

## **(6) Results**

### **6.1 ASD patients versus normal controls and comparison of the effects of catheter and surgical ASD closure on right atrial function (section 1)**

There were no significant difference in age or heart rate between normal subjects and ASD patients. There was no significant difference in heart rate before and after ASD closure in either the surgical or catheter groups.

#### **6.1.1 Two-dimensional echocardiography**

In ASD patients the right atrial  $A_{\min}$  ( $p=0.003$ ),  $A_a$  ( $p=0.000$ ) and  $A_{\max}$  ( $p=0.001$ ) were significantly higher than in normal subjects (figure 7). There was no significant difference in right atrial active emptying area fraction between the two groups (figure 8). The right atrial active emptying area ( $p=0.000$ ) (figure 9) and active/passive emptying area ratio ( $p=0.001$ ) (figure 10) were also significantly higher in ASD patients than in normal subjects. The detailed comparison between normal subjects and ASD patients is shown in table 4. In ASD patients right atrial active emptying area was significantly correlated with right atrial  $A_a$  ( $r=0.815$ ,  $p=0.000$ ) (figure 11) and  $Qp/Qs$  ( $r=0.416$ ,  $p=0.028$ ). There were no significant correlations between right atrial active emptying area fraction and right atrial  $A_a$  or  $Qp/Qs$ . In both closure groups right atrial  $A_{\min}$ ,  $A_a$ , and  $A_{\max}$  were significantly reduced after the procedures (tables 5 and 6). After ASD closure right atrial active emptying area fraction showed a significant diminution in the surgical

group ( $p=0.002$ ) while preserved in catheter group (figure 12). The detailed 2-dimensional echocardiographic results of both the ASD closure groups are shown in tables 5 and 6.

**Table 4 Comparison of right atrial performance measured by 2-dimensional echocardiography between normal subjects (n=30) and patients before ASD closure (n=30)**

	Normal subjects	Patients before ASD closure	p
	Median (range)	Median (range)	
RA $A_{\min}$ (cm <sup>2</sup> )	5.2 (1.4-10.9)	7.1 (2.6-20)	0.003
RA $A_a$ (cm <sup>2</sup> )	6.8 (2.3-15.1)	11.8 (4-28.8)	0.000
RA $A_{\max}$ (cm <sup>2</sup> )	10.4 (3.7-23.4)	16.3 (4.7-38.9)	0.001
RA active emptying fraction (%)	29 (9-59)	34 (11-61)	0.164
RA active emptying area (cm <sup>2</sup> )	1.8 (0.7-7.2)	3.5 (1.3-9.3)	0.000
RA active/passive emptying area ratio	0.5 (0.2-9.5)	1.0 (0.1-9.6)	0.001

$A_a$ : atrial area measured at onset of atrial “kick”;  $A_{\max}$ : atrial area measured when it reaches maximum;  $A_{\min}$ : atrial area measured when it reaches minimum; ASD: secundum type atrial septum defect; RA: right atrium

**Table 5 Comparison of right atrial performance measured by 2-dimensional echocardiography before and after ASD surgical closure (n=11)**

	Before closure	After closure	p
	Median (range)	Median(range)	
RA $A_{\min}$ (cm <sup>2</sup> )	8.0 (2.7-20.0)	5.7 (1.7-12.4)	0.093
RA $A_a$ (cm <sup>2</sup> )	14.8 (6.3-28.8)	6.5 (3.1-15.4)	0.012
RA $A_{\max}$ (cm <sup>2</sup> )	17.3 (9.1-38.9)	9.9 (5.2-17.6)	0.012
RA active emptying fraction (%)	36 (23-61)	20 (1-57)	0.002
RA active emptying area (cm <sup>2</sup> )	5.5 (2-9.3)	1.6 (0.1-3)	0.017
RA active/passive emptying area ratio	1.4 (0.6-6.8)	0.8 (0.1-3.7)	NS

$A_a$ : atrial area measured at onset of atrial “kick”;  $A_{\max}$ : atrial area measured when it reaches maximum;  $A_{\min}$ : atrial area measured when it reaches minimum; ASD: secundum type atrial septum defect; RA: right atrium

**Table 6 Comparison of right atrial performance measured by 2-dimensional echocardiography before and after ASD catheter closure (n=19)**

	Before closure	After closure	p
	Median (range)	Median (range)	
RA $A_{\min}$ (cm <sup>2</sup> )	7.3 (2.6-18.9)	7.8 (1.5-37.0)	NS
RA $A_a$ (cm <sup>2</sup> )	11.1 (4.0-25.0)	7.8 (2.9-22.2)	0.022
RA $A_{\max}$ (cm <sup>2</sup> )	16.1 (4.7-32.2)	12.1 (6.5-27.7)	0.027
RA active emptying fraction (%)	33 (11-52)	29 (3-65)	NS
RA active emptying area (cm <sup>2</sup> )	3.3 (1.3-8.6)	2 (0.4-6.4)	0.062
RA active/passive emptying area ratio	0.7 (0.1-9.6)	0.5 (0.2-5.2)	NS

$A_a$ : atrial area measured at onset of atrial “kick”;  $A_{\max}$ : atrial area measured when it reaches maximum;  $A_{\min}$ : atrial area measured when it reaches minimum; ASD: secundum type atrial septum defect; RA: right atrium Tissue Doppler imaging (TDI)

### Right atrial function in patients with ASD

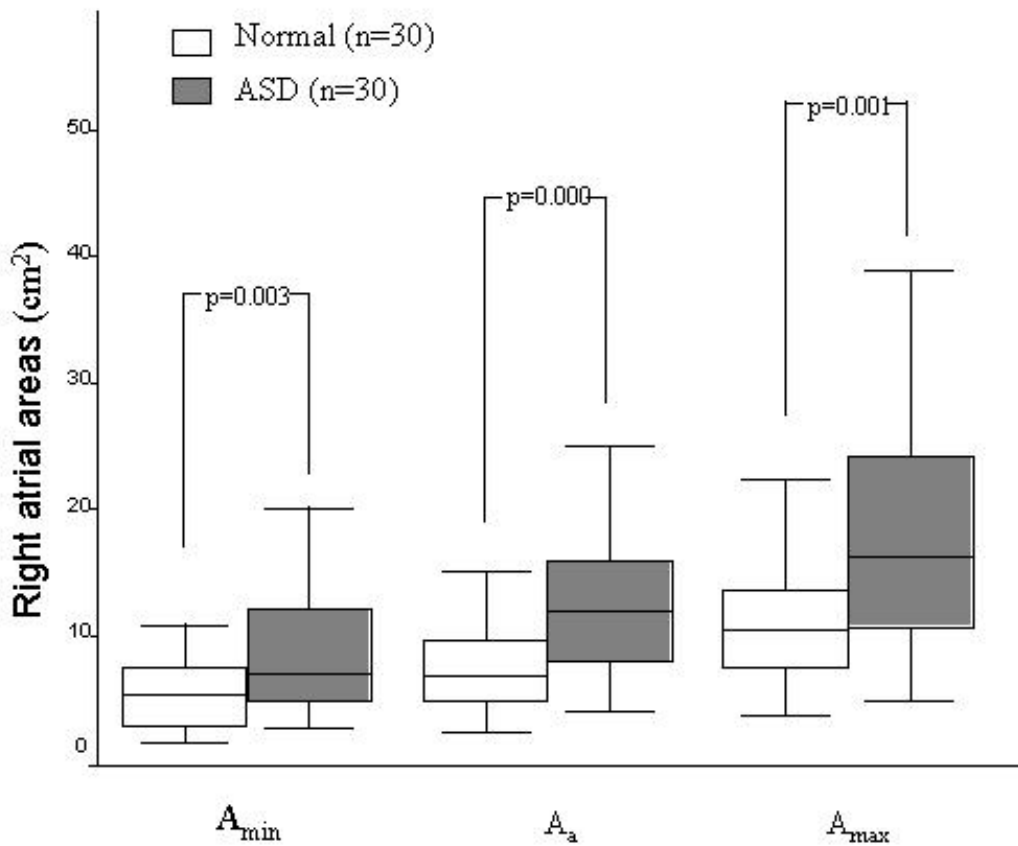


Figure 7 Comparison of right atrial areas in three phases measured by 2-D echocardiography between ASD patients and normal controls. During each phase the RA area in ASD patients was significantly larger than in controls. This may reflect right atrial volume overloading in these patients.

