Predictive Factors and Safety of Noninvasive Mechanical Ventilation in Combination With Propofol Deep Sedation in Left Atrial Ablation Procedures

Aneida Vevecka, PhD*, Carolina Schwab, MD, Mathias Forkmann, MD, Steffi Butz, MD, Ajmi Issam, MD, Oliver Turschner, MD, Christian Mahnkopf, MD, Johannes Brachmann, MD, and Sonia Busch, PhD

Catheter ablation is nowadays the core treatment of atrial fibrillation (AF). Propofol infusion sedation is an accepted safety strategy; however, respiratory depression with respiratory variations is frequent. Noninvasive mechanical ventilation (NIV) added to deep sedation could improve procedural safety and success. We sought to assess the predictive factors and safety of NIV in combination to propofol deep sedation in left atrial ablation procedures. Procedural data from 252 consecutive patients who underwent left atrial ablation (166 [66%] persistent, 86 [34%] for paroxysmal AF) were analyzed. Sedation with 1% propofol was used in all procedures and controlled by electrophysiologists. Arterial blood gas analysis was performed regularly during the procedure. NIV was indicated for respiratory depression with pH <7.25 and pCO_2 >50 mm Hg or agitated patient with the need for more profound sedation. No patient needed endotracheal intubation, and no procedure was abandoned due to adverse effects of sedation. NIV was used in 25 patients (10%). Predictive factors for the use of NIV were high-dose propofol sedation (p = 0.010), persistent AF (p = 0.029), prolonged procedure time (p = 0.006), increased body mass index (p = 0.008) and presence of obstructive sleep apnea (OSA; p <0.001). In a Cox regression analysis, OSA was an independent factor for NIV use (p = 0.016). In conclusion, propofol deep sedation for patients who underwent left atrial ablation is safe. Adding NIV in high-risk patients (i.e., OSA, high body mass index, and lengthy procedure duration) provides better respiratory homeostasis and could impact long-term procedure results.
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Atrial fibrillation (AF) is 1 crucial cause of cardiovascular morbidity and mortality in the world, making the treatment of this arrhythmia a real challenge.[1] Catheter ablation (CA) of AF is becoming increasingly prevalent and may be offered in selected patients as first-line therapy.[2−4] Among factors strengthening procedural safety and success, patient comfort and compliance are necessary for maintaining catheter stability. In this context, different sedation strategies varying from conscious sedation to general anesthesia (GA) have been used. In 2012, 50% of the members of the HRS/EHRA used GA for all AF ablation cases.[5] Di Biase et al[6,7] demonstrated that both conscious sedation and GA were useful for AF ablation with higher cure rates in patients who underwent GA, due to greater immobility of the patient, allowing regular and better controlled thoracic expansions, but in the expense of increased esophageal damage. Although some studies have proved that deep sedation using propofol infusion is safe, effective, and practical for use in AF ablation,[8−10] there is a concern regarding patients unintentionally slipping into anesthesia with the loss of spontaneous ventilation due to the narrow therapeutic window of propofol.[11] Trentman et al[12] found in a study of 208 patients who underwent various ablation procedures under sedation that 40% of patients required some form of intervention in the upper airways. Finding an approach for CA that prevents both inadequate sedation and the adverse respiratory effects of deep sedation is nowadays a challenge. Newly, periprocedural noninvasive ventilation (NIV) has been used to improve oxygenation and avoid GA.[13] Using NIV in this context is possible to maintain better respiratory dynamics and catheter stability during ablation, improving procedural safety and success. Thus, we investigated predictors and safety for the use of NIV in patients who underwent left atrial ablation procedures under propofol sedation controlled entirely by the operating cardiologist.

Methods

The study comprised 252 consecutive patients who underwent left atrial ablation from October 2016 to October 2017. All patients provided written informed consent. The average age of patients was 64 ± 10 years (59.5% male, 64% with persistent AF). All procedures were performed under sedation using propofol infusion without anesthesia pre-evaluation. Arterial blood gas analysis (BGA) was performed regularly during the procedure. NIV was indicated for respiratory depression with pH <7.25 and pCO_2 >50 mm Hg or agitated patient with the need for more profound sedation. Stand-by intensive medicine support was available during all

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*Corresponding author: Tel: 004917623869519.

E-mail address: aneidahodo@yahoo.com (A. Vevecka).

