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右美托咪定对老年患者胸腔镜肺癌根治术后肺部并发症及炎症反应的影响

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[摘要] 目的: 探究右美托咪定对老年患者胸腔镜肺癌根治术后肺部并发症及炎症反应的影响。方法: 选取2019年8月至2021年8月邯郸市中心医院收治的110例老年肺癌患者为研究对象, 按随机数字表法随机分为对照组($n=55$)与观察组($n=55$)。观察组在麻醉诱导前10 min静脉注射右美托咪定 $1.0 \mu\text{g}/\text{kg}$, 并以 $0.3 \mu\text{g}/(\text{kg}\cdot\text{h})$ 泵注至术毕; 对照组予以等量生理盐水。比较两组术中情况、血气分析指标[氧合指数(oxygenation index, OI)、肺内分流率(intrapulmonary shunt rate, Q_s/Q_t)]、肺部并发症及血清白细胞介素-6(interleukin-6, IL-6)、肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)水平。结果: 两组手术时间、麻醉时间、单肺通气时间、输液量、输血量等术中一般情况比较差异均无统计学意义(均 $P>0.05$)。与对照组相比, 观察组在单肺通气30 min(T_2)、单肺通气60 min(T_3)、恢复双肺通气15 min(T_4)时刻的OI均明显更高, Q_s/Q_t 均明显更低(均 $P<0.05$)。观察组术后肺部并发症总发生率明显低于对照组(16.36% vs 32.73%, $P<0.05$)。观察组 T_3 和术后2 h(T_5)、术后24 h(T_6)时刻血清IL-6、TNF- α 水平均明显低于对照组(均 $P<0.05$)。结论: 右美托咪定可有效改善老年患者胸腔镜肺癌根治术中的血氧状态, 减轻炎症反应, 从而降低术后肺部并发症发生率。

[关键词] 右美托咪定; 胸腔镜肺癌根治术; 老年人; 肺部并发症; 炎症反应

Effect of dexmedetomidine on pulmonary complications and inflammatory response after thoracoscopic radical resection of lung cancer in elderly patients

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Abstract **Objective:** To investigate the effect of dexmedetomidine on pulmonary complications and inflammatory response after thoracoscopic radical resection of lung cancer in elderly patients. **Methods:** A total of 110 elderly patients with lung cancer admitted to Handan Central Hospital from August 2019 to August 2021 were selected as the

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study subjects. They were randomly divided into a control group and an observation group according to the random number table method, each group with 55 cases. In the observation group, 1.0 mg/kg dexmedetomidine was intravenously injected 10 min before anesthesia induction, and 0.3 mg/(kg·h) was pumped to the end of operation. The control group was given the same amount of saline. The intraoperative conditions, blood gas analysis indexes [oxygenation index (OI), intrapulmonary shunt rate (Q_s/Q_t)], pulmonary complications, and serum inflammatory factors [interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α)] were compared between the 2 groups. **Results:** There was no statistically significant difference in the operation time, anesthesia time, one-lung ventilation time, transfusion volume, blood transfusion volume between the 2 groups (all $P>0.05$). Compared with the control group, the OI at 30 min (T_2), 60 min (T_3) of single lung ventilation and recovery of bilateral lung ventilation for 15 min (T_4) in the observation group was significantly higher, and Q_s/Q_t was significantly lower (all $P<0.05$). The total incidence of postoperative pulmonary complications in the observation group was significantly lower than that in the control group (16.36% vs 32.73%, $P<0.05$). The serum IL-6 and TNF- α levels at T_3 , and 2 h (T_5), 24 h (T_6) after the operation in the observation group were significantly lower than those in the control group (all $P<0.05$). **Conclusion:** Dexmedetomidine can effectively improve the blood oxygen status and reduce the inflammatory response in elderly patients undergoing thoracoscopic radical resection of lung cancer, thereby reducing the incidence of postoperative pulmonary complications.

