Impact of anesthesia on post-operative pulmonary complications

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AZ Sint Jan Brugge

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Review Article

Miskovic et al. BJA 2017;118:317-34

Postoperative pulmonary complications

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1. Postoperative Pulmonary Complications (PPC) have many faces

from a limited to a broad definition including hypoxia and obstructive breathing.

- Composite outcome measures
  - Respiratory infection,
  - Respiratory failure,
  - Pleural effusion,
  - Atelectasis,
  - Pneumothorax,
  - Bronchospasm,
  - Aspiration pneumonitis.
  - Hypoxia?
  - Obstructive breathing?
- Individual adverse outcomes
  - Pneumonia,
  - Acute respiratory distress syndrome,
  - Pulmonary embolus,
  - Intervential support…
    - Antibiotics, thorax drainage, steroids, physiotherapy, bronchoscopic toilet.
  - Ventilatory support…
    - O_2, CPAP, PSV, VCV, NMB, ECMO,..

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Table 1 European Perioperative Clinical Outcome definitions[1] for postoperative pulmonary complications and other defined outcome measures, shown to highlight the variation of definitions in the literature; in particular, respiratory failure and pneumonia. International statistical classification of diseases and related health problems, ninth revision (ICD-9) codes have also been used to define PPCs.[2 3] ARDS, acute respiratory distress syndrome; CXR, chest radiograph; EPCO, European Perioperative Clinical Outcome; FI_{O_2}, fraction of inspired oxygen; NIV, non-invasive ventilation; Pa_{O_2}, partial pressure of oxygen in arterial blood; PPC, postoperative pulmonary complication

Outcome measure	EPCO definitions (identical set used by Canet and colleagues[4] and subsequent studies)[5 6]	Other published definitions
Respiratory infection	Antibiotics for suspected infection with one or more of the following: new or changed sputum, new or changed lung opacities, fever, white blood cell count $>12\times10^9$ litre^{-1}	Two or more of the following for >48 h: new cough/sputum production, physical findings compatible with pneumonia, fever >38 °C, and new infiltrate on CXR[7]
Respiratory failure	Postoperative Pa_{O_2} <8 kPa (60 mm Hg) on room air, a Pa_{O_2}:FI_{O_2} ratio <40 kPa (300 mm Hg), or arterial oxyhaemoglobin saturation measured with pulse oximetry <90% and requiring oxygen therapy	Ventilator dependence for >1 postoperative day or re-intubation[8 9] Need for postoperative mechanical ventilation >48 h[10–13] Unplanned re-intubation because of respiratory distress, hypoxia, hypercarbia, or respiratory acidosis within 30 days of surgery[10 11 13–15] Re-intubation within 3 days requiring mechanical ventilation[16] Postoperative acute lung injury[17] ARDS[17–19] Requiring mechanical ventilation within 7 days of surgery[20 21] Requiring NIV[22]
Pleural effusion	CXR with blunting of costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in upright position, displacement of adjacent anatomical structures, or (in supine position) hazy opacity in one hemithorax with preserved vascular shadows	Pleural effusion requiring thoracocentesis[8 9 20]
Atelectasis	Lung opacification with mediastinal shift, hilum or hemidiaphragm shift towards the affected area, with compensatory hyperinflation in adjacent non-atelectatic lung	Requiring bronchoscopic intervention[20] Major atelectasis (one or more pulmonary segments)[23]
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura	Pneumothorax requiring thoracocentesis[20 22]
Bronchospasm	Newly detected expiratory wheeze treated with bronchodilators	Clinical diagnosis resulting in change in therapy[89] Refractory wheeze requiring parenteral drugs in addition to preoperative regimen[24]
Aspiration pneumonitis	Acute lung injury after inhalation of regurgitated gastric contents	
Pneumonia	CXR with at least one of the following: infiltrate, consolidation, cavitation;plus at least one of the following: fever >38 °C with no other cause, white cell count <4 or >12×10^9 litre^{-1}, >70 yr of age with altered mental status with no other cause;-plus at least two of the following: new purulent/changed sputum, increased secretions/suctioning, new/worse cough/dyspnoea/tachypnoea, rales/bronchial breath sounds, worsening gas exchange	Radiographic change and antibiotics[89] Antibiotics with new/changed sputum or radiographic change or fever or increased white cell count >12 000 μl^{-1} [4] Two or more of the following for ≥2 consecutive days: new cough/sputum production, examination compatible with pneumonia, temperature >38 °C, and radiographic change[7 23] New or progressive infiltrate on CXR or crackles or dullness on percussion and any of the following: new purulent/changed sputum, positive blood cultures, isolation of pathogen from sputum[20 25] Positive sputum culture or infiltrate on CXR, and diagnosis of pneumonia or pneumonitis[18] New infiltrate on CXR plus fever, leucocytosis, and positive sputum Gram stain/culture[24]
ARDS		Ventilated, bilateral infiltrates on CXR, Pa_{O_2}:FI_{O_2} ≤300, minimal evidence of left atrial fluid overload within 7 days of surgery[19]
Tracheobronchitis		Purulent sputum with normal chest radiograph, no i.v. antibiotics[8 9]
Pulmonary oedema		Pulmonary congestion/hypostasis, acute oedema of lung, congestive heart failure, fluid overload[2 3]
Exacerbation of pre-existing lung disease[23]		Not further defined
Pulmonary embolism[23]		
Death[24 26]		Not further defined

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Incidence of PPC

Dead after PPC might be better preventable than dead after cardiac problems. (dixit: Sessler on ESA 2018)

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Postoperative pulmonary complications

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Postoperative respiratory failure is the most common severe PPC.

PPC increase from 0,2% to 18,9 % when using a broader definiti
Hypoxia becomes the most common PPC

PPC After major surgery

The **30 days** mortality **30%** vs 0.2 - 3%

The **90 days** mortality **24%** vs 1.2%.

1 yr mortality 45.9% vs 8.7%

5 yr mortality 71.4% vs 41.1%.

Preventive measures & early warning for postop cardiac complications failed…

Would preventive measures & early warning for pulmonary complications fail too?

There is however time for warning before finding a patient in cardiac arrest due to a PPC!

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Table 2 Incidence and mortality rates of major studies evaluating postoperative pulmonary complications since the year 2000. Prospective studies are followed by retrospective studies in reverse chronological order. Where more than three surgical specialties are included, the term 'multi-specialty' is used. Where risk prediction model papers include a training set and a validation set, data from the validation set have been used. AAA, open abdominal aortic aneurysm; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; CXR, chest radiograph; EPCO, European Perioperative Clinical Outcome definition (Table 1); EVAR, endovascular aneurysm repair; PE, pulmonary embolus; PERISCOPE, Prospective Evaluation of a Risk Score for postoperative pulmonary COmPlications in Europe; PPC, postoperative pulmonary complication; RF, respiratory failure; Sp_{O_2}, peripheral oxygen saturation; UPI, unplanned intubation

Study	Year	Design	PPCs	Sample size	PPC incidence (%)	Mortality rate with PPC (%)	Operative specialty
Canet and colleagues[29]	2015	Secondary analysis of 'PERISCOPE' Prospective multi-centre cohort; evaluating PPCs	RF	5384	4.2	10.3 (in hospital)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Mazo and colleagues[6]	2014	'PERISCOPE' Prospective multicentre cohort; external validation of 'ARISCAT'	As per EPCO	5099	7.9	8.3 (in hospital)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Canet and colleagues[4]	2010	'ARISCAT' Prospective multicentre cohort	As per EPCO	2464	5.0	19.5 (30 day) 24.4 (90 day)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Scholes and colleagues[32]	2009	Prospective multi-centre cohort	More than four of the following: i. collapse/consolidation on CXR; ii. Sp_{O_2} <90%; iii. abnormal sputum production; iv. positive sputum culture; v. leucocytosis; vi. abnormal auscultation; or vii. physician's diagnosis	268	13.0	Not stated	Upper abdominal
McAlister and colleagues[20]	2005	Prospective single-centre cohort	RF, pneumonia, atelectasis, pneumothorax, pleural effusion	1055	2.7	Not stated	Multi-specialty (non-thoracic) elective, including abdominal
Yang and colleagues[12]	2015	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	Pneumonia, UPI, or RF	165 196	5.8	Not stated	Elective major abdominal (non-vascular)
Jeong and colleagues[5]	2014	Retrospective single-centre analysis of prospectively collected cohort regarding PPC risk	As per EPCO	2059	6.8	Not stated	Multi-specialty elective and emergency, including abdominal (open and laparoscopic), vascular, cardiac, and thoracic
Blum and colleagues[19]	2013	Retrospective single-centre cohort	ARDS	50 367	0.2	27.0 (90 day)	Multi-specialty (non-cardiothoracic) elective and emergency, including abdominal
Brueckmann and colleagues[16]	2013	Retrospective single-centre cohort	UPI	33 769	0.43	16.0	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Gupta and colleagues[13]	2013	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	Pneumonia	211 410	1.8	17.0 (30 day)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Li and colleagues[18]	2013	Retrospective single-centre cohort	Pneumonia, pulmonary oedema, atelectasis, ARDS, pleural effusion	316	18.9	Not specific to PPC	Elective and emergency infrarenal AAA
Hua and colleagues[14]	2012	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	UPI	231 548	1.9	28.0 (30 day)	Multi-specialty elective and emergency, including major abdominal, vascular (open and EVAR) cardiac, and thoracic
Kor and colleagues[17]	2011	Retrospective analysis of prospective single-centre cohort evaluating intraoperative ventilator settings and ALI	ALI/ARDS	4366	2.6	14.2	Multi-specialty elective, including abdominal (open and laparoscopic), vascular, cardiac, and thoracic
Gupta and colleagues[11]	2011	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	RF, UPI	211 410	2.6	25.6 (30 day)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Ramachandran and colleagues[15]	2011	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	UPI	222 094	0.9	9.7 (low-risk group), 30.6 (high-risk group)	Elective multi-specialty (non-cardiac)
Smith and colleagues[23]	2010	Retrospective single-centre cohort	Pneumonia, acute bronchitis, atelectasis, exacerbation of pre-existing lung disease, RF, PE	329	7.0	16.0 (30 day)	Elective and emergency laparotomy, including AAA
Johnson and colleagues[33]	2007	Retrospective analysis of multi-centre prospective cohort (non-specific to PPCs)	RF, UPI	180 359	3.0	26.5 (30 day)	Elective and emergency major vascular and general
Arozullah and colleagues[25]	2001	Retrospective analysis of multi-centre prospective cohort (non-specific to PPCs)	Pneumonia	160 805	1.5	21 (30 day)	Multi-specialty (non-cardiac), including abdominal, vascular, and thoracic
Arozullah and colleagues[34]	2000	Retrospective analysis of multi-centre prospective cohort (non-specific to PPCs)	RF	81 719	3.4	27 (30 day)	Multi-specialty (non-cardiac), including abdominal, vascular, and thoracic

