

# Relation Between High Sensitivity C-Reactive Protein And Thromboembolic Risk Markers Assessed By Echocardiography In Patients With Nonvalvular Atrial Fibrillation

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## ABSTRACT

**INTRODUCTION:** There is strong association between inflammation and atrial fibrillation (AF), as high- levels of high-sensitivity C-reactive protein(hs-CRP) have been noted to be higher among patients with AF. AF promotes thromboembolism through a variety of mechanisms, blood stasis, endothelial dysfunction and inflammation.

**OBJECTIVES:** This study aimed to assess the relationship between hs-CRP as inflammatory marker and the risk of thromboembolism in patients with non valvular AF.

**METHODS:** This study included 100 patients with non valvular AF referred to transesophageal echocardiography(TEE) before cardioversion or in patients with stroke to evaluate thromboembolic markers ( LAA thrombus, LAA low flow velocity, SEC ), transthoracic echocardiography(TTE) to measure LA anteroposterior diameter (AP), LA area, and LV EF and hs-CRP blood level .The patients divided into two groups Group ( A) included 26 patients with hs-CRP  $\geq$ 4.5 mg/dl Group ( B) included 74 patients with hs-CRP <4.5mg/dl.

**RESULTS:** Group (A) patients were significantly older ( $p = 0.003$ ), have longer duration of AF ( $P=0.003$ ), higher left atrial size (LA AP diameter. & LA area  $P<0.001$ ), lower LVEF ( $50.923 \pm 8.291\%$  vs  $57.054 \pm 7.83\%$   $P = 0.021$ ), higher incidence of thromboembolic markers as LAA thrombus ( $76.9\%$  vs  $18.92\%$   $p < 0.001$ ), dense SEC ( $53.84\%$  vs  $18.92\%$   $p < 0.001$ ) and LAA low flow velocity ( $17.058 \pm 2.751$  vs  $26.986 \pm 9.083$ ,  $p < 0.001$ ) and higher CHADSVASc score ( $4.692 \pm 1.032$  vs  $1.838 \pm 1.118$ ,  $p < 0.001$ ) compared to group (B). Hs-CRP showed significant positive correlation with age ( $r=0.514$ ,  $p < 0.001$ ), CHADSVASc ( $r=0.603$ ,  $p < 0.001$ ), LA diameter ( $r=0.628$   $p < 0.001$ ), LA area ( $r = 0.525$ ,  $p < 0.001$ ), SEC ( $r=0.603$   $p < 0.001$ ), LAA thrombus ( $r = 8.313$ ,  $p < 0.001$ ) and AF duration ( $r = 2.877$ ,  $p = 0.006$ ) and significant negative correlation with LAA emptying velocity ( $r = -0.530$ ,  $p < 0.001$ ), filling velocity ( $r = -0.487$ ,  $p < 0.001$ ), and LVEF ( $r = -0.317$ ,  $p = 0.025$ ). The cut-off value of hs-CRP  $> 4.5$  mg/ dl had sensitivity, specificity, positive & negative predictive values and accuracy 95 %, 90.3% ,92.9, 97 and 93% respectively for predicting thromboembolic risk in patients with non valvular AF.

**CONCLUSION:** High-sensitivity C- reactive protein ( hs-CRP) level is suitable to predict thromboembolic markers in patients with non-valvular AF. Therefore, it can help to predict the presence of these markers among AF patients in combination with established clinical risk score (CHA2DS2-VASc score).

**KEY WORDS:** Thromboembolic risk, hs-CRP, non valvular atrial fibrillation

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# When Is It Necessary To Resend A Residual Shunt To A Surgeon?

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## ABSTRACT

**OBJECTIVES:** Evaluation of the real volume and outcome of the problem of residual shunts after congenital heart surgery. **METHODS:** Between June 2009 and June 2015 the author operated 451 patients who needed a closure of shunting lesion and were living after 1 month postoperative; 203 males, 248 females with an age median 34 months  $\pm 2.8$ . Diagnosis: TOF (all forms) 154, VSD 151, AVSD 42, DORV 36, ASD 29, PDA 28, TGA 8, A-P window 3. All patients had median sternotomy except for 7. All patients had CPB without cooling and cold crystalloid blood enriched ante grade cardioplegia.

