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PROTECTIVE VENTILATION IMPROVES GAS EXCHANGE, REDUCES INCIDENCE OF ATELECTASES AND HOSPITAL LENGTH OF STAY IN MAJOR PANCREATODUODENAL SURGERY

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ЗАЩИТНАЯ ПЕРИОПЕРАЦИОННАЯ ВЕНТИЛЯЦИЯ УЛУЧШАЕТ ИСХОД И ПОЗВОЛЯЕТ СНИЗИТЬ ЧАСТОТУ ПОСЛЕОПЕРАЦИОННЫХ ЛЕГОЧНЫХ ОСЛОЖНЕНИЙ

Актуальность. Показано, что защитная периоперационная вентиляция улучшает исход и позволяет снизить частоту послеоперационных легочных осложнений.

Цель данного исследования – оценить влияние вентиляции с низким уровнем дыхательного объема (VT) либо отдельно, либо в сочетании с умеренной гиперкапнией при крупных панкреатодуоденальных вмешательствах.

Материалы и методы. Шестьдесят взрослых пациентов, запланированных на выборочную панкреатодуоденальную операцию длительностью >2 ч, были включены в проспективное исследование одного центра и рандомизированы на три группы: получающих высокий VT (10 мл/кг «идеальной» массы тела (PBW), группа HVT, n=20), низкий VT (6 мл/кг PBW, группа LVT, n=20) и низкий VT в сочетании с умеренной гиперкапнией и ацидозом (6 мл/кг PBW, $PaCO_2$ 45–60 мм рт. ст. в LVT+HC группе, n=20). Частота пневмокардиальных заболеваний и осложнений была зарегистрирована во время операции и в послеоперационном периоде.

Результаты и обсуждение. Значения VT были 619 (570–716), 370 (321–403) и 340 (312–430) мл/кг для HVT, в LVT и LVT+HC группах соответственно ($p<0,001$). По сравнению с группой HVT, соотношение PaO_2/FiO_2 было увеличенное в группе LVT – 392 (349–437) против 321 (289–358) мм рт. ст. через 24 ч после операции ($p<0,05$). Группа HVT имела более высокую частоту развития ателектазов (n=6), несмотря на более низкую распространенность курения, по сравнению с LVT (n=1) группой (p=0,017), и показала более длительный период пребывания в стационаре. Пациенты группы LVT+HC имели более низкие показатели артериального лактата и бикарбоната к концу оперативного вмешательства.

Выводы. При крупных панкреатодуоденальных вмешательствах превентивное использование защитного дыхательного объема улучшает послеоперационную оксигенацию, снижает частоту ателектазов, а также сокращает продолжительность пребывания в стационаре. Сочетание низкого дыхательного объема и допустимых параметров гиперкапнии и гиперкапнического ацидоза, снижающего концентрацию лактата, не имеет никаких дополнительных преимуществ и требует дальнейших исследований.

Ключевые слова: защитная вентиляция, послеоперационные легочные осложнения, ателектазы, допустимая гиперкапния, панкреатодуоденальная хирургия.

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Background: Protective perioperative ventilation has been shown to improve outcomes and reduce the incidence of postoperative pulmonary complications (PPC). The goal of this study was to assess the effects of ventilation with low tidal volume (V_T) either alone or in a combination with moderate permissive hypercapnia in major pancreatoduodenal interventions.

Materials and methods: Sixty adult patients scheduled for elective pancreatoduodenal surgery with duration >2 hrs were enrolled into a prospective single-center study. All patients were randomized to three groups receiving high V_T (10 mL/kg of predicted body weight (PBW), the HVT group, n=20), low V_T (6 mL/kg PBW, the LVT group, n=20), and low V_T combined with a moderate hypercapnia and hypercapnic acidosis (6 mL/kg PBW, $PaCO_2$ 45–60 mm Hg, the LVT+HC group, n=20). Cardiopulmonary parameters and the incidence of complications were registered during surgery and postoperatively.

