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不同肺保护性通气策略对肺切除术术中通气和术后肺部并发症的影响

陈志阳，孙丽，刘伟，魏顺民，仇庆亚，孙绪德

(空军军医大学唐都医院麻醉科，西安 710038)

[摘　要]　**目的：**评估小潮气量联合不同水平呼气末正压(positive end-expiratory pressure，PEEP)对胸腔镜下肺切除术患者通气氧合和术后肺部并发症(postoperative pulmonary complications，PPCs)的影响。**方法：**选取空军军医大学唐都医院2019年12月至2020年12月择期行胸腔镜下肺切除患者100例，采用随机数字表法分为两组：低水平PEEP组(LP组)和高水平PEEP组(HP组)；LP组于单肺通气(one lung ventilation，OLV)时设置潮气量(tidal volume，V_T)6 mL/kg，PEEP≤5 cmH_2O，HP组于相同时间点设置V_T 6 mL/kg，PEEP 6~10 cmH_2O。分别于OLV前(T1)、OLV 60 min(T2)、手术结束(T3)采取桡动脉血液行血气分析；记录T1、T2、T3的心率(heart rate，HR)、脉搏血氧饱和度(pulse oxygen saturation，SpO_2)、收缩压/舒张压(systolic blood pressure/diastolic blood pressure，SBP/DBP)、呼气末二氧化碳分压(partial pressure of end-expiratory carbon dioxide，$P_{ET}CO_2$)、V_T、吸气峰压(peak pressure，Ppeak)、平台压(plateau pressure，Pplat)；记录术后7 d内PPCs、胸腔引流管拔除时间、术后3 d内胸腔引流管引流量及术后住院时间。**结果：**与T1时比较，T2、T3时两组患者HR无明显变化；T2时平均动脉压(mean arterial pressure，MAP)明显降低(P<0.05)；两组Ppeak、Pplat明显升高，动态肺顺应性(dynamic compliance，Cdyn)明显降低(P<0.05)；两组患者氧合指数(oxygenation index，OI)明显降低，肺泡气-动脉血氧分压差(alveolar gas-arterial oxygen partial pressure difference，A-aDO_2)明显升高；T2时两组呼吸指数(respiratory index，RI)明显升高，T3时LP组RI明显升高(P<0.05)。与LP组比较，T2时HP组Ppeak明显升高；T2、T3时，HP组Pplat明显升高，驱动压(driving pressure，DP)明显降低，Cdyn明显增高(P<0.05)；T2、T3时HP组OI明显升高，A-aDO_2、RI明显降低(P<0.05)。两组术后7 d PPCs及住院时间差异无统计学意义。**结论：**小潮气量6 mL/kg联合较高水平PEEP 6~10 cmH_2O可改善胸腔镜下肺切除术患者OLV时通气氧合情况，利于术中麻醉管理。

[关键词]　肺保护性通气；小潮气量；呼气末正压通气；单肺通气；肺切除术

Effects of different lung protective ventilation strategies on intraoperative ventilation and postoperative pulmonary complications in patients undergoing thoracoscopic pneumonectomy

CHEN Zhiyang, SUN Li, LIU Wei, WEI Shunmin, QIU Qingya, SUN Xude

(Department of Anesthesiology, Tangdu Hospital, Air Force Medical University, Xi'an 710038, China)

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通信作者 (Corresponding author)：孙绪德，Email: sunxude@fmmu.edu.cn

