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# Respiratory Acidosis during Procedural Sedation and Analgesia for Pulmonary Vein Isolation: A Prospective Observational Study

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## Abstract

**Background:** Pulmonary vein isolation is widely performed under procedural sedation and analgesia (PSA). During PSA, depth and rate of ventilation are decreased which can lead to alveolar hypoventilation, resulting in increased arterial CO<sub>2</sub> levels and respiratory acidosis. This study aims to investigate the degree of respiratory depression and resulting respiratory acidosis under routine pulmonary vein isolation procedures.

**Methods and findings:** We performed a single center prospective observational study at the cardiac catheterization unit of the Radboud University Medical Centre between October 2019 and September 2020. Twenty patients, aged between 18 and 80 years, ASA 2, scheduled for pulmonary vein isolation with PSA were included. Medication used to maintain adequate PSA was limited to propofol and remifentanyl. We performed blood gas analysis before the start of PSA and every 30 minutes during PSA and recovery.

Procedural times varied considerably with a median of 50 (range 30-290) minutes. The concentration of arterial CO<sub>2</sub> increased significantly within 30 minutes from  $4.81 \pm 0.66$  kPa to  $7.13 \pm 0.84$  kPa. Thereafter, no further increase in CO<sub>2</sub> was observed. The PH decreased proportionally, from  $7.43 \pm 0.06$  to  $7.29 \pm 0.03$  and remained stable throughout the procedure until the end of PSA. After cessation of PSA, CO<sub>2</sub> normalized to baseline with 30 minutes.

**Conclusion:** During pulmonary vein isolation procedures performed with PSA a significant increase in CO<sub>2</sub> levels was found. This hypercapnia resulted in a respiratory acidosis in all patients, which stabilized within 30 minutes. Longer procedure times do not lead to higher CO<sub>2</sub> levels.

**Keywords:** Acute ischemia; Aorta; Coarctoplasty; Infra-renal coarctation; Middle aortic coarctation (MAC); Toe

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## Introduction

Pulmonary vein isolation is widely performed under procedural sedation and analgesia (PSA). PSA aims to relieve anxiety, discomfort and pain during the procedure using hypnotic and/or analgesic medication. The hallmark of PSA is that spontaneous breathing and a patent airway are preserved despite a depressed level of consciousness. During PSA, the depth and rate of ventilation are decreased because of depression of respiratory control centres [1]. This can lead to alveolar hypoventilation,

resulting in an increased arterial CO<sub>2</sub> levels and respiratory acidosis [2,3]. Acidosis can lead to myocardial suppression and arrhythmias [4]. Practice guidelines advise the use of capnography to facilitate early detection of respiratory depression [1,5]. The use of capnography greatly enhances the safety of PSA by warning of respiratory complications [6].

However, capnography during PSA is not an accurate technique for detecting hypercapnia because there is considerable mixing of room air in the sampling when not using an endotracheal

tube. The gold standard for assessing respiratory status remains arterial blood gas analysis. Although there are no obvious adverse effects of short-term respiratory acidosis, it is not a physiologically normal condition. This study aims to investigate the degree of respiratory depression and resulting respiratory acidosis over time in routine pulmonary vein isolation procedures.

## Methods

This single centre prospective observational study was performed at the cardiac catheterization unit of the Radboud University Medical Centre, Nijmegen, and The Netherlands. Ethical approval for this prospective observational study was given by the Medical Ethical Committee CMO Arnhem-Nijmegen, The Netherlands (Chairperson R. Dekhuijzen) on May 9, 2019 (METC nr 2019-5211). All the procedures were performed in accordance with the Declaration of Helsinki.

## Patients

Patients eligible for this study were all adult patients that were scheduled for pulmonary vein isolation under PSA. Patients were consecutively included between October 2019 and September 2020. Exclusion criteria were ASA classification 3 or higher, body mass index over 30 or fewer than 18, age above 80, having been diagnosed with obstructive sleep apnoea syndrome, COPD or asthma or known bleeding disorders. Inclusions stopped after reaching 20 participants.

## Study protocol

Patients were included after written informed consent. Before the start of the procedure, we inserted an intravenous cannula. Throughout the procedure patients were monitored with pulse oximeter, non-invasive arterial blood pressure measurements and continuous ECG. In addition an arterial cannula was placed in all patients. These were placed in the radial artery under local anaesthesia and ultrasound guidance by a physician or a physician assistant. The PSA was provided by a qualified physician assistant, under supervision of an anaesthesiologist. Before starting PSA, low-flow supplemental oxygen delivery was started through a nasal cannula with a side port allowing CO<sub>2</sub> sampling. EtCO<sub>2</sub> and the capnography waveform were monitored throughout the procedure for early detection of changes in ventilation.

