BRIEF COMMUNICATION

Efficacy and Safety of Echocardiographic Guidance for Post-Transplant Endomyocardial Biopsy Sampling

Eficacia y seguridad de la guía ecocardiográfica para la toma de biopsias endomiocárdicas en el postrasplante cardíaco

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ABSTRACT

Background: Endomyocardial biopsy is a very useful procedure to assess acute rejection in transplant patients, but it can cause several complications.
Objective: The purpose of this study is to demonstrate the efficacy and safety of echocardiography as a guide for endomyocardial biopsy sampling.
Methods: A retrospective analysis of transplant patients undergoing endomyocardial biopsies was carried out between November 2004 and November 2016. Demographic data and complications were analyzed with descriptive statistics.
Results: A total of 200 patients underwent 2,665 endomyocardial biopsies, with an average of 13 procedures per patient. Complications occurred in 5 patients: 2 pneumothorax (0.1%) and 3 transient alterations in the electrocardiogram (0.1%), and vascular access could not be achieved in 25 patients (0.9%). No patient died during the procedure or required emergency surgery to treat the complications.
Conclusion: Endomyocardial biopsy guided by echocardiography is a safe procedure with a low rate of complications.

Key words: Heart Transplantation - Biopsy - Echocardiography

RESUMEN

Introducción: La biopsia endomiocárdica es un procedimiento de mucha utilidad para valorar el rechazo agudo en pacientes trasplantados, sin embargo, puede causar complicaciones.
Objetivo: El propósito de este estudio es demostrar la eficacia y seguridad del ecocardiograma como guía para la biopsia endomiocárdica.
Material y métodos: Se realizó un análisis retrospectivo de pacientes trasplantados sometidos a biopsia endomiocárdica entre noviembre de 2004 y noviembre de 2016. Se analizaron datos demográficos y complicaciones mediante estadística descriptiva.
Resultados: Un total de 200 pacientes se sometieron a 2665 biopsias endomiocárdicas, con un promedio de 13 procedimientos por paciente. Se produjeron complicaciones en 5 pacientes: 2 neumotórax (0,1%), 3 alteraciones transitorias en el electrocardiograma (0,1%). No se logró acceso vascular en 25 pacientes (0,9%). Ningún paciente falleció durante el procedimiento o requirió cirugía de urgencia para tratar las complicaciones.
Conclusión: La biopsia endomiocárdica guiada por ecocardiografía es un procedimiento seguro y con baja tasa de complicaciones.

Palabras clave: Trasplante de corazón - Biopsia - Ecocardiografía

Abbreviations

EMB	Endomyocardial biopsy

INTRODUCTION

Percutaneous endomyocardial biopsy (EMB) was described by Sakakibara S. in 1962. (1) The procedure has been perfected and, due to greater histopathological understanding, it has managed to be placed as a diagnostic aid for the evaluation of patients with various heart diseases.

Although the rate of complications for EMB is low, this procedure can be associated with fatal events. Therefore, it is reasonable to explore other means to reduce major complications. Fluoroscopic guidance has been the most used method so far; however, some studies have shown the potential benefits of echocardiography-guided EMB procedures. (2. 3)

Rev Argent Cardiol 2018;86:410-413. http://dx.doi.org/10.7775/rac.v86.i6.14370

Received: 09/25/2018 – *Accepted:* 10/18/2018

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The purpose of our work was to analyze the complications associated with EMB guided by two-dimensional (2D) echocardiography.

METHODS

Patient selection

This was an observational, retrospective study on EMB performed under transthoracic echocardiographic guidance in heart transplant patients. Two hundred patients underwent 2,665 EMB in the Cardiovascular Surgery Service of the Department of Cardiac Transplantation at Hospital Italiano de Mendoza, Argentina, from November 2004 to November 2016. We analyzed the demographic data (age, gender, indication for transplant, number of samples) and the complications associated with the procedure. All patients signed and informed consent form before undergoing the EMB.