Abstract **Objective:** To evaluate the effects of low tidal volume combined with different positive end-expiratory pressure (PEEP) on intraoperative ventilation and postoperative pulmonary complications (PPCs) in patients undergoing thoracoscopic pneumonectomy. **Methods:** A total of 100 patients who underwent thoracoscopic pneumonectomy in Tangdu Hospital from December 2019 to December 2020 were randomly divided into two groups: low PEEP group (group LP) and high level PEEP group (group HP); LP group was set with tidal volume (V_T) 6 mL/kg and PEEP ≤5 cmH_2O during one lung ventilation (OLV), while HP group was set with V_T 6 mL/kg and PEEP 6~10 cmH_2O. Blood gas analysis was performed by radial artery blood before OLV (T1), at OLV 60 min (T2), and at the end of operation (T3). Heart rate (HR), pulse oxygen saturation (SpO_2), systolic blood pressure/diastolic blood pressure (SBP/DBP), partial pressure of end-expiratory carbon dioxide ($P_{ET}CO_2$), V_T, peak pressure (Ppeak), plateau pressure (Pplat) of T1, T2 and T3 were recorded. PPCs within 7 days after the operation, removal time of thoracic drainage tube, drainage volume of thoracic drainage tube within 3 days after the operation and postoperative hospital stay were recorded. **Results:** Compared with T1, there was no significant change in HR at T2 and T3. At T2, mean arterial pressure (MAP) decreased significantly (P<0.05). In both groups, Ppeak and Pplat were significantly increased, while dynamic compliance (Cdyn) was significantly decreased (P<0.05). Oxygenation index (OI) was significantly decreased and alveolar gas-arterial oxygen partial pressure difference (A-aDO_2) was significantly increased in both groups. At T2, respiratory index (RI) was significantly increased in both groups, while at T3, RI was significantly increased in LP group (P<0.05). Compared with LP group, Ppeak of HP group was significantly increased at T2. At T2 and T3, Pplat, driving pressure (DP) and Cdyn in HP group were significantly increased (P<0.05). At T2 and T3, OI and A-aDO_2 and RI in HP group were significantly increased, while A-aDO_2 and RI were significantly decreased (P<0.05). There was no significant difference in PPCs and length of stay between the two groups within 7 days after surgery. **Conclusion:** Low V_T 6 mL/kg combined with higher PEEP 6–10 cmH_2O can improve aeration and oxygenation during OLV in patients undergoing thoracoscopic pneumonectomy, which is beneficial for anesthesia management.

Keywords lung protective ventilation; low tidal volume; positive end-expiratory pressure; one lung ventilation; pneumonectomy

术后肺部并发症(postoperative pulmonary complications，PPCs)是胸科手术术后死亡的主要原因。单肺通气(one lung ventilation，OLV)可导致肺内分流、缺血-再灌注等病理生理改变，诱发急性肺损伤(acute lung injury，ALI)，严重影响患者预后，增加患者的病死率和住院时间[1]。因此，减轻OLV带来的不良影响是胸科手术麻醉管理的重点之一[2]。肺保护性通气(lung protective ventilation，LPV)包括小潮气量、PEEP和肺复张，LPV被推荐常规用于术中呼吸管理。研究[3-5]表明：LPV可改善术中通气，有效预防PPCs的发生，改善患者的预后。在一些研究中，PEEP≥5 cmH_2O较PEEP<5 cmH_2O能明显降低发生PPCs的风险[6]，也有研究[7]显示不同PEEP对PPCs的影响没有明显的差异。术中应用PEEP的水平仍存在争议。目前，关于在OLV期间施加PEEP的适宜水平的研究较少，尚还缺乏足够的循证医学证据[8-9]。同时，国内关于此方面的研究仍较少[10]。因此，本研究拟观察不同PEEP对胸腔镜下肺切除术中通气和PPCs的影响，探索适宜于OLV的PEEP水平。

1 对象与方法

1.1 对象

本研究已获得空军军医大学唐都医院医学伦理委员会批准(第K202101-05号)，患者及家属签署知情同意书。本研究纳入符合标准的因肺癌行择期全麻下行胸腔镜下肺切除术患者，性别不限，年龄18~75岁，体重指数(body mass index，BMI) 18~28 kg/m^2，美国麻醉医师协会(American Society of Anesthesiologists，ASA)分级I~III。样本量的计算通过查阅文献和预实验，采用以下公式：设定α=0.05，1−β=0.90。

$$n_1 = n_2 = \frac{\left|1.96\sqrt{2P(1-P)}\right| + 1.28\sqrt{P_1(1-P_1)+P_2(1-P_2)}}{(P_1-P_2)^2}$$

n_1和n_2分别为两干预组的样本量，并假定n_1和n_2相等；P_1和P_2分别为两种干预措施不良事件发生率；$P=|1/2(P_1-P_2)|$。根据公式计算得出$n_1=n_2\approx45$例。

