

Role of CO-Oximeter in Reduction of Post-Operative Respiratory Complications in Chronic Heavy Smokers

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Abstract

The worldwide number of smokers exceeds one billion, and about 6 million people die per year, due to tobacco use. Smoking and its hazards exert a heavy toll on healthcare expenditure as well, in countries around the world. Patients with a history of smoking have a greater risk for pulmonary complications following surgical procedures.

The Conventional technology relies on the use of arterial blood gas (ABG) analysis for monitoring gas saturation parameters in the blood but is invasive, expensive and cumbersome. Pulse CO-oximetry is a widely employed, operator-friendly, non-invasive monitoring method that yields comparable results to laboratory CO-oximetry and facilitates multi-parametric monitoring of the patients. It can accurately measure arterial oxygen saturation levels in heavy smokers who might have higher levels of circulating carboxyhemoglobin.

The technology is cost-effective, can facilitate early detection of post-operative pulmonary complications and has the potential to reduce healthcare costs and improve clinical outcomes.

Though clinical trials are yet to show benefit in patient monitoring from this technology, it is assumed to hold considerable promise in patients with risk factors for surgical complications.

Keywords: Heavy smoking; Post-operative pulmonary complications; Pulse CO-oximetry

4-7 points and the use of 15, 20 or 25 cigarettes per day often defining heavy smoking [9].

Introduction

The WHO estimates that there are 1.3 billion smokers worldwide [1]. Statistics from the U.S. reveal that 40 million people (16.8% of all adults) are smokers, and about 3200 individuals under the age of 18 start the habit every day [2]. About 6 million people die from tobacco use worldwide every year and this number may rise to 8 million, by 2030 [1]. Over two-thirds of these deaths occur in low- and middle-income countries [3]. This deadly habit also takes a heavy toll on healthcare expenditure in countries around the world. The annual economic cost of smoking in the U.S. is estimated at around \$300 billion, of which about \$176 billion is spent in direct medical care itself [4]. Tobacco use raises the risk for many diseases, including cancer, ischemic heart disease, chronic obstructive pulmonary disease (COPD), bronchitis, emphysema, stroke and lung cancer. Reports indicate that COPD will be the third leading cause of death by 2030, and about 90% of these deaths occur due to smoking alone [5].

There are no explicit guidelines that classify the extent of use of tobacco. Consumption of 1-10 cigarettes per day is considered as 'light smoking', while the use of 11-19 cigarettes constitutes 'moderate smoking'. A cumulative dose of 73000-146000 cigarettes, corresponding to 20 cigarettes per day, or 10-20 pack-years is regarded as heavy smoking and associated with high morbidity [1,6-8]. Clinical classification is often aided by Fagerström Test for Nicotine Dependence (FTND) and daily cigarette consumption, with scores of

Post-Operative Pulmonary Complications in Smokers

Post-operative pulmonary complication is generally defined as 'any pulmonary abnormality occurring in the post-operative period that produces identifiable disease or dysfunction that is clinically significant and adversely affects the clinical course' [10]. Post-operative pulmonary complications are associated with significant clinical and economic impact. Overall, these may result in longer hospital stay; increased use of antibiotics, the requirement for intensive care and mechanical ventilator support; and a higher risk for death. Some of the post-operative complications such as pneumonia can rapidly progress to acute lung injury, with limited treatment options, and cause high mortality [11].

The common post-operative pulmonary complications include pneumonia, atelectasis, chest infiltrates, fever, prolonged mechanical ventilation and respiratory failure, and depend on the type and duration of the surgery and anesthesia. Pulmonary complications occur more frequently after upper abdominal and thoracic surgeries, and to a less extent following urologic and orthopedic surgeries. Laparoscopic surgery considerably reduces the risk of pulmonary complications, by minimizing trauma to abdominal and diaphragmatic muscles and pain and facilitating rapid recovery [12].

