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Original Research

Echocardiographic findings associated with mortality in adult patients with Ebstein's anomaly

Hallazgos ecocardiográficos asociados con mortalidad en pacientes adultos con anomalía de Ebstein

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ABSTRACT. Introduction: Ebstein's anomaly (EA) is a right ventricular cardiomyopathy, current echocardiographic severity criteria are not helpful to predict disease progression or identify patients at higher risk of mortality. **Objective:** We analyzed clinical and echocardiographic data of adult patients with EA to identify predictors of mortality. **Methods and results:** Clinical and echocardiographic parameters were analyzed from historical data of 60 adult patients with EA, six of them have died. Variables were compared between groups. Among clinical characteristics only the presence of cyanosis was statistically higher in the mortality group (100 vs 26%, p <0.001). When analyzing the echocardiographic parameters, both the right and left ventricular function were worse in the mortality group (LVEF: 56.7±7 vs 49±2.2%, p <0.015, RV FAC: 27.1±11 vs 15.3±7.8%, p <0.022). Nor the severity of the EA, nor the pulmonary systolic pressure were different between groups. **Conclusion:** EA is a cardiomyopathy and not a disease limited to the tricuspid valve. Both right and left systolic dysfunction are predictors of mortality.
Keywords: Ebstein's anomaly, adult patient, echocardiographic parameters, mortality.

RESUMEN. Introducción: *La anomalía de Ebstein (AE) es una miocardiopatía del ventrículo derecho, los criterios ecocardiográficos de severidad no correlacionan con la evolución clínica y pronóstico de los pacientes.* ***Objetivo:*** *Se analizaron las variables clínicas y ecocardiográficas de pacientes adultos con AE en búsqueda de factores asociados con mortalidad.* ***Métodos y resultados:*** *Los parámetros clínicos y ecocardiográficos fueron analizados de una cohorte histórica de 60 pacientes adultos con AE, seis de ellos murieron en el seguimiento. Las variables fueron comparadas entre grupos de sobrevida y mortalidad. De las características clínicas sólo la presencia de cianosis fue significativamente mayor en el grupo de mortalidad (100 vs 26%, p <0.001). Al analizar los parámetros ecocardiográficos la función sistólica tanto del ventrículo derecho como del izquierdo fueron menores en el grupo de mortalidad (FEVI: 56.7±7 vs 49±2.2%, p <0.015, FAC VD: 27.1±11 vs 15.3±7.8%, p <0.022). Ni la severidad de la AE ni la presión sistólica pulmonar fueron diferentes entre grupos.* ***Conclusión:*** *Al ser una miocardiopatía, tanto la disfunción sistólica ventricular derecha como la izquierda se ven afectadas y correlacionan con mortalidad, estos datos deben ser útiles para el seguimiento y la toma de decisiones en pacientes con AE.*
Palabras clave: *Anomalía de Ebstein, patología congénita del adulto, parámetros ecocardiográficos, mortalidad.*

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INTRODUCTION

Ebstein's anomaly (EA) is considered a cardiomyopathy that usually involves the right ventricle, but the left ventricle could also be affected.[1,2] It is a rare disease, with a wide clinical spectrum and commonly associated with other cardiac abnormalities such as atrial septal defect. Its diagnosis is based on the hallmark of septal and/or posterior tricuspid valve leaflet adherence to the right myocardium.[3,4] Tricuspid regurgitation is common, it contributes to right chamber dilation acting as a substrate for atrial or ventricular arrhythmia. Echocardiographic severity criteria do not correlate with clinical evolution and prognosis.[3,4] Hemodynamics and clinical patterns of presentation depend on anatomical severity, degree of right-to-left atrial shunting, age at presentation and ventricular dysfunction.[5-7] We reviewed the clinical and echocardiographic data of adult patients with EA looking for factors associated to mortality.

MATERIAL AND METHODS

We analyzed an historical observational cohort of adult patients with EA from 1980 to 2015. We obtain information from the clinical records. Any patient older than 18 years, with the diagnosis of EA who had follow-up in the National Institute of Cardiology «Ignacio Chavez», Mexico, was included.

The diagnosis of EA was made through echocardiographic assessment (attachment of the septal and/or posterior tricuspid valve leaflets to the underlying myocardium, with respect to the anterior mitral valve leaflet >8 mm/m^2).[8] The severity of the anomaly was classified according to percent of septal valve as mild when it was less than 44%; moderate when it was between 44-61%; and severe when this was more than 61%.[6] As recommended for this pathology, ventricular function was evaluated through right ventricular fraction area change (RV FAC) of the functional right ventricle, left ventricular function was evaluated by Simpson's method.[9] Other echocardiographic variables were the diastolic dimension of the right and left ventricle, the severity of tricuspid regurgitation and the pulmonary systolic pressure. The surgical status was recorded. New York Heart Association (NYHA) functional classification was used to assess heart failure severity symptoms at the follow-up. Cyanosis was assessed at first evaluation. We excluded those patients who had incomplete clinical record and with

Table 1: Clinical characteristics.

