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Jakob Lüker · Arian Sultan · Tobias Plenge · Samuel Lee · Jan-Hendrik van den Bruck · Daniel Steven

Department of Electrophysiology, University Hospital Cologne, Cologne, Germany

# Effects of propofol sedation on pacing thresholds

## Results from an observational cohort study

### Background

Propofol is one of the most commonly used anaesthetic agents for surgery and sedation [1, 2]. It is also frequently used during endoscopic procedures, electrophysiology studies, and ablation procedures, as well as pacemaker and defibrillator implantation [3–8].

Propofol alters the electrophysiologic properties of the heart. Its main effects are believed to be on L-type calcium channels and potassium channels [9–11]. It caused a lengthening of the AV conduction in animal models [7, 12]. In humans, it may cause bradycardia and asystole [13].

Although the effects of other common anaesthetic agents, such as halothane, enflurane, and isoflurane, on myocardial pacing thresholds have been investigated, no influence was found [14]. To date, the effects of propofol on myocardial pacing thresholds have not been analyzed.

We sought to investigate the influence of propofol sedation on myocardial pacing thresholds in pacemaker (PM) and implantable cardioverter-defibrillator (ICD) patients in a clinical setting.

### Materials and methods

#### Inclusion criteria

Adult patients with an implanted ICD or pacemaker undergoing propofol sedation

Author contributions: J. Lüker and D. Steven designed the study. J. Lüker, A. Sultan, T. Plenge, S. Lee, and J.-H. van den Bruck collected the data and contributed to the manuscript. J. Lüker and D. Steven analyzed the data and wrote the manuscript. All authors read and approved the manuscript.

for electrophysiology (EP) study, transesophageal echocardiography (TEE), bronchoscopy, or electro-cardioversion (ECV) at the University Heart Center Cologne were included prospectively. It was mandatory for leads to be implanted for a minimum of 4 weeks. Informed consent was obtained in all patients.

#### Sedation

Patients fasted at least 6 h prior to the procedure. Propofol 1% (B. Braun Melsungen AG, Melsungen, Germany) was administered in boluses of between 0.5 mg/kg and 1 mg/kg until a Ramsay score of 5–6 (sluggish response to stimulus—no response to stimulus) was achieved [15]. Vital signs were monitored in all patients by continuous SpO<sub>2</sub>, non-invasive blood pressure measurement every 3 min, and continuous five-lead electrocardiogram (ECG). Oxygen was provided via mask or nasal tube at 2–4 l/min.

#### Device interrogation and pacing thresholds

Bipolar pacing thresholds, impedance, and sensing were assessed by device interrogation prior to sedation and after the desired sedation depth was achieved. Pacing thresholds of right atrial (RA) and (right ventricular) RV leads were assessed manually in all patients at a constant pulse duration of 0.4 ms or 0.5 ms, depending on the baseline settings. All patients were in the supine position for pre-sedation and sedation measurements.

