European Journal of Cardio-thoracic Surgery 30 (2006) 15—19

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Patient prosthesis mismatch affects short- and long-term outcomes after aortic valve replacement ☆

Thomas Walther *, Ardawan Rastan, Volkmar Falk, Sven Lehmann, Jens Garbade, Anne K. Funkat, Friedrich W. Mohr, Jan F. Gummert

Universität Leipzig, Herzzentrum, Klinik für Herzchirurgie, Strümpellstrasse 39, 04289 Leipzig, Germany

Received 29 December 2005; received in revised form 2 April 2006; accepted 13 April 2006

Abstract

Objective: The aim of this study was to evaluate the impact of patient prosthesis mismatch (PPM) and additional risk factors on outcome after aortic valve replacement (AVR). **Methods:** Four thousand one hundred and thirty-one patients who were operated between May 1996 and April 2004 were evaluated. One thousand eight hundred and fifty-six patients received bileaflet mechanical AVR and 2275 stented xenograft AVR. PPM was defined as severe if manufacturers effective orifice area (EOA) divided by body surface area (BSA) was < 0.65 cm^2/m^2 and as moderate in the range of 0.65—0.85 cm^2/m^2. PPM, age, gender, EOA index, emergency indication for surgery (within 24 h), EuroSCORE as well as requirement for additional procedures were tested. Univariate (Fisher's exact test) and multivariate logistic regression analysis as well as survival analysis (Kaplan—Meier) were performed. **Results:** Severe PPM was present in 97 (2.4%) and moderate PPM in 1103 (26.7%) patients. PPM occurs more frequently with xenograft AVR. In-hospital mortality was 5.2% for severe, 10.6% for moderate and 6.9% with no PPM ($p = 0.018$, OR 1.4). Moderate PPM was independently predictive for short- and long-term mortality. Further analysis revealed patient age > 70 years ($n = 1589$, $p = 0.002$, OR 1.85), emergency indication ($n = 374$, $p < 0.001$, OR 4.4), EuroSCORE > 10 ($n = 494$, $p < 0.001$, OR 4.7) and additional cardiac procedures ($n = 2049$, $p < 0.001$, OR 2.0) as predictors for adverse outcome after AVR. **Conclusion:** Severe PPM is rare; moderate PPM is present in a quarter of patients. PPM has a significant impact on short- and long-term mortality after AVR.

Keywords: Aortic valve replacement; Stented aortic valve prosthesis; Patient prosthesis mismatch

1. Introduction

Aortic valve replacement (AVR) has evolved as a standard procedure with low morbidity and mortality over the past decades [1]. AVR is performed in more than 10,000 patients annually in Germany. In-hospital mortality was 2.5% after mechanical valve and 3.8% after xenograft implantation in 2004 [2]. In the US the risk for isolated AVR was 4.3% in 1999 [3]. Age has been identified as an independent risk factor and subgroups, especially octogenarians have a higher risk of up to 10% following aortic valve surgery [3,4].

For AVR conventional stented xenografts or mechanical prostheses are most frequently implanted. No perfect artificial prosthesis is available at present. Conventional stents lead to some obstruction of blood flow. Stent design has evolved during the past years towards lower profiles and thinner sewing rings. Thus adequate effective orifice areas and sufficient hemodynamic function can be obtained for most patients. Residual obstruction usually is well compensated by the — frequently hypertrophied — left ventricle. However, obstruction to blood flow may also be related to an increase in perioperative and postoperative morbidity and mortality.

The concept of patient prosthesis mismatch (PPM) had been introduced by Rahimtoola [5] in the 1970s. More recently there were publications by groups in favor of the hypothesis that PPM is an independent predictor of mortality [6,7]. In contradiction there are others that found that survival after AVR appears not to be adversely affected by moderate PPM [8].

Aim of our study was to evaluate the incidence of PPM as well as its potential impact on adverse patient outcome. In addition, we thought to assess the clinical relevance of additional risk factors after AVR.

2. Materials and methods

2.1. Patients

A total of 4131 patients operated during an eight-year period between May 1996 and April 2004 were evaluated. All

☆ Presented at the joint 19th Annual Meeting of the European Association for Cardio-thoracic Surgery and the 13th Annual Meeting of the European Society of Thoracic Surgeons, Barcelona, Spain, September 25—28, 2005.

