

氧分压引导吸入氧浓度调整对老年患者胃癌根治术术后肺不张的影响

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摘 要

目的: 研究氧分压引导吸入氧浓度调整对老年患者胃癌根治术术后肺不张的影响。方法: 本研究为随机对照试验, 选择在本院接受胃癌根治术的患者90例, 随机分为两组, 每组45例。两组插管前均使用吸入氧浓度100%面罩通气3 min, 插管后行手法复张, 调整呼吸参数, 拔管后, 患者在环境空气中被转移到AICU, AICU期间设置氧流量3 L/min鼻导管吸氧。不同的是A组在插管后通过调整FiO₂观察血气分析的PaO₂值得110 ≤ PaO₂ ≤ 160。B组插管后使用80%吸入氧浓度维持。结果: 主要结局: A组的肺超声评分明显低于B组(P < 0.05), 两组差异有统计学意义, A组的肺不张发生率与B组无统计学意义(P > 0.05), A组的肺不张发生率明显低于B组(P < 0.05), 两组差异有统计学意义。次要结局: 与T0时相比, 术中各时间点(T1~T4)两组SpO₂均维持在较高且相似水平, 组间比较差异无统计学意义(P > 0.05)。术后30 min (T5)时A组SpO₂显著低于B组, 差异有统计学意义(P < 0.05)。与T0时相比, 两组患者术中HR均呈下降趋势。组间比较显示, 在T3时A组HR显著低于B组, 差异有统计学意义(P < 0.05)。其余各时间点两组HR差异均无统计学意义(P > 0.05)。两组患者术中及术后MAP均显著降低。组间比较显示, 术中及术后各时间点(T1~T5)两组MAP差异均无统计学意义(P > 0.05)。在术后手术切口感染发生率、住院时间、住院期间死亡率方面, 两组间差异无统计学意义。结论: 使用氧分压导向吸入氧浓度滴定相比固定高氧浓度可以减少术后肺不张的发生。

关键词

胃癌根治术, 肺保护性通气策略, 吸入氧浓度, 肺不张

The Effect of Arterial Oxygen Partial Pressure-Guided Titration of Inspired Oxygen Concentration on Postoperative Atelectasis in Elderly Patients Undergoing Radical Gastrectomy for Gastric Cancer

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Abstract

Objective: To investigate the effect of different intraoperative inspired oxygen concentrations (FiO₂) on postoperative atelectasis in elderly patients undergoing radical gastrectomy for gastric cancer. **Methods:** This was a randomized controlled trial. Ninety patients who underwent radical gastrectomy for gastric cancer at our hospital were randomly divided into two groups of 45 each. Both groups received 100% oxygen via face mask for 3 minutes before intubation. Manual re-expansion was performed after intubation, and respiratory parameters were adjusted. After extubation, patients were transferred to the AICU in ambient air, where they received nasal cannula oxygen at a flow rate of 3 L/min. The difference was that in group A, after intubation, PaO₂ values in blood gas analysis were adjusted by monitoring FiO₂ to ensure $110 \leq \text{PaO}_2 \leq 160$. In group B, 80% oxygen was maintained after intubation. **Results:** Primary outcomes: The lung ultrasound score of group A was significantly lower than that of group B ($P < 0.05$), and the difference between the two groups was statistically significant. The incidence of atelectasis in group A was not statistically significant compared with that in group B ($P > 0.05$), but the incidence of atelectasis in group A was significantly lower than that in group B ($P < 0.05$), and the difference between the two groups was statistically significant. Secondary outcomes: Compared to T₀, SpO₂ remained at similar and high levels in both groups at all intraoperative time points (T₁~T₄), with no statistically significant difference between the groups ($P > 0.05$). At 30 min postoperatively (T₅), SpO₂ in group A was significantly lower than that in group B ($P < 0.05$). Compared to T₀, intraoperative heart rate (HR) decreased in both groups. Intergroup comparison showed that at T₃, HR in group A was significantly lower than that in group B ($P < 0.05$). There were no statistically significant differences in HR between the two groups at any other time point ($P > 0.05$). MAP decreased significantly in both groups both intraoperatively and postoperatively. Intergroup comparison showed no statistically significant differences in MAP between the two groups at any intraoperative and postoperative time points (T₁~T₅) ($P > 0.05$). There were no statistically significant differences between the two groups in postoperative surgical site infection rate, length of hospital stay, and in-hospital mortality. **Conclusion:** Oxygen partial pressure-guided titration of inspired oxygen concentration, compared to a fixed high FiO₂ strategy, can reduce the incidence of postoperative atelectasis in elderly patients undergoing radical gastrectomy.

