

• 论著 •

肺复张对肺内/外源性急性呼吸窘迫综合征模型犬呼吸生理和肺形态学影响的比较

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【摘要】目的 探讨以压力-容积(P-V)曲线为导向的肺复张(RM)策略对肺内/外源性急性呼吸窘迫综合征(ARDSexp/ARDSp)模型犬呼吸生理和肺形态学的影响。**方法** 将24只健康杂种犬按随机数字表法均分为两组,分别以静脉注射油酸0.1 ml/kg复制ARDSexp模型,以气管内注入盐酸2 ml/kg复制ARDSp模型。每种模型再随机均分为肺保护通气策略(LPVS)组和LPVS+RM组。LPVS组采用LPVS进行机械通气(MV);LPVS+RM组先进行以P-V曲线为导向的RM,RM采用压力控制通气(PCV),压力上限为高位转折点(UIP),呼气末正压(PEEP)为低位转折点(LIP)+2 cm H₂O(1 cm H₂O=0.098 kPa),维持60 s后再按LPVS进行MV。两组MV时间均为4 h。观察动物基础状态(成模前)及RM前后的氧合指数(PaO₂/FiO₂)、呼吸力学指标变化;采用低流速法记录准静态P-V曲线并计算UIP、LIP,根据肺CT比较不同肺充气区容积占全肺容积的百分比。**结果** 成模前和RM前两组PaO₂/FiO₂及UIP、LIP比较差异均无统计学意义。RM后4 h,两种模型LPVS+RM组PaO₂/FiO₂和肺顺应性(Crs)均较同模型LPVS组显著升高[ARDSexp模型PaO₂/FiO₂(mm Hg,1 mm Hg=0.133 kPa):263.9±69.2比182.8±42.8,Crs(ml/cm H₂O):11.3±4.2比9.7±3.7;ARDSp模型PaO₂/FiO₂(mm Hg):193.4±33.5比176.4±40.2,Crs(ml/cm H₂O):10.1±3.9比9.0±3.9,P<0.05或P<0.01],气道压力明显低于同模型LPVS组[ARDSexp模型吸气峰压(PIP,cm H₂O):24.1±7.4比30.2±8.5,气道平台压(Pplat,cm H₂O):19.1±7.3比25.6±7.7;ARDSp模型PIP(cm H₂O):26.6±8.4比29.6±10.3,Pplat(cm H₂O):21.9±7.3比25.1±8.4,P<0.05或P<0.01];且ARDSexp模型改善程度较ARDSp模型更为显著(P<0.05或P<0.01)。两种模型LPVS+RM组肺组织闭合区和充气不足区所占比例均较同模型LPVS组明显减少,正常充气区所占比例明显增加[ARDSexp模型闭合区:(9.9±3.1)%比(16.3±5.2)%;充气不足区:(10.2±4.2)%比(23.4±6.7)%;正常充气区:(76.2±12.3)%比(57.5±10.1)%;ARDSp模型闭合区:(14.3±4.8)%比(18.2±5.1)%;充气不足区:(17.4±6.3)%比(24.1±5.9)%;正常充气区:(63.2±10.7)%比(54.6±11.3)%;P<0.05或P<0.01];且ARDSexp模型各充气区所占比例改善程度均明显优于ARDSp模型(均P<0.05)。**结论** 对于不同原因ARDS,以P-V曲线为导向的RM均具有增加肺氧合、改善肺顺应性和肺组织通气的作用,且对ARDSexp的治疗效果明显优于ARDSp。

【关键词】 急性呼吸窘迫综合征; 肺复张; 肺保护通气策略; 压力-容积曲线

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【Abstract】Objective To determine effects of recruitment maneuver (RM) guided by pressure-volume (P-V) curve on respiratory physiology and lung morphology in canine models of acute respiratory distress syndrome of pulmonary or extrapulmonary origin (ARDSp and ARDSexp). **Methods** Twenty-four healthy dogs were randomly divided into two groups with 12 dogs each: ARDSexp and ARDSp. Each dog in ARDSexp group was injected with oleic acid 0.1 ml/kg through femoral vein, and each dog in ARDSp group received hydrochloric acid 2 ml/kg via trachea. Subsequently, dogs with both models were randomly subdivided into lung protective ventilation strategy (LPVS) group and LPVS+RM group, respectively. Dogs in LPVS group were given LPVS only without RM. RM guided by P-V curve was performed in LPVS+RM group followed by LPVS and pressure controlled ventilation (PCV) mode was selected. Phigh was set at upper inflection point (UIP) of the P-V curve, positive end-expiratory pressure (PEEP) was set at lower inflection point (LIP)+2 cm H₂O (1 cm H₂O=0.098 kPa), and the duration of RM was 60 seconds. The duration of mechanical ventilation (MV) in both subgroups was 4 hours. The oxygenation index (PaO₂/FiO₂), relative lung mechanical indexes were measured in two ARDS models before establishment of ARDS model, and before and after RM. The UIP and LIP were calculated with P-V curve. The percentage of different volume in ventilation of lung accounting for total lung volume was compared by CT scan. **Results** The PaO₂/FiO₂, UIP and LIP did not show significant differences among all groups before ARDS.

