论著

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持续气道正压对胸腹腔镜联合食管癌根治术后肺损伤的影响

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[摘要] **目的** 观察单肺通气时,萎陷侧肺持续气道正压(continuous positive airway pressure, CPAP)对胸腹腔镜联合食管癌根治术后肺损伤的影响。**方法** 择期行胸腹腔镜联合食管癌根治术患者50例,ASA评分Ⅱ~Ⅲ级,年龄40~75岁,体质指数(BMI)18~27,按随机数字表法分为2组($n=25$):对照组,即单肺通气时萎陷侧肺及气道向大气开放;CPAP组,即单肺通气时向萎陷侧肺持续输送纯氧维持萎陷侧肺及气道压力为6 cmH_2O。分别于T1(麻醉开始前)、T2(单肺通气结束时)和T3(术后24 h)抽取患者的静脉血3 mL,用ELISA法检测血清晚期糖基化代谢产物(soluble receptor of advanced glycation end-products, sRAGE)和KL-6(krebs. von den Iungen-6)水平,同时抽取动脉血2 mL行血气分析,并计算氧合指数(oxygenation index ,OI)。**结果** 氧合指数:对照组、CPAP组于T2、T3时点,氧合指数比T1时点均显著降低($P<0.05$);在T2时点,CPAP组氧合指数比对照组显著升高($P<0.05$)。sRAGE和KL-6水平:CPAP组和对照组在T3时点与T1时点、T2时点比较sRAGE和KL-6水平均显著升高($P<0.05$);在T3时点,与对照组比较,CPAP组sRAGE和KL-6水平显著降低($P<0.05$)。**结论** 单肺通气时萎陷侧肺保持持续气道正压能减轻胸腹腔镜联合食管癌根治术所致肺损伤。

[关键词] 持续气道正压;肺损伤;血清晚期糖基化代谢产物;KL-6
[中图法分类号] R563; R572; R605.973 [文献标志码] A

Continuous positive airway pressure alleviates lung injury after thoracoscopic and laparoscopic surgery for esophageal carcinoma: report of 50 cases

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[**Abstract**] **Objective** To investigate the effect of continuous positive airway pressure (CPAP) in collapsed lung on the lung injury after the thoracoscopic and laparoscopic surgery for esophageal carcinoma. **Methods** Fifty esophageal carcinoma patients (ASA grade II to III, aged 40 to 75, with body mass index of 18 to 27) undergoing selective thoracoscopic and laparoscopic esophagectomy in our hospital were prospectively enrolled in this study. They were randomly divided into control group ($n=25$, the collapsed lung directly connected to the outside air in one lung ventilation) and CPAP group ($n=25$, application of 6 cmH_2O CPAP to the collapsed lung during one-lung ventilation). Serum levels of soluble receptor of advanced glycation end-products (sRAGE) and krebs von den lungen-6 (KL-6) were detected with ELISA at 3 time points, that is, before operation (T1), at the end of one lung ventilation (T2), and 24 h after operation (T3). Arterial blood gas analysis was carried out to calculate the oxygenation index (OI). **Results** The OI values were significantly decreased in both groups at T2 and T3 than those at T1 ($P<0.05$), and it was significantly higher at T2 in the CPAP group than the control ($P<0.05$). sRAGE and KL-6 levels were markedly elevated in both groups at T3 than T1 and T2 ($P<0.05$). sRAGE and KL-6 were significantly decreased in the CPAP group than control at T3 ($P<0.05$). **Conclusion** CPAP in collapsed lung during

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one lung ventilation might reduce the lung injury after the thoracoscopic and laparoscopic surgery for esophageal carcinoma.

[**Key words**] thoracoscopy; continuous positive airway pressure; lung injury; soluble receptor of advanced glycation end-products; krebs von den lungen-6

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胸腹腔镜联合食管癌根治术与传统食管癌根治术相比,术中出血量、手术创伤更小,住院时间更短。但是肺炎、氧合障碍、急性肺损伤和急性呼吸窘迫综合征[1]等肺部并发症仍是其手术后的主要风险。而且目前胸腹腔镜联合食管癌根治手术较传统手术耗时更长,单肺通气时间亦更长,增加了发生术后肺部并发症的风险[2-3]。在单肺通气时萎陷肺和通气肺均有损伤,且萎陷肺的肺损伤更明显[4]。

临床实践表明:萎陷侧肺保持持续气道正压(continuous positive airway pressure,CPAP)能显著改善单肺通气时的氧合状态,然而萎陷侧肺持续气道正压能否改善单肺通气所致肺损伤尚无定论。本研究拟探讨CPAP是否具有肺保护作用,为临床上缓解单肺通气时的肺损伤提供新的理论依据。目前监测急性肺损伤的生化指标较多,但其特异性和敏感性各异。可溶性晚期糖基化终末产物受体(soluble receptor of advanced glycation end-products, sRAGE)和KL-6分别高表达于肺泡Ⅰ型和Ⅱ型细胞表面,在肺功能正常的患者中表达稳定,在急性肺损伤患者血清中浓度显著增加。因此,本研究拟观察胸腔镜联合食管癌根治术患者单肺通气时,sRAGE和KL-6在血清中的表达情况,探讨持续气道正压对萎陷肺肺损伤的影响。