Keywords

Radical Gastrectomy, Lung-Protective Ventilation Strategy, Inspired Oxygen Concentration, Atelectasis

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1. 引言

机械通气为手术期间全麻患者提供必要的供氧, 然而, 机械通气期间的最佳吸入氧分数(FiO₂)仍存在

争议[1]。WHO 发布了关于减少手术部位感染的指南,建议任何接受手术麻醉、插管和机械通气的患者在麻醉期间和手术后 2~6 h 接受 FiO_2 为 80% 的氧气吸入[2]。从理论上来说吸入高浓度氧气可增加组织氧分压,以促进中性粒细胞氧化杀伤过程,从而增强免疫反应来达到预防术后手术部位感染的目的[3]。然而最新的几项荟萃分析并不支持 WHO 的这项建议[4]-[6]。两项大型随机对照试验的结果未能确定围手术期高 FiO_2 对术后感染有任何的有益影响[7] [8],并且术后吸入高浓度氧气还存在过度氧合的潜在危害[9]。虽然氧气可以预防缺氧事件,但它可能使患者处于高氧血症的危险中过量的氧气会在体内产生活性氧,促进氧化应激[10]-[12]。还能增加外周血管阻力,降低心输出量[13]-[15]。但是过量的氧气会与吸入性肺不张、重症监护室死亡率和急性肺损伤等有关[16] [17]。

氧分压导向吸入氧浓度滴定是一种动态调整 FiO_2 的方法,基于对氧分压的监测,根据患者的具体状况动态调整吸入氧浓度,以维持适当的氧分压水平,可以避免过度氧疗导致的氧毒性。研究表明, PaO_2 在 110~160 mmHg 内的患者院内病死率最低[18]。不同患者、不同病情对氧气的的需求各不相同,传统的方式可能依赖于麻醉医生的经验,但这种方式往往误差过大,难以做到精准控制,而氧分压导向吸入氧浓度滴定通过及时监测患者氧分压变化,及时调整 FiO_2 ,可以帮助限制吸氧总量,提供充分氧合的同时并保留安全余量,减少术后肺部并发症的发生风险。本实验假设通过对吸入氧浓度的精确控制和个体化调整,与传统的高 FiO_2 (80%)相比在实施肺保护性通气策略的腹部手术患者中,可以有效降低术后肺部并发症的风险,从而提高患者的手术安全性和术后恢复质量。

2. 资料与方法

2.1. 一般资料

这项随机对照实验是由医院伦理委员会批准,并在中国临床注册中心注册,在患者入组前进行获得了所有参与者的书面知情同意。纳入标准为年龄 ≥ 65 岁,择期行胃癌根治术患者;体重指数 18.5~25 kg/m^2 ; ASA 分级 II 或 III 级;肺功能未见明显异常;预计手术时间 ≥ 2 h;自愿受试并签署知情同意书。排除标准:术前高血压未得到有效控制或控制不佳(收缩压 ≥ 180 mmHg 或舒张压 ≥ 110 mmHg);严重的呼吸系统合并症(包括但不限于慢性阻塞性肺疾病、哮喘、肺癌、肺结核等);严重的肝肾功能损害;严重的心血管系统疾病:如合并严重的心律失常,心力衰竭,急性冠脉综合征等基础疾病;最近 3 个月参与其他临床研究;其他研究者认为不适合参与研究的情况。