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Who gets postoperative pulmonary complications?

Postoperative pulmonary complications

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- Patient factors
  - Advancing age
  - Co morbidity
    - COPD, OSAS, CHF, Smoking
- Procedure factors
  - General anesthesia
  - Major surgery
    - cardiac,
    - thoracic,
    - upper abdominal,
  - open vs endoscopic.
  - emergency

Miskovic et al. BJA 2017;118:317-34

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Table 3 Published risk factors for developing a postoperative pulmonary complication, categorized into patient factors, procedure factors, and laboratory testing (as defined by Smetana and colleagues),[27] further divided into non-modifiable and modifiable. Risk factors with strong evidence in the literature are discussed in more detail in the main text. AAA, abdominal aortic aneurysm; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CXR, chest X-ray; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GA, general anaesthesia; GORD, gastro-oesophageal reflux disease; NMBDs, neuromuscular blocking drugs; OSA, obstructive sleep apnoea; PACU, postanaesthesia care unit; 'Positive cough test', patient takes a deep breath and coughs once, and a positive test=ongoing coughing after the initial cough; TOF, train of four

Patient factors	Procedure factors	Laboratory testing
Non-modifiable	**Non-modifiable**	Urea >7.5 mmol $litre^{-1}$ [1 10 25]
Age[4–7 10 13 14 18 20 24 25 27 33 36]	Type of surgery:[4–7 10–13 15–18 23 25 27 29]	Increased creatinine[33]
Male sex[12 19 33]	• upper abdominal	Abnormal liver function tests[15]
ASA ≥II[5 11–14 16 19 27 33]	• AAA	Low preoperative oxygen saturation[4 6 29]
Functional dependence (frailty)[10–13 25 27 34 36]	• Thoracic	'Positive cough test'[20]
Acute respiratory infection (within 1 month)[4 6]	• Neurosurgery	Abnormal preoperative CXR[9 27]
Impaired cognition[7]	• head and neck	Preoperative anaemia (<100 g $litre^{-1}$)[4 6]
Impaired sensorium[25]	• vascular	Low albumin[5 10 27]
Cerebrovascular accident[25]	Emergency (*vs* elective)[4–6 10 11 16 18 19 23 25 29 33 36]	Predicted maximal oxygen uptake[32]
Malignancy[7 15]	Duration of procedure[6 12 14 20 22 27 29 32]	FEV_1:FVC <0.7 and FEV_1 <80% of predicted[5]
Weight loss >10% (within 6 months)[15 25]	Re-operation[18 23 36]	
Long-term steroid use[25]	Multiple GA during admission[19]	
Prolonged hospitalization[15]	**Modifiable**	
Modifiable	Mechanical ventilation strategy[3 19 63–71]	
Smoking[57 12 13 15 25 32 33 61]	GA (*vs* regional)[4 25 27 72]	
COPD[10 12 13 15–19 24 25 27 32 33 36]	Long-acting NMBDs and TOF ratio <0.7 in PACU[73]	
Asthma[20 32]	Residual neuromuscular block	
CHF[15 16 18 27 29 33]	Intermediate-acting NMBDs with surgical time <2 h (not antagonized)[21]	
OSA[62]	Neostigmine[21 74]	
BMI <18.5 or >40 kg m^{-2} [15]	Sugammadex with supraglottic airway[75 76]	
BMI >27 kg m^{-2} [7]	Failure to use peripheral nerve stimulator[21 74]	
Hypertension[15]	Open abdominal surgery (*vs* laparoscopic)[5 26 77–79]	
Chronic liver disease[29]	Perioperative nasogastric tube[18 20 22 23 25 80]	
Renal failure[19]	Intraoperative blood transfusion[19 25 36]	
Ascites[12]		
Diabetes mellitus[15 17]		
Alcohol[17 25]		
GORD[17]		
Preoperative sepsis[13–15 33]		
Preoperative shock[12]		

Can we do something to prevent PPC?

1. Reduce Co-morbidity?
   - COPD, OSAS, congestive heart failure, or chronic liver disease: 2x 3x
   - preoperative medical optimization is possible and might reduce PPC?
2. Stop Smoking?
   - Each 10 pack-yr increased PPC.
   - Stop > 4 weeks, > 1 year improves outcome
3. Treat Preoperative anaemia?
   - 3x increase in PPC.
   - Erythropoietin, vit B12, folate, iron might reduce PPC?
4. Avoiding General anaesthesia???
   - Increased PPC compared to locoregional for same procedure! 2 h > 3 h
   - Avoid general anesthesia? Avoid opioids? Less inflammation by infiltration?

Yes first 3 are obvious but limited effect. Can we do more?

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Lets focus: Postoperative respiratory failure (RF) is the most common PPC

- First signs of respiratory failure are hypercapnia followed by hypoxia.
- What causes postoperative hypoxia and how can we prevent it?

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Anesthesia Patient Safety Foundation

Section Editor: **Sorin J. Brull**

Postoperative Hypoxemia Is Common and Persistent: A Prospective Blinded Observational Study

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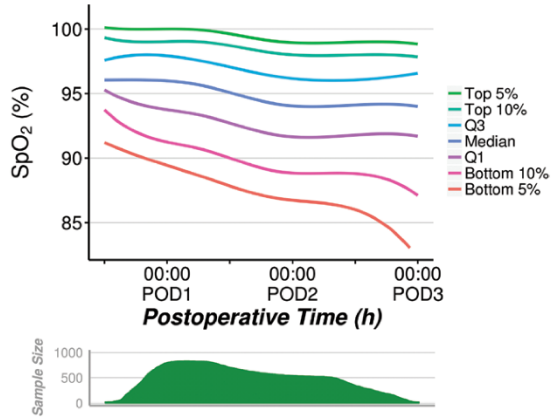

Figure 4. (Raw Spo_2 data) Distribution of Spo_2 across the patients in the sample, over postoperative time. Curves estimated using quantile regression with restricted cubic splines. POD = postoperative day.

BACKGROUND: The incidence, severity, and duration of postoperative oxygen desaturation in the general surgical population are poorly characterized. We therefore used continuous pulse oximetry to quantify arterial oxygen saturation (Spo_2) in a cross-section of patients having noncardiac surgery.

METHODS: Oxygen saturation, blinded to clinicians, was recorded at 1-minute intervals in patients >45 years old for up to 48 hours after noncardiac surgery in 1250 patients from Cleveland Clinic Main Campus and 250 patients from the Juravinski Hospital. We determined (1) the cumulative minutes of raw minute-by-minute values below various hypoxemic thresholds; and (2) the contiguous duration of kernel-smoothed (sliding window) values below various hypoxemic thresholds. Finally, we compared our blinded continuous values with saturations recorded during routine nursing care.