ASD: secundum type atrial septum defect;  $A_{min}$ : atrial area measured when it reaches minimum;  $A_a$ : atrial area measured at onset of p wave from the accompanied surface ECG;  $A_{max}$ : atrial area measured when it reaches maximum; RA: right atrium

### Right atrial function in patients with ASD

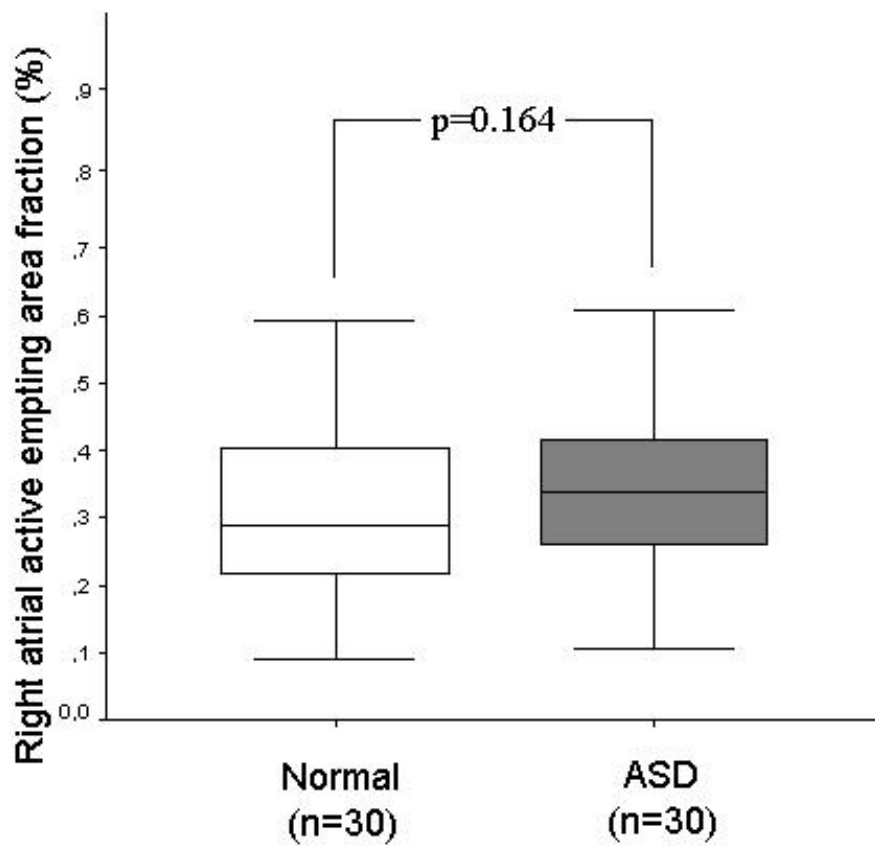


Figure 8 Comparison of the right atrial active emptying area fraction between ASD patients and normal controls. Volume overloading of right atrium had little influence on its pump function.

ASD: secundum type atrial septum defect; RA: right atrium

### Right atrial function in patients with ASD

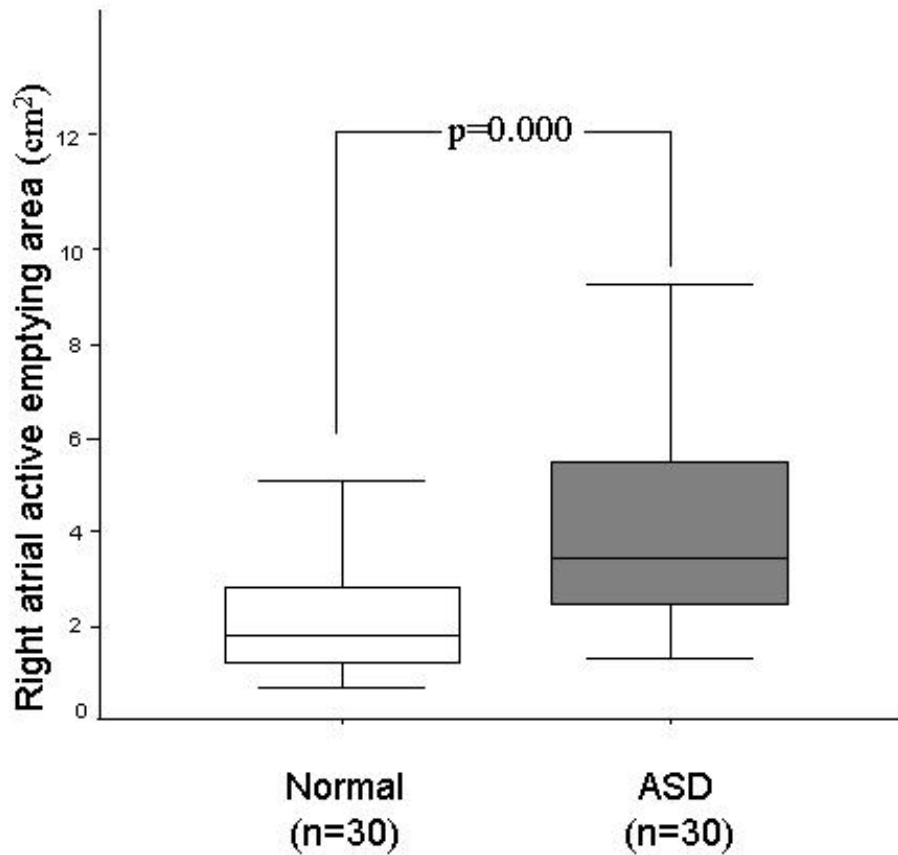


Figure 9 Comparison of the RA active emptying area between ASD patients and normal controls. In ASD patients the right atrial active emptying area was higher, which may indicate increased right atrial pump work, although the right atrial pump function was preserved.