2.2. 分组处理

严格按照纳入和排除标准选取安徽医科大学第二附属医院择期行胃癌根治术患者 90 例,按照随机数字表法将其分为两组: A 组($n=45$)和 B 组($n=45$)。两组插管前设置吸入氧浓度 100% 面罩通气 3 min, A 组:插管后行手法复张,调整呼吸参数,初始氧浓度均设为 0.5,10 分钟后测血气分析,若 $\text{SpO}_2 \geq 97\%$, $110 \leq \text{PaO}_2 \leq 160$,则维持该吸入氧浓度;若 $\text{SpO}_2 \geq 97\%$, $\text{PaO}_2 < 110$,则 FiO_2 增加 0.1,并于 10 分钟后再次测血气分析使得 $110 \leq \text{PaO}_2 \leq 160$;若 $\text{SpO}_2 \geq 97\%$, $\text{PaO}_2 > 160$,则 FiO_2 减少 0.1,并于 10 分钟后再次测血气分析使得 $110 \leq \text{PaO}_2 \leq 160$;若 $\text{SpO}_2 < 97\%$,则 FiO_2 增加 0.1,2 分钟后再次评估 SpO_2 。术中使用滴定吸入氧浓度维持。B 组:插管后启动机械通气行手法复张,调整呼吸参数,术中使用 80% 吸入氧浓度维持,拔管后,患者在环境空气中被转移到 AICU, AICU 期间设置氧流量 3 L/min 鼻导管吸氧。

2.3. 麻醉方法

所有患者术前均常规禁食 8 小时、禁水 6 小时。患者入室后平卧位,常规开放静脉通路,面罩预给氧 3 min,氧流量 4~6 L/min,常规监测 ECG、 SpO_2 、BP。局麻下行左桡动脉穿刺置管术及右颈内静脉穿

刺置管术,连续监测有创动脉压(ABP)。患者充分给氧去氮后进行麻醉诱导:静脉依次缓慢注射舒芬太尼 0.4~0.6 $\mu\text{g}/\text{kg}$ 、依托咪酯 0.3 mg/kg 、顺式阿曲库铵 0.15 mg/kg 。两组待肌肉完全肌松后在可视喉镜下行气管插管,气管插管完成后立即连接麻醉机,检查呼末二氧化碳,并听诊两肺呼吸音,确定气管导管的位置。连接呼吸机后所有患者皆使用如下呼吸机参数:① VCV 模式;② $V_t = 6 \text{ mL}/\text{kgPBW}$;③ 吸呼比 = 1:2;④ $\text{PEEP} = 5 \text{ cmH}_2\text{O}$;⑤ 动态调节呼吸频率使 PetCO_2 维持在 35~45 mmHg。

麻醉维持采用全凭静脉麻醉,静脉持续泵注丙泊酚 4~8 $\text{mg}/\text{kg}/\text{h}$,瑞芬太尼 0.1~0.2 $\mu\text{g}/\text{kg}\cdot\text{min}$,顺式阿曲库铵 0.1~0.2 $\text{mg}/\text{kg}\cdot\text{h}$,维持 BIS40~60。术后当受试者完全清醒并能够自主充分呼吸时,拔管。并转运至麻醉加强监护室观察,并通过面罩给予 3 l/min 的氧气。

2.4. 术中抢救策略

围手术期任何时间 SpO_2 低于 92%,进行抢救通气,在排除常规气道问题(如螺纹管脱落、支气管痉挛、痰栓堵塞、气管导管异位)后调整吸入氧浓度并进行持续气道正压通气,在确定无法进行后续实验时及时退出实验并记录。围术期维持患者心率在 50~100 之间,必要时使用阿托品和艾司洛尔。维持患者平均动脉压在 50~110 之间,必要时使用麻黄碱、去氧肾上腺素、去甲肾上腺素、尼卡地平类药物调整血压。

2.5. 围术期多模式镇痛

所有患者均采用多模式镇痛方案模式:术前常规予超声引导下双侧腹横肌平面阻滞;术中视情况追加舒芬太尼、瑞芬太尼等阿片类药物;术后使用非甾体类镇痛药并采取 PCIA 镇痛(PCIA 镇痛:舒芬太尼 2 $\mu\text{g}/\text{kg}$,昂丹司琼 8 mg 。背景输注(2 ml/h),单次量 2 ml,锁定时间 15 min)。

