Multicenter Survey on the Validity of the CD-ROM Guideline for Antiarrhythmic Drug Therapy Produced by the Japanese Circulation Society and the Japanese Society on Electrocardiology


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Background  A multicenter investigational survey (Japanese Guideline for Arrhythmia Management By Individual Therapy) was conducted to evaluate the validity of using CD-ROM guidelines vs physician choice for the selection of antiarrhythmic drugs.

Methods and Results  Patients with paroxysmal atrial fibrillation (PAF, n=274) or premature ventricular contractions (PVC, n=216) were enrolled. The rate of concordance for drug selection between the treating physician and the CD-ROM was 216 of 274 patients (78.8%) with PAF. Of these, 168 (61.3%) were concordant for first-line agents and the remaining 48 (17.5%) were concordant for second-line agents. The concordance for the treatment of PVC was 154/216 cases (71.3%). Of these, 106 (49.1%) were concordant for first-line agents and the remaining 48 (22.2%) were concordant for second-line agents. Nonconcordance for PAF therapy was more likely to occur for patients with underlying heart disease (p<0.05), depressed cardiac function (p<0.001), and with more frequent ECG abnormalities and renal dysfunction. These differences were not seen in patients with PVC.

Conclusion  The CD-ROM guidelines appear to be valid in the selection of antiarrhythmic drugs for both PAF and PVC, but their usefulness is influenced by the patient’s clinical characteristics.  

Key Words:  Antiarrhythmic drugs; Multicenter investigational survey; Sicilian Gambit; Therapeutic guidelines

Based on the CAST results1,2 the indication for antiarrhythmic drug therapy in patients with various arrhythmias is being revised, making the concept of the Sicilian Gambit now viable3-5. A practical guideline for the selection of antiarrhythmic drugs was also planned for Japan6 and in 2000 the joint guideline committee on antiarrhythmic drugs of the Japanese Society of Electrocardiology and the Japanese Circulation Society produced a CD-ROM version7 which is mainly based on the Sicilian Gambit. However, the usefulness of these CD-ROM guidelines has not been verified by an objective evaluation.

Therefore, we conducted a multicenter investigational survey, Japanese Guideline for Arrhythmia Management By Individual Therapy (J-GAMBIT) as an activity of the scientific committee of Japanese Circulation Society, firstly to validate drug selection using the CD-ROM guidelines and secondly to evaluate the effectiveness, safety, and utility of this method of treatment selection.

Methods

Patients  For entry into the study, the patient must have either paroxysmal atrial fibrillation (PAF) or premature ventricular contractions (PVC; nonsustained monomorphic ventricular tachycardia was included).

Patients with these arrhythmias who were treated at participating facilities were enrolled and followed up for more than 2 years to determine the efficacy and safety of the selected treatment. Most of the physicians who participated were cardiology specialists familiar with the concept of the Sicilian Gambit. All patients gave informed consent.
Consecutive patients were randomly enrolled after January 1, 1998 and necessary information was registered at the central analyzing laboratory using the Internet. Patients who received specific therapy as part of a clinical trial or who had received non-pharmacologic therapy, such as catheter ablation before entry, were excluded.

**Data Management**

Clinical information was managed at the central analyzing laboratory in the Department of Medicine, Nippon Medical School. After the Guideline CD-ROM was started up, the individual's data were input and the recommended first-line and second-line drugs, which were selected based on the guidelines, were generated by the computer.

**Analysis and Evaluation**


The name of drug selected by the physician was compared with the drug choices generated by the CD-ROM and their concordance for the PAF and PVC groups was determined. Factors that may influence drug selection were then investigated.

**Statistical Analysis**

Chi-square test was performed using SPSS software (Chicago, IL, USA) for evaluation of the concordance rate and the patient characteristics; p<0.05 was considered significant.

**Results**

**Registration**

During the registration period 544 patients were enrolled from the 20 institutes listed in Appendix 2 and of them 490 had all the necessary information needed for analysis, were selected for evaluation. There were 274 patients with PAF (182 males, 92 females; mean age 62.7±11.3 years) and 216 patients with PVC (143 males, 73 females; mean age 62.9±14.2 years).

Fig 1. Age distribution of patients with paroxysmal atrial fibrillation.