and before RM. $\text{PaO}_2/\text{FiO}_2$ and respiratory system compliance (Crs) were significantly elevated in LPVS+RM group of both models 4 hours after RM compared with corresponding LPVS group [$\text{PaO}_2/\text{FiO}_2$ (mm Hg, 1 mm Hg=0.133 kPa) of ARDSexp model, 263.9 ± 69.2 vs. 182.8 ± 42.8 , Crs (ml/cm H₂O) of ARDSexp model, 11.3 ± 4.2 vs. 9.7 ± 3.7 ; $\text{PaO}_2/\text{FiO}_2$ (mm Hg) of ARDSp model, 193.4 ± 33.5 vs. 176.4 ± 40.2 , Crs (ml/cm H₂O) of ARDSp model, 10.1 ± 3.9 vs. 9.0 ± 3.9 , $P < 0.05$ or $P < 0.01$], and the airway pressure was significantly declined compared with corresponding LPVS group [peak inspiratory pressure (PIP), cm H₂O] of ARDSexp model, 24.1 ± 7.4 vs. 30.2 ± 8.5 , plateau pressure (Pplat, cm H₂O) of ARDSexp model, 19.1 ± 7.3 vs. 25.6 ± 7.7 ; PIP (cm H₂O) of ARDSp model, 26.6 ± 8.4 vs. 29.6 ± 10.3 , Pplat (cm H₂O) of ARDSp model, 21.9 ± 7.3 vs. 25.1 ± 8.4 , $P < 0.05$ or $P < 0.01$]. Moreover, $\text{PaO}_2/\text{FiO}_2$, Crs, PIP and Pplat were improved better in ARDSexp model than ARDSp model ($P < 0.05$ or $P < 0.01$). Compared with LPVS maneuver, RM plus LPVS maneuver could significantly decrease the proportion of closure and hypoventilation region, and increase the proportion of normal ventilation region in both models [closure region of ARDSexp model, $(9.9 \pm 3.1)\%$ vs. $(16.3 \pm 5.2)\%$, hypoventilation region of ARDSexp model, $(10.2 \pm 4.2)\%$ vs. $(23.4 \pm 6.7)\%$, normal ventilation region of ARDSexp model, $(76.2 \pm 12.3)\%$ vs. $(57.5 \pm 10.1)\%$; closure region of ARDSp model, $(14.3 \pm 4.8)\%$ vs. $(18.2 \pm 5.1)\%$, hypoventilation region of ARDSp model, $(17.4 \pm 6.3)\%$ vs. $(24.1 \pm 5.9)\%$, normal ventilation region of ARDSp model, $(63.2 \pm 10.7)\%$ vs. $(54.6 \pm 11.3)\%$, $P < 0.05$ or $P < 0.01$]. All of the ventilation regions were better improved with ARDSexp model than ARDSp model (all $P < 0.05$). Conclusion RM guided by P-V curve could help obtain better oxygenation, improve pulmonary compliance and lung ventilation in ARDSexp and ARDSp, and better treatment effects are seen in ARDSexp dogs than ARDSp dogs.

【Key words】 Acute respiratory distress syndrome; Recruitment maneuver; Lung protective ventilation strategy; Pressure-volume curve

肺复张(RM)广泛用于急性呼吸窘迫综合征(ARDS)的治疗中,如何选择复张压力仍然存在很多争论^[1]。不同病因所致ARDS的临床表现、呼吸力学及对RM的反应也有较大差异^[2]。因此根据患者呼吸力学的特征来指导RM可能会更为合理。本研究中通过复制犬肺外源性ARDS(ARDSexp)和肺内源性ARDS(ARDSp)动物模型,实施以压力-容积(P-V)曲线为导向的RM和肺保护通气策略(LPVS),比较其对不同原因导致ARDS呼吸生理和肺形态学的影响,并评价其疗效和安全性。

