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# Can Antipsychotics and Antidepressants Affect the Formation or Chronicization of Aortic Dissections?

Antipsikotikler ve Antidepresanlar Aort Diseksiyonlarının Oluşumunu veya Kronikleşmesini Etkileyebilir mi?

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#### **ABSTRACT**

Acute Stanford type-A aortic dissections (STAAD) are life-threatening diseases which require emergency surgery to eliminate risks of aortic rupture, severe aortic valve insufficiency, pericardial tamponade and cerebral and/or coronary malperfusion. Only a small subset of patients go unnoticed and become chronic with unclear mechanism. These patients are usually diagnosed thru late symptoms or incidentally. Surgical techniques requiring cardiopulmonary bypass and sometimes deep hypothermia and circulatory arrest are first-line treatments with considerable mortality and complications. Herein, an incidentally diagnosed chronic STAAD patient who was receiving antipsychotic and antidepressant treatment and successfully repaired with total aortic arch replacement was presented.

Keywords: Chronic aortic dissection, Blood pressure, Antipsychotics, Antidepressants, Surgery

### ÖZ

Akut Stanford tip-A aort diseksiyonları(STAAD), aort rüptürü, ciddi aort kapak yetmezliği, perikardiyal tamponad ve serebral ve/veya koroner malperfüzyon risklerini ortadan kaldırmak için acil cerrahi gerektiren, hayatı tehdit edici hastalıklardır. Sadece küçük bir hasta alt grubu fark edilmez ve belirsiz mekanizma ile kronikleşir. Bu hastalar genellikle geç semptomlar yüzünden veya tesadüfen teşhis edilir. Kardiyopulmoner bypass ve bazen derin hipotermi ve sikülatuvar arrest gerektiren cerrahi teknikler, önemli mortalite ve komplikasyonları olan ilk basamak tedavilerdir. Burada, antipsikotik ve antidepresan tedavi alan ve total aortik ark replasmanı ile başarıyla onarılan tanısı tesadüfen konulmuş kronik STAAD hastası sunulmuştur.

Anahtar Sözcükler: Kronik aort diseksiyonu, Kan basıncı, Antipsikotikler, Antidepresanlar, Cerrahi



# INTRODUCTION

Acute aortic dissections (AD) are life-threatening conditions with incidence of 3/100000 in a year. AD are characterized by the formation of an intimal flap due to the tear in the middle layer of the aortic wall which causes a false lumen that can be best identified by contrasted CT. First 1-5cm of ascending aorta is the most seen site of primary tear. Chest and/or back pain are usually the presenting symptoms. Acute-Stanford type-A aortic dissections(A-STAAD) require emergency surgery due to the risks of aortic rupture, severe aortic valve insufficiency, pericardial tamponade and cerebral and/or coronary malperfusion. Forty percent of A-STAAD patients die before reaching to hospital. Mortality increases 1% per hour upon arrival to hospital. Chronic-STAAD(C-STAAD) are seen rarely. Most of the patients die or operated in acute phase and only a small subset of patients may go unnoticed and become chronic. Usually, dissections older than 14 days are accepted as "chronic". Surgery requirement of the C-STAAD, depends on the aortic diameter. According to current guidelines, indication for surgical repair of C-STAAD is ≥55mm ascending aorta diameter like asymptomatic ascending aortic aneurysms (1). In patients with high surgical risk, endovascular treatment modalities with custom made stent-grafts may be used.