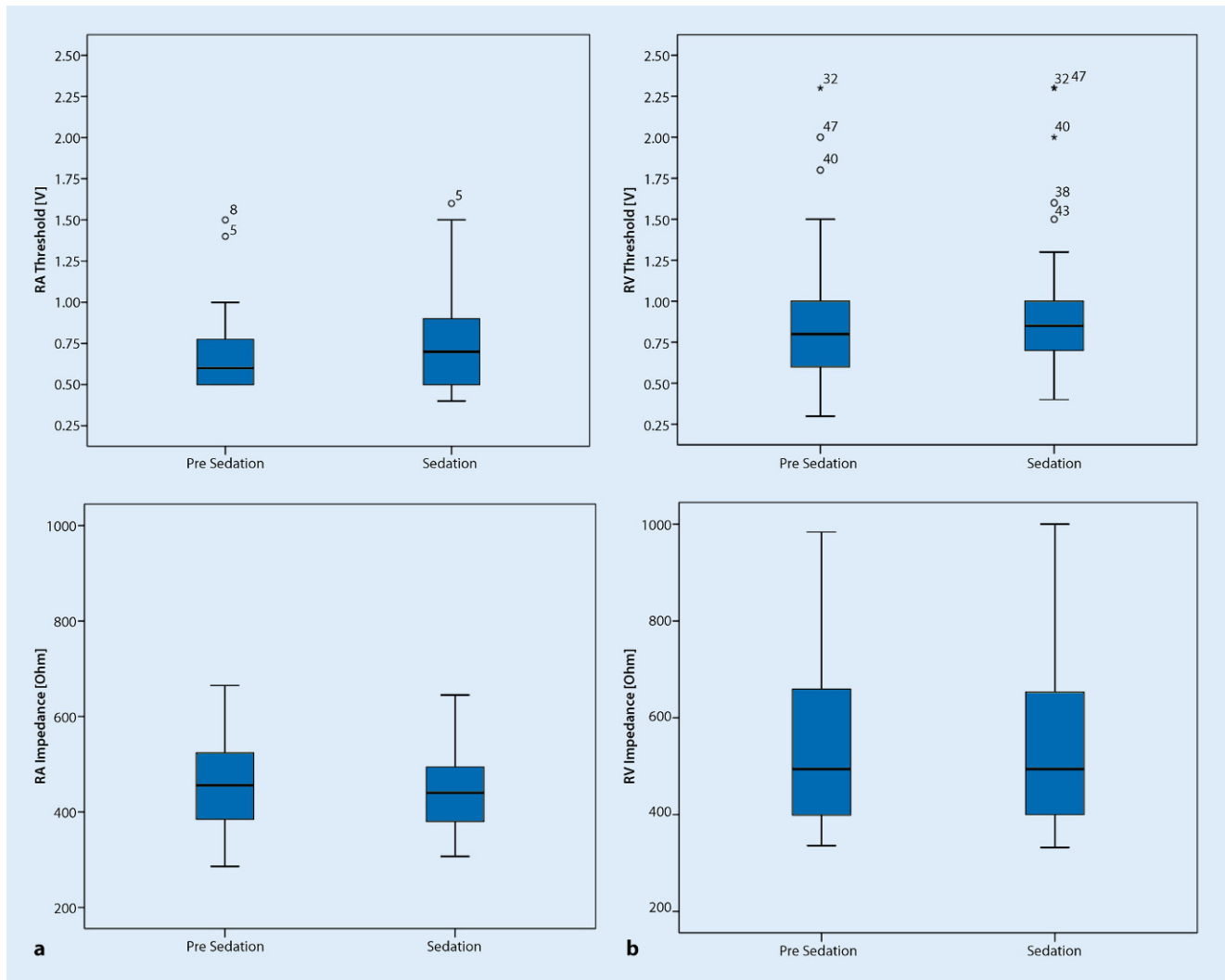
#### Study design and statistical analysis

As published data is limited, this observational study was of an explorative nature. All patients that fitted the inclusion criteria and presented over the course of 1 year (December 2014 to December 2015) were included.

Mean values of pacing threshold, sensing, and impedance prior to and during sedation were compared using a paired two-tailed student's t-test. Categorical variables expressed as numbers and percentages were compared with a Chi<sup>2</sup> test. An alpha of less than 5% was considered statistically significant. Statistical analysis was performed with SPSS Version 23 (IBM Corporation, Armonk, NY, US).

#### Abbreviations

<i>CRT</i>	Cardiac resynchronization therapy
<i>CRT-D</i>	Cardiac resynchronization therapy devices
<i>DFT</i>	Defibrillation threshold testing
<i>ECG</i>	Electrocardiogram
<i>ECV</i>	Electrocardioversion
<i>EF</i>	Ejection fraction
<i>EP</i>	Electrophysiology
<i>ICD</i>	Implantable cardioverter-defibrillator
<i>LV</i>	Left ventricular
<i>PM</i>	Pacemaker
<i>RA</i>	Right atrial
<i>RV</i>	Right ventricular
<i>TEE</i>	Transesophageal echocardiography



**Fig. 1** ▲ Pacing threshold and impedance before and under sedation for right atrial (RA) leads (a) and right ventricular (RV) leads (b)

Data are presented as means  $\pm$  standard deviation.

