

# Long-term outcomes in patients who underwent surgical correction for atrioventricular septal defect

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## ABSTRACT

**Objective:** The follow-up results of patients operated for atrioventricular septal defect (AVSD) during 1996–2016 at Başkent University are presented.

**Methods:** Data obtained from hospital records consists of preoperative echocardiographic and angiographic details, age and weight at surgery, operative details, Down syndrome presence, postoperative care details, early postoperative and latest echocardiographic findings and hospitalization for reintervention.

**Results:** A total of 496 patient-files were reviewed including 314 patients (63.4%) with complete and 181 (36.6%) with partial AVSD (48.4% of all patients had Down syndrome). Atrioventricular (AV) valve morphology was Rastelli type A in 92.2%, B in 6.5%, and C in 1.3% of patients. The operative technique used was single-patch in 21.6% (108), double-patch in 25.8% (128), and modified single-patch (Wilcox) in 52.5% (260) of patients. The follow-up time was 37.79±46.70 (range, 0–198) months. A total of 64 patients (12.9%) had arrhythmias while in the intensive care unit; pacemaker was implanted in 12 patients. A total of 78 patients (15.7%) were treated for pulmonary hypertensive crisis. The early morbidity and mortality in the postoperative first month were calculated as 38% and 10%, and the late morbidity and mortality (>1 month) were calculated as 13.1% and 1.9%, respectively. The rate of reoperation in our cohort was 8.9%.

**Conclusion:** Although the early morbidity and mortality are low in AVSD operations, the rate of reoperations for left AV valve insufficiency are still high. Although Down syndrome is not a risk factor for early mortality, the co-morbid factors, such as longer postoperative mechanical ventilator or inotropic support, lead to higher risk for morbidity. The frequency of pulmonary hypertension and consequent complications are also high. (*Anatol J Cardiol* 2018; 20: 229-34)

**Keywords:** complete AVSD, partial AVSD, Down syndrome, single-patch technique, double-patch technique, Wilcox technique

## Introduction

Atrioventricular septal defect (AVSD) constitutes 4%–5% of all the congenital heart defects. Complete AVSD is the most frequently encountered form in Down syndrome (1).

Recent studies have demonstrated markedly improved survival in AVSD after operative repair. The surgical mortality is reduced to 3%–8%, and the 20 year-survival rate is as high as 95% (2-7). In about a quarter of these patients, reoperations, which are mostly due to late complications like left atrioventricular (AV) valve insufficiency and left ventricular outflow tract obstruction (LVOTO), continue to be the main concern.

The aim of this retrospective study was to assess the early and long-term follow-up results of children who underwent surgery due to AVSD, and to analyze the major risk factors for morbidity and mortality postoperatively.

## Methods

The patient database was retrospectively scanned to identify all children who were diagnosed with AVSD, and had been operated during 1996–2016 at Başkent University. Only patients with balanced ventricles and without accompanying cardiac anomalies were eligible for inclusion. Any patient with multiple

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ventricular septal defects (VSDs), pulmonary stenosis, aortic coarctation, Fallot tetralogy, double outlet, or discordant ventriculoarterial connections were excluded. The study group comprised 496 patients. Following details were noted from the patient records: the age and weight at operation, presence of Down syndrome, preoperative catheterization data [emphasizing the pressure measurements, pulmonary vascular resistance (PVR) and flow ratios] surgical technique, surgical details (cardiopulmonary bypass and aortic cross-clamp times), details of the postoperative intensive care [durations of postoperative ventilation support, inotropic treatment, and stay in the intensive care unit (ICU)], total hospital stay, complications (infections, postoperative arrhythmias, and reoperations), operative and late mortality.

For patients with a risk of postoperative pulmonary hypertension, the pulmonary artery pressure was monitored in the ICU. If the patient had preoperative PVR >2 Wood units and/or pulmonary artery pressure >40 mm Hg or was older than 6 months, a catheter was intraoperatively placed in the main pulmonary artery.

Echocardiographic data with an emphasis on AV valve insufficiency and LVOTO was also preoperatively recorded at discharge and during the last visit. Rastelli classification was used to describe the morphology of the AV valve in patients with complete AVSD.