# **CASE REPORT**

Forty-six years-old male patient admitted to cardiovascular surgery outpatients' clinic with the complaints of constant palpitation, weight loss and breath shortness in confined spaces. He has had these complaints since 2017 and admitted to psychiatry outpatients' clinic in 2017. He was diagnosed as recurrent major depressive disorder and medical therapy (sertraline, risperidone, quetiapine, clomipramine) was started. Also, he admitted to cardiology outpatients' clinic twice (in 2017 and 2019) with his unresolved complaints. He was considered healthy in terms of aortic aneurysm, aortic dissection, hyperlipidemia, coronary artery and/or valvular heart diseases except presence of hypertension, and he was prescribed only antihypertensive medication. However, he did not use antihypertensive treatment regularly. He specified no chest and/or back pain, no hypertensive or hypotensive attack and no unconscious process recently that he remembered. In examination; except 159/108mmHg of blood pressure, no abnormal finding was present. Blood tests also including cholesterol parameters were in normal ranges, ECG was in sinus rhythm with the rate of 98/min, with no specific change. However, abnormal shadowing was present at aortic arch and descending aorta level in roentgenogram (Figure 1). Urgent contrasted thoracoabdominal CT has revealed STAAD (DeBakey type-1) with 5,7cm of ascending aorta diameter (Figures 2,3). Patient was diagnosed as C-STAAD which we do not know

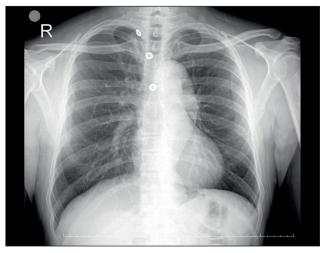


Figure 1: Patient's roentgenogram with abnormal shadowing at aorticarch and descending aorta level.



**Figure 2:** Pre-operative CT image that shows the C-STAAD in both ascending and descending aorta.



**Figure 3:** Pre-operative 3D- CT image that shows the C-STAAD false lumen in both ascending and descending aorta.

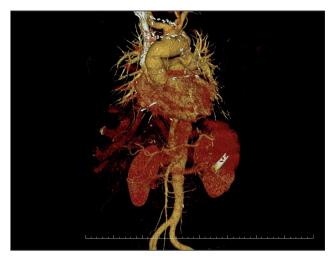
the exact occurrence time and was hospitalized. Psychiatric medications have been stopped. Amlodipine, captopril, metoprolol, alprazolam and acetylcysteine have been started. In transthoracic echocardiography, 5.8cm of ascending aorta enlargement with dissection flap was confirmed. No significant aortic valve insufficiency was present and ejection fraction was 60%.

Patient underwent surgical correction. Supracoronary ascending aorta and total aortic arch replacement were performed by right common femoral artery, brachiocephalic trunk (for antegrad cerebral perfusion) and right atrium (with two-stage venous canula) cannulations. Cardiac arrest was provided with antegrade Del Nido cardioplegia solution at 26°C of body temperature. In 23min body arrest, head and upper extremity arteries were clamped and separated as isle. Distal anastomosis of 30mm Dacron graft was performed to descending aorta. Proximal end of the graft was anastomosed to supracoronary ascending aorta. Isle was anastomosed to aortic graft by a short 20mm Dacron graft for decreasing the tension on sleazy isle tissue. Cross clamp time was 145min and bypass time was 183min. Patient successfully quit from cardiopulmonary bypass without inotropic support. He has been extubated on post-operative 6<sup>th</sup> hour without neurologic problem. He was hypertensive in intensive care unit follow up and regulated with candesartan and metoprolol. Patient was taken to cardiovascular surgery ward on post-operative 3th day and discharged on post-operative 8th day at the end of an uneventful follow up. There was no problem in his 10th day, 1st and 3th month controls (Figures 4,5).

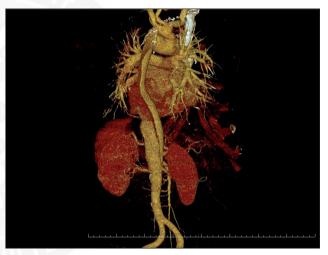
# DISCUSSION

Sharp chest and/or back pain are the presenting symptoms of A-STAAD that force patient admit to emergency service with accompanying hemodynamic disorder. A small subset of patients who are asymptomatic or have minor symptoms do not admit to emergency service and become chronic with unclear mechanism. Our patientwas diagnosed as C-STA-AD due to not specifying chest and/or back pain, hypertensive or hypotensive attack or unconscious process that he remembered recently.

