Tips and Tricks for Endomyocardial Biopsy

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Demographic features and prevalence of myocarditis in patients undergoing transarterial endomyocardial biopsy for unexplained cardiomyopathy

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INTRODUCTION

• Myocarditis is an inflammatory disease of the myocardium associated with cardiac dysfunction.

• Three forms of inflammatory CMP are recognized: Infectious, Autoimmune, and Idiopathic

• The true incidence and diagnosis of myocarditis is a challenge due to a great variation in clinical manifestations from asymptomatic changes on ECG to fulminant CHF, arrhythmias and sudden cardiac death.


IMAGING TECHNIQUES

Cardiac magnetic resonance (CMR) is the ideal technique to detect soft tissue changes such as edema and inflammation.

However, imaging techniques such as CMR or ECHO can only provide non-invasive tissue characterization but fail in revealing the true underlying causes that determine prognosis and treatment of the disease.

Endomyocardial biopsy (EMB)

- It's an invasive, diagnostic technique, which obtain histological samples from the myocardium using a biopsy forceps.
- Cardiac biopsy was initially performed in the 1950s by means of limited thoracotomy.
- EMB is the gold standard for heart disease when the common non-invasive methods do not make precise histopathological diagnosis possible.


**TABLE. Indications for Endomyocardial Biopsy**

- Monitor cardiac transplant rejection status
- Diagnose unexplained cardiomyopathies
  - Suspected myocarditis
  - Suspected infiltrative cardiomyopathy
- Diagnose cardiac tumors
- Detect suspected anthracycline toxicity
- Use in research

Endomyocardial biopsy (EMB)

- EMB can be taken from the RV or LV via the venous, or arterial route.

- EMB may be guided by Fluoroscopy, ECHO, or both.

- Because of the lack of available facilities and clinical experience, EMB appears to be infrequently used to diagnose myocarditis.

- Reported complications range from minor site hematoma, to ventricular perforation.

- Incidence of complication was less than 1% of patients.

- LV-EMB was safer and more Diagnostic than RV-EMB.
The aim of our study was to identify the demographic features and in-hospital prevalence of myocarditis in patients undergoing transarterial EMB for unexplained cardiomyopathy.

15 patients with unexplained CM were included out of 1100 pts admitted 2014

The inclusion criteria:
- Acute symptoms of HF refractory to standard TTT,
- Worsening of EF despite optimized TTT,
- Development of significant arrhythmias, particularly progressive HB and VT,
- HF with concurrent rash, fever, or peripheral eosinophilia,
- New-onset CM in the presence of known amyloidosis, sarcoidosis, or hemochromatosis.

The exclusion criteria:
- History of IHD,
- Uncontrolled HTN,
- DM,
- Congenital HD or RHD,
- Familial CM,
- Peripartum CM,
- Cardiotoxic exposure
- Alcoholic patients
Patients diagnosis protocol

All patients were subjected to

**full history** taking to identify the most common symptoms of myocarditis such as chest pain, breathlessness, fatigue, palpitations and fainting attacks. The history of flu-like symptoms (a cough, fever, malaise) and medications was used.

Then this was followed by **full physical examination, routine LAB tests, CXR and ECG**.

All patients had detailed **ECHO** study by an independent operator to analyze the suspected etiology of heart failure symptoms.

It was **after ECHO assessment that patients were included into the study as suspected unexplained Cardiomyopathy for CA if –ve…. Do EMB**

Endomyocardial biopsy (EMB)

33 EMB samples were taken from the left ventricle of 11 patients.

Zero complication rate.

**9 Tips & Trikes for safe and effective EMB**
EMB : TIP 1 --- FA, ½ dose heparin

- Insert 6F femoral sheath in left or right common femoral artery. Same as in CA
- Give 2500 IU of Heparin in the sheath only.

EMB : TIP 2 --- JR 3.5 guiding

- Insert JR 3.5 guiding cath
- Using the regular J tipped 0.038 GW
- Till the root of the Aorta
**EMB : TIP 3 ---- reach the LV apex**

- Push the JR3.5 into the LV during systole with AV opening.
- Push the wire in front of the guiding cath. till making a loop at the LV apex
  - Avoid inflow track, chordae and papillary muscles.