RESULTS: Eight hundred thirty-three patients had sufficient data for analyses. Twenty-one percent had ≥10 min/h with raw Spo_2 values <90% averaged over the entire recording duration; 8% averaged ≥20 min/h <90%; and 8% averaged ≥5 min/h <85%. Prolonged hypoxemic episodes were common, with 37% of patients having at least 1 (smoothed) Spo_2 <90% for an hour or more; 11% experienced at least 1 episode lasting ≥6 hours; and 3% had saturations <80% for at least 30 minutes. Clinical hypoxemia, according to nursing records, measured only in Cleveland Clinic patients (n = 594), occurred in 5% of the monitored patients. The nurses missed 90% of smoothed hypoxemic episodes in which saturation was <90% for at least one hour.

CONCLUSIONS: Hypoxemia was common and prolonged in hospitalized patients recovering from noncardiac surgery. The Spo_2 values recorded in medical records seriously underestimated the severity of postoperative hypoxemia. (Anesth Analg 2015;121:709–15)

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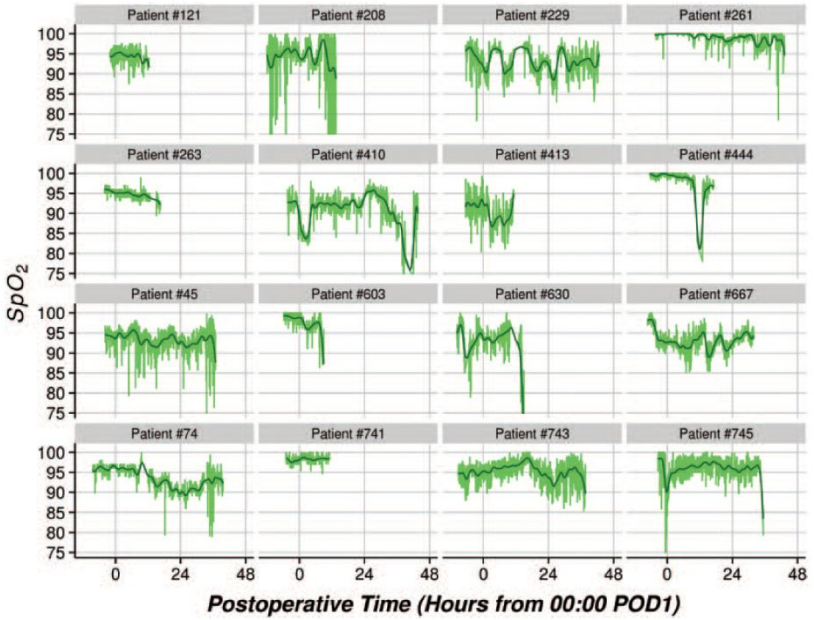

PLOS ONE

Plos one 2018; 13(3): e0194553.

RESEARCH ARTICLE

Risk factors for cardiopulmonary and respiratory arrest in medical and surgical hospital patients on opioid analgesics and sedatives

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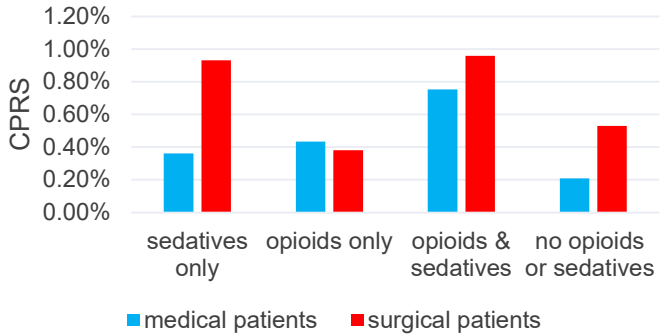
Check for updates

Risk for cardiopulmonary and respiratory arrest



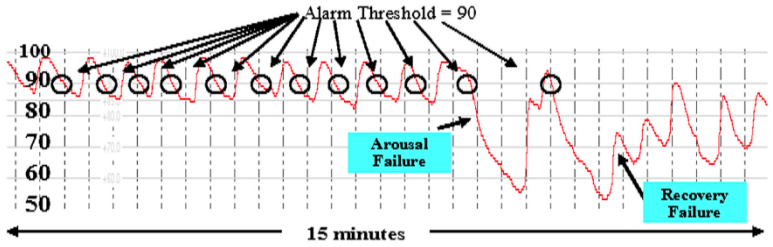
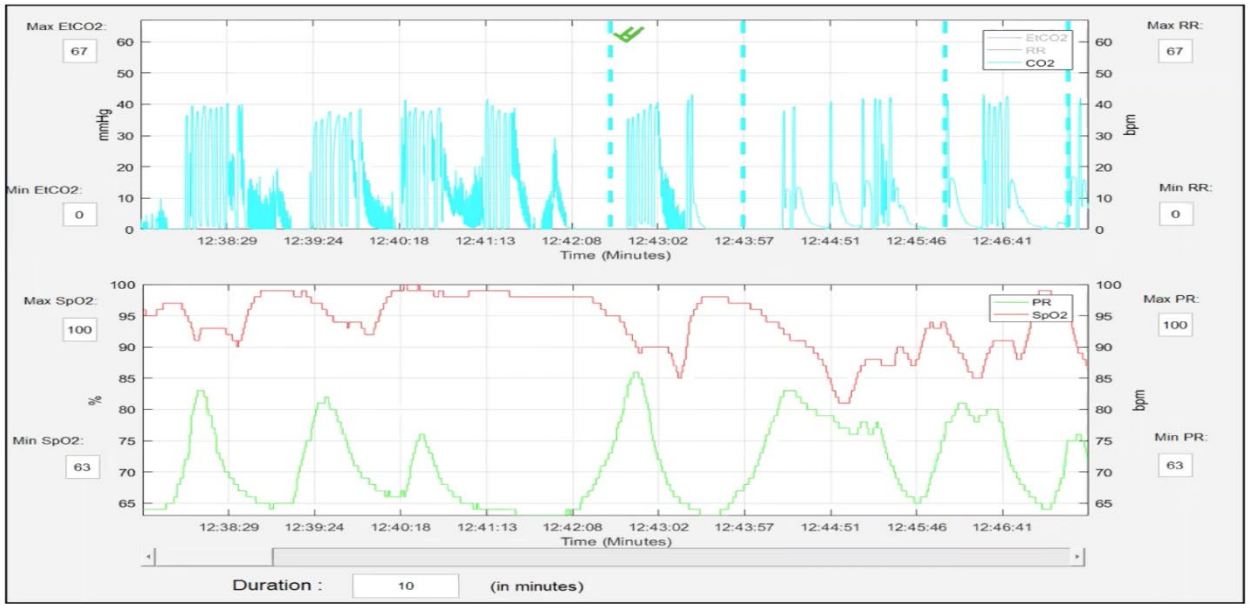
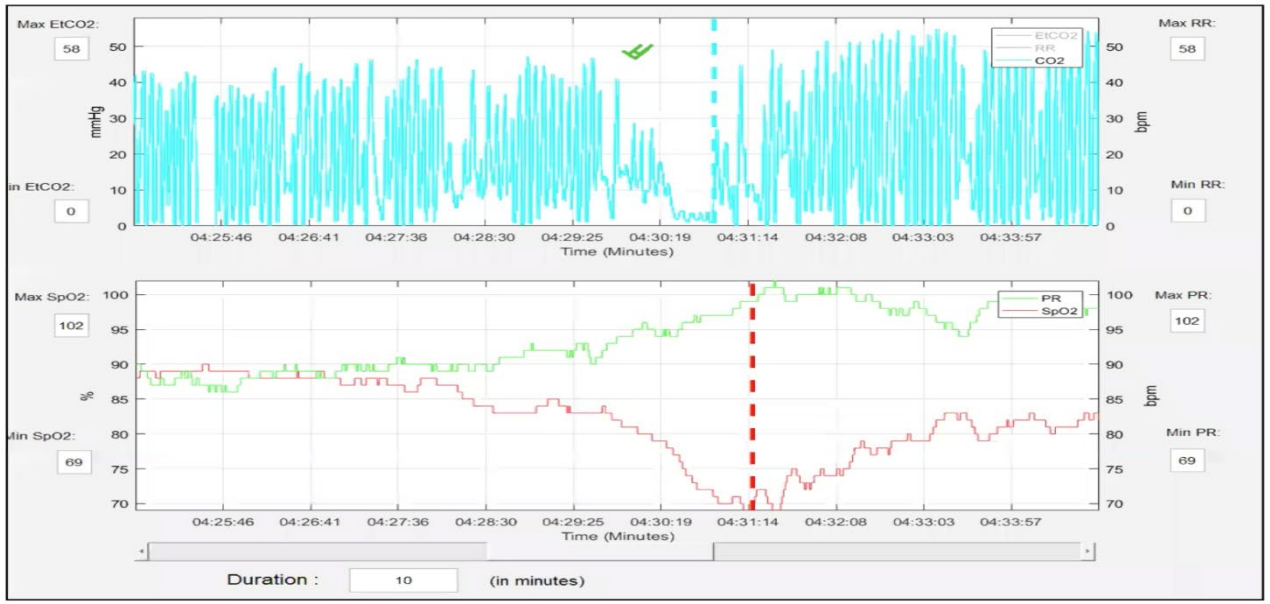


Figure 5 RECC type III pattern of respiratory dysfunction with arousal failure, recoveries, and alarm fatigue markers.