This study complies with the Declaration of Helsinki and the research protocol was approved by a locally appointed ethics committee.

## Results

### Patient population

Between December 2014 and December 2015, 838 patients undergoing transesophageal echocardiography (TEE), bronchoscopy, electrocardioversion (ECV), or electrophysiology (EP) study were screened. A total of 71 patients with a PM or ICD were identified; 21 patients declined to participate in the

study. The demographics and types of device of the  $n = 50$  patients included in the study are summarized in **Table 1**. In all, 21 (42%) pacemakers, 18 ICDs (36%), and 11 cardiac resynchronization therapy devices (CRT-Ds; 22%) were included. The population mainly carried chronically implanted leads older than 6 months (68% of RV and RA leads). The time since lead implantation was  $35 \pm 38$  months (min 1, max 142 months; median 24 months) for RV leads and  $39 \pm 39$  months (min 1, max 142 months; median 26 months) for RA leads. A total of 11 patients carried a CRT-D with a left ventricular (LV) lead.

### Procedures and use of propofol

The reason for propofol sedation was EP study in 28 patients, TEE in four patients, ECV in 17, and bronchoscopy in one patient. The mean dose of propofol administered until the desired sedation depth was achieved and device interrogation was performed was  $83 \pm 23$  mg ( $1.0 \pm 0.3$  mg/kg body weight), with a minimum dose of 40 mg and a maximum of 160 mg. The weight-adjusted dosage of propofol was  $>0.75$  mg/kg in 90% of patients. No adverse events occurred during sedation.

### Effects on lead parameters

Lead parameters at baseline and under sedation are summarized in **Table 2**.

J. Lüker · A. Sultan · T. Plenge · S. Lee · J.-H. van den Bruck · D. Steven

**Effects of propofol sedation on pacing thresholds. Results from an observational cohort study****Abstract**

**Background.** Propofol is one of the most commonly used intravenous anaesthetic drugs for surgical procedures. The use of propofol for sedation is also common practice during endoscopic procedures, electrophysiology studies, and ablation procedures, as well as pacemaker and defibrillator implantation. It was found that propofol alters the electrophysiologic properties of the heart and its conduction system. The effects of propofol on pacing thresholds are unknown and could have implications for pacemaker (PM) and defibrillator (ICD) implantation procedures, as well as sedation and anaesthesia in PM and ICD patients in general.

**Objectives.** We sought to investigate the effects of propofol sedation on atrial and right ventricular pacing thresholds in PM and ICD patients.

**Materials and methods.** A total of 50 patients with PM, ICD, or cardiac resynchronization therapy (CRT) undergoing propofol sedation for electrophysiology (EP) investigation, transesophageal echocardiography (TEE), electrocardioversion (ECV), or bronchoscopy were included prospectively. Pacing thresholds, impedance, and sensing were assessed by device interrogation immediately prior to sedation and after the desired sedation depth was achieved by the administration of propofol.

**Results.** Mean atrial (0.68 V vs 0.77 V,  $p = 0.136$ ) and mean right ventricular thresholds (0.90 V vs 0.93 V,  $p = 0.274$ ) remained unchanged. Impedances and sensing remained unaffected in all patients.

**Conclusions.** Propofol sedation did not affect pacing thresholds of atrial and right ventricular leads in this cohort of PM and ICD patients.