Smoking increases the risk for a range of intra- and post-operative pulmonary complications, [13] due primarily to the chronic lung disease it produces. The use of 10 or more cigarettes per day

considerably increases the risk for post-operative respiratory complications, mainly due to impaired mucociliary transport system, decreased macrophage function, lowering of FEV1/VC and increased tracheobronchial glandular secretion. Smoking also increases the tracheal, bronchial and laryngeal irritability. The anesthetic agents and stasis of respiratory secretions often increase the risk for peri-anesthetic laryngospasm and bronchospasm in heavy smokers [14]. Current smokers have a higher risk for post-operative pulmonary complications, even in the absence of chronic lung disease [15]. Comorbidities such as coronary vascular disease, peripheral vascular disease, and COPD may also warrant special attention in management [14]. Anesthetic agents may cause post-operative respiratory depression in heavy smokers, which make loco-regional anesthesia a safer option in these patients.

A study showed the incidence of complications such as re-intubation, laryngospasm, bronchospasm, aspiration, hypoventilation and hypoxemia during anesthesia was 5.5% among smokers, compared to 3.3% in non-smokers [16].

Moller et al. reported a higher rate of ICU admission after surgery, among patients with a history of heavy and long-term smoking [17]. In a prospective cohort study on 410 patients who underwent non-cardiac elective surgery, Bluman et al. reported a six-fold higher incidence of post-operative pulmonary complications in smokers compared to non-smokers [18].

Hulzebos et al. who studied 117 patients undergoing elective Coronary Artery Bypass Graft, reported that a history of cigarette smoking as a risk factor for post-surgical pulmonary complications [19].

In a study on 118 patients, Kinugasa et al. observed that elderly patients with a history of heavy smoking and poor lung function had a higher risk for pneumonia following esophagectomy [20].

Agostini et al. who studied 234 patients who underwent thoracic surgery observed that smoking was an independent risk factor for post-operative pulmonary complications [21].

A retrospective cohort analysis of 393,794 patients undergoing elective surgery, reported a higher incidence of post-operative pneumonia among current smokers, compared to never- and prior-smokers [22]. The authors observed a dose-dependent increase in pulmonary complications, with the use of more than 20 packs per year associated with a greater frequency of surgical complications. Recently, in a retrospective analysis of 117 patients, observed that age above 70 years, heavy smoking and presence of COPD significantly increased the risk for pulmonary complications following liver resection [23].

Hirsch et al. reported that exposure to smoke and mechanical ventilation may synergistically act to increase neutrophil influx and the risk of acute lung injury [24]. Reports have revealed that smoking is a risk factor that adversely affects the incidence and prognosis of acute lung injury and other respiratory complications in the peri-operative and ICU settings [25-31].

Iribarren et al. in a large epidemiological study reported a close association and dose-dependent effect of, smoking on acute respiratory distress syndrome (ARDS) [26].

Studies show that stopping smoking 48 hours before surgery reduces a cough, pathogen burden in lower airways, normalizes carboxyhemoglobin (COHb) levels, neutralizes cardiovascular effects of nicotine, and improves respiratory ciliary function. However,

abstinence for 1-2 weeks is required to reduce sputum production while improving symptoms and lung function may require as long as 4-6 weeks [32]. An earlier study reported a lower incidence of post-operative complications in patients who quit smoking 8 weeks prior to surgery, than those who did not [33-35].

A contrasting study by Bluman et al. reported that abstinence for 4 weeks did not reduce the complications in smokers compared to non-smoker [18]. The minimum duration of abstinence/quitting required preventing post-operative complications are not known precisely [36].

Conventional Pulse Oximetry and its Limitations

Monitoring the oxygen saturation in peripheral circulation is critical for optimal surgical outcomes, and this is commonly done either directly by arterial blood gas analysis, or non-invasively by pulse oximetry.

Arterial blood gas (ABG) analysis involves measurements of the pH, arterial oxygen partial pressure (PaO_2), arterial carbon dioxide partial pressure (PaCO_2), bicarbonate ion (HCO_3^-) concentration, base excess and oxygen saturation (SaO_2). While it remains the gold standard, ABG analysis is invasive, cumbersome, painful and expensive.

