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The Carpentier–Edwards Classic™ and Physio™ Mitral Annuloplasty Rings: A Randomized Trial

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ABSTRACT

Objective: To evaluate clinical and echocardiographic outcomes for the semi-flexible Carpentier–Edwards Physio™ and the rigid Classic™ mitral annuloplasty ring.

Methods: Ninety-six patients were randomized for either a Classic™ (n = 53) or a Physio™ (n = 43) ring from October 1995 through July 1997. Mean follow-up was 5.1 years (range .1–6.6). We included standard patient characteristics at baseline and during follow-up. Analyses were adjusted for age and gender, and for factors that differed across groups at baseline. In 2002, echocardiography was performed in 74% of the survivors.

Results: We found a 16% difference in mortality: 14% in the Physio™ group (n = 6) and 30% in the Classic™ group (n = 16) (adjusted P = .41). Life table analysis shows that the absolute risk of death after 30 months is lower in the Physio™ group. Intra-operative repair failure occurred in 3 patients (6%) of the Classic™ group, and in 4 (9%) of the Physio™ group, resulting in mitral valve replacement. Late failure occurred in 1 patient (2%) in the Classic™ group, and in 4 (9%) in the Physio™ group. At follow-up, left ventricular function did not differ across groups (ejection fraction 45% and 48% (adjusted P = .65)). The combined NYHA class III–IV had improved for the Classic™ group in 42% and for the Physio™ group in 34%.

Conclusion: Although the 16% difference in mortality did not reach statistical significance, it is considered clinically important. No differences in morbidity, valve function, and left ventricular function were found. Further research to explain the difference in mortality is required.

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INTRODUCTION

Ever since its introduction by Carpentier in 1968 [Carpentier 1969], a remodeling annuloplasty using a prosthetic ring has proven to be beneficial for the durability of mitral valve reconstruction. The rationale for the development of the ring was to restore the ratio of the antero-posterior and transverse diameters of the fibrous annulus, which is normally 3:4, during systole. Moreover, annular dilatation over time would be prevented. A serious drawback of annular fixation is caused by the fact that the posterior mitral annulus is not fixed but movable, whereas the anterior annulus (the aortic-mitral continuity or curtain) is fixed during the contractile cycle [Dall'Agata 1998, Van Rijk 1990, 1994]. Fixation of the basal segments of the left ventricle will impede left ventricular function, instead of allowing these segments to take part in ventricular contraction [Green 1998]. Also, the prosthetic ring may obstruct the left ventricular outflow tract and/or cause deterioration of left ventricular function [Green 1998, Dagum 1999]. The mechanism of outflow tract obstruction is explained by the observation that the rigid ring moves anterior, underneath the aortic valve, causing subvalvular obstruction [Dagum 1999]. The (semi-)flexible rings and posterior annulus bands are not supposed to have these disadvantages. Studies by David et al show that, shortly after the operation, patients who received a flexible ring have significantly better left ventricular systolic function than patients who received a rigid ring. However, 2 years after surgery these differences were no longer detectable [David 1989, 1995]. The aim of this study is to compare the long-term survival after mitral valve reconstruction in which rigid and semi-flexible rings were used. We also evaluate the effect on the preservation of left ventricular function expressed in echocardiographic ejection fraction and the dimensions of left atrium and left ventricle. In addition, improvement of New York Heart Association (NYHA) functional class and the occurrence of mitral valve repair failure resulting in mitral valve replacement are analyzed.

PATIENTS AND METHODS

Study Population

From October 1995 to July 1997, 96 consecutive patients were enrolled in a prospective, randomized trial. Included were

all patients suffering from mitral regurgitation grade II/IV or more. Patients with a congenital malformation of the mitral valve and isolated mitral stenosis were excluded. Other cardiac diseases were treated concomitantly. Patients were randomized on an alternating basis to either the Carpentier–Edwards Classic™ ring, model 4400, which is rigid, or the semi-flexible Carpentier–Edwards Physio™ ring, model 4450 (Edwards Lifesciences, Irvine, CA, USA). Baseline assessment was blinded for ring type. This included documentation of cardiovascular risk factors, medical history, and current drug use. The NYHA functional classification was used to quantify symptoms. Preoperative cardiac rhythm was listed as sinus rhythm, sinus arrhythmia, and atrial flutter or atrial fibrillation. Mitral valve pathology was classified using Carpentier's criteria: type I (normal leaflet motion), type II (increased leaflet motion, or prolaps), and type III (restricted leaflet motion).

