doi: 10.13241/j.cnki.pmb.2019.11.036

允许性高碳酸血症在腹腔镜直肠癌手术中的应用及对循环的影响 *

王 磊[1] 吴 婧[1] 杨丽娜[1] 张 立[1] 卫 红[2]

（1 沧州中心医院麻醉一科 河北 沧州 061001；2 河北大学附属医院麻醉科 河北 保定 071030）

摘要 目的：研究允许性高碳酸血症在腹腔镜直肠癌手术中的应用效果、最佳适宜范围及对患者循环功能的影响。**方法：**选取沧州市中心医院拟择期行腹腔镜直肠癌手术的患者 90 例，随机分为试验 1 组、2 组和对照组 3 组，每组 30 例。试验 1 组血二氧化碳分压（partial pressure of carbon dioxide，$PaCO_2$）维持在 56~65 mmHg，试验 2 组 $PaCO_2$ 维持在 46~55 mmHg，对照组 $PaCO_2$ 维持在 35~45 mmHg。观察并比较三组患者气腹时间、机械通气时间、手术时间、拔管时间、苏醒时间，气腹前 10 min(T_1)、气腹后 1 h(T_2)、气腹后 2 h(T_3)、放气后 15 min(T_4)时间点的平均动脉压、心率、气道峰压，计算动态肺顺应性、氧合指数，记录皮下气肿、呕吐、烦躁及术后认知功能障碍等并发症的发生情况。**结果：**三组患者手术时间、气腹时间、机械通气时间、拔管时间和苏醒时间比较差异无统计学意义(P>0.05)。与对照组相比，试验组 T_2、T_3 时心率（heart rate，HR）、血氧分压（partial pressure of oxygen，PaO_2）、肺动态顺应性（lung dynamic compliance，Cdyn）均明显升高，P_{max} 明显下降(P<0.05)；与 T_1 相比，试验组 T_2、T_3 时 HR、气道峰压（P_{max}）、PaO_2 均升高，Cdyn 下降(P<0.05)；与试验 2 组比较，试验 1 组 HR、P_{max} 明显更低，PaO_2、Cdyn 明显更高(P<0.05)，但三组氧合指数（oxy- genation Index，OI）比较差异无统计学意义(P>0.05)。与对照组相比，试验组 T_2、T_3 时动脉血二氧化碳分压（partial pressure of car- bon dioxide，$PaCO_2$）、Qs/Qt 均升高，氢离子浓度指数（hydrogen ion concentration，pH）、平均动脉压（mean arterial pressure，MAP）下降；与 T_1 相比，试验组 T_2、T_3 时 $PaCO_2$、Qs/Qt 均升高，pH、MAP 下降；与试验 2 组比较，试验 1 组 $PaCO_2$、$PaCO_2$ 明显更低，pH 明显更高(P<0.05)，但三组 MAP 比较差异无统计学意义(P>0.05)。手术开始 30 min 和 1 h，试验组中心静脉压（central venous pressure，CVP）、心输出量（cardiac output，CO）以及心脏指数（cardiac index，CI）较对照组更低，而试验 1 组较试验 2 组明显更低(P<0.05)。三组并发症的改善情况比较差异无统计学意义(x^2=0.1973，P=0.9954)。治疗后，试验组 MMSE 评分较治疗前明显降低，且试验组明显高于对照组，而试验 1 组又显著高于试验 2 组(P<0.05)。**结论：**允许性高碳酸血症在长时间腹腔镜直肠癌手术中在保障氧合同时降低气道压改善肺的顺应性，可一定程度上减少术后认知功能障碍的发生，有一定的脑保护作用。

关键词：允许性高碳酸血症；腹腔镜；直肠癌手术；循环功能

中图分类号：R735.37 **文献标识码：**A **文章编号：**1673-6273(2019)11-2167-05

Applications and Effects allow Hypercapnia in Laparoscopic Surgery for Colorectal Cancer Circulatory Function*

WANG Lei[1], WU Jing[1], YANG Li-na[1], ZHANG Li[1], WEI Hong[2]

(1 Department of Anesthesiology, Cangzhou Central Hospital, Cangzhou, Hebei, 061001, China;