排除标准：既往哮喘病史或者气道高反应性；严重心、肝、肾功能、凝血功能异常；严重慢性阻塞性肺病或者间质性肺病；自主呼吸空气时SpO_2<90%或者PaO_2<90 mmHg(1 mmHg=0.133 kPa)；近3个月内参加过其他临床试验。

1.2 分组及处理

采用随机数字表将患者按1:1随机分为小潮气量联合低水平PEEP组(LP组)与小潮气量联合高水平PEEP组(HP组)；LP组于单肺通气时设置V_T 6 mL/kg，PEEP≤5 cmH_2O，HP组于相同时间点设置V_T 6 mL/kg，PEEP 6~10 cmH_2O(图1)。

1.3 麻醉方法

常规术前禁食水，患者入室后持续监测心电图(electrocardiogram，ECG)、HR、SpO_2、呼吸频率(respiratory rate，RR)、脑电双频谱指数(bispectral index，BIS)，建立静脉通路，局麻下行桡动脉穿刺进行动脉血压监测(SBP/DBP)。患者仰卧位躺于手术台后，给予4 L/min O_2面罩吸氧。麻醉诱导：一次静脉注射咪唑达伦0.05 mg/kg、舒芬太尼1 μg/kg、丙泊酚2~4 mg/kg、罗库溴铵0.6 mg/kg诱导完成后行双腔支气管导管插管，纤维支气管镜确认导管位置后行机械通气。双肺通气模式：V_T 10 mL/kg，RR 10~12 min^{-1}，I:E 1:2，吸入氧浓度(fraction of inspired oxygen，FiO_2) 80%。单肺通气时根据预测理想体重{男：50+0.91×[身高(cm)−152.4]；女：45.5+0.91×[身高(cm)−152.4]}设置潮气量，根据分组设置单肺通气呼吸参数，调整呼吸频率，维持Ppeak<30 mmHg，$P_{ET}CO_2$ 35~45mmHg，I:E 1:2，FiO_2 50%~80%。麻醉维持：持续静脉滴注丙泊酚2~4 mg/(kg·h)、瑞芬太尼0.25~0.4 μg/(kg·h)、吸入1%七氟烷，间断给予顺式阿曲库铵，维持BIS值在40~60。患者翻身侧卧位后在超声引导下行手术侧胸椎旁神经阻滞：超声引导下在T4~T5穿刺至胸椎旁间隙，确定位置后注入1%罗哌卡因20 mL。术中根据患者情况和手术需要调整麻醉药物用量，必要时给与血管活性药物和输血稳定患者生命体征。术中每半小时对所有患者给予肺复张，肺复张时维持平台压35~40 cmH_2O，每次持续30 s。术毕停用麻醉药物，待患者肌力恢复，意识清醒后拔除双腔支气管导管，术后48 h所有患者镇痛均采用患者自控静脉镇痛(patient controlled intravenous analgesia，PCIA)模式，镇痛配方及给药时间一致。

