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肺保护性通气策略对老年患者腹腔镜结直肠癌手术的氧合功能及血浆炎症介质水平的影响*

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摘要 目的:探讨肺保护通气策略对老年患者行腹腔镜结直肠癌根治术肺部氧合功能及血清炎症介质水平的影响。**方法:**选择50例行择期腹腔镜结直肠癌根治术老年患者,ASA 分级(美国麻醉医师协会体格情况评估分级)Ⅰ~Ⅱ级、年龄≥60岁,采用随机数字表法将其分为两组:VCV组和PCV组。在围术期行全麻机械通气中,VCV组采用容量通气模式,潮气量为8 mL/kg,PCV组采用肺保护通气,潮气量为6 mL/kg及5 cmH₂O呼气末正压通气(positive end expiration pressure, PEEP),同时气腹后每30 min给予一次手法肺复张。记录患者气腹前5 min(T₀)、气腹后5 min(T₁)、气腹后30 min(T₂)、气腹后60 min(T₃)、气腹后120 min(T₄)、气腹停止10 min后(T₅)的呼吸力学指标、血流动力学指标于T₀、T₄、离开苏醒室时抽取血气,计算氧合指数(OI)值,于术前一天、T₄、术后一天抽取静脉血,检测血浆CRP、IL-6的值。**结果:**与VCV组比较,PCV组在T₄、T₅时刻气道压降低,T₄、T₅肺顺应性增高($P<0.05$)。两组患者血流动力学指标无明显差异。PCV组在离开苏醒室时氧合指数较高($P<0.05$);PCV组在术后一天时刻IL-6和CRP值较低($P<0.05$)。**结论:**肺保护性通气策略可以提高老年患者肺部氧合功能,减少炎症介质释放,减轻肺损伤。

关键词:肺保护性通气策略;老年;腹腔镜;结直肠;氧合;炎症介质

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Effect of Lung Protective Ventilation Strategy on the Oxygenation and Inflammatory Mediators in the Elderly Patients undergoing Laparoscopic Colorectal Cancer Surgery*

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ABSTRACT Objective: To investigate the effect of lung protective ventilation strategy on pulmonary oxygenation function and serum inflammatory mediators in elderly patients undergoing laparoscopic colorectal cancer surgery. **Methods:** 50 elderly patients undergoing elective laparoscopic colorectal cancer radical operation were classified by ASA (American Society of Anesthesiologists Physical Assessment Grade) I-II and aged over 60 years. They were divided into two groups by random number table: VCV group and PCV group. During mechanical ventilation under general anesthesia, the VCV group adopted the volume-controlled ventilation mode, and the tidal volume was set to 8 mL/kg PCV group adopted the lung protective ventilation strategy. Tidal volume was set to 6 mL/kg and 5 cm H₂O positive end expiration pressure (PEEP), and manual pulmonary resuscitation was given every 30 minutes after pneumoperitoneum. Hemodynamic parameters and respiratory mechanics indexes were recorded at 5 minutes before pneumoperitoneum (T₀), at 5 minutes after pneumoperitoneum (T₁), at 30 minutes after pneumoperitoneum (T₂), at 60 minutes after pneumoperitoneum (T₃) and at 120 minutes after pneumoperitoneum (T₄) stopped at 10 minutes after pneumoperitoneum. Blood gas was extracted at T₀, T₄ and leaving PACU, and oxygenation index (OI) was calculated. Intravenous blood was taken at one day before operation, at T₄ and one day after operation to detect the levels of CRP and IL-6 in plasma. **Results:** Compared with VCV group, PCV group had lower airway pressure at T₄, T₅ and higher lung compliance at T₄, T₅ ($P<0.05$). There was no significant difference in hemodynamic parameters between the two groups. Compared with VCV group, PCV group had a higher oxygenation index when they left PACU ($P<0.05$), IL-6 and CRP in PCV group was lower at one day after operation ($P<0.05$). **Conclusion:** Pulmonary protective ventilation strategy can improve the pulmonary oxygenation function, reduce the release of inflammatory mediators and the occurrence of lung injury in elderly patients.