Results and Discussion: The values of V_T were 619 (570–716), 370 (321–403), and 340 (312–430) mL/kg for the HVT, the LVT and the LVT+HC groups, respectively (p<0.001). Compared to the HVT group, PaO_2/FiO_2 ratio was increased in the LVT group: 392 (349–437) *vs.* 321 (289–358) mm Hg at 24 hrs postperatively (p<0.05). The HVT group had higher incidence of atelectases (n=6) despite lower incidence of smoking compared with the LVT (n=1) group (p=0.017) and demonstrated longer length of hospital stay. The patients of the LVT+HC group had lower arterial lactate and bicarbonate excess values by the end of surgery.

Conclusions: In major pancreatoduodenal interventions, preventively protective tidal volume improves postoperative oxygenation, reduces the incidence of atelectases, and shortens length of hospital stay. The combination of low tidal volume and permissive hypercapnia results in hypercapnic acidosis decreasing the lactate concentration but adding no additional benefits and warrants further investigations.

Key words: protective ventilation, postoperative pulmonary complications,, atelectasis, permissive hypercapnia, pancreatoduodenal surgery.

Introduction

Postoperative pulmonary complications (PPC) can significantly worsen the outcomes of major surgery, increasing the resource utilization and length of hospital stay. [1] The benefits of the protective mechanical ventilation with low tidal volume (V_T) resulting in improved outcome have been convincingly proved in patients with acute respiratory distress syndrome (ARDS) in large clinical studies and meta-analyses. [2, 3] Respiratory support with protective tidal volume (V_T) of 6–8 mL/kg to limit volumotrauma as well as setting of an adequate positive end-expiratory pressure (PEEP) to prevent atelectotrauma can be considered as key measures for prevention and therapy of ARDS. [4] Beyond the lower V_T, the subgroup of protectively ventilated patients with ARDS with permissive hypercapnia might have certain additional benefits. The precise mechanism of this

effect is not completely clear and may involve the suppression of inflammation, mitigation of cell apoptosis, and, finally, counteraction the biotrauma. [5–7]

During the past two decades, we observe a "paradigm shift" of preventive approach from "tertiary", targeted on the prevention of the complication and mortality in ARDS, to "secondary", aimed in the prevention of development of PPC and ARDS *per se*. [8] In patients with initially intact lungs, *i. e.* those without ARDS, the use of protective perioperative ventilation as "secondary" preventive measure can dramatically improve postoperative outcomes and reduce the risk of PPC. [9] The prevention of PPC including its most severe form, postoperative ARDS is of utmost interest in major abdominal surgery when patients have initially intact lungs but are in a risk group postoperative respiratory adverse events. [10,11]

The important components of protective perioperative ventilation are low V_T and moderate PEEP targeting low plateau and driving pressures to avoid ventilator-associated lung injury. [12] However, the independent contributing role of both parameters as well as their interaction with specific pulmonary characteristics like lung compliance and non-modifiable risk factors are to be further explored and debated. In addition, the use of the relatively low tidal volume can be accidentally accompanied by permissive hypercapnia that can interact with systemic inflammatory response, biotrauma, and extrapulmonary organ function. [6, 13]

The major pancreatoduodenal interventions include the extensive and complex resection of pancreas, liver, as well as biliary and duodenal structures. This branch of elective surgery may be potentially associated with a high risk of pulmonary and extrapulmonary postoperative complications due to history of smoking, alcohol consumption, high bleeding potential, hypoalbuminemia, and advanced age. [14–16] We hypothesized that both the protective ventilation with low V_T and combination of low V_T with moderate permissive hypercapnia and hypercapnic acidosis can reduce risk of postoperative pulmonary complications after major pancreatoduodenal surgery. The aim of our study was to assess the effects of protective ventilation on hemodynamics, gas exchange, incidence of PPC and extrapulmonary complications, and clinical outcome in this type of surgery.

Methods

The study protocol and informed consent were approved by the Ethical Committee of the Northern State Medical University, Arkhangelsk, Russian Federation. During the period 2014–2016 yrs., sixty patients (28 females/32 males, 54 (45–60) yrs.) scheduled for major pancreatoduodenal and/or hepatobiliary surgery (mostly, resection for pancreatobiliary cancer and chronic calcific pancreatitis) with expected duration of the intervention exceeding two hours were included into a prospective randomized study. All patients were visited 12 hrs before the intervention in the surgical ward and signed an informed consent.

