Adaptive-servo ventilation combined with deep sedation is an effective strategy during pulmonary vein isolation

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Aims
Pulmonary vein isolation (PVI) by catheter ablation for atrial fibrillation (AF) requires suppression of patient restlessness by sufficient sedation in addition to maintaining stable respiration. We applied adaptive-servo ventilation (ASV) and examined the effects of ASV combined with deep propofol sedation on PVI using a NavX.

Methods and results
We analysed 75 paroxysmal AF (PAF) patients (62 ± 11 years; 53 men and 22 women) who underwent PVI for treatment of PAF using an ASV system combined with deep sedation (ASV group). Control patients included 75 consecutive PAF patients (62 ± 11 years; 51 men and 24 women) who underwent PVI just before introduction of the ASV system. Deep sedation was defined as a Ramsay sedation score of 6. The ASV group had a lower frequency of restless body movements compared with the control group during PVI (1.5 ± 0.7 vs. 7.8 ± 1.4 times, \( P < 0.01 \)). The frequency of respiratory compensation and EnGuide alignment of catheter position by the NavX was lower in the ASV (4.2 ± 3.3 and 8.8 ± 7.1 times) than control group (7.1 ± 5.1 and 15.2 ± 10.0 times, \( P < 0.05 \) and \( < 0.01 \), respectively). Consequently, significantly lower total electrical energy supply (48.7 ± 6.0 KJ) was required in the ASV than control group (64.5 ± 24.9 KJ, \( P < 0.01 \)). Further, significantly shorter fluoroscopy and procedural times were observed in the ASV (28 ± 5 and 109 ± 25 min) than the control group (33 ± 6 and 141 ± 38 min, respectively, \( P < 0.01 \)) and the AF recurrence rate was significantly lower in the ASV than the control group (12 vs. 25%, \( P < 0.01 \)).

Conclusion
ASV combined with deep sedation is an effective strategy during PVI using the NavX in patients with PAF.

Keywords
Atrial fibrillation • Ablation • Ventilatory management

Introduction
Radiofrequency (RF) energy applied to circumferentially isolate the pulmonary veins (PVs) from the left atrium (LA) (pulmonary vein isolation, PVI) is now one of the most effective treatments of atrial fibrillation (AF), with a reported cure rate of 50–90%.1–6 In contrast to catheter ablation for other less complex arrhythmias such as atrioventricular node reentrant tachycardia, PVI requires a relatively long procedural time of 2–4 h, resulting in patient restlessness, which interferes with the PVI procedure. Furthermore, application of RF energy during the procedure causes considerable pain to the patients.

During the procedure, patients are expected to lie still on the operation table for an extended period of time. Hence, it is essential to provide patients with adequate sedation and analgesia to avoid patient restlessness, movement, and pain, and to stabilize their respiration. Three methods are used for sedation during PVI: (1) conscious sedation with an intravenous anaesthetic combined with an analgesic, (2) deep sedation and analgesia, and (3) general anaesthesia with tracheal intubation. Conscious sedation with an intravenous anaesthetic combined with an analgesic is widely used during catheter ablation for other arrhythmias that...
What’s new?

- To the best of our knowledge, we are the first to apply automatic portable adaptive-servo ventilation (ASV) to maintain stable respiration during deep sedation in pulmonary vein isolation (PVI) for atrial fibrillation (AF). PVI requires a relatively long time. It is essential to provide patients with adequate sedation and analgesia to avoid patient restlessness. Deep sedation has been attempted. However, deep sedation suppresses respiration and causes unstable respiration with considerable respiratory variations. Recently, reliable ASV equipment has been developed. We examined the usefulness of a portable ASV system for PVI procedures with paroxysmal AF patients. The ASV group had fewer restless body movements with stable respiration compared with the conventional conscious sedation group. Significantly lower total electrical energy supply and procedural times were observed in the ASV than the control group. We were the first to find that ASV combined with deep sedation is an effective strategy during PVI.

have a relatively short procedural time. However, conscious sedation is frequently insufficient to prevent restless body movements, relieve pain, and stabilize respiration during the relatively long procedural duration of PVI. In contrast, although general anaesthesia meets all these requirements, it requires the services of an anaesthesiologist and intubation of the patient’s trachea. Recently, deep sedation with a combination of intravenous anaesthetics and analgesics has been attempted during PVI. In another study, sedation with propofol infusion administered by cardiologists without assisted ventilation has proven safe, effective, and practical for use in AF ablation. It theoretically avoids restlessness without the need for intubation. Deep sedation, however, suppresses respiration and/or sometimes results in airway obstruction by a retracted tongue root, causing a decrease in arterial oxygen saturation. Further, it causes unstable respiration with considerable respiratory variations that interfere with the PVI procedure, including catheter positioning.