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**EMB : TIP 4 ---- safety issues**

- Remove the wire
- Measure the pressure in LV 1st (as a base line if perforation occur)
- Use a Y-connector
EMB : TIP 5… in-vitro preparation

• Prepare and test your Bioptome (Cook or small intestinal biopsy forceps compatible with 6 F guiding)
  • Check if it open and close smoothly
  • Push it in-vitro inside the JR guiding till it get out to measure the length relationship between both.
  Push the bioptom into the JR3.5 to the LV apex

A Cook Flexible Biopsy forceps (with a standard cup for tissue sampling of 5.2 Fr volume 2.25 mm³)
A Cook Flexible Biopsy forceps (with a standard cup for tissue sampling of 5.2 Fr volume 2.25 mm$^3$)

<table>
<thead>
<tr>
<th>ORDER NUMBER</th>
<th>French Size</th>
<th>Length</th>
<th>Forceps Volume mm$^3$</th>
<th>Quick Reorder Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>STANDARD CUP FORCEPS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBF-3.0-60</td>
<td>3.0</td>
<td>60 cm</td>
<td>.66</td>
<td>158482</td>
</tr>
<tr>
<td>FBF-3.0-120</td>
<td>3.0</td>
<td>120 cm</td>
<td>.66</td>
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<tr>
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<td>2.25</td>
<td>158483</td>
</tr>
<tr>
<td>FBF-5.2-120</td>
<td>5.2</td>
<td>120 cm</td>
<td>2.25</td>
<td>158484</td>
</tr>
<tr>
<td>ELONGATED CUP FORCEPS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBFE-5.2-60</td>
<td>5.2</td>
<td>60 cm</td>
<td>4.86</td>
<td>161067</td>
</tr>
<tr>
<td>FBFE-5.2-120</td>
<td>5.2</td>
<td>120 cm</td>
<td>4.86</td>
<td>161066</td>
</tr>
</tbody>
</table>

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**EMB : TIP 6 … fluoroscopic guidance**

- Use RAO 35 standard view 1$^{st}$
  - Tack the 1$^{st}$ biopsy from the apex
- Use the LAO 45 view
  - Then 2$^{nd}$ one form septum
  - To take the 3$^{rd}$ biopsy form lateral wall.
**EMB : TIP 7… avoid perforation**

Avoid perforation of the LV ventricle

- After opening the forceps out side the guiding in the LV
- Push both till reach a resistance (this is the wall for biopsy)
  - close the forceps till a grip is felt
- Pull back the hole system (JR+ bioptome together) out side the LV into the aorta …..if not the guiding will be advanced forward and perforate the LV.
- Leave the JR, and get the bioptome outside the body

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**EMB : TIP 8… samples management**

- Take 3 samples each = 2 mm --- Keep them safe
  - Use a green needle to get out your sample form the opened forceps tip.
  - Put it immediately into a bottle with saline better 10% formalin
  - Close it carefully and send it immediately to the pathologist
  - Each sample in a separate bottle with clear label.
  - Better to have an epindorf tubes with preservative (PBS)
- Don’t forget a blood sample 10 ml for viral and genetic testing.
• Final ECHO post procedure

The main reported complications were
• pericardial effusion or
• new onset mitral incompetence due to chordal involvement.

Results of EMB are usually affected by two opponents

• the 1st opponent is the fading of infiltration of inflammatory cells after treatment or in the late stage of the disease.
• The 2nd opponent is sampling errors

These factors made us to adopt the methodology in this study by taking the biopsies during the early stage of the disease and taking biopsies from different areas of LV which may help to get higher results.
Histopathological analysis

- Tissue specimens were processed and 5 ml sections were cut and stained with hematoxylin and eosin or other specific stains according to each case.
- Sections were examined by light microscopy and the following features were evaluated:
  - the presence of inflammatory cells,
  - number, and distribution of inflammatory cells,
  - the presence of necrosis or fibrosis.