* Corresponding author. Tel.: +49 341 865 1424; fax: +49 341 865 1452.
E-mail address: walt@medizin.uni-leipzig.de (T. Walther).

1010-7940/$ — see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.ejcts.2006.04.007

patients were prospectively included into the hospital's patient data management system. Based on these data entered during routine clinical therapy further analyses were performed.

All patients having elective or emergency AVR during this time period were included. Patients receiving stentless AVR were excluded from this analysis. A total of 1856 patients received bileaflet mechanical AVR and 2275 patients received conventional stented xenograft AVR. The possible impact of PPM on survival and perioperative outcome was evaluated. By intention additional analysis on the incidence of PPM in relation to the different valve prostheses was not performed as multiple criteria for individual valve selection exist.

2.2. Patient prosthesis mismatch

PPM was defined in three categories according to standard definitions as published by the Quebec group [6]. The aortic valve prosthesis effective valve orifice area (EOA) was divided by body surface area (BSA) to obtain the EOA index. PPM was then defined as none if EOA index was $>0.85\ cm^2/m^2$, as moderate for $0.65–0.85\ cm^2/m^2$ and as severe for $<0.65\ cm^2/m^2$. Effective valve orifice areas were derived from the literature as provided by the manufacturers and from scientific publications from in vitro measurements [6,9]. Values of expected effective orifice areas from in vitro measurements for the different aortic valve prostheses implanted that were used in this study are given in Table 1.

2.3. Follow-up

Individual patient contact was achieved by sending questionnaires to all patients annually after the operation. Non-responders were contacted by telephone; if no further information was available the family physicians were contacted. Follow-up results were available for all 4131 patients evaluated. Follow-up extended to 8.5 years at a mean of 5.2 ± 3.5 years.

2.4. Statistical evaluation

Results are given in a standard fashion with continuous variables expressed as mean ± standard deviation and categorical data as proportions. For continuous variables comparisons were performed using Student's *t*-test (variables with normal distribution) or the Mann–Whitney *U*-test. Categorical variables were compared by chi-square analysis. Univariate analysis of risk factors was performed calculating odds ratios (OR) with 95% confidence intervals. Several factors, patient age, gender, body weight, body surface area, diameter of the aortic valve prosthesis in millimeter, presence or absence of PPM, emergency indication, the EuroSCORE [10] value indicating the specific risk for the individual patient and requirement for additional surgery (e.g., AVR + coronary artery bypass graft (CABG) surgery or AVR + other valve ± aortic surgery) were tested.

Variables with a *p*-value less than 0.05 were consecutively subjected to a multivariate logistic regression model to assess the independent impact of the risk factors on outcome. A stepwise procedure (backward Wald) was used. A *p*-value less than 0.05 was used both to enter and eliminate variables.

Cumulative survival was calculated by Kaplan–Meier methods and differences in follow-up were calculated with 95% confidence limits and compared by log rank (Mantel cox) test.

All statistical analyses were performed using SPSS™ statistical package 13.0 (SPSS Corp., Birmingham, AL, USA). A *p*-value less than 0.05 was considered to indicate statistical significance.

3. Results

Mean age of the patients was 58.9 ± 10.2 years for mechanical AV and 72.1 ± 8.5 years for xenograft AVR. Mean patient age for the years is given in Fig. 1. As indicated, there was a steady increase in xenograft implantation in parallel to a decline in the number of mechanical prostheses used. 71.3% (mechanical AVR) and 55.9% (xenograft AVR) of the patients were male. Mean body surface area was $1.94 \pm 0.21\ m^2$ (range 1.24–2.88) for mechanical AVR and $1.87 \pm 0.2\ m^2$ (range 1.25–2.65) for xenograft AVR.

