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全身麻醉下不同脑电双频指数对老年胃肠道恶性肿瘤患者应激反应、炎症因子和术后认知功能的影响*

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摘要 目的:观察全身麻醉下不同脑电双频指数(BIS)对老年胃肠道恶性肿瘤患者应激反应、炎症因子和术后认知功能的影响。**方法:**选择2020年10月-2021年4月在新疆医科大学附属肿瘤医院初诊的住院老年胃肠道恶性肿瘤患者,共98例。据随机数字表分为浅麻醉组($n=49$, BIS值45~55)和深麻醉组($n=49$, BIS值30~40)。对比两组苏醒质量、应激反应、炎症因子、术后认知功能、血流动力学及不良反应。**结果:**浅麻醉组的苏醒时间、定向力恢复时间、气管拔管时间短于深麻醉组($P<0.05$)。插管后即刻(T1)~术毕(T5)时间点,两组心率(HR)、平均动脉压(MAP)均下降后升高($P<0.05$)。深麻醉组T1~T5时间点HR、MAP高于浅麻醉组($P<0.05$)。手术开始2h(T4)、拔管后60min(T6)时间点,两组皮质醇(Cor)、促肾上腺皮质激素(ACTH)水平呈升高趋势,且浅麻醉组高于深麻醉组($P<0.05$)。T4、T6时间点,两组白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平持续升高,但浅麻醉组低于深麻醉组($P<0.05$)。深麻醉组的术后3d、术后7d简明精神状态量表(MMSE)评分低于浅麻醉组($P<0.05$)。两组不良反应发生率组间对比无差异($P>0.05$)。**结论:**全身麻醉下老年胃肠道恶性肿瘤患者BIS值范围30~40可维持更平稳的血流动力学,应激反应低,但是其对认知功能影响相对较大;BIS值在45~55之间时,患者苏醒快,炎症因子水平更低;临床应结合实际情况合理调控BIS值。

关键词:全身麻醉;脑电双频指数;老年;胃肠道恶性肿瘤;应激反应;炎症因子;认知功能

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Effects of Different Bispectral Index on Stress Response, Inflammatory Factors and Postoperative Cognitive Function in Elderly Patients with Gastrointestinal Malignant Tumors Under General Anesthesia*

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ABSTRACT Objective: To observe the effects of different bispectral index (BIS) on stress response, inflammatory factors and postoperative cognitive function in elderly patients with gastrointestinal malignant tumors under general anesthesia. **Methods:** A total of 98 hospitalized elderly patients with gastrointestinal malignant tumors who were newly diagnosed in the Affiliated Cancer Hospital of Xinjiang Medical University from October 2020 to April 2021 were selected. According to the random number table method, they were divided into shallow anesthesia group ($n=49$, BIS value 45~55) and deep anesthesia group ($n=49$, BIS value 30~40). The awakening quality, stress response, inflammatory factors, postoperative cognitive function, hemodynamics and adverse reactions were compared between the two groups. **Results:** The awakening time, directional force recovery time and tracheal extubation time of shallow anesthesia group were shorter than those of deep anesthesia group ($P<0.05$). Heart rate (HR) and mean arterial pressure (MAP) decreased and then increased in the two groups at immediately after intubation (T1) ~ completion of operation (T5) time points ($P<0.05$). HR and MAP at T1~T5 time points of deep anesthesia group were higher than those of shallow anesthesia group ($P<0.05$). The levels of cortisol (Cor) and adrenocorticotrophic hormone (ACTH) in the two groups increased at 2 h after operation (T4) and 60 min after extubation (T6) time points, and the shallow anesthesia group was higher than the deep anesthesia group ($P<0.05$). At T4 and T6 time points, the levels of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) increased continuously, but the shallow anesthesia group was lower than the deep anesthesia group ($P<0.05$). The Mini-Mental State Examination (MMSE) score of deep anesthesia group was lower than that of shallow anesthesia group at 3 d and 7 d after operation ($P<0.05$). There was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Under general anesthesia, the BIS value range of 30~40 in elderly patients with gastrointestinal malignant tumors can maintain more stable hemodynamics and low stress response, but it has a relatively large impact on cognitive

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function. When the BIS value is between 45 and 55, the patient wakes up quickly and the level of inflammatory factors is lower. The BIS value should be adjusted and controlled reasonably in combination with the actual situation.

