ORIGINAL RESEARCH

Synchronized mandibular movement and capnography: a novel approach to obstructive airway detection during procedural sedation—a post hoc analysis of a prospective study

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Abstract

Perioperative complications related to obstructive sleep apnea still occur despite the use of partial pressure end-tidal CO_2 $\left(P_{ETCO_2}\right)$ and pulse oximetry. Airway obstruction can complicate propofol sedation and a novel monitor combining mandibular movement analysis with capnography may facilitate its detection. Patients scheduled for sleep endoscopy were recruited and monitored with standard monitoring, P_{ETCO_2}, and Jaw Activity (JAWAC) mandibular movement sensors. A post hoc analysis investigated airway obstruction prediction using a Respiratory Effort Sequential Detection Algorithm (RESDA) based on P_{ETCO_2} and mandibular movement signals. 21 patients were recruited and 54 episodes of airway obstruction occurred. RESDA detected obstructive apnea [mean $\pm$ SD (median)] 29 ± 29 (21) s, $p < 0.0001$, before P_{ETCO_2} alone. This prolonged the time between obstructive apnea detection and decrease to 90% oxygen saturation 64 ± 38 (54) versus 38 ± 20 (35) s, $p < 0.0001$. It predicted airway obstruction with a sensitivity and specificity of 81% and 93%, respectively. The RESDA algorithm, which is based on the combination of capnography with mandibular movement assessment of respiratory effort, can more rapidly alarm anesthetists of airway obstruction during propofol sedation than P_{ETCO_2} alone. However, P_{ETCO_2}, pulse oximetry, and clinical monitoring are still required.
Trial Registry numbers: ClinicalTrial.gov (NCT02909309) https://clinicaltrials.gov/ct2/show/NCT02909309.

Keywords Perioperative medicine · Monitoring · Postoperative complications · Respiratory insufficiency · Obstructive sleep apnea syndrome · Anesthesia

1 Introduction

Propofol sedation can produce airway collapse in patients at risk of developing obstructive sleep apnea [1]. Although it is the desired effect in sleep endoscopy, this technique can cause airway obstruction, hypoventilation, and hypoxemia in other procedures requiring sedation [2]. American and European anesthesia societies recommend partial pressure of end-tidal CO_2 $\left(P_{ETCO_2}\right)$, i.e. capnography, as the monitor of choice for detecting obstructive apnea during sedation [3–5]. Unfortunately, P_{ETCO_2} does not always detect obstruction in time to allow physicians to prevent potentially life-threatening complications [1, 2]. Novel technologies capable of quantifying respiratory effort, however, may bridge the gap in time from obstruction to detection.

The Brizzy mandibular movement analysis system (Nomics, Belgium) provides a sinusoidal Jaw Activity (JAWAC) signal that corresponds to respiratory effort [6, 7]. During airway obstruction, increased respiratory effort appears with increasing flow limitation. JAWAC activity has been shown to correspond with respiratory effort during obstructive sleep apnea and has been validated against diaphragmatic electromyography [6]. However, mandibular movements are not specific to respiratory effort and can occur, for example, with facial movement following nociception or manual manipulation of the airway. Using both JAWAC and P_{ETCO_2} simultaneously may rapidly detect airway obstruction. The Respiratory Effort Sequential Detection Algorithm (RESDA), which integrates data from these two signals, is a prototype monitor which was developed to detect airway obstruction during sedation.

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The goal of this pilot study was to determine if the proposed RESDA threshold could reliably detect airway obstruction (e.g. obstructive apnea) more rapidly than P_{ETCO_2} alone. The secondary goal was to evaluate if RESDA would increase the time from detection of airway obstruction to oxygen desaturation.

2 Methods

This prospective pilot study took place at the Erasme Hospital in Brussels, Belgium, was approved by the local ethical committee, and was registered on ClinicalTrial.gov (NCT02909309) (principal Investigator Nicolas Ponthieu; date of registration: on September 21st, 2016). The article adheres to the STROBE guidelines as well as the 1964 Helsinki declaration and its later amendments. Patients gave written consent and participated in the study from March 1st to July 31st, 2017. They were adults suspected of having obstructive sleep apnea. Patients were excluded if they refused to participate, were underage, had facial burns, or had a history of jaw or thoracic surgery. Since this was a pilot study, a small group of 21 patients was considered sufficient.