ASD: secundum type atrial septum defect; RA: right atrium



### Right atrial function in patients with ASD

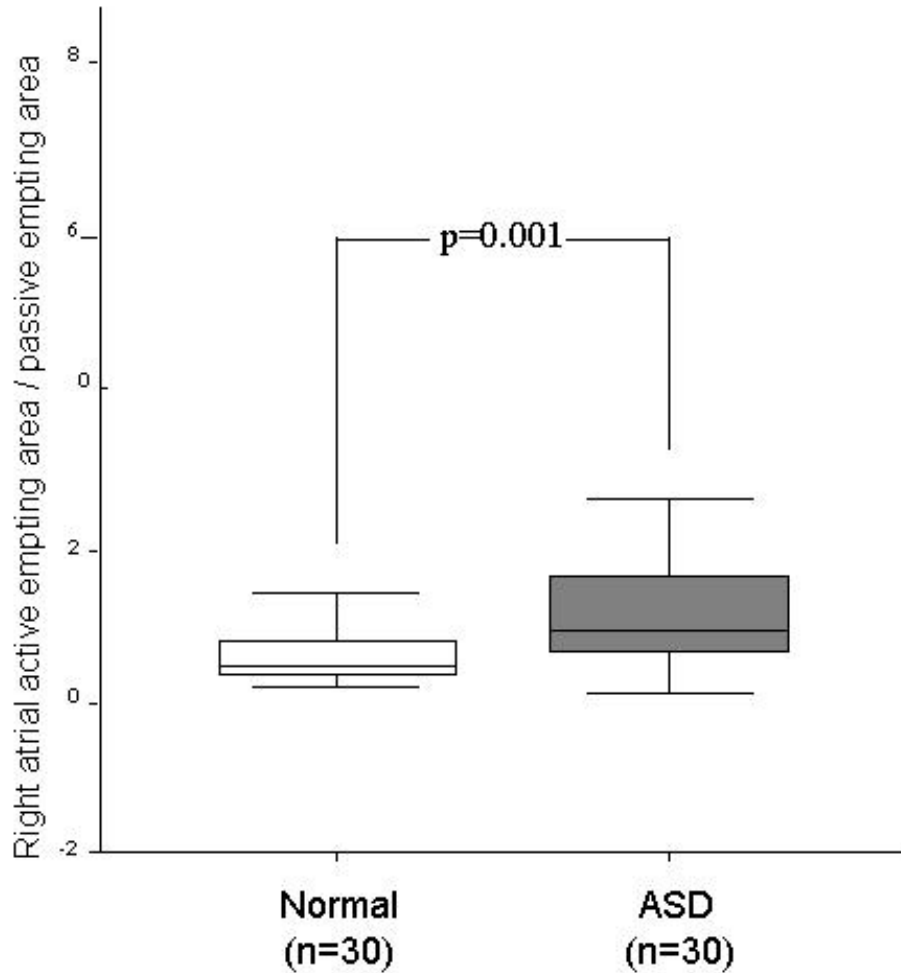


Figure 10 Comparison of the right atrial active emptying area/passive emptying area between ASD patients and normal controls. In ASD patients adequate right ventricular filling requires relatively more active atrial pump in late diastole.

ASD: secundum type atrial septum defect; RA: right atrium; RV: right ventricle

### Right atrial function in patients with ASD

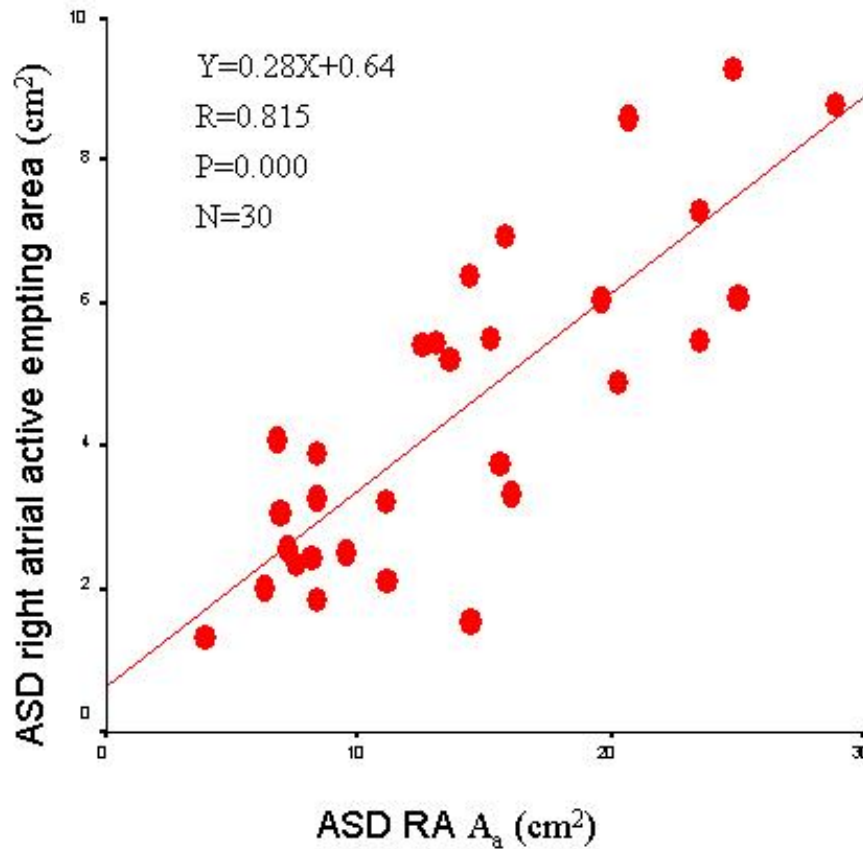


Figure 11 Correlation between right atrial late diastolic strain rate peak and right atrial active emptying area in ASD patients. The right atrial pump volume is increased with elevated preload secondary to the left to right shunt across the ASD.

A<sub>a</sub> : atrial area measured at onset of atrial "kick"; ASD: secundum type atrial septum defect;  
RA: right atrium

## Right atrial function in patients with ASD

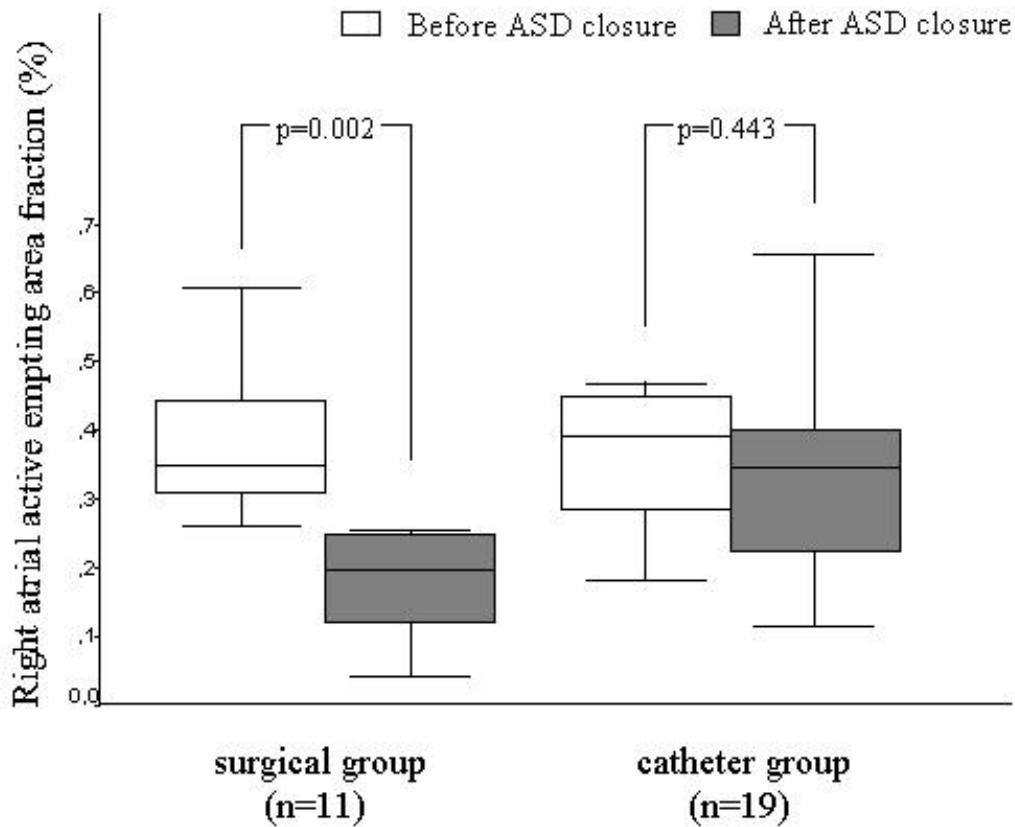


Figure 12 Comparison of right atrial active emptying area fraction before and after surgical or catheter ASD closure. The right atrial pump function was significantly reduced after surgical ASD closure while preserved through the interventional procedure. Myocardial damage secondary to cardiopulmonary bypass, hypothermia and surgical incision may explain the reduced right atrial pump function in the surgical group.