Perioperative ventilation

Before anesthesia and start of mechanical ventilation, the patients were randomized using the envelope method to three groups receiving either high V_T (10 mL/kg of predicted body weight (PBW); the HVT group, n=20) or low V_T (6 mL/kg PBW; the LVT group, n=20). An additional group combined low V_T with moderate permissive hypercapnia (V_T 6 mL/kg PBW and $PaCO_2$ 45–60 mm Hg: the LVT+HC group, n=20). In all groups, PEEP of 4 cm H_2O was set (Table 1).

The standard preoxygenation lasting for at least 3 minutes was performed in all the patients using 80 % oxygen (Datex Ohmeda Avance, GE, Madison, WI, USA). Initial FiO_2 was set at 30 % to achieve SpO_2 at least 95 %. In case of SpO_2 below 95 %, FiO_2 was increased with increment of 5 % to achieve the target SpO_2 value. In all patients, the respiratory support was discontinued using standard criteria and spontaneous breathing trial; the tracheal extubation was performed in the ICU by an independent ICU physi-

Table 1

Ventilator settings in the studied groups

Group	Acronym	Settings
High tidal volume	HVT	Tidal volume **10 mL/kg PBW**. Initial respiratory rate was set at 12 per min and tailored to achieve $EtCO_2$ 35 mm Hg. **Goal: PaO_2 90–150 mm Hg, $PaCO_2$ 32–48 mm Hg**
Low tidal volume	LVT	Tidal volume **6 mL/kg PBW**. Initial respiratory rate was set at 14 per min and tailored to achieve $EtCO_2$ 35 mm Hg. **Goal: PaO_2 90–150 mm Hg; $PaCO_2$ 32–48 mm Hg**
Low tidal volume + permissive hypercapnia	LVT+HC	Tidal volume **6 mL/kg PBW**. Initial respiratory rate was set at 8–10 per min and tailored to achieve $EtCO_2$ 45 mm Hg. **Goal: PaO_2 90–150 mm Hg; $PaCO_2$ 45–60 mm Hg**

Note. PBW — predicted body weight.

cian. The criteria for discontinuation of respiratory support were as follows: the ability to tolerate 30 minutes of spontaneous breathing trial *via* the pressure support ventilation with pressure support level of 6–8 cm H_2O, PaO_2/FiO_2 > 200 mm Hg, spontaneous minute volume < 10 L/min and respiratory rate < 30/min (f/V_T < 65 and V_T > 6 mL/kg PBW) as well as normal body temperature, no obvious bleeding or anemia, hemodynamic stability and adequate analgesia.

Anesthesia

Before the interventions, all patients received premedication with sedative (phenazepam 1. 0 mg) and antacid (omeprazol 20 mg). After transfer to the operating room, the catheterization of peripheral vein was performed and sedation with diazepam 5–10 mg intravenously was provided. The radial arterial line and thoracic epidural catheterization (Th_7–Th_9) were set in all patients. Combined epidural anesthesia (ropivacain 20 mg and fentanyl 100 mcg) was provided prior the start of surgery. General anesthesia was induced using propofol (1.5–2.0 mg/kg) and fentanyl (100 mcg); muscular blockade was achieved with atracurium besilate (0. 6 mg/kg). Thereafter the anesthesia was maintained with sevoflurane 1.5–2.5 vol. % with fresh gas flow of 1 L/min and continuous infusion of fentanyl (100 mcg/hr) and atracurium (25 mg/hr). Gastric tube and urinary catheter were set after the induction and intubation of the patients. Mean arterial pressure was maintained >65 mm Hg, if necessary using the titrated infusion of norepinephrine. Continuous infusion of a balanced crystalloid solution (4–5 mL/kg/hr) was performed intraoperatively.