Key words: Pulmonary protective ventilation strategy; Elderly patients; Laparoscopy; Colorectal; Oxygenation; Inflammatory mediators

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前言

随着人口老龄化,高龄患者的手术量日渐增多,高龄患者由于特殊的生理功能状态易在围术期出现肺不张、肺内感染等术后肺部并发症^[1],术后肺部并发症的发生严重影响了高龄患者的术后恢复及预后,成为其术后死亡的主要原因之一。随着外科手术的发展,微创技术应运而生,腹腔镜具有比开放性手术更好的微创性,但操作困难,对麻醉管理要求高。众多研究证明二氧化碳气腹可能会引起机体一系列生理和病理改变^[2],肺内皮细胞和上皮细胞因受机械刺激产生大量白细胞介素(interleukin, IL)例如 IL-6、IL-8、IL-10 及肿瘤坏死因子 α , C 反应蛋白(CRP)等炎症因子,进而损伤肺组织引起肺部乃至全身性炎症反应^[3]。因此,行腹腔镜手术的高龄患者是术后肺部并发症的高危人群。

肺保护性通气策略现已证实可以改善氧合,减少术后肺部并发症的发生。肺保护策略^[4]主要包括小潮气量、适当的呼气末正压及定时的肺复张策略。但对于老年患者,肺保护性通气策略是否能改善老年人的呼吸功能,减少肺损伤,仍需要进一步研究。本研究采用肺保护性通气策略,通过监测氧合指数(OI)、肺顺应性、CRP、IL-6 等指标,探讨了肺保护性通气策略对老年患者腹腔镜结直肠癌手术患者呼吸功能的影响,以期为临床麻醉过程中合理选择机械通气方式提供参考。

1 资料与方法

1.1 一般资料

本研究经医院伦理委员会批准,患者术前均签署知情同意书。选择我院 2018 年 4 月~2018 年 10 月 50 例 ASA 分级 I~II 级、行择期腹腔镜结直肠癌根治术的老年患者,年龄 60~80 岁, BMI 18.5~25 kg/m², 无心、肝、肾等重要脏器疾病,无基础的肺部疾病,如慢支、哮喘、术前上呼吸道感染、嗜烟史等,术前胸片正常。将所有患者随机分为两组: VCV 组和 PCV 组,每组 25 例。

1.2 麻醉方法

患者入室后开放上肢静脉通路,给予乳酸钠林格氏液。常规监测 ECG、SpO₂、BP 和 HR(监护仪:迈瑞 PM 7000),局麻下行右侧桡动脉穿刺,监测有创动脉压。麻醉诱导:静注依托咪脂乳状注射液(江苏恩华药业股份有限公司)0.2 mg/kg、顺式苯磺酸阿曲库铵(江苏恒瑞医药股份有限公司)0.2 mg/kg、枸橼酸舒芬太尼注射液(宜昌人福药业有限公司)0.3 μ g/kg,待患者自主呼吸消失后,采取小潮气量手法辅助通气,在可视喉镜引导下,插入 7.0 或 7.5 号加强丝导管,两组均采用 8 mL/kg 的潮气量,

呼吸频率为 12~15 次/分,控制 PETCO₂ 为 35~45 mmHg (1 mmHg=0.133 kPa),气腹后 VCV 组继续采用 8 mL/kg 的潮气量, PCV 组采用 6 mL/kg 潮气量, 5 cmH₂O 的 PEEP, 调整呼吸频率为 12~20 次/分,控制 PETCO₂ 为 35~45 mmHg, 每 30 分钟给予一次手法肺复张(lung recruitment maneuver, LRM), 每次控制气道压不超过 30 cmH₂O, 持续时间 30 s。麻醉维持采用静吸复合麻醉,术中持续吸入七氟烷 1.5%~2.5%、静脉输注瑞芬太尼 0.1~0.3 μ g $\cdot$ kg⁻¹ $\cdot$ min⁻¹, MAC 值维持在 1.0~1.3, 术中间断追加舒芬太尼、顺式阿曲库铵。手术结束前 10 min 停药,待患者自主呼吸和气道反射恢复后拔除气管导管,术后送入恢复室(PACU)。