Data on all 4131 patients receiving AVR were available for further evaluation on the relevance of PPM. Two thousand and eighty-two patients (50.4%) had isolated AVR and 2049

Table 1
Values of expected effective orifice areas (EOA) for the different aortic valve prostheses implanted used in this study

	19 mm	21 mm	23 mm	25 mm	27 mm	29 mm
Mechanical prosthesis						
Advantage		1.65	2.17	2.80	3.3	3.9
ATS Std.	1.2	1.5	1.75	2.15	2.5	3.1
Carbomedics	1.06	1.41	1.75	2.19	2.63	3.07
On-X	1.5	1.7	2	2.4	3.2	3.2
Regent	1.84	2.47	2.91	3.34	4.28	4.8
SJM HP	1.51	2.03	2.59	3.08	3.73	
Stented xenograft						
CE porcine	1.06	1.4	1.46	1.52	1.88	2.18
CE Perimount	1.22	1.82	1.96	2.12	2.38	2.66
Epic		1.14	1.4	1.7		
Mosaic	1.02	1.13	1.56	1.8	1.97	2.22

Data are derived from the literature [6,7,9]. EOA in square centimeter.

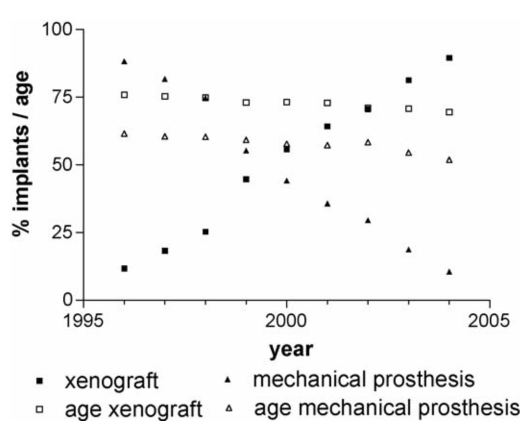

Fig. 1. Percentage of xenografts and mechanical prostheses as implanted over the years. There was a steady increase in xenograft use. In addition, mean patient age for the xenograft and mechanical valve groups is given.

Table 2
Univariate predictors for adverse outcome

	n	*p*	Odds ratio	95% confidence interval
Age > 70	1589	0.002	1.85	1.5—2.4
Emergency indication	374	<0.001	4.4	3.4—5.9
EuroSCORE > 10	494	<0.001	4.7	3.6—6.0
Requirement for additional procedures	2049	<0.001	2.0	1.6—2.6
PPM	1200	<0.001	1.5	1.2—1.9

PPM indicates patient prosthesis mismatch.

Table 3
Independent predictors for adverse outcome at multivariate logistic regression analysis

	n	*p*	Odds ratio	95% confidence interval
Age > 70	1589	0.006	1.43	1.1—1.9
Emergency indication	374	<0.001	3.27	2.4—4.5
EuroSCORE > 10	494	<0.001	2.73	2—3.7
Requirement for additional procedures	2049	<0.001	1.81	1.4—2.3
PPM	1200	0.016	1.37	1.1—1.8

PPM indicates patient prosthesis mismatch.

required additional procedures, mostly additional coronary artery bypass grafting. A total of 2931 (71%) patients had no PPM, 1103 patients (26.7%) had moderate PPM and 97 patients (2.3%) had severe PPM. In-hospital and 30-day mortality was 6.9% if no PPM was present, 10.6% in presence of moderate PPM, and 5.2% in presence of severe PPM. Due to the relatively small number of patients having severe PPM, no further separate statistical evaluation was performed for this subgroup. Moderate PPM was identified as being independently predictive for in-hospital and 30-day mortality. Patients were further evaluated according to presence (EOA/BSA $< 0.85\ cm^2$) or absence of PPM. Longer term outcome is summarized in Fig. 2. Five-year survival was $84.9 \pm 0.7\%$ if no PPM was present and $79.6 \pm 1.3\%$ with PPM, $p < 0.01$. Eight and a half year survival was $81.4 \pm 1\%$ if no PPM was present and $76.8 \pm 1.7\%$ with PPM, $p < 0.01$.