1 对象与方法

1.1 病例及分组

该研究为随机对照试验,该研究方案已通过重庆医科大学附属第一医院伦理委员会审批。每位受试者均了解该试验并签署知情同意书。收集重庆医科大学附属第一医院胸外科普胸组,择期拟行胸腹腔镜联合食管癌根治术患者50例,ASA分级Ⅱ~Ⅲ级。采用随机数字表法分为2组:对照组,即单肺通气时萎陷侧肺及气道向大气开放;CPAP组,即单肺通气向萎陷侧肺及气道持续输送纯氧维持气道压力为6 cmH_2O。纳入标准:①拟行胸腹腔镜联合食管癌根治术患者;②年龄40~75岁;③患者心功能Ⅰ~Ⅱ级;d ASA分级Ⅱ~Ⅲ级。排除标准:①既往患慢性阻塞性肺病[肺功能检查:吸入支气管舒张药后第1秒用力呼气量(forced expiratory volume in 1s, FEV1)小于预测值的80%和FEV1与用力肺活量的比值(forced vital volume, FVC)小于70%];②慢性肾衰竭(血清肌酐>200 μmol/l);③体温超过38 ℃或者低于36 ℃;④1个月内有皮质激素服药史;⑤白细胞计数超过10×10^9/L或者低于4×10^9/L,以及胸片提示肺部感染者。

1.2 临床资料收集

制定专用实验数据表格记录术中参数及术后血清指标数据。包括①患者姓名、性别、年龄、诊断;②术中生命体征;③单肺通气时间,手术持续时间;④血气分析结果。

1.3 实验方法

分别于T1(麻醉开始前)、T2(单肺通气结束时)和T3(术后24 h)采集动脉血2 mL及时进行血气分析、计算氧合指数(OI),并于同时点抽取静脉血3 mL注入抗凝管中,立即使用离心机以1500转/min的转速离心10 min,取上清液,按照Biovendor公司sRAGE和KL-6试剂盒操作指南,用ELISA法检测各组血清sRAGE和KL-6水平。

1.4 统计学分析

采用SPSS 17.0统计软件。计量资料以$\bar{x}\pm s$表示,组内比较采用重复测量设计的方差分析,组间比较采用成组t检验,计数资料比较采用χ^2检验。

2 结果

2.1 患者一般情况

2组患者年龄、体质指数、性别、ASA分级、FEV1/FVC和单肺通气时间比较差异无统计学意义(表1)。

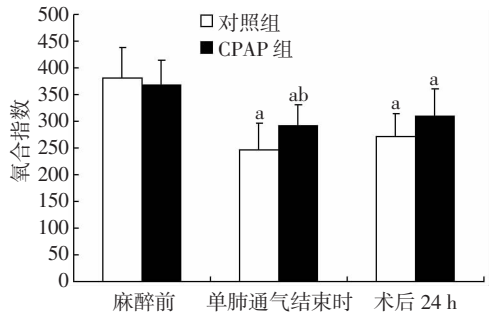
表1 2组患者一般情况

组别	年龄(岁)	体质指数	性别(男/女)	ASA(Ⅱ/Ⅲ)	FEV1/FVC	单肺通气时间(min)
对照组	60±8	22±5	16/9	18/7	75±11	105±21
CPAP组	58±9	22±4	18/7	20/5	73±10	96±25

2.2 2组患者术中及术后氧合状态及血清标志物水平

2.2.1 氧合指数 组内比较:对照组:T2、T3与T1比较,氧合指数均明显下降($P<0.05$),而T3与T2比较无统计学意义($P>0.05$)。CPAP组:T2、T3与T1

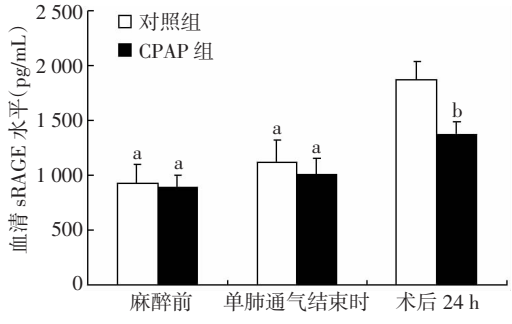
比较,氧和指数均明显下降($P<0.05$),T2与T3比较无统计学意义($P>0.05$);组间比较:T2时,CPAP组较对照组氧合指数显著升高($P<0.05$),其余各时点无统计学差异(图1)。