**Keywords**

Electrophysiology · Anaesthetics, intravenous · Bronchoscopy · Implantable cardioverter/defibrillator · Cardiac Resynchronization Therapy

**Effekte der Propofolsedierung auf die Reizschwellen. Ergebnisse einer Kohortenstudie****Zusammenfassung**

**Hintergrund.** Propofol gehört zu den am häufigsten verwendeten intravenösen Narkotika im Rahmen chirurgischer Eingriffe. Es wird zudem oft im Rahmen der Sedierung für endoskopische Prozeduren, elektrophysiologische Untersuchungen (EPU) und Ablationen sowie die Implantation von Herzschrittmachern (SM) und Defibrillatoren (ICD) eingesetzt. Die elektrophysiologischen Eigenschaften des Herzens werden von Propofol beeinflusst. Die Effekte auf die Reizschwelle von SM und ICD sind nicht bekannt, könnten aber Einfluss auf das Implantationsverfahren sowie auf die Sedierung und Anästhesie bei SM- und ICD-Patienten im Allgemeinen haben.

**Ziel der Arbeit.** Die Effekte von Propofol auf die atrialen und rechtsventrikulären Reizschwellen bei Patienten mit SM oder ICD wurden untersucht.

**Material und Methoden.** Prospektiv wurden 50 Patienten mit SM, ICD oder kardialer Resynchronisationstherapie eingeschlossen, die mittels Propofol im Rahmen einer EPU, transösophagealen Ultraschalluntersuchung, Elektrokardioversion oder Bronchoskopie sediert wurden. Reizschwellen, Impedanzen und Wahrnehmung wurden mithilfe einer SM/ICD-Abfrage unmittelbar vor Beginn der Sedierung und unter Propofolsedierung bestimmt.

**Ergebnisse.** Die atriale (0,68 V vs. 0,77 V,  $p = 0,136$ ) und rechtsventrikuläre Reizschwelle

(0,90 V vs. 0,93 V,  $p = 0,274$ ) blieben unter Sedierung unverändert. Ebenso zeigte sich keine signifikante Veränderung von Impedanzen und Wahrnehmung unter Sedierung.

**Schlussfolgerungen.** Die Propofolsedierung hatte keinen Effekt auf Stimulationsreizschwellen rechtsatrialer und rechtsventrikulärer Elektroden in dieser Kohorte von SM- und ICD-Patienten.

**Schlüsselwörter**

Elektrophysiologie · Intravenöse Anästhetika · Bronchoskopie · Implantierbarer Kardioverter/Defibrillator · Kardiale Resynchronisationstherapie

Right ventricular (RV) pacing thresholds remained unchanged under sedation in 19 patients (38%). RV pacing threshold was determined to be lower under sedation in 13 patients (26%), while in 18 patients (36%) it had increased when measured under sedation. Mean RV pacing threshold did not change significantly from pre-sedation ( $0.91 \pm 0.4$  V) to under sedation ( $0.93 \pm 0.43$  V;  $p = 0.274$ ; **Fig. 1**). Maximum and minimum RV threshold delta (pre-sedation to under sedation) were  $-0.5$  V and  $+0.5$  V (**Fig. 2**).

Of the 50 patients, 16 pts with an RA lead present were in sinus rhythm. The pacing threshold in the RA remained unchanged in eight patients (53%), decreased in two patients (13%), and increased in six patients (40%). The mean RA pacing threshold remained unchanged under sedation ( $0.73 \pm 0.31$  V to  $0.77 \pm 0.35$  V;  $p = 0.203$ ). The maximum and minimum RA threshold delta (pre-sedation to under sedation) was  $-0.2$  V and  $+0.25$  V.

**Differences between patients according to threshold assessment during sedation**

Comparing the group of patients with an increase in RV pacing threshold under sedation with those in whom the RV pacing threshold remained unchanged or decreased, no significant differences in baseline or lead parameters were evident (**Table 3**).

