Mechanical ventilation is frequently used as a supportive strategy in intensive care medicine and anaesthesiology despite its potential to aggravate or even initiate lung injury. Indeed, overdistension of nondependent lung regions and repetitive opening and closing of dependent lung regions may cause mechanical stress and strain, eventually worsening or causing lung damage.1,2 Critically ill patients with acute respiratory distress syndrome (ARDS) requiring long-term mechanical ventilation (i.e. for days) have been found to benefit from lung-protective mechanical ventilation settings that limit airway pressures and tidal volumes.3,4 Therefore, use of such lung-protective mechanical ventilation strategies is currently recommended in these patients.5 There is growing evidence that critically ill patients at risk for, but not yet suffering from, lung injury also benefit from pressure and tidal volume limitation during long-term mechanical ventilation.6–8 Although higher levels of positive end-expiratory pressure (PEEP) with or without recruitment manoeuvres during long-term mechanical ventilation benefit selected patients with ARDS, its use is not widely recommended.4 Evidence for beneficial effects of higher PEEP levels and recruitment manoeuvres during long-term mechanical ventilation in patients with uninjured lungs is lacking.

The effects of short-term mechanical ventilation (i.e. for hours) on pulmonary integrity are still to be defined.9 The potential benefits of lung-protective mechanical ventilation strategies during general anaesthesia for surgery in patients with uninjured lungs are even questioned.10 However, results from preclinical studies of short-term mechanical ventilation in animals without lung injury suggest possible beneficial effects of pressure and tidal volume limitations and the use of higher PEEP levels.2,11,12 In addition, intraoperative lung-protective mechanical ventilation may attenuate postoperative lung inflammation and prevent postoperative pulmonary complications.9,13 During short-term postoperative ventilation, pressure and tidal volume limitation may also be protective.8,14,15 Although potentially beneficial, there is insufficient evidence as to whether the use of higher levels of PEEP during surgery prevents postoperative pulmonary complications.16

Consensus on optimal mechanical ventilation settings during general anaesthesia for surgery is largely lacking. Knowledge on intraoperative mechanical ventilation settings is very limited. One observational study, conducted in 49 centres in France, showed that 18% of patients undergoing general anaesthesia for surgery received tidal volumes more than 10 ml kg$^{-1}$ predicted body weight.
during mechanical ventilation in the operating room. In addition, 81% received mechanical ventilation without PEEP.\textsuperscript{17} Information beyond this study is scarce, although some observational studies suggest poor use of pressure and volume-limited mechanical ventilation during general anaesthesia for surgery.\textsuperscript{9,14,16} Thus, it is unclear how widely the concept of lung-protective mechanical ventilation is applied in other countries.

Postoperative pulmonary complications are a major contributor to postoperative morbidity, with a reported incidence varying from 2.6 to 5.0%.\textsuperscript{19,20} Perhaps postoperative pulmonary complications are dependent on intraoperative mechanical ventilation settings? Considering the large number of surgical procedures performed worldwide daily, estimated to be over 600,000, and the high incidence of complications (25%) and mortality (from 3.5 to 7%) in this patient population, even a small beneficial effect of lung-protective mechanical ventilation during general anaesthesia for surgery on postoperative pulmonary complications could have significant importance.\textsuperscript{21,22}

The LAS VEGAS study aims to characterise current mechanical ventilation practices during general anaesthesia for surgery and assess the dependence of postoperative pulmonary complications on intraoperative mechanical ventilation settings. As secondary end-points, we plan to assess intraoperative complications possibly related to mechanical ventilation settings, as well as the variation of applied mechanical ventilation settings within centres and between centres on an international basis.

This large observational study will provide valuable data that can guide optimisation of intraoperative mechanical ventilation to attenuate intraoperative and postoperative pulmonary complications. Prevention of ventilator-associated lung injury (VALI) could have substantial impact on postoperative pulmonary complications, postoperative clinical course and length of hospital stay.

The LAS VEGAS study is an international, observational, prospective noninterventional cohort study. It will include consecutive adult patients undergoing mechanical ventilation during general anaesthesia for surgery within a 7-day study period in the first months of 2013. Patients are followed during 5 postoperative days for postoperative pulmonary complications. At day 28 after surgery, length of hospital stay and in-hospital mortality are recorded. Patients undergoing obstetric surgical procedures or any procedure during pregnancy, surgical procedures outside the operating room and surgical procedures involving extracorporeal circulation are excluded from participation. Two specific patient groups will be included in the study, but analysed separately: patients undergoing one-lung ventilation during surgery, and ICU patients (i.e. patients who may already have received mechanical ventilation before the surgical procedure).