The clinical indication for the procedure is based on the International Society of Heart and Lung Transplantation Guidelines for the care of cardiac transplant candidates (4) and the protocol specifications for transplanted patient management in our unit. All procedures were programmed, with prior 6- and 8-hour fasting for pediatric and adult patients, respectively. The EMB was performed with local anesthesia under continuous echocardiographic guidance and electrocardiographic monitoring. An electrocardiogram was performed after the procedure. The frequency of biopsies was: one per week for six weeks; then, one every fifteen days for six weeks more (until the third month), one per month for three months and one every two months for the rest of the year; finally, one every six months after one year. This scheme is subject to modifications according to the patient's clinical evolution, changes in medication, etc. The result of the first 117 patients has been previously published, (5) with a descriptive analysis by conventional statistics.

Echocardiography

All patients underwent 2D echocardiography, using Philips 5500 and General Electric Vivid 7 systems. Studies were recorded and stored in the video library of endocavitary biopsies, and apical 4-chamber, subcostal and parasternal views with the patient in supine decubitus position were used. The most satisfactory view was the one corresponding to the apical 4-chamber image where the right atrium, the tricuspid valve and the right ventricle are best displayed. The subcostal and parasternal views were not so useful for the aim of the study.

Endomyocardial biopsy

All procedures to obtain the biopsy samples were performed by the same operator in supine position under electrocardiographic monitoring (ECG). After the administration of local anesthesia and antisepsis, the heart was accessed by puncture of the right internal jugular vein and insertion of the introducer. The correct puncture and introducer position were controlled by the injection of 5 ml of physiological solution and the visualization of bubbles in the right chambers by 2D echocardiography. The 8 or 9 French Stanford Caves-Schultz bioptome or a 7 French Cordis Bipal disposable bioptome was then inserted through the introducer and its progress through the right atrium and the tricuspid valve was controlled by 2D echocardiography (Figures 1 and 2).

The bioptome was opened in the right ventricle and its tip contact with the endocardium was identified by echocardiographic control. The biopsy was taken by closing the clamp to retrieve a myocardial sample, a procedure that was repeated 5 to 10 times.

After the procedure, 2D echocardiography ruled out pericardial effusion. All the biopsies in which special care was taken in the search for pericardial tissue were analyzed by optical microscopy.

Complications

Complications were classified as major and minor.

Major complication were death related to the procedure, need for emergency cardiac surgery, pericardial effusion requiring pericardiocentesis, sustained ventricular tachycardia, severe tricuspid regurgitation, and pneumothorax or hemopneumothorax. Minor complications were electrocardiographic changes, pericardial effusion not requiring pericardiocentesis, bleeding at the puncture site and mild to moderate tricuspid regurgitation.

Statistical analysis

A conventional descriptive analysis was performed. Discrete variables are described as number and percentage, and continuous variables as mean and standard deviation or median and interquartile range according to their type of distribution. SPSS 17.0 for Windows (IBM Corp., Armonk, NY, USA) was used to perform statistical analyses.

RESULTS

From November 2004 to November 2016, 200 cardiac transplant patients underwent 2,665 EMB.

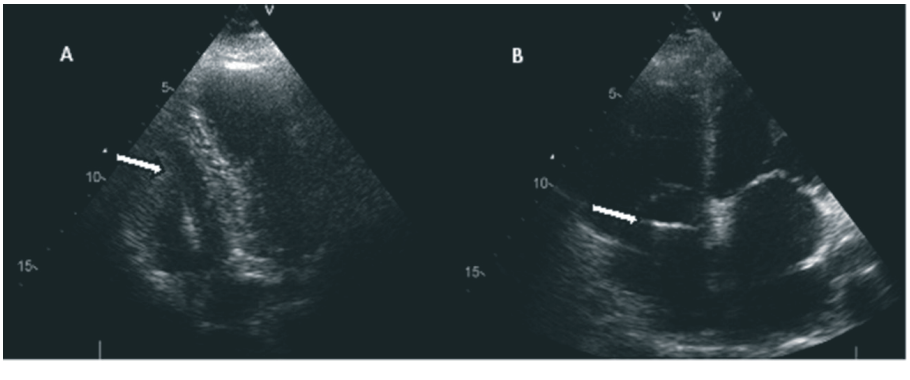

Fig. 1. Two-dimensional echocardiography in apical 4-chamber view; the tip of the bioptome (*white arrow*) can be seen in image A ready to take a biopsy sample in the free wall of the right ventricle; and in image B before crossing the tricuspid plane.