**Table 1** Baseline parameters of the study cohort according to device

	All (n = 50)	Pacemaker (n = 21)	ICD (n = 18)	CRT (n = 11)	P
Age (years)	57 ± 32	57 ± 34	56 ± 30	58 ± 33	0.868
BMI (kg/m <sup>2</sup> )	26 ± 4	26 ± 4	26 ± 6	25 ± 1	0.600
LV-EF (%)	44 ± 16	59 ± 11	42 ± 14	30 ± 8	0.031
Hypertension	30 (60%)	13 (62%)	11 (61%)	6 (55%)	0.915
Hyperlipidemia	14 (28%)	4 (19%)	6 (33%)	4 (36%)	0.479
Diabetes	12 (24%)	3 (14%)	5 (28%)	4 (36%)	0.341
Ischemic cardiomyopathy	22 (44%)	6 (29%)	5 (28%)	7 (64%)	0.134
Dilative cardiomyopathy	9 (18%)	1 (5%)	5 (28%)	3 (27%)	0.116
<i>Medication</i>					
Betablockers (%)	45 (90%)	16 (76%)	18 (100%)	11 (100%)	0.022
Amiodarone (%)	12 (24%)	1 (5%)	7 (39%)	4 (36%)	0.025
Class Ic drugs (%)	1 (2%)	1 (5%)	0	0	0.494

ICD implantable cardioverter-defibrillator, CRT cardiac resynchronization therapy, LV-EF left ventricular ejection fraction, BMI body mass index

**Table 2** Lead parameters before sedation and under sedation

	Pre-sedation	Post-sedation	P
<i>RA leads</i>			
Sensing (mV)	2.3 ± 1	2.8 ± 1.4	0.126
Impedance (Ohm)	457 ± 95	449 ± 98	0.450
Pacing threshold (V)	0.73 ± 0.31	0.77 ± 0.35	0.203
Pacing threshold delta (V)	–	+0.04 ± 0.1	–
<i>RV leads</i>			
Sensing (mV)	12 ± 6	12.3 ± 6	0.514
Impedance (Ohm)	553 ± 187	549 ± 183	0.335
Pacing threshold (V)	0.91 ± 0.4	0.93 ± 0.43	0.274
Pacing threshold delta (V)	–	+0.03 ± 0.19	–

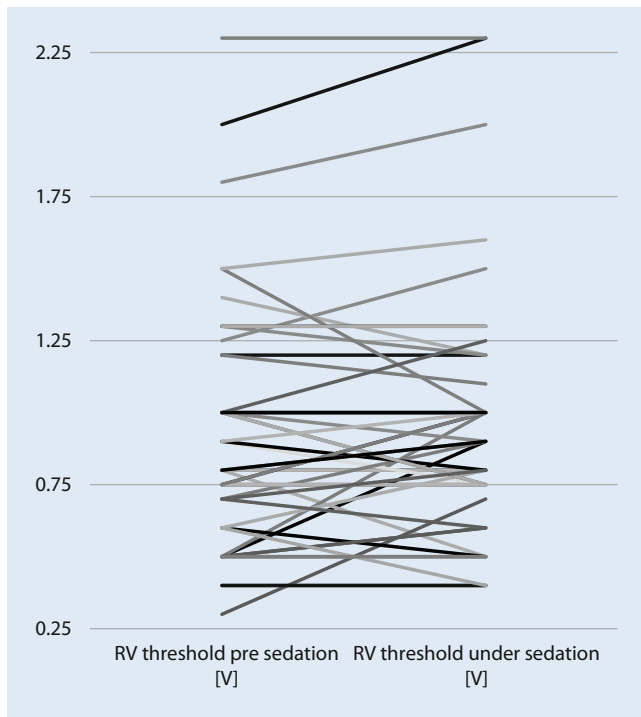
Pacing threshold delta is the change between pre-sedation assessment to assessment under propofol sedation.