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procedures. Clinical data, procedural parameters, minor (persistent hypotension defined as systolic blood pressure (BP) <90 mm Hg at minimum sedation level) and major complication (pericardial effusion [PE] requiring intervention, major bleeding defined as bleeding requiring surgery or transfusion of ≥2 U or associated with a decrease in hemoglobin of ≥2.0 g/L and stroke/transient ischaemic attack (TIA)) were recorded. All data and arrhythmia recurrence besides the 3 months were analyzed to assess the safety of deep sedation with propofol infusion and the predictive factors for using noninvasive ventilation.

Patients were placed horizontally on the catheter laboratory table. Oxygen was administered through a nasal cannula starting at 4 L/min, and fentanyl (2.5 to 5 mg/kg) was administered as an analgesic. Sedation was performed by propofol infusion (bolus dose 1 to 1.5 mg/kg, maintenance 2 to 4 mg/kg/hour), which was administered and monitored by catheter lab nurses under the direction of the practicing electrophysiologist. Appropriate sedation was considered to have been achieved upon interruption of body movements and failure to respond to verbal commands. After sedation, an oropharyngeal airway tube was inserted from the outset of the procedure (Intersurgical Guedel tube). Peripheral oxygen saturation, heart rate, electrocardiogram, and invasive BP through a femoris arterial access were monitored continuously. Mean arterial pressure was conserved above 70 mm Hg during the entire procedure. In case of persistent hypotension and after exclusion of PE, propofol infusion was initially interrupted until the mean arterial pressure was ≥70 mm Hg and then resumed at the half-dose, aiming for a minimum level of sedation. Arterial BGAs were collected approximately 30 minutes after initiation of propofol infusion, and were repeated depending on peripheral oxygen saturation during the procedure. The majority of the patients obtained preprocedural a urinary catheter to measure the fluid balance. In the event of fluid retention, a bolus of furosemide (20 to 40 mg Lasix, 20 mg/ml) was administered. NIV was performed with a Respironic latex-free total face mask connected to Garbin ventilator. The ventilator settings were adjusted by serial measurement of BGA applying incorporated algorithms to improve patient-ventilator synchrony by adjusting to changing breathing patterns and dynamic leaks. I-PAP, E-PAP, and respiratory rate were modified according to the clinical response, including tolerance of the patient to obtain an exhaled tidal volume of 6 to 8 ml/kg; the FIO_2 requirement was 40% or less to maintain the oxygen saturation above 92%. The efficacy of NIV was checked with BGA every 30 minutes during the procedure. Sedation and mechanical ventilation discontinued at the end of the CA procedure.

All patients abstained from food and water on the day of the examination and underwent transesophageal echocardiography to exclude left atrial thrombus before the procedure. Access was acquired through right femoral venous cannulation under local anesthesia (lidocaine 1%). The left femoral artery was cannulated for BP monitoring purposes. The left atrium (LA) was approached with the Lasso and ablation catheter through a single transseptal puncture through a deflectable sheath (Agilis; St. Jude Medical) and a long sheath (SR0 sheath) to enhance stability. The sheaths were continuously irrigated with heparinized saline. A single bolus of 70 IU/kg of heparin was administered after left atrial access and continuous intravenous heparin was injected to maintain an activated clotting time of 280 to 350 seconds. CA procedure was performed using radiofrequency energy or cryoablation balloon ablation catheter (Arctic Front, Medtronic, Minneapolis, Minnesota). The radiofrequency ablation procedure was guided by electroanatomical mapping (NavX, St. Jude Medical Inc., Minneapolis, Minnesota or CARTO-3 mapping system, Biosense Webster, Diamond Bar, California) reconstruction of the LA. In patients with paroxysmal AF, pulmonary vein isolation (PVI) only was usually performed. In patients with persistent AF, PVI was performed and depending on the patient's characteristics, different ablation's lines, complex fractionated atrial electrograms (CFAE), or low-voltage areas ablation were added as described before.[14] Atrial tachycardias arising during the procedure were ablated according to the AT mechanism.[15] All patients were observed in a recovery unit for 240 minutes before returning to the ward. Full neurological recovery was assessed in all patients 30 minutes after completion of the procedure. All patients were kept under surveillance on the central ward after ablation for at least 1 day before discharge. Procedural documentation of all AF ablations was analyzed in detail. Baseline clinical details including basic patient demography, peripheral oxygen saturation, heart rate, electrocardiogram, and invasive BP were registered. Procedural details as total procedure time (time from induction of sedation to sheath removal), intraprocedural complication, propofol and analgesia doses were recorded. Arterial BGA was performed infrequently during the procedure. By the 3-month follow-up visits, the arrhythmia recurrence was analyzed. Primary end point included procedural safety and completion. Secondary end points included respiratory depression with the need for NIV, the presence of any other complications, and 3-month arrhythmia recurrence.

