National Survey of the Use of Endomyocardial Biopsy in Japan

Shinya Hiramitsu, MD; Michiaki Hiroe, MD*; Akihisa Uemura, MD; Katsutomo Kimura, MD; Hitoshi Hishida, MD; Shin-ichiro Morimoto, MD

A national survey of endomyocardial biopsy procedures was conducted in Japan. Questionnaires were mailed to 852 institutions and statistical analysis of the 213 completed questionnaires (25.0% of the total) was performed. Cardiac biopsies were being performed at 134 of these institutions (62.9%), representing a 5.5-fold increase over 1980. A total of 19,964 cardiac biopsies have been performed in Japan. Specimens were obtained from the right ventricle at 113 institutions, and from the left ventricle at 76 centers. The Konno-Sakakibara bioprome was used at 32 institutions, whereas the long sheath method was used at 98 institutions. Sixty of the institutions (44.8%) had encountered ventricular wall perforation. The perforation rate of the two ventricles combined was 0.7% (147 of 19,964 cases), with a mortality rate of 0.05% (10 of 19,964 cases). Endomyocardial biopsy has become widespread in Japan, and its safety was ascertained by this national survey. (Jpn Circ J 1998; 62: 909–912)

Key Words: Complications; Endomyocardial biopsy; Mortality; Questionnaire

Methods

Questionnaires

In 1992, we sent a detailed questionnaire to 852 institutions (circulation training institutions and circulation training-related institutions designated by the Japan Circulation Society), and 213 responses (25.0% of the total) were analyzed statistically.

Statistical Analysis

Mortality rates in patients with left or right ventricular perforation were compared using Fisher’s exact test with Statview 4.5 statistical software package. A p value of <0.05 was considered statistically significant.

Results

Current Status of Endomyocardial Biopsy

Responses were obtained from 213 institutions: 58 university hospitals and 155 general hospitals. Of the 213 institutions that completed the questionnaire, 134 (62.9%) performed endomyocardial biopsy, and the remaining 79 (37.1%) gave the following reasons for not using this method: 58 institutions stated that it was technologically impossible, 25 reported that it was too dangerous, 10 described it as meaningless and 7 reported that there were no patients with indications for this procedure. Some 134 institutions were performing cardiac biopsies: 49 out of 58 (84.5%) university hospitals, and 85 out of 155 (54.8%) general hospitals.

Fig 1 illustrates the change in the number of institutions performing endomyocardial biopsy. At the time of the 1980 survey by Sekiguchi et al there were only 23 such institutions; by 1992, the number had risen 5.5-fold to 126.

A total of 16,820 adults (118 institutions) and 3,144 children (71 institutions) have undergone endomyocardial biopsy in Japan. Out of that combined total of 19,964 cases, 2,452 endomyocardial biopsies were performed during the last year surveyed [2,264 adults (113 institutions) and 188 children (61 institutions)].

Diseases of the patients studied are listed in Table 1. Cardiomyopathy was present in 7,866 cases, representing 3,177 cases with dilated cardiomyopathy, 3,438 cases with hypertrophic cardiomyopathy, and 276 cases with restrictive cardiomyopathy. Specific cardiomyopathy was present in 2681 cases, with myocarditis accounting for 1515 cases and alcoholic cardiomyopathy accounting for 233 cases. The remaining 2049 cases included patients with hypertensive heart disease, diabetes mellitus, and various arrhythmias such as ventricular tachycardia or complete atrioventricular block.
Accessing the heart with bioptome was via the femoral artery/vein at the majority of institutions, with the right heart biopsied at 108 institutions (101 via the femoral vein, 7 via the saphenous vein, 5 via the right internal jugular vein, 2 via the right subclavian vein, and 2 via the right brachio-cubital vein), and the left heart biopsied at 74 institutions (via the femoral artery at all 74, and via the right brachial artery at 7 centers).

As regards the instruments used for endomyocardial biopsy, the long sheath method was used at the majority (98) of the institutions (Table 2), but in many cases the specific brand was not recorded. However, in most cases the tip of the sheath was either straight or bent at a 45° angle. Bioptomes manufactured by Cordis Co, (Miami, FL, USA) were the most frequently used (65 institutions), followed by those manufactured by Mansfield Co, (Watertown, MA, USA; 15 institutions). Bioptomes with small jaws were used at 59 institutions and those with large jaws were used at 11 centers. The Konno-Sakakibara bioptome was used at 32 institutions, with small or medium-sized jaws used in the majority.

Methods of accessing the heart with bioptome were via the femoral artery/vein at the majority of institutions, with the right heart biopsied at 108 institutions (101 via the femoral vein, 7 via the saphenous vein, 5 via the right internal jugular vein, 2 via the right subclavian vein, and 2 via the right brachio-cubital vein), and the left heart biopsied at 74 institutions (via the femoral artery at all 74, and via the right brachial artery at 7 centers).

As regards the instruments used for endomyocardial biopsy, the long sheath method was used at the majority (98) of the institutions (Table 2), but in many cases the specific brand was not recorded. However, in most cases the tip of the sheath was either straight or bent at a 45° angle. Bioptomes manufactured by Cordis Co, (Miami, FL, USA) were the most frequently used (65 institutions), followed by those manufactured by Mansfield Co, (Watertown, MA, USA; 15 institutions). Bioptomes with small jaws were used at 59 institutions and those with large jaws were used at 11 centers. The Konno-Sakakibara bioptome was used at 32 institutions, with small or medium-sized jaws used in the majority.