1 材料与方法

1.1 动物分组和模型制备:普通级健康杂种犬24只,体重(17.6 ± 3.1)kg,雌性10只、雄性14只,由广州医学院实验动物中心提供,动物合格证号:粤SCXK2009-009。按随机数字表法将动物均分为两组制备ARDSexp和ARDSp模型,每种模型再随机分为LPVS组和LPVS+RM组,每组6只。麻醉成功后行气管插管机械通气。ARDSexp模型:20 ml生理盐水和油酸(0.1 ml/kg)充分混合后经中心静脉导管缓慢注入,20 min注完。ARDSp模型:pH值1.0的盐酸2 ml/kg气管内注入。90 min后行动脉血气分析,氧合指数($\text{PaO}_2/\text{FiO}_2$)<200 mm Hg(1 mm Hg=0.133 kPa)并稳定30 min为ARDS模

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型复制成功。

1.2 通气方法:LPVS组采用LPVS进行机械通气4 h,潮气量(V_T)8 ml/kg,频率(f)30次/min,吸入氧浓度(FiO_2)1.00,呼气末正压(PEEP)为低位转折点(LIP)+2 cm H₂O(1 cm H₂O=0.098 kPa)。LPVS+RM组先实施RM,压力控制通气(PCV),压力上限为P-V曲线高位转折点(UIP),PEEP为LIP+2 cm H₂O,维持60 s;RM后继续LPVS机械通气4 h。

1.3 监测指标:①动脉血气:pH值、动脉血氧分压(PaO_2)、动脉血二氧化碳分压(PaCO_2)和动脉血氧饱和度(SaO_2);②呼吸力学:气道平台压(Pplat)、吸气峰压(PIP)、气道阻力(Raw)、肺顺应性(Crs);③准静态P-V曲线:采用低流速法,容量控制通气(VCV),恒流, V_T 20 ml/kg,f 5次/min,吸气流速为5 L/min,由呼吸功能监护仪记录准静态P-V曲线,将数据导出,Origin 8.0软件分析数据,采用双向直线回归法计算曲线的LIP和UIP水平。

1.4 肺CT扫描:通气4 h后进行CT扫描。使用ImageJ软件进行影像学分析,计算全肺肺组织容积、全肺气体容积和总肺容积。根据像素HU值进行全肺充气状况分区,CT值≤-900 HU为过度充气区;-900 HU<CT值≤-500 HU为正常充气区;-500 HU<CT值≤-100 HU为充气不足区;CT值>-100 HU为闭合区。计算各充气区的容积及其占总肺容积的比例^[3]。

1.5 统计学处理:使用SPSS 13.0统计软件进行数据处理。结果以均数±标准差($\bar{x} \pm s$)表示,各组间进行方差分析, $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 一般情况(表1):成模前各组 PaO_2 、 PaCO_2 及RM前LIP、UIP差异无统计学意义(均 $P > 0.05$)。

2.2 RM对 $\text{PaO}_2/\text{FiO}_2$ 的影响(表2):与LPVS组相比,ARDSexp和ARDSp两种模型LPVS+RM组实施RM后4 h $\text{PaO}_2/\text{FiO}_2$ 明显升高($P < 0.01$ 和 $P < 0.05$);与ARDSp模型相比,ARDSexp模型LPVS+RM组 $\text{PaO}_2/\text{FiO}_2$ 改善明显($P < 0.01$)。

2.3 RM对呼吸力学的影响(表2):RM后4 h ARDSexp和ARDSp两种模型LPVS+RM组PIP和Pplat均较RM前有一定程度下降,且明显低于同模型LPVS组($P < 0.05$ 或 $P < 0.01$);Crs较RM前增加,且明显高于同模型LPVS组($P < 0.01$ 和 $P < 0.05$);Raw均无明显变化(均 $P > 0.05$)。与ARDSp模型相比,ARDSexp模型实施RM后4 h PIP、Pplat和Crs改善程度更为显著(均 $P < 0.05$)。

2.4 RM对肺组织不同充气区分布的影响(表1):与LPVS组比较,两种模型LPVS+RM组肺组织闭合区和充气不足区所占比例均明显减少,正常充气区所占比例明显增加($P < 0.05$ 或 $P < 0.01$),而过度充气区所占比例差异无统计学意义。与ARDSp模型相比,ARDSexp模型实施RM后肺组织闭合区和充气不足区减少比例及正常充气区增加比例更为明显(均 $P < 0.05$)。

3 讨 论

小 V_T 的LPVS是至今为止在ARDS诸多治疗中惟一证实能够改善ARDS预后的措施^[4]。小 V_T 有其明显的缺陷,容易导致肺膨胀不全而发生肺泡萎陷。为保证氧合,必须将萎陷的肺泡再度开放,并维持其开放状态。1991年Lachmann^[5]率先提出开放肺泡的概念,近年来RM策略被认为是LPVS的有效补充,在临床得到广泛的应用。但是RM具有双刃剑效应,应用不当可能导致呼吸机相关性肺损伤(VILI)。如何进行RM,尤其是复张压力的选择需要进一步的探索。