Conventional pulse oximetry was developed in 1972 and offers non-invasive, safe and inexpensive measurement of oxygen saturation. In pulse oximetry, a probe is placed over a vascular bed (fingertip or ear lobe). Light Emitting Diodes (LED) in the probe emits light of two wavelengths (red and infra-red), which is absorbed by the arterial and venous blood as well as the tissue. Subsequently, a photodetector detects the light that passes through the tissue. Oxyhemoglobin absorbs more infra-red light compared to hemoglobin, and the differences in absorption are measured, and the absorbance ratio compared with the SpO_2 values.

Conventional pulse oximeters employ transmission sensors with light emitters and detectors located on opposite sides of the tissue bed, and suitable for measurements from fingertips, toes or earlobes [37,38]. Pulse oximeter probes using reflectance sensors (with emitter and detector placed adjacently) have also become available, which can obtain measurements from the forehead [39].

Reflectance forehead probes have a shorter response time, compared to fingertip probes, as they obtain the readings from the supraorbital artery which has abundant blood flow and is less subject to peripheral vasoconstriction [40].

Studies show the bias (difference between SpO_2 and SaO_2) and precision of pulse oximetry measurements deteriorate at SaO_2 levels less than 90% [41,42]. Though pulse oximetry shows high accuracy in one-point measurements of SaO_2 , it has poor reliability in predicting trends in SaO_2 , especially in ICU patients [42,43].

However, pulse oximetry has a number of limitations. The oximetry readings can be affected by the presence of dyshemoglobins (carboxyhemoglobin and methemoglobin), intravenous dyes, low perfusion states, skin pigmentation, anemia, use of nail polish, motion artifacts as well as poor operator knowledge [38].

In particular, the accuracy of pulse oximetry can be compromised by high concentrations of carbon monoxide. Carbon monoxide combines readily with hemoglobin, with an affinity 245 times higher than oxygen, forming carboxyhemoglobin (COHb). In non-smokers, COHb is found in concentrations less than 1.5%, while the levels range between 3 to 15%, in current smokers [32].

In a preliminary study on 50 non-smoking subjects in a non-smoking environment reported an average COHb level of 1%. The authors subsequently studied COHb levels in 33 smokers and 27 non-smokers in a smoking environment, using Rad-57 pulse co-oximeter. The results showed that the non-smokers had a mean COHb level of 2.49% (range, 1-6%) while it was 5.04% (range, 1-16%) in the smokers [44].

An earlier study revealed that methemoglobinemia is a common clinical entity, and occurs in patients over a broad range of ages-from 4 days to 86 years [45]. Many drugs, including benzocaine, lidocaine, nitroglycerin, inhaled nitric oxide and dapson can cause methemoglobinemia.

Methemoglobin and carboxyhemoglobin are incapable of oxygen transport and can reduce blood oxygenation and produce tissue hypoxemia. Methemoglobinemia and carboxyhemoglobinemia often manifest as flu-like symptoms and hence go undiagnosed, till very high levels of arterial carboxyhemoglobin saturation (SpCO₂) and arterial methemoglobin saturation (SpMet) are reached. Low levels of methemoglobin do not have significant clinical effects, but morbidity increases with increase in concentration, and death may occur at high levels.

Several reports show that pulse oximetry may lead to overestimation of arterial oxygenation in patients with higher levels of COHb, the extent of overestimation approximately being equal to the level of COHb [46-48].

Pulse CO-Oximetry

Pulse CO-oximetry is technology developed by Masimo Corp (Irvine, CA, USA) that enables continuous, non-invasive estimation of hemoglobin, carboxyhemoglobin, methemoglobin, oxygen level and Pleth Variability Index along with oxygen saturation, pulse rate and perfusion index [49]. The measurements are obtained using multi-wavelength sensors (single-use, adhesive type for continuous monitoring; or re-usable finger-clip sensors for spot checking) [50]. Radical-7 and Rad-87 are two versions of devices with this technology that aid bedside monitoring, while Rad-57 and Pronto are hand-held devices suitable for spot checking.

Erroneous readings and false alarms caused by patient movement have been a drawback of pulse oximeters [51-55]. However, devices with improved signal processing techniques (e.g., Masimo signal extraction technology (SETTM)) has addressed this problem effectively [56-58].

Berkow et al. reported comparable accuracy of continuous non-invasive monitoring of hemoglobin (SpHb) with that of laboratory CO-oximetry, upon analysis of 130 arterial blood gas samples from patients who underwent spine surgeries [59]. Causey et al. also reported similar findings in surgical and intensive care patients [60].