ASD: secundum type atrial septum defect; RA: right atrium

### **6.1.2 Tissue Doppler imaging**

According to the tissue Doppler imaging evaluation there were no significant differences of strain rate systolic ( $S_{SR}$ ), early diastolic ( $E_{SR}$ ) and late diastolic ( $A_{SR}$ ) peaks in right atrial lateral wall or in atrial septum between ASD patients and the normal subjects (table 7, figure 13). After surgical closure the  $A_{SR}$  measured by tissue Doppler imaging at the right atrial lateral wall ( $p=0.047$ ) was significantly reduced while the parameter remained unchanged at the atrial septum (figures 14 and 15). In the catheter group none of the locations showed a significant change in  $A_{SR}$  before and after the interventional closure (figures 14 and 15). Detailed comparison of the TDI results before and after ASD closure is shown in tables 8 and 9.

**Table 7 Comparison of right atrial performance measured by tissue Doppler imaging in normal subjects (n=30) and patients before ASD closure (n=30)**

	Normal subjects	Patients before ASD closure	p
	Median (range)	Median (range)	
$S_{SR}$ (1/s)	5.9 (0.8-9.8)	5.7 (2.4-11.8)	NS
$E_{SR}$ (1/s)	5.6 (0.6-11.4)	5.5 (1.5-11.1)	NS
$A_{SR}$ (1/s)	4.0 (0.6-11.9)	4.6 (0.3-11.1)	NS

$A_{SR}$ : late diastolic peak strain rate; ASD: secundum type atrial septum defect;  $E_{SR}$ : early diastolic peak strain rate;  $S_{SR}$ : systolic peak strain rate; SR: strain rate

**Table 8 Comparison of right atrial regional performance measured by tissue Doppler imaging before and after surgical closure (n=11)**

	Before closure	After closure	p
	Median (range)	Median (range)	
<b>RA lateral wall</b>			
S <sub>SR</sub> (1/s)	5.7 (2.5-11.8)	3.4 (2.2-6.2)	0.006
E <sub>SR</sub> (1/s)	5.3 (2.2-8.7)	3.5 (2.5-6.6)	0.022
A <sub>SR</sub> (1/s)	5.3 (0.3-11.1)	2.9 (0.5-6.2)	0.047
<b>Atrial septum</b>			
S <sub>SR</sub> (1/s)	2.1 (1.5-5.5)	1.7 (1.5-3)	NS
E <sub>SR</sub> (1/s)	2.9 (0.7-6.8)	3.3 (1.1-7.1)	NS
A <sub>SR</sub> (1/s)	2.4 (0.7-6.4)	1.7 (0.8-5.2)	NS

A<sub>SR</sub>: late diastolic peak strain rate; E<sub>SR</sub>: early diastolic peak strain rate; RA: right atrium;

S<sub>SR</sub>: systolic peak strain rate; SR: strain rate; TDI: tissue Doppler imaging

**Table 9 Comparison of right atrial regional performance measured by tissue Doppler imaging before and after catheter closure (n=19)**

	Before closure	After closure	p
	Median (range)	Median (range)	
<b>RA lateral wall</b>			
S <sub>SR</sub> (1/s)	5.6 (2.4-10.8)	5.1 (2.5-10)	NS
E <sub>SR</sub> (1/s)	5.5 (1.5-11.1)	5 (1.8-8.1)	NS
A <sub>SR</sub> (1/s)	3.9 (0.7-7.6)	4 (0.8-15)	NS
<b>Atrial septum</b>			
S <sub>SR</sub> (1/s)	2.4 (0.4-3.4)	2.7 (1.5-10.1)	NS
E <sub>SR</sub> (1/s)	2.4 (0.9-6.9)	3 (0.5-6.7)	NS
A <sub>SR</sub> (1/s)	1.6 (0.2-5.6)	2.8 (0.6-6.3)	NS

A<sub>SR</sub>: late diastolic peak strain rate; E<sub>SR</sub>: early diastolic peak strain rate; RA: right atrium;

S<sub>SR</sub>: systolic peak strain rate; SR: strain rate; TDI: tissue Doppler imaging

## Right atrial function in patients with ASD

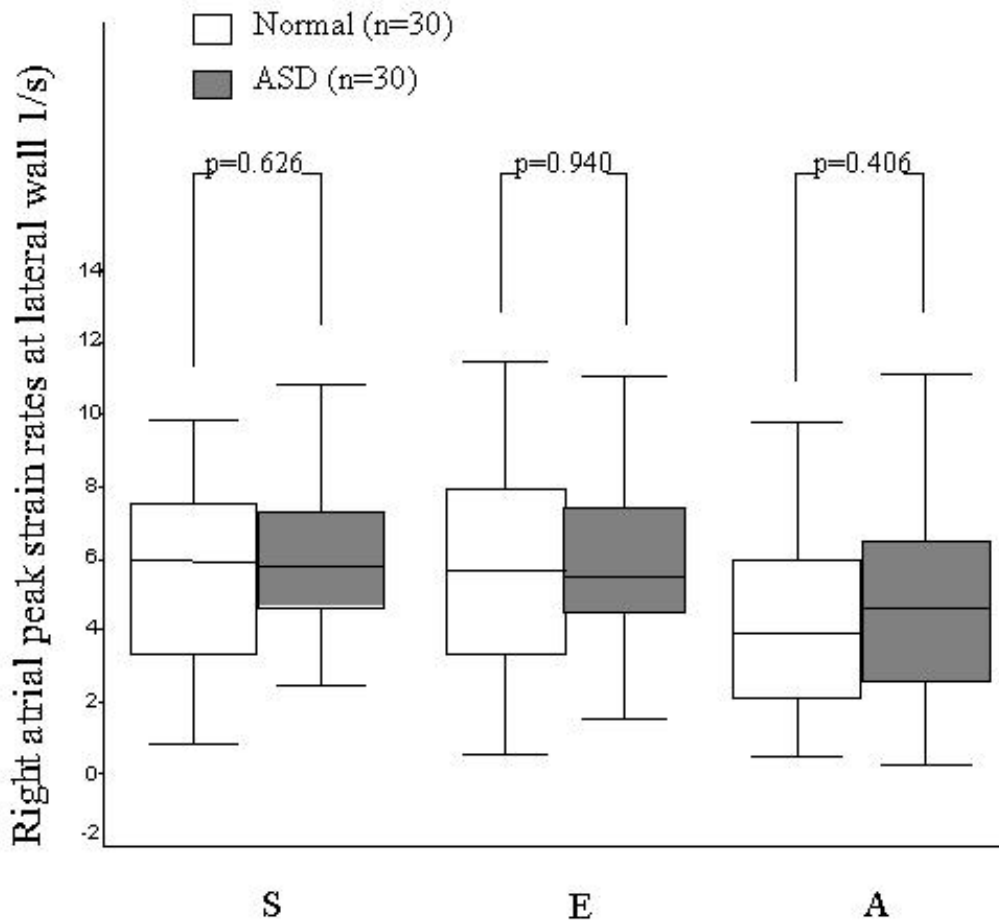


Figure 13 Comparison of the right atrial lateral wall peak strain rates measured by tissue Doppler imaging between ASD patients and controls. Volume overloading secondary to the left to right shunt across the ASD did not significantly alter the regional RA performance.