Keywords dexmedetomidine; thoracoscopic radical resection of lung cancer; the elderly; pulmonary complications; inflammatory response

胸腔镜肺癌根治术为我国肺癌外科治疗最主要的手段, 具有创伤小、恢复快、效果好等优势^[1]。但外科手术的创伤性不可避免, 加之老年患者各器官系统功能减退、合并症较多等, 其手术及术后并发症风险较中青年患者更高, 更应予以重视^[2]。麻醉是手术顺利进行的必要保障, 但麻醉药物、手术创伤及疼痛等的刺激均可加重患者机体应激反应^[3]。同时, 术中单肺通气技术的应用也可能导致急性肺损伤, 增加术后肺部并发症发生风险^[4]。右美托咪定是麻醉常用药物, 具有镇静、催眠、镇痛之效, 还可通过减少儿茶酚胺的释放来减轻应激反应^[5]。近年研究^[6]还发现: 右美托咪定对创伤、感染等诱导的肺损伤具有一定保护作用。基于此, 本研究旨在探究右美托咪定对老年患者胸腔镜肺癌根治术后肺部并发症及炎症反应的影响, 为临床研究提供一定参考。

1 对象与方法

1.1 对象

本研究通过邯郸市中心医院医学伦理委员会审批(审批号: 2021031)。本实验开始前基于统计学原理, 参考文献[7]进行了样本量估算, 计算结果为: 当两组病例数相等时, 每组不应少于40例, 计算公式为: $n_1=n_2=2[(t_{\alpha/2}+t_{\beta})s/\delta]^2$ 。本研

究选取2019年8月至2021年8月邯郸市中心医院收治的110例老年肺癌患者为研究对象。纳入标准: 1) 择期行胸腔镜下肺叶切除或肺楔形切除术治疗; 2) 年龄 ≥ 60 岁; 3) 美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级 $\leq III$; 4) 术前肺功能正常; 5) 预计单肺通气时间 ≥ 1 h; 6) 患者及家属知情同意参与研究, 且治疗配合度高。排除标准: 1) 术前合并严重心肝肾肾疾患、高血压、糖尿病; 2) 术前2周内发生急性上呼吸道感染; 3) 有肺气肿、哮喘等严重肺部疾病或脑梗死、脑出血、脑外伤既往史; 4) 术中由胸腔镜转为开胸手术; 5) 单肺通气时间 >4 h; 6) 有精神类药物长期应用史或近2周内有镇痛、镇静药治疗史。按随机数字表法将患者随机分为对照组与观察组, 每组55例。

1.2 麻醉方法

两组均由同一组医师实施胸腔镜肺癌根治术。入室后, 常规建立动、静脉通道, 监测心电图、脉搏、血压、脑电双频指数(bispectral index, BIS)等。观察组在麻醉诱导前10 min静脉输注右美托咪定(2 mL:0.2 mg, 四川国瑞药业有限责任公司, 国药准字H20110097)1.0 $\mu\text{g}/\text{kg}$, 并以0.3 $\mu\text{g}/(\text{kg}\cdot\text{h})$ 的速率泵注至术毕; 对照组予以等容量生理盐水。术中采用全凭静脉麻醉, 以