RA right atrial, RV right ventricular

**Table 3** Baseline, procedural, and device parameters according to RV threshold change under sedation

	RV threshold increased (n = 18)	RV threshold unchanged or decreased (n = 32)	P
Age (years)	48.9 ± 39.7	61.7 ± 26.3	0.177
BMI (kg/m <sup>2</sup> )	25 ± 4	26 ± 4	0.517
LV-EF (%)	47 ± 16	42 ± 16	0.437
Propofol dose (mg)	78 ± 25	86 ± 22	0.232
Propofol dose per bodyweight (mg/kg)	1.02 ± 0.43	1.06 ± 0.25	0.715
<i>Device Parameters</i>			
Time since RV lead implantation (months)	27 ± 32	40 ± 42	0.364
ICD	9 (50%)	9 (28%)	0.211
Pacemaker	7 (39%)	14 (44%)	
CRT	2 (11%)	9 (28%)	
<i>Medication</i>			
Betablockers (%)	16 (89%)	29 (90%)	0.844
Amiodarone (%)	5 (28%)	7 (22%)	0.639
Class Ic drugs (%)	1 (6%)	0	0.178

BMI body mass index, CRT cardiac resynchronization therapy, ICD implantable cardioverter-defibrillator, LV-EF left ventricular ejection fraction, RV right ventricular, CRT cardiac resynchronization therapy



**Fig. 2** ◀ Line graph of right ventricular (RV) pacing thresholds of individual patients pre-sedation and under sedation

## Discussion

In this cohort of patients receiving a mean of 1 mg/kg of propofol until a Ramsay score of 5–6 was achieved, RA and RV pacing thresholds were not affected. Mean sensing and impedances of atrial, right, and left ventricular leads also remained unchanged under propofol sedation.

Thus, in this cohort of patients undergoing propofol sedation, no clinically relevant implications for PM and ICD myocardial pacing thresholds were found.

It is known that propofol has significant effects on cardiac output and systemic vascular resistance, often resulting in hypotension [3, 4, 16, 17]. Propofol sedation also affects the electrophysiologic properties of the heart. It was shown to affect calcium influx and to have negative inotropic effects in isolated myocytes [9–11]. It prolonged the intra-atrial and His-Purkinje conduction in a Langendorff rabbit heart model [12] and also in animal studies [7]. Slowing of the heart rate was observed in rabbit hearts [12] and confirmed to occur in humans [13]. In a case report, concern was raised that propofol sedation may alter the defibrillation threshold during ICD implantation and testing [18], which was not

confirmed in a small study comparing propofol versus thiopental for defibrillation threshold testing (DFT) [19].

There is a gap in the evidence to date regarding the effects of propofol on the pacing thresholds of pacemaker and ICD leads. Since propofol is a widely used anesthetic agent for endoscopic procedures [8], surgical procedures [1, 20], sedation [2], and electrophysiology procedures [4, 21], any effects on pacing thresholds may have implications for PM, ICD, and CRT patients.

This study revealed no indication of a relevant influence of propofol sedation on RA and RV pacing thresholds.

Significant effects of propofol sedation on RA and RV pacing thresholds can be excluded based on the findings presented here.

## Limitations

Thresholds were measured during bipolar pacing, and the present results may not be transferrable to unipolar pacing. The effects of higher doses of propofol and deeper sedation, such as during induction of general anaesthesia, on pacing thresholds remain to be investigated.

## Conclusions

Propofol sedation does not affect RA and RV myocardial pacing thresholds in pacemaker and ICD patients.

## Corresponding address

**J. Lüker, MD**

Department of Electrophysiology, University Hospital Cologne  
Kerpener Straße 62, 50823 Cologne, Germany  
jakob.lueker@uk-koeln.de

## Compliance with ethical guidelines

**Conflict of interest.** J. Lüker, A. Sultan, T. Plenge, S. Lee, J.-H. van den Bruck, and D. Steven declare that they have no competing interests.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. Ethics approval was obtained from the ethics committee of the University Hospital Cologne (ref. nr 14-418) and all patients gave informed written consent. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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