Perioperative measurements and monitoring

Hemodynamics, gas exchange, and laboratory parameters were registered at the beginning of surgery, at the end of the intervention and during 72 hrs of the postoperative period. The invasive arterial blood pressure (radial artery), central venous pressure, and SpO_2 were monitored continuously (B40 Patient monitor, GE Medical Systems, Freiburg, Germany) Inspiratory and end-expiratory sevoflurane concentration, FiO_2 and FeO_2, and $EtCO_2$ were monitored using integrated monitor of anesthesia machine and Capnostream™ 20 monitor (Covidien, USA). Intra- and postoperatively, arterial and venous blood gases, lactate concentration, bicarbonate excess (BE) and hemoglobin concentration were regis-

tered. The incidence of the postoperative complications including atelectases (plain chest x-ray), postoperative ileus, pneumonia, bleeding, and anastomosis leakage, lengths of the ICU and hospital stay and mortality were analyzed up to the Day 28 after surgery.

Statistics

The data distribution was assessed using Shapiro–Wilk test. The data are presented as median (25^{th}–75^{th} percentiles). For data analysis, we used SPSS Statistics software (ver. 17, IBM, USA). Intergroup comparisons was performed using Kruskal–Wallis *H*-test followed by pairwise post-hoc Mann–Whitney *U*-test or χ^2-test for nominal data when appropriate. The intragroup differences were explored using Wilcoxon test. A *p* value below 0. 05 was regarded as statistically significant.

Results

We did not find any significant baseline differences between the groups except for the history of smoking that was lower in the HVT group (Table 2). The duration of both intra — and postoperative respiratory support as well as the overall duration of surgery were not different between the groups.

The values of V_T and $PaCO_2$ at the start and completion of the surgery for the HVT, the LVT, and the LVT+HC groups are depicted in Figure 1. Compared with the HVT group, PaO_2/FiO_2 ratio at 24 hrs postoperatively was higher in the LVT group: 333 (301–381) vs. 382 (349–423) mm Hg (p=0.027), but not in the LVT+HC group (Figure 2). Notably, the transient improvement of the postoperative oxygenation was achieved regardless the significantly higher incidence of smokers in the LVT group compared with the HVT group (p=0.025; Table 1).

During surgery, we observed significantly increased V_E and peak pressure in the HVT group (Figure 1, Table 3). The LVT+HC group had higher $PaCO_2$ and $EtCO_2$ compared with other groups. In parallel with development of hypercapnia, arterial pH, BE and lactate concentration reduced significantly (p<0.03 and <0.02 compared with the HVT and the LVT groups, respectively, Table 3).

The length of hospital but not the length of ICU stay was significantly longer in the HVT group compared with the LVT group (Figure 3). The overall mortality at Day 28 was 5 % (n=1 in the HVT group and n=2 in the LVT+HC group), and the overall incidence of postoperative complications was 40 % (n=24). We registered higher incidence of the postoperative complications, particularly, atelectases (Figure 4) in the HVT group compared with the LVT group. We found no differences in the overall incidence of complications and atelectases between the HVT and the LVT+HC groups.

Discussion

Our study demonstrated transiently improved postoperative oxygenation, reduced incidence of postoperative pulmonary atelectases, and shortened length of hospital stay in the patients ventilated with protective tidal volume of 6 mL/kg PBW during major pancreatoduodenal surgery. The combination of protective V_T with moderate hypercapnia and hypercapnic acidosis did not affect pulmonary function, but could potentially interplay with perioperative acid-base balance.

The improvement of oxygenation (PaO_2/FiO_2) was transient and registered at 24 hrs of the postoperative period only in the LVT, but not LVT+HC group. Moreover, we showed the decreased incidence of atelectases and tendency to reduced overall incidence of the postoperative complications in the LVT group that was accompanied by increased length of the hospital stay in the group ventilated with high V_T. In compliance with our results, Severgnini P. *et al*. have shown that in open abdominal surgery lasting more than two hours ventilation with relatively high V_T of 9 mL/kg and zero PEEP, resulted in com-