Repeated apneic events



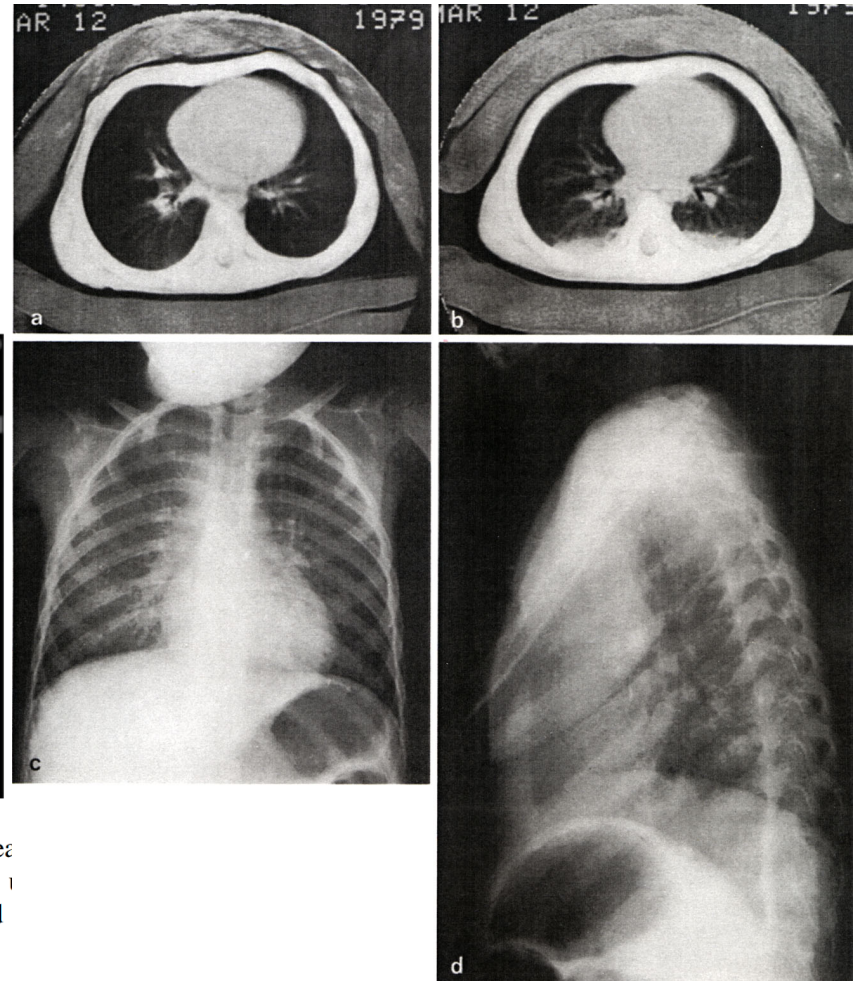
Apnea and hypoxemia



Atelectasis is problem no 1 after anaesthesia but unrecognised

90 % of the patients have atelectasis post general anaesthesia

- Basal lung area
- Not seen on X-ray
- Visible on Echo or CT scan



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Journal of Anesthesia
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Review article

Atelectasis during anesthesia: Can it be prevented?

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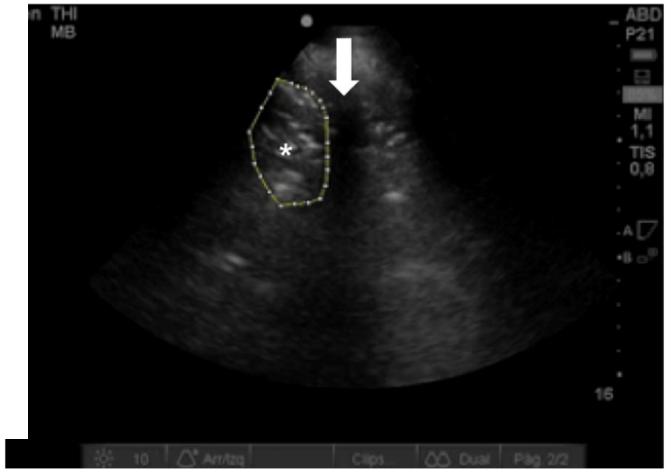


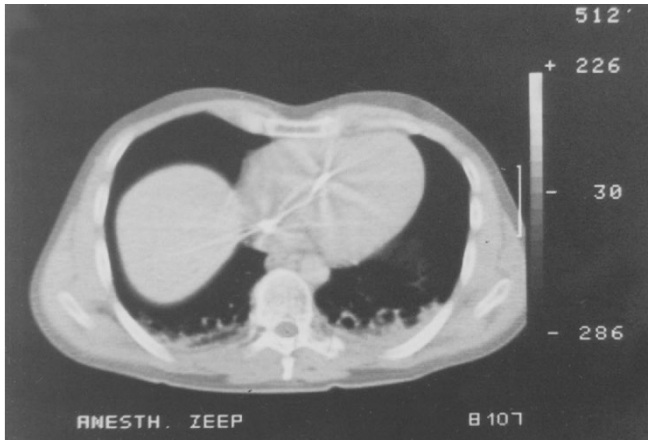
Can J Anesth/J Can Anesth (2019) 66:1328–1337
Pediatr Radiol. 1980 Apr;9(3):145-8

Fig. 4 Arrow = border of the rib with acoustic shadowing benea
Asterisk = lung consolidation. Consolidation area is outline
manual tracing tools in ImageJ software. Area is calculated
adjusting scale with the same software

Atelectasis (freq reason for PPC) has more than one cause

Postoperative hypoxemia = atelectasis if no O2 is given, if no hemodynamic reason, if sat probe is correct, finger not cold, if not breathing hypoxic air,…

1. Opioids induce obstructive breathing and hypoventilation after surgery inducing atelectasis
2. PORC (post operative residual curarisation) induce obstructive breathing and hypoventilation inducing atelectasis
3. Sedation induce obstructive breathing and hypoventilation, inducing atelectasis.
4. Extubation without CPAP, at 100 % O2, without LRM before, aspiration during extubation, all induce atelectasis



Failure until today to reduce PPC sufficiently?

Large patient groups & Multifactorial

- Avoiding PORC is not enough to avoid PPC
- LPV not followed till extubation!
  - LPV guidelines are available.
- Opioids, oxygen, laying flat, no mobilisation in PACU.
  - New guidelines needed on O_2, opioids,
- Remote Inflammation due to surgical stress, sympathic stress, obesity.
  - Research needed to block better sympathic stress & inflammation.
- Early warning post PACU:
  - O_2 saturation while no oxygen, Monitoring breathing, et CO_2, …

The essential LPV (Lung Protective ventilation) guidelines for every adult patient. Young C. BJA 2019:123: 898-913

1. LPV ?

Induction of anesthesia

1. Always **beach chair (30°) during induction**; (avoid flat supine position during induction in every patient).
2. **Use always CPAP** prior to the loss of spontaneous ventilation.
3. Monitor during induction for an obstructive breathing pattern and use a combination of appropriate techniques.

Maintenance of anesthesia

4. After induction start with **$FiO_2 \leq 0.4$**. Thereafter, use the lowest possible FiO2 to achieve SpO2 ≥94%.
5. The ventilator should be set to deliver **$V_T \leq$ 6-8 mL/kg IBW** with PEEP minimal 5 cmH2O. **Higher PEEP** may be required in **obese** patients, during **pneumoperitoneum**, and during prone or **Trendelenburg** positioning.
6. Dynamic **compliance**, driving pressure (P_{Plat}-PEEP), and P_{Plat} should be monitored in every patient. **Decreasing compliance should be treated** with **recruitment** combined with sufficient PEEP. RMs should be performed using the **lowest effective P_{Plat}** (30-40 cmH2O in non-obese, 40-50 cmH2O in obese) and **shortest effective time** or fewest number of breaths. The bag-squeezing RM should be avoided in favor of a **ventilator-driven RM**

Emergence from anesthesia

7. **Avoid ETT suctioning** immediately prior to tracheal extubation.
8. Extubate patient in **Beach chair**, under **CPAP** &
9. **Low FiO_2 (<0.4) during emergence** from general anesthesia can improve pulmonary function in the postoperative period.
    - When high FiO2 (>0.8) is used during emergence, the use of low $Fi0_2$ (<0.3) CPAP immediately following tracheal extubation may reduce the risk of resorption atelectasis.

Postoperative care

10. **Avoid routine application of supplemental oxygen** without investigating and treating the underlying cause. Postoperative oxygen is recommended when room air $Sp0_2$ falls **below 94%.**

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BMJ Open 2018

Risk factors for opioid-induced respiratory depression in surgical patients: a systematic review and meta-analyses

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Opioid induced post operative respiratory depression

- Incidence: 0.5%
- 85% occurred within the first 24 h.
- Increased risk:
  - cardiac disease
  - pulmonary disease
  - OSA.
  - higher doses of opioids
- Safety by monitoring of
  - Level of sedation
  - Ventilation (respiratory rate & tidal vol)
  - pulse oximetry and capnography

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BJA

Opioids ?