1.3 观察指标

记录气腹前 5 min(T₀)、气腹后 5 min(T₁)、气腹后 30 min(T₂)、气腹后 60 min(T₃)、气腹后 120 min(T₄)、气腹停止 10 min 后(T₅)的呼吸力学指标(潮气量、呼吸频率、气道峰压、气道平台压、呼气末 CO₂、肺顺应性),血流动力学指标(心率、收缩压、舒张压、平均动脉压、血氧饱和度)进行观察;于 T₀、T₄、离开苏醒室时抽血行血气分析(西门子公司,德国),计算氧合指数(OI, OI= 动脉氧分压/吸入氧浓度),并与术前一天、T₄、术后一天抽取静脉血,检测血浆 CRP、IL-6 的值。

1.4 统计学分析

采用 SPSS22.0 统计学软件进行数据分析。计量资料以均数 $\pm$ 标准差($\bar{x}\pm s$)表示,组间比较采用成组 t 检验,计数资料采用 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组基本情况的比较

本研究共纳入 53 例研究对象,其中 1 例因术后出血,2 例因拒绝接受实验而被排除研究,最终共纳入 50 例研究对象。所有患者均行腹腔镜结直肠癌根治术,两组患者性别、年龄、体重等一般情况和麻醉时间、手术时间、气腹时间、入液量、失血量及尿量比较差异无统计学意义($P<0.05$,见表 1)。

2.2 两组不同时间点呼吸力学指标的比较

与 VCV 组比较, PCV 组在 T₄、T₅ 时刻气道压显著降低, T₄、T₅ 肺顺应性明显增高($P<0.05$),见表 2。

2.3 两组不同时间点血流动力学指标的比较

如表 3 所示,两组不同时间点血流动力学指标如心率、收缩压、舒张压、平均动脉压、血氧饱和度比较无明显差异均无统计学意义($P>0.05$)。

2.4 两组不同时间点氧合功能的比较

与 VCV 组比较, PCV 组在离开苏醒室时氧合指数显著增

表 1 两组患者性别、年龄、体重、身高一般情况及麻醉时间、手术时间、气腹时间、入液量、失血量、尿量围术期比较($\bar{x}\pm s$)

Table 1 Comparison of the sex, age, weight, height, anesthesia time, operation time, pneumoperitoneum time, fluid intake, blood loss and urine volume between two groups during perioperative period ($\bar{x}\pm s$)

Groups	Sex	Age	Weight	Height	Anesthesia time	Operation time	Pneumoperitoneum time	Fluid Intake	Blood Loss	Urine Volume
VCV	18/7	67.08 $\pm$ 5.75	65.28 $\pm$ 8.88	167.64 $\pm$ 6.26	269.32 $\pm$ 80.93	250.36 $\pm$ 79.11	189.04 $\pm$ 54.48	2570.00 $\pm$ 712.98	113.20 $\pm$ 83.20	550.00 $\pm$ 358.28
PCV	15/10	66.08 $\pm$ 5.57	64.24 $\pm$ 10.29	166.32 $\pm$ 6.47	220.60 $\pm$ 44.61	205.40 $\pm$ 45.75	153.84 $\pm$ 33.25	2044.00 $\pm$ 316.33	60.00 $\pm$ 20.41	364.00 $\pm$ 172.31

表 2 两组患者潮气量,气道峰压,气道压,呼吸频率,PETCO₂,肺顺应性等呼吸力学情况比较($\bar{x} \pm s$)Table 2 Respiratory mechanics of tidal volume, peak airway pressure, airway pressure, respiratory frequency, PETCO₂ and lung compliance in two groups ($\bar{x} \pm s$)