Table 2

The characteristics of the patients

Data	HVT	LVT	LVT+HC	*P* value
Age, yrs	56 (48–61)	53 (45–63)	51 (41–58)	0.345
Weight, kg	70 (64–80)	62 (60–77)	69 (56–83)	0.539
Predicted Body Weight, kg	64 (56–71)	59 (53–67)	66 (52–71)	0.533
Gender (F / M)	8 / 12	11 / 9	9 / 11	0.626
Duration of surgery, min	160 (135–250)	190 (138–234)	225 (180–264)	0.269
Duration of mechanical ventilation, min	360 (270–525)	370 (265–499)	400 (295–473)	0.961
Length of ICU stay, hrs	44 (24–85)	43 (22–68)	45 (27–76)	0.711
Hospital stay, days	42 (25–51)	28 (21–38)	31 (26–41)	0.117
Smoking history, n (%)	6 (30)*	14 (70)	13 (65)	0.025
All complications, n (%)	11 (55)	5 (25)	8 (40)	0.131
Atelectases, n (%)	6 (30)*	1 (5)	2 (10)	0.047
Mortality, n (%)	1 (5)	0 (0)	2 (10)	0.315

Note. HVT, high tidal volume group; LVT, low tidal volume group LVT+HC, high tidal volume group combined with hypercapnia. Data are presented as median (25th–75th percentiles), numbers or percentage. p values are calculated using Kruskal–Wallis H-test with *post hoc* Mann–Whitney *U*-test or χ^2-test when appropriate for nominal data. * $p<0.05$ between the HVT and LVT groups.

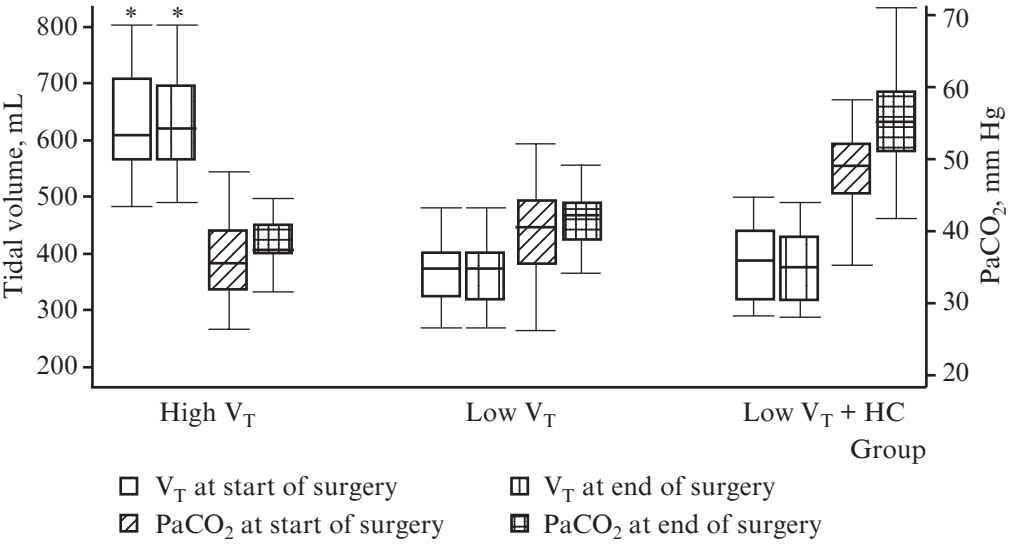

Fig. 1. The values of tidal volume and arterial partial pressure of CO_2 in the groups at the beginning and end of the surgery.

Note. Data are presented as median (25th–75th percentiles). *p* values are calculated using Kruskal–Wallis *H*-test followed by *post hoc* Mann–Whitney *U*-test. for the LVT group vs. the HVT group for tidal volume and the LVT group vs. the LVT+HC group for $PaCO_2$ at the start and end of surgery. * — $p<0.001$.

