European Heart Journal (2007) **28**, 1358–1365
doi:10.1093/eurheartj/ehm001

What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery?

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Received 17 July 2006; revised 5 February 2007; accepted 9 February 2007; online publish-ahead-of-print 9 March 2007

See page 1281 for the editorial comment on this article (doi:10.1093/eurheartj/ehm156)

KEYWORDS
Mitral regurgitation;
Mitral valve replacement;
Mitral valve repair;
Decision-making

Aim To identify the proportion and characteristics of patients with severe symptomatic mitral regurgitation (MR) who are denied surgery.
Methods and results In the Euro Heart Survey on valvular heart disease, 396 patients had severe symptomatic MR as assessed by Doppler-echocardiography (grade $\geq$3/4) and New York Heart Association class II or greater. Patient characteristics were analysed according to the decision to operate or not. A decision not to operate was taken in 193 patients (49%). In multivariable analysis, decreased left ventricular ejection fraction (LVEF) [OR = 1.39 per 10% decrease, 95% CI (1.17–1.66), $P = 0.0002$], non-ischaemic aetiology [OR = 4.44, 95% CI (1.96–10.76), $P = 0.0006$], older age [OR = 1.40 per 10-year increase, 95% CI (1.15–1.72), $P = 0.001$], increased Charlson comorbidity index [OR = 1.38 per 1 point increase, 95% CI (1.12–1.72), $P = 0.004$], and grade 3 MR [OR = 2.23, 95% CI (1.28–3.29), $P = 0.005$] were associated with the decision not to operate. One-year survival was 96.0 $\pm$ 1.4% in patients with a positive decision for intervention vs. 89.5 $\pm$ 2.3% in those with a negative decision ($P = 0.02$).
Conclusion Surgery was denied in 49% of patients with severe symptomatic MR. Impaired LVEF, older age, and comorbidity were the most striking characteristics of patients who were denied surgery. The weight of age and LVEF in the decision do not seem justified according to current knowledge.

Introduction

Mitral regurgitation (MR) is the second most frequent valvular heart disease in industrialized countries.[1] A number of contemporary series, taking into account the changes resulting from the shift from rheumatic to degenerative aetiologies, have improved knowledge on spontaneous prognosis as well as results of surgery in MR.[2–14] Although there is controversy regarding the optimal timing of intervention in asymptomatic patients, a consensus exists that valvular surgery should be advised in symptomatic patients who present with severe MR, as shown by the corresponding class I recommendation in ACC/AHA guidelines.[15] However, the actual application of guidelines has not been studied so far in the latter group of patients.

We used the data from the Euro Heart Survey on valvular heart disease to estimate the actual proportion of symptomatic patients with severe MR in whom a decision not to operate was taken. This was possible because this survey was designed to evaluate practices and, thus, included patients regardless of therapeutic decision. It was also possible to analyse patient characteristics according to the decision to operate or not.

Methods

Study population

The Euro Heart Survey on valvular heart disease was conducted between April and July 2001 in 92 centres from 25 European countries. Recruitment took place in medical and surgical wards, as well as in outpatient clinics in a variety of hospitals. Details of the methodology of the study have been described previously.[1]

Of the 5001 patients included during the 4 months of the study, 877 had isolated MR on a native valve, i.e. without associated mitral stenosis with a valve area $\leq$2 cm^2, aortic regurgitation $\geq$2/4, or aortic stenosis with a maximum jet velocity $\geq$2.5 m/s. Of them, 546 had severe MR, as defined by a grade $\geq$3/4 assessed

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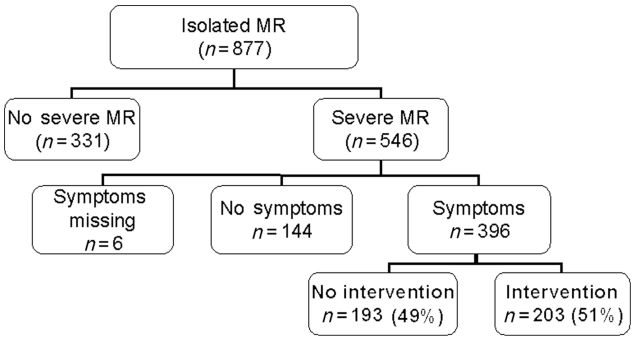

Figure 1 Distribution of patients with isolated MR.

using semi-quantitative Doppler-echocardiography, as pre-specified in the survey.[1] Among these 546 patients, 396 had dyspnea New York Heart Association (NYHA) class II or greater and 144 were in NYHA class I, functional status being missing in six patients (*Figure 1*). The 396 patients with severe MR and symptoms, i.e. dyspnea NYHA class II or greater, form the basis of the present study.