Recently, automatic portable adaptive-servo ventilation (ASV) equipment has been developed and its reliability established. To compensate for the disadvantages of deep sedation noted above, we hypothesized that use of a portable ASV system with deep sedation would allow adequate control of restlessness while stabilizing respiration, which would improve the success of the PVI procedure, including a higher AF-free rate. Accordingly, we evaluated the usefulness of ASV with deep sedation during PVI and compared the results with ablation procedures performed under conventional conscious sedation with relatively low-doses of an intravenous anaesthetic–analgesic combination.

Patients and methods

Patients

We analysed the efficacy of the ASV system (AutoSet-CS™, ResMed LTD, Sydney, Australia) with deep sedation during PVI in 75 consecutive patients with paroxysmal AF (PAF) (ASV group) who underwent their first PVI from March, 2011 to September, 2011. Seventy-five consecutive PAF patients who had undergone their first PVI just before the introduction of ASV with deep sedation from August 2010 to February 2011 were included as controls. PAF was defined by the presence of (1) an initial episode of AF verified by ECG, and (2) documented conversion to sinus rhythm either spontaneously or after treatment during hospitalization. All patients had repetitive episodes of drug-refractory. The clinical characteristics of the patients in ASV and control groups are summarized in Table 1. Patients with allergy to constituents of propofol, such as egg and soybeans, were excluded from this study. None of the patients had pulmonary organic disease. The examination procedure complied with the rules of the Helsinki Declaration; written informed consent was obtained from all subjects and the study was approved by the institutional ethics committee of the Okayama Heart Clinic for human research.

Sedation and adaptive servo ventilation

Sedation levels were determined using the Ramsay sedation scale and deep sedation was defined as sedation level 6 on the scale. In addition, a brain monitoring system (A-3000 BIS Platform™, Aspect Medical System, Natick, MA, USA) was used to confirm the depth of sedation to avoid excessive sedation or awakening. ASV supports inspiratory pressure when expiratory positive airway pressure (EPAP) is low; the ventilatory support is increased when breathing effort decreases and vice versa. ASV was performed with a full face mask (Mirage Quattro™; ResMed Ltd). The normal settings used during treatment were EPAP, 5 cm H₂O; inspiratory positive airway pressure, minimum 3 cm H₂O, maximum 10 cm H₂O. ASV monitored tidal and minute volumes to avoid hypoventilation. Supplemental oxygen was administered at the rate of 6 L/min. Heart rate, blood pressure, and arterial oxygen saturation were continuously monitored during the PVI procedure.

Propofol and pentazocine hydrochloride were used for sedation and analgesia, respectively, in both ASV and control groups. The

<table>
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<tr>
<th>Table 1 Patient’s characteristics</th>
<th>ASV group</th>
<th>Control group</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62 ± 11</td>
<td>62 ± 10</td>
</tr>
<tr>
<td>Male (%)</td>
<td>71</td>
<td>68</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>34</td>
<td>39</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Heart failure (%)</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Left atrial size (mm)</td>
<td>39 ± 6</td>
<td>39 ± 6</td>
</tr>
<tr>
<td>Left atrial volume (cm³)</td>
<td>85.1 ± 3.1</td>
<td>91.1 ± 29.5</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>67 ± 6</td>
<td>67 ± 6</td>
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ASV, adaptive servo-ventilation; LVEF, left ventricular ejection fraction; NS, not significant.
Catheters were positioned in the LA: two decapolar ring catheters within 300–350 s in order to avoid thrombus formation. Three tered via a peripheral vein to maintain Activated Clotting Time Before transseptal catheterization, bolus intravenous heparin brought technique, with all sheaths over one puncture site. St. Paul, MN, USA) were advanced to the LA by the Brocken- right jugular vein. Three 8-F SL0 sheaths (St. Jude Medical, Inc., femoral vein and a 6-F catheter in the coronary sinus via the Lifeline Co., Ltd., Tokyo, Japan) at the His bundle region via a trophysiology catheters were positioned: a 4-F catheter (Japan venous accesses were performed as follows. Two standard elec- trophysiology catheters were positioned: a 4-F catheter (Japan Lifeline Co., Ltd., Tokyo, Japan) at the His bundle region via a femoral vein and a 6-F catheter in the coronary sinus via the right jugular vein. Three 8-F SL0 sheaths (St. Jude Medical, Inc., St. Paul, MN, USA) were advanced to the LA by the Brockenbrough technique, with all sheaths over one puncture site. Before transseptal catheterization, bolus intravenous heparin sodium (100 units/kg) was administered. After transseptal cather- ization, a continuous heparinized saline infusion was adminis- tered via a peripheral vein to maintain Activated Clotting Time within 300–350 s in order to avoid thrombus formation. Three catheters were positioned in the LA: two decapolar ring catheters (Japan Lifeline Co., Ltd.) and one ablation catheter (CoolPath Duo, St. Jude Medical, Inc. or Safire Blu Duo, St. Jude Medical, Inc.).