Surgical Procedure

Preoperative assessment of the severity, and of the mechanism of mitral regurgitation as well as information on left ventricular function were obtained by means of transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) (Hewlett-Packard Sonos 5500, Hewlett-Packard, Andover, MA, USA) ultrasound system equipped with a 2.5 MHz transducer. A standard cardio-pulmonary bypass and myocardial preservation protocol was adhered to in all cases. The mitral valve was exposed through either a Guiraudon incision (right atrial and septal incision extending into the roof of the left atrium) or a direct left atrial incision posterior to Waterston's groove. All reconstructions were performed using Carpentier's techniques [Carpentier 1983, Deloche 1990] and either of the two rings was implanted using interrupted 2/0 or 3/0 non-absorbable sutures. The intra-operative result of the repair was evaluated by TEE after discontinuation of cardiopulmonary bypass. Residual regurgitation more than grade I/IV was not accepted, nor was systolic anterior movement (SAM). In those cases bypass was re-instituted and if a correction of the repair was impossible the valve was replaced.

Outcome Measurements

The outcome status of the patients was defined as 30-days, 6-months, and late mortality. Early failure of valve repair was defined as residual mitral incompetence during intraoperative echocardiographic assessment up to one year postoperatively. Late failures occurred more than one year after the initial operation. In these cases of recurrent mitral incompetence, requiring valve replacement, patients were re-operated in our department.

Follow-up Echocardiography

All surviving patients with a functioning mitral valve plasty were contacted by telephone and invited for a repeat TTE in our hospital. At the completion of follow-up (average 5.1 years), transthoracic echocardiography was performed with a Hewlett-Packard Sonos 5500. The presence and severity of mitral regurgitation was quantified, as was tricuspid valve incompetence. Grading of the mitral regurgitation was done by means of color Doppler total regurgitation area in comparison to left atrial area. According to Helmcke et al, 20–40% regurgitation area/left atrial area corresponds with moderate, grade II mitral regurgitation; more than 40% corresponds with severe, grade III mitral regurgitation. Trivial mitral regurgitation was defined as a small circumscript color Doppler signal just underneath the plane of the mitral valve annulus [Helmcke 1987]. Pulmonary arterial pressures were deducted from tricuspid regurgitation velocity. In patients with mitral regurgitation greater than grade I, the effective regurgitant orifice (ERO) was calculated by the PISA (Proximal Isovelocity Surface Area) method [Enriquez-Sarano 1995]. We evaluated left ventricular function by calculating the wall motion score and the ejection fraction using the Hewlett-Packard™ acoustic quantification technology in the four- and two-chamber apical views. Chamber dimensions were recorded and the mitral valve area (MVA) was calculated using the pressure half-time method [Otto 2000].

Since pre-operatively left ventricular function was mostly expressed as ejection fraction measured by angiography, we were not able to evaluate echocardiographic changes of left ventricular function over time.

Data Analysis

General characteristics of the study population are presented as percentages, or as means with standard deviations. Comparison of baseline medical history between patients receiving a Classic™ and a Physio™ ring were evaluated with a *t*-test for continuous variables and with chi-square test for dichotomous variables.

Indicators of left ventricular function assessed by echocardiography were compared across treatment groups using linear regression models. Apart from age and gender, adjustments were made for those baseline risk factors that differed across treatment groups ($P < .20$) in the 46 subjects in whom quantitative echocardiography evaluation was performed.

To evaluate NYHA functional class and morbidity, two types of analyses were performed. First, we compared pre- and postoperative and end-of-follow-up NYHA classes (dichotomized: equal to and above or below III) across treatment groups at the time of measurement using chi-square tests. Next, we computed the difference between the end-of-follow-up NYHA class, and directly postoperative NYHA class, and compared the mean differences in rate of change across groups using a linear regression model.

