CARDIOVASCULAR MEDICINE

Prevalence and clinical significance of incidental paraprosthetic valvar regurgitation: a prospective study using transoesophageal echocardiography

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Objective: To assess the prevalence, mechanisms, and significance of paraprosthetic regurgitation detected incidentally by transoesophageal echocardiography (TOE) in patients after heart valve replacement.
Design: Prospective observational study.
Setting: Tertiary referral centre.
Patients: 360 consecutive patients (mean (SD) age 65.8(9.5) years, 193 women) undergoing elective first ever valve replacement.
Methods: Postoperative and follow up TOE, and tests for haemolysis and anaemia.
Results: There were 243 aortic, 90 mitral, and 27 double valve replacements, using 316 mechanical and 44 tissue valves, giving 270 aortic and 117 mitral valves. One patient with severe paraprosthetic mitral regurgitation underwent immediate reoperation and was excluded from subsequent analyses. Paraprosthetic jets were detected around 16 (6%) of the aortic and 38 (32%) of the mitral valves ($p < 0.05$) at the postoperative study. Follow up TOE was available for 151 aortic and 67 mitral valves, 0.9 (0.5) years after operation. Paraprosthetic jets were present in 15 (10%) of the aortic and 10 (15%) of the mitral valves (NS). Two thirds of the aortic and a fifth of the mitral jets were new. Paraprosthetic jets were more common in aortic valves in a supra-annular (12 of 88, 14%) than in an intra-annular position (4 or 182, 2%; $p < 0.005$) and in mitral valves inserted with continuous (36 of 88, 41%) rather than interrupted sutures (2 of 28, 7%; $p < 0.001$). Lactate dehydrogenase concentration was higher in patients with paraprosthetic jets than in those without (752 (236) *v* 654 (208) IU/l, $p < 0.001$). Haemoglobin and haptoglobin concentrations were not different.
Conclusions: Small paraprosthetic leaks are common, are related to surgical factors, are not associated with increased subclinical haemolysis, and are benign during the first year after heart valve replacement.

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Paraprosthetic regurgitation, defined as abnormal retrograde flow between the sewing ring and the native valve annulus, is a well recognised complication of prosthetic valves. Paraprosthetic jets detectable by the diagnostic methods available until the 1970s were frequently caused by infective endocarditis of the prosthetic valve and were associated with unequivocal clinical signs. The diagnosis was confirmed by angiography, severe haemolysis was generally present, and treatment usually involved reoperation.[1] Paraprosthetic regurgitation was thus a severe and feared complication of prosthetic heart valves.

Now that transoesophageal echocardiography (TOE) is widely available, a different picture is emerging.[2] Small and asymptomatic paraprosthetic jets are often detected incidentally as a result of the high sensitivity of colour flow mapping,[3–5] mainly when it is used with TOE.[6] However, important clinical issues have not yet been adequately studied, such as the prevalence of these jets, their cause and time course, and their clinical consequences. Answers to these questions are clinically relevant for deciding which (if any) patients with small paraprosthetic jets, detected either incidentally or because of systematic study, need more careful follow up or even a repeat operation.

Intravascular haemolysis is often considered an unavoidable consequence of paraprosthetic regurgitation.[7] This notion dates from the pre-echocardiographic era, when the only paraprosthetic jets that came to medical attention were severe and haemodynamically significant, and it may not apply to small jets detected incidentally by colour flow mapping. Most published studies have relied on measurement of lactate dehydrogenase (LDH) concentration to diagnose haemolysis[8] but LDH may be raised from other causes and LDH concentrations may be high preoperatively.

To address these questions we studied prospectively a large cohort of patients undergoing elective valve replacement.

PATIENTS AND METHODS

Inclusion criteria

The Cardiff embolic risk factor study took place between June 1995 and July 1999 in the tertiary cardiac centre for Wales, UK. All patients undergoing elective valve replacement were eligible. The exclusion criteria were previous valve replacement, operation for infective endocarditis, emergency operations, aortic root replacement, and unwillingness to give informed consent for the study. All patients had an interview at the outset, when their New York Heart Association functional status was ascertained.

All patients gave informed consent and the ethical committee at our institution had approved the study protocol.

