Title: Is the perioperative change in ultrasound-based diaphragmatic inspiratory amplitude predictive of postoperative atelectasis? A prospective observational study in obese patients undergoing bariatric surgery.

Protocol 994/19

Introduction

Obese patients undergoing bariatric surgery, are at high risk for postoperative respiratory complications but predictive variables, risk factors and criteria for postoperative ICU admission are debated (1-3). In these patients, postoperative respiratory complications are related to various pathophysiological mechanisms that include: decreased lung volumes, respiratory muscle dysfunction and atelectasis (4). Very recently it has also been demonstrated a possible role of molecules that would mediate the fibro-adipogenic remodeling of the diaphragm in the obese, thus increasing the respiratory disability (5).

Pulmonary atelectasis appears within minutes after anesthesia induction, complicate 85-90% of the cases -involving up to 15% of the lungs and inducing a 5 to 10% of cardiac output intra pulmonary shunting- and determine an increased incidence of postoperative morbidity (with higher incidence of pneumonia) (6-11). Furthermore, in the perioperative period, obese patients are more likely to develop atelectasis that resolves more slowly than in non-obese patients (12). Surgical handling of sub diaphragmatic region, as during sleeve gastrectomy, can impair diaphragmatic excursions thus contributing to postoperative pulmonary dysfunction (12-17). The same upper abdominal surgery represents a risk factor for the development of pulmonary complications in the perioperative period and alteration of the respiratory function indices (18).

Ultrasounds (US) imaging is a real-time, bedside, non-invasive technique that allows the quantitative evaluation of amplitude, force and velocity of diaphragmatic movement, including: diaphragmatic inspiratory amplitude (DIA) and diaphragmatic thickening (19). The US-DIA is a qualified quantitative approach to assess diaphragmatic function and has been reported to linearly correlate with vital capacity (20-26). In obese patients undergoing sleeve gastrectomy there are no conclusive criteria for discharge and indications to postoperative ICU admission, as recently defined for patients with OSAS (27,28). We hypothesize that perioperative change in US-DIA predicts postoperative atelectasis, thus providing a clinically useful tool to stratify the need for higher intensity monitoring including ICU admission (3,27).

Aim of this prospective observational study, in obese patients undergoing sleeve gastrectomy, is to evaluate the relationship between pre to postoperative changes in US-DIA and PaO_2/FiO_2.

Methods

After IRB approval from the University of Rome and having the patient's written consent, 40 consecutive patients morbidly obese (BMI >30 Kg/m^2), aged >18 years, undergoing laparoscopic sleeve gastrectomy will be enrolled in this prospective observational study. Exclusion criteria will be any of the following: sign and symptoms of heart failure, neuromuscular diseases or previous thoracic surgery, American Society of Anesthesiology physical (ASA) status >III.

Study protocol

Perioperative monitoring will include continuous 3-lead electrocardiogram, heart rate (HR), invasive (arterial line) systolic, diastolic and mean arterial pressure (MAP), SpO2, end-Tidal CO2, end-Tidal desflurane, diuresis and body temperature. In all patients anesthesia will be induced, according available guidelines, with propofol (2 mg/kg of IBW) and fentanyl (2 mg/kg of IBW) (4). To facilitate endotracheal intubation and mechanical ventilation, neuromuscular block will be induced with rocuronium dose (0.6 mg/kg) based on the patient's real body weight, and will be monitored throughout anesthesia using an acceleromyographic train-of-four stimulus to the adductor pollicis (3). After anesthesia induction trachea will be intubated, and mechanical ventilation with intermittent positive pressure ventilation (IPPV) will be started at a Tidal volume of 7 mL/kg of IBW and with 12 breaths per minute. Lungs will be ventilated with air/O2 mixture to keep PaO2 between 100 and 200mm Hg. After the beginning of mechanical ventilation, desflurane will be started maintaining a minimum alveolar concentration (MAC) of 6% and a fresh gas flow of