**RESULTS:** Median cross clamp time 21.8 minutes, cardiopulmonary bypass time 43.6 minutes, ICU stay 2.6 days and hospital stay 8.2 days. Only one patient had a sudden deterioration on the 6<sup>th</sup> postoperative day just before being discharged; echo showed detachment of a part of the patch that was not seen in the earlier echo. Follow up duration median was 25 months  $\pm 2.8$ . A residual shunt was detected in the pre discharge echo of 129 patients (28.6%) they were called group II; 16 at the atrial level (12.4%), 105 at the ventricular level (81.4%) and 8 at both levels (6.2 %). The number of shunts  $\leq 2$ mm we called type A was 92 (71.3%), 34 (26.4%)  $> 2$ mm and  $\leq 4$ mm; type B and 3 residuals  $> 4$  mm (3.1%); type C. At 3 months postoperative 390 patients (86.5%) had echo. 117 of Group II patients (90.7%) had echo and only 109 patients were still showing residuals 74 of type A (67.9%), 32 type B (29.4%), 3 type C (2.8%). Spontaneous closure in 8 patients out of 117 examined patients (6.8%) were all of type A. Only one patient needed reoperation 7 months after the operation.

**CONCLUSION:** Tiny residuals may close spontaneously. Medium and large residual shunts are associated with longer clamping and CPB time as well as ICU and hospital stay. Only shunts larger than 4mm may need intervention. Shunts less than 4 mm needs more patient reassurance than treatment. Residual shunts should be mentioned in the operative consent

## INTRODUCTION

Residual is a term that usually represents the persistent of a part of a lesion or a development of a new lesion. Residuals presents a very important issue in pediatric cardiac surgery both from the clinical outcome and medicolegal point of view.

The most common types of residuals are: 1. Residual shunts.  
2. Residual gradients. 3. Residual lesions as tumors, abscess... etc

The evaluation of the residual and its effect as well as the need and ways of management is a point of controversy. [1]

Residual shunts result from incomplete closure of an original shunt or creation of a new shunt. Residual shunts size is usually over estimated due to earlier under estimation of the original shunt and defective measurement of the shunt surface area in relation to the defect size. Causes of residual shunts can vary between Imperfect estimation of the defect as regard the size or multiplicity, Imperfect defect closure, Slipped or broken suture, muscle tear, over dissection or excision, ischemia or sometimes it can be left on purpose.

The objective of our study is the evaluation of the real volume and outcome of the problem of residual shunts after congenital heart surgery.

## PATIENTS AND METHODS

Between June 2009 and June 2015 the author operated 451 patients who had a repair that included a need for a closure of shunting lesion and were living after 1 month postoperative. Age median 34 months  $\pm 2.8$  and the body weight median was 12.1  $\pm 2.3$  kg. there were 203 males and 248 females.

The diagnosis was Tetralogy of Fallot (all forms) in 154 patients,

VSD in 151, atrioventricular septal defect (AVSD) in 42, double outlet right ventricle in 36, ASD in 29, PDA in 28, TGA (who had atria with the technique of Senning) in 8, aorto pulmonary window in 3. All patients had median sternotomy except for 7 patients who had right posterior mimithoracotomy for ASD closure.

All patients had CPB with no cooling. Cold crystalloid blood enriched ante grade homemade cardioplegia was used in all patients. We used Dacron patches for VSD closure while ASD, AVSD, P-A window was closed by pericardium either fresh or Glutaraldehyde fixed and PDA ligation by silk suture. Non absorbable 5/0 monofilament for suturing. Resection was used only for fibrous tissues and interruption for muscle bands. Us aim is always to keep aortic clamping time at minimum.