A: late diastolic peak strain rate; ASD: secundum type atrial septum defect;  
E: early diastolic peak strain rate; RA: right atrium;  
S: systolic peak strain rate; TDI: tissue Doppler imaging



## Right atrial function in patients with ASD

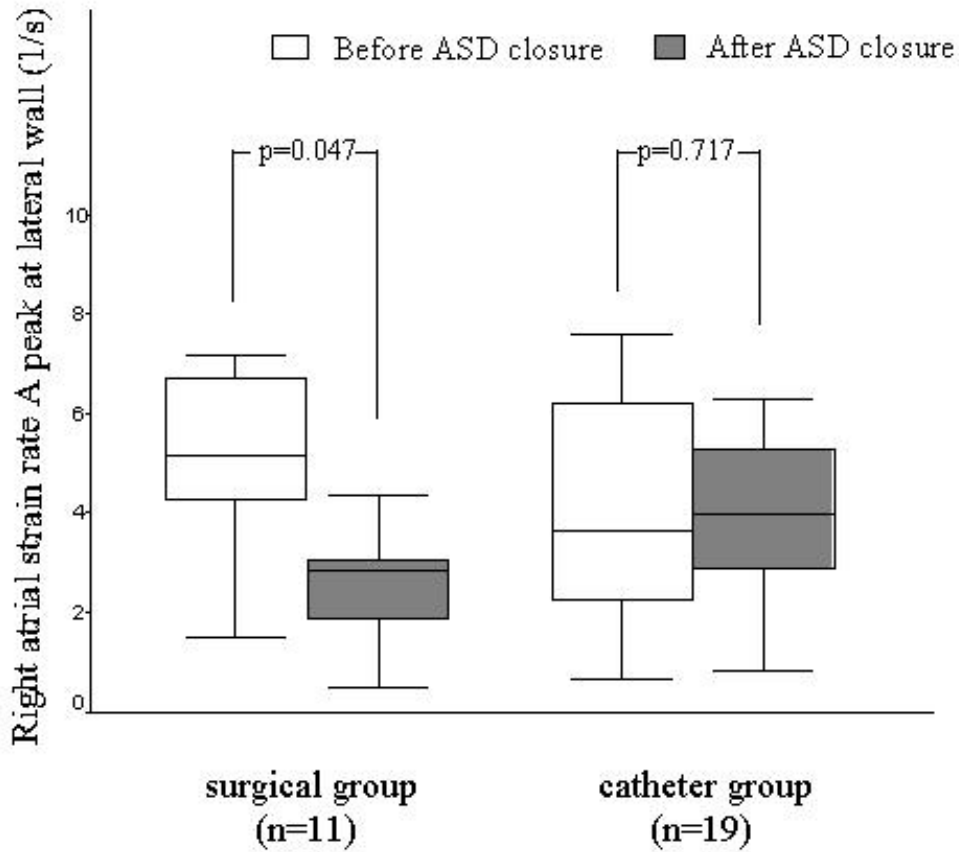


Figure 14 Comparison of RA lateral wall late diastolic strain rate peak before and after surgical or catheter ASD closure. The tissue Doppler imaging results confirmed that the regional right atrial pump function was reduced after surgical ASD closure while preserved through the interventional procedure

A peak: late diastolic peak; ASD: secundum type atrial septum defect; RA: right atrium

## Right atrial function in patients with ASD

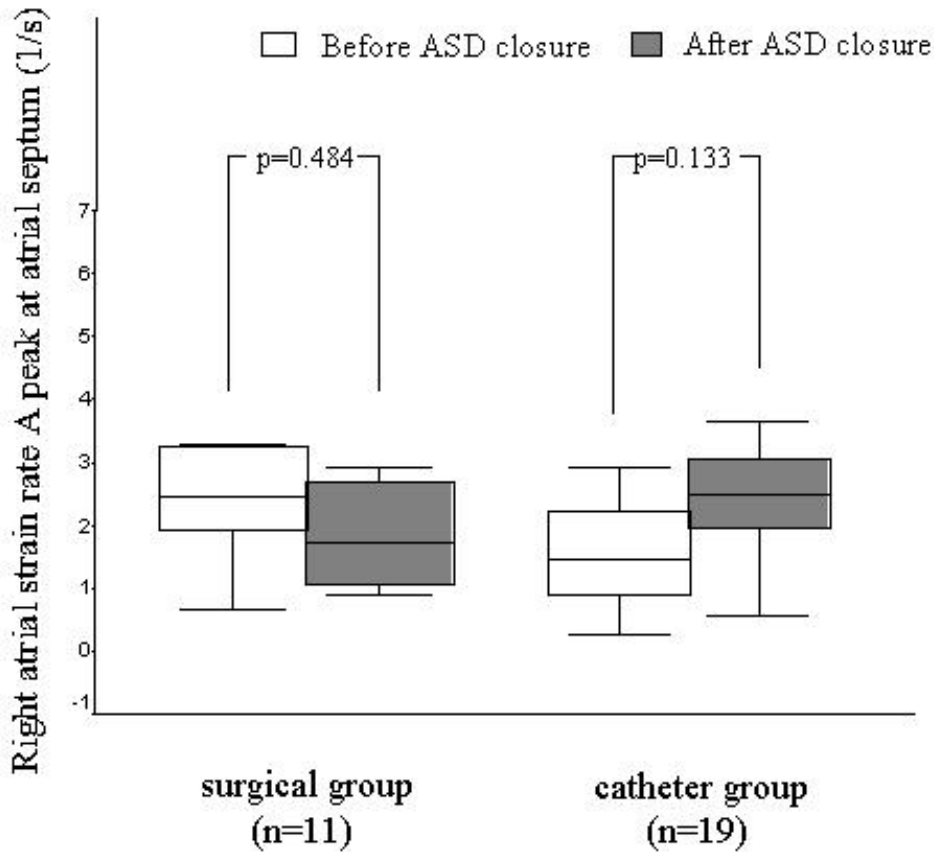


Figure 15 Comparison of atrial septum late diastolic peak strain rate before and after surgical or catheter ASD closure. The regional right atrial pump function at the atrial septum was not influenced by either of the ASD closure procedures. Figures 14 and 15 suggest that the atrial lateral wall incision is the main reason for acute right atrial pump function reduction after surgical ASD closure.

A peak: late diastolic peak; ASD: secundum type atrial septum defect; RA: right atrium

## **6.2 Right atrial pump function and its relation to right ventricular function in patients following corrective surgery of TOF (section 2)**

There were no significant difference in age or heart rate between the normal subjects and the patients after corrective surgery of tetralogy of Fallot.

### **6.2.1 Two dimensional echocardiographic examination**

In TOF patients the right atrial  $A_{\min}$  ( $p=0.000$ ),  $A_a$  ( $p=0.000$ ) and  $A_{\max}$  ( $p=0.013$ ) were significantly higher than in normal subjects (figure 16). The right atrial active emptying area fraction ( $p=0.005$ ) (figure 17) was significantly lower, while the active/passive emptying area ratio ( $p=0.001$ ) (figure 18) was significantly higher in TOF patients when compared to normal subjects. Detailed comparison between normal subjects and TOF patients is shown in table 10. There was no difference in right atrial active emptying area fraction between the TOF patients with right ventricular ejection fraction more than 50% and those with right ventricular ejection fraction less than 50%. Comparison of the two ejection fraction groups is shown in table 11.

Two of the patients undergoing magnetic resonance tomography, and three of the other 30, showed a Doppler pattern of restrictive right ventricular physiology, which was diagnosed when antegrade pulmonary flow in late diastole was detected throughout the respiratory cycle [54, 55].