	Survival group n=54 (%)	Mortality group n=6 (%)	p
Age (years)	34.8±12.4	38±8.4	0.555
Female gender	35 (64.8)	5 (83.3)	0.361
Surgery	12 (22.2)	3 (50)	0.136
Cyanosis	14 (26)	6 (100)	0.001
NYHA functional class			
I	12 (22.2)	0	0.083
II	38 (70.4)	4 (66.7)	
III	4 (7.4)	2 (33.3)	
WPW syndrome	19 (35.2)	1 (16.7)	0.361
AF/flutter	9 (16.7)	0	0.578
AV blocks	9 (16.7)	1 (16.7)	0.997
Ablation procedure	17 (31.5)	1 (16.7)	0.453
Pacemaker	4 (7.4)	1 (16.7)	0.436
Ventricular tachycardia	1 (1.8)	1 (16.7)	0.192
Stroke	3 (5.6)	1 (16.7)	0.351

NYHA = New York Heart Association; WPW = Wolff Parkinson White; AF = atrial fibrillation; AV = atrioventricular.

absence of late follow-up (all patients should have at least one-year of follow up in our institution).

Statistical analysis

Information was stored on an electronic Excel spreadsheet and processed using STATA 12.1 statistical software package. All continuous variables were assessed for normality with the Shapiro-Wilk test, they are expressed as mean value and standard deviation and comparation between groups was made with t-Student test. Categorical variables are expressed as number and percentage in relation to the population at risk, comparation between groups was made with χ^2 test. We considered a p value <0.05 as indicative of statistical significance.

RESULTS

Sixty patients met our inclusion criteria, 40 patients were female (67%), the average age at diagnosis was 36.1 years old (25-42.4).

Table 2: Echocardiographic characteristics.

	Survival group (n=54)	Mortality group (n=6)	p
Severity (%)			0.217
Mild	18 (33.3)	0	
Moderate	15 (27.8)	3 (50)	
Severe	21 (39)	3 (50)	
LVEDD (mm)	38.3±5.7	35.6±5.7	0.146
LVESD (mm)	25.3±5.6	22.3±5.5	0.238
RVEDD (mm)	56±9.4	64.3±12.1	0.058
RV FAC (%)	27.1±11	15.3±7.8	0.022
TR (%)			0.221
Mild	3 (5.5)	0	
Moderate	17 (31.5)	0	
Severe	34 (63)	6 (100)	
PSP (mmHg)	29.5±11.6	30.5±7.8	0.846
ASD (%)	24 (44.4)	3 (50)	0.795
Tricuspid annulus (mm)	49.2±9.7	53.5±11.38	0.461
LVEF (%)	56.7±7	49±2.2	0.015

LVEDD = left ventricle end-diastolic dimension; LVESD = left ventricle end-systolic dimension; RVEDD = right ventricle end-diastolic dimension; FAC = fractional area change; TR = tricuspid regurgitation; PSP = pulmonary systolic pressure; ASD = atrial septal defect; LVEF: left ventricle ejection fraction.

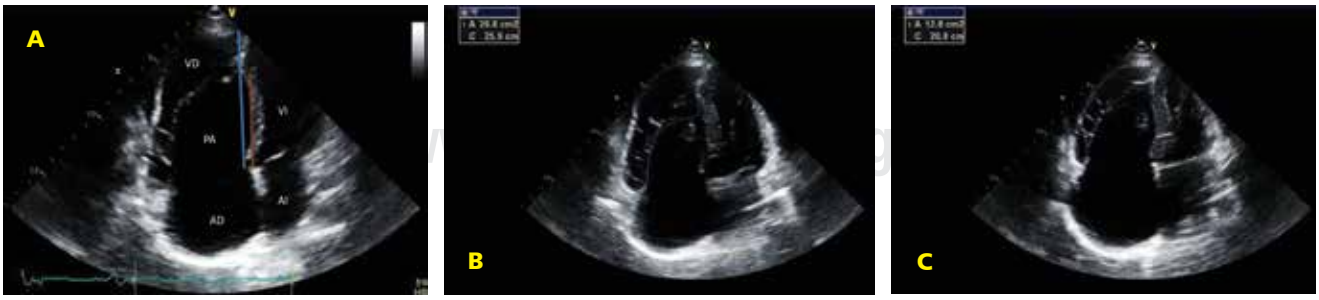

Figure 1: Patient con severe EA. **A)** Severe septal valve attachment (orange line) to the right ventricular septum (blue line). **B)** Diastolic area of the functional right ventricle (26.8 cm^2). **C)** Systolic area of the functional right ventricle (12.8 cm^2). In this specific case the RV FAC was 52.2%.