When different methods were available to assess left ventricular ejection fraction (LVEF), priority was given to ventricular angiography, followed by radionuclide and, finally, echocardiographic evaluation. Left ventricular end-diastolic diameter, end-systolic diameter, and left atrial diameter were assessed using time-motion echocardiography. Systolic pulmonary artery pressure was derived from maximum gradient between right ventricle and atrium using continuous-wave Doppler.

Therapeutic decision

The analysis of the therapeutic decision was based on the decision to operate during the index evaluation and not on the actual performance of surgery. Patient characteristics were compared according to whether there was a decision to operate or not. Reasons advocated by responsible practitioners who were interviewed were also analysed for in-hospital patients who were denied surgery.

Outcome

Follow-up started from the inclusion date in the survey. One-year follow-up was pre-specified in the Euro Heart Survey on valvular heart disease. It was available in 392 of 396 cases (99%).

Statistical analysis

Quantitative variables were expressed as mean $\pm$ standard deviation. Predictive factors of the decision not to operate were analysed by comparing 25 patient characteristics related to demographics, risk factors, comorbidity, symptoms, and investigations, as listed in *Tables 1* and *2*. Definitions of risk factors and comorbidities are detailed in the appendix. Comorbidities were analysed individually and combined using the Charlson comorbidity index.[16] Univariable comparisons used the unpaired Student *t*-test for quantitative variables and the χ^2 test for qualitative variables. Variables with $P < 0.25$ were entered in a multivariable logistic model and were selected using a backward procedure with a threshold of $P = 0.05$. An internal validation of the model was performed using the bootstrap resampling technique.[17] The model was applied to 1000 replicated bootstrap samples. The c-index (area under the receiver operating characteristic curve) was calculated for each bootstrap sample and subtracted from the initial c-index obtained in the original population. The average of the differences between the initial c-index and the c-index from the bootstrap samples was then subtracted from the initial c-index to obtain the corrected c-index with the bootstrap technique.

One-year survival was analysed using the Kaplan–Meier method. Univariable analysis of the predictive factors of 1 year mortality used a Cox univariable model. Variables with $P < 0.25$ were entered into a multivariable Cox model and selected using a backward procedure with a threshold of $P = 0.05$, except for the variable 'decision to operate' which was kept in the model. The assumption of proportional hazard hypothesis was verified graphically. All tests were two-sided. A *P*-value <0.05 was considered significant. Analysis was performed with SAS statistical software (SAS Institute Inc. release 8.2).

Results

Patient characteristics

The majority of patients were in-hospital [224 (56%) were included in a medical department, 106 (27%) in a surgical department], and 66 (17%) outpatients.

Mean age of the 396 patients was 66 $\pm$ 13 years; 137 (35%) of them were aged between 70 and 80 and 40 (10%) over 80. Degenerative valve disease with valve prolapse was the most frequent aetiology, being present in 209 (53%) patients. At least one comorbidity was present in 160 (40%) patients. The mean Charlson comorbidity index was 1.24. Coronary artery disease was present in 100 of the 228 (44%) patients in whom coronary angiography was performed: 29 (13%) had single-vessel disease, 29 (13%) had double-vessel disease, 40 (17%) had triple-vessel disease, and two (1%) had left main disease.

Most patients were on medication at inclusion: 272 (69%) received diuretics, 238 (60%) angiotensin-converting enzyme inhibitors, 154 (39%) β-blockers, 98 (25%) nitrates, and 64 (16%) calcium-channel blockers.

Therapeutic decision

Of the 396 symptomatic patients included in this study, surgery was denied in 193 (49%). A decision to operate was taken in 203 patients, among whom 135 (67%) underwent surgery in a participating centre during the survey period and 68 (33%) were scheduled for intervention. Valve replacement was performed in 79 patients (59%) and valve repair in 56 (41%). Coronary artery bypass grafting (CABG) was combined in 39 patients (29%) in the whole population and in 15 of the 18 (83%) patients who underwent surgery for ischaemic MR. Five patients (3.7%) died during the 30 post-operative days: four of the 39 patients (10,3%) who underwent mitral valve repair or replacement combined with CABG, one of the 60 patients (1.7%) who had mitral valve replacement without CABG, and there were no deaths in the 36 patients who had mitral valve repair without CABG.