**Table 10 Comparison of right atrial performance measured by two- dimensional echocardiography between normal subjects (n=30) and TOF patients (n=50)**

	Normal subjects	TOF patients	p
	Median (range)	Median (range)	
RA area parameters			
RA $A_{\min}$ (cm <sup>2</sup> )	6.1 (2.5-10.9)	9.9 (4.3-24.8)	0.000
RA $A_a$ (cm <sup>2</sup> )	8.1 (4.2-15.1)	12.5 (6.2-27.2)	0.000
RA $A_{\max}$ (cm <sup>2</sup> )	12.8 (7.5-23.4)	15.7 (7.2-29.2)	0.013
RA active emptying fraction (%)	25 (9-52)	18 (1-56)	0.005
RA active emptying area (cm <sup>2</sup> )	1.8 (0.9-7.2)	2.4 (0.2-8.8)	NS
RA active/passive emptying area ratio	0.4 (0.2-0.9)	0.9 (0.1-3.3)	0.001

$A_a$ : atrial area measured at onset of atrial “kick”;  $A_{\max}$ : atrial area measured when it reaches maximum;  $A_{\min}$ : atrial area measured when it reaches minimum; RA: right atrium; TOF: tetralogy of Fallot

**Table 11 Comparison of the TOF patients with right ventricular ejection fraction more than 50% and those with right ventricular ejection fraction less than 50%**

	RV EF $\geq$ 50%	RV EF < 50%	p
	n=8	n=12	
	Mean (range)	Mean (range)	
Age (years)	12 (10-30)	16 (8-28)	NS
Heart rate (bpm)	61 (50-84)	66 (55-88)	NS
ESV / BSA (ml / m <sup>2</sup> )	39 (26-58)	46 (33-106)	0.069
EDV / BSA (ml / m <sup>2</sup> )	81 (64-126)	84 (45-150)	NS
RA TDI derived A <sub>SR</sub> (1/s)	2.6 (1.1-3.6)	3.6 (1.5-7.1)	0.021
RA active emptying area fraction (%)	19 (3-25)	13 (6-29)	NS

bpm: beats per minute; BSA: body surface area; EDV: end diastolic volume; EF: ejection fraction; ESV: end systolic volume; RA: right atrium; RV: right ventricle; A<sub>SR</sub>: peak late diastolic strain rate; TDI: tissue Doppler imaging; TOF: tetralogy of Fallot

## Right atrial function in patients with corrected TOF

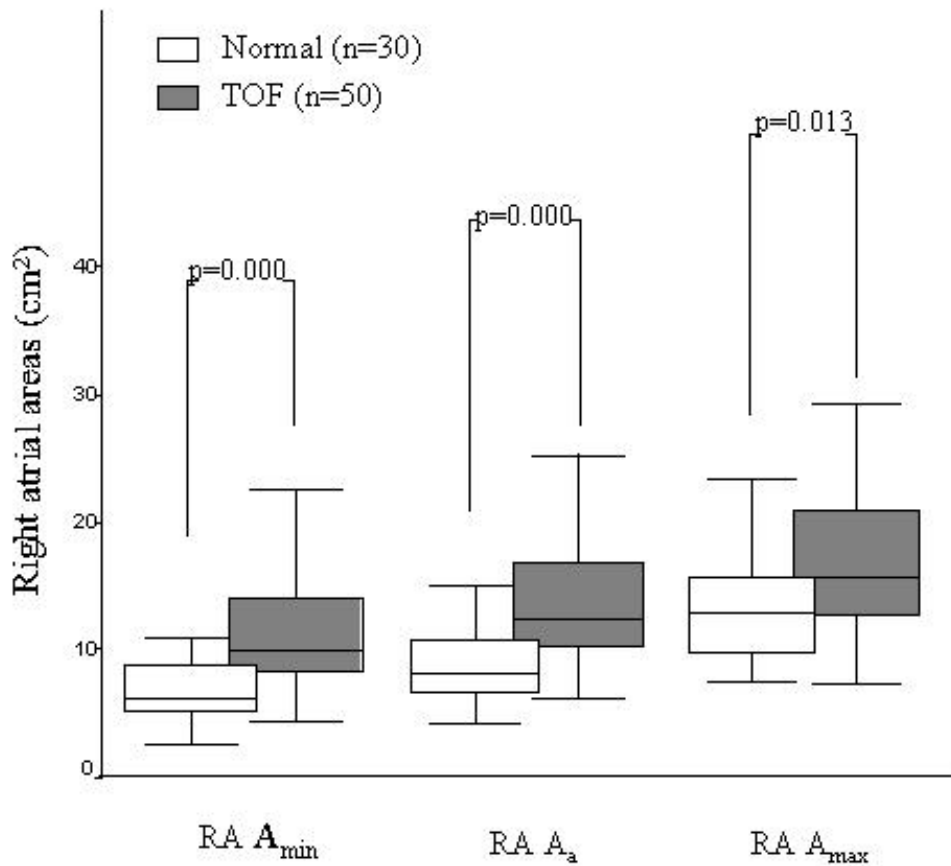


Figure 16 Comparison of right atrial areas between patients with corrected TOF and normal subjects in three different phases of a cardiac cycle (end-diastolic, end-systolic, onset of the p-wave of the accompanied ECG) measured by 2-D echocardiography. During every phase the right atrial area among TOF patients was significantly larger than in controls.

$A_{min}$ : atrial area measured when it reaches minimum;  $A_a$ : atrial area measured at onset of atrial “kick”;  $A_{max}$ : atrial area measured when it reaches maximum; RA: right atrium; TOF: tetralogy of Fallot

## Right atrial function in patients with corrected TOF

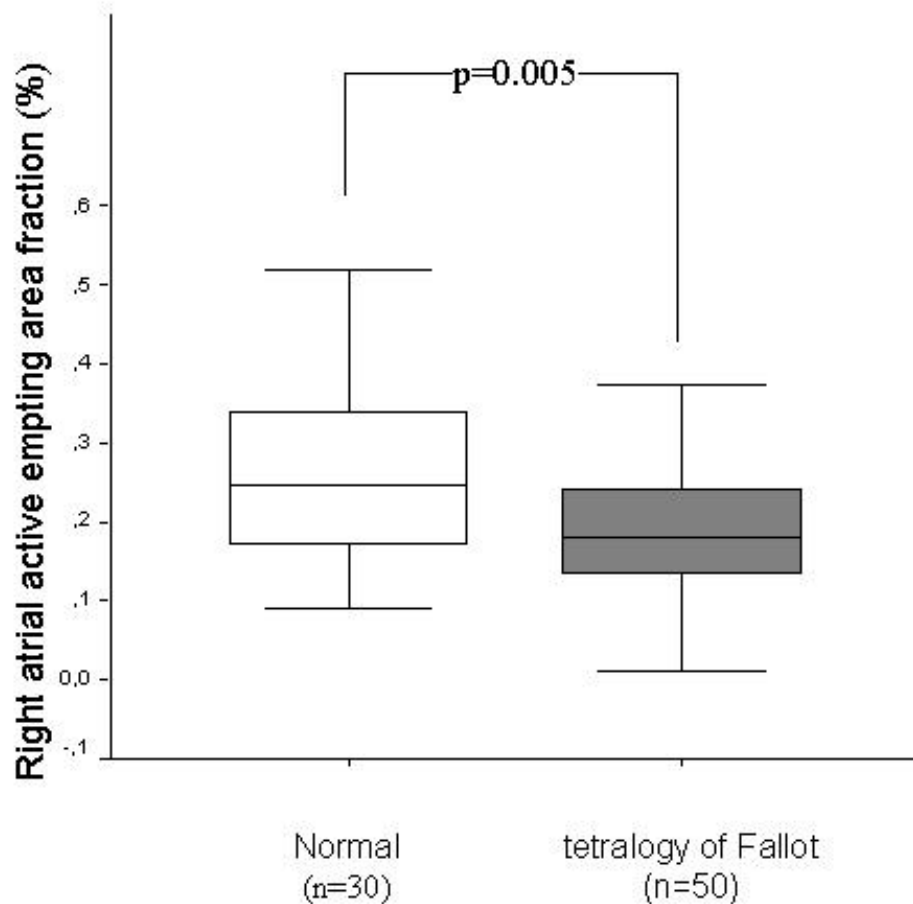


Figure 17 Comparison of right atrial active emptying area fraction between patients with corrected TOF and normal controls. Global right atrial pump function was reduced in TOF patients. This can be explained by the preoperative hypoxia and surgical right atrial myocardial insult in TOF patients.