Cyanosis was found in 33% of patients during the first follow-up. Four patients had stroke (6.6%). According to echocardiographic criteria for severity, 18 patients were classified as having mild EA (33.3%), 15 as moderate EA (27.8%) and 21 patients as severe EA (39%) *(Figure 1)*. Fifteen patients underwent corrective or palliative surgery. Ablation procedure was made in 18 patients. Six patients died at follow-up.

When comparing the clinical characteristics between the mortality and the survival groups we only found difference in the prevalence of cyanosis, being more frequent in the mortality group, there were no difference in age, gender, surgical status, functional class or prevalence or rhythm disorders *(Table 1)*.

The echocardiographic findings showed no difference for the severity or EA between groups, nor the severity of tricuspid regurgitation or the systolic pulmonary pressure were different. The end-diastolic and end-systolic dimensions of the left ventricle showed no difference, the end-diastolic dimension of the right ventricle showed a tendency to be larger in patients who died. Systolic dysfunction of both ventricles was more prevalent in the mortality group, with a mean RV FAC of 27.1 vs 15.3%, p <0.022, and a mean LVEF of 56.7 vs 49% p <0.015 for the survival and mortality group respectively *(Table 2)*.

DISCUSSION

This study showed that in adult patients with EA right ventricular systolic dysfunction measured by FAC and left ventricular systolic dysfunction measured by LVEF correlate with mortality regardless of the severity of the disease or the surgical status. The pre-excitation and WPW syndrome are more frequently in EA than in general population,[10] the downward displacement of the septal leaflet, associated with discontinuity of the central fibrous body and septal atrioventricular ring, generates direct muscular connections, allowing persistence of accessory atrioventricular pathways.[8,11] Complete heart block is rare in EA,[4,7] when this occurs it is explained by compression of the AV node and the abnormal formation of the central fibrous body. Early age at presentation, right ventricular outflow obstruction, right ventricular systolic dysfunction, hemoglobin/hematocrit values, male sex and severe EA have been associated with higher mortality.[5,6,12] In our study, only the ventricular systolic dysfunction of both ventricles were associated to higher mortality. No difference in age, gender or severity of the pathology was found.

Right ventricular dysfunction has been previously associated to mortality.[12] The myopathic nature of this disease, affecting the entire anatomy of the right ventricle,[8] leads to ventricular dysfunction.

Study limitations: The retrospective character of the study is the principal limitation. New techniques for the evaluation of RV systolic function were not assessed.

CONCLUSION

Right ventricular and left ventricular systolic dysfunction are importantly associated to higher mortality in adult patients with Ebstein's anomaly regardless or the severity of the pathology or the surgical status.

REFERENCES

1. Dearani JA, Mora BN, Nelson TJ et al. Ebstein anomaly review: what's now, what's next? Expert Rev Cardiovasc Ther. 2015; 13: 1101-1109.
2. Monibi AA, Neches WH, Lennox CC et al. Left ventricular anomalies associated with Ebstein's malformation of tricuspid valve. Circulation. 1978; 57: 303-306.
3. Brown ML, Dearani JA. Ebstein malformation of the tricuspid valve: current concepts in management and outcomes. Curr Treat Options Cardiovasc Med. 2009; 11: 396-402.
4. Attenhofer CH, Connolly HM, Edwards WD, et al. Ebstein's anomaly - review of a multifaceted congenital cardiac condition. Swiss Med Wkly. 2005; 135: 269-281.
5. Celermajer DS, Bull C, Till JA et al. Ebstein's anomaly: presentation and outcome from fetus to adult. J Am Coll Cardiol. 1994; 23: 170-176.
6. Attie F, Rosas M, Rijlaarsdam M et al. The adult patient with Ebstein anomaly. Outcome in 72 unoperated patients. Medicine. 2000; 79: 27-36.
7. Giuliani ER, Fuster V, Brandenburg RO et al. Ebstein's anomaly: the clinical features and natural history of Ebstein's anomaly of the tricuspid valve. Mayo Clin Proc. 1979; 54: 163-173.
8. Edwards WD. Embryology and pathologic features of Ebstein's anomaly. Prog Pediatr Cardiol. 1993; 2: 5-15.
9. Warnes CA, Williams RG, Bashore TM et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American

College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults with Congenital Heart Disease). J Am Coll Cardiol. 2008; 52: e143-e163.

10. Sarubbi B, D'Alto M, Vergara P et al. Electrophysiological evaluation of asymptomatic ventricular pre-excitation in children and adolescents. Int J Cardiol. 2005; 98: 207-214.
11. Frescura C, Basso C, Thiene G et al. Anomalous origin of coronary arteries and risk of sudden death: a study based on an autopsy population of congenital heart disease. Hum Pathol. 1998; 29: 689-695.
12. Sarris GE, Giannopoulos NM, Tsoutsinos AJ et al. Results of surgery for Ebstein anomaly: a multicenter study from the European Congenital Heart Surgeons Association. J Thorac Cardiovasc Surg. 2006; 132: 50-57.