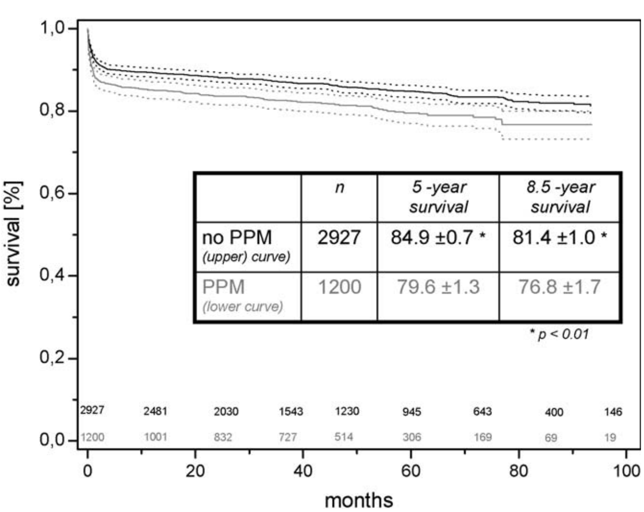

Fig. 2. Kaplan—Meier cumulative survival for patients with patient prosthesis mismatch (PPM) and with no mismatch. Five-year as well as 8.5-year survivals together with 95% confidence intervals are illustrated. Patients having no PPM are represented by the upper (black) and patients having PPM by the lower (gray) curve. Patients at risk are indicated at the bottom.

Besides PPM all other parameters tested were evaluated regarding their impact on survival after AVR with or without additional procedures. Several of the factors tested were found to be univariate predictors for an adverse outcome. These were patient age more than 70 years ($n = 1589$, $p = 0.002$, OR 1.85), emergency indication ($n = 374$, $p < 0.001$, OR 4.4), EuroSCORE > 10 ($n = 494$, $p < 0.001$, OR 4.7) and requirement for additional procedures, mostly additional coronary artery bypass grafting ($n = 2049$, $p < 0.001$, OR 2.0). These additional risk factors are summarized in Table 2.

At multivariate logistic regression analysis all these parameters were identified as independent predictors for an adverse outcome. This is indicated in Table 3.

4. Discussion

AVR is routinely performed using conventional xenografts or mechanical prostheses. AVR like all other cardiac surgical interventions is associated with a change in patient profile towards a continuously increasing age at the time of the operation. This is associated with an increase in additional risk factors. The steady increase in patient age leads to a change of indications towards more frequent implantation of xenografts.

In the presence of excellent perioperative outcome after AVR factors possibly affecting the longer term functionality gain more and more importance. Besides valve durability the effective hemodynamic properties of the implanted prosthesis may have a direct impact on follow-up mortality. As such surgeons strive to implant the largest valve possible in order to obtain the best hemodynamic performance. However, some residual obstruction remains. This may lead to impaired hemodynamic function and residual gradients, especially under exercise conditions. Thus theoretically the concept of PPM is important and should be considered whenever AVR is performed.

The concept of PPM is currently being controversially discussed in the scientific literature. Several studies support

Table 4
Patient prosthesis mismatch (PPM) and its relevance: overview of the current literature

Author	Year	Study design	Patient number	OP interval	Definition	Findings	PPM is important	Ref.
Fuster et al.	2005	One center	339	03/94–11/01	(a)	Important in presence of severe LVH	Yes	[18]
Tasca et al.	2005	One center	111	09/97–04/03	(a)	Larger EOA result in better LVM regression	Yes	[19]
Ruel et al.	2004	One center	1563	1976–2001	(c)	Prosthesis size has influence on heart failure	Yes	[20]
Blais et al.	2003	One center	1266	01/92–12/01	(a)	PPM is independent predictor of short term mortality	Yes	[6]
Blackstone et al.	2003	Multicenter	13258	1970–1999	(c)	Increased risk with indexed orifice area < 1.2 cm^2/m^2	Yes	[16]
Rao et al.	2000	Two center	2981	1976–1996	(b)	PPM predicts valve related mortality	Yes	[7]
Pibarot et al.	1998	One center	392	1986–1995	(a)	Less symptomatic improvement	Yes	[14]
Pibarot et al.	1996	One center	61	n/a	(a)	Worse hemodynamic performance	Yes	[15]
Moon et al.	2006	One center	1400	06/92–05/04	(b)	PPM important in young and large patients	Yes	[17]
Koch et al.	2005	One center	1014	06/95–05/98	(c)	Functional recovery evaluated	No	[11]
Frapier et al.	2002	One center	90	1986–1990	(a)	10-year follow-up	No	[12]
Hanayama et al.	2002	One center	1129	1990–2000	(c)	No influence, severe PPM is rare	No	[13]
Medalion et al.	2000	One center	892	1978–1996	(c)	Patient risk factors but not PPM are important	No	[8]