Baseline patient characteristics are shown in Table 1. Seventy-two percent of patients were male and mean age of 54±15 years. An average of 13±3 EMB was performed per patient and 90% of biopsies were done on an outpatient basis. The most frequent indication for heart transplantation was ischemic-necrotic dilated cardiomyopathy (34%), followed by idiopathic dilated cardiomyopathy (19%) (Table 2).

Vascular access for EMB was not achieved in 0.9% of patients (n=25).

Major complications occurred in 0.1% of cases (n=2): one patient with hemopneumothorax and another patient with pneumothorax, both requiring the implantation of a pleural drainage tube. No patient died during the procedure or immediately after, nor did we observe cardiac tamponade or complex ventricular arrhythmias.

Minor complications were found in 0.1% of cases (n=3): two patients with sinus bradycardia during instrumentation and frequent ventricular premature beats and one patient with bleeding at the puncture site. There was low incidence of severe tricuspid valve regurgitation.

DISCUSSION

Despite the progress in diagnostic studies, EMB remains indispensable for the follow-up of the transplant patient. Given that EMB per se carries a risk of complications, its role in the multi-imaging era has been transferred to other pathologies; (6) however, histological confirmation is still necessary in the follow-up of cardiac transplant patients.

In our study, we presented a low rate of complications, related with the puncture (pneumothorax).

Table 1. Demographic data of the population

Parameter	%
Age	54±15 years
Male sex	72%/144
Ambulatory EMB	89.9%/2,397
Number of EMB/patient	13±3
Number of samples/patient	3.8±2

EMB: Endomyocardial biopsy

Table 2. Indications for heart transplantation

Cause	%
Ischemic-necrotic dilated cardiomyopathy	34%/67
Idiopathic dilated cardiomyopathy	19%/37
Chagasic cardiomyopathy	11%/22
Congenital heart disease	2.5%/5
Heart valve dilated cardiomyopathy	7.5%/15
Cardiovascular: Ischemic - graft vascular disease.	0.5%/1
Others (COPD, primary pulmonary hypertension, cystic fibrosis, etc.)	26%/53

COPD: Chronic obstructive pulmonary disease

Cardiac tamponade is the most feared complication by physicians performing EMB. During the 12 years of our EMB series, no cardiac tamponade was encountered. Other authors report an incidence of cardiac tamponade in fluoroscopy- guided EMB ranging from 0.8% (n=4 in 490 cases) (7) to 0.4% (n=2 in 546 cases). (8)

We believe that the systematic use of 2D echocardiographic guidance, which allows the visualization of the bioptome and its correct position at the time of biopsy sampling, is responsible for the low rate of complications observed in this work. Echocardiography also provides high sensitivity and reliable detection of pericardial effusion and associated complications that can be resolved without delay. Moreover, it improves the sensitivity of biopsy sampling by enabling the selection of specific sites (right ventricular outflow tract, right interventricular septum, sites with greater edema or suspicion of fibrosis) for specimen retrieval. In transplant patients who are going to be subjected to multiple imaging studies, this procedure decreases the accumulated radiation.

Tricuspid regurgitation occurs frequently in transplant patients, due to the successive repetition of EMB. Some series report up to 6.8% of severe tricuspid regurgitation. (9) This complication was not found in our work as the possibility of observing the tricuspid valve plane avoids injuring the subvalvular apparatus, preventing regurgitation.

Another relevant fact regarding the use of echocardiography as guidance for EMB sampling is the advantage of not moving the patient, since it can be done on the bed of the transplant unit. In addition, it allows estimating ventricular function data, segment motility changes, ventricular filling patterns and, even, filling pressures.

CONCLUSIONS

Complications associated with echocardiography-guided EMB were low.

It is performed on an outpatient basis, without the need for hospitalization. In hospitalized patients, who cannot be transferred to the hemodynamics lab or surgery, it can be done in the ward.

Endomyocardial biopsy with echocardiographic guidance is cost-effective and has a low rate of complications in experienced hands.

As limitation, this was a retrospective study, carried out in a single center and by the same operators.

As strengths, we believe that it is a reproducible method, easy to perform and that the number of biopsies, associated to the low rate of complications, supports the study. In addition, it decreases the accumulated radiation in patients undergoing transplantation.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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