2 Department of Anesthesiology, Affiliated Hospital of Hebei University, Baoding, Hebei, 071030, China)

ABSTRACT Objective: To study the effect of permissible hypercapnia in laparoscopic rectal cancer surgery, the optimal range of application and the effect on the patient's circulatory function. **Methods:** 90 cases with rectal cancer were researched to undergoing laparoscopic surgery according to the random number table they were divided into Test 1 group, 2 groups and control group, 30 cases in each group. The $PaCO_2$ of the test group 1 was maintained at 56-65 mmHg, the $PaCO_2$ of the test group 2 was maintained at 46-55 mmHg, and the $PaCO_2$ of the control group was maintained at 35-45 mmHg. They were compared with Pneumoperitoneum time, mechanical ventilation time, operation time, extubation time, wake-up time, mean arterial pressure, heart rate, and airway pressure at 10 minutes before pneumoperitoneum (T_1), 1 hour after pneumoperitoneum (T_2), 2 h after pneumoperitoneum (T_3), and 15 min after deflation (T_4). dynamic lung compliance, oxygenation index, recording of complications such as subcutaneous emphysema, vomiting, irritability and postoperative cognitive impairment. **Results:** There was no significant difference in the operation time, pneumoperitoneum time, mechanical ventilation time, extubation time and recovery time between the three groups (P>0.05). Compared with the control group, HR, PaO_2, and Cdyn in the test group significantly increased at T_2 and T_3, and P_{max} decreased significantly; compared with T_1, HR, P_{max}, and PaO_2 in the test group increased at T_2 and T_3, and Cdyn decreased; Compared with the experimental group 2, the HR and P_{max} of the experimental group 1 were significantly lower, PaO_2 and Cdyn were significantly higher, and the difference between the three groups was significant (P<0.05), but there was no significant difference in the OI between the three groups (P>0.05). Compared with the control

* 基金项目：沧州市重点研发计划指导项目（172302086）；河北省科技支撑计划项目(122077179D)

作者简介：王磊(1983-)，男，硕士，主治医师，研究方向：临床麻醉方向，E-mail：chenqihanhz@163.com，电话：15731701656

(收稿日期：2018-12-22 接受日期：2019-01-18)

group, the $PaCO_2$, Qs/Qt of the test group increased at T_2 and T_3, and the pH and MAP decreased. Compared with T_1, the $PaCO_2$, Qs/Qt of the test group increased at T_2 and T_3, and the pH and MAP decreased. Compared with the experimental group 2, the Pa- CO_2 and $PaCO_2$ in the experimental group 1 were significantly lower and the pH was significantly higher (P<0.05), but there was no sig- nificant difference in the MAP between the three groups (P>0.05). There was no significant difference in preoperative CO, CVP, and CI between the three groups (P>0.05). At 30 min and 1 h after surgery, CO, CVP, and CI were lower in the experimental group than in the control group, while the experimental group 1 was significantly more lower than the experimental group 2 (P<0.05). There was no signifi- cant difference in the improvement of complications between the three groups (x^2=0.1973, P=0.9954); the MMSE score after treatment was significantly lower than before treatment, and the test group was significantly higher than the control group, and the test group 1 was significantly higher than the test 2 group (P<0.05). **Conclusion:** Permissive hypercapnia protects lung compliance by reducing airway pres- sure during oxygen laparoscopic surgery for prolonged laparoscopic rectal cancer surgery, and can reduce the occurrence of postoperative cognitive impairment to a certain extent, it has a certain degree of brain protection.

Key words: Permissive hypercapnia; laparoscopic; rectal cancer surgery; circulatory function

Chinese Library Classification(CLC): R735.37 Document code: A

Article ID: 1673-6273(2019)11-2167-05

前言

直肠癌是一种常见的消化道肿瘤,好发于中年人群,近年来年轻人直肠癌的发病率也有上升的趋势[1,2]。因直肠解剖关系较为复杂且深入盆腔,传统手术治疗存在不彻底、术后复发率高等特点[3,4]。随着腹腔镜技术的发展,腹腔镜直肠癌手术已经取代了传统开腹手术,但由于腹腔镜术中建立人工气腹需要采用 CO_2 灌注,由此会导致患者大量吸收 CO_2,从而引发患者体内 $PaCO_2$ 水平显著升高,最终引起高碳酸血症的发生[5,6]。

