**Orijinal Araştırma**

# Rate Of Abnormal Coagulation Test Results in Patients with Congenital Heart Disease

# Konjenital Kalp Hastalığı Olan Hastalarda Anormal Koagülasyon Test Sonuçlarının Oranı

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## Özet

Giriş: Konjenital kalp hastalığı olan kişilerde pıhtılaşma bozuklukları beklenmektedir. Bu çalışmada siyanotik ve nonsiyanotik konjenital kalp hastalığı olan çocuklarda anormal koagulasyon test sıklığı ve bunun klinik önemi araştırılmıştır.

Materyal ve Metod: Konjenital kalp hastalığı olan ve cerrahi müdahele ihtiyacı duyan 49 çocuk hasta prospektif olarak çalışmaya alınmıştır. Hastaların demografik bilgileri, primer tanıları, cerrahi müdahele ve sonrasında oluşan kanama bozukluğu ve hastaların prognozu kayıt edilmiştir.hastaların trombosit sayıları, protrombin zamanı, aktive parsiyel tromboplastin zamanı ile kan fibrinojen düzeyleri cerrahi müdahele öncesi saptanmıştır.

Bulgular: 16 hastanın uzun PT, 13 hasta düşük fibrinojen düzeyi, 10 hastanın uzun aPTT ve 5 hastanın ise düşük trombosit sayısı olduğu saptanmıştır.

Sonuç: Her ne kadar bozulmuş koagulasyon test sonuçları ile ilişkili artmuış bir komplikasyon saptanmamış olsa da bu hastalarda dikkatli olmak gerekmektedir.

Anahtar Kelimeler: Koagülasyon testleri, Konjenital kalp hastalığı, yaygın damariçi pıhtılaşma, fibrinoliz

## Abstract

Introduction: Coagluation abnormalities are expected in patients with congenital heart disease. We searched the rate of abnormal coagulation test in children with both cyanotic and non-cyanotic heart disease and investigated the clinical relevance of these abnormal tests.

Material and Method: 49 children who have congenital heart disease and needed surgical intervention were prospectively enrolled to this study. Demographic data, primary diagnosis, bleeding complication during and after the intervention and prognosis of the patients were recorded. Platelet counts, prothrombin time, activated partial thromboplastine time and blood fibrinogen levels were measured prior to intervention.

Results: 16 patients had prolonged PT, 13 patients had low fibrinogen level, 10 patients had prolonged aPTT and 5 patients had low platelet count.

Conclusion: There was no increased complication risk in patients with abnormal test results, but caution must be taken during operation of these patients.

Key words: Coagulation test, Congenital Heart Disease, Disseminated Intravascular Coagulation, Fibrinolysis.

## Introduction

Coagulation abnormalities are expected in patients with cyanotic heart disease. Bleeding tendency in patients with cyanotic heart disease has been known for at least 50 years (1,2). Various type of coagulation abnormalities including thrombocytopenia (3), factor deficiency (4), fibrinolysis and disseminated intravascular coagulation (5-7) have been reported in these patients. It is also well known that adults with congenital heart disease who undergo operation have more bleeding following operation (8).

In this study, we searched the rate of abnormal coagulation test in children with both cyanotic and non-cyanotic heart disease and investigated the clinical relevance of these abnormal tests.

## Material and Method

Children who have congenital heart disease and need an intervention between June 2004 and February 2005 in Ege University Hospital were prospectively enrolled to this study. Demographic data, primary diagnosis, bleeding complication during and after the intervention and prognosis of the patients were recorded. Platelet counts, prothrombin time, activated partial thromboplastine time and blood fibrinogen levels were measured prior to intervention. A standardized questionnaire about the bleeding history was administered to all patients and informed consent was obtained from all the patients or their parents. We determined the rate of abnormal coagulation test, the relation between the abnormal coagulation test and bleeding history and bleeding complication during surgery.

## Results

We enrolled 49 patients with congenital heart disease (32 male, 17 female) totally. Mean age of the patients was 3.8±5.1 years (1 day-18 year). Children with both cyanotic and non-cyanotic heart disease were included to study. Primary diagnosis of the patients is demonstrated in Table 1.

Mean PT of the patients prior to intervention was 14.1±1.5 (11.5-18.4)sec. 16 patients were found to have prolonged PT. Of these, four patients had non-cyanotic heart disease and 12 patients had cyanotic heart disease. None of the patients with prolonged PT had a bleeding history ($p<0.05$). Mean aPTT of the patients was 35.0±5.6 (23.9-47.5) sec. 10 patients had prolonged aPTT. All of these patients had cyanotic heart disease. Only one patient with prolonged aPTT had a history of bleeding but this was not statistically significant ($p>0.05$). The mean fibrinogen level of the patients was 228.4±91 (90-589) mg/dL. 13 patients were found to have low fibrinogen level. Five of these patients had non-cyanotic heart disease. Only one patient with low fibrinogen level had bleeding history but this was not statistically significant (Table 2). None of the patients suffered from bleeding complication during and after surgery. During surgery, no additional hematological support is needed. Seven patients had prolonged PT and aPTT and 12 patients had abnormality in at least two tests.

Mean platelet count of patients was 251.000/mm3 (102.000-496.000/mm3). Five patients had thrombocytopenia (platelet count <150.000/mm3). One of these patients had non cyanotic heart disease (Atrial Septal Defect), and the others had cyanotic heart disease.

11 patients (nine male and two female) died after the operation. Of these patients, four had prolonged PT, three had prolonged APTT and three had low fibrinogen level. However there was not a statistically significant relationship between abnormal coagulation test result and prognosis of patients and none of the patients died due to bleeding complication.

