Defining Postoperative Respiratory Depression: The Need for a Universally Accepted Definition

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BACKGROUND

Postoperative respiratory depression (PORD) can arise from reduced pulmonary function caused by prolonged supine positioning[1], anesthetics and analgesics utilized, and exacerbated by certain surgeries like thoracic or abdominal procedures that further diminish lung capacity[2]. The majority of respiratory depression events (85%) occur within the initial 24 hours post-surgery.[3] Atelectasis occurring at the induction of anesthesia and possibly persisting post-surgery,[1] can lead to varying degrees of respiratory depression. These effects may have unpredictable long-term consequences, contributing to heightened morbidity and mortality beyond the time of hospital discharge.[4]

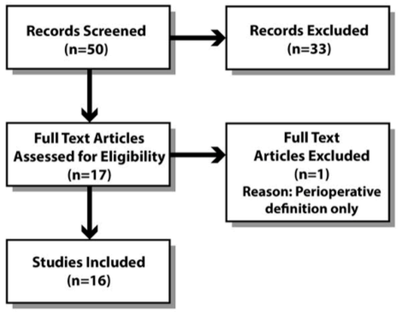
The American Society of Anesthesiologists Task Force on Neuraxial Opioids and American Society of Regional Anesthesia and Pain Medicine define PORD by (1) reduction in respiratory rate (<10 breaths/min), (2) reduced arterial oxygen saturation (<90%), or (3) hypercapnia/hypercarbia (PCO2 >50 mmHg).[5] However, this definition is not consistently utilized in clinical practice or across clinical trials making it difficult to quantify how often PORD occurs. The goal of this review is to demonstrate the variability across recent clinical trials in assessing respiratory depression and the need for a universally accepted and clinically meaningful definition of PORD.

METHODS

In June 2023, using the PubMed database of the National Library of Medicine, part of the National Institutes of Health, the keyword "postoperative respiratory depression" was searched and results were limited to clinical trials or randomized clinical trials; with associated data; published in the past five years; and in English. We obtained 50 results.

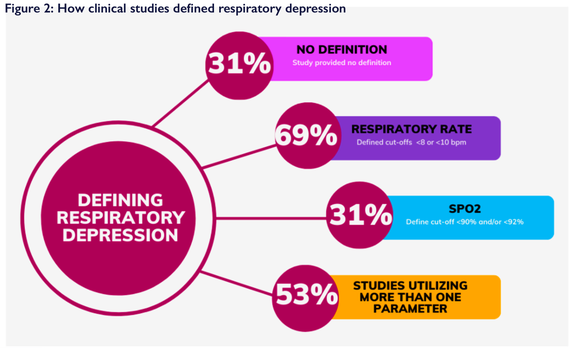
The goal of each search was to determine how postoperative respiratory depression was defined, whether as a specific metric, diagnostic criteria, or outcome. While all articles were searched for definition(s) of postoperative respiratory depression, the lack of a definition was not an exclusion criterion. Definitions for perioperative respiratory depression were excluded and studies that did not specifically evaluate postoperative respiratory depression were excluded. Articles were excluded if they were not clinical trials or randomized clinical trials, if they were not in English, and if they were not indexed in PubMed. Systematic reviews and meta-analyses were excluded since they synthesize results from multiple studies which may have differing definitions. The abstracts of the 50 articles identified were reviewed and 33 articles were excluded because they did not include postoperative respiratory depression as a study endpoint (primary or secondary) or otherwise met exclusion criteria. This resulted in 17 articles for consideration. When full texts were evaluated, one more article was excluded because it used only a perioperative definition of respiratory depression. This left 16 articles included. **See Figure 1.**

Figure 1: Flowchart of study inclusions



Articles were included for all types of surgical interventions (i.e., open surgery, laparoscopic surgery, orthopedic surgery, brain surgery, and so on) and for all populations, such as pediatric, geriatric, and others.