To analyze the changes in consecutive time that could possibly affect the outcome, follow-up period was arbitrarily divided into three phases considering the date of the operation. Each operation phase was 5 years in duration and was designated as 1996–2001 (first phase), 2002–2007 (second phase), and 2008–2016 (third phase).

### Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences software (version 20 for Windows; SPSS, Chicago, IL, USA). Continuous variables were reported as mean±standard deviation of the mean, and categorical variables were presented as frequencies and percentages. Univariate comparisons of continuous variables were made using t-test. Categorical variables were compared using  $\chi^2$  test. A two-sided p value less than 0.05 was considered statistically significant. Binary logistic regression analysis was used to examine the relationship between potential risk factors and early mortality. Results are shown as odds ratios (ORs) with 95% confidence intervals (CI). Logistic regression analysis, using all variables in stepwise method, was performed to identify independent risk factors. Cox proportional hazard models were used to examine the predictors for reoperation. Results are shown as a hazard ratio (HR) with 95% CI.

## Results

There were 215 male (43.3%) and 281 female (56.7%) patients. A total of 240 patients (48.4%) were diagnosed with Down syndrome. Of all the patients, 63.4% (314 patients) had complete

AVSD, and 36.6% (181 patients) had intermediate-partial AVSD. The mean age of patients with complete AVSD was  $10.01\pm 12.01$  (range, 2–84; median, 6; 25 and 75 percentiles, 5 and 9, respectively) months. The mean age of patients with partial-intermediate AVSD was  $46.59\pm 44.01$  (range, 2–240; median, 30; 25 and 75 percentiles, 17 and 63, respectively) months. The mean body weight during the operation was  $9.26\pm 8.25$  (range, 2.5–64) kg.

Atrial septal defect (ASD) and patent ductus arteriosus (PDA) were observed in 26.2% of the patients. Rastelli type A morphology was seen in 92.2% of the patients with complete AVSD whereas 6.5% had type B and 1.3% had type C morphology.

Twelve patients (2.4%) had pulmonary banding prior to total correction. AVSD closure technique used was single-patch in 108 patients (21.8%), modified single-patch (Wilcox technique) in 260 patients (52.4%), and double-patch in 128 patients (25.8%).

The early postoperative morbidity and mortality within first month were calculated as 38% and 10%, respectively. Common causes of early morbidity were pericardial effusion (38 patients), pneumonia (30 patients), pleural effusion (21 patients), and subglottic edema and stenosis due to prolonged intubation (19 patients). A total of 48 patients died in the first postoperative month. Death within 24 h was due to hemodynamic instability and was observed in 28 patients. Early mortality beyond 24 h was seen in the remaining patients due to cardiac failure, pulmonary hypertensive crisis, arrhythmia, or septicemia.

Postoperative infections, confirmed by blood, urine, or tracheal aspirate cultures, were seen in 21% of the patients.

Pulmonary artery pressure catheter was placed in 189 patients, of which 78 had pulmonary hypertensive crisis (15.7%) and 3 died. No complications related to the placement or removal of the catheters was noted.

There was postoperative third-degree AV block in 64 patients (12.9%). Only 12 patients had permanent block and had permanent cardiac pacemaker implanted.

Morbidity and mortality observed beyond 1 month was considered a late result, and the rates were calculated as 13.1% and 1.9%, respectively. The most prevalent cause of morbidity was reoperation (8.9%; 44 patients). Other causes were cardiac failure (2.6%; 13 patients), upper airway obstruction due to subglottic stenosis (1%; 5 patients), and infection (0.8%; 4 patients).

Among 44 patients who were reoperated, 12 patients had undergone mitral valve repair (2.4%) and 18 patients had undergone mitral valve replacement (3.6%). LVOTO developed in 19 patients postoperatively, among which 10 (2%) were operated. Two patients had undergone residual VSD closure, and one patient had aortic coarctation repair. In two patients, the residual patent ducts were postoperatively closed with coils.

Considering the echocardiographic results at discharge, no correlation was observed between the surgical technique and degree of left AV valve insufficiency ( $p=0.67$ ). However, the AV valve insufficiency degree measured at the last follow up echocardiography was significantly lower in the double patch group ( $p=0.002$ ).