Dallas criteria

The confirmed diagnosis of myocarditis was according to the Dallas criteria

Limitations of Dallas criteria

- High inter-observer variability in interpreting biopsy (especially borderline myocarditis).

- EMB is considered to be positive for inflammation by immunohistochemical detection of focal or diffuse mononuclear infiltrates with >14 cells/mm². 

EMB diagnostic potential in cardiac dis.

<table>
<thead>
<tr>
<th>Clinically suspected disease</th>
<th>EMB diagnostic potential and histological notes</th>
<th>Technical aspects and tissue usage</th>
<th>Grading of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocarditis/inflammatory cardiomyopathy</td>
<td>Recommended: In addition to formal fixation, two fragments (or one if greater than 3 mm²) can be snap-frozen or preserved in RNA-later for viral molecular investigations. One peripheral blood sample (5-10 ml) collected in EDTA or sodium citrate tube.</td>
<td>Recommended: Congo red, modified aldehyde fuchsin, or Braak T stains. IHC, IF, immunohistochemistry, protein sequencing, and/or mass spectrometry to establish the type of amyloid. Frozen tissue is required for IF and protein sequencing</td>
<td>M: Cardiomyopathy</td>
</tr>
<tr>
<td>Cardiovascular disease due to drugs and chemical “tort”</td>
<td>Probable/predisposed hypertension: myocardial hypertrophy and fibrosis (histological findings suggestive of the disease).</td>
<td>Fresh sample may be useful for viral molecular biology. Important: EMB timing.</td>
<td>M</td>
</tr>
<tr>
<td>Cardiac amyloidosis</td>
<td>Recommended: Congo red, modified aldehyde fuchsin, or Braak T stains. IHC, IF, immunohistochemistry, protein sequencing, and/or mass spectrometry to establish the type of amyloid. Frozen tissue is required for IF and protein sequencing.</td>
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<td>M</td>
</tr>
<tr>
<td>Iron overload</td>
<td>Iron staining is advisable for all diagnostic EMBs from patients with untreated DCM.</td>
<td>Iron staining is advisable for all diagnostic EMBs from patients with untreated DCM.</td>
<td>S</td>
</tr>
</tbody>
</table>

**Note:** The grading of recommendation (M: Moderate; S: Strong) reflects the strength of the evidence supporting the use of EMB in these specific cardiac conditions. Further details and systematic reviews are recommended for a comprehensive understanding.
Results of our study

The in-hospital prevalence of Unexplained CM =1.4%
Myocarditis =0.63%.

EMB showing the absence of inflammation or necrosis and diagnosed as negative for myocarditis (H&Ex400)
**Acute myocarditis** showing diffuse infiltrate by mixture of polymorphs and lymphocytes (arrows) with cardiomyocyte necrosis.

**Borderline myocarditis**: demonstrating few inflammatory cells without cardiomyocytes necrosis.
**Cardiac amyloidosis** showing homogenous structureless pink material (amyloid) in between cardiac muscles

![Image](image_url)

**Limitations**

- Small number of biopsy samples,
- No follow-up samples, Nor CMR.
- Lack of immune histochemical analysis of biopsy samples and
- Lack of molecular analysis with DNA-RNA extraction and
- RI-PCR amplification of the viral genome to rule in/out viral etiology was not performed.

However, this is our first report and our main concern was to develop the system to implement EMB sampling technique and set in motion the process of the preservation of samples and the onward collaboration with a specialist in the pathology department to handle and study all cardiac specimens in this early report of our continuing project on unexplained CM patients.
THE MAIN FINDING IN OUR STUDY

1. The in-hospital prevalence of
   • Unexplained CM was 1.4%
   • Myocarditis was 0.63%.

2. Myocarditis proved by pathological examination of EMB represents 64% of these patients.

3. EMB from the LV using Cook bioptomes via transfemoral artery sheath is safe and essential in confirming the diagnosis.

THANKS

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