In a comparison of SpHb measurements with capillary hemoglobin and laboratory methods, Lamhaut et al. observed that the techniques yielded comparable results, though the non-invasive monitoring produced a marginal increase in outliers [61].

Lindner and Exadaktylos suggested that the real utility of SpHb measurement lies in its capability as an indicator for subtle changes in hemoglobin trends during occult bleeding or following blood transfusion. The authors remarked that the technology can improve

clinical care by augmenting conventional laboratory-based monitoring [51].

A randomized controlled study on 327 surgical patients revealed that addition of SpHb monitoring to the standard care reduced blood transfusion rates from 4.5% to 0.6%, and the number of mean units (0.1 vs. 0.01) transfused per patient [62].

In a prospective observational study on 28 surgical patients, Yamaura et al. reported that SpHb measurements in anesthetized patients were significantly affected by thermoregulatory vasoconstriction and perfusion state [63]. Similar findings were reported by Isosu et al. in a study on Japanese surgical patients [64].

Yamada et al. reported good relative trending accuracy of SpHb measurements made using a Radical-7 pulse co-oximeter in a series of 12 patients undergoing hemodialysis in an ICU, reflecting the potential of pulse co-oximetry in evaluating relative changes in blood volume [65].

Barker et al. evaluated the accuracy of Masimo Rainbow-SET Rad-57 pulse co-oximeter (Masimo Corporation, Irvine, CA, USA) in measuring dyshemoglobins, in healthy volunteers receiving induction of carboxyhemoglobinemia (0 to 15%) and methemoglobinemia (0 to 12%). A comparison of the COHb values estimated using the instrument and a standard laboratory CO-oximeter revealed a low bias (-1.22%), and a precision of 2.19%. The corresponding values for MetHb measurements were 0.0% and 0.45%, respectively [66].

The study by Feiner et al. showed a bias and precision of -0.7% and 4.0%, respectively, in pulse CO-oximeter-based measurements of COHb at SaO₂ levels less than 95%. However, the technique failed to detect COHb when the levels were lower than 85%. [67] A low bias (3%) was also reported between CO-oximeter-based and laboratory CO-oximeter based estimation of COHb in patients with suspected carbon monoxide poisoning [68,69].

Since the limits of agreement between the two types of measurements were large, some authors have recommended against replacing laboratory CO-Hb measurements by pulse CO-oximeter readings [68-70].

According to Hare et al. anesthesia-transition periods are associated with a high risk for hypoxemia (SpO₂ less than 90%) [71]. Pulse oximetry may facilitate early detection of hypoxemia in these settings [41,72].

Another important application of pulse oximetry could be in the reliable titration of fractional inspired oxygen concentration (FIO₂) in patients receiving mechanical ventilation. Rice et al. analyzed data from 1074 patients with acute lung injury or ARDS to evaluate whether the ratio of SpO₂ to FIO₂ (S/F ratio) can be a surrogate for the ratio of PaO₂ to FIO₂ (P/F ratio). They observed that the S/F ratio was a reliable proxy for P/F ratio in surgical patients requiring mechanical ventilation [73].

A subsequent study reported that S/F ratios can be a reliable surrogate for P/F ratio in the calculation of sequential organ failure assessment score, in critically ill patients [74].

Pulse oximetry can also be a cost-effective strategy in the emergency and ICU settings, compared to ABG analysis; [75,76] however, explicit guidelines for its optimal use are still lacking.

A randomized study on 1219 surgical patients compared the utility of pulse oximetry in determining the requirement for ICU transfer of

the patients from a surgical floor [77]. The authors noted that the rate of ICU transfer for pulmonary complications was lower among the patients monitored by oximetry, compared to a control group. Oximetry-based monitoring also reduced the total estimated cost of the study (\$15,481 compared to \$18,173 in control group).

Despite the obvious advantages of pulse oximeters, clinical trials thus far have failed to show improvement in clinical outcomes with their use. This is attributed to the signal-to-noise ratio, [41,78] and the requirement for a larger sample size [41].