Figure 2: How clinical studies defined respiratory depression



CONCLUSION

- The term postoperative respiratory depression (PORD) is widely used in clinical practice and clinical trials, but it lacks a consensus definition
- Without a universally accepted and clinically measurable definition for PORD, our ability to study and quantify its occurrence is profoundly hampered
- The lack of quantification puts patient safety at risk in the near term and potentially long-term

bpm, breaths per minute; CO2, carbon dioxide; ETCO2, end tidal carbon dioxide; GI, gastrointestinal; IT, intrathecal; IV, intravenous; L/min, liters per min; mmHg, millimeters of mercury; NIV, noninvasive ventilation; O2 oxygen; Pa02FiPO2, peripheral blood oxygen saturation/fraction of inspired oxygen; PK, pharmacokinetic; PORD, postoperative respiratory depression; RCT, randomized controlled trial; RD, respiratory depression; RR, respiratory rate RT, randomized trial; SpO2, oxygen saturation

Author	Study Design/ Procedure/ Intervention(s)	PORD Definition or Relevant Information
Abrard 2022[6]	RT/ Elective or semi-urgent surgery/ Intermittent prophylactic face mask NIV for 6-8 h per day or usual care	Utilized "acute respiratory failure" rather than PORD. Acute respiratory failure was defined as ventilatory frequency > 34 bpm, O_2 saturation <92% or 90% on air, PaO_2FiPO_2 ratio <250, the need for fractional inspired O_2 >50% or inhaled oxygen >5 L/min.
Albrecht 2020[7]	RCT, triple blind/ Hip arthroplasty/ IT morphine vs placebo	Oxygen saturation and ventilatory rate were used as surrogates for respiratory depression. Authors stated they did not use "respiratory depression" because there was no official consensus definition.
Amer 2020[8]	RCT/ Pediatric upper GI endoscopy (ages 2-7 years)/ Dexmedetomidine as sedative vs. propofol against background IV ketamine infusion	O_2 saturation <92%
Comelon 2021[9]	RCT/ Laparoscopic hysterectomy/ Tapentadol vs. Oxycodone	No definition of PORD utilized. However, respiratory variables were recorded: RR, $ETCO_2$, SpO_2 and compared to baseline.
Cosgrave 2019[10]	RCT/ Major hepatobiliary surgery/ Low-dose naloxone after IT morphine	RR <10 bpm and/or O_2 saturation <90% or increase in fraction of inspired O_2 to maintain saturation of >92%
Dereu 2019[11]	RCT/ Cesarean section/ Clonidine vs. IT morphine	RR <8 bpm for >5 minutes during first 6 h or 1 episode or RR < 8 bpm from 6 to 24 hours
Dhaliwal 2019[12]	RCT/ Lumbar fusion/ IT morphine vs. placebo	RR <10 bpm
Han 2018[13]	RCT/ Abdominal surgery under GA/ Oxycodone vs. IV sufentanil PCA	Both SpO_2 <90% and RR <10 bpm
He 2021[14]	RCT/ Intracranial surgery for brain tumor/ Dexmedetomidine 0.1 μg/kg/h vs. placebo	Arterial partial pressure of CO_2 >50 mmHg or RR <10 bpm
Morue 2018[15]	RCT/ Oocyte retrieval/ Placebo vs. low-dose ketamine in addition to remifentanil for conscious sedation	Hypopnea= RR < 8 bpm without oxygen desaturation Moderate RD = SpO_2 between 90% and 94% Major RD = SpO_2 <90%
Ranganathan 2019[16]	RCT/ Gastric bypass/ Intraoperative dexmedetomidine v. placebo	No definition but secondary endpoints included SpO_2 and RR
Sadhasivam 2021[17]	Multi-dose PK study/ Pediatric spinal fusion (10-17 years old)/ methadone	SpO_2 <90% and/or RR < 8 bpm breathing room air for 1 minute
Shanthanna 2018[18]	RCT/ Outpatient surgery/ Morphine vs. hydromorphone	No definition, but recorded as occurring when treatment was required.
Shim 2018[19]	RCT/ Robot-assisted laparoscopic prostatectomy/ IT morphine and bupivacaine vs. placebo	No definition
Xing 2019[20]	RCT/ Pediatric craniotomy (1-to 12-year-olds)/ Four groups: fentanyl, morphine, tramadol, and placebo	A clinically significant decline in RR which required intervention with SpO_2 <92%
Xu 2022[21]	RCT/ Hip fracture/ All patients received 12.5 mg of 0.5% hyperbaric bupivacaine; one group has low-dose IT morphine 100 μg and the other low-dose sufentanil 100 μg	RR < 10 bpm Hypopnea was defined as a 30% decrease in respiratory signal flow along with a 3% drop in oxygen saturation.

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