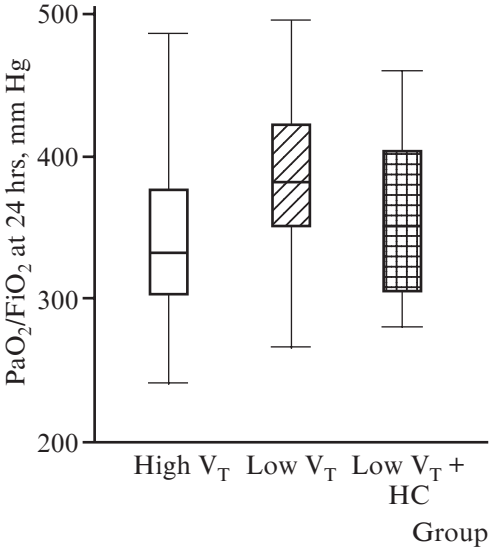

Fig. 2. The ratio of PaO_2/FiO_2 at 24 hours after surgery.

Note. Data are presented as median (25^{th}–75^{th} percentiles). *p* values are calculated using Mann–Whitney *U*-test between the HVT and the LVT groups; * — p =0.027 compared with the LVT group.

promised pulmonary function, worsened oxygenation, and increased incidence of PPC in comparison with protective ventilation (V_T of 7 mL/kg of ideal body weight, PEEP of 10 cm H_2O and recruitment maneuvers). [10] By contrast, Treschan T. A. *et al*. demonstrated that the application of low V_T of 6 mL/kg PBW in major abdominal surgery did not improve postoperative lung function as compared with high V_T values of 12 mL/kg PBW with the similar PEEP level (5 cm H_2O) [17]. In the large randomized controlled trial, Futier E. *et al.* have demonstrated a reduction in the incidence of the major pulmonary and extrapulmonary complications within seven days following major abdominal surgery by 17 % in the protective ventilation (V_T 6–8 mL/kg PBW and PEEP 6–8 cm H_2O) compared with the conventional ventilation group (V_T 10–12 mL/kg PBW and zero PEEP). In consistency with our results, this study convincingly proved that protective ventilation was associated with shorter length of hospital stay. [11]

Table 3

The characteristics of the patients

Group	Stage				
	Start	End	6 hrs.	24 hrs.	48 hrs.	72 hrs.
	Peak pressure, cm H_2O					
HVT	15 (14–19)	16 (15–19)				
LVT	12 (11–13)*	13 (12–15)*		—		
LVT+HC	12 (11–14)*	12 (11–15)*				
	Driving pressure, cm H_2O					
HVT	5 (2–9)	4 (4–8)				
LVT	5 (2–7)	5 (2–8)		—		
LVT+HC	3 (2–6)	3 (2–8)				

Mean arterial pressure, mm Hg						
HVT	65 (57–79)	78 (64–83)	—			
LVT	73 (58–80)	74 (63–83)				
LVT+HC	63 (56–81)	75 (68–78)				
Heart rate, 1/min						
HVT	72 (67–83)	69 (63–79)				
LVT	68 (57–76)	72 (61–83)				
LVT+HC	65 (55–77)	72 (66–89)				
pH of arterial blood						
HVT	7.41 (7.32–7.47)	7.30 (7.28–7.38)	7.36 (7.34–7.40)	7.42 (7.39–7.44)	7.43 (7.40–7.46)	7.44 (7.41–7.47)
LVT	7.35 (7.30–7.40)	7.28 (7.25–7.32)	7.37 (7.35–7.39)	7.41 (7.36–7.45)	7.43 (7.41–7.46)	7.43 (7.40–7.44)
LVT+HC	7.27 (7.23–7.33)*	7.16 (7.13–7.24)*	7.33 (7.31–7.37)†	7.40 (7.37–7.42)	7.42 (7.41–7.43)	7.44 (7.40–7.45)
BE, mmol/L						
HVT	–2.2 (–3.9–0.0)	–5.9 (–7.5…–3.1)	–5.2 (–7.8…–3.1)	–2.2 (–4.0…–0.6)	–1.3 (–3.7…–0.2)	–2.6 (–4.8…–0.4)
LVT	–3.0 (–4.7…–1.4)	–6.8 (–7.4…–3.2)	–5.1 (–6.1…–3.4)	–2.7 (–5.8…–0.7)	–3.0 (–5.0…–0.8)	–2.6 (–3.8…–0.5)
LVT+HC	–3.8 (–5.5…–2.1)	–8.0 (–8.8…–6.3)*	–6.1 (–7.8…–5.4)†	–4.1 (–4.9…–2.1)	–3.0 (–4.9…–0.9)	–2.8 (–4.2…–0.6)
Arterial lactate, mmol/L						
HVT	0.8 (0.6–1.1)	1.1 (0.8–1.8)	1.7 (0.8–2.3)	1.2 (0.8–1.5)	0.8 (0.8–1.1)	0.8 (0.7–1.1)
LVT	0.7 (0.5–0.8)	1.1 (0.7–1.5)	1.5 (1.0–3.1)	1.1 (0.9–1.5)	0.9 (0.7–1.2)	0.7 (0.6–1.2)
LVT+HC	0.6 (0.5–0.7)*	0.7 (0.5–1.0)*,†	1.3 (1.0–2.4)	1.4 (1.0–2.2)	0.9 (0.7–1.6)	0.9 (0.7–1.2)
$EtCO_2$, mm Hg						
HVT	32 (28–35)	32 (29–35)	—			
LVT	36 (35–42)	36 (34–38)				
LVT+HC	45 (42–47)*,†	47 (45–50)*,†				