British Journal of Anaesthesia, 123 (3): 378–391 (2019)

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Review Article

RESPIRATION AND THE AIRWAY

Characterisation and monitoring of postoperative respiratory depression: current approaches and future considerations

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Editor's key points

- Use of conventional opioids for the management of acute pain in the postoperative setting is associated with unacceptable adverse events, including opioid-induced respiratory depression.
- Monitoring respiratory safety events is imperative for timely institution of intervention and prevention of catastrophic cardiorespiratory arrest, anoxic brain injury and mortality.

Postoperative respiratory depression

Pulmonary dysfunction after surgery and anaesthesia is common with a reported incidence of 0.3–17% depending upon the metric evaluated.[1,5,24] The heterogeneity in anaesthetic practice and postoperative monitoring strategies used makes it difficult to accurately assess the true incidence of this problem. Postoperative respiratory failure has been rated as the fourth most common patient safety event by the Agency for Healthcare Research and Quality, and is associated with increased mortality and hospital length of stay.[25] Despite the magnitude of this problem and the high likelihood of catastrophic consequences in affected patients, a universal definition is lacking.

with the duration and extent of oxygen desaturation events in these patients.[39] Although best practices for optimal detection of postoperative respiratory depression are still not universally available, experts advocate for the increasing use of capnography (or ventilation monitoring) in addition to pulse oximetry (oxygenation monitoring) at least in those patients receiving opioids. In addition, the judicious use of supplemental oxygen in the postoperative recovery room and general care floor, along with better education of healthcare providers with respect to early recognition of impending respiratory deterioration patterns, is essential.[40] Continuous, portable bedside monitors with an effective central alarm and noise filter will also be essential in decreasing alarm fatigue, whilst maintaining patient safety and vigilant surveillance.[21,41,42]

Mulier

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All opioids reduce dose dependent the respiratory drive

Respiratory depression and brain hypoxia induced by opioid drugs: Morphine, oxycodone, heroin, and fentanyl

Eugene A. Kiyatkin

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7. Between-drug differences in NAc oxygen decreases

During the final stage of our analyses we compared four primary parameters of NAc oxygen decrease (latency, peak, time to peak, and duration) induced by heroin, fentanyl, oxycodone, and morphine at different doses (Fig. 10). As can be seen, NAc oxygen decreases occurred with relatively similar onset latencies for each drug and each dose (40–70 s), with minimal values for fentanyl (32 s) and maximal for oxycodone (65 s) and morphine (70 s). These onset latencies also remained relatively stable with increases in drug doses. These latencies obviously reflect a definite time that is necessary for the drug delivered intravenously to reach centrally and peripherally located opioid receptors and induce centrally-mediated depression of respiratory activity. Each of the four drugs tested also decreased oxygen levels with different potency, and this effect was clearly dose-dependent for each drug. The most robust between-drug differences in NAc oxygen response were found with respect to the time to maximal effect, which was shortest for fentanyl (62, 78, and 80 s for 3, 10 and 40 μg/kg, respectively), slightly larger for heroin (120 and 140 s for 0.1 and 0.2 mg/kg doses) and oxycodone (150 and 210 s for 0.6 and 1.2 mg/kg doses) but much larger for morphine (20 min). Similar between-drug differences were found in duration of NAc oxygen decrease, which was short for fentanyl, heroin, and oxycodone, but clearly longer for morphine. While morphine was found to be ~10-fold less potent than fentanyl in respiratory-depressive effects as assessed by plethysmography following intracerebral injections, the effects of morphine were much more prolonged (Kuo et al., 2015). As shown in latter study, centrally administered oxycodone was 2–3-fold less potent than morphine and its effects were shorter than those for morphine.

8. Conclusions and clinical implications

Respiratory depression appears to be a basic effect of all μ-opioid receptor agonists (Baud, 2009; Jaffe et al., 1997; Simon, 1997). As shown above, each of four opioids considered in this review decreased NAc oxygen levels, indicating brain hypoxia. However, these drugs had significant differences in their potency to decrease brain oxygen levels.

Respiratory effects with increasing dose:

1. Irregular and slower frequency
2. Larger variability in tidal volume
3. Decrease in minute volume
4. 50 % depression of hypercapnic response
5. Hypercapnia
6. Respiratory arrest

levels (up to 40-20% of baseline) if these decreases are transient. It is also known that brain cells tolerate robust but transient hypoxia, but cellular damage is greatly progressing if hypoxia becomes prolonged

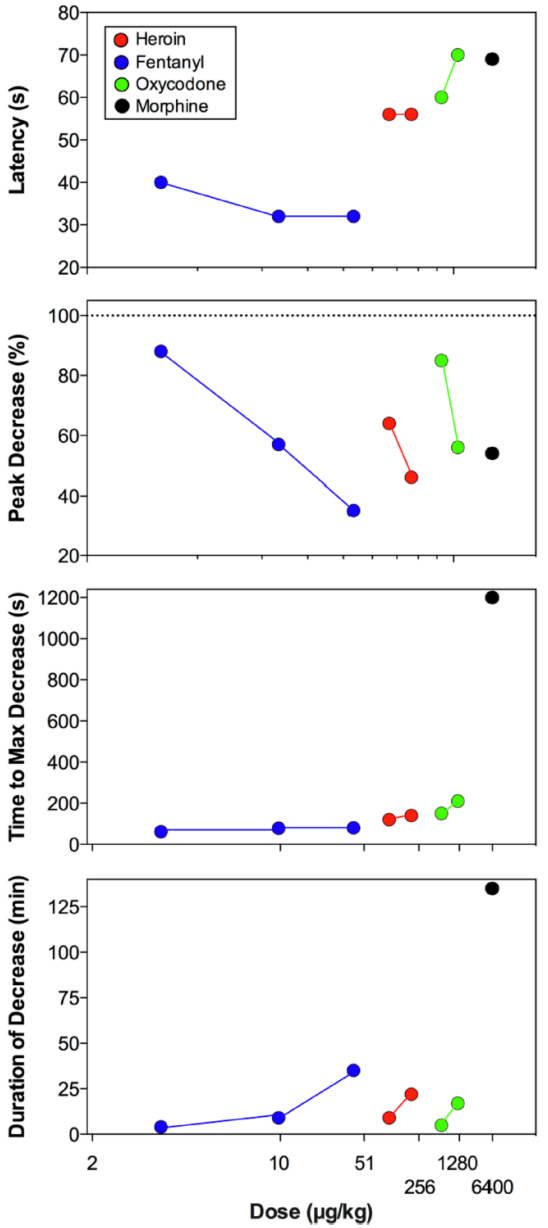

Fig. 10. Mean values of different parameters of NAc oxygen decreases induced by heroin, fentanyl, oxycodone and morphine, shown in log-scale. Latency to decrease is the time from the onset of the injection to the first significant point of decrease. Peak decrease is the lowest point of oxygen decrease vs. baseline (=100%). Time to maximum decrease is the time from the onset of the injection to the point of maximum decrease. Duration of decrease is the time from onset of the injection to the last significant value in drug-induced brain oxygen decrease.

Journal of Clinical Anesthesia and Pain Medicine

A Randomized Controlled, Double-Blind Trial Evaluating the Effect of Opioid-Free Versus Opioid General Anaesthesia on Postoperative Pain and Discomfort Measured by the QoR-40

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Postoperative saturation in the post-anaesthesia care unit while giving a 6 l/min O2 mask was lower in the OA group with a higher incidence of hypertension, postoperative nausea and vomiting, shivering or feeling cold and a higher VAS score. The following morning patients in the OFA group had higher QoR-40 scores and lower VAS scores and cortisol levels.

Table 3: Postoperatively in the post-anaesthesia care unit (PACU).

yes/no mean (SD)	OA(22)	OFA(23)	p-value *	test
lowest saturation < 94% with 6 l/min oxygen mask yes/no	11/11	2/21	0.002 *	chi-square

Impact of opioids on saturation:

Study by Lieselot Geerts
& Eliza Jarahyan at AZ Sint Jan
Retrospecrtive analysis of 64 obese pt

	Before Opioid in PACU OFA & OA	After opioid in PACU OFA (3,4mg) & OA (15 mg)
Saturation without O2	97,37 %	94,76 %

Lin regression analysis of factors before M+

	coef	p
age	**-0.083**	**0.019**
BMI	**-0.239**	**0.003**
gender	1.334	0.190
OFA	**1.72**	**0.030**

Saturation is lower when older, high BMI or OA.

Lin regression analysis of factors after M+

	coef	p
age	**-0.135**	**0.001**
BMI	0.028	0.762
gender	-1.546	0.145
OFA	**1.749**	**0.041**
total M given post op	**-0.198**	**0.048**

Sat is lower when older, OA or high M+ dose.