2.1 Anesthesia technique

No premedication was given before the procedure. Patients were placed in supine position. A bispectral index sensor (BIS Extend, Medtronic, Belgium) was placed on the patient's forehead and an Agilia V4e infusion device (Fresenius, Germany) administered Propofol target-controlled infusion (TCI) sedation using the Marsh pharmacokinetic model [8]. The initial target propofol plasma concentration was started at 2 μg ml^{-1}. When the effect site concentration was attained, the plasma concentration was progressively increased by 1 μg ml^{-1} to reach a BIS value of 60. This sedation simulates sleep adequately for obstructive airway assessment [9]. All patients received 2 l min^{-1} of oxygen through nasal cannula. If oxygen saturation decreased below 90%, jaw-thrust and chin-lift techniques were applied to release airway obstruction.

2.2 Monitoring and data collection

The Brizzy Mandibular Movement Magnetic Sensor System (Nomics, Belgium) measured and recorded mandibular movement (i.e. the JAWAC signal). This sensor consists of parallel coupled resonant circuits positioned on the patient's chin and forehead. The currents of each emitter circuit generates pulsed magnetic waves. The sensor circuits detect changes in magnetic field which correlate with jaw movements and give an instantaneous assessment of mandibular

movement. Measurement resolution is 0.05 mm. The CapnoLine sensor (FilterLine, Family of P_{ETCO_2} sampling lines, Medtronic, Belgium), connected to the monitoring system (Ohmeda S/5 Anesthesia Monitor, Datex, GE Healthcare, Finland) measured P_{ETCO_2} and administered oxygen.

The Computer Assisted Sedation Comfort Kit (CASCK) software (Nomics, Belgium) was specifically designed for this study and collected on a single multi-graph file screen intraoperative data including pulse oximetry, propofol infusion rate, P_{ETCO_2}, and mandibular movement. Apios software (Nomics, Belgium) then checked for consistency and analyzed the recordings. Apios identified and highlighted in pink the zones that corresponded to the defined criteria for respiratory effort (Fig. 1).

RESDA combines mandibular movement analysis with capnography to predict airway obstruction. CASCK software collected data and the Apios software measured JAWAC frequency, P_{ETCO_2} frequency, and the mandibular movement amplitude. The respiratory effort threshold for RESDA required fulfillment of the following three criteria for six seconds (s): sinusoidal-like mandibular movement pattern, mandibular movement amplitude > 0.15 mm, and mandibular movement frequency equal to P_{ETCO_2} frequency (Fig. 2). Each criterion gives a yes/no answer. Investigators visually assessed the results from the Apios analysis and determined if all three criteria were present. If so, the algorithm was positive for airway obstruction. JAWAC and P_{ETCO_2} signals were recorded at 10 samples per second (sps) and 25 sps, respectively. Mathematical morphology methods were used to determine maxima and minima zones. The intervals between these extrema were then used to calculate frequency signals. Worst case precision of period calculation concerned the JAWAC signal and can be estimated to 0.2 s. For respiration frequencies between 0.15 and 0.5 Hz, this represents an error from 1.3 to 10%. A median filtering with a window length of 6 s was performed on both frequency signals. The equality of JAWAC and P_{ETCO_2} frequencies was determined with an allowed difference of 15%. Distance measured by the JAWAC sensor is computed 10 times per second. No further filtering was perfomed on this signal.