Patient characteristics associated with decision not to operate in univariable analysis are summarized in *Tables 1* and *2*. Surgery was denied more frequently in older patients (*Figure 2*), in those with congestive heart failure, diabetes, and comorbidity as attested by a higher comorbidity Charlson index (*Figure 3*). Patients with ischaemic MR were more often considered candidates for surgery than those with non-ischaemic, in particular degenerative, MR (*Table 2*). Patients were more frequently denied surgery when LVEF was $<60\%$ and MR was graded 3/4 vs. 4/4 (*Figure 4*).

There was no significant difference between the four European regions regarding the proportion of decision not

Table 1 Patient characteristics associated with therapeutic decision. Univariable analysis (I)

Variable	Decision not to operate ($n = 193$) mean $\pm$ SD or *n* (%)	Decision to operate ($n = 203$) mean $\pm$ SD or *n* (%)	*P*
Demographics			
Age	69 $\pm$ 13	63 $\pm$ 12	<0.0001
Male gender	90 (46.6)	108 (53.2)	0.19
Previous percutaneous coronary intervention	12 (6.2)	11 (5.4)	0.73
Previous CABG	14 (7.3)	7 (3.4)	0.09
Previously known valve disease	128 (66.3)	159 (78.3)	0.008
Risk factors			
Current smokers	23 (11.9)	21 (10.3)	0.62
Hypertension	103 (53.4)	95 (46.8)	0.19
Diabetes	40 (20.7)	21 (10.3)	0.004
Insulin-treated	9 (4.7)	6 (3.0)	0.37
Dyslipidemia	57 (29.5)	63 (31.0)	0.75
Family history	30/147 (20.4)	34/165 (20.6)	0.97
Comorbidity			
Previous myocardial infarction	54 (28.0)	37 (18.2)	0.02
Carotid atherosclerosis	9 (4.7)	4 (2.0)	0.13
Lower limb atherosclerosis	18 (9.3)	7 (3.5)	0.02
Creatinine >200 μMol/L	10 (5.2)	5 (2.5)	0.16
Neurological dysfunction	18 (9.3)	9 (4.4)	0.054
Chronic obstructive pulmonary disease	41 (21.2)	22 (10.8)	0.005
≥1 comorbidity	97 (50.3)	63 (31.0)	<0.0001
Charlson comorbidity index			<0.0001
0	44 (22.8)	101 (49.8)	
1	63 (32.6)	57 (28.1)	
2	48 (24.9)	27 (13.3)	
3	23 (11.9)	10 (4.9)	
>3	15 (7.8)	8 (3.9)	
Symptoms			
Angina pectoris	64 (33.2)	63 (31.0)	0.65
NYHA class			0.36
II	58 (30.0)	72 (35.5)	
III	104 (53.9)	95 (46.8)	
IV	31 (16.1)	36 (17.7)	
Heart failure at admission	94 (48.7)	59 (29.1)	<0.0001
Atrial fibrillation	70 (36.3)	64 (31.5)	0.32

In case of missing data, the number of patients with available data is specified at the denominator. Definitions of risk factors and comorbidities are detailed in the appendix.

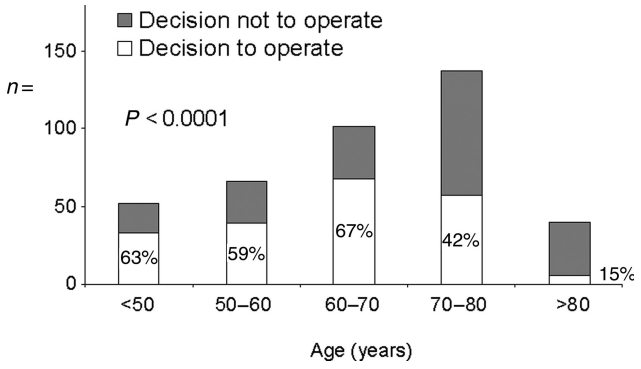

Figure 2 Decision to operate according to age range.

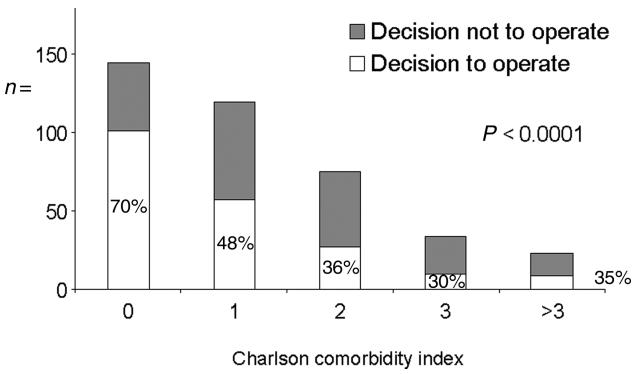

Figure 3 Decision to operate according to the Charlson comorbidity index.