Repair failure resulting in valve replacement during follow-up across groups was evaluated using Cox proportional hazards model with adjustment for factors that differed across treatment groups at baseline.

Finally, overall survival is expressed in percentages with standard errors and was estimated using Kaplan–Meier analysis and life table analysis for both intervention groups separately. Differences in survival between the intervention groups were evaluated using a Cox proportional hazards model with adjustment for baseline factors that differed across treatment groups. The statistical analyses were performed using SPSS software (version 8.0).

RESULTS

Baseline Characteristics

For 5 patients randomized to receive the flexible ring the original alternating device allotment protocol was breached

Table I. General Pre-operative Characteristics of the Study Population*

	Classic Ring (n = 53)	Physio Ring (n = 43)	*P* Value for Difference across Groups
Age, mean (SD)	65.6 (10.6)	62.0 (12.0)	.15
Women, %	40%	40%	1.0
NYHA class, %			
I	11.5	7.1	.76
II	28.0	26.2	
III	53.8	57.1	
IV	5.8	9.5	
Rhythm, %			
Sinus	73.6	78.0	.63
Atrial fibrillation	22.6	22.0	
History, %			
Arrhythmia	42	31	.22
Systemic hypertension	45	43	.68
Pulmonary hypertension	40	48	.55
Coronary arterial disease	43	36	.36
Myocardial infarction	23	19	.59
Congestive heart failure	25	26	.59
Endocarditis	9	2	.15
TIA/CVA	8	7	.89
Renal failure	6	7	.81
Diabetes mellitus	11	12	.99
Smoking – current	6	7	.81
Smoking – past	17	15	.66
Anticoagulation, %			
Coumadines	2	0	.37
Aspirin	8	5	.54
Medication, %			
Diuretics	82	61	.04
Calcium antagonists	18	29	.27
Anti-arrhythmic drugs	20	5	.04
Beta-blockers	20	21	.99
Antihypertensive med.	46	39	.71
vasodilators	24	24	.73
ACE inhibitors	42	29	.16
Other	12	5	.25
Body mass index, mean (SD)	24.8 (3.3)	25.2 (3.2)	.32

*NYHA indicates New York Heart Association; TIA, transient ischemic attacks; CVA, cerebral vascular accidents; ACE, Angiotensin-converting enzyme.

on the basis of preference of the individual surgeon. Baseline characteristics in Table 1 are given according to the received ring. Both groups were comparable for age, sex, NYHA functional class, and the presence of atrial fibrillation. Preoperative use of diuretics and of anti-arrhythmic drugs was significantly lower in the Physio™ group compared to Classic™ group. Other factors did not differ across treatment groups.

The main cause of mitral regurgitation was degenerative disease (65%). Other causes included isolated annular dilatation (21%), rheumatic valve disease (4%), ischemic valve disease (3%), and acute endocarditis (3%). In 26% of the patients normal leaflet motion was observed (Type I), 60% had type II (increased leaflet motion), and 14% type III (restricted leaflet motion).

In Table 2 all the repair techniques that have been used in addition to the annular remodeling are given. All the techniques are distributed over both groups equally. Concomitant coronary artery bypass grafting (CABG) was performed in 35 patients (36.5%), tricuspid valve plasty (TVP) in 9 (9%), the Cox–Maze III procedure in 8 (8%), and aortic valve replacement (AVR) in 4 patients (4%). Two patients underwent CABG together with an AVR, 1 patient CABG and TVP, and yet another patient AVR and TVP.

The mean hospital stay was 12.1 days (SD 9.3), with a median of 10 days. One patient was hospitalized for 66 days because no other suitable facility was available. Only 1 patient died in the hospital due to cerebral damage caused by cardiac tamponade 3 days after surgery.