2.3 Outcome definitions

Oxygen desaturation was defined as pulse oximetry under 90%. Start of oxygen desaturation was defined as the moment when pulse oximetry began to decrease progressively from its baseline value towards its lowest value. The proposed respiratory effort threshold, defined by RESDA, was passed if the following conditions were fulfilled for at least 6 s: sinusoidal-like mandibular movement pattern, mandibular movement amplitude > 0.15 mm, and mandibular movement frequency equals P_{ETCO_2} frequency. Obstructive apnea was defined as a period of at least 10 s absence of P_{ETCO_2} signal
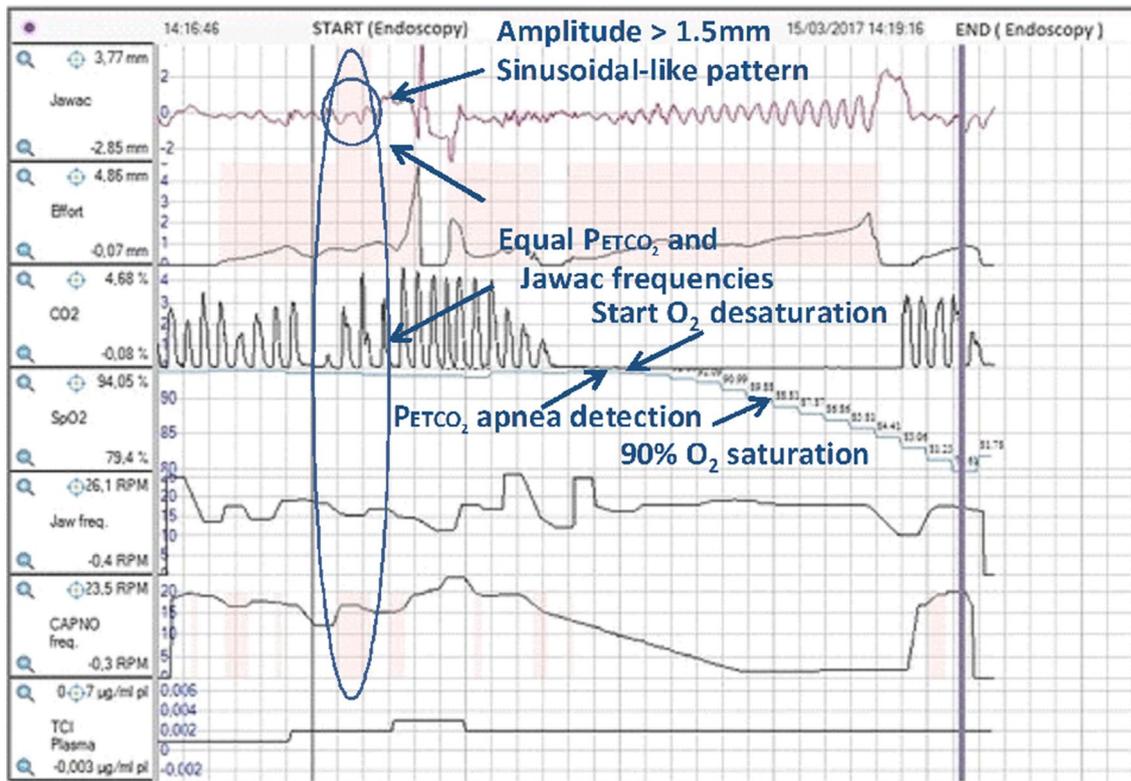
Fig. 1 Prediction of obstructive apnea using RESDA. RESDA is based on P_{ETCO_2} and mandibular movement. CASCK software collected data and Apios software measured JAWAC frequency, P_{ETCO_2} frequency, and the mandibular movement amplitude. Respiratory effort was detected when the following conditions were present: sinusoidal-like mandibular movement pattern, mandibular movement amplitude is > 0.15 mm, and mandibular movement frequency equals P_{ETCO_2} frequency. Obstructive apnea was defined as a period of at least 10 s loss of P_{ETCO_2} signal. Oxygen desaturation was defined as pulse oximetry under 90%. Start of oxygen desaturation was defined as the moment when pulse oximetry begins to decrease progressively from its baseline value towards its lowest value. CASCK Computer Assisted Sedation Comfort Kit RESDA Respiratory Effort Sequential Detection
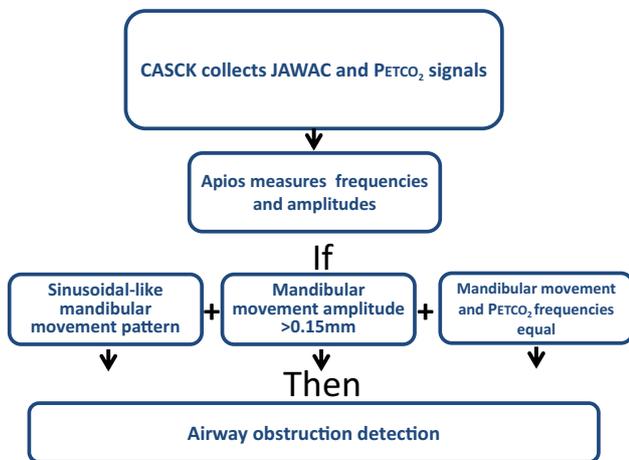
Fig. 2 RESDA flowchart. RESDA is based on P_{ETCO_2} and mandibular movement. Respiratory effort is detected when the following conditions are present: sinusoidal-like mandibular movement pattern, mandibular movement amplitude is > 0.15 mm, and mandibular movement frequency equals P_{ETCO_2} frequency. The equality of JAWAC and P_{ETCO_2} frequencies was determined with an allowed difference of 15%. CASCK Computer Assisted Sedation Comfort Kit RESDA Respiratory Effort Sequential Detection

