Variable versus conventional lung protective mechanical ventilation during open abdominal surgery (PROVAR) – A randomized controlled trial

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Rationale

- Postoperative pulmonary complications contribute to perioperative morbidity and mortality.
- Experimental studies showed that variable lung protective ventilation (CVV) improves lung function and attenuates lung injury compared to conventional lung protective ventilation (CNV).
- Therefore, CVV may have the potential to improve lung protection in the perioperative setting.
- In the present study, we compared CVV vs. CNV in patients undergoing open abdominal surgery. We hypothesized that CVV compared to CNV improves respiratory function in the intra- and postoperative periods.

Methods

Figure 1: Time course of interventions

- Single center RCT** (clinicaltrials.gov #NCT01683578)
- 50 patients undergoing open abdominal surgery**
- Inclusion criteria:** 1) expected duration of surgery > 3h; 2) American Society of Anesthesiologists (ASA) classification 2 or 3; 3) expected extubation in the operation room; 4) written informed consent
- Exclusion criteria:** 1) other chronic lung diseases than COPD GOLD stages I and II, untreated bronchial asthma; 2) BMI > 40 kg/m²; 3) allergy against drugs administered during the study; 4) participation of the patient in another clinical trial within the preceding 30 days; 5) any mental status possibly affecting informed consent; 6) pregnancy or breastfeeding; 7) suspected low patient compliance; 8) contraindication for magnetic resonance imaging (MRI); 9) mechanical ventilation within the last 30 days.
- Patients were randomly assigned to receive either CVV or CNV.**
1.CNV: mean VT – 8 mL/kg (PBW) and PEEP – 5 cmH₂O
2.CVV: mean VT – 8 mL/kg (PBW) and PEEP – 5 cmH₂O, random variation of VT (normal distribution, coefficient of variation of 30%)
- Modified triple blind design:** Patients and assessors of the postoperative period were blinded to the treatment, the intraoperative investigator was blinded to the pre- and postoperative measurements
- Primary endpoint:** forced vital capacity (FVC) on postoperative day 1
Secondary endpoints: oxygenation, non-aerated lung volume, distribution of ventilation, pulmonary and extrapulmonary complications until postoperative day 5

Results

- CVV did not improve intraoperative respiratory function, nor impaired hemodynamics compared to CNV.
- FVC did not differ between groups on postoperative day 1 (61.9±23.6% versus 61.5±22.1%, CVV and CNV, p = 0.190) and thereafter (p = 0.161).
- Forced expiratory volume at the first second (FEV1) and FEV1/FVC showed a greater deterioration with time in CVV compared with CNV.
- Oxygenation, distribution of ventilation, atelectasis formation, and incidence of postoperative pulmonary and extrapulmonary complications did not differ between groups.

Conclusion

In patients submitted to open abdominal surgery, CVV did not improve intra- and postoperative respiratory function compared to CNV.

Figures

Figure 2: CONSORT Diagram. Patient flow in the PROVAR study according to the CONSORT guidelines. 188 patients were screened for eligibility and 50 were finally enrolled in the trial. 25 patients were randomly assigned to receive either controlled variable ventilation or controlled non-variable ventilation, respectively. One patient in each group withdrew informed consent on day 1 or day 3, respectively. Intention to treat (ITT) analysis was performed in 24 patients per group.

Variable	Group	Preop. day -1 (24) (25)	Postop. day 1 (23) (24)	Postop. day 3 (23) (23)	Postop. day 5 (21) (20)	Discharge (17) (19)	Group	Time
FEV ₁ (%)	CNV CVV	95.6 ± 17.9 93.2 ± 22.7	58.8 ± 20.5 51.5 ± 21.4	59.7 ± 25.1 59.8 ± 23.4	70.5 ± 21.1 68.5 ± 24.6	86.4 ± 18.9 83 ± 23.3	P=0.569	P=0.881
FVC (%)	CNV CVV	100.2 ± 16.2 103.3 ± 20.4	61.9 ± 23.6 61.5 ± 22.1	68.8 ± 27.1 62.4 ± 21.5	81.4 ± 22.7 72.2 ± 22.4	95.9 ± 17.4 87.6 ± 22.8	P=0.161	P=0.789
PEF (%)	CNV CVV	84.8 ± 21.6 85.8 ± 24.4	46.3 ± 20.1 41.8 ± 20.6	49.1 ± 23.7 51.5 ± 22.9	61.6 ± 17.9 60.1 ± 20.6	75.9 ± 23 74.2 ± 22.5	P=0.914	P=0.183
FEV ₁ /FVC (%)	CNV CVV	76.3 ± 12.2 73.5 ± 9.6	77.2 ± 13.8 68.6 ± 17.9	75.6 ± 11.9 75.7 ± 17.9	75.7 ± 11.5 72.5 ± 11.4	76.5 ± 10.7 71.2 ± 18.5	P=0.766	P=0.032
SpO ₂ (%)	CNV CVV	97.4 ± 2.2 97.2 ± 2.0	93.6 ± 4.8 93.7 ± 4.2	93.1 ± 4.3 90.8 ± 5.4	94.6 ± 4.2 90.7 ± 1.6	97.3 ± 2.3 96.4 ± 2.5	P=0.234	P=0.483
PcO ₂ (mmHg)	CNV CVV	78.0 ± 10.5 75.0 ± 11.3	66.0 ± 10.5 62.3 ± 12.0	63.0 ± 10.5 57.8 ± 9.8	66.8 ± 9.8 65.3 ± 12.0	78.0 ± 11.3 72.8 ± 12.8	P=0.754	P=0.931

Table 1: Pre- and postoperative pulmonary function tests and oxygenation, values are given as mean ± standard deviation. Pulmonary function tests refer to expected normal values of patients (%). Groups did not differ significantly preoperatively, as assessed by Student's t-test. General linear model statistics were used to assess group and time effects. p < 0.05 was considered statistically significant.

Figure 3: Single magnetic resonance tomography scans of thorax in representative patients of the CNV and CVV groups. Images were obtained during spontaneous breathing preoperatively and at postoperative day 1. R = right; L = left.

Figure 6: Center of ventilation along the ventral-dorsal axis. Closed circles represent CNV, open circles represent CVV. Red lines represent median and interquartile ranges. * p < 0.05 versus the respective preoperative value.