Note. HVT — high tidal volume group; LVT — low tidal volume group LVT+HC — high tidal volume group combined with hypercapnia. Data are presented as median (25th–75th percentiles), numbers or percentage. *p* values are calculated using Kruskal–Wallis *H*-test followed by post hoc Mann–Whitney *U*-test when appropriate. * — $p<0.05$ compared with the HVT group, † — $p<0.05$ compared with the LVT group.

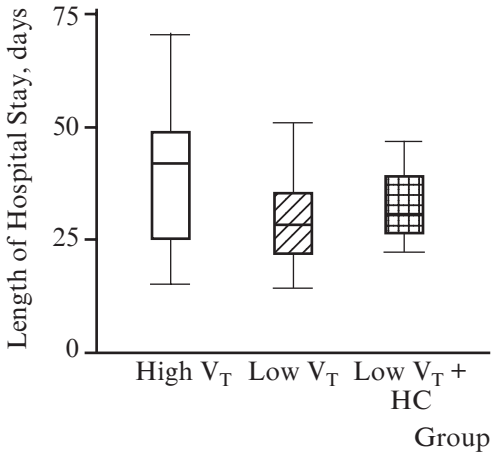

Fig. 3. The length of the hospital stay.

Note. Data are presented as median (25th–75th percentiles). p values are calculated using Kruskal–Wallis *H*-test followed by *post hoc* Mann–Whitney *U*-test. between the HVT and the LVT groups; * — p=0.049 compared with the LVT group.

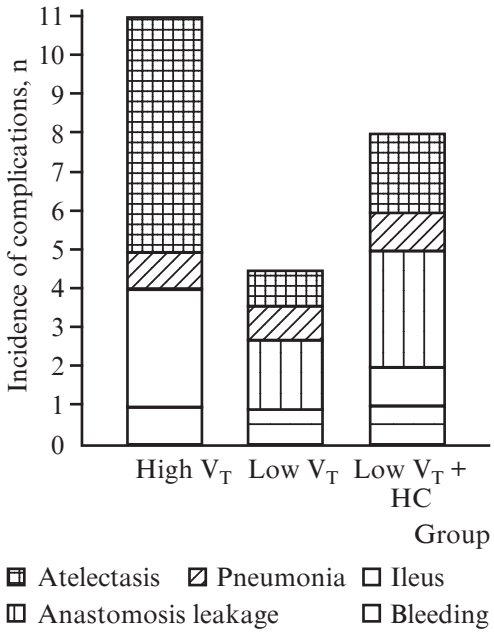

Fig. 4. The incidence of the postoperative complications in the study groups.