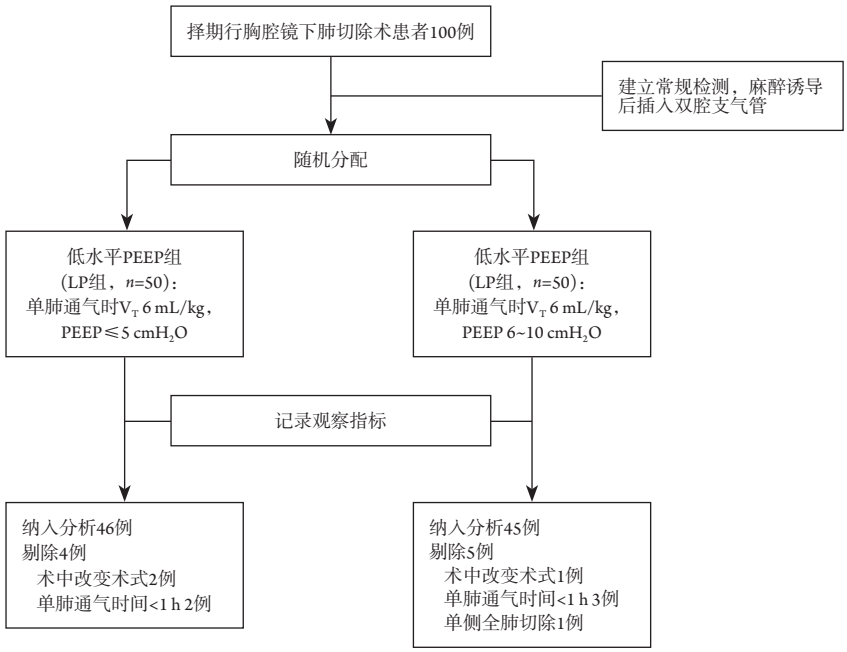

图1 试验流程图

Figure 1 Flow diagram of this study

1.4 观察指标

1.4.1 主要指标

术后7 d内肺部并发症，包括肺不张、胸腔积液、肺部感染等。

1.4.2 术中通气及氧合相关指标

记录OLV前(T1)、OLV 60min(T2)及手术结束时(T3)的HR、SpO_2、SBP/DBP、$P_{ET}CO_2$、V_T、Ppeak、Pplat，计算DP和Cdyn。分别于T1、T2、T3抽取桡动脉血进行血气分析，测得动脉血氧分压(partial arterial oxygen pressure，PaO_2)及动脉血二氧化碳分压(arterial partial pressure of carbon dioxide，$PaCO_2$)，计算$OI=PaO_2/FiO_2$、$A\text{-}aDO_2=(PB-PH_2O)\times FiO_2-PaCO_2/RQ-PaO_2$及$RI=A\text{-}aDO_2/PaO_2$；室温下，大气压PB=760 mmHg，饱和水蒸气压(PH_2O)=47 mmHg，呼吸商(RQ)=0.8。

1.4.3 术后其他指标

记录胸腔引流管拔除时间、术后3 d内胸腔引流管引流量及术后住院时间。

1.5 统计学处理

采用SPSS 25.0统计学软件进行数据分析。正态分布计量资料以均数±标准差($\bar{x}\pm s$)表示，不同时间点测量资料采用重复测量分析，组间比较采用t检验；计数资料以例(%)表示，采用χ^2检验或者Fisher精确概率法检验。$P<0.05$为差异有统计学意义。

2 结果

2.1 两组患者纳入排除情况及基线资料对比

本研究共入组患者100例，排除9例，最终LP组纳入分析46例，HP组纳入分析45例(图1)。两组患者性别、年龄、BMI、ASA分级、手术部位、麻醉时间、手术时间、OLV时间、失血量、术中补液量及既往史情况比较，差异无统计学意义($P>0.05$，表1)。

2.2 两组患者不同时间点血流动力学对比

两组间各时间点HR和MAP比较差异无统计学意义($P>0.05$)。与T1时比较，两组患者T2和T3时HR无明显波动($P>0.05$)；T2时两组MAP明显降低($P<0.05$，表2)。

表1 两组患者一般情况及术中情况的比较

Table 1 Comparison of basic and intraoperative indicators between the two groups

项目	LP组(n=46)	HP组(n=45)	P
性别(男/女)/例	20/26	23/22	0.531
年龄/岁	57.02 ± 10.91	56.49 ± 10.90	0.489
BMI/($kg\cdot m^{-2}$)	23.65 ± 2.55	23.61 ± 3.08	0.207
ASA(I/II/III级)/例	8/36/2	6/35/4	0.692
手术部位(左/右)/例	11/35	9/36	0.054
麻醉时间/min	145.98 ± 45.64	161.68 ± 49.18	0.432
手术时间/min	117.21 ± 44.68	130.41 ± 45.57	0.643
OLV时间/min	110.33 ± 45.61	121.33 ± 45.96	0.679
失血量/mL	97.83 ± 87.89	76.33 ± 67.18	0.797
输液量/mL	1 484.78 ± 358.37	1 473.33 ± 321.90	0.694
既往史/例			
糖尿病	5	5	0.971
高血压	13	14	0.821
冠心病	4	2	0.677
非心脏手术史	15	20	0.285
吸烟史	13	16	0.505

2.3 两组患者不同时间点呼吸力学指标对比

与T1时比较，T2、T3时两组患者Ppeak、Pplat明显升高，Cdyn明显降低；LP组T2时DP明显升高(P<0.05)。与LP组比较，T2时HP组Ppeak明显升高；T2、T3时，HP组Pplat明显升高，DP明显降低，Cdyn明显增高(P<0.05，表3)。