Today, antipsychotic and antidepressant treatments those were given to our patient are also used for pain treatment. Sertaline(SSRI-antidepressant) and clomipramine(tricyclic antidepressant) are used for negative neuropathic pain, due to their such effect mechanisms; a-Effects on mood, b-Blockade of norepinephrine and serotonin, c-Blockade of sodium channels, d-Effects on visceral nerve fibers, e-Sympathetic blockades, and f-Antagonism of NMDA(N-metil-D-aspartat) glutamate receptor. Risperidone and quetiapine are both atypical antipsychotics which may be used for pain with positive psychotic symptoms too (2). However, atypical



**Figure 4:** Post-operative 3D-CT image that shows the supracoronary 30mm Dacron graft and the anastomosis of the isle to the aortic graft via 20 mm Dacron graft.



**Figure 5:** Post-operative 3D-CT image that shows the thrombosed false and patent true lumens of the C-STAAD.

antipsychotics may lead cardiovascular side effects such as deviations in blood pressure and arrhythmias. Rarely, congestive heart failure, myocarditis and sudden death have been reported. They increase blood pressure through Dopamine (D) receptors which D1, D3, and D4 receptors interact with rennin-angiotensin-aldosterone system, which D2 and D5 receptors interact with the sympathetic nervous presynaptic post-ganglia (3). In the multicenter study of Falissard et al. (4) 2270 schizophrenia patients receiving antipsychotic therapy, in 12 European countries were evaluated. Related to antipsychotics; in 34.8% of patients' hypertension and in 11.7% of patients' hypotension was determined. Similarly, Dania et al. (5) determined increase in systolic blood pressure in 57 patients, increase in diastolic blood pressure in 50 patients after use of atypical antipsychotics. In our patient; antipsychotics might have caused the already

hypertensive patient to undergo uncontrolled higher blood pressure attacks which could lead aortic dissection. Also, antipsychotics and antidepressants might have caused the patient to remain asymptomatic by eliminating the chest and/or back pain which develops during the aortic dissectionand by blocking the sympathetic activity. Anyway, patients receiving such treatments should be kept under regular cardiologist control. Previous studies have determined the estimated mortality rate for A-STAAD in the first 2 weeks at 57-74%, unless surgery was performed. In the remaining unoperated and survived patients, after 2 weeks, mortality rates decrease significantly due to increase of thickness and stiffness of the flap and false lumen wall throughout the remodelling (6). Different surgical techniques have been suggested for aortic arch pathologies in C-STAAD but definite technique is still controversial. Mortality rates are given at 1-15% for the surgery of ascending aorta or aortic arch. Advanced age, multiple co-morbidities and previous thoracic surgery increase the mortality risk significantly, regardless of canters' experience. Although C-STAAD patients are usually operated in better conditions than A-STAAD patients, total aortic arch replacement is still a hard procedure due to bleeding risk and poor visceral organ response to circulatory arrest. Isle-en bloc and branched graft techniques are the most used techniques to simplify anastomoses. Combination of these 2 techniques was performed by 20mm Dacron graft between isle and aortic graft in this patient.

In young, hypertensive patients who receive antidepressant and/or antipsychotic treatments, the blood pressure regulation may break even if these patients receive antihypertensive medications. Possible hypertensive attacks which may occur under these uncontrolled conditions, may lead to the development of aortic dissections. Also, antidepressant and/or antipsychotic treatments may conceal acute phase of the aortic dissections by decreasing the pain and may lead to chronicization. Therefore, we recommend close follow up of these patients by cardiologists in regular periods.

#### **Acknowledgment**

None.

# **Author Contributions**

Buğra Harmandar performed the operation together with Burak Can Depboylu. Burak Can Depboylu reviewed the literature and wrote the case report. Buğra Harmandar performed the critical and English review. Kadir Arslan reviewed the literature and wrote the case report. Serkan Yazman wrote the case report and performed the critical review.

### **Conflicts of Interest**

None.

## Financial Support

No financial support was received for this case report.

# Ethical Approval and/or Written Informed Consent of the Patient

Since this manuscript was a case report, ethics committee approval was not required. The written informed consent form of the patient was obtained on 13.01.2020 and submitted to the system of the Medical Journal of Western Black Sea.

#### **Review Process**

Extremely peer-reviewed.

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