Survival

Follow-up was complete with a mean interval of 61.4 months (SD 20.1) ranging from 3 days to 79 months. During this follow-up 9 patients (9%) died with congestive heart failure (of which 6 in the Classic™ group), 5 (5%) had sudden death (3 in the Classic™ group), 1 (1%) from cerebral hemorrhage (Classic™ group), 5 (5%) from pneumonia (4 [4%]) in the Classic™ group) and in 2 (2%) the cause of death remained unknown (both in the Classic™ group). At completion of follow-up a total of 22 patients had died (23%), yielding an overall mortality rate of 4.5 per 100 patient years. Of these 16 patients (30%) were from the Classic™ group and 6 (14%) from the Physio™ group. We consider this 16% difference in mortality between groups clinically important, but it did not reach statistical significance. The adjusted hazard ratio for the Physio™ ring compared to the Classic™ ring was .66 (95% CI: .24–1.80; $P = .41$).The first year, third year, and fifth year survival rates were 94% (SE = 3.2), 86.5% (4.7), and 79% (5.7) in the Classic™ group and 91% (2.3), 89% (4.8), and 89% (4.8) in the Physio™ group. The Figure shows that after 30 months of follow-up the flexible ring clearly is superior to the rigid ring in terms of absolute risk of death.

Mitral Valve Replacement

Out of the 96 patients, mitral valve repair was unsuccessful in 7 (7%), 3 in the Classic™ group and 4 in the Physio™ group. In these patients the valve was replaced instantly by a mechanical or biological prosthesis. During follow-up, an additional 5 patients (5%) had recurrent mitral regurgitation for which valve replacement was performed: one in the Classic™ group and four in the Physio™ group (adjusted $P = .12$). There was no in-hospital mortality in this group of patients.

Improvement of NYHA Class

Pre-operatively, 60% of the patients in the Classic™ group were in NYHA III or IV (Table 1), and 67% of the Physio™ group ($P = .39$). At the end of follow-up, 18% of the patients of the Classic™ group were in NYHA III or IV as compared to 33% in the Physio™ group ($P = .24$).

In the period immediately after surgery until the end of follow-up, the mean change in NYHA class III–IV was

Table 2. Repair Techniques Performed During Surgery*

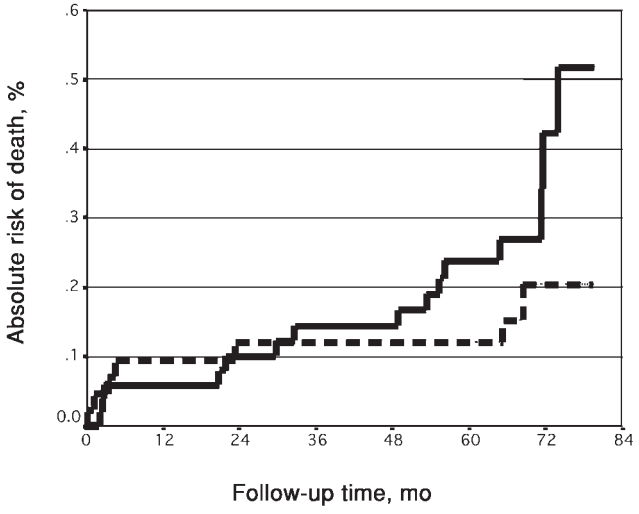
Repair Technique, n (%)	Classic Ring, n = 53	Physio Ring, n = 43	Total, n = 96
Ring annuloplasty alone	20 (37%)	18 (42%)	38 (40%)
Quadrangular resection PML	23 (43%)	15 (35%)	38 (40%)
Quadrangular resection PML + sliding annuloplasty	2 (4%)	2 (5%)	4 (4%)
Triangular resection AML	1 (2%)	5 (11%)	6 (6%)
Miscellaneous	3 (6%)	2 (5%)	5 (5%)
No information available	4 (8%)	1 (2%)	5 (5%)

*PML indicates posterior mitral leaflet; AML, anterior mitral leaflet.

.19 (.85) in the Classic™ group and .43 (.84) in the Physio™ group, an adjusted mean difference of .57 [95% CI – .03, 1.18], P = .06, adjusted for history of anti-arrhythmic drug use, the use of ACE inhibitors and smoking.