However, in view of its ability to yield multiparametric data, facile operation and cost-effectiveness, pulse oximetry may still hold considerable value in the post-operative monitoring for pulmonary complications in patients with a history of smoking.

Conclusion

Smoking exerts a heavy toll on human morbidity and mortality worldwide, and on healthcare expenditure in most countries. Patients with a history of heavy smoking face a greater risk for perioperative pulmonary complications, and systematic monitoring for these is essential for optimal clinical outcomes. Compared to ABG analysis, pulse oximetry affords a non-invasive, cost-effective and facile technology to monitor multiple parameters important to clinical monitoring of these patients. Pulse-CO-oximetry can aid early detection of hypoxemia, and reliable measurements of multiple parameters, even during periods of patient movement and low peripheral perfusion. The utility of this technology needs to be evaluated further in broader settings and larger cohorts of surgical patients.

Disclosures

- The authors declare that they have no conflict of interest.
- This article does not contain any studies with human participants or animals performed by any of the authors.
- There was no prior publication or presentation of this study.
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References

1. World Health Organization (2011) WHO Report on the Global Tobacco Epidemic. Geneva.
2. US Department of Health and Human Services (2014) The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, US.
3. Lozano R, Murray CJL, Lopez A [2012] Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 380: 2224-2260.
4. Xu X, Bishop EE, Kennedy SM, Simpson SA, Pechacek TF (2015) Annual healthcare spending attributable to cigarette smoking: an update. *Am J Prev Med* 48: 326-333.
5. World Health Organization (2016) Burden of COPD.
6. US Centers for Disease Control and Prevention (2016) Smoking & Tobacco Use.
7. Kruger J, O'Halloran A, Rosenthal A (2015) Assessment of compliance with U.S. Public Health Service clinical practice guideline for tobacco by primary care physicians. *Harm Reduct J* 12: 7.
8. Kamholz SL (2004) Pulmonary and cardiovascular consequences of smoking. *Med Clin North Am* 88: 1415-1430, ix-x.
9. Neumann T, Rasmussen M, Heitmann BL, Tønnesen H (2013) Gold standard program for heavy smokers in a real-life setting. *Int J Environ Res Public Health* 10: 4186-4199.
10. O'Donohue WJ Jr (1992) Postoperative pulmonary complications. When are preventive and therapeutic measures necessary? *Postgrad Med* 91: 167-170, 173-175.
11. Weingarten TN, Kor DJ, Gali B, Sprung J (2013) Predicting postoperative pulmonary complications in high-risk populations. *Curr Opin Anaesthesiol* 26: 116-125.
12. Doyle RL (1999) Assessing and modifying the risk of postoperative pulmonary complications. *Chest* 115: 77S-81S.
13. Egan TD, Wong KC (1992) Perioperative smoking cessation and anesthesia: a review. *J Clin Anesth* 4: 63-72.
14. Worlee GM (1988) Common perioperative problems and the anaesthetist. The Netherlands: Kluwer Academic Publishers.
15. Rudra A, Das S (2006) Postoperative pulmonary complications. *Ind J Anaesth* 50: 89-98.
16. Schwilk B, Bothner U, Schraag S, Georgieff M (1997) Perioperative respiratory events in smokers and non-smokers undergoing general anaesthesia. *Acta Anaesthesiologica Scandinavica* 41: 348-355.
17. Moller AM, Pedersen T, Villebro N, Munksgaard A (2003) Effect of smoking on early complications after elective orthopaedic surgery. *J Bone Joint Surg Br* 85: 178-181.
18. Bluman LG, Mosca L, Newman N, Simon DG (1998) Preoperative smoking habits and postoperative pulmonary complications. *Chest* 113: 883-889.
19. Hulzebos EH, Van Meeteren NL, De Bie RA, Dagnelie PC, Helders PJ (2003) Prediction of postoperative pulmonary complications on the basis of preoperative risk factors in patients who had undergone coronary artery bypass graft surgery. *Phys Ther* 83: 8-16.
20. Kinugasa S, Tachibana M, Yoshimura H, Ueda S, Fujii T, et al. (2004) Postoperative pulmonary complications are associated with worse short- and long-term outcomes after extended esophagectomy. *J Surg Oncol* 88: 71-77.
21. Agostini P, Cjeslik H, Rathinam S, Bishay E, Kalkat MS, et al. (2010) Postoperative pulmonary complications following thoracic surgery: are there any modifiable risk factors? *Thorax* 65: 815-818.
22. Hawn MT, Houston TK, Campagna EJ, Graham LA, Singh J, et al. (2011) The attributable risk of smoking on surgical complications. *Ann Surg* 254: 914-920.
23. Choudhuri AH, Chandra S, Aggarwal G, Uppal R (2014) Predictors of postoperative pulmonary complications after liver resection: Results from a tertiary care intensive unit. *Indian J Crit Care Med* 18: 358-362.
24. Hirsch J, Chalkley RJ, Bentley T, Burlingame AL, Frank JA (2014) Double impact of cigarette smoke and mechanical ventilation on the alveolar epithelial type II cell. *Crit Care* 18: R50.
25. McCulloch TM, Jensen NF, Girod DA, Tsue TT, Weymuller EA Jr (1997) Risk factors for pulmonary complications in the postoperative head and neck surgery patient. *Head Neck* 19: 372-377.
26. Iribarren C, Jacobs DR Jr, Sidney S, Gross MD, Eisner MD (2000) Cigarette smoking, alcohol consumption, and risk of ARDS: a 15-year cohort study in a managed care setting. *Chest* 117: 163-168.
27. Tandon S, Batchelor A, Bullock R, Gascoigne A, Griffin M, et al. (2001) Peri-operative risk factors for acute lung injury after elective oesophagectomy. *Br J Anaesth* 86: 633-638.
28. TenHoor T, Mannino DM, Moss M (2001) Risk factors for ARDS in the United States: analysis of the 1993 National Mortality Followback Study. *Chest* 119: 1179-1184.
29. Zingg U, Smithers BM, Gotley DC, Smith G, Aly A, et al. (2011) Factors associated with postoperative pulmonary morbidity after esophagectomy for cancer. *Ann Surg Oncol* 18: 1460-1468.