Failure until today to reduce PPC because?

- LPV not followed till extubation!
  - LPV guidelines are available.
- Opioids, PORC, oxygen, laying flat, no mobilisation in PACU.
  - New guidelines needed on O_2, opioids, PORC.
- Remote Inflammation due to surgical stress, sympathic stress, obesity.
  - Research needed to block better sympathic stress & inflammation.
  - Research needed to block inflammation through obesity.

- Early warning post PACU:
  - Monitoring breathing, CO_2, O_2 saturation if no oxygen

Only Visceral fat is Pro-inflammatory! and attract macrophages

Adipocyte death defines macrophage localization and function in adipose tissue of obese mice and humans

Saverio Cinti,* Grant Mitchell,† Giorgio Barbatelli,* Incoronata Murano,* Enzo Ceresi,* Emanuela Faloia,§ Shupei Wang,† Melanie Fortier,† Andrew S. Greenberg,[1,] and Martin S. Obin****

Institute of Normal Human Morphology* and Endocrinology Unit,§ University of Ancona, Ancona, Italy; Division of Medical Genetics,† Research Center, Hopital Ste.-Justine, Montreal, Canada; and Obesity and Metabolism Laboratory,** Jean Meyer United States Department of Agriculture-Human Nutrition Research Center on Aging at Tufts University, Boston, MA

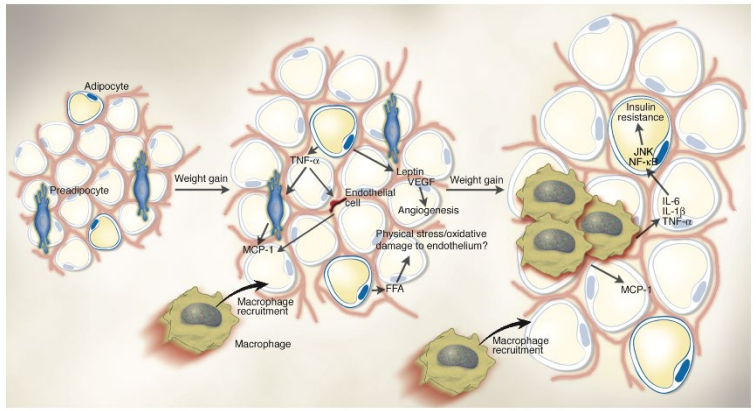

Figure 1
Obese adipose tissue is characterized by inflammation (1) and progressive infiltration by macrophages as obesity develops (10, 11). Changes in adipocyte and fat pad size lead to physical changes in the surrounding area and modifications of the paracrine function of the adipocyte. For example, in obesity, adipocytes begin to secrete low levels of TNF-α, which can stimulate preadipocytes to produce monocyte chemoat-

Visceral fat cells die, Macrophages infiltrate, release cytokines (induce inflammation in lungs)
Macrophage Clean up celdebris,
And swell with fat again...
(macrophages are embryologic fat cells!)

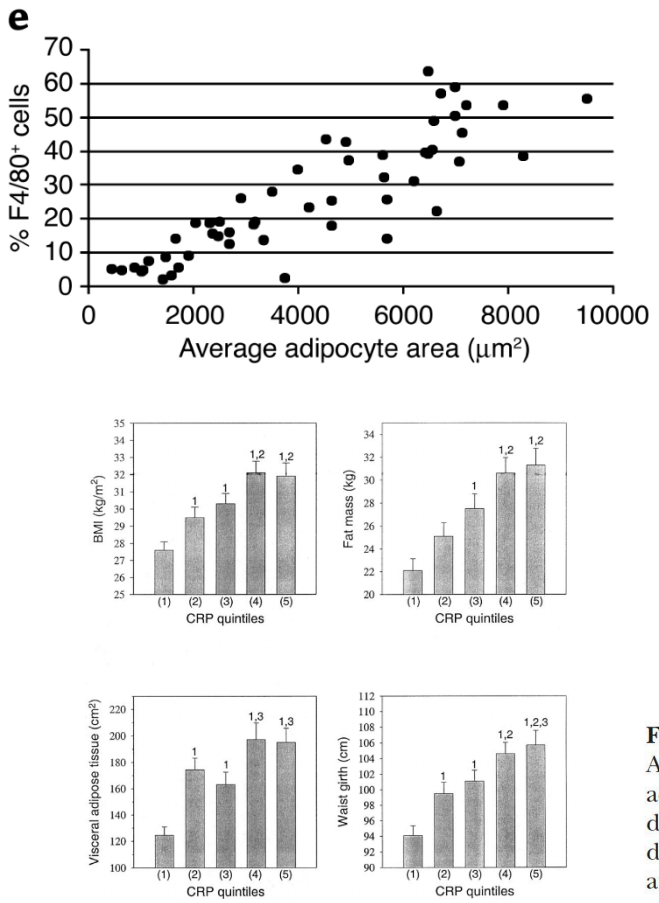

Figure 1. BMI, body fat mass, visceral AT area, and waist girth according to quintiles of plasma CRP levels. The significant difference ($P<0.0001$) from the corresponding quintiles is indicated above the standard error.

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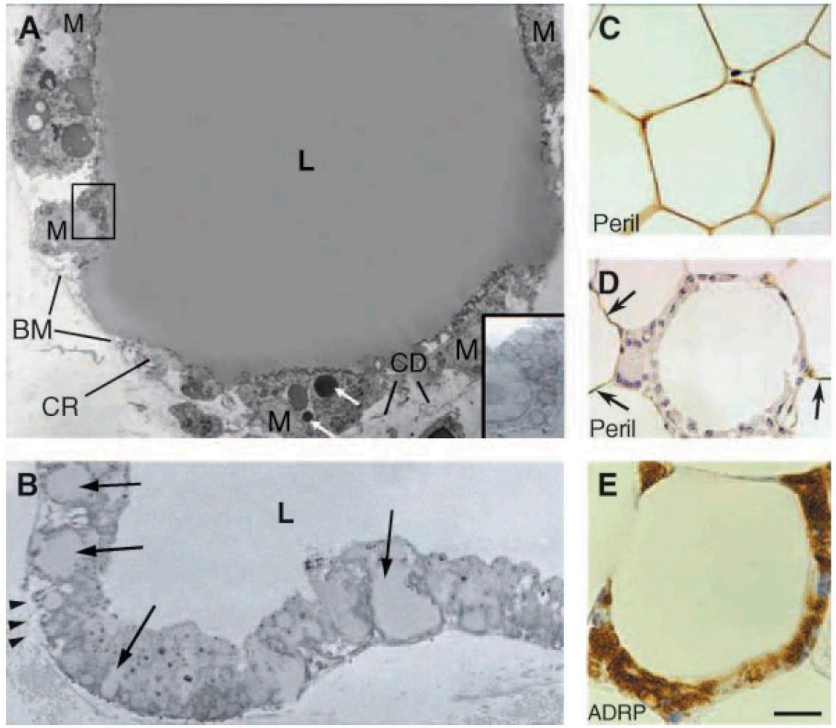

Fig. 2. CLS form exclusively at sites of adipocyte death and scavenge the residual adipocyte lip
A: Electron micrograph showing CLS macrophages (M) surrounding the residual lipid droplet (L
adipocyte. Evidence of necrosis includes disrupted basal membrane (BM), cytoplasmic remnants
debris (CD) in the interstitium, and the apparent degeneration of the unilocular lipid droplet
droplets. White arrows indicate lipid-laden phagolysosomes. The inset shows an enlargement of t
area showing small adipocyte lipid droplets engulfed by a macrophage. B: Necrotic features in *d*
adipocyte before recruitment of CLS macrophages. Note the rupture of basal membrane (arrow
the loss of lipid droplet (L) integrity manifest as small lipid droplets in the cytoplasm (arrows).
droplet degeneration in necrotic adipocytes can be detected at the light microscope level by the
droplet-associated proteins. All adipocytes of lean mice (C) are perilipin (Peril) immunoreactiv
whereas adipocytes surrounded by CLS in obese mice (D) are not immunoreactive for perilipin
cyte differentiation-related protein (ADRP); not shown]. Note that viable adipocytes (not surr
CLS) in obese mice (D) retain perilipin immunoreactivity (arrows). E: Scavenging of residual adip

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Yonsei Medical Journal YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