For PSA we used propofol and remifentanyl in a dose range of 4-8 mg.kg.hr<sup>-1</sup> and 0.01-0.05 µg.kg.min<sup>-1</sup> respectively. No other sedatives were administered. The PSA depth was estimated

using the Ramsay sedation scale and maintained at 5-6 [7,8]. Upper airway obstruction was managed with manual airway manoeuvres, placement of an oral pharyngeal airway (OPA) device or nasal pharyngeal airway (NPA) device. If apnoea persisted despite a patent airway, PSA depth was reduced and ventilation was supported through facemask ventilation until spontaneous breathing recovered.

The data recorded included patient characteristics, the start and end times of PSA (determined as starting and stopping of propofol infusion) and arterial blood gas analyses. Blood gas analysis was performed before starting PSA, and every 30 minutes during the PSA. At the end of the PSA, a sample was taken at the moment propofol was stopped, and after 30 and 60 minutes.

The recorded blood gas values were pH, pCO<sub>2</sub>, pO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>, base excess and lactate. Other data recorded were heart rate (HR), blood pressure (BP) and oxygen saturation as measured by pulse-oximeter (SpO<sub>2</sub>). All blood gas measurements were made using a point-of-care analyser (i-STAT<sup>®</sup>, Abbott, CG4+-cartridges).

## Statistical analysis

The primary outcome of this study was the change in arterial CO<sub>2</sub> over time compared to baseline measurement during prolonged PSA. Secondary outcomes were changes in arterial pH and other blood gas parameters. Data are expressed as mean ± SEM, or median (range), depending on their distribution. Differences over time between groups were analysed with repeated measures two-way analysis of variance (ANOVA), providing that data were normally distributed. In the case of non-normally distributed data, we compared the areas under the concentration-time curve using Mann-Whitney U tests. Differences in group means or medians were tested with Student's t-tests for parametric data or Mann-Whitney U tests for non-parametric data. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA) and Graphpad Prism, version 5.03 for Windows (GraphPad Software, San Diego California USA, www.graphpad.com).

## Results

Demographic data are presented in Table 1.

Twenty patients were included in the study. All patients underwent an uneventful pulmonary vein isolation procedure. Procedure times varied considerably with a median of 50 (30-290) minutes. In most patients (85%) the procedures took 80 minutes or less, while in 3 patients, procedure times were much longer

**Table 1:** Baseline characteristics of patients undergoing pulmonic vein isolation under PSA.

	Total (n=20)
Age (Year)	61 ± 7.4
Male (n)	17 (85%)
Weight (kg)	84.0 ± 9.8
BMI	25.5 ± 2.3
ASA 2 (n)	20 (100%)