30. Paul DJ, Jamieson GG, Watson DI, Devitt PG, Game PA (2011) Perioperative risk analysis for acute respiratory distress syndrome after elective oesophagectomy. *ANZ J Surg* 81: 700-706.
31. Ando K, Doi T, Moody SY, Ohkuni Y, Sato S, et al. (2012) The effect of comorbidity on the prognosis of acute lung injury and acute respiratory distress syndrome. *Intern Med* 51: 1835-1840.
32. Pearce AC, Jones RM (1984) Smoking and anaesthesia: preoperative abstinence and perioperative morbidity. *Anesthesiology* 61: 576-584.
33. Warner MA, Divertie MB, Tinker JH (1984) Preoperative cessation of smoking and pulmonary complications in coronary artery bypass patients. *Anesthesiology* 60: 380-383.
34. Warner DO, Warner MA, Offord KP, Schroeder DR, Maxson P, et al. (1999) Airway obstruction and perioperative complications in smokers undergoing abdominal surgery. *Anesthesiology* 90: 372-379.
35. Warner MA, Offord KP, Warner ME, Lennon RL, Conover MA, et al. (1989) Role of preoperative cessation of smoking and other factors in postoperative pulmonary complications: a blinded prospective study of coronary artery bypass patients. *Mayo Clin Proc* 64: 609-616.
36. Warner DO (2000) Preventing postoperative pulmonary complications: the role of the anesthesiologist. *Anesthesiol* 92: 1467-1472.
37. Clayton DG, Webb RK, Ralston AC, Duthie D, Runciman WB (1991) Pulse oximeter probes. A comparison between finger, nose, ear and forehead probes under conditions of poor perfusion. *Anaesthesia* 46: 260-265.
38. Jubran A (2015) Pulse oximetry. *Crit Care* 19: 272.
39. Branson RD, Mannheim PD (2004) Forehead oximetry in critically ill patients: the case for a new monitoring site. *Respir Care Clin N Am* 10: 359-367, vi-vii.
40. MacLeod DB, Cortinez LI, Keifer JC, Cameron D, Wright DR, et al. (2005) The desaturation response time of finger pulse oximeters during mild hypothermia. *Anaesthesia* 60: 65-71.
41. Jubran A, Tobin MJ (2013) Monitoring during mechanical ventilation: In: Tobin MJ, editor. *Principles and Practice of Mechanical Ventilation*. New York: McGraw-Hill Inc 261-287.
42. Van de Louw A, Cracco C, Cerf C, Harf A, Duvaldestin P, et al. (2001) Accuracy of pulse oximetry in the intensive care unit. *Intensive Care Med* 27: 1606-1613.
43. Perkins GD, McAuley DF, Giles S, Routledge H, Gao F (2003) Do changes in pulse oximeter oxygen saturation predict equivalent changes in arterial oxygen saturation? *Crit Care* 7: R67.
44. Light A, Grass C, Pursley D, Krause J (2007) Carboxyhemoglobin levels in smokers vs. non-smokers in a smoking environment. *Respir Care* 52: 1576.
45. Ash-Bernal R, Wise R, Wright SM (2004) Acquired methemoglobinemia: a retrospective series of 138 cases at 2 teaching hospitals. *Medicine (Baltimore)* 83: 265-273.
46. Shippy MB, Petterson MT, Whitman RA, Shivers CR (1984) A clinical evaluation of the BTI Biox II Ear Oximeter. *Respir Care* 29: 730-735.