Definitions: (a) moderate PPM: EOA/BSA = 0.65–0.85 cm^2/m^2; severe PPM: EOA/BSA < 0.65 cm^2/m^2; (b) PPM: EOA/BSA < 0.75 cm^2/m^2; (c) full spectrum of size values normalized to patient size evaluated.

the concept of PPM while others question its impact on outcome. This includes studies from single centers with longer term follow-up or multicenter evaluations. A summary of the pros and cons is given in Table 4. There are four studies that found no impact of PPM on patient outcome [8,11–13]. These were published by the groups from Cleveland [8,11], one group from Toronto [13] and Montpellier [12]. The authors concluded that other than valve size related factors are important for short- and long-term outcomes of the patients [8,12,13]. In addition, functional recovery was shown not to be adversely affected in the presence of PPM [11]. All other studies, especially from the Quebec group [6,14,15] as well as from another group in Toronto [7] came to the conclusion that there is a significant impact of PPM upon patient outcome after AVR. The Quebec group deserves the credit to bring the whole concept to the attention of cardiac surgeons. Interestingly, in a multicenter evaluation of more than 13,000 patients including data from Cleveland an increased risk associated with an indexed orifice area $<$1.2 cm^2 was found [16]. This underlines the functional importance of the presence of PPM. However, an important additional conclusion of this multicenter evaluation was that PPM rarely occurs as the smaller sized xenografts were implanted rather infrequently [16]. Recently, PPM was found to be important in younger as well as in older patients [17].

In accordance with several of the mentioned studies [6,7,14,15,18–20] we found a significant impact of moderate PPM on long-term survival. Furthermore, relatively few patients presented with severe PPM, which is in accordance with Blackstones' findings [16]. Surprisingly, survival was slightly better in presence of severe versus moderate PPM in our population. However, due to the small number of patients presenting with severe PPM a meaningful statistical comparison was not justified for that group. Data evaluation was therefore performed focusing on the comparison of two groups, patients without versus patients with moderate PPM. The survival shown in Fig. 1 revealed that there is a significant impact of PPM on short and intermediate term outcome up to 8.5 years. Subgroup comparisons between different products were not performed as this was not the goal of the study.

Can we exclude any bias possibly occurring from technical aspects? Only experienced surgeons performed AVR in this series. Valve size selection was performed using valve specific standard sets of sizers after complete resection of the stenotic native valve cusps and complete decalcification of the AV annulus. The largest suitable valve was always selected for a given patient. Valve implantation was performed routinely using horizontal mattress sutures. This technique with pledget reinforced sutures results in a slightly supraannular position of all implanted AV prostheses. Aortic root enlargement techniques are not routinely performed in presence of small aortic annuli in our center to avoid any possible increase in operative risk.

The implantation of stentless valves may be an alternative for patients presenting with a small aortic annulus in order to avoid PPM. This has been shown by several studies [21–24]. However, stentless valve implantation can be technically more demanding and there is no proof as yet whether this will lead to improved long-term survival in the elderly.

The present study was based on data extracted from a routine patient data management system with retrospective analysis. Further prospective evaluation of the impact of PPM upon longer term hemodynamic function will be important. Assessment of the potential regression of left ventricular hypertrophy in parallel to an improvement in transvalvular gradient and in relation to overall patient outcome would be advantageous to select the optimal therapy for the individual patient.

This study clearly underlines that PPM is an important factor. To avoid PPM in future knowledge about the specific characteristics of the selected prosthetic heart valve together with detailed preoperative echocardiographic analysis of the individuals' annular diameter will allow to define suitable valve sizes for a given patient preoperatively. In case the selected sizer will not fit intraoperatively other strategies, such as root enlargement, use of stentless valves or even root replacement techniques may be chosen. This will lead to an optimal result with long lasting functional outcome.