临床治疗中维持 $PaCO_2$ 水平主要采用增大呼吸频率和潮气量的方法,但该方法会造成肺损伤和气道压增高[7,8]。相关研究结果显示允许性高碳酸血症作为一种保护性通气策略,可有效避免气道压增高和肺损伤,已经广泛应用于呼吸系统需要机械通气的疾病[9,10]。同时,该方法在一些妇科短小手术中也取得较大成功[11,12]。目前,国内外关于允许性高碳酸血症在腹腔镜直肠癌这种时间较长的手术中是否可行,其最佳适宜范围是多少的报道较少。因此,本研究主要探讨了允许性高碳酸血症用于腹腔镜直肠癌手术患者的安全性、有效性以及对循环的影响。现将结果报道如下。

1 资料与方法

1.1 临床资料

选取我院 2018 年 3 月至 2019 年 3 月收治的 90 例拟择期行腹腔镜直肠癌手术的患者,按照动脉血二氧化碳分压随机分为试验 1 组、2 组和对照组 3 组,每组各 30 例。其中,试验 1 组 $PaCO_2$ 维持在 56~65 mmHg, 试验 2 组 $PaCO_2$ 维持在 46~55 mmHg,对照组 $PaCO_2$ 维持在 35~45 mmHg。试验 1 组患者中,男 18 例,女 12 例,年龄 45~75 岁,平均(58.4± 3.9)岁。试验 2 组患者中,男 20 例,女 10 例,年龄 46~73 岁,平均(57.2± 4.1)岁。对照组患者中, 男 21 例, 女 9 例, 年龄 47~74 岁, 平均(57.6± 4.3)岁。

1.2 麻醉方法

所有患者均行全麻, 于术前半小时肌注 1 mg 盐酸戊乙奎醚注射液(生产厂商:成都力思特制药股份有限公司,生产批号:20160912,规格:1 mL:1 mg× 6 支 / 盒)。进入手术室后,开放静脉通路,监测心电图、平均动脉压、气道压。行气管插管后接入麻醉机,潮气量为 6~10 mL/kg,吸氧浓度(FiO_2)100%,呼吸频率为每分钟 10~20 次,气道峰压(P_{max})在 35 cm H_2O 以下,呼气末正压(PEEP)为 4~8 cm H_2O。CO_2 气腹后,调整呼吸参数,试验 1 组 $PaCO_2$ 维持在 56~65 mmHg, 试验 2 组 $PaCO_2$ 维持在 46~55 mmHg,对照组 $PaCO_2$ 维持在 35~45 mmHg,pH 值在7.20 以上。将麻醉深度维持在 37~56 之间,行桡动脉穿刺置管备用。

1.3 观察指标

观察记录三组患者气腹时间、机械通气时间、手术时间、拔管时间、苏醒时间,气腹前 10 min(T_1)、气腹后 1 h(T_2)、气腹后 2 h(T_3)、放气后 15 min(T_4)时间点的平均动脉压(MAP)、心率(HR)、气道峰压(P_{max}),计算动态肺顺应性(Cdyn)[13]、氧合指数(OI)[14],观察并记录手术前、手术开始 30 min 和手术开始 1h 后中心静脉压(CVP)、心输出量(CO)、心脏指数(CI),记录皮下气肿、呕吐、烦躁及术后认知功能障碍等并发症发生情况。

认知功能评价标:采用 MMSE 量表[15]对患者认知功能进行评估。

1.4 统计学分析

应用 SPSS11.5 统计软件对本次实验数据进行处理, 计量资料($\bar{x}$± s)表示,两样本均数比较采用 t 检验,计数资料以率(%)表示,两组间比较应用 x_2 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 三组患者手术情况的比较

三组患者机械通气时间、手术时间、拔管时间、气腹时间和苏醒时间比较均无明显统计学差异(P>0.05),见表 1。

2.2 三组患者术中血流动力学和呼吸参数比较

与对照组相比,试验组 T_2、T3 时 HR、PaO_2、Cdyn 均明显升高(P<0.05),P_{max} 明显下降(P<0.05);与 T1 相比,试验组 T_2、T_3 时 HR、P_{max}、PaO_2 均升高(P<0.05),Cdyn 下降(P<0.05);与试验 2 组比较,试验 1 组 HR、P_{max} 明显更低(P<0.05),PaO_2、Cdyn 明显更高(P<0.05)。三组 OI 比较差异无统计学意义(P>0.05),见表 2。