Data are extended as the mean value + standard deviation or as the median and first or third quartile if appropriate. Continuous measures were differentiated using the Student's *t* test or the rank sum test and noncontinuous variables using ×2 or Fisher's exact test to a 0.05 level of significance. A Cox regression analysis including the factors associated with NIV use was performed to assess the independent factors. A receiver-operating characteristic (ROC) curve analysis was performed to assess the correlation between propofol doses and NIV use. Statistical analysis was performed, and figures were generated with a commercially available software package (SPSS, Version 21, IBM SPSS Inc., Chicago, Illinois).

Results

The average age of patients was 64 ± 10 years, and 59.5% were male. In the majority of patients (81%), a radiofrequency ablation was performed. Most of our patients suffer from obesity and arterial hypertension. Obstructive sleep apnea (OSA) was diagnosed in 8.3% of patients before ablation (Table 1—clinical characteristics). Among the 252 patients included in the study, NIV was used in 25 patients (22 patients [90%] with respiratory depression and in 3 patients (10%) with the need for more

Table 1
Characteristics of the study sample and the differences between the 2 groups of patients

Characteristic	All patients (n = 252)	Deep sedation only (n = 227)	Deep sedation and NIV (n = 25)	p value
Age (years)	64 ± 10	64 ± 10	61 ± 8	0.1
Men	150 (59.5%)	133 (58.6%)	17 (68%)	0.036
Body mass index (kg/m^2)	31 ± 5	30 ± 5	34 ± 7	0.008
Persistent AF	161 (64%)	139 (61%)	22 (88%)	0.029
CHA2DS2-VASc scores	2,73 ± 1,41	2,76 ± 1,43	2,42 ± 1,23	0.206
Arterial hypertension	215 (85.3%)	192 (84.6%)	23 (92%)	0.059
Obstructive sleep apnea	21 (8.3%)	13 (5.7%)	8 (32%)	<0.001
Chronic obstructive pulmonary disease	17 (6.7%)	14 (6.2%)	3 (12%)	0.27
Smoking	32 (12,7%)	26 (12,1%)	6 (23%)	0,13
Left ventricular ejection fraction (%)	57 ± 11	57 ± 10	56 ± 11	0.343
Left atrial diameter (mm)	48,4 ± 5,7	48,5 ± 7,3	50,1 ± 6,6	0,25

profound sedation). None of our patients declined the NIV therapy after the insertion. The timing of the NIV insertion was 56 ± 34 minutes after propofol initiation and the average time of NIV use was 116 ± 66 minutes. No intervention was discontinued due to the side effect of sedation, and no endotracheal intubation was necessary. There were no differences regarding age, CHA2DS2-VASc score, left atrial diameter, smoking, left ventricular ejection fraction (LVEF), and presence of chronic obstructive pulmonary disease between the 2 groups of patients. NIV patients had a significantly higher body mass index (BMI) compared with patients who did not need NIV. In patients with NIV need, persistent AF and OSA were significantly more frequently diagnosed compared with the group of patients without NIV need. The mean procedure time was 184.5 ± 64 minutes and significantly longer in patients with NIV requirement compared with patients without NIV. Mean propofol dose was 639.5 ± 348.5 mg. In patients with NIV need, a higher dose of propofol was necessary to achieve the optimal sedation compared with patients without NIV need. Persistent hypotension was the common intraprocedural complication and occurred in 15% of our patients. Arterial hypotension was diagnosed significantly more frequently in patients with NIV need compared with non-NIV patients (Table 2). Under NIV, treatment was achieved a better arterial blood gas balance (Table 3). Severe complications occurred in 1.9% of patients, without difference between groups. Four patients had significant bleeding due to vascular complications (pseudoaneurysms), 3 of them were managed conservatively, and 1 had required surgical intervention. One patient had PE during the procedure and was successfully treated with percutaneous pericardiocentesis.