associated with oxygen desaturation and airway obstruction was defined as any episode of desaturation associated with either a 10 s loss of etCO$_2$ or positive RESDA signal (i.e. obstructive apnea and hypopnea).

The RESDA algorithm was applied post hoc and gave a binary answer. Several time intervals were studied when both RESDA and P_{ETCO_2} predicted airway obstruction. Studied intervals were time from RESDA prediction to P_{ETCO_2} obstructive apnea detection, time from either RESDA prediction or P_{ETCO_2} obstructive apnea detection to start of desaturation, and time from either RESDA prediction or P_{ETCO_2} obstructive apnea detection to 90% saturation.

2.4 Statistical analysis

Time from RESDA prediction to P_{ETCO_2} obstructive apnea detection, start of oxygen desaturation, and time to 90% oxygen saturation were calculated for all patients. Sensitivity and specificity to predicted obstructive apnea was determined for RESDA and Cohen's Kappa Correlation Coefficient was used to define the agreement between RESDA and

P_{ETCO_2}. Wilcoxon matched-pairs signed rank test evaluated continuous variables. Systat v 5.0 for DOS (Systat Software, Inc., Chicago, IL, USA) software was used for statistical analysis. A p-value of 0.05 is considered statistically significant. Since this was a pilot study and no preliminary data was available, no power analysis was undertaken. There was no missing data.

3 Results

Of the 21 patients recruited, 19 developed airway obstruction. Baseline characteristics were determined at the preanesthesia consultation and can be found in Table 1. Overall, 54 obstructive airway episodes occurred during propofol TCI sedation. RESDA detected 44 episodes of airway obstruction, three of which were not detected by P_{ETCO_2}. In the 41 cases where both P_{ETCO_2} and RESDA detected airway obstruction, RESDA detected obstructive apnea before P_{ETCO_2} in every case except one [mean ± SD (median)] 29 ± 29 (21) s versus 0 ± 0 (0) s, p < 0.0001. RESDA sensitivity and specificity were 81% and 93%, respectively, for prediction airway obstruction. The Cohen's Kappa correlation was 0.68, indicating good agreement [10].

Since RESDA detected airway obstruction before P_{ETCO_2}, there was an increase in time from detection to start of desaturation [mean ± SD (median)] 29 ± 29 (22) versus 0 ± 24

(7) s, p < 0.0001, and 90% saturation 64 ± 38 (54) versus 38 ± 20 (35) s, p < 0.0001.

4 Discussion

In this pilot study, RESDA detected episodes of airway obstruction during propofol sedation for sleep endoscopy with a sensitivity and specificity of 81% and 93%, respectively. This novel monitor detected airway obstruction before capnography and prolonged the time from detection of obstruction to desaturation. Patients who receive supplemental oxygen can have normal pulse oximetry signal even after the loss of P_{ETCO_2} due to obstructive apnea [11–13]. This is contrary to our results, however, and may be due to the short duration and low flow of supplementary oxygen which were inadequate to compensate hypoventilation in our patient population. In the 41 obstructive apneic episodes detected by both RESDA and etCO2, RESDA predicted airway obstruction an average of 29 s before P_{ETCO_2} alone. This period of roughly half a minute may have corresponded to hypopnea, which decreased oxygen reserves and led to rapid desaturation upon onset of apnea. Hypopnea seems to have occurred in the three episodes of airway obstruction predicted by RESDA alone. Although RESDA was unable to predict 10 episodes of obstructive apnea, its capability to detect obstructive hypopnea and apnea is an advantage