Note. Data are presented as stacked numbers of the complications. p values are calculated using χ^2-test between the HVT and the LVT groups; * — p=0.02 for the incidence of atelectases between the HVT and LVT groups and p=0.13 for incidence of all complications between the HVT and the LVT groups.

The ability of preventive low V_T to counteract the potential injurious and pro-inflammatory effects of inadvertent lung overdistension related to conventional ventilation is still a matter of debates [18, 19]. Thus, Cai H. *et al.* showed by means of computed tomography that ventilation with protective V_T of 6 mL/kg alone without PEEP was not associated with any difference both in the incidence of atelectases and in oxygenation compared with the V_T of 10 mL/kg. [20] In routine practice, low V_T is associated with the rather unjustified fair of atelectases, which probably could be counteracted by an adequate PEEP. Since our study included the patients with body mass index within the relatively normal range of 23.2 (21.3–28. 4) kg/m^2, the empiric relatively low PEEP of 4 cm H_2O could be considered adequate to reduce the risk of atelectases. As a result, low V_T was accompanied by a significant reduction of the atelectases incidence compared with the HVT group that makes this approach attractive for a wider use in clinical practice.

As noted, the PPC have been considered to be strongly associated with prolonged hospital stay [21] that was also confirmed by the presented results. Despite our study confirms the conclusions of several similar investigations showing that protective ventilation can improve gas exchange, lung mechanics and attenuate the risk of PPC and extrapulmonary adverse events [10, 11, 22], its results could contribute to the pool of the evidences favoring protective ventilation in major pancreatoduodenal surgery due to relatively homogenous patient population and insights into effects of permissive hypercapnia.

In our study, we induced a moderate degree of hypercapnia in the LVT+HC group aiming to prevent significant hemodynamic effects, risk of organ dysfunction, and increased consumption of anesthetic drugs. The patients assigned to this group did not show any additional improvement in oxygenation or reduced incidence of PPC and, namely, atelectases compared with both the LVT and the HVT groups. We found that only minor and transient metabolic effects in the LVT+HC group are reduced arterial lactate concentration combined with res-

piratory acidosis and lower bicarbonate excess values. Hypercapnia and acidosis could interact with inflammation, modulate biotrauma, and attenuate ARDS that mostly explored so far in isolated lungs and *in vivo* experimental studies [23–25]. In addition, the exact values of hypercapnic acidosis and hypercapnia are not settled ranging from 6.90–7.40 and 40–100 mm Hg, respectively and the distinct mechanism of the protection remains unrevealed. [26, 27] However, beyond the experimental attenuation of the cytokine release, hypercapnia can exert several deleterious effects *via* overproduction of nitric oxide, impaired plasma membrane repair, immunosupression, and possible promotion of the bacterial growth. [6] These effects combined with influence of hypercapnia on cardiovascular and central nervous systems can prevent physician to avoid this maneuver in patients without ARDS. [28–30] The reduction in lactate concentration observed in our study can be explained by the metabolic acid-base effect of hypercapnic acidosis rather than any modification of organ perfusion. Indeed, it is suggested that the decreased lactate concentration during hypercapnia might actually result from the inhibition of phosphofructokinase activity, suppressed transport of lactic acid from muscles, and augmented rate of lactate oxidation. [31–33] Therefore, the effects of hypercapnia associated with hypercapnic acidosis and low tidal volume on PPC incidence might worth further investigations to clarify the value of this approach for routine clinical practice.

Limitations

The limitations of our study include the relatively small number of observations. Applying low tidal volume, we did not consider the specific targets for pulmonary compliance, peak, plateau and driving pressures that can also limit the applicability of the findings. The population of patients is heterogeneous in respect of the type of surgery and underlying pathology, therefore both cancer- and not cancer-related interventions were included.

Conclusions

In major elective pancreatoduodenal surgery, preventive reduction of tidal volume to protective values results in transiently improved postoperative oxygenation, reduced incidence of atelectases, and shortened length of the hospital stay. The combination of low tidal volume and permissive hypercapnia leads to transient decrease in lactate concentration but does not add any substantial benefits to the outcome and organ function and warrants further investigations.

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