Radiofrequency ablation
The ablation strategy was the same in all groups. PVI was per- formed in all patients. Electrophysiological mapping was performed with a 3.5-mm-tip ablation catheter inserted via the transeptal sheath. Each PV ostium was identified using an electroanatomic integration mapping system (Ensite-NavX system, St. Jude Medical Inc.). After LA reconstruction, each PV ostium was identified by se- lective venography and tagged on the electroanatomic map. Two decapolar ring catheters were placed within the ipsilateral superior and inferior PVs or within the superior and inferior branches of a common PV during RF delivery. Irrigated RF energy was delivered with a target temperature of 42°C, a maximal power limit of 35 W (20–30 W for posterior wall abla- tion and 30–35 W for anterior wall ablation) and an infusion rate of 13 mL/min via the irrigated ablation catheter. RF energy was applied for 30 s until the maximal local electrogram amplitude decreased by 70% was noted. Irrigated RF ablation was performed in the posterior wall >0.5–1 cm, and in the anterior wall >5 mm from the angiographically or electrophysiologically defined PV ostia. The temperature of the oesophagus was continuously mon- itored by a catheter with a temperature sensor (SensiTherm TM, St. Jude Medical Inc.) during ablation to avoid oesophageal damage from the high energy supplied. When the temperature exceeded 40°C, the energy supply was discontinued. The end point of PVI was defined as (1) elimination of PV poten- tials recorded by the two ring catheters within the ipsilateral PVs and lack of LA capture during intra-PV, isthmus, and PV atrium pacing at least 30 min after isolation and (2) no recurrence of PV spikes within all the PVs after intravenous administration of 20 to 40 mg of adenosine triphosphate during sinus rhythm or coronary sinus pacing.

Postablation care and follow-up
After the procedure, anticoagulation therapy was continued at least 3 months after the AF ablation in all groups. All patients received monthly follow-ups at our centre for at least 6 months after the AF ablation. The initial follow-up was made at 2 weeks after AF ablation. All previously ineffective antiarrhythmic drugs were withdrawn just after ablation. At follow-up, surface ECG and transthoracic echocardiography were performed at our centre. All patients had a telemetry ECG recorder (Omron Co., Ltd., Kyoto, Japan) to document symptomatic arrhythmias or to transfer an ECG once per week if asymptomatic for 6 months. An AF recurrence was defined as an AF episode lasting for >30 s that was analysed during the latter 4 months of the 6 month follow-up period as the initial 2 month blanking period was excluded. When patients presented complaints that suggested oesophageal damage, endoscopic examination was performed.

**Table 2 Sedation and ventilatory management of the two groups during pulmonary vein isolation**

<table>
<thead>
<tr>
<th>Dose of propofol</th>
<th>ASV group</th>
<th>Control group</th>
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<tbody>
<tr>
<td>Initial intravenous dose</td>
<td>10–100 mg</td>
<td>40–100 mg</td>
</tr>
<tr>
<td>Maintenance dose</td>
<td>150–350 mg/h</td>
<td>100 mg/h</td>
</tr>
<tr>
<td>Additional dosage at body movement</td>
<td>20–30 mg</td>
<td>20–30 mg</td>
</tr>
<tr>
<td>Dose of pentazocine hydrochloride</td>
<td>7.5–15 mg</td>
<td>15–30 mg</td>
</tr>
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RSS scores
- On entering the catheterization-ablation room: 5
- During the procedure: 6
- When leaving the catheterization-ablation room: 2
- Ventilatory management: Adaptive-servo ventilation with full face mask vs. Manual airway management with use of an airway and oxygen mask
- Supplemental oxygen (L/min): 6

Table 2: Sedation and ventilatory management of the two groups during pulmonary vein isolation

ASV, adaptive servo-ventilation; RSS, Ramsey sedation scale.