Transoesophageal echocardiography

Multiplane or biplane TOE probes interfaced with commercially available scanners (Hewlett Packard Sonos 1500 and

Abbreviations: CABG, coronary artery bypass grafting; LDH, lactate dehydrogenase; TOE, transoesophageal echocardiography

2500, Hewlett Packard, Andover, Massachusetts, USA) were used. The probe was inserted in the anaesthetic room, with the patients fully anaesthetised and mechanically ventilated, immediately before they were taken to the operating theatre. The initial TOE was performed in theatre in the early stages of the operation.

Patients had a second TOE two hours after the operation in the intensive therapy unit. The prosthetic valve was first scanned using grey scale imaging. Multiplane scanning with colour flow mapping was then used, and particular attention was given to identifying small paraprosthetic leaks and their location relative to the four quadrants of the prosthesis (anterior, posterior, lateral, and medial). The vena contracta of any paraprosthetic leak was measured in the imaging plane where it was broadest.[9] We also documented the maximal length of paraprosthetic jets, as this has often been reported in studies of intraprosthetic and paraprosthetic regurgitation,[2–5] but since we did not use constant colour gain settings, this length is not an accurate guide to severity.

Patients were followed up in the outpatient clinic in our centre. Reoperation, infective endocarditis, and death were documented by examining the medical records and by interview. Patients who consented had a follow up TOE 6–12 months after the operation under light sedation with midazolam and the same protocol as for the early postoperative study.

Surgical details

The following parameters were documented by the surgeon at operation: the degree of calcification of the annulus of the diseased valve and of the aortic wall, the size of the annulus, the type of anatomical lesion (regurgitation, stenosis, or mixed), its aetiology (rheumatic, degenerative, myxomatous, senile calcification, congenital), the configuration of the aortic valve (bicuspid or tricuspid), the size of the prosthetic valve, the type of sutures used (continuous or interrupted, pledgeted or not), and the implant position (intra-annular or supra-annular).

Laboratory studies

Patients had the following tests preoperatively, one week after the operation, and at follow up: full blood count, haemoglobin, serum haptoglobin, serum LDH, and serum bilirubin. At the preoperative study, reticulocyte count was also measured. For the follow up study, the blood samples were taken on the same day as the TOE study or as close to it as feasible.

Subclinical haemolysis was defined as the combination of an increased LDH concentration (> 440 IU/l) with a decreased haptoglobin concentration (< 0.007 g/l). Haemolytic anaemia was defined as the presence of haemolysis and of haemoglobin < 1.78 mmol/l in women and < 2.09 mmol/l in men.

Statistical methods

Means and standard deviations of continuous variables were compared using the *t* test for independent samples. Median values were calculated where meaningful. Categorical variables were compared using the χ^2 test. The denominator for proportions by valve position was calculated as follows:

total number of mitral valves = number of mitral valve replacements + number of double valve replacements

total number of aortic valves = number of aortic valve replacements + number of double valve replacements.

Logistic regression was used for assessing the influence of variables on the presence of paraprosthetic jets. The presence or absence of paraprosthetic jets at either of the two postoperative TOE studies was used as the dependent categorical variable. The following independent categorical variables were included in the analysis of all jets, regardless of their position: identity of the operating surgeon, concomitant coronary artery bypass grafting (CABG), aetiology of valve lesion, dominant type of lesion, and type of prosthetic valve. The size of the prosthetic valve used was included as a continuous variable.

For mitral paraprosthetic jets the degree of calcification of the annulus and the suture technique used were added for the regression. For paraprosthetic jets in the aortic position the following variables were added: degree of calcification of the annulus, degree and extent of calcification of the aortic wall, aetiology of valve disease, and its configuration (bicuspid or tricuspid).

Linearised rates were calculated for the end points by dividing the number of events by the total years of follow up and were compared using the formula described by Grunkemeier.[10] The level of significance was set at $p < 0.05$ for all tests. All statistical calculations were performed using a commercially available statistical package (SPSS version 6.1, SPSS Inc, Chicago, Illinois, USA).

RESULTS

Patients and operations

We studied 360 patients (193 women) with a mean (SD) age of 65.8 (9.5) years. They underwent 243 aortic, 90 mitral, and 27 double valve replacements, using 44 tissue and 316 mechanical valves, giving 270 aortic and 117 mitral valves. One hundred and three patients (29%) had concomitant CABG: 33% of those undergoing aortic valve replacement, 24% of those undergoing mitral valve replacement, and 7% of those having double valve replacement. Tables 1 and 2 summarise the types of valves used.