Follow up was made by the use of echocardiography with the following milestones: before the patient is discharged from the hospital, every 3 months twice then every year after.

A hemodynamic study by catheter was used to estimate residual shunt associated with hemodynamically significant stenosis.

One hundred forty-seven patients were incompliant to follow up (32.6%). The median cross clamp time  $21.8 \pm 4.7$  minutes, the median cardiopulmonary bypass time  $43.6 \pm 8.1$  minutes, the median ICU stay  $2.6 \pm 1.9$  days, the median hospital stays  $8.2 \pm$  Th days. Only one patient had a sudden deterioration on the 6 postoperative day just before being discharged; echo showed detachment of a part of the patch that was not seen in the earlier echo. Follow up duration median was 25 months  $\pm 2.8$ . A residual shunt was detected in the pre discharge echo of 129 patients (28.6%) they were called group II. Of those residual shunts there were 16 at the atrial level (12.4%), 105 at the ventricular level (81.4%) and 8 at both the atrial and ventricular levels (6.2 %).

The distribution in relation to the diagnosis is listed in the table 1.

The number of shunts  $\leq 2$ mm we called type A was 92 (71.3%), 34 (26.4%)  $> 2$ mm and  $\leq 4$ mm; type B and 3 residuals  $> 4$  mm (3.1%); type C. Group II and its sub groups A, B and C characteristics are listed on the table 2. At 3 months postoperative 390 patients (86.5%) had echo.

117 of Group II patients (90.7%) had echo and only 109 patients were still showing residuals 74 of type A (67.9%), 32 type B (29.4%), 3 type C (2.8%).

Spontaneous closure in 8 patients out of 117 examined patients (6.8%) were all of type A. Only one patient needed reoperation 7 months after the operation.

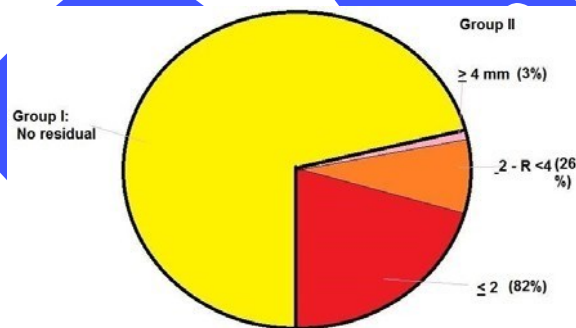


Fig 1: distribution of patients' population.

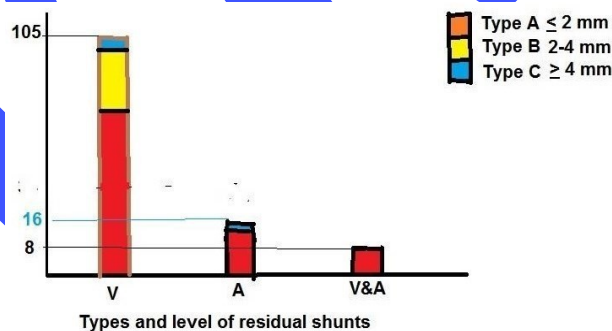


Fig 2: Types and levels of the residuals

AVSD repairs was associated with highest rate of residuals (45%) while TOF repair had the highest rate of moderate size residuals of group II b (29%) and DORV repair had the highest rate of large residuals of group II c (11%). Table 2 shows that aortic cross clamping time was higher in Group II and special in the sub groups b with P value 0.036 and c with a P value 0.029.

The same remark was found with CPB time with statistically significant risk in II b (P = 0.048) and II c P = 0.031).

