Simple Minimal Sedation for Catheter Ablation of Atrial Fibrillation

Noboru Ichihara, MD; Shinsuke Miyazaki, MD; Hiroshi Taniguchi, MD; Eisuke Usui, MD; Takamitsu Takagi, MD; Jin Iwasawa, MD; Akio Kuroi, MD; Hiroaki Nakamura, MD; Hitoshi Hachiya, MD; Yoshito Iesaka, MD

Background: Deep sedation or general anesthesia is generally used during atrial fibrillation (AF) ablation. The aim of this study was to report the safety and feasibility of minimal sedation during AF ablation.

Methods and Results: One thousand and fifty-two AF ablation procedures in 819 patients (62±11 years, 621 men, 506 paroxysmal) were included. Boluses of intravenous hydroxyzine pamoate and pentazocine were administered, with a maximal dose of 100 mg of hydroxyzine and 60 mg of pentazocine in response to pain. If the pain was intolerable or patients requested deeper sedation, moderate sedation using dexmedetomidine or propofol was introduced. Among 819 consecutive first procedures, the procedure was completed under minimal sedation in 795 (97.1%) patients without inotropic drugs or respiratory support, whereas in 20 (2.4%) patients, anesthesia was switched to moderate sedation due to pain. Patients requiring a switch to moderate sedation were significantly younger than those without (53.6±2.3 vs. 62.6±10.4, P<0.01). No procedures were abandoned due to adverse effects of sedation. Significant intra-procedural blood pressure decreases requiring inotropic drugs were not observed in any patients. Among 233 patients who underwent repeat procedures, 6 (2.6%) requested moderate sedation before the procedure. The mean procedure time was 151±54 min. Cardiac tamponade, unrelated to sedation, was observed in 7 (0.66%) procedures.

Conclusions: Minimal sedation might be acceptable anesthesia in the vast majority of AF ablation procedures performed in electrophysiological laboratories.

Key Words: Atrial fibrillation; Catheter ablation; Sedation
Minimal Sedation Protocol
Catheters were manipulated under local anesthesia. Boluses of hydroxyzine pamoate (Atarax-P® 25 mg and pentazocine (Sosegon®) 15 mg were administered intravenously prior to the start of radiofrequency (RF) application. If necessary, each drug was added with a maximal dose of hydroxyzine of 100 mg and pentazocine of 60 mg in response to pain. If the pain was intolerable or patients requested deeper sedation during the procedure, moderate sedation using dexmedetomidine or propofol was introduced. The peripheral oxygen saturation, heart rate, and blood pressure (BP) were monitored continuously. Femoral arterial access is routinely acquired for continuous arterial pressure monitoring. Supplemental oxygen was used to avoid hypoxemia if necessary, starting with a flow rate of 3 L/min via a nasal cannula. When the BP fell significantly during the procedure, we added a fluid infusion while evaluating the possibility of cardiac tamponade.

The procedures were performed by 2 electrophysiologists. The cases were assisted by 1 nurse. All operators were trained in advanced on life support, including tracheal intubation and cardiopulmonary resuscitation. The administration of sedation and analgesics, monitoring the patients and documentation were performed by a designated nurse under supervision and according to the instructions of the electrophysiologist. The recommended appropriate emergency equipment, including a defibrillator, advanced airway management equipment and emergency medications, were always present in the electrophysiology laboratory.

Mapping and Ablation Protocol
All antiarrhythmic drugs were discontinued for at least 5 half-lives prior to the procedure, with the exception of amiodarone. All patients were effectively anticoagulated for >1 month before the procedure. Transesophageal echocardiography was performed to exclude any atrial thrombi. The surface electrocardiogram and bipolar intracardiac electrograms were continuously monitored and stored on a computer-based digital recording system (LabSystem PRO, Bard Electrophysiology, Lowell, MA, USA). The bipolar electrograms were filtered from 30 to 500 Hz. A 7-F 14 pole 2-site mapping catheter (Irvine Biomedical Inc, Irvine, CA, USA) was inserted through the right jugular vein for pacing, recording and internal cardioversion.

The ablation was performed according to the strategy described previously. In brief, after a single transseptal puncture, 2 long sheaths (SL0; St. Jude Medical, Minneapolis, MN, USA) were placed in the superior and inferior PVs, and mapping catheters (Lasso; Biosense Webster, Diamond Bar, CA, USA) were inserted through the right jugular vein for monitoring. The end-point of the procedure was the activation of the cavo-tricuspid isthmus. If AF continued after the substrate ablation, the patients underwent internal electrical cardioversion. If AF was converted to an atrial tachycardia, it was mapped and ablated by using activation 3D mapping and entrainment maneuvers. When a critical isthmus of a macroreentrant circuit was identified, the lesions were deployed to achieve complete a bidirectional conduction block. The cavotricuspid isthmus was also ablated to create a bidirectional conduction block.