Five cardiac surgeons performed the operations. All aortic valves were sutured with interrupted sutures. Mitral valves were sutured either with interrupted or with continuous sutures, according to each surgeon's preference. When continuous sutures were used, three separate sutures were placed, one around each third of the circumference of the valve.

Postoperative TOE

At the early postoperative study, one patient had dehiscence and instability of a mitral valve after one of the continuous sutures had unravelled; he required immediate reoperation

Table 1 Prevalence of paraprosthetic jets at the early transoesophageal echocardiographic study by valve type and position

	Paraprosthetic jets		
Prosthesis type	**Absent**	**Present**	**Total**
Aortic			
Carpentier-Edwards			
Pericardial	34	2 (6%)	36
Porcine	8	0	8
Medtronic Hall	74	1 (1%)	75
St Jude	105	11 (10%)	116
Ultracor	33	2 (6%)	35
Total	254	16 (6%)	270
Mitral			
Medtronic Hall	25	12 (32%)	37
St Jude	43	17 (28%)	60
Ultracor	10	9 (47%)	19
Total	78	38 (33%)	116

Table 2 Prevalence of paraprosthetic jets at the follow up TOE study by valve type and position

Prosthesis type	Paraprosthetic jets		
	Absent	Present	Total
Aortic			
Carpentier-Edwards			
Pericardial	16	4 (5%)	20
Porcine	6	0	6
Medtronic Hall	39	2 (5%)	41
St Jude	57	8 (12%)	65
Ultracor	18	1 (5%)	19
Total	136	15 (10%)	151
Mitral			
Medtronic Hall	16	3 (16%)	19
St Jude	33	2 (6%)	35
Ultracor	8	5 (38%)	13
Total	57	10 (15%)	67

and was excluded from subsequent analyses. Fifty four other patients (15%) had small paraprosthetic jets (table 1).

Follow up TOE

A follow up TOE study was available for 206 patients at an average of 0.9 (0.5) years, a median of 1.8 years, and a range of 0.1–3.8 years after the operation (total follow up 423 years). There were 151 patients with aortic valves (12 with double valves) and 67 with mitral valves (including 12 double), representing 56% and 57% of the initial groups, respectively. Twenty eight patients died before the follow up study, 128 refused the TOE, and one patient was lost to follow up. Paraprosthetic jets were present in 25 patients (12%).

Aortic jets

There were 16 aortic jets at the early postoperative study (6% of all aortic valves). Paraprosthetic jets were located predominantly in the posterior or medial quadrant of the valve (69%). The mean length of aortic jets on colour flow mapping was 1.5 (0.9) cm and the mean width of the vena contracta of the jets was 0.3 (0.2) cm.

The average size of aortic valves with paraprosthetic leaks was not different from that of valves without paraprosthetic leaks. There was no difference in the proportion of valves with or without pledgeted sutures that had paraprosthetic regurgitation.

At the follow up TOE study, there were 15 jets in the aortic position (10% of aortic valves), of which 10 were new. Seven of these new jets were in the posterior and medial quadrants of the valve. Three of the initial early postoperative jets (43%) had disappeared, and eight of the patients who had paraprosthetic jets at the initial study did not have a follow up study (fig 1). At the early postoperative study paraprosthetic jets were more common in aortic valves in a supra-annular (12 or 88, 14%) than in an intra-annular position (4 of 182, 2%; $p < 0.005$) and this remained true at follow up study (9 of 48, 19% *v* 6 of 103, 6%; $p < 0.05$).

The proportion of patients with paraprosthetic leaks was not different when patients were stratified according to any of the following criteria: extent and severity of annular calcification, size of the aortic root and of the prosthetic valve, use of pledgeted sutures, aetiology of aortic valve disease, concomitant CABG, and identity of the operator.

Mitral jets

There were 38 mitral paraprosthetic jets at the early TOE study (32% of all mitral valves, $p < 0.05$ *v* aortic valves), of which four occurred in patients with double valves. Seventy six per cent of the jets were posteromedial. There was a trend for mitral valves with leaks to be larger than those without (mean size 2.9 (0.2) cm *v* 2.8 (0.2) cm; $p = 0.05$).

The mean length and the width of the vena contracta were 2.4 (1.2) cm and 0.5 (0.6) cm, respectively, significantly more than for the aortic jets ($p < 0.005$ and $p < 0.05$, respectively). Forty one per cent of the valves implanted with continuous sutures had leaks, compared with 7% of those with interrupted sutures ($p < 0.001$), but the use of pledgets made no difference to the prevalence of paraprosthetic jets.

