²⁹ and is probably an illustration that the decision making process cannot apply only to chronological age but should rather take into account a balance of several factors, including the cardiologist's and surgeon's preference. Valve repair, homograft or autograft valve replacement, which account for a large part of the contemporary surgical literature, are performed in only a small percentage of patients in real life. 30-32 Finally, the data from the survey confirm that percutaneous aortic valvuloplasty has virtually disappeared from practice.33

In mitral valve disease more conservative techniques are gaining popularity. In MR nearly half of the patients underwent mitral valve repair. This encouraging figure probably reflects the increasing confidence in the technique due to the accumulation of data showing its good short and long term efficacy. 34-36 However, the answers of the physicians in the survey show that the absence of local expertise in conservative surgery remains a significant limitation for a larger use of conservative techniques. In the other patients, mechanical valves are usually preferred over bioprosthesis. In MS, the therapeutic alternatives are either percutaneous balloon commissurotomy, which is performed in over one third of cases, or prosthetic valve replacement, most often using a mechanical prosthesis. 33 Surgical commissurotomy has become an unusual procedure.³⁷

Another characteristic of contemporary valve intervention is that it is frequently associated with other procedures. 12,13 This is particularly true in patients with aortic valve disease in whom an associated procedure is performed in between one third and half of cases. This is most often bypass grafting, while the use of combined percutaneous intervention remains exceptional in current practice. 38 The high frequency of concomitant lesions of the ascending aorta in degenerative AR explains why one fifth of patients who undergo surgery also require replacement of the ascending aorta.³⁹ Finally, associated anti-arrhythmic surgery is the subject of growing attention, in particular in patients with mitral valve disease, but very patients underwent this procedure in the survey.⁴⁰

Operative mortality and morbidity

The risk of valve replacement was low in the aortic position. The risk of intervention in MS was very low due to the fact that a significant proportion of patients underwent balloon commissurotomy. As regards MR, our findings confirm the lower risk of valve repair in comparison with that of valve replacement, although selection bias may have partially accounted for this. ^{34,35} Consistent with other series, mortality was higher in patients where bypass grafting was associated, especially in mitral position. ^{12,13} However it should be stressed that combined surgery in MR frequently applies to patients who have ischaemic MR and whose operative mortality is always higher than in patients with other aetiologies. ⁴¹

Overall mortality and morbidity figures after valve intervention observed in the survey are slightly lower than in the most recent surgical registries such as the STS database in the USA and the United Kingdom Cardiac Surgical Register (Table 9), but this may be related to differences in the centres involved. 12,13,42,43 The large proportion of medical centres in the survey may account for different patient characteristics and presentations as compared with registries comprising only surgical centres. In particular, only 2.0% of patients underwent emergency surgery in the present survey although the figure was 14% in the surgical registry from the UK12 and this factor has a significant impact on operative mortality in VHD. In addition, the figures from the EHS and these registries are somewhat different from those of the current literature, but may not be strictly comparable as the survey represents a snapshot in 2001 whereas most literature series originate from selected centres

and cover a long period of time during which changes in practice may have occurred. 44-46

Limitations

This survey was not a population-based epidemiological study and it is not possible to derive any information on the prevalence of different types of VHD, because the selection of participating centres may have introduced a selection bias. The results of this survey should therefore not be generalized to all centres within a particular country or region. On-site auditing concerned only a limited number of centres, and the audit only focused on the accuracy of data entry and not on the validity of the diagnosis. Although medical centres were required to enroll consecutive patients with VHD, we were not able to verify this due to our limited audit. Thirty-day follow-up status was missing for a small minority of patients and it was unlikely to affect mortality rates. Because patient management was based on the working diagnosis made by the attending physician, our analysis is suitable for the evaluation of patient management. Due to the nature of the survey and the limits of the existing guidelines, more than performing a strict head to head comparison with guidelines the aim was here to analyse the rationale for management

Conclusions

The EHS on VHD confirms that it is possible to perform such a survey in a large number of European countries. It provides a unique contemporary data set on the presentation and management of patients with VHD. The findings in this survey show that VHD is now mostly degenerative in origin, AS being the most frequent. The patients concerned are often old with a number of cardiovascular risk factors and comorbidities. In accordance with the guidelines, coronary angiography is frequently performed in the evaluation of these patients. However there is a trend towards too much use of catheterization and insufficient use of exercise testing. Today valvular intervention consists mostly of valve replacement for aortic valve disease and conservative techniques being used more frequently in mitral valve disease. In keeping with the characteristics of the population, combined procedures are often necessary. The early timing of intervention balances the otherwise higher risk profile and may account for the relatively low mortality and morbidity. Finally, the survey shows that there is an important need for

further trials, in particular in the field of patients who have undergone previous operation who represent an important sub-group. Such trials will allow for new and more comprehensive guidelines which will then need to be implemented and scrutinised by new surveys in order to improve patient care.