Key words: General anesthesia; Bispectral index; Elderly; Gastrointestinal malignant tumors; Stress response; Inflammatory factors; Cognitive function

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前言

胃肠道恶性肿瘤是临床的常见疾病,而手术切除是其有效的治疗方案之一^[1]。伴随着人民生活结构不断变化,加上老龄化的日益加重,老年胃肠道恶性肿瘤患者不断增加^[2-3]。但是由于老年患者各项重要脏器功能退化,药物敏感性下降,且老年患者在手术过程中的调节能力也相对更弱,致使术后易出现一种或多种并发症^[4,5]。既往麻醉医师常常依据患者手术中一般症状体征主观地判断患者意识水平及麻醉深度,可能存在麻醉过浅或过深的情况,及时给予相关处理措施,也存在滞后性,会对患者造成一定程度上的不利影响^[6]。脑电双频指数(BIS)可有效反映个体麻醉镇静深度,也是临床常用的监测麻醉镇静深度的指标^[7,8]。但有关 BIS 的最佳数值尚存在一定的争议。本次研究观察 BIS 值 45~55、BIS 值 30~40 这两种麻醉状态下,老年胃肠道恶性肿瘤患者应激反应、炎症因子和术后认知功能的变化,以期临床选择合理的麻醉方案提供参考。

1 资料与方法

1.1 一般资料

选择 2020 年 10 月 -2021 年 4 月在新疆医科大学附属肿瘤医院初诊的住院老年胃肠道恶性肿瘤患者,共 98 例。纳入标准:(1)年龄 ≥ 65 岁,性别、民族不限;(2)拟在全身麻醉下行胃肠道恶性肿瘤择期手术的患者;(3)同意参加本研究,并签署知情同意书;(4)美国麻醉医师协会(ASA)分级为 II~III 级^[9]。排除标准:(1)存在神经病史、中枢神经损伤的患者;(2)术前 3 个月内接受过免疫治疗;(3)术中出现严重过敏反应;(4)发生房颤,外周血管疾病,主动脉瓣持续返流或动脉置管禁忌者;(5)合并严重心肝肾等疾病者;(6)无法耐受既定麻醉深度需加用血管活性药物或大量出血者;(7)严重心率失常者。新疆医科大学附属肿瘤医院医学伦理委员会已批准本研究。根据随机数字表法将所有患者分为浅麻醉组(n=49, BIS 值 45~55)和深麻醉组(n=49, BIS 值 30~40),两组一般资料对比无差异($P>0.05$)。见表 1。

表 1 一般资料分析
Table 1 Analysis of general data

General data	Shallow anesthesia group (n=49)	Deep anesthesia group (n=49)	t/χ^2	P
Age(years)	71.87 $\pm$ 5.16	73.02 $\pm$ 5.47	-1.071	0.287
Gender(male/female)	28/21	27/22	0.041	0.839
BMI(kg/m ²)	24.93 $\pm$ 4.26	24.52 $\pm$ 3.15	0.542	0.589
Years of schooling(years)	7.78 $\pm$ 2.43	7.71 $\pm$ 3.29	0.120	0.905
ASA classification(II/III)	18/31	17/32	0.044	0.833
Preoperative MMSE(scores)	27.38 $\pm$ 0.99	27.32 $\pm$ 1.16	0.275	0.784
Operation time(min)	253.44 $\pm$ 53.92	255.75 $\pm$ 57.38	-0.205	0.838
Anesthesia time(min)	261.06 $\pm$ 51.63	267.48 $\pm$ 63.05	-0.551	0.583