**Compared parameters**

The following parameters were compared between ASV with deep sedation and conventional sedation groups: experienced pain, rest- lessness and body movement, compensation by the NavX system for catheter movement caused by respiratory variation and
EnGuide™ alignment to readjust the catheter position to the three-dimensional navigation model, i.e. to the $x$–$y$–$z$ axis. The presence of pain during PVI was assessed during the procedure and confirmed by an interview conducted after completion of the procedure. Body movement restlessness was defined as present when the NavX system detected positional catheter movement of $>4$ mm from the preceding position concomitantly with body movement. In addition, total energy supply for PVI, fluoroscopic time and procedural duration were compared. Finally, AF-free rate was also compared.

**Data and analysis**

The same operators (authors H.Y. and T.M.) with adequate experience in PVI $>$300 cases performed PVI for both control patients and patients with ASV group. Similarly, the same nursing team carried out ventilatory and sedation management for both control and ASV groups. PVI was performed within 7 months in both control and ASV groups. Real-time and recorded data were analysed by other doctors and nurses in a blind manner.

**Statistics**

Data were analysed using PASW Statistics 17.0 (SPSS Inc., Chicago, IL, USA). For univariate analyses, Student’s t-test and $\chi^2$ test with a $2 \times 2$ table were applied for continuous and categorical variables, respectively, to compare clinical characteristics, procedural parameters, and clinical outcomes between patients with ASV combined with deep sedation and control patients with conscious sedation groups. Comparison of AF recurrence between ASV and control groups was performed using the Kaplan–Meier survival analysis with a log-rank test. Data are expressed as mean ± standard deviation. Differences of $P < 0.05$ were considered statistically significant.

**Results**

All patients in both groups reached the endpoint of PVI, so that the initial success rate was not different between the two groups. There were no patients associated with oesophageal damage in both group.

Decrease of arterial oxygen saturation to $<90\%$ was not observed at any point during PVI under ASV with deep sedation. Further, no hypventilation was observed by the ASV self-monitoring system for tidal and minute volumes in ASV with deep sedation. In contrast, decrease in arterial oxygen saturation due to airway obstruction by the tongue root was occasionally observed in approximately one-third of the patients with PVI under conventional conscious sedation. Maintaining an appropriate position of the patient’s neck to avoid airway obstruction was required during PVI under conventional conscious sedation while no additional airway management was necessary during ASV with deep sedation.

Post-procedure patient interviews demonstrated that none of the ASV group patients experienced pain during PVI (Figure 1, upper left panel), while 59% (44 of 75) of patients with conventional conscious sedation with analgesia experienced pain during the procedure. Restlessness and body movement occurred less frequently in the ASV (1.5 ± 0.7 times) than the control group (7.8 ± 1.4 times) (Figure 1, upper right panel). Respiratory compensation by the NavX system for catheter movement was also required significantly less frequently in the ASV (4.2 ± 3.3 times) than the control group (7.1 ± 5.1 times) (Figure 1, lower left panel). Similarly, the ASV group needed significantly less frequent EnGuide™ alignment to readjust the catheter position (8.8 ± 7.1 times) as compared with the control group (15.2 ± 10.0 times) (Figure 1, lower right panel). As a result of these, the ASV group...
required a significantly lower total energy supply for PVI (47.8 ± 16.5 KJ) than the control group (64.4 ± 25.3 KJ) (Figure 2, upper left panel). Further, fluoroscopic time was significantly shorter in the ASV group (28 ± 5 min) as compared with the control group (33 ± 6 min) (Figure 2, upper right panel). Similarly, significantly shorter procedural duration was observed in the ASV group (109 ± 28 min) than in the control group (141 ± 38 min) (Figure 2, lower left panel).

The Kaplan–Meier survival analysis with a log-rank test revealed that the ASV group had a significantly higher AF-free rate (88%, 66 of 75) than the control group (75%, 56 of 75) during the latter 4 months of the 6-month follow-up period as the initial 2-month blanking period was excluded.

Discussion

The present results revealed that ASV with deep sedation during PVI maintained stable respiration without a decrease in oxygen saturation, eliminated pain, and patient movements which significantly decreased the energy required for the isolation, as well as fluoroscopy and procedural times, as compared with conventional conscious sedation. Further, patients who received ASV achieved a higher AF-free rate at 6 months compared with control patients. These results demonstrate the clinical efficacy of ASV during PVI in patients with PAF.

To the best of our knowledge, we were the first to apply the ASV system to attain stable and quiet respiration. In fact, respiratory compensation by the NavX system was required less frequently in the ASV than in the control group. The reliability and efficacy of ASV has been previously demonstrated in several studies, especially for patients with chronic heart failure and those with obstructive sleep apnea. The ASV system provided smooth and stable maintenance of the airway and ventilation without any decrease in arterial oxygen saturation, demonstrating its efficacy. Additional maneuvers to maintain neck position to avoid airway obstruction were required in control patients who received conventional conscious sedation while no such maneuvers were required under ASV with deep sedation. These findings revealed that ASV could effectively and safely maintain respiration during PVI procedures.