The hospital stay duration median calculation proved that being in group II c is a statistically significant risk factor with a P value of 0.019.

|           | TOF | VSD | AVSD | DORV | ASD | PDA | TGA | A-P window |
|-----------|-----|-----|------|------|-----|-----|-----|------------|
| No.       | 154 | 151 | 42   | 36   | 29  | 28  | 8   | 3          |
| residuals | 38  | 41  | 19   | 9    | 7   | 3   | 4   | 0          |
| ≤2 mm     | 26  | 37  | 15   | 6    | 4   | 2   | 3   |            |
| 2 - < 4   | 11  | 12  | 4    | 2    | 3   | 1   | 1   |            |
| 4 ≤       | 1   |     | 1    | 1    |     |     |     |            |

**Table 1:** residual and its sizes shunts per diagnosis

**DISCUSSION**

Residual shunts can be a nightmare for each pediatric cardiac surgeon due to ethical, medicolegal and financial causes. Small residual shunts can be very noisy and cause a great psychological problem to the patient especially if he or she was provoked by any misleading information by any medical personnel. Large defects can be catastrophic causing severe hemodynamic disturbance and may need urgent management by percutaneous intervention or reoperation. Echocardiographic examination has a tendency for over estimation of the size of residual shunts specially if the surface area of the residual

|      | Group I | Group II | II A | II B | II C |
|------|---------|----------|------|------|------|
| No.  | 322     | 129      | 92   | 34   | 3    |
| CXT  | 20.9    | 23.2     | 22.1 | 27.3 | 29.1 |
| CPB  | 38.2    | 45       | 44.6 | 62.1 | 66.9 |
| ICU  | 2.4     | 3.2      | 2.5  | 4.1  | 4.7  |
| Hosp | 8.6     | 9.1      | 7.4  | 8.5  | 16.3 |
| Reop | 0       | 0        | 0    | 0    | 1    |

**Table 2:** statistics of Group I (no residuals) and II (residuals) with its sub groups A (< 2 mm), B (2 - < 4 mm) and C (4 < mm), dark cells = P < 0.05 (significant)

Shunt column or neck is not calculated. If there was no mention of the possibility of such a complication to the patient and in the preoperative consent a residual shunt can result in serious medicolegal problems. Financially the increased cost due to longer ICU, hospital stay and medications raises another issue and this will be a real problem in case of a need for reintervention; usually the insurance authority is reluctant to pay without investigations. The psychological effect on the patient varies according to the patient personality and the family reaction, some psychological effects can be long term or life time up to the need for continuous psychiatric treatment.

Endocarditis and its prevention remains an issue especially in case of small residuals. Hemolysis is another problem that can be seen with small residual shunts and up to a life threatening condition.

Dodge and colleagues concluded in their study that up to 1 third of residual VSDs < 2 mm may close spontaneously within a year and that has suggested that nonsignificant residuals should be left alone. [1]

Preoperative preparation of the patient and the choice of the suture type and technique can help in residual avoidance. Proper intraoperative assessment of the shunt closure should be the role and immediate closure of any significant shunt should be done. [2,3,4] There is a consensus among all authors that the management of residual shunts depends on the hemodynamic effects above all. Slightly significant residuals are treated medically (diuretics – vasodilators) or by percutaneous intervention. Residuals with significant hemodynamic effect might need urgent management by catheter or surgery. A residual shunt is a nightmare for interventional cardiologists too as with

expansion of percutaneous closure higher numbers of residual shunt are seen. [5,6]

The higher clamping time in groups II b and c means that residual shunts are more common with complex lesions and more difficult ones. From all the above we can see that minimizing the risk of having residual shunt associated problems starts with preoperative patient preparation and awareness, intraoperative proper exposure and closure with transesophageal echo monitoring and postoperative proper communication and early management.

#### Conclusion

Tiny residual shunts may close spontaneously. Residual shunts are serious problems no matter how small they are and should be avoided by all means. Medium and large sized residual shunts are associated with longer clamping and CPB time as well as ICU and hospital stay. Only shunts larger than 4mm may need intervention. Shunts less than 4 mm needs more patient reassurance than treatment.

Residual shunts should be mentioned in the operative consent. Ethically and legally a doctor should notify the referring doctor and not the patient.

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