Echocardiography Follow-up Results

Of all patients alive with a functional repair (n = 62), 46 (74%) participated in an echocardiography study (Classic™ n = 24, Physio™ n = 22). Of those who declined, 3 suffered from dementia, 2 moved to a different country, and 11 patients gave a variety of other, mostly practical reasons not to participate. In Table 2 the main findings of the various indicators of left ventricular function are summarized. No statistically significant differences across treatment groups were found. Differences in echocardiograhic parameters were additionally adjusted for the following baseline factors which were all more common in the Classic™ group compared to the Physio™ group: history of anti-arrhythmic drugs (25% versus 4.8%, P = .07); history of use of ACE-inhibitors (45% versus 23.8%, P = .15); and smoking history (28.6% versus 8.7%, P = .09). None of the left ventricular function parameters differed across treatment groups after adjustment (Table 3).



Absolute risk of death by follow-up time per treatment group. The black line indicates the Classic group and the dotted line indicates the Physio group.

DISCUSSION

This randomized trial includes 96 patients with mitral valve regurgitation to be treated with either a rigid annuloplasty ring or a semi-flexible one. In a prospective, alternating fashion the Carpentier–Edwards Classic™ and Physio™ mitral annuloplasty rings were used. Follow-up of the patients was complete with a maximum duration of 6.6 years. At baseline the two groups were comparable with respect to determinants of survival and morbidity. At completion of the follow-up at 5.1 years on average, 22 patients had died and 12 had undergone replacement of the repaired mitral valve (12.5%): 7 patients immediately at the initial intervention, 5 patients later postoperatively, with a mean interval of 19.4 months. The reported relatively large difference in mortality of 16% is considered clinically important, but did not reach statistical significance, most probably due to the limited study size (adjusted hazard ratio = .66; 95% CI: .24–1.80; P = .41). After 30 months of follow-up the absolute risk of death is unequivocally lower in the Physio™ ring.

Of the remaining 62 surviving patients with a competent reconstruction, 46 patients (74%) could be studied extensively by echo. A significant difference in left ventricular function, or diameter between the two groups could not be detected. Residual mitral regurgitation was also equally divided over the two groups.

Due to surgeons preference 5 patients randomized to the flexible ring received the rigid ring. Since we presented the results according to the ring received, we had to deal with potential confounders in our analyses. Given the results of our adjusted analyses, it is unlikely that these 5 deviations from the randomization sequence and the minor differences in baseline status influenced the results of our study.

The concept of stabilizing and remodeling the annulus as part of reconstructing the mitral valve is generally accepted. The advantages and disadvantages of the use of a rigid ring as opposed to a flexible ring or band have been discussed extensively [Kreindel 1986, David 1989, Cosgrove 1995, Borghetti 2000]. In order to avoid the disadvantages of a rigid ring but to keep the advantages of a rigid prosthesis, a semi-flexible device, the Physio™ ring was developed [Carpentier 1995]. The latter is kidney-shaped with a 3:4 ratio between the antero-posterior and transverse diameter. This allows efficient annulus remodeling and increased orifice area. The ring geometry conforms to the natural "saddle-shape" configuration of the mitral annulus. The flexibility of the posterior curvature, created by the Elgiloy bands sepa-

Table 3. Follow-up Echocardiographic Data*

	Classic Ring, n = 53	Physio Ring, n = 43	Adjusted *P* Value†
LV dimensions			
LVESD, mm	38.9 (9.7)	39.0 (11.1)	.52
LVEDD, mm	55.1 (8.4)	51.5 (8.26)	.45
LA dimensions			
LA parasternal, mm	47.3 (10.0)	43.04 (6.8)	.68
LA 4chamber, mm × mm			
LV function			
Wall motion score	3.32 (4.44)	4.04 (4.61)	.65
AQU (EF) 4chamber	44.8 (10.0)	48.0 (13.1)	.69
AQU (EF) 2chamber	46.7 (10.0)	45.6 (12.9)	.54
Mitral incompetence			
Grade	.95 (1.0) (FUMI)	.92 (.88)	.85
ERO (PISA), cm^2	.44 (1.26)	.23 (.72)	.50
SAM, y/n + LVOT gradient	0%	n = 1	Not calculated
Tricuspid incompetence			
Grade	.68 (.84) (FUTI)	.58 (.78)	.71
Pulmonary artery pressure	19.6 (16.5)	19.0 (12.9)	.71
Effective mitral valve area			
Gradient *P* max/*P* mean	2.6 (.74)	2.5 (.73)	.85
MVA (p t1/2 method), cm^2	3.16 (.98)	3.20 (1.02)	.93