RA: right atrium; TOF: tetralogy of Fallot

## Right atrial function in patients with corrected TOF

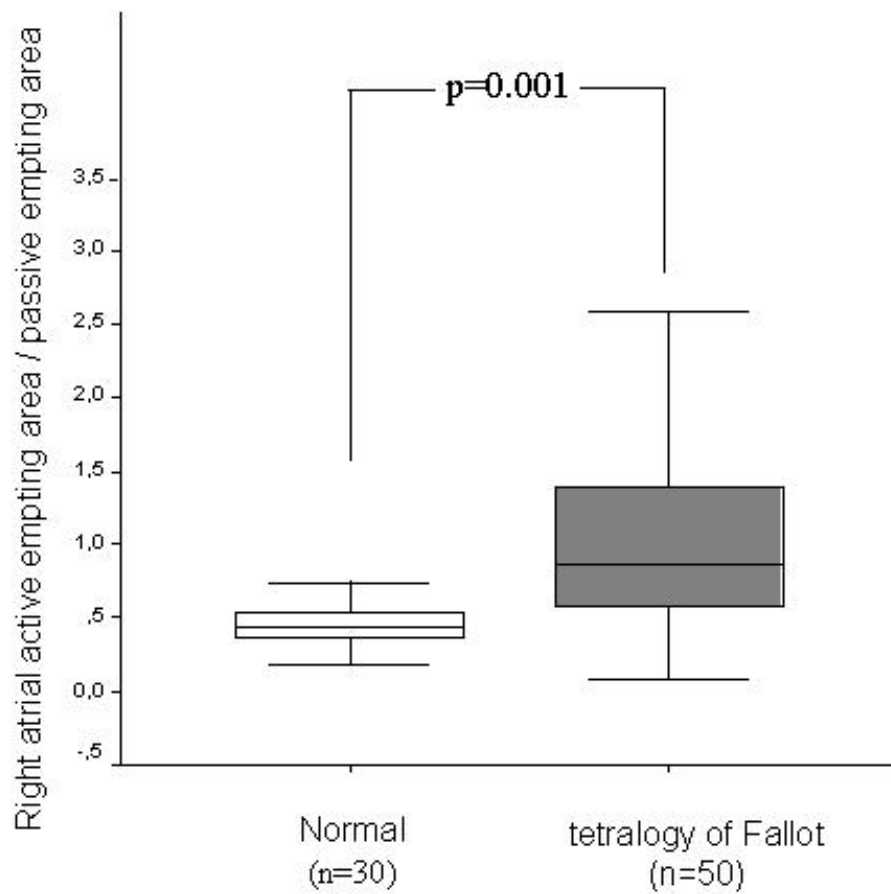


Figure 18 Comparison of the RA active emptying area/passive emptying area between patients with corrected TOF and normal controls. In TOF patients adequate right ventricular filling requires relatively more right atrial pump in late diastole to compensate the reduced right ventricular relaxation.

RA: right atrium; RV: right ventricle; TOF: tetralogy of Fallot



### **6.2.2 Tissue Doppler imaging**

According to the tissue Doppler imaging evaluation the RA lateral wall  $S_{SR}$  ( $p=0.000$ ),  $E_{SR}$  (0.038) and  $A_{SR}$  ( $p=0.002$ ) peaks were significantly reduced in TOF patients compared to normal subjects (table 12, figures 19 and 20). In TOF patients with right ventricular ejection fraction less than 50% right atrial tissue Doppler derived SR A peak was significantly higher than in those with right ventricular ejection fraction more than 50% ( $p=0.021$ ) (figure 21).

**Table 12 Comparison of right atrial and right ventricular performance measured by tissue Doppler imaging between normal subjects (n=30) and TOF patients (n=50)**

	Normal subjects	TOF patients	p
	Median (range)	Median (range)	
Right atrial tissue Doppler derived			
strain rate			
S <sub>SR</sub> (1/s)	6.4 (2.7-10.3)	4.6 (0.7-10)	0.000
E <sub>SR</sub> (1/s)	5.9 (1.9-11.7)	4.3 (0.7-11.5)	0.038
A <sub>SR</sub> (1/s)	5.2 (2.2-11.8)	3.2 (0.2-7.7)	0.002
Right ventricular tissue Doppler			
derived strain rate			
S <sub>SR</sub> (1/s)	3.5 (1-5)	1.8 (0.9-2.6)	0.000
E <sub>SR</sub> (1/s)	3.5 (1.3-5.5)	2.3 (1.4-4.2)	0.016
A <sub>SR</sub> (1/s)	2.5 (0.4-4.6)	1 (0.3-1.7)	0.001

A<sub>SR</sub>: late diastolic peak strain rate; E<sub>SR</sub>: early diastolic peak strain rate; S<sub>SR</sub>: systolic peak strain rate; SR: strain rate; TOF: tetralogy of Fallot

## Right atrial function in patients with corrected TOF

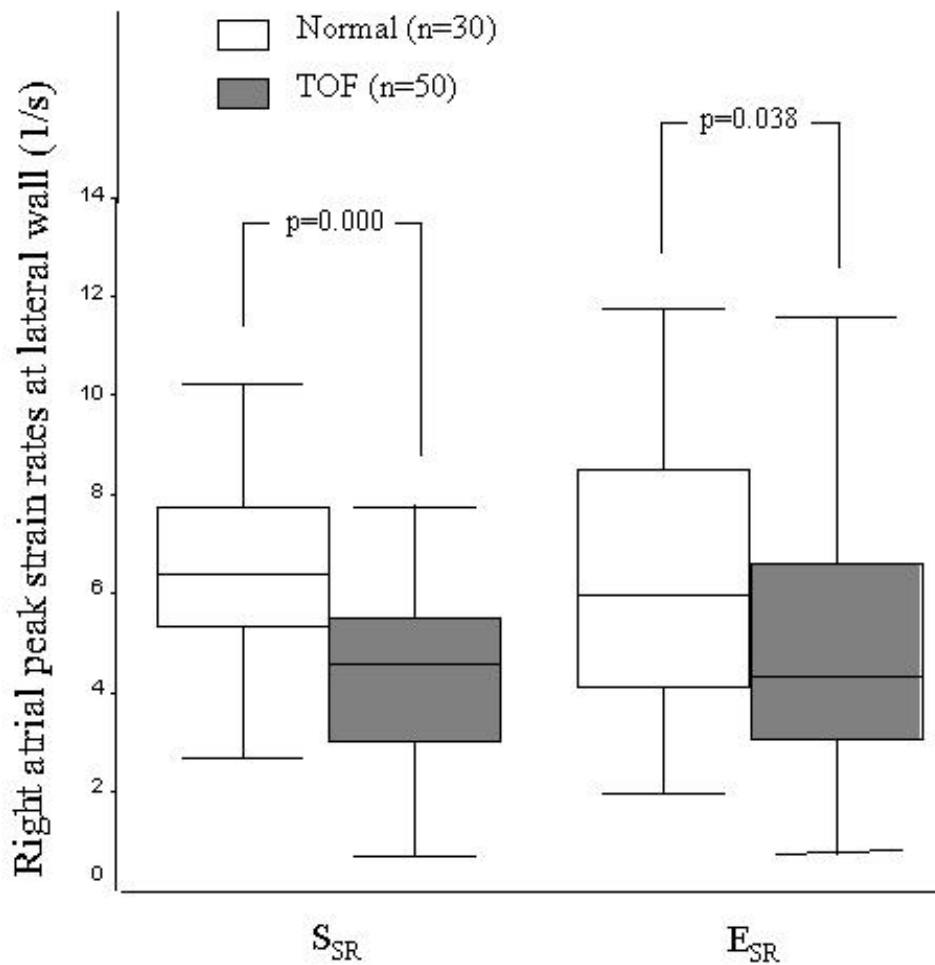


Figure 19 Comparison of right atrial lateral wall systolic and early diastolic strain rate peaks measured by tissue Doppler imaging between corrected TOF patients and normal subjects. In postoperative TOF patients the regional right atrial systolic and early diastolic performances were reduced, which may reflect the global right ventricular contraction and relaxation.