咪达唑仑(3 mL:15 mg, 江苏恩华药业股份有限公司, 国药准字H20153019)0.05 mg/kg、舒芬太尼(5 mL:250 μ g, 宜昌人福药业有限责任公司, 国药准字H20054256)0.2 g/kg、依托咪酯(10 mL:20 mg, 江苏恩华药业股份有限公司, 国药准字H20020511)0.3 mg/kg、阿曲库铵(25 mg, 上海恒瑞医药有限公司, 国药准字H20061298)0.15 mg/kg进行麻醉诱导, 5 min后行双腔支气管插管术, 机械通气, 设置呼吸比为1:2, 维持双肺通气时潮气量(tidal volume, V_t)为6~8 mL/kg, 呼吸频率(respiratory rate, RR)为12~14次/min; 单肺通气时 V_t 为6 mL/kg, RR为14~16次/min, 呼气末二氧化碳分压(arterial partial pressure of end-tidal carbon dioxide, $P_{et}CO_2$)为35~45 mmHg(1 mmHg=0.133 kPa)。以丙泊酚(100 mg:10 mL, 西安力邦制药有限公司, 国药准字: H20010368)4~8 mg/(kg·h)、舒芬太尼0.2~1.0 μ g/(kg·h)持续泵注进行麻醉维持, 术中维持BIS为40~50, 血压、心率波动幅度控制在基础水平的20%以内。术后, 待患者意识恢复、满足拔管条件时拔除气管导管, 入麻醉后恢复室(post anesthesia care unit, PACU); 同时接自控静脉镇痛泵, 舒芬太尼2 μ g/kg+生理盐水稀释至100 mL, 背景剂量为2 mL/h, 单次按压剂量为0.5 mL, 锁定15min。控制疼痛视觉模拟评分法(visual analog scales, VAS)评分 \leq 3, VAS评分 $>$ 3时静脉注射曲马多100 mg进行镇痛补救。

1.3 观察指标

1)患者入院后即收集两组性别、年龄、体重指数(body mass index, BMI)等一般资料。2)术中情况: 记录两组手术时间、麻醉时间、单肺通气时间、输血量、输血量。3)血气分析: 于单肺通气即刻(T_1)、单肺通气30 min(T_2)、单肺通

气60 min(T_3)、恢复双肺通气15 min(T_4)时采集两组桡动脉、颈静脉血, 进行血气分析, 计算氧合指数(oxygenation index, OI)、肺内分流率(intrapulmonary shunt rate, Q_p/Q_s)。4)术后肺部并发症: 记录两组术后住院期间肺部感染、肺不张等并发症发生情况。5)炎症反应: 于麻醉诱导前(T_0)、 T_3 、术后2 h(T_5)、术后24 h(T_6)时采集两组静脉血, 检测血清白细胞介素-6(interleukin-6, IL-6)、肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)水平。

1.4 统计学处理

采用SPSS 24.0统计学软件分析数据。正态分布计量资料以均数 \pm 标准差($\bar{x}\pm s$)表示, 2组比较行两独立样本 t 检验或配对 t 检验; 计数资料以例(%)描述, 2组比较行 χ^2 检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 一般资料

两组性别、年龄等一般资料比较差异均无统计学意义(均 $P>0.05$, 表1)。

2.2 术中情况

两组手术时间、麻醉时间、单肺通气时间、输血量、输血量等术中一般情况比较差异均无统计学意义(均 $P>0.05$, 表2)。

2.3 血气分析参数

两组 T_1 时刻OI、 Q_p/Q_s 比较差异均无统计学意义(均 $P>0.05$)。与对照组相比, 观察组在 T_2 、 T_3 、 T_4 时刻的OI均明显更高, Q_p/Q_s 明显更低, 组间比较差异均有统计学意义(均 $P<0.05$, 表3)。

表1 两组一般资料比较($n=55$)

Table 1 Comparison of general data between the 2 groups ($n=55$)

组别	性别(男/女)/例	年龄/岁	BMI/(kg·m ⁻²)	患侧(左/右)/例	ASA分级(II/III)/例	术前FEV ₁ /FVC/%	吸烟史(有/无)/例	手术方式(肺叶切除/肺楔形切除)/例
观察组	33/22	69.73 \pm 5.46	22.38 \pm 2.74	28/27	35/20	88.95 \pm 7.23	31/24	27/28
对照组	34/21	69.45 \pm 5.89	22.42 \pm 2.55	26/29	37/18	88.64 \pm 6.97	32/23	29/26
t/χ^2	0.038	0.259	0.079	0.146	0.161	0.229	0.037	0.146
P	0.845	0.796	0.937	0.703	0.688	0.819	0.847	0.703

表2 两组术中情况比较($n=55$)Table 2 Comparison of intraoperative conditions between the 2 groups ($n=55$)