表 1 三组患者手术情况的比较($\bar{x}\pm s$)

Table 1 Comparison of the surgical conditions among three groups of patients($\bar{x}\pm s$, min)

Groups	n	Operation time	Pneumoperitoneum time	Mechanical ventilation time	Extubation time	Wake up time
Test group 1	30	176.32± 23.64	69.35± 9.89	108.89± 10.59	35.56± 17.63	27.46± 15.92
Test group 2	30	175.14± 21.37	68.91± 9.37	107.98± 11.03	35.87± 17.48	27.57± 15.77
Control group	30	179.29± 24.15	67.99± 9.52	109.78± 10.95	31.39± 13.75	25.53± 11.38

表 2 三组患者术中血流动力学和呼吸参数比较($\bar{x}\pm s$)

Table 2 Comparison of the intraoperative hemodynamics and respiratory parameters among three groups of patients($\bar{x}\pm s$)

Index	Groups	T_1	T_2	T_3	T_4
HR(次 /min)	Test group 1	74.23± 11.89	78.65± 11.49△*▲	79.38± 12.17△*▲	77.35± 11.34
	Test group 2	74.19± 12.05	81.62± 12.38△*	82.46± 12.77△*	77.34± 11.65
	Control group	73.13± 12.12	75.07± 12.83	74.19± 12.54	75.16± 10.39
$P_{max}(cmH_2O)$	Test group 1	16.62± 3.12	25.67± 3.54△*▲	26.49± 3.77△*▲	16.41± 3.32
	Test group 2	16.63± 3.25	28.27± 3.22△*	29.18± 3.16△*	17.27± 3.39
	Control group	16.13± 3.08	31.25± 3.16△	31.98± 3.29△	17.37± 3.41
$PaO_2(mmHg)$	Test group 1	79.24± 10.28	87.24± 11.18△*▲	86.87± 13.06△*▲	80.28± 11.95
	Test group 2	79.19± 10.26	83.14± 11.21△*	84.46± 13.01△*	80.13± 11.68
	Control group	78.55± 10.73	77.89± 11.17	76.98± 12.36	79.28± 12.13
$Cdyn(mL/cmH_2O)$	Test group 1	45.11± 5.28	37.27± 5.84△*▲	38.19± 5.98△*▲	43.19± 7.14
	Test group 2	44.35± 5.66	31.15± 5.86△*	32.27± 5.89△*	41.38± 7.12
	Control group	45.02± 5.71	29.45± 5.68△	28.34± 5.58△	42.14± 7.18
OI(mmHg)	Test group 1	418.39± 66.92	398.28± 65.68△	381.38± 66.96△	413.28± 63.71
	Test group 2	419.28± 66.18	393.78± 65.89△	378.24± 66.89△	411.35± 63.54
	Control group	413.76± 66.93	388.65± 65.13△	371.28± 66.91△	406.86± 63.38

Note: Compared with the control group, *P<0.05, Compared with T_1, △ P<0.05, Compared with the Test group 2, ▲P<0.05.

2.3 三组患者动脉血气和 Qs/Qt 比较

与对照组相比，试验组 T_2、T_3 时 $PaCO_2$、Qs/Qt 均升高，pH、MAP 下降；与 T1 相比，试验组 T_2、T_3 时 $PaCO_2$、Qs/Qt 均升高，pH、MAP 下降；与试验 2 组比较，试验 1 组 $PaCO_2$、$PaCO_2$ 明显更低，pH 明显更高，三组比较差异显著(P<0.05)，但三组 MAP 比较差异无统计学意义(P>0.05)，见表 3。

表 3 三组患者动脉血气和 Qs/Qt 比较($\bar{x}\pm s$)

Table 3 Comparison of the arterial blood gas and Qs/Qt among three groups of patients($\bar{x}\pm s$)