Acknowledgements

We thank Pr Maarten L. Simoons and Pr David A. Wood, Past-Chairman and Chairman of the Euro Heart Survey Programme for their continuing support.

Appendix A

Organisation of the Survey

Expert Committee: Alec Vahanian (Survey Chairman), France; Bernard lung (Survey Coordinator), France; Christa Gohlke-Bärwolf, Germany; Pilar Tornos, Spain; Eric G. Butchart, United Kingdom; François Delahaye, France; Jean-Louis Vanoverschelde, Belgium; Frank Vermeer, Netherlands; Olaf W. Levang, Norway.

Coordination and Data Management Centre (Euro Heart House, Sophia-Antipolis, France): Renaud Longelin (EHS Director); Malika Manini (EHS Operations Manager); Ronald Schravendeel, Charles Taylor (EHS Data Managers); Claire Bramley (EHS Data Monitor); Susan Del Gaiso (EHS Assistant).

Data Analysis Centre (Epidemiology, Biostatistic, and Clinical Research Department, Bichat Hospital, Paris, France): Philippe Ravaud, Gabriel Baron.

National Coordinators: Belgium, Guy De Backer; Switzerland, Peter Buser; Czech Republic, Roman Cerbak; Germany, Uwe Zeymer; Denmark, Per Thayssen; Spain, Angeles Alonso; Finland, Seppo Lehto; France, Jean-Jacques Blanc; United Kingdom, Kevin Fox; Greece, Dennis Cokkinos; Hungary, Kristof Karlocai; Israel, Sholmo Behar; Italy, Aldo Maggioni; Lithuania, Virginija Grabauskiene; Netherlands, Jaap W. Deckers; Poland, Janina Stepinska; Russia, Vyacheslav Mareev; Sweden, Annika Rosengren; Turkey, Tugrul Okay.

There was no national coordinator in the participating countries which are not mentioned in the above list.

Sponsors: European Society of Cardiology; Dutch Heart Foundation; Fédération Française de Cardiologie/Société Française de Cardiologie; Hellenic Cardiological Society; Swedish Heart and Lung Foundation; European Commission Grant (Infermed/Mansev Project); Toray Medical Company.