References

[1] Bonow RO, Carabello B, deLeon AC, Edmunds Jr LH, Fedderly BJ, Freed MD, Gaasch WH, McKay CR, Nishimura RA, O'Gara PT, O'Rourke RA, Rahimtoola SH. ACC/AHA practice guidelines. Guidelines for the management of patients with valvular heart disease. Executive summary. Circulation 1998;98:1949—84.

[2] Gummert JF, Funkat A, Krian A. Cardiac Surgery in Germany during 2004: a report by the German Society for Thoracic and Cardiovascular Surgery. Thorac Cardiovasc Surg 2005;53:391—9.

[3] Jamieson WR, Edwards FH, Schwartz M, Bero JW, Clark RE, Grover FL, for the Database Committee of the Society of Thoracic Surgeons. Risk stratification for cardiac valve replacement. National cardiac surgery database. Ann Thorac Surg 1999;67:943—51.

[4] Chiappini B, Camurri N, Loforte A, Di Marco L, Di Bartolomeo R, Marinelli G. Outcome after aortic valve replacement in octogenarians. Ann Thorac Surg 2004;78:85—9.

[5] Rahimtoola SH. The problem of valve prosthesis-patient mismatch. Circulation 1978;58:20—4.

[6] Blais C, Dumesnil JG, Baillot R, Simard S, Doyle D, Pibarot P. Impact of valve prosthesis-patient mismatch on short-term mortality after aortic valve replacement. Circulation 2003;108:983—8.

[7] Rao V, Jamieson WR, Ivanov J, Armstrong S, David TE. Prosthesis-patient mismatch affects survival after aortic valve replacement. Circulation 2000;102:III-5—9.

[8] Medalion B, Blackstone EH, Lytle BW, White J, Arnold JH, Cosgrove DM. Aortic valve replacement: is valve size important? J Thorac Cardiovasc Surg 2000;119:963—74.

[9] Marquez S, Hon RT, Yoganathan AP. Comparative hydrodynamic evaluation of bioprosthetic heart valves. J Heart Valve Dis 2001;10:802—11.

[10] 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 19,030 patients. Eur J Cardiothorac Surg 1999;15:816—22.

[11] Koch CG, Khandwala MS, Estafanous FG, Loop FD, Blackstone EH. Impact of prosthesis-patient size on functional recovery after aortic valve replacement. Circulation 2005;111:3221—9.

[12] Frapier JM, Rouviere P, Razcka F, Aymard T, Albat B, Chaptal PA. Influence of patient-prosthesis mismatch on long-term results after aortic valve replacement with a stented bioprosthesis. J Heart Valve Dis 2002;11:543—51.

[13] Hanayama N, Christakis GT, Mallidi HR, Joyner CD, Fremes SE, Morgan CD, Mitoff PR, Goldman BS. Patient prosthesis mismatch is rare after aortic valve replacement: valve size may be irrelevant. Ann Thorac Surg 2002; 73:1822—9.

[14] Pibarot P, Dumesnil JG, Lemieux M, Cartier P, Metras J, Durand LG. Impact of prosthesis-patient mismatch on hemodynamic and symptomatic status, morbidity and mortality after aortic valve replacement with a bioprosthetic heart valve. J Heart Valve Dis 1998;7:211—8.

[15] Pibarot P, Honos GN, Durand LG, Dumesnil JG. The effect of prosthesis-patient mismatch on aortic bioprosthetic valve hemodynamic performance and patient clinical status. Can J Cardiol 1996;12:379—87.

[16] Blackstone E, Cosgrove DM, Jamieson WRE, Birkmeyer NJ, Lemmer JH, Miller DC, Butchart EG, Rizzoli G, Yacoub M, Chai A. Prosthesis size and long-term survival after aortic valve replacement. J Thorac Cardiovasc Surg 2003;126:783—96.

[17] Moon MR, Pasque MK, Munfakh NA, Melby SJ, Lawton JS, Moazami N, Codd JE, Crabtree TD, Barner HB, Damiano RJ. Prosthesis-patient mismatch after aortic valve replacement: impact on age and body size on late survival. Ann Thorac Surg 2006;81:481—9.