Index	Groups	T_1	T_2	T_3	T_4
pH	Test group 1	7.41± 0.06	7.35± 0.05△*▲	7.33± 0.05△*▲	7.40± 0.06
	Test group 2	7.42± 0.05	7.30± 0.06△*	7.28± 0.06△*	7.38± 0.05
	Control group	7.41± 0.05	7.39± 0.06	7.38± 0.07	7.39± 0.06
MAP(mmHg)	Test group 1	416.39± 66.94	393.29± 65.39	369.37± 71.37*	414.28± 63.71
	Test group 2	417.37± 66.89	388.93± 69.12	365.39± 71.84*	413.19± 63.49
	Control group	413.74± 66.91	398.62± 65.32	371.23± 66.93	406.87± 63.72
$PaCO_2(mmHg)$	Test group 1	40.49± 3.45	51.38± 3.72△*▲	54.39± 2.81△*▲	42.17± 3.01
	Test group 2	41.38± 3.28	57.73± 6.38△*	60.28± 2.78△**	45.28± 3.08
	Control group	40.71± 3.59	40.76± 3.61	41.79± 2.98	40.57± 3.07
Qs/Qt	Test group 1	13.83± 3.02	15.17± 3.19△*▲	17.37± 3.86△*▲	13.93± 2.89
	Test group 2	13.72± 3.04	16.93± 3.48△*	18.09± 3.96△*	14.04± 2.99
	Control group	13.55± 3.01	14.55± 3.38	14.85± 3.59	14.32± 3.01

Note: Compared with the control group, *P<0.05, Compared with T_1, △ P<0.05, Compared with the Test group 2, ▲P<0.05.

2.4 三组患者循环功能的比较

三组患者术前 CO、CVP 以及 CI 比较差异无统计学意义(P>0.05);手术开始 30 min 和 1 h,试验组 CO、CVP 以及 CI 较对照组更低,而试验 1 组较试验 2 组明显更低(P<0.05),见表 4。

表 4 三组患者循环功能指标比较($\bar{x}\pm s$)

Table 4 Comparison of the circulatory function indexes among the three groups($\bar{x}\pm s$)

Index	Groups	Before surgery	At 30min after surgery	At 1h after surgery
CO(L/min)	Test group 1	4.19± 1.29	5.76± 1.32△ *▲	4.51± 1.34△ *▲
	Test group 2	4.18± 1.31	5.85± 1.33△ *	4.66± 1.31△ *
	Control group	4.18± 1.26	6.29± 2.02△	7.67± 1.64△
CVP(cmH_2)	Test group 1	8.35± 2.14	10.42± 3.12△ *▲	9.78± 3.18△ *▲
	Test group 2	8.33± 2.12	10.83± 3.15△ *	10.12± 3.17△ *
	Control group	8.38± 2.13	11.57± 3.41△	13.97± 3.81△
CI[L/(min·m^2)]	Test group 1	3.07± 1.14	3.66± 1.47△ *▲	3.24± 1.50△ *▲
	Test group 2	3.03± 1.13	3.79± 1.55△ *	3.75± 1.37△ *
	Control group	3.04± 1.16	3.92± 1.77△	4.55± 1.58△

Note: Compared with the control group, *P<0.05, Compared with before surgery, △ P<0.05, Compared with the Test group 2, ▲P<0.05.

2.5 三组患者并发症发生情况及手术前后认知功能评分变化的比较

治疗后，实验 1 组并发症发生率为 23.33%(7/30)，试验 2 组并发生发生率为 46.67%(14/30)，对照组并发生发生率为 66.67%(20/30),三组比较差异无统计学意义(x^2=0.1973,P=0.9954);三组患者治疗前 MMSE 评分比较无统计学意义(P>0.05),但治疗后,三组 MMSE 评分均较治疗前明显降低,且试验组 MMSE 评分明显高于对照组,而试验 1 组 MMSE 评分显著高于试验 2 组(P<0.05),见表 5。

表 5 三组患者并发症发生情况及手术前后认知功能评分变化的比较

Table 5 Comparison of the incidence of complications and changes of cognitive function scores before and after surgery among three groups of patients

Groups	n	Subcutaneous emphysema[n(%)]	Vomiting[n(%)]	Irritability[n(%)]	MMSE score(point)	
					Before treatment	After treatment
Test group 1	30	2(6.67)	2(6.67)	3(10.00)	24.98± 5.89	19.74± 4.17△ *▲
Test group 2	30	4(13.33)	5(16.67)	5(16.67)	23.33± 5.17	16.78± 4.23△ *
Control group	30	5(16.67)	7(23.33)	8(26.67)	23.02± 5.01	14.49± 5.15△

Note: Compared with the control group, *P<0.05, Compared with before treatment, △ P<0.05, Compared with the Test group 2, ▲P<0.05.