组别	手术时间/min	麻醉时间/min	单肺通气时间/min	输血量/mL	失血量/mL
观察组	172.38 ± 25.48	181.82 ± 22.56	102.36 ± 17.25	1158.26 ± 243.89	49.33 ± 13.76
对照组	177.26 ± 27.04	186.21 ± 23.41	104.47 ± 18.12	1196.13 ± 251.34	53.48 ± 14.47
<i>t</i>	0.974	1.001	0.625	0.802	1.541
<i>P</i>	0.332	0.319	0.533	0.424	0.126

表3 两组血气分析参数比较($n=55$)Table 3 Comparison of blood gas analysis parameters between the 2 groups ($n=55$)

组别	OI/mmHg				Q _s /Q _t /%			
	T ₁	T ₂	T ₃	T ₄	T ₁	T ₂	T ₃	T ₄
观察组	457.64 ± 39.52	314.53 ± 25.64*	324.53 ± 28.26*	462.57 ± 37.59*	3.41 ± 0.25	12.66 ± 3.34*	19.68 ± 3.89*	11.05 ± 2.34*
对照组	461.08 ± 41.25	243.28 ± 23.96*	287.54 ± 30.17*	421.36 ± 35.46*	3.37 ± 0.31	18.52 ± 3.71*	23.46 ± 5.72*	16.37 ± 4.22*
<i>t</i>	0.447	15.057	6.636	5.914	0.745	8.706	4.053	8.176
<i>P</i>	0.656	0.001	0.001	0.001	0.458	0.001	0.001	0.001

与同组T₁时刻比较, * $P < 0.05$ 。1 mmHg=0.133 kPa。

Compared with the same group at T₁, * $P < 0.05$. 1 mmHg=0.133 kPa.

2.4 术后肺部并发症

观察组术后肺部并发症总发生率为16.36%(9/55), 对照组术后肺部并发症总发生率为32.73%(18/55), 组间比较差异有统计学意义($P < 0.05$, 表4)。

2.5 炎症反应

T₀时刻, 两组血清IL-6、TNF- α 水平比较差异均无统计学意义(均 $P > 0.05$)。T₃、T₅和T₆时刻, 观察组血清IL-6、TNF- α 水平均明显低于对照组, 组间比较差异均有统计学意义(均 $P < 0.05$, 表5)。

表4 两组术后肺部并发症发生情况比较($n=55$)Table 4 Comparison of postoperative pulmonary complications between the 2 groups ($n=55$)

组别	肺部感染/[例(%)]	肺不/[例(%)]	胸腔积液/[例(%)]	低氧血症/[例(%)]	总发生/[例(%)]
观察组	6 (10.91)	2 (3.64)	1 (1.82)	0 (0.00)	9 (16.36)
对照组	10 (18.18)	4 (7.27)	2 (3.64)	2 (3.64)	18 (32.73)
χ^2					3.976
<i>P</i>					0.046

表5 两组血清炎症因子水平比较($n=55$)Table 5 Comparison of serum inflammatory factors between the 2 groups ($n=55$)

组别	IL-6/(pg·mL ⁻¹)				TNF- α /(pg·mL ⁻¹)			
	T ₀	T ₃	T ₅	T ₆	T ₀	T ₃	T ₅	T ₆
观察组	19.12 ± 3.38	38.24 ± 9.67*	86.96 ± 13.59*	66.73 ± 11.28*	8.72 ± 1.14	13.45 ± 2.28*	27.65 ± 7.28*	16.11 ± 3.27*
对照组	19.19 ± 3.04	51.76 ± 11.05*	123.78 ± 16.83*	83.69 ± 10.54*	8.63 ± 1.07	15.36 ± 2.79*	34.31 ± 8.64*	22.26 ± 3.89*
<i>t</i>	0.114	6.828	12.623	8.147	0.427	3.931	4.371	8.975
<i>P</i>	0.909	0.001	0.001	0.001	0.670	0.001	0.001	0.001

与同组麻醉诱导前(T₀)比较, * $P < 0.05$ 。

Compared with the same group before anesthesia induction (T₀), * $P < 0.05$.