*LV indicates left ventricle; LVESD, left ventricle end systolic diameter; LVEDD, left ventricle end diastolic diameter; LA, left atrium; AQU, acoustic quantification, EF, ejection fraction; ERO, effective orifice area; PISA, proximal isovelocity surface area; SAM, systolic anterior movement; LVOT, left ventricle outflow tract; FUMI, mitral incompetence at follow-up; FUTI, tricuspid incompetence at follow-up; MVA, mitral valve area.

†*P* values are adjusted for age, gender, anti-arrhythmic drugs at baseline, ACE-inhibitor use at baseline and smoking habit.

rated by plastic bands, is variable, displaying more flexion proceeding up to the anterior region. When compared to the Classic™ model, this ring is closed and the dimensions have been optimized so as to fulfill the requirements of degenerative and ischemic valvular diseases that are prevalent indications for mitral valve repair.

Despite the promising characteristics described above, sheep model studies of Dagum and co-workers [Dagum 1999] showed that when compared to the flexible Duran ring, the Physio™ ring was associated with perturbations in annular dynamics that caused changes in papillary muscle geometry, which may explain displacement of the anterior leaflet into the left ventricular outflow tract after annuloplasty.

The first report on the effects of rigid and flexible prosthetic rings on annular dynamics and left ventricular performance was by David et al [1989]. Although at short-term follow-up, a flexible annuloplasty proved to be beneficial, this advantage faded away on longer follow-up. Gillinov et al [2002] also pointed out the theoretical advantages of flexible, posterior annuloplasty as opposed to rigid, circumferential annuloplasty. Clinical benefits, however, have not been shown. Green and co-workers [1998] showed that postoperative left ventricular function both generally, and in the region of the base of the left ventricle (near the mitral annulus) was not altered by either a semi-rigid or a flexible ring, resulting in fixation of the mitral annulus. This study was done in sheep, 7 to 10 days after surgery. Long-term results were not given.

Three-dimensional reconstruction of the mitral annulus using multiplane transesophageal echocardiography revealed that mitral annular configuration and dynamics are more physiological in patients with a flexible Duran ring than with a rigid Carpentier ring [Yamaura 1995]. The Cosgrove–Edwards™ ring maintains its flexibility early after implantation and demonstrates significant systolic–diastolic changes in the orifice area during the cardiac cycle [Dall'Agata 1998]. There are no long-term echo data that specifically focus on these changes. Van Rijk et al [1989, 1990] compared rigid (Carpentier) and flexible (Duran) rings for annuloplasty in an acute porcine model. They found that Duran rings interfere less with valvular function and filling of the base of the left ventricle, although the differences are small. Again, no long-term follow-up is given.

We have compared a rigid and a semi-flexible ring, but were unable to show a relationship between ring type and echocardiographic data and clinical endpoints at long term. Most probably the differences in design of these two rings are too subtle to show a significant difference on left ventricular function and related morbidity. In view of this, and our relatively limited sample size, we were unable to detect such a statistically significant relationship. However, we do consider the magnitude of the difference in mortality important as well as the absolute risk of death which diverges clearly after 30 months, in favor of the Physio™ ring group. Therefore, to our opinion the Physio™ ring should be preferred over the Classic™ ring in reconstructive surgery of the regurgitant mitral valve.

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REVIEW AND COMMENTARY

1. Editorial Board Member ST351 writes:

(a) I believe the total number of patients undergoing echo exam at five years to be fairly low (22 and 24 in each group). I am concerned that some of the conclusions may be incorrect because of the limited power of the study.

(b) There were several non-cardiac related deaths in the classic cohort, so can we really conclude the classic ring contributes to a higher mortality?