2.4 两组患者不同时间点氧合情况对比

与T1时比较，T2、T3时两组患者OI明显降低，A-aDO_2明显升高；T2时两组RI明显升高，T3时LP组RI明显升高(P<0.05)。与LP组比较，T2、T3时HP组OI明显升高，A-aDO_2、RI明显降低(P<0.05，表4)。

2.5 两组患者术后情况对比

术后7 d两组PPCs、胸腔引流管拔除时间及术后住院时间差异无统计学意义。与LP组比较，HP组术后3 d胸腔引流管引流量明显减少(P<0.05，表5)。

表2 两组患者不同时间点血流动力学的比较

Table 2 Comparison of hemodynamic between the two groups at different time

组别	n	HR/min^{-1}			MAP/mmHg		
		T1	T2	T3	T1	T2	T3
LP组	46	64.41 ± 9.46	65.67 ± 11.04	65.54 ± 10.87	93.11 ± 15.38	85.36 ± 12.93*	91.84 ± 12.99
HP组	45	63.53 ± 10.16	62.60 ± 10.33	65.60 ± 11.51	96.87 ± 49.05	87.16 ± 10.05*	92.41 ± 10.64

与本组T1比较，*P<0.05。

Compared with T1 in this group, *P<0.05.

表3 两组患者不同时间点呼吸力学相关指标的比较

Table 3 Comparison of respiratory-mechanics-related indicators between the two groups at different time

项目	LP组(n=46)			HP组(n=45)		
	T1	T2	T3	T1	T2	T3
Ppeak/mmHg	15.58 ± 3.34	21.30 ± 3.49*	17.24 ± 3.57*	15.15 ± 3.99	23.57 ± 3.47*	18.18 ± 4.54*
Pplat/mmHg	7.76 ± 3.28	12.43 ± 4.82*	9.57 ± 3.64*	8.29 ± 4.37	16.91 ± 4.04*#	11.31 ± 3.19*#
DP/mmHg	13.76 ± 3.25	17.62 ± 3.54*	7.67 ± 4.03	13.27 ± 4.18	13.69 ± 3.18#	6.87 ± 4.52#
Cdyn/(mL·H_2O^{-1})	32.29 ± 8.14	23.31 ± 9.31*	21.81 ± 4.40*	35.67 ± 12.16	27.01 ± 6.56*#	28.03 ± 6.56*#

与本组T1比较，*P<0.05；与LP组比较，#P<0.05。

Compared with T1 in this group, *P<0.05; compared with Group LP, #P<0.05.

表4 两组患者不同时间点氧合相关指标的比较

Table 4 Comparison of oxygenation-related indicators between the two groups at different time

项目	LP组(n=46)			HP组(n=45)		
	T1	T2	T3	T1	T2	T3
OI	362.21 ± 90.50	163.79 ± 88.68*	340.85 ± 96.63*	364.13 ± 99.34	202.77 ± 87.93*#	408.45 ± 96.34*#
A-aDO_2/mmHg	262.65 ± 9.62	421.50 ± 11.58*	288.37 ± 11.53*	268.78 ± 9.61	368.26 ± 12.79*#	275.72 ± 11.25*#
RI	0.93 ± 0.53	4.24 ± 1.86*	1.26 ± 0.16*	0.83 ± 0.67	3.31 ± 1.31*#	0.71 ± 0.48#

与本组T1比较，*P<0.05；与LP组比较，#P<0.05。

Compared with T1 in this group, *P<0.05; compared with Group LP, #P<0.05.

表5 两组患者术后肺部并发症及术后情况的比较

Table 5 Comparison of PPCs and postoperative indicators between the two groups

组别	*n*	PPCs≥1项/[例(%)]	肺不张/[例(%)]	胸腔积液/[例(%)]	肺部感染/[例(%)]	胸腔引流管拔管时间/d	术后3 d引流量/mL	术后住院时间/d
LP组	46	11 (23.9)	0 (0.0)	7 (15.2)	4 (8.7)	5.74 ± 3.33	637.02 ± 301.81	7.30 ± 3.19
HP组	45	9 (20.0)	2 (4.4)	3 (6.7)	7 (15.6)	6.76 ± 3.88	562.00 ± 242.44$^{\#}$	8.51 ± 4.28
P		0.801	0.242	0.315	0.354	0.588	0.005	0.110

与LP组比较，$^{\#}P$<0.05。

Compare with Group LP, $^{\#}P$<0.05.