**Left ventricular outflow tract obstruction**

Among 19 patients who had late postoperative LVOTO, 14 patients had undergone repair using Wilcox technique, 4 patients with double-patch, and 1 patient with single-patch technique. Although Wilcox technique was more frequent among patients with LVOTO, the correlation between surgical technique and LVOTO was not significant (p=0.11). Additionally, the type of AVSD (complete vs. partial AVSD) was not related to development of LVOTO (p=0.31).

**Early mortality**

We tested the following possible risk factors for early mortality in patients with postoperative AVSD: age, body weight, Down syndrome presence, degree of preoperative and postoperative left AV valve insufficiencies, type of AVSD, surgical technique, and the surgical era. Even though each of these factors were significant models according to binary logistic regression analysis (p<0.001), only low body weight was found to have significant correlation with early mortality (p=0.018). The assessment of risk factors for early mortality using binary logistic regression analysis is given in Table 1.

The early mortality in complete AVSD group was determined as 12.5%, whereas in the partial-intermediate group it was 5.5%. When comparison analysis was made with respect to early mortality; having younger age and lower body weight at operation, complete AVSD, postoperative arrhythmia, pulmonary hypertension, high PVR and pulmonary hypertensive crisis were significantly related with early mortality (p<0.01). On the other

hand, the degree of preoperative or postoperative left AV valve insufficiency, Down syndrome presence, or infections were not significantly related with early mortality.

Early postoperative mortality for the three time phases were calculated as 13% (between first phase), 9.9% (second phase), and 9.4% (third phase), whereas the overall mortality was 10%. The decrease in mortality was significant after the first phase, and the correlation between the surgical era and mortality was found as statistically significant (p=0.036). Low body weight was found to be a risk factor for early mortality in each phase (p<0.05).

The late mortality was 1.9% (nine patients), and all patients died because of progressive cardiac failure.

**Reoperation**

The assessment of risk factors for reoperation using Cox regression analysis is given in Table 2. The factors determined as significant risk factors for reoperation for valve repair were severe preoperative or postoperative left AV valve insufficiency and early surgical era (higher risk in the first phase) (p<0.05 for each). On the other hand, surgical era, age, and body weight were significantly related to reoperation for LVOTO.

The rates of reoperations were significantly high in patients with partial AVSD and those operated with Wilcox technique (p=0.001) as well.

**Down syndrome and complete AVSD**

Patients with Down syndrome were young and light-weighted during operation. They had more preoperative pulmonary hypertension, higher PVR, (CPB), aortic cross-clamp, and ventilation and inotropic support than patients not affected by Down syndrome. They also had more frequent infections (Table 3) than those without Down syndrome.

Because Down syndrome was significantly more frequent among patients with complete AVSD than partial AVSD, similar findings were pertinent for patients with complete AVSD as well (Table 4).

Although overall early morbidity was more frequent in Down syndrome, patients without Down syndrome had more frequent and higher degree of left AV valve insufficiency at their last visit. This also resulted as a higher rate of mitral valve repair and mitral valve replacement.

Therefore, higher late morbidity in patients without Down syndrome may be attributed to the fact that AV valve complications and reoperations were more frequent among patients in the partial/intermediate AVSD group.

**Discussion**

In our retrospective study of 496 patients with AVSD, who were postoperatively followed for up to 20 years in a tertiary health center, we observed a decrease in early mortality from 13% to 9.9% after 2001. This was parallel to the rate of reopera-

**Table 1. Assessment of risk factors for early mortality using Binary logistic regression analysis**

| Variable                           | Early mortality OR (95% CI) | P value |
|------------------------------------|-----------------------------|---------|
| Down                               | 2.18 (0.54-8.85)            | 0.272   |
| Preop left AV valve insufficiency  | 0.74 (0.20-2.75)            | 0.659   |
| Type of AVSD                       | 0.48 (0.69-3.35)            | 0.461   |
| Years of operation                 |                             | 0.936   |
| 1996–2001                          | 1                           |         |
| 2002–2007                          | 0.86 (0.74-10.05)           | 0.905   |
| 2008–2016                          | 0.71 (0.11-4.34)            | 0.717   |
| Associated cardiac anomalies       | 1.49 (0.34-6.56)            | 0.592   |
| Age                                | 1.00 (0.83-1.22)            | 0.931   |
| Weight                             | 0.44 (0.22-0.86)            | 0.017   |
| Cleft closure                      | 1.41 (0.11-17.93)           | 0.791   |
| Technique                          | 0.10 (0.11-1.03)            | 0.053   |
| Postop left AV valve insufficiency | 1.30 (0.35-4.71)            | 0.688   |