Regarding the early arrhythmia recurrence, 54.8% of our patients were free of arrhythmia at 3 months. Although only 44% of NIV patient was free of arrhythmia in 3 months, the difference between the 2 groups did not reach the statistical significance threshold (Table 4).

Predictive factors for the use of NIV were high-dose propofol sedation, persistent AF, prolonged procedure time, increased BMI, and presence of OSA. There was a strong correlation between propofol doses and NIV use (area under the curve (AUC) = 0.69, p = 0.002). A dose of 581 mg had the most discriminatory potential and predicted NIV use with a sensibility of 84.6% and a specificity of 54%. In a Cox regression analysis, OSA was an independent factor for NIV use (p = 0.016). Higher BMI and longer procedure time also remained essential factors (Table 5). A strong correlation was also found between procedure duration and NIV use (AUC = 0.687, p = 0.002). The point associated with the most discriminatory potential was a procedure duration of 178.5 minutes. It predicted NIV use with a sensibility of 80.8% and a specificity of 55.3%. Regarding the BMI, a value of 30.65 kg/m^2 had the most discriminatory potential and predicted NIV use with a sensibility of 80% and a specificity of 58.1% (AUC = 0.698, p = 0.001).

Discussion

In our large cohort of patients with deep propofol sedation for LA ablation, NIV use enhanced the safety of the procedure

Table 2
Intraprocedural data and the differences between the 2 groups of patients

Characteristic	All patients (n = 252)	Deep sedation only (n = 227)	Deep sedation and NIV (n = 25)	p value
Time of procedure (minutes)	184 ± 64	180 ± 63	219 ± 62	0.004
Radiofrequency energy ablation	204 (81%)	179 (78,9%)	25 (100%)	<0.001
Mean Propofol dosis (mg)	639 ± 348	617 ± 336	843 ± 394	0.01
Mean SBP basal (mm Hg)	130 ± 21	130 ± 22	127 ± 15	0.02
Intra procedural arterial hypotension	39 (15.5%)	31 (13.7%)	8 (32%)	0.008

Table 3
Arterial blood gas analysis features and the differences between the 2 groups of patients

Arterial blood gas analysis features	All patients (n = 252)	Deep sedation only (n = 227)	Deep sedation and NIV (n = 25)		p value
			Before NIV	After NIV	
Mean pH	7.29 ± 0.06	7.29 ± 0.06	7.27 ± 0.06	7,31 ± 0,04	0.03
Mean SO_2 (%)	96 ± 3	96 ± 3	95 ± 2.5	96,9 ± 1,64	0.08
Mean $PaCO_2$ (mm Hg)	48 ± 8	47 ± 7	54 ± 9	47,4 ± 7,06	0.02

Table 4
Complications and early arrhythmia recurrence—the differences between the 2 groups of patients

Characteristic	All patients (n = 252)	Deep sedation only (n = 227)	Deep sedation and NIV (n = 25)	p value
Major complication	5 (1.9%)	5 (2.2%)	0	NA
Pericardial effusion	1 (0.4%)	1 (0.4%)	0	
Stroke/TIA	0	0	0	
Major bleeding	4 (1.6%)	4 (1.7%)	0	
Early arrhythmia recurrence (AF/AT >30 s, 7 d Holter or ILR)	114 (45.2%)	100 (44.1%)	14 (56%)	0.31

Table 5
Predictive factors of noninvasive mechanical ventilation

Variable	Univariate Cox regression		Multivariate Cox regression	
	Score	p value	Score	p value
Persistent atrial fibrillation	4,039	0.044	1,430	0.232
Body mass index	12,391	<0.001	3,507	0.061
Obstructive sleep apnea	16,625	<0.001	5,767	0.016
Procedure duration	6,811	0.009	3,544	0.060
Propofol dosis	6,945	0.008	0.003	0.955

and was particularly useful in patients with OSA and higher BMI. No intervention was discontinued due to the side effect of sedation, and no endotracheal intubation was necessary. The most common intraprocedural complication was arterial hypotension, which occurred in 15% of our patients. Our data are in harmony with the findings of Salukhe et al who have demonstrated on 1,000 patients that sedation with propofol infusion is safe, effective, and practical for use in AF ablation without serious or residual complications. In this setting, intraprocedural persistent hypotension is the most common acute adverse effect (13.6%) requiring cessation of propofol in ca. 14%.[8] A complete interruption of propofol infusion was necessary for none of our patients. Recovery of arterial BP was achieved due to the propofol dose reduction or the intravenous administration of fluids. In our study, arterial hypotension was diagnosed significantly more frequently in patients with need of NIV compared with non-NIV patients, which can be explained by the high propofol dose that was needed in these patients.