There were 10 paraprosthetic jets in the 67 mitral valves scanned at follow up (that is, a prevalence of 15%), of which two were new. Fourteen of the initial 22 jets (64%) had disappeared and 16 patients with paraprosthetic jets at the initial study did not have a follow up TOE (fig 1).

The length and vena contracta of aortic compared with mitral jets were not different at follow up (2.0 (1.4) cm *v* 2.6 (2.1) cm, and 0.3 (0.2) cm *v* 0.4 (0.2) cm, respectively).

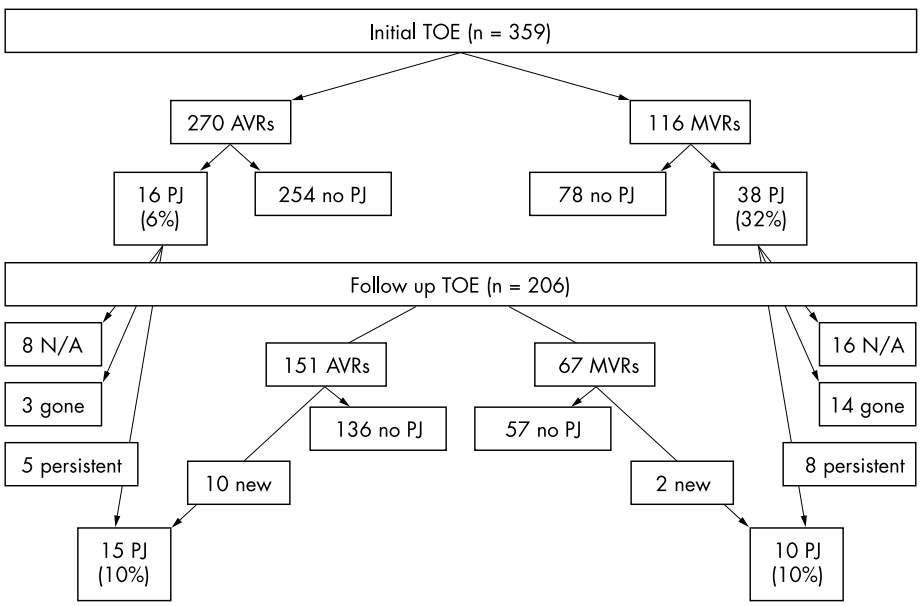

Figure 1 Prevalence and course of incidental paraprosthetic regurgitation. AVR, aortic valve replacement; MVR, mitral valve replacement; N/A, not available; PJ, paraprosthetic jet; TOE, transoesophageal echocardiogram.

Logistic regression and clinical end points

On univariate logistic regression the following categorical variables were associated with postoperative paraprosthetic jets: mitral position ($p < 0.001$, $r = 0.34$), supra-annular aortic implant ($p < 0.005$, $r = 0.22$), and continuous sutures in the mitral position ($p < 0.005$, $r = 0.21$).

Subclinical haemolysis and haemolytic anaemia

The proportion of patients with an abnormal LDH concentration increased from 33% preoperatively to 91% one week after the operation, and it was 76% at the follow up study. The proportion of patients with normal haemoglobin but with increased LDH and decreased haptoglobin concentrations was 9% at the preoperative study, 10% at the postoperative study, and 42% at follow up. Paraprosthetic jets were present in 17% and 12% of these patients at the early and late TOE studies, respectively.

The proportion of patients with haemolytic anaemia was 2%, 6%, and 3% at the preoperative, postoperative, and follow up studies, respectively. Paraprosthetic jets were present in 9% and 0% of these patients at the early and late TOE studies, respectively.

Haemolysis and paraprosthetic jets

Indices of haemolysis were similar in patients with paraprosthetic jets and those without, either as a group or by valve position, except for LDH concentrations. These were higher in patients with paraprosthetic jets both one week after the operation (752 (236) IU/l *v* 654 (208) IU/l, $p = 0.01$) and at follow up (731 (447) IU/l *v* 605 (221) IU/l, $p = 0.07$).

DISCUSSION

This is the first large prospective study of paraprosthetic regurgitation to use serial TOE and haematological indices of haemolysis in patients with normally functioning prosthetic valves.

Prevalence of paraprosthetic regurgitation

Paraprosthetic jets have been a major complication of prosthetic valves since the early days of cardiac surgery.[1] Haemodynamically significant jets caused by infective endocarditis or technical failures at surgery[11] were usually diagnosed clinically, confirmed at angiography, and treated by re-replacement of the valve.