Patients will be recruited in both teaching and community centres worldwide. We aim to include a minimum of 4800 patients in at least 96 centres. Taking into account an expected minimum incidence of postoperative pulmonary complications of 2.6%, we anticipate that, in order to provide a sample of 120 events, inclusion of at least 4800 patients is required. This will allow for inclusion of up to 12 covariates (including but not limited to mechanical ventilation settings, fluid loading, blood transfusion, ARISCAT risk score) in a logistic regression model to analyse the effect on postoperative pulmonary complications.\textsuperscript{20} For a logistic regression analysis, the number of events divided by the number of predictor variables should be at least 10.\textsuperscript{23}

The data to be collected are all collected as part of routine clinical care. Predefined risk factors for postoperative pulmonary complications (including, but not restricted to, physical status, smoking status, chronic comorbidity, transfusion of red blood cells, urgency of surgery, surgical procedure, fluid loading, use of epidural anaesthesia), intraoperative mechanical ventilation settings (ventilatory mode, airway pressures, tidal volume, PEEP, respiratory rate), intraoperative complications possibly related to the mechanical ventilation strategy (oxygen desaturation, need for unplanned recruitment manoeuvres, need for pressure reduction, need for expiratory flow limitation, hypotension, need for vasoactive drugs, new arrhythmias) and postoperative pulmonary complications (new or prolonged invasive or noninvasive mechanical ventilation, need for oxygen therapy, respiratory failure, pneumonia, ARDS, pneumothorax) are recorded from the medical chart.\textsuperscript{19,20,24} In patients who are admitted to the ICU after surgery, a more detailed follow-up is performed. These patients will be part of an elective substudy that can provide important information on postoperative critical care.

All data are collected on paper case-record forms, unless a local electronic system to register intraoperative and/or postoperative data is used (e.g. a patient data management system). All collected data are transcribed by local investigators into a web-based electronic Case Report Form (open source software OpenClinica).

In this multicentre study, we will check for design effects. Design effects measure the effect of clustering due to multisite recruitment of individuals. Student’s $t$-test or Mann–Whitney $U$-test will be used to compare continuous variables, and $\chi^2$ tests for categorical variables. Comparison between and within groups will be performed using one-way analysis of variance (ANOVA) and posthoc analyses for continuous variables. Study parameters of patients receiving mechanical ventilation prior to operation and of patients undergoing one-lung ventilation during surgery will be analysed separately. Data from the ICU substudy will be analysed separately. To identify potential factors associated with intraoperative and postoperative
pulmonary complications, univariate analyses will be performed. A multivariate logistic regression model will be used to identify independent risk factors for postoperative pulmonary complications. To enter new terms into the model, a stepwise approach will be used, with a limit of a $P$ value of less than 0.05 to enter the terms. Time to event variables will be analysed using Cox regression and visualised by Kaplan–Meier curves. Statistical significance will be considered at a $P$ value of less than 0.05.

All participating centres will submit the study protocol to their local Institutional Review Board for ethical judgement and obtain documentary proof that the study has been subjected to ethical review and granted approval/favourable opinion. If required, ethical approval must be obtained before the start of inclusion. The study is registered at Clinicaltrials.gov with registration identifier NCT 01601223.

The study will be performed by the LAS VEGAS collaboration on behalf of the European Society of Anaesthesiology (ESA). National coordinators will identify and recruit local participating centres, translate all study documents and ensure that all local necessary ethical and regulatory approvals are obtained before start of patient inclusion. They will assist, train and monitor local centres, ensuring that the study is conducted according to the Good Clinical Practice guidelines of the International Conference on Harmonisation (ICH–GCP). Local coordinators in individual participating centres will provide scientific and structural leadership in their centre. They will guarantee the integrity of data collection and ensure timely completion of the dataset.

After publication of the primary results in a peer-reviewed medical journal, the pooled dataset will be available for all members of the LAS VEGAS collaboration on request for secondary analyses after judgement and approval of scientific quality and validity by the Steering Committee.

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