35 patients (72%) were between 0-60 months-old, seven patients (14%) were between 61-120 months old and seven patients (14%) between 121-216 months old. All the expired patients were below five years old age.

**Table 1: Diagnosis of the enrolled patients.**

| Diseases | Patient Count (n) | Ratio (%) |
|---|---|---|
| Aberrant right subclavian artery | 1 | 2.0 |
| Aort coarctation | 1 | 2.0 |
| Aortic Stenosis | 3 | 6.1 |
| ASD | 5 | 10.1 |
| ASD+VSD | 1 | 2.0 |
| ASD+VSD+PDA | 1 | 2.0 |
| Cor Triatum | 1 | 2.0 |
| DORV+ PS | 1 | 2.0 |
| ECD | 1 | 2.0 |
| Incomplete AV canal defect | 1 | 2.0 |
| PA | 1 | 2.0 |
| PA+TA+RV hypoplasia | 1 | 2.0 |
| PA + Truncus Arteriosus Type 4+ VSD | 1 | 2.0 |
| PDA | 2 | 4.1 |
| PDA+ASD | 1 | 2.0 |
| PS+PFO | 1 | 2.0 |
| Single Ventricule+PS+VSD | 2 | 4.0 |
| Subaortic discrete membrane | 1 | 2.0 |
| TA+VSD+ASD+Pulmonary hypoplasia | 1 | 2.0 |
| TAPVDA | 1 | 2.0 |
| TGA | 6 | 12.2 |
| TGA+TA | 1 | 2.0 |
| TGA+TA+PS | 1 | 2.0 |
| Truncus Arteriosus Tip 4 | 3 | 6.0 |
| TOF | 4 | 8.2 |
| TOF+ASD | 1 | 2.0 |
| VSD | 4 | 8.2 |
| VSD+Pulmonary Atresia | 1 | 2.0 |
| Total | 49 | 100.0 |

**Table 2: Distribution of hemostatic test results of the patients.**

| | Normal (%) | Prolonged or Low Level (%) |
|---|---|---|
| PT | 33 (68%) | 16 (32%) |
| APTT | 39 (80%) | 10 (20%) |
| Fibrinogen | 36 (74%) | 13 (26%) |

## Discussion

Presence of bleeding diathesis has been known for more than 50 years and the contributing factors for this diathesis has been defined as hyperviscosity, DIC and primary fibrinolysis (1,2).

Lenk et al reported in 1975 that patients with cyanotic heart disease who had elevated haematocrit levels usually had abnormal coagulation test results as well as hyperfibrinolysis and thrombocytopenia (9). He stated that the cause of these abnormalities is mainly DIC present in these patients. Thereafter, Henriksson studied 41 patients with cyanotic heart disease and stated that haemostatic abnormalities noted in these patients is mainly due to deficient synthesis of coagulation factors by the liver (10). He did not find any clue for the activation of coagulation system or fibrinolytic system in these patients. According to Henriksson, the decrease in synthesis of vitamin K dependant coagulation molecules is the result of stagnation of blood in hepatic microcirculation due to polycytemia as well as systemic hypoxia affecting synthetic activity of the liver.

We found that 35 of 49 patients with congenital heart disease (70%) had at least one abnormal haemostatic test result. 12 patients had at least two abnormal results and seven patients had abnormal results both in PT an aPTT. Fibrinogen level was low in 13 patients (26.5%). This result suggests that consumption coagulopathy may be the main underlying pathology in these patients. Colon-Otero et al found abnormal coagulation tests in 45 of 235 patients (19%) with congenital heart disease (11). 16 patients (7%) had more than one abnormal test results. They stated that not only DIC but also hypoxia and deficiency in vitamin

K dependant carboxylation were responsible from these abnormal tests. One patient with normal and two patients with abnormal haemostatic test results developed severe bleeding postoperatively. Goel et al has also reported that abnormal haematologic test results is common in cyanotic heart disease patients (64%) and according to them, the underlying mechanisms in these abnormal results are reduced synthesis of coagulation factors, subclinic compensated DIC and impaired platelet aggregation (12). Although, rate of abnormal test results in children with congenital heart disease varies greatly, our abnormal test results seem to be higher compared with other studies. The reason may be that DIC in our patients may be more severe than other patients due to severity of their primary diagnosis and resultant polycytemia.

Colon-Otero et al found that the mostly affected tests were PT and aPTT and these abnormal results are usually found in frank cyanotic patients who had impaired cardiac function and high haematocrit levels (11). In our patients, the mostly affected coagulation tests were PT and fibrinogen level. 32.6% of patients had prolonged PT and 26.5% of patients had decreased fibrinogen level. However, prolonged aPTT was also not scarce. Approximately 20% of patients had prolonged aPTT. In addition, five patients (10.2%) had low platelet count. Most of the thrombocytopenic patients (80%) were in cyanotic group. This finding also supports that subclinial compensated DIC is present in these patients. Moreover, thrombocytopenia may also be due to impaired platelet aggregation and increased platelet secondary to degraded von Willebrand factor (13). We determined in a study that von Willebrand factor is deficient in 12.2% of congenital heart disease patients due to high shear stress over von Willebrand Factor in heart diseased children.(14).

Although we did not determine increased risk or hemorrhage during or after the operation in any patient, Colon-Otero reported that one patient with normal and 2 patients with abnormal haemostatic test results developed severe bleeding postoperatively (11). Besides, Andre et al reported that patients with aortic stenosis who have bleeding history and low von Willebrand factor preoperatively develop major bleeding complication during intervention (15). Nevertheless, there was no statistically significant relation between prognosis of the patients and abnormal test results in our patients.

Thus, we concluded that abnormal haemostatic test results are common in patients with congenital heart disease and despite bleeding complication is not frequent in these patients caution must be taken during any surgical intervention.

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