a:$P<0.05$,与麻醉前比较;b:$P<0.05$,与单肺通气结束时的对照组比较

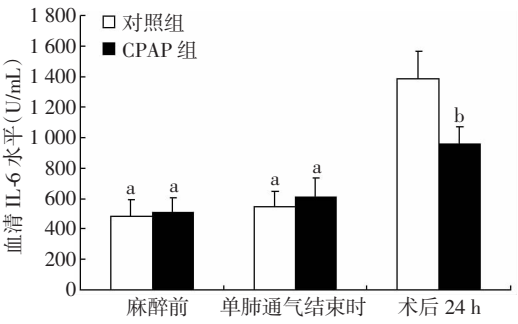
图1 2组患者不同时间点及组间氧合指数比较

2.2.2 sRAGE和KL-6水平 组内比较:对照组:T3较T1、T2,sRAGE和KL-6水平明显升高($P<0.05$),具有统计学差异,而其余各时点间比较无统计学差异。CPAP组:T3较T1、T2时sRAGE和KL-6水平均有明显升高($P<0.05$),而其余各时间点比较无统计学差异。组间比较:CPAP组于T3时较对照组sRAGE和KL-6水平显著降低($P<0.05$),而其余各时间点两组比较无统计学差异(图2、3)。



a:$P<0.05$,与术后24 h比较;b:$P<0.05$,与对照组比较

图2 2组患者不同时间点及组间血清sRAGE水平



a:$P<0.05$,与术后24 h比较;b:$P<0.05$,与对照组比较

图3 2组患者不同时间点及组间血清KL-6水平

3 讨论

大量文献研究提示,单肺通气可导致急性肺损伤[5-9]。临床上常以肺损伤血清标志物水平在机械通气前后变化判断其肺损伤程度。sRAGE是免疫球蛋白超家族中的一员,在肺泡Ⅰ型细胞和内皮细胞中高度表达[10]。研究表明:sRAGE可作为反映肺损伤的指标[11-13]。KL-6是一种表达于肺泡Ⅱ型细胞膜表面的肺泡上皮黏液素,在急性肺损伤或急性呼吸窘迫综合征患者血浆内KL-6含量增加[14-16]。本研究中,所有受试者均进行胸腹腔镜联合食管癌根治术,因此避免了肺叶切除等手术操作造成的肺叶损伤对本实验结果的影响。本研究发现,在胸腹腔镜联合食管癌根治术单肺通气结束时血清中sRAGE和KL-6水平升高,至手术结束24 h时血清sRAGE和KL-6水平升高更为显著,提示该手术使肺泡Ⅰ型细胞和肺泡Ⅱ型细胞均遭受损伤。这可能与胸腹腔镜联合食管癌根治术,单肺通气导致萎陷侧肺肺不张,萎陷侧肺泡细胞代谢出现紊乱,通气血流比例失衡;而通气侧肺过度通气可使其肺组织受到强烈的牵张力和剪切力,导致肺泡细胞受损;且手术操作对肺反复牵拉和挤压,亦可造成肺损伤。受损的肺泡Ⅰ型和Ⅱ型细胞大量分泌sRAGE和KL-6,导致血清中sRAGE和KL-6逐渐堆积,出现显著升高。

现有文献报道CPAP能够改善单肺通气时的氧合状态[17]。本研究亦发现采用CPAP患者术后氧合指数较对照组显著提高,提示胸腹腔镜联合食管癌根治术中使用CPAP能显著改善单肺通气时的氧合状态。CPAP改善氧合的原因可能与萎陷侧肺少量正压气流进入,纠正该侧肺极端的通气/血流比例失调有关。此外,本研究还提示:相较于对照组,CPAP组在手术结束24 h时血清sRAGE和KL-6水平有明显降低,提示CPAP对胸腹腔镜联合食管癌根治术后肺损伤具有一定的保护作用。但CPAP减轻肺损伤的具体机制尚不明确,可能与CPAP改善萎陷侧肺泡氧合以及减少萎陷侧肺肺泡的萎陷程度,进而改善肺泡Ⅰ型及Ⅱ型细胞代谢状态有关。当单肺通气时,缺血性肺血管收缩在减少萎陷侧肺组织血供的同时,亦使该侧肺组织处于相对缺血状态,当再次通气时,可能会出现缺血再灌注损伤[18-19],CPAP可改善萎陷侧肺的氧供并使该侧肺缺血性肺血管收缩所致肺泡缺血损害降低。这可能是CPAP能减轻肺损伤的原因之一。近年来有研究报道,在胸腹腔镜联合食管癌根治术中,萎陷侧肺给予

5 cmH_2O 的 CPAP 能显著减轻肺内灌洗液中白介素1α、白介素1β、白介素10和肿瘤坏死因子α等的水平[20],提示CPAP在单肺通气时能显著减少肺泡炎性反应,从而减轻肺损伤,达到肺保护作用。目前在临床中很多医院在单肺通气时CPAP常常采用5~10 cmH_2O,而我医院采用的CPAP为4~7 cmH_2O。因为文献指出6 cmH_2O CPAP具有较好的作用,因此我们选择了6 cmH_2O 的CPAP,且不会造成肺部分膨胀,从而影响手术操作。

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