Table 2 Patient characteristics associated with therapeutic decision. Univariable analysis (II)

Variable	Decision not to operate ($n = 193$) mean ± SD or *n* (%)	Decision to operate ($n = 203$) mean ± SD or *n* (%)	*P*
Aetiology			0.03
Degenerative	117 (60.6)	92 (45.4)	
Rheumatic	30 (15.6)	35 (17.2)	
Ischaemic	12 (6.2)	26 (12.8)	
Endocarditis	3 (1.6)	10 (4.9)	
Inflammatory disease	2 (1.0)	5 (2.5)	
Congenital	7 (3.6)	10 (4.9)	
Other or unknown	22 (11.4)	25 (12.3)	
Investigations			
LVEF (%)	48 ± 16	56 ± 13	<0.0001
30–60%	94 (58.0)	92 (48.1)	
<30%	24 (14.8)	4 (2.1)	
Left ventricular end-diastolic dimension (mm)	57 ± 8	59 ± 8	0.014
Left ventricular end-systolic dimension (mm)	41 ± 10	40 ± 8	0.22
Indexed left ventricular end-diastolic dimension (mm/m^2 body surface area)	32 ± 5	33 ± 5	0.01
Indexed left ventricular end-systolic dimension (mm/m^2 body surface area)	23 ± 6	22 ± 5	0.55
Left atrium diameter (mm)	49 ± 10	51 ± 9	0.18
Systolic pulmonary artery pressure (mmHg)	43 ± 21	49 ± 21	0.03
Grade 4/4 MR	38 (19.7)	72 (35.5)	0.0005
Coronary angiography performed	57 (29.5)	173 (85.2)	<0.0001
Coronary artery disease	34/57 (59.7)	66/173 (38.2)	0.005

In case of missing data, the number of patients with available data is specified at the denominator.

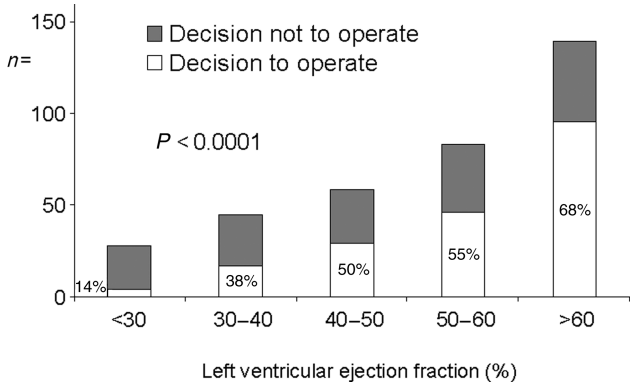

Figure 4 Decision to operate according to LVEF.

to operate, which was 42% in Northern Europe, 46% in Eastern Europe, 50% in Western Europe, and 53% in Mediterranean Europe ($P = 0.63$).

In multivariable analysis, the five characteristics linked to the decision not to operate were lower LVEF, non-ischaemic aetiology, older age, higher Charlson comorbidity index, and grade 3 MR (*Table 3*). The c-index of the final logistic model was 0.760 in the original population and the corrected c-index was 0.735 when validated using the bootstrap technique.

The most frequent reasons advocated by practitioners against surgery, either singly or in combination, were: resolution of symptoms under medical treatment (45%), followed by the presence of comorbidity (37%), advanced age (28%), patient refusal (23%), and terminal heart failure (18%).

Table 3 Factors associated with a decision not to operate. Multivariable analysis

	P	Odds ratio	95% CI
LVEF (per 10% decrease)	0.0002	1.39	(1.17–1.66)
Aetiology	0.0006		
Ischaemic		1	
Non-ischaemic		4.44	(1.96–10.76)
Age (per 10-year increase)	0.001	1.40	(1.15–1.72)
Charlson comorbidity index (per 1 point increase)	0.004	1.38	(1.12–1.72)
Degree of MR	0.005		
Grade 4/4		1	
Grade 3/4		2.23	(1.28–3.29)

Hosmer-Lemeshow goodness-of-fit $\chi 2 = 9.84$ (df = 8), $P = 0.28$.