Groups	Time	Tidal Volume	Peak Airway Pressure	Airway Pressure	Respiratory Frequency	PETCO ₂	Lung Compliance	Temperature
VCV	T ₀	6.49± 0.73	12.56± 2.68	11.44± 2.40	12.00± 0.00	34.88± 4.90	52.80± 12.14	36.22± 0.53
	T ₁	7.38± 1.13	21.28± 4.00	20.84± 3.75	13.60± 1.58	34.49± 4.03	29.28± 7.31	36.12± 0.51
	T ₂	7.33± 1.18	21.60± 3.57	20.80± 3.72	14.00± 1.61	34.68± 3.33	28.65± 7.83	36.04± 0.50
	T ₃	7.44± 1.17	22.12± 3.33	20.60± 3.82	14.12± 1.36	34.92± 3.19	27.53± 5.92	35.90± 0.49
	T ₄	7.36± 1.20	21.64± 4.11	20.56± 4.17	14.04± 1.31	40.14± 6.78	27.94± 5.55	35.81± 0.50
	T ₅	6.76± 1.51	15.00± 3.27	14.32± 3.34	12.68± 2.02	35.68± 4.53	42.92± 9.52	35.74± 0.54
PCV	T ₀	6.22± 0.88	12.12± 2.35	11.60± 2.42	12.00± 0.00	35.12± 2.57	56.01± 8.27	36.12± 0.50
	T ₁	6.26± 0.90	19.96± 3.01	18.08± 2.64	15.28± 1.28	34.18± 7.50	29.18± 6.40	36.09± 0.50
	T ₂	6.19± 0.90	20.08± 2.97	19.16± 3.02	15.64± 1.60	36.72± 1.55	30.93± 3.37	35.98± 0.48
	T ₃	6.33± 0.89	20.80± 2.96	19.28± 2.85	15.60± 3.32	37.72± 1.93	27.20± 5.77	35.84± 0.50
	T ₄	6.41± 0.79	19.84± 3.00	18.48± 2.87 ^a	16.44± 1.96	41.23± 5.74	31.57± 4.61 ^b	35.75± 0.49
	T ₅	5.83± 1.12	13.20± 2.66	11.48± 2.35 ^a	13.08± 1.61	37.10± 3.39	50.87± 9.99 ^b	35.67± 0.49

Note: Compared with VCV group, the airway pressure in PCV group decreased at T₄ (t = 0.046) and T₅ (t = 0.001), $P < 0.05$. Compared with VCV group, the lung compliance in PCV group increased at T₄ (t = 0.015) and T₅ (t = 0.006), $P < 0.05$.

表 3 两组患者不同时点心率、收缩压、舒张压、平均动脉压、血氧饱和度等血流动力学指标比较($\bar{x} \pm s$)Table 3 Comparison of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, oxygen saturation and at different time points between the two groups ($\bar{x} \pm s$)

Groups	Time	HR	SBP	MAP	DBP	SPO ₂
VCV	T ₀	58.76± 8.08	118.36± 19.00	68.64± 8.11	85.16± 13.75	99.12± 1.01
	T ₁	66.60± 11.17	134.68± 18.30	87.60± 14.17	99.32± 15.12	99.32± 0.69
	T ₂	67.76± 11.94	132.80± 16.93	80.64± 12.56	101.84± 14.06	99.04± 0.98
	T ₃	61.56± 8.33	125.76± 15.88	78.68± 11.97	97.56± 13.12	99.12± 1.09
	T ₄	62.00± 8.32	126.64± 14.76	74.88± 9.78	95.16± 11.21	99.28± 0.98
	T ₅	64.68± 11.61	127.08± 13.62	72.00± 13.71	91.60± 12.69	99.44± 0.82
PCV	T ₀	61.96± 11.99	113.16± 20.58	71.00± 16.82	84.88± 14.77	99.20± 1.08
	T ₁	67.12± 13.57	137.92± 20.44	87.36± 16.52	104.76± 13.03	99.28± 0.89
	T ₂	66.52± 10.62	126.00± 17.25	79.96± 15.98	96.12± 15.33	99.00± 0.91
	T ₃	66.08± 9.18	125.28± 15.86	77.12± 13.30	94.08± 13.72	98.84± 0.85
	T ₄	65.76± 11.81	129.24± 12.91	75.12± 8.45	92.80± 11.60	99.08± 0.76
	T ₅	63.20± 10.43	121.20± 19.90	68.00± 15.47	85.04± 18.00	99.12± 0.88