$E_{SR}$ : early diastolic peak strain rate; RA: right atrium; RV: right ventricle;  $S_{SR}$ : systolic peak strain rate; TDI: tissue Doppler imaging; TOF: tetralogy of Fallot

## Right atrial function in patients with corrected TOF

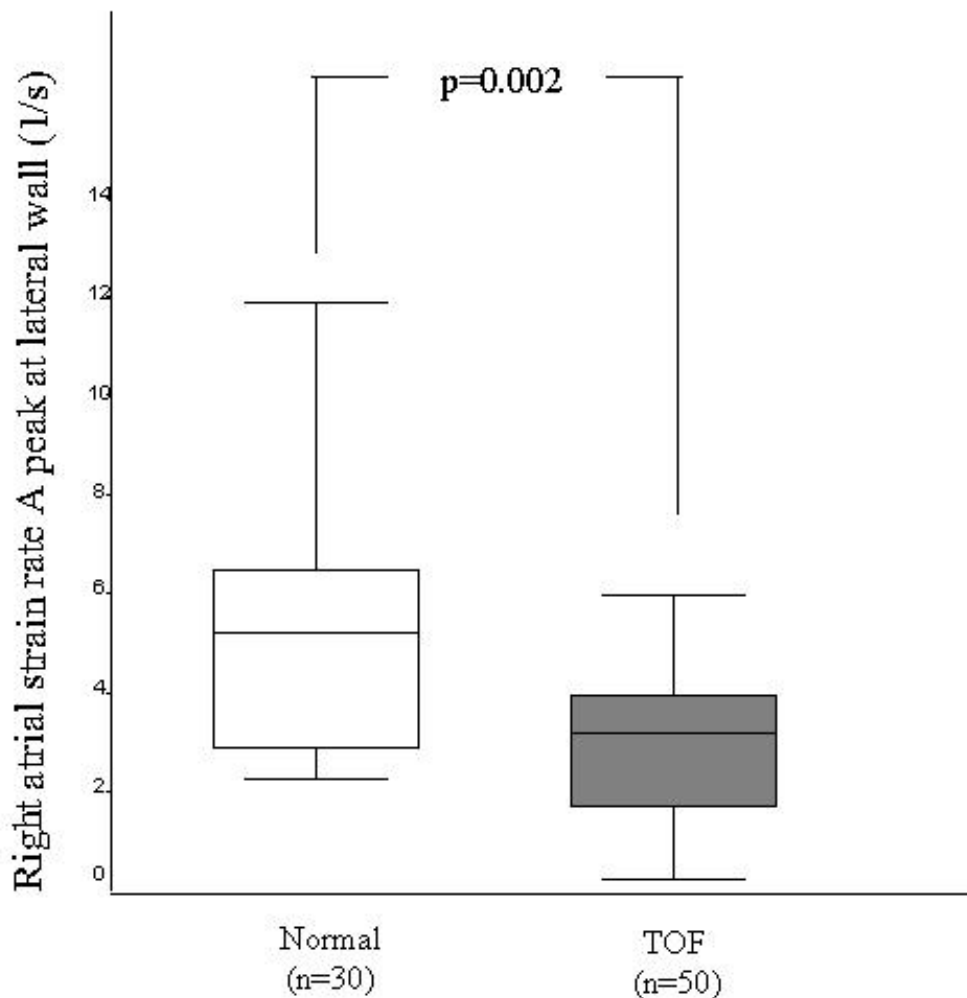


Figure 20 Comparison of right atrial lateral wall late diastolic strain rate peak measured by tissue Doppler imaging between patients with corrected TOF and normal subjects. In addition to the well-known global right ventricular dysfunction, tissue Doppler imaging results demonstrate that the regional right atrial pump function in TOF patients is also reduced

A peak: late diastolic peak; RA: right atrium; TDI: tissue Doppler imaging; TOF: tetralogy of Fallot

## Right atrial function in patients with corrected TOF

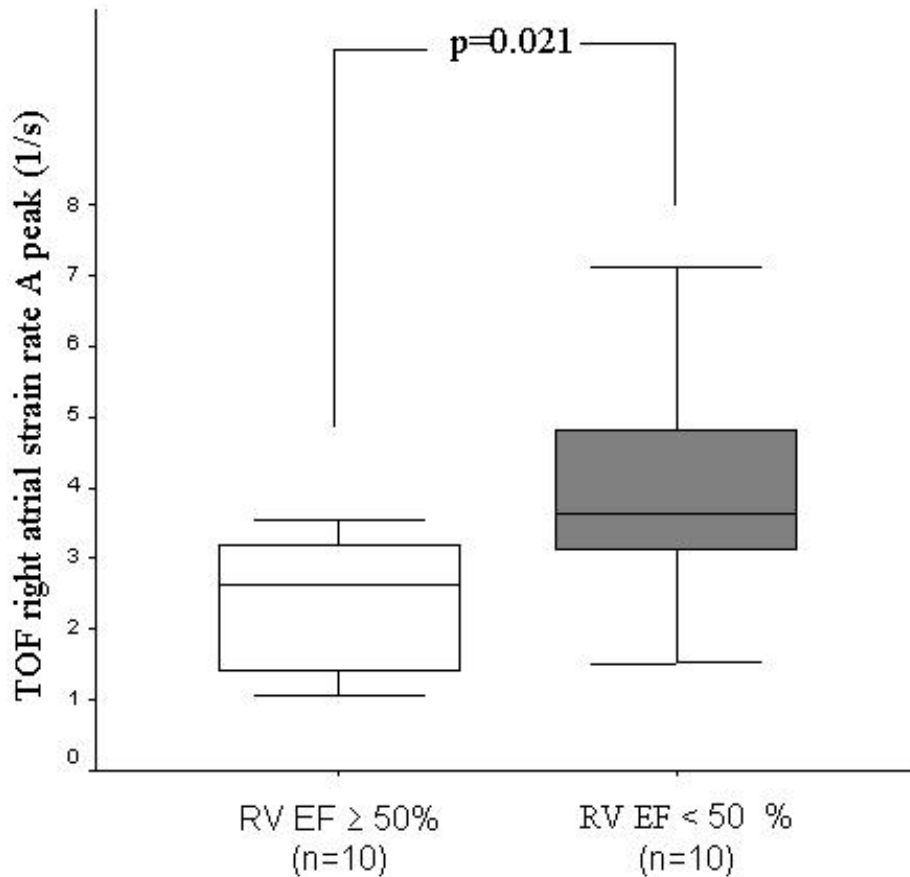


Figure 21 Comparison of right atrial lateral wall late diastolic peak strain rate in corrected TOF patients between those with right ventricular ejection fraction more than 50% and those less than 50%. TOF patients with reduced systolic function (ejection fraction less than 50%) have relatively increased longitudinal atrial myocardial shortening indicating increased atrial pump function. This may be an adaptive compensatory mechanism of the right atrium to prevent further deterioration of the RV haemodynamics.

A peak: late diastolic peak; EF: ejection fraction; RA: right atrium;  
RV: right ventricle; SR: strain rate; TOF: tetralogy of Fallot