Participating Centres and Investigators with numbers of patients included per country: Czech Republic (627): J. Bruthans, Praha; J. Cerny, Brno; P. Bocek, Plzen. Spain (609): L. Lopez Bescos, Madrid; A. Castro Beiras, La Coruna; J.L. Diago Torrent, Castellon; F. Fernandez Avilés, Valladolid; F. Malpartida, Malaga; R. Melgares Moreno, Granada; J.A. Velasco Rami, Valencia; V. Palacios Motilla, Valencia; M. Soledad Alcasena Juango, Pamplona; A. Aloso Garcia, Madrid; C. Martin Luengo, Salamanca. Netherlands (557): J. Deckers, Rotterdam; F. Vermeer, R. Nieuwlaat, Maastricht; M.J. De Boer, Zwolle; J.W.M.G. Widdershofen, Tilburg; M. Bijl, Dordrecht. Israel (396): A. Sagie, Petach Tikva; B.S. Lewis, Haifa; D. Gilon, Jerusalem; W. Markiewicz, S. Rispler, Haifa; N. Roguin, Nahariya; N. Kogan, Nazareth; S. Shimoni, Rehovot; M. Leitman, Beer Yakov; C. Yosefy, Ashkelon; N. Liel-Cohen, Beer Sheva; C. Cafri, Beer Sheva. France (362): G. Montalescot, Paris; A. Cohen-Solal, Clichy; J.C. Daubert, Rennes; J.P. Bassand, Besançon. Lithuania (317): R. Jonkaitiene, Kaunas; A. Laucevicius, Vilnius. Germany (304): J. Niebauer, Leipzig; H. Klepzig, Offenbach; U. Zeymer, Kassel; R. Erbel, Essen; E. Fleck, Berlin; A. Gitt, Ludwigshafen am Rhein. Hungary (192): A. Temesvari, Budapest; K. Karlocai, Budapest; A. Kalina, F. Szaboki, Budapest; A. Katona, Gyula; A. Mohacsi, Debrecen. Finland (178): S. Lehto, Kuopio; M.S. Nieminen, Helsinki. Belgium (175): L. Piéard, V. Legrand, Liège; B. Marchandise, Yvoir. Italy (161): G. Rosano, Rome; F. Valagussa, Monza; D. di Marco, G. Levantesi, Vasto; E. Cecchi, Torino; A. Desideri, Castlefranco Veneto; C. Mazzone, Trieste. Greece (157): D. Cokkinos, Athens; S. Stametelopoulos, Athens; K. Oikonomou, P. Makridis, Edessa; M. Marketou, Heraklion; G. Psaltiras, Athens; C. Samara, Thessaloniki. Turkey (121): K. Sonmez, Istanbul; S. Aytekin, Sisli; J. Cordan, Bursa; B. Gorenek, Meselik-Eskisehir. Ukraine (121): Y.A. Ivaniv, Lviv; M. Orynchak, Ivano-Frankivsk. Romania (112): I.S. Benedek, Targu-Mures; E. Carasca, C. Suciu, Targu-Mures; G. Georgescu, Iasi; A. Iancu, Cluj-Napoca. Poland (105): M. Tendera, Katowice; A. Rynkiewicz, Gdansk; M. Trusz-Gluza, Katowice. United Kingdom (103): J.G.F. Cleland, Kingston-upon-Hull; M. Cowie, Aberdeen; D. Wood, London. Latvia (90): J. Romanova, Riga. Russia (85): A.A. Alexandrovsky, Saransk; D. Aronov, Moscow; A. Galiavitch, Kazan. Yugoslavia (74): M. Miric, Beograd; N. Radovanovic, Sremska Kamenica; B. Vujisic-Tesic, Belgrade. Denmark (60): P. Thayssen, Odense. Sweden (59):

A. Rosengren, Göteborg; L. Rydén, Stockholm. Bulgaria (19): V. Sirakova, Varna. Switzerland (9): J. Turina, Zurich. Croatia (8): D. Pocanic, Zagreb.

Appendix B

Definitions of terms

Smoking: cigarette, cigar, pipe.

Hyperlipidemia: Diagnosis previously made by physician, receiving lipid-lowering therapy, or total cholesterol >190 mg/dl or >5 mmol/l, HDL <40 mg/dl or <1 mmol/l, TG >190 mg/dl or >2 mmol/l.

Hypertension: Diagnosis previously made by physician, receiving medications to lower blood press-

ure, or known blood pressure values of ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic on ≥ 2 occasions.

Diabetes: Fasting blood glucose level ≥ 7 mM/l. on ≥ 2 samples or previous diagnosis of diabetes, whatever the treatment.

Family history of premature coronary artery disease: History of angina pectoris, myocardial infarction, or sudden death among first-degree relatives before the age of 55 years.

Chronic obstructive pulmonary disease: Diagnosis previously made by physician, or patient receiving bronchodilators, or values of FEV1 <75% of expected value, arterial pO2 <60 mmHg, or arterial pCO2 >50 mmHg in prior studies.

Carotid atherosclerosis: stenosis >50%, previous or planned surgery.

Lower limbs atherosclerosis: claudication, previous or planned surgery.

Neurological dysfunction: neurological disease severely affecting ambulation or day-to-day. functioning.

References

- Boersma E, Manini M, Wood DA, et al. Cardiovascular Diseases in Europe. Euro Heart Survey and National Registries of Cardiovascular Diseases and Patient Management. European Society of Cardiology, Sophia Antipolis, France, 2002.
- EUROASPIRE II Study Group. Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries: principal results from EUROASPIRE II Euro Heart Survey Programme. Eur Heart J 2001;22:554–72.
- Hasdai D, Behar S, Wallentin L et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin:the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). Eur Heart J 2002;23:1190–201.
- Bonow RO, Carabello B, DeLeon AC et al. ACC/AHA Guidelines for the management of patients with valvular heart disease. J Am Coll Cardiol 1998;32:1486–588.

