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AHA/ACCF/ESC SCIENTIFIC STATEMENT

The Role of Endomyocardial Biopsy in the Management of Cardiovascular Disease

A Scientific Statement From the American Heart Association, the American College of Cardiology, and the European Society of Cardiology

Endorsed by the Heart Failure Society of America and the Heart Failure Association of the European Society of Cardiology

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The role of endomyocardial biopsy (EMB) in the diagnosis and treatment of adult and pediatric cardiovascular disease remains controversial, and the practice varies widely even among cardiovascular centers of excellence. A need for EMB exists because specific myocardial disorders that have unique prognoses and treatment are seldom diagnosed by noninvasive testing (1). Informed clinical decision making that weighs the risks of EMB against the incremental diagnostic, prognostic, and therapeutic value of the procedure is especially challenging for nonspecialists because the relevant published literature is usually cited according to specific cardiac diseases, which are only diagnosed after EMB. To define the current role of EMB in the management of cardiovascular disease, a multidisciplinary group of experts in cardiomyopathies and cardiovascular pathology was convened by the American Heart Association (AHA), the American College of Cardiology (ACC), and the European Society of Cardiology (ESC). The present Writing Group was charged with reviewing the published literature on the role of EMB in cardiovascular diseases, summarizing this information, and making useful recommendations for clinical practice with classifications of recommendations and levels of evidence.

The Writing Group identified 14 clinical scenarios in which the incremental diagnostic, prognostic, and therapeutic value of EMB could be estimated and compared with the procedural risks. The recommendations contained in the present joint Scientific Statement are derived from a comprehensive review of the published literature on specific cardiomyopathies, arrhythmias, and cardiac tumors and are categorized according to presenting clinical syndrome rather than pathologically confirmed disease. The ultimate intent of this document is to provide an understanding of the range of acceptable approaches for the use of EMB while recognizing that individual patient care decisions depend on factors not well reflected in the published literature, such as local availability of specialized facilities, cardiovascular pathology expertise, and operator experience. The use of EMB in the posttransplantation setting is beyond the scope of this document.

This Scientific Statement was approved for publication by the governing bodies of the American Heart Association, the American College of Cardiology, and the European Society of Cardiology and has been officially endorsed by the Heart Failure Society of America and the Heart Failure Association of the European Society of Cardiology.

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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The classifications of recommendations used in this document are

- *Class I:* conditions for which there is evidence or there is general agreement that a given procedure is beneficial, useful, and effective;
- *Class II:* conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment;
  - *Class IIa:* conditions for which the weight of evidence/opinion is in favor of usefulness/efficacy;
  - *Class IIb:* conditions for which usefulness/efficacy is less well established by evidence/opinion; and
- *Class III:* conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

The levels of evidence are

- *Level A (highest):* multiple randomized clinical trials;
- *Level B (intermediate):* limited number of randomized trials, nonrandomized studies, and registries; and
- *Level C (lowest):* primarily expert consensus.

Technique and Risks of EMB

The first nonsurgical techniques for heart biopsy were reported in 1958 (2). In the 1960s the safety of heart biopsy improved, with vascular access through the right external or internal jugular vein, sampling of the right interventricular septum, and designation of the heart borders by right heart catheterization before biopsy (3). Sakakibara and Konno (4) introduced the use of a flexible bioptome with sharpened cusps that allowed EMB by a pinching as opposed to a cutting technique. Caves et al (5) modified the Konno biopsy forceps (Stanford Caves-Shulz bioptome) to allow percutaneous biopsies through the right internal jugular vein with only local anesthesia and rapid tissue removal. The reusable Stanford-Caves bioptome and its subsequent modifications became the standard device for EMB for approximately 2 decades (6,7). Single-use bioptomes and sheaths allow access through the right and left jugular or subclavian veins, right and left femoral veins, and right and left femoral arteries and may be associated with lower risk of pyrogen reaction and transmission of infection than reusable bioptomes.

The right internal jugular vein is the most common percutaneous access site for right ventricular EMB in the United States. In Germany and Italy, the femoral vein is commonly used for percutaneous access (8). Sonographic techniques to identify the location, size, and respirophasic variation in size of the internal jugular vein decrease the duration of the procedure and complications (9,10). Monitoring should include electrocardiographic rhythm, blood pressure, and pulse oximetry. The subclavian vein also may be used occasionally.

The femoral artery may be used as a percutaneous access site for left ventricular biopsy (11,12). This approach requires insertion of a preformed sheath to maintain arterial patency. All arterial sheaths must be maintained under constant pressurized infusion to avoid embolic events. Aspirin or other antiplatelet agents may be used in addition to heparin during left heart biopsy procedures to decrease the risk of systemic embolization. No comparative studies exist on which to base a recommendation for left versus right ventricular biopsy; however, left ventricular biopsy has been used in case series to define cardiomyopathic processes limited to the left ventricle (13).

EMB usually is performed safely under fluoroscopic guidance. Fluoroscopy is generally better than 2-dimensional echocardiography to guide EMB because it provides more information to the operator about the course of the bioptome and site of biopsy (14,15). The echocardiographic technique without fluoroscopy has been used primarily to biopsy intracardiac masses. Some operators use fluoroscopy and echocardiography in combination to enhance entry into the right ventricle and direction of the bioptome. Noninvasive computed tomography (CT) or cardiac magnetic resonance (CMR) imaging may be of value in patients scheduled for EMB. CT scanning may be used to assess the angle of the intraventricular septum relative to the superior vena cava or inferior vena cava. Knowledge of this angle may lessen the risk of inadvertent biopsy of the right ventricular free wall during a fluoroscopically directed biopsy. In addition, CMR detection of a focal disease process may identify the area of the left or right ventricle that would be most likely to demonstrate the underlying pathological process (13,16). Three-dimensional echocardiography may enhance visualization and reduce the reliance on radiographic imaging in the future (17).

The risks of EMB may be divided into those that are acute and those that are delayed. Immediate risks of biopsy include perforation with pericardial tamponade, ventricular or supraventricular arrhythmias, heart block, pneumothorax, puncture of central arteries, pulmonary embolization, nerve paresis, venous hematoma, damage to the tricuspid valve, and creation of arterial venous fistula within the heart. The risks of EMB likely vary with the experience of the operator, clinical status of the patient, presence or absence of left bundle-branch block, access site, and possibly bioptome. The use of a long sheath that crosses the tricuspid valve may decrease the risk of bioptome-induced tricuspid valve trauma. Delayed complications include access site bleeding, damage to the tricuspid valve, pericardial tamponade, and deep venous thrombosis. Most complications are known from case reports, and therefore the precise frequency of these events is not known.

The data on EMB risks are derived from several single-center experiences and registries that have been reported in the literature. Fowles and Mason (18) reported an overall complication rate of $<1\%$ in >4000 biopsies performed in transplantation and cardiomyopathy patients, including 4 with tamponade (0.14%), 3 pneumothorax, 3 atrial fibrillation, 1 ventricular arrhythmia, and 3 focal neurological complications (18). Olsen, in an unpublished series referenced by Fowles and Mason (18), reported an overall complication rate of 1.55% in 3097 cardiomyopathy patients biopsied in Europe. Sekiguchi and Take (19) reported a 1.17% complication rate in a worldwide questionnaire of 6739 patients, including perforation in 28 patients (0.42%) and death in 2 patients