AV – atrioventricular, AVSD – atrioventricular septal defect, CI – confidence interval, OR – odds ratio

**Table 2. Assessment of risk factors for reoperation using Cox regression analysis**

| Variable  | Reoperation<br>HR (95%CI) | P value      | Valve op<br>HR (95% CI) | P value      | LVOTO<br>HR (95% CI) | P value      |
|---|---------------------------|--------------|-------------------------|--------------|----------------------|--------------|
| Down  | 0.49 (0.17-1.41)          | 0.191        | 0.84 (0.21-3.37)        | 0.812        | 0.45 (0.11-1.85)     | 0.271        |
| <b>Preoperative left AV valve insufficiency</b> |                           | <b>0.048</b> |                         | <b>0.050</b> |                      | <b>0.767</b> |
| Minimal   | 1                         | 0.754        | 1                       | 0.801        |                      | 1            |
| Mild  | 1.41 (0.16-12.41)         | 0.787        | 0.73 (0.06-7.90)        | 0.410        |                      | 0.950        |
| Moderate  | 0.74 (0.08-6.36)          | 0.402        | 0.37 (0.03-3.85)        | 0.615        |                      | 0.952        |
| Severe  | 2.43 (0.30-19.60)         |              | 1.76 (0.19-16.24)       |              |                      | 0.948        |
| <b>Type of AVSD</b>                             | 0.51 (0.20-1.28)          | 0.155        | 0.17 (0.04-0.64)        | <b>0.009</b> | 0.68 (0.16-2.88)     | 0.603        |
| <b>Years of operation</b>                       |                           | <b>0.008</b> |                         | 0.074        |                      | <b>0.004</b> |
| 1996–2001                                       | 1                         | <b>0.014</b> | 1                       | 1            | 1                    | 0.001        |
| 2002–2007                                       | 0.21 (0.06-0.72)          | <b>0.003</b> | 0.68 (0.14-3.28)        | 0.635        | 0.002 (0.00-0.09)    | 0.054        |
| 2008–2016                                       | 0.22 (0.08-0.60)          |              | 0.27 (0.76-0.96)        | <b>0.043</b> | 0.20 (0.04-1.02)     |              |
| <b>Associated cardiac anomalies</b>             | 1.30 (0.63-2.68)          | 0.476        | 1.44 (0.55-3.75)        | 0.452        | 1.00 (0.33-3.00)     | 0.987        |
| <b>Age</b>                                      | 0.99 (0.95-1.02)          | 0.686        | 1.03 (0.99-1.078)       | 0.098        | 0.88 (0.81-0.97)     | <b>0.009</b> |
| Weight  | 1.03 (0.89-1.18)          | 0.663        | 0.82 (0.65-1.03)        | 0.095        | 1.37 (1.07-1.76)     | <b>0.012</b> |
| Cleft closure                                   | 0.48 (0.10-2.31)          | 0.366        | 0.30 (0.03-2.62)        | 0.279        | 2.12 (0.18-23.94)    | 0.541        |
| Technique                                       | 1.26 (0.59-2.68)          | 0.549        | 2.13 (0.50-9.03)        | 0.303        | 1.46 (0.60-3.57)     | 0.403        |
| <b>Postop left AV valve insufficiency</b>       | 1.90 (1.25-2.88)          | <b>0.002</b> | 3.26 (1.87-5.66)        | <b>0.000</b> | 0.49 (0.23-1.05)     | 0.067        |

AV – atrioventricular, AVSD – atrioventricular septal defect, CI – confidence interval, HR – hazard ratio, LVOTO - left ventricular outflow tract obstruction