3 讨论

目前,临床上腹腔镜直肠癌手术仍然以增大潮气量和气道压的方法维持 $PaCO_2$ 在正常水平的全身麻醉为主,但临床上提出将允许性高碳酸血症用于腹腔镜直肠癌手术中,这为临床麻醉应用提供了一种新的选择[16,17]。2016 年,刘晶[18]等人报道妇科腹腔镜手术肥胖患者采用允许性高碳酸血症在降低气道压的同时保障了氧合,对改善肺顺应性是安全可行的。2016 年,曲良超[19]等研究发现允许性高碳酸血症对腹腔镜肾部分切除术的患者是安全的,对肾功能无明显影响。允许性高碳酸血症可显著降低高容量和高气道压造成的肺损伤，且有学者认为[20,21]允许性高碳酸血症对患者脑、肝脏、肺、心肌等重要脏器具有保护作用。

本研究按照 $PaCO_2$ 水平不同将 90 例择期行腹腔镜直肠癌手术的患者分为三组,通过比较三组不同时间点以及组间各指标差异以分析二氧化碳分压的最佳适宜范围。当分别与对照组和 T1 时间点比较时，发现其 T2、T3 时 HR 和 MAP 水平均出现升高,这可能与在 CO_2 气腹时需要保持 $PaCO_2$ 正常水平而提高 P_{max} 的高水平通气，从而减少回心血量的循环抑制有关[22,23]。此外,与 T1 时间点比较时,P_{max} 升高,Cdyn 下降,其原因可能为人工体位和气腹改变导致气道压升高。但最终结果显示试验组 P_{max} 均下降,Cdyn 均上升且试验 1 组各指标数据明显优于试验 2 组,说明二氧化碳分压的最佳适宜范围为 56~65 mmHg。大量研究表明引起机械通气相关性肺损伤的主要危险因素有高 P_{max} 和大潮气量。而本研究结果则说明允许性高碳酸血症能有效降低气道压和潮气量,改善肺顺应性,减轻肺损伤。

此外,既往研究结果表明允许性高碳酸血症可有效改善组织氧合。本研究中,与 T_1 时间点比较,其 T_3 时间点 PaO_2 和 OI 均出现下降,与上述研究结果一致。另外,试验 1 组 CO、CVP 以及 CI 明显优于试验 2 组和对照组，表明其可有效优化循环功能,其原因可能是提高患者手术体位适应度,避免术中摆放不当挤压循环通路,从而改善循环功能。

综上,允许性高碳酸血症在长时间腹腔镜直肠癌手术中肺通气保护策略在降低气道压改善肺顺应性的同时,不增加心脑血管的并发症,还能对脑组织有一定的保护作用,可缩短住院时间,降低住院费用,值得临床推广。

参 考 文 献(References)

[1] Dwyer RH, Scheidt MJ, Marshall JS, et al. Safety and efficacy of syn-

chronous robotic surgery for colorectal cancer with liver metas- tases [J]. Journal of robotic surgery, 2018, 12(4): 603-606

[2] Schaap DP, Ogura A, Nederend J, et al. Prognostic implications of MRI-detected lateral nodal disease and extramural vascular invasion in rectal cancer [J]. The British journal of surgery, 2018, 105(13): 1844-1852

[3] Zhang XY, Wang S, Li XT, et al. MRI of Extramural Venous Invasion in Locally Advanced Rectal Cancer: Relationship to Tumor Recurrence and Overall Survival[J]. Radiology, 2018, 289(3): 677-685

[4] Kondo A, Tsukada Y, Kojima M, et al. Effect of preoperative chemotherapy on distal spread of low rectal cancer located close to the anus [J]. International journal of colorectal disease, 2018, 33(12): 1685-1693

[5] Prete FP, Pezzolla A, Prete F, et al. Robotic Versus Laparoscopic Minimally Invasive Surgery for Rectal Cancer: A Systematic Review and Meta-analysis of Randomized Controlled Trials[J]. Annals of surgery, 2018, 267(6): 1034-1046

[6] Nonaka T, Fukuda A, Maekawa K, et al. The Feasibility and Efficacy of Laparoscopic Extended Total Mesorectal Excision for Locally Advanced Lower Rectal Cancer[J]. In vivo (Athens, Greece), 2018, 32(3): 643-648