1.2 方法

两组常规禁食禁饮。入室后开通静脉输液通路,监测心率(HR)、平均动脉压(MAP),连接 BIS 麻醉深度监护仪监测 BIS 值。局麻下行右侧锁骨下静脉及左侧桡动脉穿刺。麻醉诱导:咪达唑仑注射液(国药准字 H20067040,宜昌人福药业有限责任公司,规格:2 mL:2 mg)0.015~0.03 mg/kg、丙泊酚/长链脂肪乳注射液(国药准字 H20213012,扬子江药业集团有限公司,规格:20 mL:0.2 mg)1.5~2.5 mg/kg、枸橼酸舒芬太尼注射液(国药准字 H20054171,宜昌人福药业有限责任公司,规格:按 C₂₂H₃₀N₂O₂S 计 1 mL:50 μ g)0.3~0.6 μ g/kg、苯磺顺阿曲库铵注射液[国药准字 H20213438,杭州澳亚生物技术股份有限公司,规格:5 mL:10 mg(以顺阿曲库铵计)]0.2 mg/kg。面罩吸氧

5 min 后进行气管插管,行机械通气,呼吸参数设定:呼气末二氧化碳维持 35~45 mmHg 左右,吸呼比为 2:1,潮气量 8~10 mL/kg,氧浓度 100%,呼吸频率 10~12 次/min。术中:全凭静脉维持麻醉,丙泊酚靶控维持麻醉,效应室浓度为 2~2.5 μ g/mL,苯磺顺阿曲库铵 5 mg/30 min,注射用盐酸瑞芬太尼[国药准字 H20123421,国药集团工业有限公司廊坊分公司,规格:2 mg(以瑞芬太尼 C₂₀H₂₈N₂O₃ 计)]靶浓度 2~4 μ g/mL,其中浅麻醉组维持 BIS 值 45~55,深麻醉组维持 BIS 值 30~40。手术结束后依据 BIS 值及麻醉苏醒状况待病人自然苏醒拔出气管导管。

1.3 观察指标

(1)苏醒质量:记录两组患者定向力恢复时间、苏醒时间、气管拔管时间。(2)血流动力学:分别记录两组患者麻醉诱导前

(T0)、插管后即刻(T1)、手术开始时(T2)、手术开始 1h(T3)、手术开始 2 h(T4)以及术毕(T5)的 HR、MAP。(3)应激反应、炎症因子:分别于 T0、T4、拔管后 60 min(T6)时间点采集患者中心静脉血 4 mL,采用电化学发光法测定血清皮质醇(Cor)、促肾上腺皮质激素(ACTH)水平。采用酶联免疫吸附法检测白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平。试剂盒购自武汉华美生物工程有限公司。(4)术后认知功能:分别于术前、术后 3 d、术后 7 d 采用简明精神状态量表(MMSE)^[10]对患者认知功能进行评估,MMSE 总分 30 分,分数越高,认知障碍越严重。(5)安全性评价:记录两组患者围术期不良反应。

1.4 统计学方法

采用 SPSS25.0 软件进行统计学分析,计数资料采用($\bar{x} \pm s$)表示,组间比较选用独立样本 t 检验;组内各时间点如血流动力学参数、应激反应、炎症因子、MMSE 评分等比较采用单组的重复测量方差分析。计数资料以%表示,实施 χ^2 检验。检验水准为 $\alpha=0.05$ 。

2 结果

2.1 苏醒时间、定向力恢复时间、气管拔管时间对比

浅麻醉组的苏醒时间、定向力恢复时间、气管拔管时间短于深麻醉组($P<0.05$),见表 2。

表 2 苏醒时间、定向力恢复时间、气管拔管时间对比($\bar{x} \pm s$, min)

Table 2 Comparison of awakening time, directional force recovery time and tracheal extubation time ($\bar{x} \pm s$, min)