2.6. 观察指标

主要观察指标为术后 30 min 肺超声诊断术后肺不张的发生率及严重程度以及术后 30 min 低氧血症的发生率。次要观察指标为 T0(术前)、T1(手术切开前)、T2(手术 1 h)、T3(手术 2 h)、T4(术毕)、T5(拔管后 30 分钟)一般生命体征、血气分析参数;术后第 2 d、术后第 7 d 对患者进行肺功能测试,临床肺部感染评分,术后肺部并发症,手术切口感染发生率、住院期间死亡率等。

2.7. 肺超声评估

在到达 AICU 后 30 分钟进行肺部超声检查。肺超声检查由对熟练掌握肺超声检查和对分组不知情的研究人员进行。采用 Sonosite Edge 超声系统(Fuji Film, Bothell, WA)在仰卧位进行超声检查频率为 6~12 mhz 的线性探头。按照 Monastesse 及其同事描述的肺部超声检查方法[19],对患者进行仰卧位扫描胸腔被腋窝前线、腋窝后线和乳头下方的一条水平线所分割。对 12 个区域的肋间隙分别进行扫描和分析。通过计算改进的 LUSS 来评估曝气损失,该方法对曝气损失的检测具有足够的灵敏度。两名肺部超声检查人员在肺部扫描同时检查后,为每个区域提供评分。然后将 12 个单独象限的得分相加,计算胸腔 LUSS (0~36),得分越高表明通气损失越严重。曝气程度评分为 0~3 分:0 分:0~2 条 B 线;1 分: ≥ 3 条 B 线或 1 条或多条胸膜下实变被一条正常胸膜线隔开;2 分:由增厚或不规则胸膜线隔开的多个合并 B 线或多个胸膜下实变;3 分:以及直径超过 1 厘米 \times 2 厘米的实变或小的胸膜下实变。

2.8. 统计分析

采用 SPSS 软件进行统计学分析,计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示,连续变量的组间比较采用独立的两样本 t 检验,组内不同时点各指标比较采用重复测量数据的方差分析检验后使用 Bonferroni 校正,分类变量采用卡方检验或确切概率法。 $P < 0.05$ 为差异有统计学意义。

3. 结果

本研究将纳入的 90 例患者随机分为 A 组($n = 45$)和 B 组($n = 45$)。两组患者的性别、年龄、ASA、BMI、手术时间、住院时间无明显差异(表 1)。

Table 1. Comparison of general information between the two groups of patients

表 1. 两组患者一般情况的比较

组别	A	B
性别(男/女)	33/12	30/15
年龄	72.9 ± 4.5	72.8 ± 3.9
BMI (kg/m^2)	21.5 ± 2.5	21.7 ± 2.0
ASA II/III级(例)	30/15	24/21
高血压[例(%)]	24/45	21/45
糖尿病	5/45	8/45
手术时间(min)	269.8 ± 46.3	234.8 ± 42.7
住院时间	24.8 ± 10.2	23.9 ± 9.7
FiO ₂	34.7 ± 4.7	80
PaO ₂	131.5 ± 17.3	385 ± 45.1

A 组的肺超声评分明显低于 B 组($P = 0.042$)，两组差异有统计学意义，A 组的肺不张发生率与 B 组无统计学意义($P = 0.153$)，A 组的肺不张发生率明显低于 B 组($P = 0.049$)，两组差异有统计学意义(表 2)。

Table 2. Comparison of lung ultrasound findings, atelectasis, and 30-min postoperative hypoxemia between groups

表 2. 两组肺超声、肺不张、术后 30 min 低氧血症发生率的比较

组别	A ($n = 45$)	B ($n = 45$)	P 值
肺超声评分	9.9 ± 2.6	11.4 ± 4.1	0.042
肺不张发生率	19/45	25/45	0.153
术后 30 min 低氧血症发生率	9/45	15/45	0.049

Table 3. Comparison of vital signs at different time points between the two groups