(c) There is no information on ring sizing: how was this done and what were the sizes? Could differences between the groups been influenced by different degrees of "down-sizing" of the mitral annulus?

(d) Why did the classic cohort have a stronger improvement in heart failure class; and how do you reconcile this with the higher mortality in this group?

Author's Response by Dr. Ghada M.M. Shahin:

(a) The number of patients who underwent follow-up echocardiography is fairly low. We included patients from all Dutch cities. Hence many patients had to travel more than considerable distance for this follow-up. However, patients with a follow-up echocardiography are equally distributed over both groups (22 and 24, respectively). The follow-up echocardiographies did not show a difference in left ventricular function nor diameters between the two groups. In spite of this, however, we are aware of the limited power of these echocardiographic data.

(b) Only for the two patients for which the cause of death was unknown were the causes of death considered to be cardiac-related. Cerebral hemorrhage developed due to anticoagulation for atrial fibrillation. Pneumonia occurred in the presence of heart failure and pulmonary edema. We therefore believe that we can validly conclude the mortality rate in the Classic ring group is higher.

(c) Ring sizing was performed according to the instructions of Edwards Lifesciences: the intertrigonal distance and the surface area of the anterior mitral leaflet should match that of the templates. All surgeons of our institution apply the same sizing technique. The sizes of rings used were 32, 34, and 36 mm. Only very occasionally a 30 mm ring was used. Therefore it is unlikely that possible individual sizing errors have led to down-sizing, and are a probable explanation for the differences between both groups.

(d) The higher mortality rate in the Classic group could lead to a stronger improvement in NYHA class because of the death of those with a likely poor NYHA class in this group. At the same time, the higher repair failure rate in the Physio group is likely to result in mitral valve replacement

and (further) reduction of the postoperative NYHA heart failure class in this group.

2. Editorial Board Member SC389 writes:

(a) Preop EF from the echo is not described.

(b) The etiology for MR is broken down by overall cohort and should also be broken down by the type of ring used. The overall group of patients is only 96 and 5 of the randomized patients were crossovers.

(c) Please ask the authors to address the clinical significance of the higher incidence of MVReplacement, failed MV repair and lower NYHA class in the flexible ring group.

Author's Response by Dr. Ghada M.M. Shahin:

(a) The preoperative left ventricular ejection fraction was not accurately measured by echocardiography in all patients as this was already done during catheterization. The preoperative echo concentrated on description of the function of several cardiac segments and measurement of the dimensions of ventricles and atria.

(b) In our study randomization should warrant equal groups regarding the cause of mitral regurgitation. Still, different decisions regarding performing concomitant surgery are likely to be related to the cause of regurgitation. Therefore we adjusted in our analysis for concomitant surgery and found that this adjustment did not affect the outcomes of our study.

(c) The preoperative NYHA class was comparable in both the Classic and Physio group. Our study shows a higher rate of repair failure, leading to mitral valve replacement, in the Physio group. This difference is not statistically significant. Clinically however this might contribute to the smaller improvement in NYHA heart failure class in the semi-flexible ring group.

3. Editorial Board Member XA55 writes:

I do not understand how the authors can claim that there's a difference in the groups when there's no statistical difference. I showed this paper to others who also said that with no statistical difference, the conclusions are invalid.

One of the individuals, who has worked at Stanford, showed in their studies that these rings solidify in days and thus the whole 'flexible ring' concept is flawed from the outset.

Author's Response by Dr. Ghada M.M. Shahin:

There are three important issues we would like to emphasize: First, the validity of the study does not depend on statistical precision. Second, it is the magnitude of the difference (or the size of the effect) that can be considered clinically important. Lastly, the difference can be statistically significant. Statistical significance depends, amongst others, on the magnitude of the difference. In our study we found a difference that we consider clinically important, yet did not reach statistical significance.

The aim of our study was to evaluate clinical and echocardiographic outcomes of the rigid and semi-flexible annuloplasty rings for mitral valve repair. Although we do appreciate the statement that flexible rings solidify over time we would like to stress that the justification of the concept of flexibility of annuloplasty rings was not the goal of our study.