Table 1 Baseline characteristics of included patients	Patient number	Age	Weight	Height	BMI	Male gender	ASA score
	1	63	75	1.75	24.5	1	2
	2	50	87	1.79	27.2	1	2
	3	46	73	1.60	28.5	0	2
	4	53	82	1.70	28.4	1	2
	5	41	60	1.68	21.3	0	2
	6	57	85	1.67	30.5	1	2
	7	39	108	1.73	36.1	0	2
	8	69	65	1.71	22.2	1	2
	9	54	83	1.65	30.5	0	2
	10	45	90	1.85	26.3	1	2
	11	49	93	1.73	31.1	1	2
	12	27	82	1.82	24.8	1	2
	13	60	95	1.58	38.1	0	2
	14	28	95	1.74	31.4	1	2
	15	47	98	1.78	30.9	1	2
	16	47	75	1.65	27.5	0	2
	17	41	70	1.69	24.5	1	2
	18	32	95	1.87	27.2	1	2
	19	53	80	1.72	27.0	1	2
	20	47	75	1.59	29.7	0	2
	21	65	74	1.74	24.4	1	2

of JAWAC technology and could prove useful in the future. Mandibular movement analysis has been shown to be reliable in detecting obstructive apnea during sleep lab tests [6, 7] and our results indicate that there is considerable potential in combining mandibular movement and P_{ETCO_2} during propofol sedation to rapidly detect airway obstruction.

This post hoc analysis of a prospective study had several strengths and limitations. It is the first study to show the potential of RESDA during procedural sedation, it compares RESDA to the recommended respiratory monitor (i.e. P_{ETCO_2}), and it shows that RESDA can detect apnea before P_{ETCO_2} and pulse oximetry. Although it is a post hoc analysis, this study was initially planned to determine a posteriori an appropriate threshold for apnea detection with RESDA since no previous study had investigated this issue. Another limitation is that we defined apnea as a 10 s drop in P_{ETCO_2} signal. Although capnography is the recommended monitor for apnea detection during sedation [3–5], it does not have perfect sensitivity and specificity and it may have missed or falsely detected apnea [13]. This is underlined by our observation that P_{ETCO_2} was unable to detect three RESDA predicted episodes of hypopnea that led to desaturation. However, the association of loss of signal with desaturation probably decreased the number of false positive results (e.g. CapnoLine sensor disconnection). Future studies should nevertheless compare RESDA and capnography to a "gold standard" test of airflow detection, such as pneumotachography. Additionally, this study may have both selection and measurement biases. These preliminary results can only be interpreted in the context of patients having a clinical suspicion of obstructive apnea who receive propofol TCI administered by progressive steps of 1 μg ml^{-1} during sleep endoscopy. Other procedures requiring sedation, such as colonoscopy, may introduce movement artefacts rendering mandibular movement analysis less reliable. Measurement bias, on the other hand, was probably minimized by the continuous recording of all parameters of interest, which allowed an off-line analysis using predefined criteria. Finally, RESDA probably has limited to no use in predicting central apnea, which is not associated with oscillatory mandibular movement. However, central apneas can be detected with JAWAC during or immediately following the event because they have a characteristic non-oscillating mandibular movement that is regularly interrupted by an abruption [14]. It may consequently be possible to develop another algorithm based on the mandibular movement patterns of central apnea that could predict its occurrence.

This study opens the way to several potential fields of research. The first step is to develop a real-time obstructive apnea monitor which could be prospectively assessed and validated in the anesthetic setting. Anesthetists could then apply real-time RESDA to different sedation techniques, populations, perioperative periods, and fields of medicine.