高($P < 0.05$), 见表 4。

2.5 两组不同时点血浆 IL-6 和 CRP 水平的比较

与 VCV 组比较, PCV 组在术后一天时刻血浆 IL-6、CRP 水平均明显降低($P < 0.05$), 见表 5。

3 讨论

近些年来, 腹腔镜手术飞速发展, 其具有损伤小、出血少、快速康复、腹部切口美观等诸多优点, 但也给患者带来许多不良影响, 如气腹。CO₂ 气腹可以引起 CO₂ 蓄积进而导致酸中毒, 血压和心率上升, 形成皮下气肿, 腹腔压力增加, 膈肌上抬导致

肺底部肺泡萎陷、不张^[5,6]。此外, CO₂ 入血可导致气栓等等。腹腔镜手术的危险因素包括 Trendelenburg 体位^[7]抑制患者循环功能和呼吸指标; 长时间人工气腹的建立, 引起腹腔脏器缺血性损伤, 如肾功能不全等; 肺内通气血流比失调, 影响患者呼吸循环功能^[8], 容易引起肺不张发生。高龄患者是术后肺部并发症的高危人群之一, 这种风险在接受腹腔镜手术时尤为明显, 肺部并发症的发生严重影响老年人的预后^[9]。

在全麻过程中, 我们以前多采用 10~15 mL/kg 的潮气量代偿气腹所带来的 CO₂ 蓄积, 最近的研究表明常规的机械通气模式不能有效扩张小气道的肺组织, 改善氧合功能的能力相对有

表 4 两组患者不同时点氧分压、PETCO₂、氧合指数等氧合情况比较($\bar{x} \pm s$)Table 4 Comparison of the partial pressure of oxygen, PETCO₂ and oxygenation index at different time points between two groups ($\bar{x} \pm s$)

Groups	Time	Partial Pressure Of Oxygen	PETCO ₂	Oxygenation Index
VCV	T ₀	192.69± 42.09	35.28± 4.96	411.24± 103.07
	T ₄	165.71± 39.19	39.50± 9.81	347.99± 90.01
	Leaving the recovery room	70.27± 17.26	41.71± 3.89	320.50± 34.43
PCV	T ₀	196.74± 44.00	35.95± 3.54	399.01± 88.79
	T ₄	199.70± 34.02	43.82± 5.61	403.38± 73.83
	Leaving the recovery room	74.11± 10.03	39.42± 3.47	352.86± 47.80

Note: Compared with VCV group, PCV group had higher oxygenation index ($t = 0.021$) when it left the recovery room, $P < 0.05$.

表 5 两组患者不同时点血浆 IL-6、CRP 水平的比较($\bar{x} \pm s$)Table 5 Comparison of the plasma IL-6 and CRP levels at different time points between two groups ($\bar{x} \pm s$)

Groups	Time	IL-6	CRP
VCV	At 1 day before operation	8.11± 6.92	4.59± 3.77
	T ₄	14.32± 7.91	4.67± 4.23
	At 1 day after operation	13.53± 4.96	47.56± 24.58
PCV	At 1 day before operation	7.38± 6.86	6.47± 5.58
	T ₄	15.76± 5.58	5.06± 4.23
	At 1 day after operation	10.07± 3.26 ^e	27.74± 13.03 ^f

Note: e Compared with VCV group, the value of IL-6 in PCV group was lower at one day after operation ($t = 0.005$), $P < 0.05$. f Compared with VCV group, the value of CRP in PCV group was lower at one day after operation ($t = 0.001$), $P < 0.05$.

限,同时会肺泡过度膨胀,甚至导致呼吸机相关性肺损伤^[10,11]。虽然在麻醉中使用容量控制通气模式可以保证分钟通气量,但恒定的气流量可能会导致更高的峰值吸气压力,增加气压伤的发生率,造成肺气体分布不平衡^[12]。呼吸机相关性肺损伤的机制是由于大量炎症因子释放导致的肺功能损伤。动物实验显示大潮气量的机械通气可刺激细胞因子产生,释放炎症物质(如 CRP、IL-6 等)和炎性细胞聚集^[13,14],导致急性肺损伤^[15,16]。