47. Buckley RG, Aks SE, Eshom JL, Rydman R, Schaidler J, et al. (1994) The pulse oximetry gap in carbon monoxide intoxication. *Ann Emerg Med* 24: 252-255.
48. Hampson NB (1998) Pulse oximetry in severe carbon monoxide poisoning. *Chest* 114: 1036-1041.
49. O'Brien D (2006) Audible alarms in medical equipment. *Med Devices Diagnostic Industry* 28: 98-103.
50. Lindner G, Exadaktylos AK (2013) How Noninvasive Haemoglobin Measurement with Pulse CO-Oximetry Can Change Your Practice: An Expert Review. *Emerg Med Int* 2013: 701529.
51. Moller JT, Johannessen NW, Espersen K, Ravlo O, Pedersen BD, et al. (1993) Randomized evaluation of pulse oximetry in 20,082 patients: II. Perioperative events and postoperative complications. *Anesthesiology* 78: 445-453.
52. Runciman WB, Webb RK, Barker L, Currie M (1993) The Australian Incident Monitoring Study. The pulse oximeter: applications and limitations-an analysis of 2000 incident reports. *Anaesth Intensive Care* 21: 543-550.
53. Reich DL, Timcenko A, Bodian CA, Kraidin J, Hofman J, et al. (1996) Predictors of pulse oximetry data failure. *Anesthesiology* 84: 859-864.
54. Rheineck-Leyssius AT, Kalkman CJ (1997) Influence of pulse oximeter lower alarm limit on the incidence of hypoxaemia in the recovery room. *Br J Anaesth* 79: 460-464.
55. Dumas C, Wahr JA, Tremper KK (1996) Clinical evaluation of a prototype motion artifact resistant pulse oximeter in the recovery room. *Anesth Analg* 83: 269-272.
56. Barker SJ, Shah NK (1997) The effects of motion on the performance of pulse oximeters in volunteers (revised publication). *Anesthesiology* 86: 101-108.
57. Barker SJ (2002) "Motion-resistant" pulse oximetry: a comparison of new and old models. *Anesth Analg* 95: 967-972.
58. Petterson MT, Begnoche VL, Graybeal JM (2007) The effect of motion on pulse oximetry and its clinical significance. *Anesth Analg* 105: S78-84.
59. Berkow L, Rotolo S, Mirski E (2011) Continuous noninvasive hemoglobin monitoring during complex spine surgery. *Anesth Analg* 113: 1396-1402.
60. Causey MW, Miller S, Foster A, Beekley A, Zenger D, et al. (2011) Validation of noninvasive hemoglobin measurements using the Masimo Radical-7 SpHb Station. *Am J Surg* 201: 590-596.
61. Lamhaut L, Apriotesei R, Combes X, Lejay M, Carli P, et al. (2011) Comparison of the accuracy of noninvasive hemoglobin monitoring by spectrophotometry (SpHb) and hemocue with automated laboratory hemoglobin measurement. *Anesthesiology* 115: 548-554.
62. Ehrenfeld JMHJ (2010) Impact of continuous and noninvasive hemoglobin monitoring on intraoperative blood transfusions. *Proceedings of the Annual Meeting of the American Society of Anesthesiologists*. San Diego.
63. Yamaura K, Nanishi N, Higashi M, Hoka S (2014) Effects of thermoregulatory vasoconstriction on pulse hemoglobin measurements using a co-oximeter in patients undergoing surgery. *J Clin Anesth* 26: 643-647.