Another common side effect of propofol is respiratory depression. Tang et al.[16] compared conscious sedation using midazolam/fentanyl with unconscious sedation with propofol and showed that the latter had a higher incidence of respiratory complications. The initial higher mean $PaCO_2$and lower mean pH in our patients with NIV use reflect the indication for its use. NIV allows reducing the risk of hemodynamic and respiratory complications secondary to improper ventilation in patients with respiratory depression or patients with the need for more profound sedation. The use of NIV in our study group was safe and led to a better arterial blood gas balance.

Other complications unrelated to sedation protocol and NIV use, such as PE and significant bleeding occurred in 1.9% of patients. There was no difference between the 2 groups of patients. A similar incidence of significant complications was reported. The most recent data that reflect real-life scenario come from the European EORP Pilot registry with an overall complication rate of 7.7%, of which 1.7% was major.[17]

Our data support the use of NIV during LA ablations by patients with OSA and increased BMI. It allows longer procedure duration, with a need for high-dose propofol sedation, for example, in persistent AF, without the risk of hemodynamic and respiratory complications secondary to improper ventilation. The predictive factors for NIV use during AF ablation are closely related to each other, defining a patient with a high cardiovascular profile, whereby the ablation process itself is expected to be challenging with a high risk of AF relapse after ablation. Obesity is one of the strong links between OSA and AF.[18,19] As a growing epidemic, it increases the risk of developing AF by about 50% in the general population, and the risk escalates in parallel with increased BMI, which is an independent risk factor for AF.[20−22] Despite a higher incidence of AF relapse after ablation in high-BMI patients, these patients benefit more from ablation in the context of quality-of-life improvement.[23,24] Nowadays, it is a challenge to increase the success rate of AF ablation in this growing up category of patients. In this study, we showed that a higher BMI is a predictive factor for the use of NIV during the AF ablation, and the rate of success of ablation is lower compared with patients who did not need NIV, but without achieving statistical significance. The data can be explained in the context of a better BGA balance and potentially better controlled thoracic expansions improving catheter stability in this category of patients. The most predictive independent factor for the use of NIV in our study was the presence of OSA. Of note, a systematical OSA screening was not part of our protocol. The incidence of OSA in our patient population represented only patients with established therapy at the time of the procedure. Therefore, even if OSA diagnosis might be underestimated in our study, this finding is important considering the confirmed strong association between OSA and AF.[25] Gami et al[26] showed that approximately half of the patients with AF had OSA and that this association was more significant compared with other risk factors such as BMI and hypertension. Moreover, OSA was an independent predictor of failed CA. Matiello et al[27] found that 24% of patients with AF who underwent CA had some degree of OSA and the severity of OSA influenced the success of procedure. Although it has been demonstrated that patients who underwent continuous positive airway pressure (CPAP) therapy were equal regarding the risk of AF recurrence to the non-OSA patients the impact of NIV during the CA in these patients is still unknown.[28,29] The implication of our study is to use a prophylactic NIV therapy in these high-risk patients, which improves the safety of ablation procedure and may positively affect the long-term results. These results are lacking, but our findings showed that despite the high cardiovascular risk profile of patients with NIV use, early arrhythmia recurrences as a predictor for late recurrences[30] were comparable in both groups. Of note, early recurrences were assessed using an implantable loop recorder (ILR) in 62% of patients. We conclude that adding NIV in high-risk patients (i.e., OSA, high BMI, and lengthy procedure duration) provides better respiratory homeostasis and could impact long-term procedure results.

The study has 2 main limitations. First, this is an observational and not a randomized study, comparing an alternative sedation form. Second, we are aware that the study may underestimate the actual incidence of OSA, as systematical screening for OSA was not performed. However, it provides real-world data from a large AF ablation registry.

In conclusion, propofol deep sedation for patients who underwent left atrial ablation is safe. Adding NIV in high-risk patients (i.e., OSA, high BMI, and lengthy procedure duration) provides better respiratory homeostasis, better arterial blood gas balance, and could impact long-term procedure results.

Disclosures

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