In the present study, the prevalence of paraprosthetic jets was 15% in unselected consecutive patients immediately after elective valve replacement. Paraprosthetic jets were more common in the mitral than in the aortic position (prevalence 33% *v* 10%, $p < 0.05$). All jets were small and the valves were functioning normally. No patient required late reoperation.

Several large series from the pre-echocardiographic era reported a much lower prevalence of paraprosthetic regurgitation: 2.5% in two series[12 13] where almost all patients presented with heart failure, endocarditis, or haemolytic anaemia and more than two thirds had to have repeat operations; and 1.7% in another,[14] where all had repeat operations. In this latter study, two thirds of the patients who eventually required repeat operations had had a transthoracic echocardiogram five months after the initial operation. Only a small proportion had leaks at that stage.

Such historic controls had paraprosthetic regurgitation detected only when it produced symptoms, and so the prevalence was much lower than in the present study.

Aortic paraprosthetic regurgitation

Paraprosthetic regurgitation was detected in 6% of the aortic valves and it was more prevalent in the supra-annular position. This new finding is probably explained by the greater difficulty in ensuring good contact between the sewing ring and the supra-annular tissues, particularly in the commissural area or in areas of residual irregularity after incomplete decalcification.

There are only scant data in the literature about aortic paraprosthetic jets. In a study using transthoracic echocardiography, Rallidis and colleagues[15] report a prevalence of 48% for aortic paraprosthetic jets one week after valve replacement, 90% of which were small. There was no difference in the prevalence of jets between tissue and metallic valves. Chambers and colleagues[4] reported paraprosthetic jets in 28–73% of aortic valves, according to valve type, with the highest prevalence in Starr-Edwards valves.

Mitral paraprosthetic regurgitation

In the present study, mitral paraprosthetic regurgitation was three times more common than aortic paraprosthetic regurgitation and was detected in approximately a third of the mitral valves scanned. This proportion is in keeping with some of the earlier studies.

A cross sectional study by Skudicky and colleagues[16] reported a 31% prevalence of mitral paraprosthetic jets after mitral valve replacement with a mechanical valve, two thirds of which had been secured with continuous sutures. A lower prevalence of paraprosthetic regurgitation was reported by Bonnefoy and colleagues,[17] who found narrow regurgitant jets in 14% of patients studied with transthoracic echocardiography and TOE within one day after mitral valve replacement. Small jets between a suture and the edges of the hole produced by the needle can disappear quite soon after the operation, so delaying the echocardiographic study by even several hours may account for the lower incidence than in the present study. Chambers and colleagues,[4] in a cross sectional study using transthoracic echocardiography, found paraprosthetic jets in 6–27% of mitral prostheses, according to valve type.

Meloni and colleagues[18] reported paraprosthetic jets in 60% of patients studied at the time of mitral valve replacement. Their findings, similar to ours, was that paraprosthetic jets were associated with continuous sutures (76% of continuous versus 33% of interrupted sutures had paraprosthetic jets).

We found that mitral jets were more frequent on the medial aspect of the prosthetic valve and that they were associated with the use of continuous sutures. This is the region of the annulus sutured last with the in situ continuous suture technique used in this study. When the patient's annulus is larger then the prosthesis this is the area where any remaining size mismatch must be corrected and it is possible for a small paraprosthetic jet to occur through a fold of puckered annular tissue (a ''dog ear''). If there is concern about the integrity of the suture line in such cases of size mismatch, it is preferable to complete the last few centimetres of the suture line with interrupted pledgeted sutures. In the absence of infection, the association of continuous sutures with paraprosthetic regurgitation has been reported by Dhasmana and colleagues[19] for mitral prostheses (where it was also associated with annular calcification) and by Hjelms and associates[20] for aortic prostheses. However, both reports referred to the ''parachute'' technique, in which the prosthesis is slid down to its implant position only once all the sutures are in place. In this technique, tightening all the loops of the suture evenly can be problematic.

Time course of paraprosthetic regurgitation

In our patients, the prevalence of paraprosthetic regurgitation was 12% at the follow up TOE study performed at an average of nine months after surgery. The majority of aortic jets were new, while mitral jets were mostly persistent, and the prevalence by valve position was similar (10% in aortic and

15% in mitral valves). There are not many prospective studies of paraprosthetic regurgitation but the data available confirm that new regurgitant jets can often develop during follow up.