One-year outcome

Follow-up was available in 191 of the 193 patients (99%) who were denied surgery and in 201 of the 203 cases (99%) in whom operation was decided upon. One-year survival was lower in those who were denied surgery than in those who were considered surgical candidates (89.5 ± 2.3% vs. 96.0 ± 1.4% respectively, $P = 0.02$). In multivariable analysis, older age and higher Charlson comorbidity index were the two predictive factors of a higher 1-year mortality, while therapeutic decision was not a significant predictor (*Table 4*).

Of the 193 patients who were initially denied surgery, 19 (9.8%) underwent mitral surgery during the year following

Table 4 Predictive factors of 1-year mortality. Multivariable analysis

	P	Hazard ratio	95% CI
Age (per 10-year increase)	0.005	1.73	(1.18–2.53)
Charlson comorbidity index (per 1 point increase)	<0.0001	1.48	(1.27–1.73)
Decision	0.85		
Intervention		1	
No intervention		1.08	(0.50–2.33)

inclusion, so that a total of 222 patients were finally operated on. One-year survival was $96.3 \pm 1.3\%$ in the 222 operated patients vs. $88.2 \pm 2.5\%$ in the 174 non-operated patients ($P = 0.003$).

Discussion

In this contemporary pan-European survey including a wide range of centres, 49% of symptomatic patients with severe MR were denied surgery, although surgery is strongly recommended in symptomatic MR according to current guidelines. The characteristics independently associated with a decision not to operate were lower LVEF, non-ischaemic aetiology, older age, higher Charlson comorbidity index, and grade 3 MR.

Population

Most series on MR include hospitalized patients from tertiary centres, who were scheduled for operation. A particularity of the Euro Heart Survey was to screen a wide range of centres and to also include outpatient clinics. Thus, the present study is likely to limit inclusion bias in the analysis of decision-making.

The characteristics of patients with severe and symptomatic MR were consistent with those in published series in industrialized countries.[2–14] The predominance of degenerative aetiologies is associated with relatively advanced age. Forty-five percent of the patients were aged ≥70 in this survey, which may account for the fact that 40% of the patients presented at least one comorbidity. Published series do not always detail comorbidity and, moreover, are likely to report lower rates since most of them are surgical series, with inherent selection bias.

Therapeutic decision and associated patient characteristics

The decision not to operate on approximately half of symptomatic patients with severe MR seems particularly high in the light of ACC/AHA guidelines.[15]

When analysing patient characteristics linked to the therapeutic decision, it is necessary to take into account their respective impacts on the results of surgery as well as on the spontaneous outcome in severe, symptomatic MR.[3,5]

Low LVEF is a predictive factor of spontaneous mortality,[3,5,13] post-operative mortality,[18] and post-operative LVEF[19] in MR. Despite a higher operative risk and less satisfying late results than when LVEF is >60%, symptomatic patients with moderately impaired left ventricular function benefit from surgery since they have a particularly poor outcome under medical therapy.[5] Thus, surgery is a class I recommendation in ACC/AHA guidelines in patients with severe MR and LVEF between 30 and 60%.[15] However, we observed in this survey that this range of LVEF, which accounted for 53% of the population, was associated with a frequent decision not to operate in univariable and multivariable analyses. On the other hand, the recommendation for surgery is less strong in patients who have left ventricular end-systolic dimension >55 mm or ejection fraction <30% (class IIa).[15] However, the latter patients accounted for only 11% of our study population.

In this survey, patients with ischaemic MR were more often considered as candidates for surgery than those with organic MR, in particular degenerative diseases. This may seem somewhat unexpected given the lower risk-benefit ratio in ischaemic when compared with non-ischaemic MR, which explains that indications for mitral surgery are more debated in ischaemic MR.[20] Coronary disease was probably the main reason for indicating surgery in patients with ischaemic MR, since the majority (83%) of operated patients with ischaemic MR underwent associated CABG. It can be supposed that mitral valve surgery was more likely to be associated rather than being the primary reason for surgery. Nevertheless, this association points out that patients with non-ischaemic MR were frequently denied surgery, although most of them had degenerative MR, a condition for which the risk-benefit analysis strongly supports the performance of mitral surgery in symptomatic patients.