Data are presented as number (n) or as mean ± SD

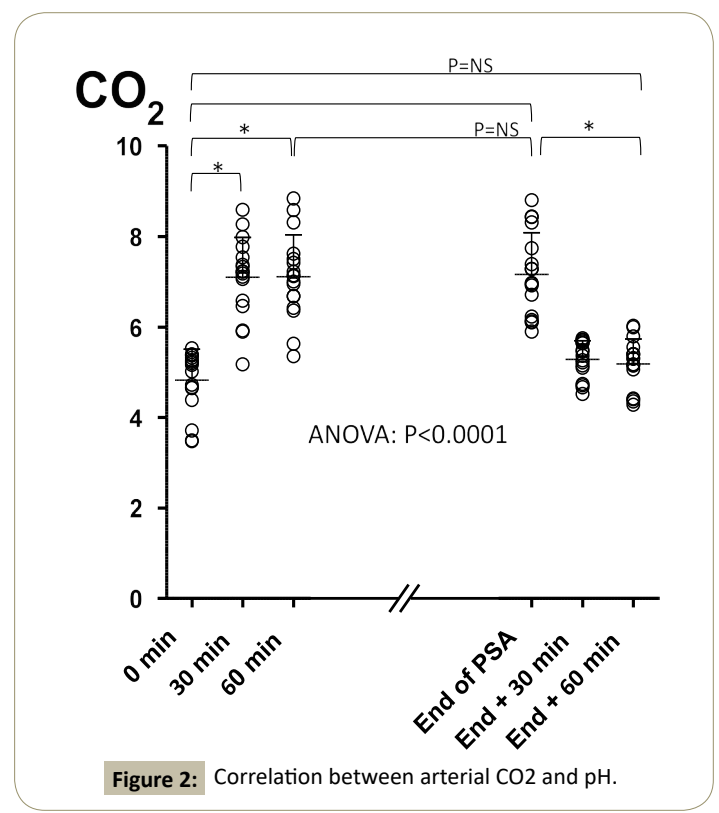
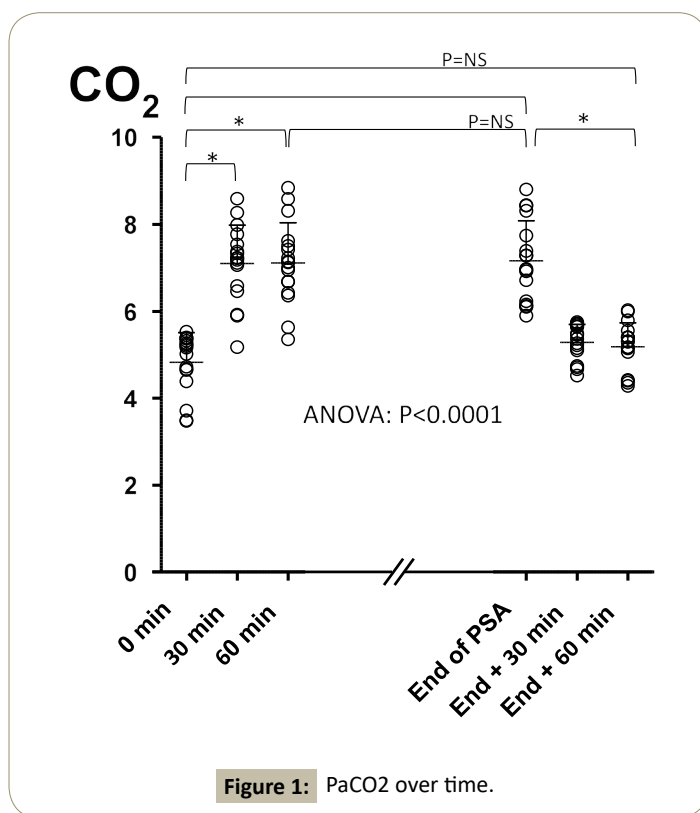
(122-290 minutes). All patients awoke promptly after propofol and remifentanyl administration were ceased, irrespective of the duration of the procedure. At the time of the intraoperative blood gas analysis, all patients had a Ramsay score of 5-6. We were able to maintain an open airway at all time and no persistent apnoea was observed.

The concentration of arterial CO<sub>2</sub> increased significantly within 30 minutes from  $4.81 \pm 0.66$  kPa at the start of PSA to  $7.13 \pm 0.84$  kPa at t=30 min (Figure 1). After that no further increase in CO<sub>2</sub> was observed. In the 3 patients with extended procedure times, no increase was noted compared with t=30 min. No correlation was found between procedure time and arterial CO<sub>2</sub> at the end

of the procedure (Spearman  $r=0.33$ ,  $P=0.19$ ). In addition, no correlation was found between remifentanyl or propofol dose and CO<sub>2</sub> at T=30 and T=60 minutes. After cessation of PSA, CO<sub>2</sub> normalized to baseline with 30 minutes.

As expected, pH decreased proportionally, from  $7.43 \pm 0.06$  at baseline to  $7.29 \pm 0.03$  at t=30 min, and remained stable throughout the procedure until the end of the PSA. There was a good correlation between arterial CO<sub>2</sub> and pH (Spearman  $r = -0.87$ ) indicating that acidosis was primarily caused by respiratory depression (Figure 2).

Other blood gas parameters are displayed in Table 2, dosages of medication are displayed in Table 3.



**Table 2:** Blood gas analyses throughout PSA.

	start PSA (n=18)	30 min (n=19)	60 min (n=20)	end PSA (n=20)	30 min after end PSA (n=20)
pH	$7.43 \pm 0.06$	$7.29 \pm 0.03$	$7.29 \pm 0.04$	$7.30 \pm 0.04$	$7.40 \pm 0.04$
pCO <sub>2</sub> (kPa)	$4.81 \pm 0.66$	$7.13 \pm 0.84$	$7.06 \pm 0.87$	$7.16 \pm 0.86$	$5.28 \pm 0.39$
pO <sub>2</sub> (kPa)	$13.08 \pm 1.75$	$18.59 \pm 8.69$	$19.85 \pm 8.22$	$16.77 \pm 5.66$	$11.56 \pm 1.95$
HCO <sub>3</sub> <sup>-</sup> (mmol/l)	$23.73 \pm 2.24$	$25.50 \pm 2.34$	$25.62 \pm 2.45$	$26.13 \pm 2.75$	$24.64 \pm 2.25$
BE (mmol/l)	$-1.18 \pm 1.91$	$-1.28 \pm 2.45$	$-0.90 \pm 2.57$	$-0.89 \pm 2.11$	$-0.67 \pm 1.68$
Lactate (mmol/l)	$1.08 \pm 0.43$	$0.85 \pm 0.46$	$0.66 \pm 0.33$	$0.83 \pm 1.14$	$0.66 \pm 0.30$