[7] Cheung HYC, Dent OF, Richardson GL, et al. Pathological outcomes in rectal cancer following laparoscopic surgery [J]. Asia-Pacific journal of clinical oncology, 2018, 14(2): e175-e180

[8] Chen TC, Liang JT. Robotic D4 lymphadenectomy for the treatment of rectal cancer with metastasis to N3-N4 lymph nodes - a video vignette [J]. Colorectal disease: the official journal of the Association of Coloproctology of Great Britain and Ireland, 2018, 20(4): 352-353

[9] Rabe H, Fernandez-Alvarez JR. Permissive hypercapnia in preterm infants: the discussion continues [J]. The Lancet Respiratory medicine, 2015, 3(7): 499-501

[10] Thome UH, Genzel-Boroviczeny O, Bohnhorst B, et al. Permissive hypercapnia in extremely low birthweight infants (PHELBI): a randomised controlled multicentre trial [J]. The Lancet. Respiratory medicine, 2015, 3(7): 534-543

[11] Nayak S, Jindal A. Permissive hypercapnia: Is there any upper limit [J]. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine, 2015, 19(1): 56-57

[12] Victor S, McKeering CM, Roberts SA, et al. Effect of permissive hypercapnia on background cerebral electrical activity in premature babies[J]. Pediatric research, 2014, 76(2): 184-189

[13] Patel KP, Giraud AS, Samuel CS, et al. Combining an epithelial repair factor and anti-fibrotic with a corticosteroid offers optimal treatment for allergic airways disease[J]. British journal of pharmacology, 2016, 173(12): 2016-2029

[14] Reeves KW, Okereke OI, Qian J, et al. Depression, Antidepressant Use, and Breast Cancer Risk in Pre- and Postmenopausal Women: A Prospective Cohort Study [J]. Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 2018, 27(3): 306-314

[15] Kanchanatawan B, Hemrungrojn S, Thika S, et al. Changes in Tryptophan Catabolite (TRYCAT) Pathway Patterning Are Associated with Mild Impairments in Declarative Memory in Schizophrenia and Deficits in Semantic and Episodic Memory Coupled with Increased False-Memory Creation in Deficit Schizophrenia[J]. Molecular neurobiology, 2018, 55(6): 5184-5201

[16] Victor S, McKeering CM, Roberts SA, et al. Effect of permissive hypercapnia on background cerebral electrical activity in premature babies[J]. Pediatric research, 2014, 76(2): 184-189

[17] Beitler JR, Hubmayr RD, Malhotra A. CrossTalk opposing view: there is not added benefit to providing permissive hypercapnia in the treatment of ARDS [J]. The Journal of physiology, 2013, 591(11): 2767-2769

[18] Liu J, Wang LN. The efficacy and safety of riluzole for neurodegenerative movement disorders: a systematic review with meta-analysis[J]. Drug delivery, 2018, 25(1): 43-48

[19] Qu K, Zaba LC, Satpathy AT, et al. Chromatin Accessibility Landscape of Cutaneous T Cell Lymphoma and Dynamic Response to HDAC Inhibitors[J]. Cancer cell, 2017, 32(1): 27-41.e4

[20] Tregub P, Kulikov V, Bespalov A. Tolerance to acute hypoxia maximally increases in case of joint effect of normobaric hypoxia and permissive hypercapnia in rats[J]. Pathophysiology: the official journal of the International Society for Pathophysiology, 2013, 20(3): 165-170

[21] Curley GF, Laffey JG, Kavanagh BP. CrossTalk proposal: there is added benefit to providing permissive hypercapnia in the treatment of ARDS[J]. The Journal of physiology, 2013, 591(11): 2763-2765

[22] Zhang JS, Wang T, Du HP, et al. Impact of interval between noeadjuvant chemoradiotherapy and surgery on short and long-term outcomes of patients with rectal cancer [J]. Zhonghua zhong liu za zhi [Chinese journal of oncology], 2018, 40(11): 833-836

[23] Jones K, Qassem MG, Sains P, et al. Robotic total meso-rectal excision for rectal cancer: A systematic review following the publication of the ROLARR trial [J]. World journal of gastrointestinal oncology, 2018, 10(11): 449-464