Fig 2. Age distribution of patients with premature ventricular contractions.
There were no differences in the frequency of underlying heart disease (p<0.05) or complications such as renal dysfunction compared with concordant patients. Concordant patients were more likely to have more frequent ECG abnormalities, renal dysfunction, and underlying diseases (p<0.05) or complications such as any complications compared with discordant patients. Based on the present data, discordant patients in the PAF group tended to have more frequent underlying diseases, a perception of the Sicilian Gambit is understood, and it is thought that an empiric factor strongly influences most cases. It is important to determine what caused the discordance in drug selection between the CD-ROM and the physician. Based on the present data, discordant patients in the PAF group tended to have more frequent underlying diseases, a depressed ejection fraction, liver or renal dysfunction. In the clinical setting, a physician must consider many factors comprehensively (eg, presence or absence of any underlying diseases, their severity, the degree of cardiac dysfunction, and the pharmacokinetics and pharmacodynamics of the agents). Each physician weighs the importance of these factors differently. Although several large-scale studies have been done to create better therapeutic strategies for PAF, it has not even been confirmed whether rhythm control or rate control is superior. We hypothesize that these complicated factors may be related to the discordance in the PAF group. In Japan, it has been reported that rhythm control is superior to rate control for PAF and its prognosis depends on its progressive nature. However, the long-term prognosis may be different and improved if the CD-ROM guided treatment of PAF is standardized and every physician tends to use antiarrhythmic agents according to the guideline.

**Concordance Rate for Drug Selection**

**PAF** The treatment chosen by the physician was concordant with the drug selected by the CD-ROM in 216 of the 274 patients (78.8%) with PAF. There was concordance for first-line agents in 168 patients (61.3%) and for second-line agents in the remaining 48 (17.5%). When we analyzed the 58 cases (21.1%) in which the selection was not concordant, 42 cases (15.3%) were completely discordant and in the remaining 16 cases (5.8%) either the physician or the CD-ROM guidelines had determined that drug therapy was unnecessary.

**PVC** The concordance rate for PVC was 154/216 cases (71.3%) and there was concordance for first-line agents in 106 cases (49.1%) and for second-line agents in the remaining 48 (22.2%). The selection was discordant in 62 cases (28.7%), of which 53 cases (24.5%) were completely discordant and 9 cases (4.2%) did not require drug therapy.

**Comparison of the Clinical Characteristics of Concordant and Discordant Patients**

Table 1 shows the clinical characteristics of patients with PAF with regard to the concordance of drug selection. There were only slight differences in the age and gender of the patients. Discordant patients were more likely to have underlying heart disease (p<0.05) or complications such as depressed cardiac function (p<0.001), and tended to have more frequent ECG abnormalities, renal dysfunction, and any complications compared with concordant patients. There were no differences in the frequency of underlying diseases or complications in patients with PVC (Table 2).

**Discussion**

To evaluate the usefulness of the Japanese version of the Sicilian Gambit Guideline on CD-ROM, we conducted a multicenter investigational survey, J-GAMBIT to evaluate the validity of computer-generated selection of antiarrhythmic treatment compared with physician selection. The overall concordance rate for drug selection between CD-ROM and physician was 78.8% for PAF and 71.3% for PVC. Because the CD-ROM generates 2 or more drugs with similar pharmacologic properties, we considered the choices were concordant when the physician-selected drug was included in the list generated by the CD-ROM. The concordance rate for first-line agents was 61% for PAF and 49% for PVC.

Drug selection using a CD-ROM is based on the concept of the Sicilian Gambit, which uses a pathophysiologic approach that considers the underlying mechanism and the vulnerable parameters of each arrhythmia. In contrast, a physician’s selection is mainly based on experience, even if the concept of the Sicilian Gambit is understood, and it is thought that an empiric factor strongly influences most cases.

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In contrast, such differences were not seen in the PVC group and the reason for the low concordance rate cannot be explained. We presume that the theoretical drug selection using the pathophysiologic approach of the CD-ROM cannot be applied to PVC because the mechanism responsible for PVC is not identical in each patient. Generally speaking, one cannot identify the precise mechanism of PVC, other than for idiopathic PVCs with specific QRS morphologies (ie, right bundle branch block with superior axis or left bundle branch block with inferior axis). In this report we focused on the evaluation of concordance of the selected therapy for PAF or PVC between the guideline CD-ROM and the physician. Further evaluation of the efficacy and safety of the selected drugs, including the actual clinical effectiveness and adverse events, are
needed and will elucidate the true clinical utility of the CD-ROM guidelines.

Acknowledgment

The authors express sincere thanks to all participants.

References


Appendix 1


Appendix 2

The institutes that participated in the study are listed here in arbitrary order.

Second Department of Medicine, Keio University; First Department of Medicine, Niigata University; Department of Medicine, Keio University; Department of Medicine, Tokyo Medical and Dental University; Heart and Blood Pressure Institute, Tokyo Women’s Medical College; First Department of Medicine, Nippon Medical School; Department of Cardiology, Metropolitan Hiroo Hospital; Third Department of Medicine, Chiba University; Department of Medicine, Inza Hospital; Department of Medicine, Yokohama Minami Kiyosaki Hospital; Department of Medicine, Nagoya University; Higashihakata Hospital; Department of Cardiology, Fujita Health University; Second Department of Medicine, Toyama Medical and Pharmaceutical University; Department of Cardiology, Okayama University; Ohsaka Hospital; Department of Medicine, Oita Medical College; Oita Kyoritsu Hospital; Ogata Choritsu General Hospital; USA Ichio Hospital.