Age was strongly associated with the decision not to operate. In univariable analysis, patients aged between 70 and 80 were more often denied surgery although the increase in the risk of surgery is only moderate in this group.[21,22] The relationship between age and the therapeutic decision remained highly significant in multivariable analysis. Given life expectancy in industrialized countries, the comparative assessment of spontaneous outcome and the results of surgery does not support denial of surgery on the sole basis of age in patients aged between 70 and 80, who represented a high proportion of the study population. Surgical denial may be more justified in patients aged over 80, who accounted for only 10% of our study population.

The presence of comorbidities, as attested by a higher Charlson comorbidity index, was associated with a more frequent decision not to operate. This may be understandable since an increased Charlson comorbidity index has a negative impact on life expectancy[16] and most comorbidities also increase operative risk.[21,22] The high frequency of comorbidities is a probable explanation for the high proportion of patients who were denied surgery in the present study. Coronary artery disease increases operative risk, but its weight in the decision to operate cannot be objectively assessed since the performance of coronary angiography is closely linked to the decision to operate.[15] This leads to a bias in the evaluation of the prevalence of coronary disease in non-operated patients. This is the reason why we did not include the presence of coronary artery disease in the multivariable analysis, thereby precluding the analysis of its impact on decision-making. Although there is no

ideal method for controlling the role of comorbidities in decision-making, the Charlson index is widely validated and enables comorbidities to be weighted according to their prognostic impact.

In this survey, patients with grade 3 MR were less frequently considered candidates for surgery when compared with those with grade 4 MR. This suggests that practitioners may not have attributed symptoms to grade 3 MR. However, there is no evidence to support a reluctance to consider surgery in symptomatic patients with grade 3 MR. Semi-quantitative grading of MR has been described according to the angiographic quantitation scale and guidelines advise intervention in symptomatic patients with grade 3 or 4 MR.[15]

Besides objective patient characteristics associated with therapeutic decision, reasons advocated by medical practitioners provided additional, although more subjective, insights into decision-making. Resolution of symptoms under medical therapy was considered as a reason not to operate in nearly half of the patients, either singly or associated with other reasons. This is in contradiction with the predictive value of symptom onset, which is the strongest predictor of mortality, even if resolved under medical treatment.[5] Vasodilators may decrease the regurgitant volume in organic MR.[23] However, their efficacy on survival has not been proven so far, which explains that guidelines do not recommend the use of vasodilators in MR.[15] Consistently with objective patient characteristics identified in this study, age, and comorbidities were also cited as reasons for a decision not to operate. Patient refusal was mentioned in 21% of the patients. However, in particular for the latter reason, the subjective component makes it difficult to interpret, and patient refusal may be strongly influenced by the conviction of the responsible practitioner.

In this survey, the high proportion of patients who were denied surgery is not related to the infrequency of performance of valve repair. Valve repair should be favoured when possible and its feasibility can be a further incentive for intervention. Forty-one percent of the operated patients had valve repair in this study. This can be related to the frequency of degenerative MR and is consistent with the findings of contemporary surgical registries.[24] Moreover, in patients with severe symptomatic MR, surgery should be performed using any kind of technique.[15]

Patient characteristics linked to the decision not to operate in patients with severe MR are consistent with those identified in aortic stenosis in the elderly in the same survey, in particular older age and impaired LVEF.[25] Although prognostic implications of LVEF differ between aortic stenosis and MR, these findings show that treatments tend to be under-used in the patients who have the highest risk profile, as in other heart diseases.

Outcome

Operative mortality was relatively low in this series. This is likely to be a consequence of the frequent performance of valve repair and, more importantly, the selection of patients at relatively low risk for surgery, as attested by the factors linked to the therapeutic decision.

One-year mortality was mainly related to age and comorbidities. Unlike in univariable analysis, decision-making was not significantly linked to 1-year outcome in multivariable analysis. However, this finding should be interpreted with great caution because multivariable analyses have limitations for controlling the respective strengths of strongly linked predictive factors. The absence of predictive value of the decision to operate on survival may also be explained by the short duration of follow-up. When a decision to operate was taken, most deaths were observed during the post-operative period, while their occurrence was more progressive in non-operated patients. Therefore, longer follow-up of at least several years would be required to assess the benefit of surgery.

Even when taking into account the 19 patients who were initially denied surgery, but who underwent subsequent intervention, there were no relevant changes in 1-year survival of operated and non-operated patients.

Study limitations

The Euro Heart Survey enables actual practices in the surgical treatment of valvular heart diseases to be better ascertained than in series from surgical or tertiary centres. However, the true proportion of patients who were denied surgery cannot be estimated since this survey only included patients who were referred to cardiologists. Thus, it is likely that this proportion is even higher in the general population.