3.0 l/min. Intraoperative normothermia will be warrant with forced air systems. The total amount of remifentanil infused through a dedicated venous line during the surgical procedure will be recorded. At the end of anesthesia, neuromuscular block will be reversed with sugammadex. The dose of sugammadex used will depend on the level of neuromuscular block to antagonize according to the following modalities. If the recovery from the rocuronium-induced block will reach a value of at least 1-2 PTC (Post tetanic count), the dose of sugammadex used will be 4 mg/kg bw. In the presence of a spontaneous recovery reached until the reappearance of T2 the dose used will be 2mg/kg. The median time to restore a value of 0.9 of the ratio T4/T1 will be registered, then inhalational anesthesia will be discontinued. After skin closure and reversal of neuromuscular block, desflurane administration will be stopped and to speed up anesthetic washout the fresh gas flow will be increased to 10 l/min. Postoperatively, supplemental O_2 will be provided with the minimal FiO_2 needed to keep SpO_2 >93% as prescribed by guidelines on OSAS (27).

Measurements

Demographics (age, gender, BMI) and clinical characteristics including: ASA and comorbidities and pre and post operative respiratory function [PaO_2/FiO_2 ratio, Blood gas analysis (BGA)] and US-DIA will be recorded. These data will be collected according to time sequence:

T0: preoperative <24hours before surgery: US-DIA, BGA while the patient is breathing minimal supplement FiO_2 needed to keep SpO_2 >93%.

T1: Post op: at 60 min after extubation: Aldrete, US-DIA, BGA.

T2: Post op at 240 min: Aldrete, BGA.

Occurrence and severity of postoperative atelectasis, duration of surgery, RASS, Aldrede score, VAS, intraoperative fluid balance, premedication and intraoperative use of opioids and neuromuscular blocking drugs used will be also recorded.

Primary endpoint will be to detect the relationship between perioperative changes in DIA during forced breath and occurrence and severity of postoperative atelectasis (PaO_2/FiO_2) at 240 min after extubation (T2).
Secondary endpoints will be: amount of muscle relaxants, opioids and fluids used intraoperatively, BGA at T0, T1 and T2 with $PaCO_2$ and ph, difference in pre and postoperative DIA during a quite breath, incidence of pneumonia at second postoperative day, LOS, needs of postoperative ICU recovery, mortality at hospital discharge.

Ultrasound evaluation

In eligible patients, a preoperative baseline ultrasound evaluation of the diaphragm and lungs is accomplished. A Philips HD7X3 (Philips Medical Systems, Bothell, WA, USA) US machine will be used and equipped with a 4 MHz convex probe. Evaluation will be performed by a single operator, blinded to the arterial blood gas analysis values. In a semi recumbent position (bed slope of 45°) patients will be asked to rest and breath quietly with their eyes closed. An anterior approach will be carried out applying freehand transducer on abdomen at the right midclavicular line immediately below the costal margin with firm pressure, steering in cranial direction. A B-mode transverse scanning will be performed looking across the liver for inferior vena cava (IVC) on the right of the screen and gallbladder in the middle. Measurements will be recorded by the M-mode frozen images using the US machine calibration and algorithm. The M-mode modality will be used to study DIA, regulating the lowest possible gain setting to enhance the trace: the best sinusoidal curve will be considered for measurements. During resting and forced breathing, measurement of DIA will be recorded drawing a vertical line from the leading edge of the inspiratory peak on the sinusoidal curve to the leading edge of the imaginary horizontal line passing through the baseline, corresponding to the end of normal expiration. The inspiratory and expiratory times will be finally measured both during resting (t0, t1 respectively) and forced breathing (T0, T1 respectively).

Moreover, to reduce the measurement error and calculate the intraobserver variability, every recording will be taken three times, both during resting and forced breathing: the highest value of these three measurements will be considered. Data on pre and post operative spirometry will be recorded when available.

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