表 3. 两组患者不同时间点生命体征的比较

指标	组别	T0 (患者入室时)	T1 (手术开始)	T2 (术中 1 h)	T3 术中 2 h	T4 (术毕)	T5 (术后 30 min)
SpO ₂	A	97.0 ± 1.7	97.8 ± 1.1	98.1 ± 0.9	97.7 ± 0.8	98.6 ± 0.6	95.8 ± 1.6
	B	96.7 ± 1.8	98.2 ± 0.9	98.3 ± 0.9	98.2 ± 1.0	98.2 ± 1.3	97.5 ± 1.3
HR	A	74.6 ± 6.2	64.5 ± 11.1	60.8 ± 14.1	58.8 ± 7.4	64.5 ± 6.6	72.0 ± 3.7
	B	73.5 ± 8.9	65.4 ± 11.6	64.4 ± 13.1	65.4 ± 9.4	67.0 ± 12.6	73.7 ± 11.5
MAP	A	110.2 ± 12.6	90.7 ± 17.1	84.4 ± 11.5	84.7 ± 10.3	82.8 ± 12.8	85.9 ± 19.9
	B	102.7 ± 15.8	86.0 ± 16.9	82.6 ± 10.9	83.5 ± 9.8	79.6 ± 13.3	79.9 ± 17.9

与 T0 时相比，术中各时间点(T1~T4)两组 SpO₂ 均维持在较高且相似水平，组间比较差异无统计学意义($P > 0.05$)。术后 30 min (T5)时 A 组 SpO₂ 为(95.8 ± 1.6)%，显著低于 B 组的(97.5 ± 1.3)%，差异有统

计学意义($P < 0.05$)。与 T0 时相比, 两组患者术中 HR 均呈下降趋势。组间比较显示, 在 T3 时 A 组 HR 为(58.8 ± 7.4)次/分, 显著低于 B 组的(65.4 ± 9.4)次/分, 差异有统计学意义($P < 0.05$)。其余各时间点两组 HR 差异均无统计学意义($P > 0.05$)。与 T0 时比较, 两组患者术中及术后 MAP 均有不同程度的降低。组间比较显示, 术中及术后各时间点(T1~T5)两组 MAP 差异均无统计学意义($P > 0.05$) (表 3)。

在术后手术切口感染发生率、住院时间、住院期间死亡率方面, 两组间差异无统计学意义(表 4)。

Table 4. Comparison of surgical site infection, hospital stay, and in-hospital mortality between groups

表 4. 两组患者手术切口感染发生率、住院时间与住院期间死亡率比较

组别	A	B	P 值
手术切口感染率	12/45	18/45	0.180
住院时间	23.9 ± 9.7	24.8 ± 10.2	0.669
住院时间死亡率	1/45	1/45	0.999

4. 讨论

胃癌是一种常见的消化道恶性肿瘤, 受饮食习惯、生活方式、区域环境等因素影响, 胃癌发生率逐年升高[20]。中国是胃癌的高发国家之一, 每年胃癌新发病例占全球发病病例的 1/3 以上, 病死率居全球各国家第 6 位, 给人们健康造成极大威胁, 同时也给社会带来沉重负担[21] [22]。胃癌根治术是治疗胃癌的最有效方案, 但该手术创伤较大, 术后并发症发生率较高, 其中肺部并发症(PPCs)尤为常见[23] [24]。所以围术期管理是保障手术安全和提高术后恢复质量的关键环节之一。小潮气量(6~8 mL/kg)、PEEP 和肺复张等肺保护性通气策略, 已被证实可明显减少患者术后呼吸系统并发症的发生[25], 其中小潮气量和肺复张等已经被麻醉医生广泛接受并应用于临床, 然而吸入氧浓度(FiO_2)对肺部的潜在影响仍饱受争议。