The severity of MR was assessed using semi-quantitative and not quantitative Doppler-echocardiography and there was no central reading. However, in this survey, MR grade should be interpreted with caution given the limitations inherent to semi-quantitation. The combination of different methods, including quantitative echocardiography, is now recommended and quantitation of MR has a prognostic value.[26,27] However, these recommendations had not been published at the time the survey was performed. The requirement of quantitative methods would have limited the inclusion of patients from non-tertiary centres and would have precluded practices being evaluated in a wide range of health care structures.

Selection bias cannot be ruled out in the present survey. Although there was a wide range of participating centres, they were not selected at random and this study cannot be considered as epidemiologically representative.

The lack of external validation limits the accuracy of the factors linked to the decision not to operate. However, the predictive ability of the logistic model was attested by the low decrease in its discriminant accuracy, as assessed by the c-index, when using the bootstrap technique to limit the bias inherent to internal validation.

This survey enables the reasons of actual decisions in patients for whom guidelines advise intervention, to be assessed for the first time. However, it does not enable the whole process of decision-making to be assessed and the appropriateness of the decision to be analysed in each individual patient.

Conclusion

This contemporary survey shows that as many as a half of symptomatic patients presenting with severe MR were denied surgery.

The fact that non-operated patients were older and more frequently have moderate impairment of LVEF than operated patients suggests that the decision not to operate may

not be always justified by the corresponding risk-benefit analysis of surgery. The relationship between comorbidities and the decision not to operate may seem more justified and this has an important impact given the increase in age and inherent proportion of comorbidites in patients with valvular diseases in industrialized countries.

Further prospective studies are warranted to address in particular the impact of comorbidities, and their interaction with other characteristics in the risk-benefit analysis of the decision to operate.

Acknowledgements

The Euro Heart Survey on valvular heart disease was funded by: 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.

Conflict of interest: B.I. received speaker's honoraria from Edwards Lifesciences. A.V. is consultant for Edwards Lifesciences.

Appendix: definitions

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 pressure, or known blood pressure values of ≥140 mmHg systolic or ≥90 mmHg 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 forced expiratory volume <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.

Coronary artery disease: ≥1 stenosis >50% of vessel diameter on coronary angiography.

Congestive heart failure: clinical sign of congestive heart failure at admission.