Statistical Analysis
Continuous data are expressed as the mean±standard deviation for normally distributed variables or as the median [25th, 75th percentiles] for non-normally distributed variables, and were compared using a Student’s t-test or Mann-Whitney U-test, respectively. Categorical variables were compared using a chi-squared test. The time-course patterns of the BP were compared with a 2-way layout ANOVA between the patients undergoing AF ablation under minimal sedation and moderate sedation. Sequential data measurements in each group were analyzed by a repeated-measures analysis of variance (repeated measures ANOVA), and the data were analyzed with a Bonferoni’s multiple comparison. The difference in the arrhythmia-free survival was evaluated using the log-rank test. A probability value of P<0.05 indicated statistical significance.

Results
In total, 819 patients (62±11 years, 621 male, 506 paroxysmal AF) underwent a total of 1052 ablation procedures (mean 1.28±0.52 per patient). Among 819 consecutive first AF ablation procedures, the procedures were completed under minimal sedation in 795 (97.1%) patients, with a mean of 45.1±20.0 mg of hydroxyzine pamoate and 32.2±10.6 mg of pentazocine, whereas in 20 (2.4%) patients, a switch to moderate sedation using dexmedetomidine (17 patients) or propofol (3 patients) was required due to pain; this was in addition to a mean of 34.9±27.5 mg of hydroxyzine pamoate and 31.6±14.0 mg of pentazocine. Among those 20 patients, moderate sedation was introduced due to severe pain during RF deliveries at the posterior part of the left ipsilateral PVs and during the femoral puncture in 17 and 3 patients, respectively. In the remaining 4 (0.5%) patients, moderate sedation was introduced from the beginning of the procedure because they were foreigners (non-Japanese) and good communication with the laboratory staff was difficult. The 20 patients in whom minimal sedation was switched to moderate sedation due to pain were significantly younger than those without moderate sedation (53.6±2.3 vs. 62.6±10.4, P<0.01), whereas there were no other differences in the clinical characteristics. The mean total procedure time (from the femoral puncture to the removal of the sheaths) and the mean procedure time required for the PVAI were 151±54 and 69±26 min, respectively. The freedom from arrhythmia recurrence after the initial ablation procedure was similar be-
Minimal Sedation During AF Ablation

required in any patients. The mobilization could be controlled by the operator’s command. In 24 patients who required moderate sedation for any reason, the systolic BP prior to the procedure, just after the LA access, just after the left PVAI, just after the right PVAI, and at the end of the procedure was 155.0±24.2, 154.5±25.4, 142.4±23.4, 136.4±22.0, and 134.6±21.6, respectively. The BP significantly decreased gradually over the time-course, and the time-course pattern of the BP was similar between the patients undergoing AF ablation under minimal and moderate sedation (P=0.972, Figure).

No adverse effects of the sedation resulted in procedural complications or a reason to switch to another analgesic in any of the patients. The only reason to switch the analgesia was to control the pain during the procedure. Cardiac tamponade requiring pericardiocentesis was observed in 7 (0.66%) procedures, and was unrelated to the analgesia.

Discussion

We here present the results of a single-center study on the procedural feasibility of simple minimal sedation during AF ablation. To the best of our knowledge, this is the first report describing minimal sedation during AF ablation procedures. Although 2.4% of the procedures required a switch to moder-
ate sedation due to pain, the procedure was completed under minimal sedation without any sedation-related complications, such as persistent hypotension or respiratory depression in the remaining 97.1% of the patients. The rate of cardiac tamponade (0.66% in the study collective) seems to be acceptable.

**General Anesthesia and Moderate/Deep Sedation**

General anesthesia is widely used in a large number of centers. Although general anesthesia provides the most sufficient control of movement and pain, it has certain disadvantages. Of those, excessive hypotension and (when combined with muscle relaxants) reduced sensitivity to high-output phrenic nerve mapping, are particularly relevant. In addition, the anesthesiologist is required to perform monitoring throughout the procedure even for short procedure times. While propofol-based deep sedation is common practice in a wide range of electrophysiological procedures, there is a risk of airway complications under a strong anticoagulated state, which requires well-trained personnel and adequate monitoring. Besides that, propofol may alter the arrhythmia inducibility and it can lead to hypokalemia, especially after a prolonged infusion. A prior report has clearly shown that the important limitation of deep sedation is persistent hypotension, and 15.6% of the patients with propofol sedation required a switch to midazolam sedation. Due to its profound cardiovascular depressive effects by reducing the myocardial contractility and systemic vascular resistance and preload, propofol should be administered slowly at a small divided dose and titrated on an individual basis. Careful hemodynamic and respiratory monitoring are important, particularly in elderly cardiac patients, or those with hypovolemia, poor ventricular function, concurrent negative inotropic medications, or vasodilating medications. After the procedure, the patients were allowed to recover from anesthesia and were transferred to an intermediate care unit for monitoring of their vital signs. Deep sedation or general anesthesia might delay the diagnosis of thromboembolic events leading to transient ischemic attacks or strokes.