[18] Fuster RG, Argudo JAM, Albarova OG, Sos FH, López SC, Codoner MB, Minano JAB, Albarran IR. Patient-prosthesis mismatch in aortic valve replacement: really tolerable? Eur J Cardiothorac Surg 2005;27:441—9.

[19] Tasca G, Brunelli F, Cirillo M, Tomba MD, Mhagna Z, Troise G, Quaini E. Impact of the improvement of valve area achieved with aortic valve replacement on the regression of left ventricular hypertrophy in patients with pure aortic stenosis. Ann Thorac Surg 2005;79:1291—6.

[20] Ruel M, Rubens FD, Masters RG, Pipe AL, Bédard P, Hedry PJ, Lam BK, Burwash IG, Goldstein WG, Brais MP, Keon WJ, Mesana TG. Late incidence and predictors of persistent or recurrent heart failure in patients with aortic prostheses. J Thorac Cardiovasc Surg 2004;127:149—59.

[21] Ennker J, Rosendahl U, Albert A, Dumlu E, Ennker IC, Florath I. Stentless bioprostheses in small aortic roots: impact of patient-prosthesis mismatch on survival and quality of life. J Heart Valve Dis 2005;14:523—30.

[22] Borger MA, Carson SM, Ivanov J, Rao V, Scully HE, Feindel CM, David TE. Stentless aortic valves are hemodynamically superior to stented valves during mid-term follow-up: a large retrospective study. Ann Thorac Surg 2005;80:2180—5.

[23] Petracek MR. Assessing options for the small aortic root. J Heart Valve Dis 2002;11(Suppl. 1):S50—5.

[24] Walther T, Falk V, Diegeler A, Gummert J, Autschbach R, Mohr FW. Stentless valve replacement in the small aortic root. Cardiovasc Surg 1997;5:229—34.

Appendix A. Conference discussion

Dr A. Moritz (*Frankfurt*, *Germany*): As you had this large set of data, why didn't you risk adjust your survival curves? As you identified that age and additional surgery is a risk, if I understood this right, then maybe you simply have in the small aortic valve group, a higher percentage of these risk factors. Then of course you have a higher mortality, but this is not due to the small prosthesis but more due to the risk factors.

Dr Walther: Well, we could do that, of course. We are going to do subgroup analysis in the next month.

Dr Moritz: But it may well be in the results you presented now, that the groups mismatch versus non-mismatch have different risk factors.

Dr Walther: Could be, yes. But I assume from the large number that they're kind of equally distributed.

Dr Moritz: Well, in our experience, you have most probably the highest chance to have a mismatch in the old ladies with very hypertrophic ventricles. Male patients usually have either a tendency to enlarge their ventricles, so you usually get a larger valve size and already this causes a risk difference.

Dr P. Herijgers (*Leuven*, *Belgium*): I have two questions that are in fact referring to the same.

Yesterday we heard from the presentation of Bart Meuris that it's very important which reference values for effective orifice area you use, especially when you use, for example, in your series freestyle valves or St. Jude valves.

Can I ask you, how was the composition of your patient group, which valves were used, and which reference values for the effective orifice areas did you use to calculate patient prosthesis mismatch?

Dr Walther: Well, basically, that's an important comment. Stentless valves were not included in this presentation. This was an evaluation of stented prostheses. So the freestyle valve is not included in this series.

Regarding the question on which reference values we used, we rely on the work published by the group from Blais and Dumesnil in Circulation where I showed the table in the beginning giving most of the reference values. It's a kind of summary of different literature which is quoted in their manuscript, and in their paper.

Dr R. Lorusso (*Brescia*, *Italy*): If you look at your results, you have higher mortality in the moderate group and not in the severe group. I know that you have a small number of patients in the second one, but could you elaborate more, because this is a very controversial topic. In your opinion, why do you have in the moderate group higher mortality, not in the severe one? And what about the mode of death, and why these patients should die more frequently.

Dr Walther: I'm a bit careful. Of course, you're right. We have seen in these 97 patients who are having severe mismatch that the mortality is lower. But I was a bit careful to pronounce that because the number is rather low in comparison to the rather bigger numbers in the other two groups.