近年来,学者们在临床试验中逐渐摸索出了适合腹腔镜手术的通气模式即肺保护性肺通气策略,而其较早应用于 ARDS 的临床治疗,核心环节是重新开放塌陷的肺泡。目前,临床多采用小潮气量进行机械通气以限制潮气量和降低气道压,并且在呼气末加用适当的 PEEP,使肺泡保持开放^[17]及萎陷的肺泡复张,以及定时给予肺复张^[18]。研究表明肺保护性通气策略可以提高腹部、妇科手术或者肥胖患者的氧合功能,减少术后肺部并发症的发生^[19],但对于老年患者行腹腔镜手术时使用肺保护性通气策略能否改善氧合功能,减少肺部并发症的发生仍有待研究。Gu 等学者^[20]在 Meta 分析中发现手术期间接受小潮气量通气的患者发生围手术期肺损伤和术后肺部感染的风险比接受大潮气量通气的患者低。Serpa 等^[21]发现采用 6 mL/kg 的小潮气量复合 5 cmH₂O 呼气末正压能够有效改善高龄患者术后低氧血症,减少术后肺部并发症的发生同时对高龄患者术中的血流动力学没有明显影响。PEEP 值的选择同样是关键,过高的 PEEP 可增加胸腔内压力,引起术中血流动力学的不稳定^[22],不但不能进一步增加肺泡容积,改善通气血流比例,反而会加重死腔通气比降低通气效率更进一步减少肺组织的血流灌注,导致通气血流不匹配,长时间使用压力较高的 PEEP 导致肺内气

体滞留,引发肺组织的炎症反应发生^[23]。因此,如果需在围术期行机械通气时应避免使用过高的 PEEP 通气,对于最佳呼气末正压的设定两项回顾性研究认为肺复张策略后给予 5 cmH₂O 的呼气末正压是可以减少系统炎症反应和改善通气血流比值失衡、减少肺部并发症的最佳方法^[24-26]。小潮气量与低水平呼气末正压更适合于高龄患者的特殊生理状态,加强气体交换、改善氧合^[27]。Girgis^[28]等研究发现短时间的机械通气中使用肺复张可以充分加强 PEEP 对肺组织通气的有利作用。也有多项研究显示 PEEP 联合肺复张可以提高健康肺组织的顺应性,明显减少死腔样通气增加肺的功能残气量,减少肺部炎症,而这些效应比在肺复张前使用 PEEP 更明显^[29]。

本研究主要探讨了肺保护性通气策略对于行腹腔镜手术老年患者的肺部功能及炎症因子的影响,以为老年患者术中麻醉管理提供参考依据。实验组采用 6 mL/kg 的潮气量+5 cmH₂O PEEP+ 肺复张的肺保护性通气策略,而对照组采用传统的 8 mL/kg 潮气量,不给予 PEEP 及肺复张。结果显示与 VCV 组比较,PCV 组在 T₄、T₅ 时刻气道压降低,T₄、T₅ 肺顺应性增高。与 VCV 组比较,PCV 组在离开苏醒室时氧合指数较高。肺顺应性定义为在一定单位的跨肺压下肺容量的改变能力,主要反映了肺扩张的难易程度以及肺组织的弹性能力,是衡量肺泡通气功能和肺功能损害的主要参数^[30]。在我们的研究中,腹腔镜建立气腹后,两组患者的肺顺应性都出现下降,但在 T₄、T₅ 时刻,PCV 组肺顺应性较 VCV 组高,提示肺保护性通气策略可以改善老年患者的肺部功能。氧合指数可以反映肺不张及肺内分流的存在,我们观察到在离开苏醒室时 PCV 组的氧合指数高于 VCV 组,表明肺保护性通气策略同时可以提高老年患者的氧

合功能。在术后一天时,PCV 组血浆 CRP 和 IL-6 水平低于 VCV 组,可见肺保护性通气策略可以减少肺部炎症介质的产生,从而减少肺功能损伤,保护肺功能。虽然 PCV 组较 VCV 组呼吸频率和呼吸末 CO₂ 的数值有所增高,但并不对患者的循环功能产生影响,因此可以安全应用在临床工作中。

综上所述,保护性肺通气策略可以改善行腹腔镜结直肠手术老年患者的肺功能,表现为气道压下降、肺顺应性提高、氧合指数明显改善,同时减少炎症介质的产生,肺保护策略可以作为老年患者行腹部微创手术时安全的术中通气策略,但其能否改善老年患者术后肺部并发症的发生仍需进一步研究证实。

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