Groups	Awakening time	Directional force recovery time	Tracheal extubation time
Shallow anesthesia group(n=49)	18.17 $\pm$ 1.36	27.18 $\pm$ 2.28	22.69 $\pm$ 2.16
Deep anesthesia group(n=49)	23.95 $\pm$ 2.21	32.34 $\pm$ 3.19	27.71 $\pm$ 2.25
t	-15.592	-9.212	-11.266
P	0.000	0.000	0.000

2.2 HR、MAP 对比

T0 时间点, 两组 HR、MAP 组间对比无差异($P>0.05$)。

T1~T5 时间点, 两组 HR、MAP 均下降后升高($P<0.05$)。深麻醉组 T1~T5 时间点 HR、MAP 较浅麻醉组高($P<0.05$)。见表 3。

表 3 HR、MAP 对比($\bar{x} \pm s$)

Table 3 Comparison of HR, MAP($\bar{x} \pm s$)

Groups	Time points	HR(beats/min)	MAP(mmHg)
Shallow anesthesia group(n=49)	T0	79.46 $\pm$ 5.11	96.69 $\pm$ 5.63
	T1	73.11 $\pm$ 3.75 ⁱ	88.70 $\pm$ 4.51 ⁱ
	T2	69.33 $\pm$ 4.57 ⁱ	84.65 $\pm$ 5.49 ⁱ
	T3	65.56 $\pm$ 3.30 ⁱ	80.65 $\pm$ 6.59 ⁱ
	T4	70.16 $\pm$ 6.59 ⁱ	85.71 $\pm$ 5.68 ⁱ
	T5	74.64 $\pm$ 5.91 ⁱ	90.45 $\pm$ 6.56 ⁱ
Deep anesthesia group(n=49)	T0	79.19 $\pm$ 4.40	96.47 $\pm$ 4.15
	T1	76.68 $\pm$ 3.99 ^{at}	92.67 $\pm$ 5.32 ^{at}
	T2	73.30 $\pm$ 4.73 ^{at}	88.72 $\pm$ 4.57 ^{at}
	T3	69.90 $\pm$ 3.27 ^{at}	84.74 $\pm$ 5.60 ^{at}
	T4	74.27 $\pm$ 4.33 ^{at}	89.45 $\pm$ 6.39 ^{at}
	T5	78.23 $\pm$ 3.26 ^a	95.77 $\pm$ 6.37 ^a
Repeated measurement and overall analysis	HF correction factor	0.9471	0.9846
	Inter group F, P	78.173, 0.000	49.818, 0.000
	In group F, P	78.782, 0.000	77.966, 0.000
	Interaction F, P	3.533, 0.007	2.884, 0.022

Note: compared with T0, ⁱ $P<0.05$. Compared with shallow anesthesia group, ^a $P<0.05$.

2.3 Cor、ACTH 对比

T0 时间点, 两组 Cor、ACTH 水平对比无差异($P>0.05$)。

T4、T6 时间点, 两组 Cor、ACTH 水平持续升高, 且浅麻醉组高

于深麻醉组($P<0.05$), 见表 4。

2.4 IL-6、TNF- α 对比

T0 时间点, 两组 IL-6、TNF- α 水平对比无差异($P>0.05$)。

T4、T6 时间点,两组 IL-6、TNF- α 水平呈升高趋势,但浅麻醉组 低于深麻醉组($P<0.05$),见表 5。

表 4 Cor、ACTH 对比($\bar{x}\pm s$)
Table 4 Comparison of Cor, ACTH($\bar{x}\pm s$)