For example, many patients suffering from obstructive sleep apnea undergo anesthesia without being diagnosed and there is a need for easily accessible preoperative diagnostic tests [15]. Mandibular movement analysis has been shown to be reliable in screening for sleep apnea [7] and an ambulatory monitor using this technology may be useful in screening patients preoperatively. In the postoperative period, patients that receive opiates are at risk of respiratory depression [16] and monitoring these patients with RESDA could help detect obstructive apneic episodes and prevent hypoxemia associated complications.

In conclusion, the RESDA algorithm, which is based on the combination of capnography with mandibular movement assessment of respiratory effort, can more rapidly alarm anesthetists of airway obstruction during propofol sedation than P_{ETCO_2} alone. However, P_{ETCO_2}, pulse oximetry, and clinical monitoring are still required.

Compliance with ethical standards

Conflict of interest The authors declares that they have no conflict of interest.

References

1. Metzner J, Posner KL, Domino KB. The risk and safety of anesthesia at remote locations: the US closed claims analysis. Curr Opin Anaesthesiol. 2009;22(4):502–8.
2. Coté GA, Hovis RM, Ansstas MA, et al. Incidence of sedation-related complications with propofol use during advanced endoscopic procedures. Clin Gastroenterol Hepatol. 2010;8:137–42.
3. New Standards Monitoring. Association of Anaesthetists of Great Britain and Ireland. 2016. https://www.aagbi.org/news/new-standards-monitoring-which-mandate-capnography-during-anaesthesia-recovery-and-sedation-aim. Accessed 1 May 2018.
4. Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018 A Report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons. American College of Radiology, American Dental Association,

American Society of Dentist Anesthesiologists, and Society of Interventional Radiology. Anesthesiology. 2018;128(3):437–79.

5. Hinkelbein J, Lamperti M, Akeson J, et al. European Society of Anaesthesiology and European Board of Anaesthesiology guidelines for procedural sedation and analgesia in adults. Eur J Anaesthesiol. 2018;35(1):6–24.

6. Martinot JB, Le-Dong N, Cuthbert V, et al. Mandibular movements as accurate reporters of respiratory effort during sleep: validation against diaphragmatic electromyography. Front Neurol. 2017;8:353.

7. Cattrysse F, Peeters M, Calaerts S, Ferson K, Degryse JM. Detection of sleep apnea by case-finding and home monitoring with Somnolter a pilot study. BMC Res Notes Sep. 2014;7:616.

8. Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. Br J Anaesth. 1991;67:41–8.

9. Traxdorf M, Tschaikowsky K, Scherl C, et al. Drug-induced sleep endoscopy (DISE) with target controlled infusion (TCI) and bispectral analysis in obstructive sleep apnea. J Vis Exp. 2016. https://doi.org/10.3791/54739.

10. Landis JR, Koch GG. An application of hierarchical kappa-type statistics in the assessment of majority agreement among multiple observers. Biometrics. 1977;33(2):363–74.

11. Niesters M, Mahajan RP, Aarts L, Dahan A. High-inspired oxygen concentration further impairs opioid-induced respiratory depression. Br J Anaesth. 2013;110(5):837–41.

12. Vincent JL, Einav S, Pearse R, et al. Improving detection of patient deterioration in the general hospital ward environment. Eur J Anaesthesiol. 2018;35(5):325–33.

13. Applegate R, Lenart J, Malkin M. Meineke M. Qoshlli S, et al. Advanced monitoring is associated with fewer alarm events during planned moderate procedure-related sedation: a 2-part pilot trial. Anesth Analg. 2016;122(4):1070–8.

14. Maury G, Senny F, Cambron L, Albert A, Seidel L, Poirrier R. Mandible behaviour interpretation during wakefulness, sleep and sleep-disordered breathing. J Sleep Res. 2014;23:709–16.

15. Cavalcante A, Martin Y, Sprung J, Imsirovic J, Weingarten T. Low minute ventilation episodes during anesthesia recovery following intraperitoneal surgery as detected by a non-invasive respiratory volume monitor. J Clin Monit Comput. 2017;32(5):909–935.

16. Faßbender P, Haddad A, Bürgener S, Peters J. Validation of a photoplethysmography device for detection of obstructive sleep apnea in the perioperative setting. J Clin Monit Comput. 2018. https://doi.org/10.1007/s10877-018-0151-2.