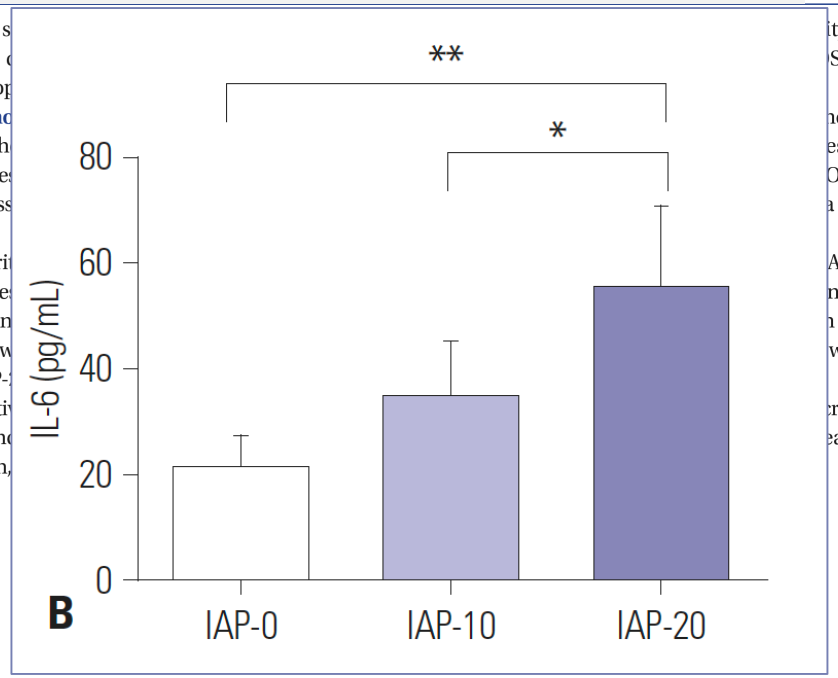
2 h pneumoperitoneum at 0, 10, or 20 mmHg

Effect of Pneumoperitoneum on Oxidative Stress and Inflammation via the Arginase Pathway in Rats

Seokyung Shin[1], Sungwon Na[1], Ok Soo Kim[2], Yong Seon Choi[1], Shin Hyung Kim[1], and Young Jun Oh[1]
iversity College of

Higher Pressure of pneumoperitoneum
-> more inflammation local & distance

Purpose: Oxidative s ity of nitric oxide (NO). However, the S), and arginase during CO_2 pneumop
Materials and Metho nduction, the ab- dominal cavities of th essures of 10 mm Hg and 20 mm Hg, re O was measured, while protein express a and lung tissue samples.
Results: Plasma nitri AP-20 compared to IAP-0. While expre nificantly greater in group IAP-20 than n in group IAP-0, while iNOS activity w was significantly greater in group IAP-
Conclusion: The acti reased, a change that contributes to in eased during CO_2 pneumoperitoneum,



Local inflammation with higher IAP

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Lung injury score based on
interstitial cellular infiltration, alveolar protein exudation, tissue hemorrhage

Remote inflammation in lungs without touching!

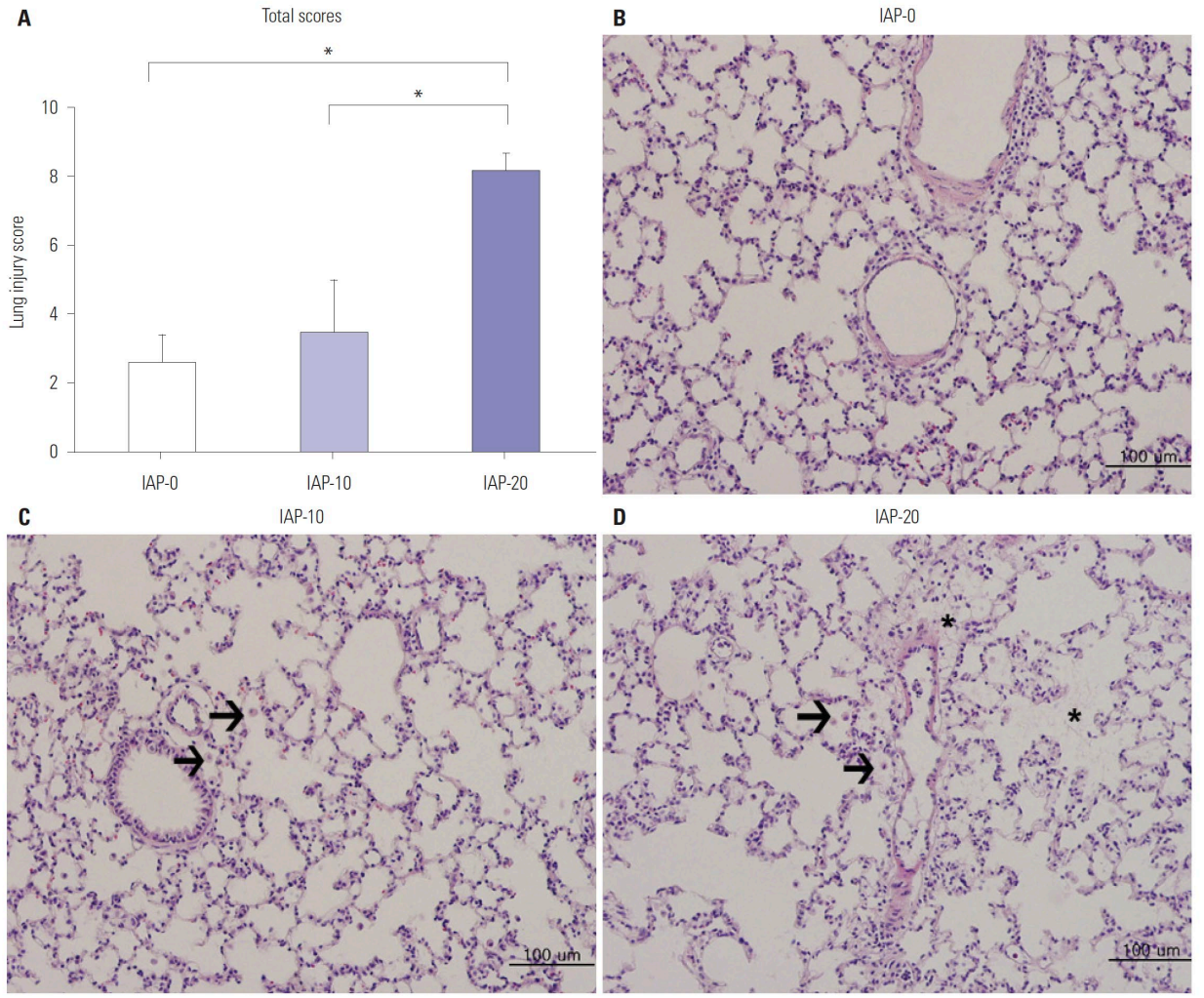


Fig. 5. The effects of different IAPs on histopathological changes in CO_2 pneumoperitoneum-induced lung injury in rats. (A) Total scores of lung injury were significantly higher in group IAP-20 than in groups IAP-0 and IAP-10. (B) Normal lung tissue is seen in the IAP-0 group. (C) A slight increase in cellularity (arrows) is seen in the IAP-10 group. (D) Inflammatory cell infiltration (arrows) with protein exudation (asterisks) and alveolus collapse is seen in the IAP-20 group. *p<0.001. IAP, intra-abdominal pressure.

Failure until today to reduce PPC because?

- LPV not followed till extubation!
  - LPV guidelines are available.
- Opioids, PORC, oxygen, laying flat, no mobilisation in PACU.
  - New guidelines needed on O_2, opioids, PORC.
- Remote Inflammation due to surgical stress, sympathic stress, obesity.
  - Research needed to block better sympathic stress & inflammation.
  - Research needed to block inflammation through obesity.
- Early warning post PACU:
  - Monitoring breathing, CO_2, O_2 saturation if no oxygen

Pulse oximetry may be a late symptom of apnea if Oxygen is given!

Curry and Jungquist *Patient Safety in Surgery* 2014, **8**:29
http://www.pssjournal.com/content/8/1/29

PATIENT SAFETY IN SURGERY

REVIEW Open Access

A critical assessment of monitoring practices, patient deterioration, and alarm fatigue on inpatient wards: a review

J Paul Curry[1*] and Carla R Jungquist[2]

Abstract

Approximately forty million surgeries take place annually in the United States, many of them requiring overnight or lengthier post operative stays in the over five thousand hospitals that comprise our acute healthcare system. Leading up to this Century, it was common for most hospitalized patients and their families to believe that being surrounded by well-trained nurses and physicians assured their safety. That bubble burst with the Institute of Medicine's 1999 report: To Err Is Human, followed closely by its 2001 report: Crossing the Quality Chasm. This review article discusses unexpected, potentially lethal respiratory complications known for being difficult to detect early, especially in postoperative patients recovering on hospital general care floors (GCF). We have designed our physiologic explanations and simplified cognitive framework to give our front line clinical nurses a thorough, easy-to-recall understanding of just how these events evolve, and how to detect them early when most

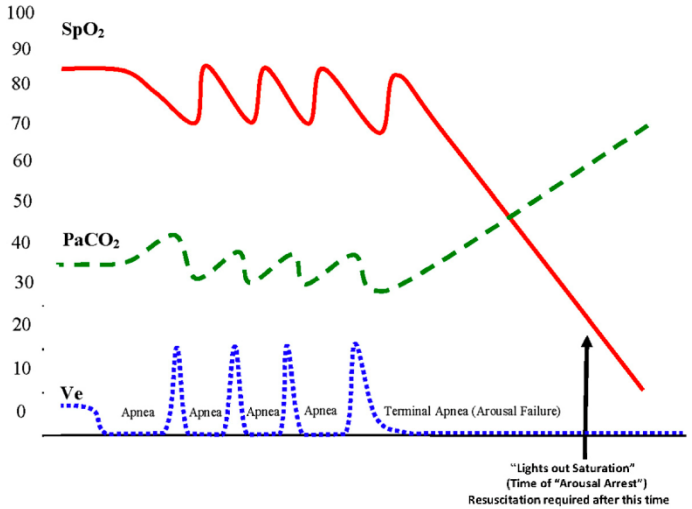


Figure 4 RECC Type III pattern of respiratory dysfunction (OSA).