**Table 3. Comparison of patients with Down syndrome and those without Down syndrome**

|                                  | Down syndrome<br>(n=240) | Not affected by<br>Down syndrome<br>(n=256) | P value |
|----------------------------------|--------------------------|---|---------|
| Age (months)                     | 14.54±22.61              | 31.59±39.09                                 | <0.001  |
| Weight (kg)                      | 7.14±6.12                | 11.24±9.43                                  | <0.001  |
| PAP                              | 38.59±11.88              | 28.17±12.12                                 | <0.001  |
| PVR                              | 2.21±1.86                | 1.67±1.37                                   | <0.001  |
| CPB time (min)                   | 99.66±29.41              | 88.50±40.51                                 | 0.01    |
| Aortic cross-clamp<br>time (min) | 71.61±20.27              | 60.72±25.13                                 | 0.01    |
| Inotrop time (day)               | 4.34±4.12                | 3.13±5.50                                   | <0.001  |
| MV duration (h)                  | 83.79±228.22             | 43.40±109.15                                | 0.02    |

PAP - pulmonary arterial pressure, PVR - pulmonary vascular resistance, CPB - cardiopulmonary bypass, MV - mechanical ventilation

tion that declined from 13% to 5.9% (p=0.012). Within past 20 years, the surgical success of AVSD has increased due to our better understanding of the defect structure, advanced myocardial protection and perfusion methods, increased use of periop-

erative transesophageal echocardiography, and better postoperative care.

Our results are concordant with the literature, in which more than 20-year experience is presented. Similarly in the reported studies, the mortality has been reported as high as 15%–20% in the first year, which has significantly decreased to 5.7%–10% in the following years (2-8). Crawford and Stroud (8) have reported current mortality as 3%–6%. The authors listed the factors that led to the drop in the mortality as performing early surgery (before pulmonary hypertension develops), encountering less postoperative low cardiac output syndrome, decline in the rate of hemodynamically important residual defects, and third-degree AV block. In the study by Hooenkerk et al. (2), early mortality was reported to decrease from 16% to 8.3% in 30 years. They also similarly reported higher mortality in patients with complete AVSD. Their mortality in the complete AVSD group were 10.5% compared with 3.9% in the partial-intermediate group. The corresponding rates in our study were 12.5% and 5.5%, respectively.

The median age of our patients with complete AVSD during operation was 6 months. Therefore, we relate higher mortality in our cohort to older age at operation. In patients with AVSD, pulmonary arterial pressure and PVR increase with time (9). In these patients, pulmonary hypertensive crisis is a known risk factor for early mortality. We also observed postoperative pul-

**Table 4. Comparison of patients with complete-partial atrioventricular septal defect**

|                             | <b>cAVSD<br/>(n=315)</b> | <b>pAVSD<br/>(n=181)</b> | <b>P value</b> |
|-----------------------------|--------------------------|--------------------------|----------------|
| Age (months)                | 9.99±11.99               | 46.59±44.01              | <0.001         |
| Weight (kg)                 | 5.99±2.63                | 14.94±11.14              | <0.001         |
| PAP                         | 39.12±11.46              | 22.85±8.51               | <0.001         |
| PVR                         | 2.18±1.81                | 1.50±1.19                | <0.001         |
| CPB                         | 106.78±35.24             | 71.53±24.44              | <0.001         |
| Aortic cross-clamp          | 76.35±18.92              | 47.99±19.57              | <0.001         |
| Inotrop duration<br>(days)  | 4.57±4.82                | 2.25±4.77                | <0.001         |
| Inotrop score               | 18.42±65.81              | 5.82±11.21               | 0.001          |
| MV duration (h)             | 87.95±217.79             | 20.34±44.84              | <0.001         |
| ICU stay (days)             | 9.40±17.53               | 3.96±9.19                | <0.001         |
| Time to discharge<br>(days) | 14.72±22.81              | 6.83±4.00                | <0.001         |

AVSD - atrioventricular septal defect, PAP - pulmonary arterial pressure, PVR - pulmonary vascular resistance, CPB - cardiopulmonary bypass, MV - mechanical ventilation, ICU - intensive care unit

monary hypertensive crisis as an important risk factor for early mortality, which is especially prevalent in patients with complete AVSD. Because patients with complete AVSD comprise the majority of our cohort, the mortality might have been influenced by patient distribution as well.