64. Isosu T, Obara S, Hosono A, Ohashi S, Nakano Y, et al. (2013) Validation of continuous and noninvasive hemoglobin monitoring by pulse CO-oximetry in Japanese surgical patients. *J Clin Monit Comput* 27: 55-60.
65. Yamada H, Saeki M, Ito J, Kawada K, Higurashi A, et al. (2015) The relative trending accuracy of noninvasive continuous hemoglobin monitoring during hemodialysis in critically ill patients. *J Clin Monit Comput* 29: 107-112.
66. Barker SJ, Curry J, Redford D, Morgan S (2006) Measurement of carboxyhemoglobin and methemoglobin by pulse oximetry: a human volunteer study. *Anesthesiology* 105: 892-897.
67. Feiner JR, Rollins MD, Sall JW, Eilers H, Au P, et al. (2013) Accuracy of carboxyhemoglobin detection by pulse CO-oximetry during hypoxemia. *Anesth Analg* 117: 847-858.
68. Sebbane M, Claret PG, Mercier G, Lefebvre S, Théry R, et al. (2013) Emergency department management of suspected carbon monoxide poisoning: role of pulse CO-oximetry. *Respir Care* 58: 1614-1620.
69. Touger M, Birnbaum Am, Wang J, Chou K, Pearson D, et al. (2010) Performance of the RAD-57 pulse CO-oximeter compared with standard laboratory carboxyhemoglobin measurement. *Ann Emerg Med* 56: 382-388.
70. Maisel WH, Lewis RJ (2010) Noninvasive measurement of carboxyhemoglobin: how accurate is accurate enough? *Ann Emerg Med* 56: 389-391.
71. Hare GM, Kavanagh BP (2010) Hypoxemia during surgery: learning from history, science, and current practice. *Can J Anaesth* 57: 877-881.
72. Pretto JJ, Roebuck T, Beckert L, Hamilton G (2014) Clinical use of pulse oximetry: official guidelines from the Thoracic Society of Australia and New Zealand. *Respirology* 19: 38-46.
73. Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, et al. (2007) Comparison of the SpO₂/FIO₂ ratio and the PaO₂/FIO₂ ratio in patients with acute lung injury or ARDS. *Chest* 132: 410-417.

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74. Pandharipande PP, Shintani AK, Hagerman HE, St Jacques PJ, Rice TW, et al. (2009) Derivation and validation of Spo₂/Fio₂ ratio to impute for Pao₂/Fio₂ ratio in the respiratory component of the Sequential Organ Failure Assessment score. *Crit Care Med* 37: 1317-1321.
 75. Solsona JF, Marrugat J, Vázquez A, Masdeu G, Álvarez F, et al. (1993) Effect of pulse oximetry on clinical practice in the intensive care unit. *Lancet* 342: 311-312.
 76. Le Bourdellès G, Estagnasié P, Lenoir F, Brun P, Dreyfuss D (1998) Use of a pulse oximeter in an adult emergency department: impact on the number of arterial blood gas analyses ordered. *Chest* 113: 1042-1047.
 77. Ochroch EA, Russell MW, Hanson WC 3rd, Devine GA, Cucchiara AJ, et al. (2006) The impact of continuous pulse oximetry monitoring on intensive care unit admissions from a postsurgical care floor. *Anesth Analg* 102: 868-875.
 78. Shah A, Shelley KH (2013) Is pulse oximetry an essential tool or just another distraction? The role of the pulse oximeter in modern anesthesia care. *J Clin Monit Comput* 27: 235-242.