Prendergast B, Manning AP, Hall RJC. Valvular heart disease:recommendations for investigation and management.
 Summary of guidelines produced by a working group of the British Cardiac Society and the Research Unit of the Royal College of Physicians. J R Coll Physicians Lond 1996; 30:309–15.

- Classen M, Dierkesmann R, Heimpel H, et al. Rationale Diagnostik und Therapie in der inneren Medizin. Ein Beitrag zur Qualitatzssicherung in Klinik und Praxis. Munchen: Urban und Fischer, Dezember 1999.
- Azpitarte J, Alonsi A, Garcia Gallego F et al. Guias de practica clinica de la Sociedad Espanola de Cardiologia en valvulopatias. Rev Esp Cardiol 2000;53:1209–78.
- 8. Delahaye F, Rial MO, de Gevigney G et al. A critical appraisal of the quality of the management of infective endocarditis. *J Am Coll Cardiol* 1999;33:788–93.
- Bouma BJ, van den Brink RBA, van der Meulen JHP et al. To operate or not on elderly patients with aortic stenosis: the decision and its consequences. *Heart* 1999;82:143–8.
- Bouma BJ, van der Meulen JHP, van den Brink RBA et al. Variability in treatment advice for elderly patients with aortic stenosis: a nationwide survey in the Netherlands. Heart 2001;85:196–201.
- 11. lung B, Gohlke-Bärwolf C, Tornos P et al. Working Group Report. Recommendations on the management of the asymptomatic patient with valvular heart disease. *Eur Heart J* 2002;**23**:1253–66.
- National Adult Cardiac Surgical Database Report 1999–2000.
 The United Kingdom Cardiac Surgical Register. http://www.ctsnet.org/doc/853 accessed Aug 23, 2002.
- US Society of Thoracic Surgeons National Database. http:// www.ctsnet.org/section/stsdatabase, accessed Feb 28, 2003
- 14. Unger F. Worldwide survey on cardiac interventions 1995. *Cor Europaeum* 1999;7:128–46.
- 15. Dare AJ, Vienot JP, Edwards WD et al. New observations on the etiology of aortic valve disease: a surgical pathologic study of 236 cases from 1990. *Human Pathology* 1993; 24:1330–8.
- Passik CS, Ackermann DM, Pluth JR et al. Temporal Changes in the causes of aortic stenosis: a surgical pathological study of 646 cases. Mayo Clin Proc 1987;62:119–23.
- 17. Olsen LJ, Subramanian R, Ackerman DM et al. Surgical pathology of the mitral valve: a study of 712 cases spanning 21 years. *Mayo Clin Proc* 1987;62:22–34.
- Dare AJ, Harrity PJ, Tazelaar HD et al. Evaluation of surgically excised mitral valves: Revised recommendations based on changing operative procedures in the 1990s. *Hum Pathol* 1993;24:1286–93.
- Stewart BF, Siscovick D, Lind BK et al. Clinical factors associated with calcific aortic valve disease. Cardiovascular Health Study. J Am Coll Cardiol 1997;29:630–4.
- Cheitlin MD, Alpert JS, Armstrong WF et al. ACC/AHA guidelines for the clinical application of echocardiography. Circulation 1997;95:1686–744.
- 21. Roudaut R, Touche T, Cohen A et al. Recommandations de la Société Française de Cardiologie concernant la formation des échocardiographistes et la réalisation des échocardiogrammes. Arch Mal Cœur 1994;87:791–8.
- 22. Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 Guideline update for exercise testing: summary article. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee to update the 1997 exercise testing Guidelines). Circulation 2002;106:1883–1892.