Our methods of catheter ablation for AF were essentially the same as recently described improved methods. For both control patients and patients in the ASV group, the same operators having adequate experience in PVI performed PVI within 7 months. Therefore, operator experience had no effect on the present results. The fluoroscopic and procedural times in our PVI procedures performed under conventional sedation were comparable to those in recent reports. Our ablation success rates and AF-free status for patients with conventional conscious sedation were also identical to the results of recent studies. These results for procedural parameters and clinical outcome indicate that our methods for catheter ablation of PAF were satisfactory. The clinical and echocardiographic parameters did not differ between the two groups. Data were analysed by other doctors and nurses in a blind manner. These considerations validate any comparisons between the results.

Deep sedation with analgesia under ASV diminished pain during the procedure. Reportedly, the initial success rate of PVI is 70–80%, with the remaining patients requiring additional PVI procedures. When patients experience considerable pain during the primary PVI procedure, they are more likely to hesitate undergoing a secondary procedure. Pain results in body movement that interferes with the PVI procedure; deep sedation with analgesia, by minimizing pain, is better able to prevent body movement than conventional conscious sedation. General anaesthesia, on the other hand, while allowing painless PVI, has been found to be associated with a higher incidence of oesophageal damage. This is because an increase in oesophageal temperature and the resultant oesophageal damage cause pain. One demerit of both general anaesthesia and deep sedation is diminution of the pain associated with oesophageal temperature increments, which may thus increase the likelihood of undetected oesophageal damage. Hence, to avoid oesophageal damage, oesophageal temperature was continuously monitored in our series of patients, ensuring that no oesophageal damage occurred. Thus, oesophageal temperature monitoring can overcome the demerit of painless PVI with respect to oesophageal damage.

In our study, deep sedation with ASV was performed safely without any complications related to deep sedation. The few other studies that have evaluated deep sedation for PVI have revealed similar safety as our study. These studies did not, however, use ASV. Although not during PVI, the safety of propofol administered in the absence of an anaesthesiologist has been indicated in a previous position statement paper on gastrointestinal endoscopy. The training guidelines for non-anaesthesiologist administration of propofol indicate that an airway workshop is essential to teach maintenance of respiration. In contrast, ASV does not need airway training. This is a definite clinical advantage of the use of ASV combined with deep sedation. In fact, no adverse respiratory events occurred in our series of PVI with deep sedation combined with ASV. On the other hand, few studies have definitively examined the safety and clinical utility of general anaesthesia for PVI. The efficacy of general anaesthesia for PVI procedures has not been fully clarified; further, it requires tracheal intubation and the services of an anaesthesiologist. However, since the control group in this study were patients who underwent PVI under conventional conscious sedation rather than general anaesthesia, further comparison of our results with the reported findings of general anaesthesia for PVI is not appropriate.

This study demonstrated that ASV with deep sedation significantly decreased the total energy requirements and procedural time for PVI when compared with conventional conscious sedation. Further, the ASV group showed a significantly higher AF-free rate at 6 months than the control group. The reasons for the favourable results were that ASV with deep sedation eliminated restlessness and achieved a stable respiratory cycle without deep inspiration, which enabled sufficient and successful PVI. In fact, the frequency of restlessness, respiratory compensation, and EnGuide alignment of catheter position by the NavX were lower in the ASV group than in controls. Although previous studies have evaluated the safety of deep sedation for PVI, these studies did not include a control group. These studies could, thus, not compare procedural parameters with conscious sedation. To
the best of our knowledge, this study is the first to demonstrate that ASV with deep sedation significantly improves PVI procedural parameters and the AF-free rate compared with procedures performed under conscious sedation.

Another important observation of our study was that ASV with deep sedation reduced fluoroscopy duration. PVI procedures for AF require a considerably long duration of 2–4 h, including fluoroscopy time. Although radiation exposure determined by the film-badge was within the allowable range, recent studies have recommended a reduction of radiation exposure. The present results clearly demonstrated that ASV with deep sedation has clinical benefits with respect to reduction of the duration of radiation exposure.

Limitations of this study were that analysis was performed retrospectively, and it included a relatively small number of study patients. However, the clinical backgrounds of patients in the two groups were not significantly different from each other. Careful statistical analysis provided clear differences, suggesting that an increase in the number of patients is not likely to evoke different results.

In conclusion, the present results revealed that ASV with deep sedation is a clinically effective management strategy during PVI in patients with PAF.

Conflict of interest: none declared.

References