References

1. Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Barwolf C, Levang OW, Tornos P, Vanoverschelde JL, Vermeer F, Boersma E, Ravaud P, Vahanian A. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on valvular heart disease. *Eur Heart J* 2003;**24**:1231–1243.
2. Olson LJ, Subramanian R, Ackermann DM, Orszulak TA, Edwards WD. Surgical pathology of the mitral valve: a study of 712 cases spanning 21 years. *Mayo Clin Proc* 1987;**62**:22–34.
3. Delahaye JP, Gare JP, Viguier E, Delahaye F, De Gevigney G, Milon H. Natural history of severe mitral regurgitation. *Eur Heart J* 1991;**12** (Suppl B):5–9.
4. Rosen SE, Borer JS, Hochreiter C, Supino P, Roman MJ, Devereux RB, Kligfield P, Bucek J. Natural history of the asymptomatic/minimally symptomatic patient with severe mitral regurgitation secondary to mitral valve prolapse and normal right and left ventricular performance. *Am J Cardiol* 1994;**74**:374–380.
5. Ling LH, Enriquez-Sarano M, Seward JB, Tajik AJ, Schaff HV, Bailey KR, Frye RL. Clinical outcome of mitral regurgitation due to flail leaflet. *N Engl J Med* 1996;**335**:1417–1423.
6. Crawford MH, Souchek J, Oprian CA, Miller DC, Rahimtoola S, Giacomini JC, Sethi G, Hammermeister KE. Determinants of survival and left ventricular performance after mitral valve replacement. Department of Veterans Affairs cooperative study on valvular heart disease. *Circulation* 1990;**81**:1173–1181.
7. Reed D, Abbott RD, Smucker ML, Kaul S. Prediction of outcome after mitral valve replacement in patients with symptomatic chronic mitral regurgitation. The importance of left atrial size. *Circulation* 1991;**84**:23–34.
8. Lee EM, Shapiro LM, Wells FC. Importance of subvalvular preservation and early operation in mitral valve surgery. *Circulation* 1996;**94**: 2117–2123.
9. Gillinov AM, Cosgrove DM, Blackstone EH, Diaz R, Arnold JH, Lytle BW, Smedira NG, Sabik JF, McCarthy PM, Loop FD. Durability of mitral valve repair for degenerative disease. *J Thorac Cardiovasc Surg* 1998;**116**: 734–743.
10. Mohty D, Orszulak TA, Schaff HV, Avierinos JF, Tajik JA, Enriquez-Sarano M. Very long-term survival and durability of mitral valve repair for mitral valve prolapse. *Circulation* 2001;**104**(Suppl. 1):I1–I7.
11. Braunberger E, Deloche A, Berrebi A, Abdallah F, Celestin JA, Meimoun P, Chatellier G, Chauvaud S, Fabiani JN, Carpentier A. Very long-term results (more than 20 years) of valve repair with Carpentier's techniques in nonrheumatic mitral valve insufficiency. *Circulation* 2001;**104**(Suppl. I): I8–I11.
12. Ruel M, Rubens FD, Masters RG, Pipe AL, Bedard P, Mesana TG. Late incidence and predictors of persistent or recurrent heart failure in patients with mitral prosthetic valves. *J Thorac Cardiovasc Surg* 2004;**128**: 278–283.
13. Avierinos JF, Gersh BJ, Melton LJ 3rd, Bailey KR, Shub C, Nishimura RA, Tajik AJ, Enriquez-Sarano M. Natural history of mitral valve prolapse in the community. *Circulation* 2002;**106**:1355–1361.
14. David TE, Ivanov J, Armstrong S, Christie D, Rakowski H. A comparison of outcomes of mitral valve repair for degenerative disease with posterior, anterior, and bileaflet prolapse. *J Thorac Cardiovasc Surg* 2005;**130**: 1242–1249.
15. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, Gaasch WH, Whitney Lytle B, Nishimura RA, O'Gara PT, O'Rourke RA, Otto CM, Shah PM, Shanewise JS. ACC/AHA 2006 Guidelines for the Management of Patients With Valvular Heart Disease A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2006;**48**:e1–e148.
16. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**:373–383.
17. Steyerberg EW, Harrell FE Jr, Borsboom GJJM, Eijkemans MJC, Vergouwe Y, Habbema JDF. Internal validation of predictive models: efficiency of some procedures for logistic regression models. *J Clin Epidemiol* 2001;**54**:774–781.
18. Enriquez-Sarano M, Tajik AJ, Schaff HV, Orszulak TA, Bailey KR, Frye RL. Echocardiographic prediction of survival after surgical correction of organic mitral regurgitation. *Circulation* 1994;**90**:830–837.
19. Enriquez-Sarano M, Tajik AJ, Schaff HV, Orszulak TA, Mc Goon MD, Bailey KR, Frye RL. Echocardiographic prediction of left ventricular function after correction of mitral regurgitation: results and clinical implications. *J Am Coll Cardiol* 1994;**24**:1536–1543.
20. Levine RA, Schwammenthal E. Ischaemic mitral regurgitation on the threshold of a solution: from paradoxes to unifying concepts. *Circulation* 2005;**112**:745–758.
21. Ambler G, Omar RZ, Royston P, Kinsman R, Keogh BE, Taylor KM. Generic, simple risk stratification model for heart valve surgery. *Circulation* 2005; **112**:224–231.
22. Roques F, Nashef SA, Michel P, Gauducheau E, de Vincentiis C, Baudet E, Cortina J, David M, Faichney A, Gabrielle F, Gams E, Harjula A, Jones MT, Pintor PP, Salamon R, Thulin L. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. *Eur J Cardiothorac Surg* 1999;**15**:816–823.

23. Levine HJ, Gaasch WH. Vasoactive drugs in chronic regurgitant lesions of the mitral and aortic valves. *J Am Coll Cardiol* 1996;**28**: 1083–1091.
24. US Society of Thoracic Surgeons National Database. http://www.sts.org/section/stsdatabase://www.sts.org/section/stsdatabase (19 November 2005).
25. Iung B, Cachier A, Baron G, Messika-Zeitoun D, Delahaye F, Tornos P, Gohlke-Bärwolf C, Boersma E, Ravaud P, Vahanian A. Decision making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J* 2005;**26**:2714–2720.
26. Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, Nihoyannopoulos P, Otto CM, Quinones MA, Rakowski H, Stewart WJ, Waggoner A, Weissman NJ. American Society of Echocardiography Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr* 2003;**16**:777–802.
27. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, Detaint D, Capps M, Nkomo V, Scott C, Schaff HV, Tajik AJ. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med* 2005;**352**: 875–883.