3 讨论

肺癌是临床常见恶性肿瘤,在我国发病率、病死率均较高,且呈上升趋势,严重危害人民生命健康^[8]。胸腔镜肺癌根治术为临床肺癌治疗常用术式,可在胸腔镜的辅助下尽可能缩小手术切口,获得高清视野,为肿瘤的精准切除创造有利条件。但老年患者因机体功能减退、自我修复能力、免疫力较差等易发生术后肺部感染等并发症,影响预后。因此,选择对机体免疫、应激、炎症反应等影响小的麻醉方法具有重要临床意义^[9]。

侧卧位、单肺通气等均会引起机体发生一系列病理生理变化,加之麻醉剂也会抑制缺氧性肺血管收缩,患者易出现低氧血症、肺内分流等症状,另外,手术创伤、术后疼痛等导致的肺缺血再灌注损伤、肺不张等均是胸腔镜肺癌根治术中麻醉所面临的问题^[10]。右美托咪定为 α_2 肾上腺素受体激动剂,具有镇痛、镇静、降低交感活性等作用。近年研究^[11]发现:右美托咪定还具有肺保护作用,在胸外科麻醉中应用具有一定优势:右美托咪定可通过抑制脂多糖诱导的线粒体功能障碍来改善肺组织细胞黏附、线粒体膜电位及血管通透性,并可抑制细胞凋亡,从而提高OI。右美托咪定还可提高肺组织中超氧化物歧化酶、血红素氧合酶1等的活性和表达来减轻麻醉期间患者机体的炎症与氧化应激程度,有利于低氧血症和肺内分流的改善^[12]。另有研究^[13]发现:右美托咪定可通过提高肺的动态顺应性、减少生理无效腔来纠正通气/血流比例,提高肺癌患者在术中与术后的OI,避免低氧血症的发生。基础实验^[14-15]也证实:右美托咪定可通过调节 α_7n ACh R介导的TLR4/NF- κ B通路、 α_2 AR介导的ERK1/2通路等来减轻急性肺损伤。另外,右美托咪定可减轻舒芬太尼大剂量应用而导致的疼痛过敏现象,有效缓解患者术后疼痛,有利于肺功能的恢复^[16]。本研究结果显示:与对照组相比,观察组在 T_2 、 T_3 、 T_4 时刻的OI均明显更高, Q_e/Q_t 均明显更低,且术后肺部并发症总发生率更低,表明右美托咪定可有效改善老年胸腔镜肺癌根治术患者术中缺氧状态,发挥肺保护效应而减少术后肺部并发症的发生,与李伟靖等^[17]研究结果一致。

炎症反应被认为是导致肺组织损伤、感染等多种术后并发症的重要因素^[18]。单肺通气操作可诱发多种细胞因子释放,激发全身性炎症反应^[19]。IL-6、TNF- α 均参与了机体炎症反应。右美托咪定对 α_2 肾上腺素受体的特异性选择作用可经TLR4/

MyD88/MAPK信号通路来下调TNF- α 、IL-6的表达^[20]。王磊等^[21]研究也发现右美托咪定可明显降低肺癌患者肺组织中TGF- β 、TNF- α 、IL-6等的表达。本研究也发现:观察组 T_3 、 T_5 和 T_6 时刻血清IL-6、TNF- α 水平均明显低于对照组,表明右美托咪定可有效抑制老年患者胸腔镜肺癌根治术围手术期炎症反应,进而减轻肺损伤、降低术后肺部并发症发生风险,这得益于右美托咪定的抗炎作用^[22]。

综上所述,在老年患者胸腔镜肺癌根治术中应用右美托咪定,可有效改善患者围手术期血氧状态,抑制炎症反应,从而降低术后肺部并发症发生风险,有利于术后康复。但本研究仍存在样本量较小的局限性,结果难免存在一定偏倚,未来仍需多中心、大样本量的随机对照研究进一步验证和完善结果。

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