Data are presented as mean  $\pm$  SD

**Table 3:** dosages of medication throughout PSA.

	30 min	60 min
Propofol (mg.kg.h <sup>-1</sup> )	$6.08 \pm 1.05$	$5.46 \pm 1.06$
Remifentanyl ( $\mu$ g.kg.min <sup>-1</sup> )	$0.018 \pm 0.008$	$0.017 \pm 0.006$

Data are presented as mean  $\pm$  SD

## Discussion

This prospective observational study shows a significant increase in arterial CO<sub>2</sub> levels in pulmonary vein isolation performed under PSA. This hypercapnia resulted in a respiratory acidosis in all patients and which remained constant throughout the procedure. During PSA, airway patency was maintained by routine use of oropharyngeal airways, and capnography was used to detect any airway obstruction. The increased PaCO<sub>2</sub> was therefore due to a decreased depth and rate of ventilation by depression of respiratory control centres. CO<sub>2</sub> levels rose and stabilized after 30 minutes indicating a new set point in the respiratory control centre. This is in concordance with a previous study in which a statistically significant PaCO<sub>2</sub> increase was shown as soon as 5 minutes after starting PSA levelling off after 10 minutes.

During PSA, EtCO<sub>2</sub> monitoring is advised to monitor ventilation in order to prevent unnoticed CO<sub>2</sub> retention. In this study, we demonstrated that CO<sub>2</sub> retention is present in all patients during pulmonary vein isolation under PSA, also in patients with a patent airway who are breathing spontaneously throughout the procedure. A PaCO<sub>2</sub> > 6 kPa is common during PSA [9]. It occurs more often in patients who receive supplemental O<sub>2</sub> [10]. The degree of CO<sub>2</sub> increase depends on the depth of the sedation and the sedatives used. A previous study in patients under moderate or conscious sedation (Ramsey sedation score of 3) showed that sedation with dexmedetomidine and fentanyl or remifentanyl resulted in a median PaCO<sub>2</sub> of 5.32 (4.80-6.00) kPa, whereas patients sedated using propofol had a PaCO<sub>2</sub> of 5.86 (5.33-6.53) kPa [11,12]. When a combination of fentanyl and midazolam was used to achieve a Ramsey sedation score of 3, PaCO<sub>2</sub> reached levels between 5.5 and 7 kPa [10]. In our study, PaCO<sub>2</sub> increased to 7.13 ± 0.84 kPa, which is likely due to a deeper level of sedation in this study, corresponding with a Ramsey score of 5 to 6. Regardless of the duration of the procedure and PaCO<sub>2</sub> concentration, post-procedural arterial blood gas values in our patients normalized within 30 minutes after stopping propofol infusion.

The hypercapnia during the procedure had no apparent negative consequences for the patients in this study. The effects of permissive hypercapnia in critically ill patients with severe respiratory failure are well described [13], but to our knowledge there has been no previous research into the effects of short-term hypercapnia and acidosis.

Limitations of our study include the single-centre prospective observational study design. Furthermore, the physician assistants who administered the sedation were not blinded to the results although the results did not lead to any change in the PSA. Only three patients underwent an extended PSA procedure, the majority of the procedures were completed within 90 minutes. The interval between measurements chosen is too large to indicate precisely how fast the new respiratory equilibrium is reached and how fast the patient recovers from the hypercapnia after the procedure. Finally, patients with respiratory problems such as obstructive sleep apnoea syndrome, COPD or asthma, were excluded from our study, but further research into the effects of PSA on the respiratory drive is warranted to assess the safety of deep PSA in these patients.

## Conclusion

During pulmonary vein isolation procedures performed with PSA a significant increase in CO<sub>2</sub> levels was found. This hypercapnia resulted in a respiratory acidosis in all patients, which stabilized within 30 minutes. Longer procedure times did not lead to higher CO<sub>2</sub> levels.

During pulmonary vein isolation procedures performed with PSA a significant increase in CO<sub>2</sub> levels was found.

## Declarations

### Availability of data

Data is available on request from the authors.

### Funding

Departmental funding only

### Conflicts of interest

None to declare

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