In a study with transthoracic echocardiography, Glisenti and others[5] detected new paraprosthetic jets in 10% of the mitral and 5% of the aortic valves followed up for five months. All patients underwent repeat operation because they had severe paraprosthetic regurgitation.

Movsowitz and colleagues[21] followed up eight patients who had either mild (six patients) or moderate paraprosthetic mitral regurgitation detected by TOE at the time of the valve replacement. The two patients with moderate regurgitation and two of the patients with mild regurgitation deteriorated clinically during a mean follow up of 16 months, and the authors conclude that moderate paraprosthetic jets should be corrected at the time of surgery.

Haemolysis

Haemolysis following heart valve replacement has been noted since 1954 when anaemia was described following the implantation of Hufnagel ball valves into the aorta.[22] Thereafter, the reported frequency and severity of this complication declined, from 55% in 1975,[1] to 7% in 1983,[19] to less than 4% in 1993.[23] The mechanisms of haemolysis include high shear stress, even in normally functioning valves,[24 25] collision of jets with solid boundaries resulting in rapid deceleration, and interaction of red blood cells with foreign surfaces.[26] Many patients with artificial heart valves have a state of compensated, mild subclinical haemolysis, which does not require treatment.[27] Cases of severe haemolytic anaemia are usually associated with severe paraprosthetic leaks or other types of valve dysfunction.[28]

In the present study, the mean LDH concentration was increased regardless of the presence or absence of paraprosthetic jets. However, patients with paraprosthetic jets had higher LDH concentrations than those without paraprosthetic jets. The peak LDH concentration was recorded postoperatively, probably reflecting tissue damage from surgery as well as haemolysis. There was a steady increase in the proportion of patients having both an increased LDH and a low haptoglobin concentration during follow up, suggesting worsening haemolysis, but this was independent of the presence of paraprosthetic jets. The proportion of patients with anaemia was not different according to whether a paraprosthetic jet was present.

Limitations

Follow up was not complete because a substantial proportion of our patients did not consent to the follow up TOE study. This was not unexpected, given the semi-invasive character of TOE and the fact that the studies were performed purely for research, in patients who were well and asymptomatic. Similar consent rates have been noted in other studies where TOEs were performed without a clinical indication.[29] The change in paraprosthetic jets at follow up is reported only in those patients who had both immediate and late postoperative TOE studies.

Conclusion

Paraprosthetic jets are frequently detected by TOE in normally functioning valves where they are associated with continuous sutures in the mitral position and with supra-annular implants in the aortic position. They do not cause anaemia but they produce subclinical haemolysis, as shown by increased LDH concentrations. Over a mean follow up of nine months, there was no difference in outcomes between patients with and those without paraprosthetic jets. Therefore, small leaks detected incidentally by TOE in asymptomatic patients with normally functioning valves are benign in the short term.

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IMAGES IN CARDIOLOGY

Echocardiographic detection of systemic air embolism during positive pressure ventilation

A healthy 50 year old woman was admitted to hospital with abdominal pain. Abdominal *x* ray revealed pneumoperitoneum and she was taken to the operating room with suspected perforation of the viscera. The duodenum was operated on because of the perforation with accompanying peritonitis, and the patient required dopamine for blood pressure support. The haemodynamic status was compatible with septic shock. Thoracic x ray during the following 48 hours showed progressive development of respiratory distress syndrome. Positive pressure ventilation was administrated. Fifty six hours after surgery, the patient became acutely cyanotic with decreased systolic arterial blood pressure and arterial oxygen saturation; a new loud systolic retrosternal murmur, that was not present before, had also developed. Transthoracic echocardiography using harmonic imaging showed normal left ventricular function and normal valvar function (AO, aortic valve). The right ventricle (RV) appeared slightly dilated but with normal function. Air bubbles were seen in left atrium (LA) and left ventricle (LV) during mechanical ventilation in the inspiratory phase (arrows, panel A). No air bubbles were seen during apnoea. There was no evidence of an atrial or ventricular septal defect, as indicated by the absence of abnormal colour Doppler flow and by the lack of contrast material seen in the left side of the heart after intravenous injection of agitated saline solution. This event was time limited (another study that did not show bubbles was performed, panel B) and the patient's haemodynamic status improved within three minutes while tidal volume was reduced. The patient died three days after the event from refractory hypoxaemia and hypotension.

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