- 23. Omran H, Schmidt H, Bernhardt P et al. Valvular aortic stenosis: Risk of cerebral embolism in patients undergoing retrograde catheterisation on the aortic valve. Prospective randomized study. *J Am Coll Cardiol* 2002; **39**(suppl. A):426A (abstract).
- 24. Logeais Y, Langanay T, Roussin R et al. Surgery for aortic stenosis in elderly patients. A study of surgical risk and predictive factors. *Circulation* 1994;**90**:2891–8.
- 25. Lund O. Preoperative risk evaluation and stratification of long-term survival after valve replacement for aortic stenosis. Reasons for earlier operative interventions. *Circulation* 1990;82:124–39.
- 26. Parsonnet V, Dean D, Bernstein AD. A method of uniform stratification of risk evaluating the results of surgery in acquired adult heart disease. *Circulation* 1989;79(suppl. I):3–12.
- 27. Roques F, Nashef SAM, Michel P et al. Risk factors and outcomes in European cardiac surgery:analysis of the Euro-SCORE multinational database of the 19030 patients. *Eur J Cardiothorac Surg* 1999;15:816–23.
- 28. Hammermeister K, Sethi GK, Henderson WG et al. Outcomes 15 years after valve replacement with a mechanical versus a bioprosthetic valve: final report of the Veterans Affairs randomized trial. *J Am Coll Cardiol* 2000;36:1152–8.
- 29. Taylor KM. The United Kingdom heart valve registry: the first 10 years. *Heart* 1997;77:295–6.
- 30. Duran C, Kumar N, Gometza B, Al-Halees Z et al. Indications and limitations of aortic valve reconstruction. *Ann Thorac Surg* 1991;52:447–54.
- Takkenberg JJ, van Herwerden LA, Eijkemans MJ et al. Evolution of allograft aortic valve replacement over 13 years: results of 275 procedures. Eur J Cardiothorac Surg 2002;21:683–91.
- 32. Ross D. Pulmonary valve autotransplantation (the Ross operation). *J Card Surg* 1988;3(suppl):313–9.
- 33. Vahanian A. Valvuloplasty. In: Topol EJ, editor. Textbook of cardiovascular medicine: Lippincott & Wilkins, Philadelphia; 2002, p. 1767–82.
- 34. Acar J, Michel P, Luxereau P et al. Indications for surgery in mitral regurgitation. *Eur Heart J* 1991;12:52–4.

- 35. Lee EM, Shapiro LM, Wells FC. Superiority of mitral valve repair in surgery for degenerative mitral regurgitation. *Eur Heart J* 1997;18:655–63.
- 36. Braunberger E, Deloche A, Berrebi A et al. Very longterm results (more than 20 years) of valve repair with Carpentier's techniques in non rheumatic mitral valve insufficiency. *Circulation* 2001;104:5(Suppl 1):18–21.
- 37. Palacios IF. Farewell to surgical mitral commissurotomy for many patients. *Circulation*. 1998;97:223–6.
- Aranki SF, Rizzo RJ, Couper GS et al. Aortic valve replacement in the elderly; effect of gender and coronary artery disease on operative morality. *Circulation* 1993;88(part 2):17–23.
- Gott VL, Greene PS, Alejo DE et al. Replacement of the aortic root in patients with Marfan Syndrome. N Engl J Med 1999;340:1307–13.
- 40. Yuda S, Nakatani S, Kosakai Y et al. Long-term follow-up of atrial contraction after the maze procedure in patients with mitral valve disease. *J Am Coll Cardiol* 2001;37:1622–7.
- 41. Grossi EA, Goldberg JD, LaPietra A et al. Ischemic mitral valve reconstruction and replacement: comparison of long-term survival and complications. *J Thorac Cardiovasc Surg* 2001;16:328–32.
- 42. Edwards FH, Grover FL, Shroyer AL et al. The Society of Thoracic Surgeons National Cardiac Surgery Database: current risk assessment. *Ann Thorac Surg* 1997;63:903–8.
- Jamieson WRE, Edwards FH, Bero J et al. Cardiac valve replacement surgery: the Society of Thoracic Surgeons national database experience. *Ann Thorac Surg* 1999; 67:943–51.
- 44. Dujardin K, Enriquez-Sarano M, Schaff HV et al. Morality and morbidity of aortic regurgitation in clinical practice. A long-term follow-up study. *Circulation* 1999;**99**:1851–7.
- 45. Tribouilloy C, Enriquez-Sarano M, Schaff HV et al. Impact of preoperative symptoms on survival after surgical correction of organic mitral regurgitation. Rationale for optimizing surgical indications. *Circulation* 1999;99:400–5.
- Edwards FH, Peterson ED, Coombs LP et al. Prediction of operative mortality after valve replacement surgery. J Am Coll Cardiol 2001;37:885–92.