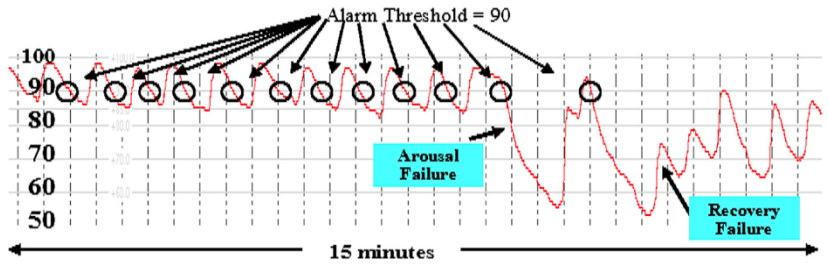


Figure 5 RECC type III pattern of respiratory dysfunction with arousal failure, recoveries, and alarm fatigue markers.

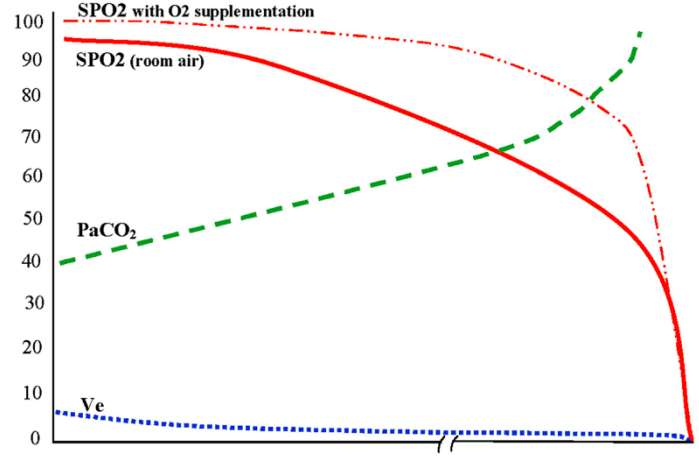


Figure 3 RECC Type II pattern of respiratory dysfunction (CO_2 Narcosis).

Therefore we need non invasive monitoring of

- Breathing tidal volume
- End tidal CO_2 or transcut CO_2
- Saturation without giving O_2

In every patient postoperative on the ward

2020 Mulier

Respiration and Sleep Medicine

Section Editor: **David Hillman**

SYSTEMATIC REVIEW ARTICLE

Continuous Pulse Oximetry and Capnography Monitoring for Postoperative Respiratory Depression and Adverse Events: A Systematic Review and Meta-analysis

Thach Lam, MD,* Mahesh Nagappa, MD,† Jean Wong, MD,* Mandeep Singh, MD, MSc,* David Wong, MD,* and Frances Chung, MBBS*

BACKGROUND: Death and anoxic brain injury from unrecognized postoperative respiratory depression (PORD) is a serious concern for patient safety. The American Patient Safety Foundation has called for continuous electronic monitoring for all patients receiving opioids in the postoperative period. These recommendations are based largely on consensus opinion with currently limited evidence. The objective of this study is to review the current state of knowledge on the effectiveness of continuous pulse oximetry (CPOX) versus routine nursing care and the effectiveness of continuous capnography monitoring with or without pulse oximetry for detecting PORD and preventing postoperative adverse events in the surgical ward.

METHODS: We performed a systematic search of the literature databases published between 1946 and May 2017. We selected the studies that included the following: (1) adult surgical patients (>18 years old); (2) prescribed opioids during the postoperative period; (3) monitored with CPOX and/or capnography; (4) primary outcome measures were oxygen desaturation, bradypnea, hypercarbia, rescue team activation, intensive care unit (ICU) admission, or mortality; and (5) studies published in the English language. Meta-analysis was performed using Cochrane Review Manager 5.3.

RESULTS: In total, 9 studies (4 examining CPOX and 5 examining continuous capnography) were included in this systematic review. In the literature on CPOX, 1 randomized controlled trial showed no difference in ICU transfers (6.7% vs 8.5%; $P = .33$) or mortality (2.3% vs 2.2%). A prospective historical controlled trial demonstrated a significant reduction in ICU transfers (5.6–1.2 per 1000 patient days; $P = .01$) and rescue team activation (3.4–1.2 per 1000 patient days; $P = .02$) when CPOX was used. Overall, comparing the CPOX group versus the standard monitoring group, there was 34% risk reduction in ICU transfer ($P = .06$) and odds of recognizing desaturation (oxygen saturation [Spo_2] <90% >1 hour) was 15 times higher ($P < .00001$). Pooled data from 3 capnography studies showed that continuous capnography group identified 8.6% more PORD events versus pulse oximetry monitoring group (CO_2 group versus Spo_2 group: 11.5% vs 2.8%; $P < .00001$). The odds of recognizing PORD was almost 6 times higher in the capnography versus the pulse oximetry group (odds ratio: 5.83, 95% confidence interval, 3.54–9.63; $P < .00001$). No studies examined the impact of continuous capnography on reducing rescue team activation, ICU transfers, or mortality.

CONCLUSIONS: The use of CPOX on the surgical ward is associated with significant improvement in the detection of oxygen desaturation versus intermittent nursing spot-checks. There is a trend toward less ICU transfers with CPOX versus standard monitoring. The evidence on whether the detection of oxygen desaturation leads to less rescue team activation and mortality is inconclusive. Capnography provides an early warning of PORD before oxygen desaturation, especially when supplemental oxygen is administered. Improved education regarding monitoring and further research with high-quality randomized controlled trials is needed. (Anesth Analg 2017;125:2019–29)

Continuous Pulse oximetry and no oxygen
To detect desaturations

Or

Continuous capnography and oxygen
To detect respiration being obstructive / arresting

Or in the Future

Continuous non invasive monitoring of minute volume ventilation …

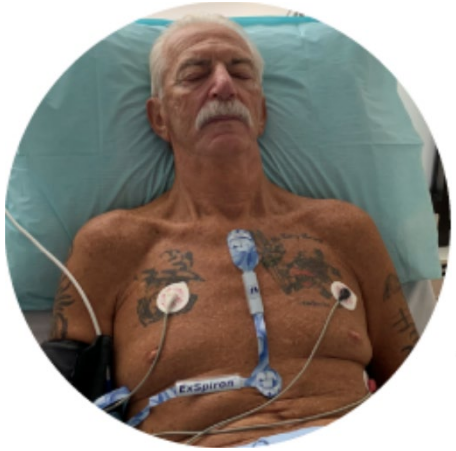
er

Section Editor: **Maxime Cannesson**

The Evaluation of a Noninvasive Respiratory Volume Monitor in Pediatric Patients Undergoing General Anesthesia

Andrea D. Gomez-Morad, MD,* Joseph P. Cravero, MD,* Brian C. Harvey, PhD,† Rachel Bernier, MPH,* Erin Halpin, MSN, RN,* Brian Walsh, PhD, RRT-NPS,* and Viviane G. Nasr, MD*

Continuous non invasive monitoring of minute volume ventilation ? …



- The ExSpiron 1Xi measures bioelectrical impedance, which is the tissue's opposition to carrying an alternating electrical current.
- Impedance measurements across the chest correlate with the volume of air in the lungs.
- The system consists of a single-use PadSet sensor and a monitor unit with integrated display

OR ?

"NEVER MISS A BREATH" WITH MINUTE VENTILATION MONITORING

FOR NON-INTUBATED PATIENTS

- Just OFA,
  - no sedation,
    - never PORC,
      - perfect LPV till extubation,

- No oxygen & No need for ExSpiron ???

) Mulier

Conclusion: What to do in every patient

1. PPC are frequent and happen every day if you take the broad definition.
   - Atelectasis, desaturation, obstructive breathing,… are PPC
2. Risk scoring before surgery. (who is at risk?)
   - Improve pre operative, weight reduction, stop smoking, treat anemia, …
3. Avoid PORC by measuring NMT objective in every patient getting NMB.
   - Reverse with Sugammadex when TOF < 4 and verify that TOF returns to 100 %
4. Apply LPV guidelines in every patient to avoid ateletasis.
   - Avoid oxygen postoperative, avoid sedation, avoid laying flat.
5. Reduce opioids postoperative by working multimodal.
   - Pulse oxymetry without oxygen therapy to identify risks
   - Capnography/breathing frequency if oxygen & opioids are given.

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