传统的高氧策略, 其理论基础在于最大化增加组织的氧储备以预防意外低氧血症, 并通过氧的抗生素效应降低手术部位感染风险。但是医源性高氧血症本身可能是一种隐匿性的医源性损伤, 其带来的危害可能远超其理论上的益处。高 FiO_2 可能造成对肺毛细血管内皮功能受损和氧化应激等潜在不利影响。过量的氧气可通过线粒体分裂导致肺内皮细胞损伤[26]。Romagnoli 等人证明, 最低 FiO_2 水平的保护性通气使 $SpO_2 \geq 95\%$, 通过产生较少的 ROS 生成来降低氧毒性[27]。吸收性肺不张还可促进肺分流并引起低氧血症, 肺不张区趋向于低通气/灌注比。高氧也是肺泡上皮细胞凋亡的重要因素, 并降低表明肺组织损伤的表面活性剂蛋白水平[28]。

本研究通过滴定将 A 组的 FiO_2 维持在 34.7 ± 4.7 , 在之前的一项研究中, Wei Xia 等人使用 SpO_2 来滴定 FiO_2 以减少术中高氧及术后肺不张[29], 结果只需要 27% 的氧浓度即可达到正常氧合, 我们认为, 这种差异主要与研究独特的人群特征及手术类型密切相关。本实验研究对象主要是 65 岁以上的老年患者, 年龄导致的肺生理学改变是 FiO_2 增高的重要影响因素; 其次, 本实验涉及的胃癌根治术手术时间较长, 长时间的手术与麻醉本身即是术后肺部并发症的独立危险因素。这种差异恰恰反映了基于氧分压的滴定策略能够根据患者的实际生理和手术需求进行动态调节。另外, 关于本实验一个有趣的发现是 A 组在术后 30 min 的 SpO_2 要低于 B 组, 但 A 组的肺超声评分更高, 这可能正好揭示了 SpO_2 作为单一评价术后肺不张的局限性, B 组可能依赖术中高氧暂时补偿了吸收性肺不张的肺内分流, A 组虽然 SpO_2 略低, 但是仍然处于安全阈值之上, 而且更加可以反映真实的氧合状态。这可以通过肺部超声体现出来。在标准的临床环境中, 高氧血症通常定义为 $PaO_2 \geq 100$ mmHg。根据以往的研究, 全麻期间 PaO_2 的平均值为 206 mmHg [30], 然而, 在我们日常的麻醉管理中, 有时 PaO_2 高达 400~500 mmHg。据报道, 危重患者的 PaO_2 高氧临界值低至 150 mmHg [31]。不同患者因其年龄、合并症、手术类型等其氧合能力存在较大差

异, 个体化维持术中吸入氧浓度可以根据患者的实时生理反馈进行动态调整。个体化策略从根本上减少了吸收性肺不张的发生, 改善了肺通气/血流比例, 从而显著降低了术后肺炎、肺不张和需要呼吸支持的重度低氧血症的发生率。根据我们的研究结果, 将 PaO_2 维持在 110~160 mmHg 时, 对应的 FiO_2 当处在 30~45 的区间, 这样既可以避免不必要的给氧, 降低高氧血症的风险, 又能维持机体正常的供氧。

当然, 本研究也存在一定的局限性。首先, 本研究在单一中心进行, 样本量有限, 虽然结果表明了显著的临床差异, 但对于某些罕见的严重肺部并发症, 我们的研究可能效能不足。其次, 个体化策略的实施需要更频繁的动脉血气分析或严密监测, 这对医疗资源提出了一定要求, 可能在一定程度上限制其普适性。未来研究应致力于更经济、无创的方案来可靠地指导 FiO_2 滴定。第三, 本研究主要纳入的是接受胃癌根治术的老年患者, 结果能否对其他人群或手术有利仍需要进一步研究验证。第四, 在本试验中, 仅评估了术后 30 分钟内肺不张的发生率, 而没有检查肺不张的后续时间点。虽然这是评估全麻恢复期患者肺不张的常见时间点[32][33], 但如果术后病区相关混杂因素能够得到有效管理, 延长观察时间可能会提供更多证据。

本研究结果表明, 采用个体化氧浓度管理(以维持生理性氧合为目标)在改善患者术后肺功能、减少肺不张和降低氧化应激方面, 显著优于传统的固定高浓度给氧方案。个体化给氧最大限度地实现了肺保护与预防低氧之间的平衡。

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