3 讨论

目前，PLV已被广泛推荐用于术中通气管理，但是对于术中应用PEEP的大小尚无统一的意见[11]。本研究选择术前肺功能无明显异常的肺癌患者为对象，在胸腔镜下肺切除术中OLV期间应用小潮气量联合不同PEEP的肺保护性通气策略，结果表明，与低水平PEEP组(PEEP≤5 cmH_2O)比较，高水平PEEP组(PEEP 6~10 cmH_2O)可明显改善OLV和术毕时的通气氧合情况和肺顺应性，具有减轻患者术中肺部损伤的潜力。

肺切除术由于手术损伤和OLV、PPCs的发生率明显高于其他手术，可高达30%以上，严重影响了患者的预后和远期生存率[12]。全麻可导致呼吸肌功能下降，通气/血流比失调[13]。OLV会进一步加重了上述病理生理过程，增加发生PPCs的风险。已有较多研究[3,14-15]表明：机械通气期间应用肺保护性通气策略可有效减少PPCs发生，改善术中通气氧合情况和预后。应用较高PEEP(PEEP≥5 cmH_2O)可减少PPCs，减少肺不张和术中肺泡剪切伤，改善术中通气氧合情况和肺顺应性[16]。但是，Généreux等[17]和Bluth等[18]研究显示：术中应用不同水平PEEP对PPCs发生率没有明显差异。本研究结果显示两组患者在术后7 d内的PPCs发生情况无统计学差异。HP组术后胸腔引流管拔除时间和术后住院时间稍长于LP组，但是并无明显统计学差异。PPCs的发生是围手术期多种因素的综合结果，麻醉医生难以参与患者术后管理的全过程，不同PEEP对PPCs的影响可能会被其他因素所掩盖。HP组术后3 d内胸腔引流量较LP组更少，术后胸腔引流量与肺部损伤渗出有关，提示HP组的肺部损伤可能较LP组更轻，但需进一步的研究。

高水平PEEP会影响血流动力学稳定，影响心输出量，导致血压降低，使组织灌流不足[19]。本研究结果显示：与LP组比较，OLV后HP组HR和MAP并无明显下降，提示OLV期间6~10 cmH_2O PEEP对血流动力学的影响尚能在患者代偿范围之内。同时两组患者手术时间没有明显差异，说明OLV期间应用6~10 cmH_2O PEEP不会影响手术操作。OLV后HP组的Ppeak和Pplat较LP组高，但是驱动压明显低于LP组，Cdyn明显高于LP组。两组患者OLV期间OI明显下降，手术结束时较OLV时有所升高，但是仍低于OLV前；A-aDO_2、RI明显升高，术毕较OLV期间有所降低，但仍高于OLV前，提示OLV明显影响患者的肺功能，主要表现为肺通气和氧合功能下降。OLV组时HP组的OI、Cdyn均高于LP组，A-aDO_2、RI和驱动压均低于LP组，提示OLV期间，HP组患者肺功能改善情况优于LP组，这可能与较高水平的PEEP可以在OLV期间维持更多的肺单位扩张有关。

本研究在胸腔镜下肺切除术OLV期间应用V_T 6 mL/kg联合不同水平PEEP，辅以规律肺复张，结果提示：两组患者在术后短期内PPCs的发生情况无明显差异，但是PEEP>5 cmH_2O的应用更利于围手术期管理，有改善患者预后的潜力。本研究的不足之处在于：为单中心临床试验，临床样本量较小，所得出的结果还需大样本量的多中心临床研究加以验证。本研究仅观察了部分术后肺部并发症的发生情况。同时，对患者术后随访时间较短，对术后患者长期的恢复情况未能有效评估。

综上所述，小潮气量6 mL/kg联合6~10 cmH_2O可更好地改善胸腔镜下肺切除术患者OLV时通气氧合情况，利于术中麻醉管理。

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