Complications

Sixty institutions had encountered ventricular perforation (44.8%), 59 had experienced arrhythmias (44.3%) and one reported valve perforation (0.7%).

The underlying disease of ventricular perforation was recorded in a total of 111 cases, dilated cardiomyopathy in 34 cases (30.1%), hypertrophic cardiomyopathy in 34
Endomyocardial biopsy in Japan

Endomyocardial biopsy has become widely used in Japan in the 36 years since its development, because of the wealth of information that is provided by a few milligrams of biopsied tissue. Its use has expanded beyond morphological research to include the biochemical, immunological, and genetic engineering fields. Indications for the procedure are not limited to patients with cardiomyopathy and specific heart muscle disease. Patients receiving heart transplants can also benefit from the procedure, which serves to determine the presence/absence of rejection and to evaluate the therapeutic effect of immunosuppressant agents.

The present study was designed to assess the use of endomyocardial biopsy in Japan. Questionnaires were mailed to all 852 institutions, while only 213 (25.0%) of these responded. Because the circulation training-related institutions are certified on the basis of one board certified member of the Japanese Circulation Society and 15 hospital beds, we assumed that many of the hospitals targeted by the present study were too small to be equipped with cineangiographic devices. We thought this was one of the reasons for the low response rate. Among the 58 university hospitals responding there were 49 (84.5%) that performed cardiac biopsies, and they more or less typify present conditions in Japan. However, general hospitals used this method at a high rate (85 of 153 institutions, or 54.8%). This would appear to indicate a low response rate from institutions where the procedure was not in place. The size of these general hospitals, their use/non-use of cineangiographic systems, etc could not be determined just by the questionnaire results. The number of institutions that performed endomyocardial biopsy has increased more than 5-fold since 1980, when Sekiguchi et al conducted their survey, with the number of cases reaching 2,500 per year in 1991. Use of the Konno-Sakakibara biopomel is the most common method at the time of the previous survey, has largely been replaced by the long sheath method. Endomyocardial biopsy alone was performed in rather few cases, usually being performed in conjunction with cardiac catheterization. Therefore, in the majority of cases, specimens were collected from the right ventricle via the inguinal approach. The mean number of specimens obtained per procedure was 2.6 from the right ventricle and 2.8 from the left ventricle, which is rather low, considering the possibility of sampling error.

The most troublesome complication was perforation, which was encountered in a relatively high percentage of the institutions (60 of 134, 45%). Symptoms and signs at the time of perforation, in addition to those of cardiac tamponade, were frequently those induced by the vasovagal reflex. Few cases progressed quickly to death after the perforation, especially in cases of right ventricle perforation, suggesting that such cases could be rescued if appropriate treatment was administered. The following measures are recommended when perforation does occur. When bradycardia develops, atropine sulfate should be administered intravenously to counteract the vasovagal reflex. Intravenous fluids replacement should be administered as soon as possible to prevent dehydration, because endomyocardial biopsy is usually performed with the patient in a fasting or near-fasting state. In previous studies, complications such as coronary artery fistula and ruptured chordae tendineae of the tricuspid valve were reported. The mortality rate due to perforation in our survey was 0.05% (10 of 19,964 cases), which was similar to the rate of 0.08% (3 of 3,931 cases) noted in the survey of Sekiguchi et al and confirmed the safety of this procedure. The fact that the mortality rate had not risen, despite the significant increase in the number of institutions performing endomyocardial biopsy, suggests that this examination can be performed safely even by less experienced physicians. Mortality rates were somewhat higher among...
patients with left ventricular perforation (12.9%, 4/31 cases) than in those with right ventricular perforation (5.2%, 6/115 cases). Additional investigation of mortality rates is needed to devise more definitive safety measures, as the outcome after perforation was unclear in some cases, and details were not available for some of the fatalities.

In a survey of patients undergoing coronary arteriography from 1984 to 1987 recorded by the US Society for Cardiac Angiography and Interventions (SCAI)\(^4\) a mortality rate of 0.1% (218 of 222,553 cases) was reported, which exceeds the rate in the present survey. These figures do not point to endomyocardial biopsy as a particularly high-risk heart catheterization procedure. When heart transplantation becomes accepted in Japan, the number of cases undergoing endomyocardial biopsy will increase further. Baraldi-Junkins et al studied a series of 2,454 cases undergoing right ventricle endomyocardial biopsy after heart transplantation and reported an incidence of right ventricle perforation of only 0.08% (2 cases) and no deaths.\(^{15}\) This incidence was lower than that reported by Deckers et al\(^{16}\) in a series of 546 patients with cardiomyopathy (perforation rate: 1.3%, mortality rate: 0.3%), which illustrates the safety and usefulness of endomyocardial biopsy in post-transplant patients. Baraldi-Junkins et al also noted that because there is no pericardium in heart transplant patients, cardiac tamponade does not develop even if perforation occurs, thus explaining the high survival rate in their series.\(^{15}\)

Recently, in addition to histopathological examinations of biopsied myocardium, research involving virological, immunohistochemical, cytochemical and biochemical techniques has expanded. Study methods using micromaterials have been refined and can be applied to myocardial biopsy as well. In the future, we will focus on the instruments and methods used for this procedure and discuss improvements that can further enhance its safety and availability.

**Acknowledgments**

The authors express their gratitude to all the physicians who generously took the time to complete the questionnaire.

**References**