Groups	Time points	Cor($\mu\text{g/dl}$)	ACTH(pmol/L)
Shallow anesthesia group($n=49$)	T0	13.85 $\pm$ 3.28	5.02 $\pm$ 0.33
	T4	28.33 $\pm$ 4.41 ¹	12.15 $\pm$ 0.41 ¹
	T6	46.31 $\pm$ 4.77 ¹	25.74 $\pm$ 0.79 ¹
Deep anesthesia group($n=49$)	T0	13.32 $\pm$ 2.81	4.91 $\pm$ 0.48
	T4	22.73 $\pm$ 4.26 ^{ad}	8.71 $\pm$ 0.86 ^{ad}
	T6	36.00 $\pm$ 4.30 ^{ad}	14.51 $\pm$ 1.07 ^{ad}
Repeated measurement and overall analysis	HF correction factor	0.9835	0.5205
	Inter group F, P	167.107, 0.000	3, 209.098, 0.000
	In group F, P	1, 143.932, 0.000	11, 991.723, 0.000
	Interaction F, P	27.934, 0.000	1, 654.181, 0.000

Note: compared with T0, ¹ $P<0.05$. Compared with shallow anesthesia group, ^a $P<0.05$.

表 5 IL-6、TNF- α 对比($\bar{x}\pm s$, pg/mL)
Table 5 Comparison of IL-6, TNF- α ($\bar{x}\pm s$, pg/mL)

Groups	Time points	IL-6	TNF- α
Shallow anesthesia group($n=49$)	T0	23.65 $\pm$ 4.41	5.12 $\pm$ 0.48
	T4	35.83 $\pm$ 4.34 ¹	11.02 $\pm$ 1.25 ¹
	T6	48.61 $\pm$ 5.39 ¹	17.93 $\pm$ 2.29 ¹
Deep anesthesia group($n=49$)	T0	23.15 $\pm$ 5.26	5.29 $\pm$ 0.37
	T4	49.72 $\pm$ 4.15 ^{ad}	16.79 $\pm$ 2.15 ^{ad}
	T6	60.53 $\pm$ 5.06 ^{ad}	28.52 $\pm$ 3.07 ^{ad}
Repeated measurement and overall analysis	HF correction factor	0.8480	0.6675
	Inter group F, P	249.969, 0.000	620.665, 0.000
	In group F, P	1, 012.517, 0.000	2, 267.136, 0.000
	Interaction F, P	62.201, 0.000	189.945, 0.000

Note: compared with T0, ¹ $P<0.05$. Compared with shallow anesthesia group, ^a $P<0.05$.

2.5 术后认知功能对比

术前两组 MMSE 评分对比无差异($P>0.05$)。术后 3 d、术后 7 d 两组 MMSE 评分下降后升高($P<0.05$)。深麻醉组术后 3 d、术后 7 d MMSE 评分较浅麻醉组低($P<0.05$)。见表 6。

2.6 两组不良反应发生率对比

浅麻醉组出现 1 例寒战、1 例恶心呕吐, 不良反应发生率为 4.08%。深麻醉组出现 1 例恶心呕吐、1 例低血压、1 例寒战, 不良反应发生率为 6.12%。两组不良反应发生率组间对比无差异(校正 $\chi^2=0.211$, $P=0.000$)。均予以相关药物对症处理, 不良反应消失。

3 讨论

全身麻醉是指采用麻醉药物对中枢神经系统进行暂时抑制, 从而出现全身痛觉消失、神志消失、反射抑制、遗忘等临床症状^[1]。此类抑制属于完全可逆过程, 当药物被人体代谢后, 患