Compared to deep sedation, moderate sedation with midazolam carries a reduced risk of airway complications or hemodynamic impairment. In general, benzodiazepines have minimal effects on the cardiovascular system within the therapeutic dose range; however, the infusion of midazolam alone often does not provide an adequate anesthetic outcome for a prolonged procedure. Halfway sedation often leads to an unpredictable patient response. Procedural discomfort may be increased during moderate sedation and patient movements may be more likely. Usually, it is difficult to control patient movements in such a situation when communicating with the patient is difficult.

**Minimal Sedation**

Despite the development of AF ablation procedures and the increasing experience with the procedures, few studies are available on a minimal sedation strategy. Because anesthetics typically have a narrow therapeutic window and patient's sensitivity to anesthetics varies with age, body weight, composition, genetics, medical conditions, and concomitant use of other medications, a more prominent or prolonged sedative effect might unexpectedly occur at an apparently lower administered dose. Furthermore, when used in combination, the inhibitory effects of anesthetics on the brain function, spontaneous respirations and hemodynamic status are synergistic. The use of this type of minimal sedation was started in our institute more than 10 years ago, and the same convincing results have been achieved in several thousand patients. In the experience in our group, mutual communication with the patient under minimal sedation can control the depth of breathing, and avoid unpredictable patient movements because they can be controlled by the operator's command. One of the major advantages is that minimal sedation does not lead to sedation-related adverse effects, such as hypotension and hypoxia. Thus, the use of ionotropic drugs and an airway does not need to be considered. In the present study, the BP during the procedure was similar between the patients undergoing ablation under minimal sedation and those who required moderate sedation because there were few patients in whom moderate sedation was introduced from the beginning of the procedure. Thromboembolic events could be evaluated during and immediately after the procedure, which is clearly comfortable for the operator. Neither an anesthesiologist nor special equipment, such as assisted ventilation and an intermediate care unit is required for the procedure, which is also an important advantage from the economical standpoint. In addition, the perception of severe pain during the RF energy application has been described as a possible measure to reduce the risk of esophageal injury.

In the present study, patients who were eligible for AF ablation were included and thus represent a typical population encountered in clinical practice with a broad range of age and comorbidities. Patients requiring a switch to deeper sedation were younger compared with those who tolerated minimal sedation. Pain is subjective and is also largely influenced by one’s mental state. We speculate that the tolerability to pain is lower in young patients than elderly patients during the procedure, presumably because young patients have less experience of previous invasive procedures. Recent advancements in mapping systems and procedural experience have contributed to the shorter procedure time and explosive spread of AF ablation procedures in clinical practice. Given the above advantages and economical standpoint, we believe that minimal sedation could be a standard anesthesia method used during AF ablation, and that deeper sedation should be applied in specific populations. Further exploration and efforts should be continued to find better medications to control the pain, and in which patients, deeper sedation is suitable.

**Hydroxyzine and Opioids**

Opioid analgesics are among the oldest known medications. In spite of their long usage, clinical success in controlling pain in many settings appears to be limited by a lack of understanding of the clinical pharmacology of these agents. Efforts to achieve better outcomes often focus on the use of adjunctive agents, such as hydroxyzine, in an attempt to control postoperative pain with a minimum of toxicity. Hydroxyzine is classified as an antihistamine, antipsychotic, anxiolytic and is also used as a tranquilizer. Unlike most other first-generation antihistamines, it has negligible affinity for the mACh receptors. For many years, it was especially preferred for its ability to boost the effectiveness of opioids by slowing the metabolism of opiates by inhibiting certain enzymes.

**Study Limitations**

The study was retrospective and observational by design, and the patients were not randomized against a comparison group with an alternative form of sedation. In fact, the study included few patients in whom moderate sedation was introduced from the beginning of the procedure.

**Conclusions**

In the vast majority of the general population eligible for AF ablation, AF ablation procedures can be completed under sim-
ple minimal sedation and minimal equipment, with an acceptable complication rate. Minimal sedation might be an acceptable anesthesia method during AF ablation procedures conducted in electrophysiological laboratories.

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Disclosures

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References