We prefer to operate on patients with complete AVSD before 3–4 months and patients with partial AVSD at approximately 2 years of age. However, in this cohort, most of the patients with complete AVSD were referred late for operation, especially during the earliest surgical era; hence, our median age for operation was significantly increased.

Younger age and lower weight at operation, especially for patients with partial/intermediate AVSD, during the early surgical era were the other significant risk factors for early mortality.

The rate of reoperation for AVSDs has been reported as 5%–15% (5, 8, 10). The most common cause for reoperation was left AV valve insufficiency followed by LVOT stenosis (5, 8, 10). The rate of reoperation in our cohort was 8.9%, and the reoperations mainly were mitral valve replacement or mitral repair. Operations directed to LVOT stenosis comprised only a fifth of all reoperations. The degree of preoperative and postoperative left AV valve insufficiencies and the earlier surgical era seem to be significant in terms of reoperation. In our study, valve operations were more frequent among patients with partial/intermediate AVSD, in which the degree of residual regurgitation is higher probably due to unsewn cleft in the left AV valve. Partial AVSD was more frequent among patients without Down syndrome, which is why one can assume that these patients had more frequent valve reoperations.

Because of the favorable anatomy, modified single-patch (Wilcox) technique is usually the preferred operation in partial or intermediate AVSDs. It is performed by directly suturing the common AV valve leaflet to the crest of the ventricular septum. In this technique, directly pulling the AV valve leaflets down to the crest causes crowding of the LVOT and has the potential for LVOTO. This is why double-patch technique is usually claimed to be a better alternative because the patch used to close the ventricular component of the AVSD helps widen the LVOT. Furthermore, in Wilcox technique, the AV valve drawn down to the septum has a non-physiological height of hinge point that also causes concern for potential residual VSD and left AV valve insufficiency. On the other hand, this simpler technique has the advantage of not having the need to divide the AV valves (11, 12). We also preferred Wilcox technique in our patients with partial AVSD. This may be another reason why valvular reoperations were more frequent among these patients.

In our study group, LVOTO was more frequently patients operated with Wilcox technique, but this did not reach statistical significance. Other risk factors for LVOTO were earlier surgical era, younger age, and lower body weight at operation. In the study conducted by Ginde et al. (5), Wilcox technique was not found to be a risk factor in reoperation for LVOTO, but it was a risk factor for residual VSD. Residual VSD was an infrequent finding in our study regardless of the operation technique; only two patients were reoperated due to residual VSD.

Early morbidity was high in patients with Down syndrome. Even though they underwent successful cardiac surgery, the recovery time and the rate of complications are influenced by the co-morbid factors in these patients. Most of them have complete AVSD, high pulmonary artery pressure, and PVR. They also have long aortic cross-clamp and CPB times that may explain the longer postoperative inotropic support and mechanical ventilator support times. However, early mortality was not affected by Down syndrome presence. Remarkably, late morbidity was higher in patients not affected by Down syndrome, which was mostly related to the high rate of left AV valve insufficiency and more frequent valve-related reoperations.

Comparing these results to those previously reported, there are studies stating that total correction operations in patients with Down syndrome, if performed early, and have similar mortality and morbidity risks compared to patients not affected by Down syndrome (2, 5, 6, 8, 10, 13). Nevertheless it is important to indicate that our patients with complete AVSD were relatively old during operation that might have created the difference in terms of mortality and mortality.

#### Study limitation

The study was limited by its retrospective nature. Although all patients had clear documentation of preoperative and postoperative variables. Additionally, some patients have short follow-up. Because these patients continued follow-up at centers near their country.

## Conclusion

Although the morbidity and mortality of AVSD operations are lower in recent years, the frequency of reoperations is still high. More frequently encountered left AV valve insufficiency in patients with partial AVSD rationalizes the high rate of valve-related reoperations in this group. Although Down syndrome is not a risk factor for early mortality, it causes high risk of morbidities, such as longer postoperative ventilation and inotropic support. The frequency of pulmonary hypertension and the consequent complications are also high in patients with Down syndrome. The optimal surgical technique for AVSD repair still remains a vexed question. Further research is warranted to determine whether any surgical technique (i.e. Wilcox technique as suggested in our study) is an important risk factor for long-term morbidities in patients undergoing surgical correction for AVSD.

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