者的神志及各种反射反映可逐步恢复^[12]。随着老龄化的趋势加重, 加上医学水平的进步, 各种疾病的检出率不断增加, 老年疾病也日益增加, 越来越多的老年患者需要在全身麻醉下完成手术^[13]。然而相较于年轻群体, 老年人的体液减少, 全身生理机能退化, 脂肪比例增加, 代谢降低, 药物敏感性下降, 以上诸多原因导致老年患者的全身麻醉方案应慎重选择^[14,15]。此外, 老年人血管壁内脂质沉积, 管壁增厚, 术中易出现血流动力学波动及心律失常^[16]。而且老年患者经常合并多种基础性疾病, 这些生理特点导致老年患者术中麻醉深度不易掌控^[17]。以往一般通过对患者肌松、生命体征等情况进行监测来判断麻醉深度, 主观性较强, 且可能和实际情况存在不同步性^[18]。如今进行麻醉深度监测的技术方法主要有 BIS, BIS 可用 0~100 的数值来反映患者所处的意识状态水平^[19]。现在全身麻醉时常用的 BIS 值多在 0~60 之间, 但 BIS 也存在最佳麻醉深度争议。麻醉深度不够会增加心血管应激反应, 而不必要的麻醉过深, 可能引起低

表 6 术后认知功能对比($\bar{x} \pm s$, 分)
Table 6 Comparison of postoperative cognitive function($\bar{x} \pm s$, scores)

Groups	Time points	MMSE score
Shallow anesthesia group(n=49)	Before operation	27.35± 0.98
	3 d after operation	25.20± 0.57 ^t
	7 d after operation	26.45± 0.36 ^t
Deep anesthesia group(n=49)	Before operation	27.35± 1.17
	3 d after operation	23.35± 0.79 ^{at}
	7 d after operation	25.20± 0.42 ^{at}
Repeated measurement and overall analysis	HF correction factor	0.7348
	Inter group F, P	123.645, 0.000
	In group F, P	400.044, 0.000
	Interaction F, P	37.777, 0.000

Note: compared with before operation, ^t $P < 0.05$. Compared with shallow anesthesia group, ^a $P < 0.05$.

血压和循环功能紊乱及苏醒延迟^[20]。因此本研究把设置两个麻醉深度:30~40 和 45~55,探讨老年胃肠道恶性肿瘤患者全麻围术期更合理的 BIS 值范围。

本次研究结果显示,BIS 值处于 30~40 的患者其血流动力学更平稳,应激反应更低。可能因为较深麻醉抑制动脉压力感受器功能相对减弱,中枢交感神经使迷走神经相对亢进所致,从而有效稳定机体血流动力学^[21,22]。同时 BIS 值 30~40 能降低应激激素 Cor 的水平,更好的抑制机体的应激反应^[23]。而胃肠道肿瘤手术的手术创伤应激导致激活了单核-巨噬细胞,可导致促炎性细胞因子大量释放到血液中,如 TNF- α 、IL-6 等^[24,25]。以往人们往往会认为相对深的麻醉下可以降低炎症因子的分泌^[26],但本次研究结果发现 BIS 值处于 45~55 的患者炎症反应反而更轻。出现这一结果的原因可能与以下几点有关:BIS 值处于 45~55 的患者的术中丙泊酚用量相对更少,从而减轻丙泊酚对循环的抑制作用^[27]。有研究表明丙泊酚可能会引起微循环灌注的不同,从而导致不同的炎症反应^[28]。此外,麻醉水平较深可能会改变患者免疫反应,而促凝反应、免疫抑制等会损害脏器^[29]。除此之外,BIS 值处于 30~40 的患者其认知功能损害相对更严重,苏醒质量相对更差。究其原因,老年患者对药物代谢差,麻醉药比较敏感,过深的麻醉常会延长苏醒时间^[30]。同时过多的麻醉药物蓄积于体内,可能导致患者术后认知功能恢复较慢。而两组不良反应发生率组间对比无差异,可见两种麻醉深度均具有较好的安全性,不会明显增加不良反应发生率。

综上所述,全麻下胃肠道恶性肿瘤患者 BIS 值范围 30~40 可维持更平稳的血流动力学,应激反应低,但是深麻醉认知功能损害相对更大;BIS 值在 45~55 之间时,患者苏醒快,炎症因子更低。此外,有关炎症反应的结论,由于人体内有多种的炎症因子,本研究只选择了 IL-6、TNF- α ,并不能非常准确的反应整体的炎症反应改变,有待后续进一步的深入分析。

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