表1 ARDSexp/ARDSp犬成模前动脉血气和RM前呼吸力学的比较及RM后犬肺组织不同充气区分布的影响($\bar{x} \pm s$)

模型	组别	动物数	PaO_2 (mm Hg)	PaCO_2 (mm Hg)	LIP(cm H ₂ O)	UIP(cm H ₂ O)	闭合区(%)	充分不足区(%)	正常充气区(%)	过度充气区(%)
ARDSexp	LPVS组	6	440.1±72.6	44.2±10.3	9.9±3.2	32.3±8.5	16.3±5.2	23.4±6.7	57.5±10.1	2.8±1.1
	LPVS+RM组	6	453.3±68.9	42.5±8.9	10.3±2.7	31.9±8.1	9.9±3.1 ^a	10.2±4.2 ^a	76.2±12.3 ^a	3.7±1.3 ^a
ARDSp	LPVS组	6	462.3±85.2	42.8±8.4	10.2±2.1	32.4±7.4	18.2±5.1	24.1±5.9	54.6±11.3	3.1±0.9
	LPVS+RM组	6	435.9±92.8	40.7±9.5	10.6±2.1	33.1±9.2	14.3±4.8 ^b	17.4±6.3 ^b	63.2±10.7 ^b	5.1±1.3 ^b

注:ARDSexp:外源性急性呼吸窘迫综合征,ARDSp:内源性急性呼吸窘迫综合征,RM:肺复张,LPVS:肺保护通气策略, PaO_2 :动脉血氧分压, PaCO_2 :动脉血二氧化碳分压,LIP:低位转折点,UIP:高位转折点;与同模型LPVS组比较,^a $P < 0.05$,^b $P < 0.01$;与ARDSp模型同组比较,^a $P < 0.05$;1 mm Hg=0.133 kPa,1 cm H₂O=0.098 kPa

表2 RM对ARDSexp/ARDSp犬 $\text{PaO}_2/\text{FiO}_2$ 及呼吸力学的影响($\bar{x} \pm s$)

模型	组别	时间	动物数	$\text{PaO}_2/\text{FiO}_2$ (mm Hg)	PIP(cm H ₂ O)	Pplat(cm H ₂ O)	Raw(cm H ₂ O·s ⁻¹ ·L ⁻¹)	Crs(ml/cm H ₂ O)
ARDSexp	LPVS组	基础	6	456.2±89.3	11.3±2.6	6.8±1.8	5.3±1.2	17.9±4.9
		RM前	6	113.2±22.5	28.2±7.2	23.5±6.9	11.2±2.4	8.9±2.7
		RM后4 h	6	182.8±42.8	30.2±8.5	25.6±7.7	11.0±4.2	9.7±3.7
	LPVS+RM组	基础	6	441.3±88.4	12.2±2.9	7.3±1.4	5.7±1.9	18.4±5.6
		RM前	6	118.5±31.7	29.1±8.4	24.8±7.2	11.6±3.2	9.1±3.3
		RM后4 h	6	263.9±69.2 ^d	24.1±7.4 ^c	19.1±7.3 ^c	10.3±3.9	11.3±4.2 ^c
ARDSp	LPVS组	基础	6	439.5±92.1	11.9±3.1	6.7±1.9	4.9±1.7	18.7±4.9
		RM前	6	120.6±26.8	28.9±8.4	22.8±8.3	11.8±3.5	9.3±2.3
		RM后4 h	6	176.4±40.2	29.6±10.3	25.1±8.4	11.6±3.7	9.0±3.9
	LPVS+RM组	基础	6	452.3±98.7	12.4±4.2	7.0±1.5	5.2±2.1	18.1±5.3
		RM前	6	115.1±19.8	28.4±9.1	23.4±8.9	11.1±3.7	8.8±3.1
		RM后4 h	6	193.4±33.5 ^b	26.6±8.4 ^b	21.9±7.3 ^b	11.2±4.6	10.1±3.9 ^b

注:RM:肺复张,ARDSexp:外源性急性呼吸窘迫综合征,ARDSp:内源性急性呼吸窘迫综合征, $\text{PaO}_2/\text{FiO}_2$:氧合指数,LPVS:肺保护通气策略,PIP:吸气峰压,Pplat:气道平台压,Raw:气道阻力,Crs:顺应性;与同模型LPVS组同期比较,^a $P < 0.01$,^b $P < 0.05$;与ARDSp模型同组同期比较,^c $P < 0.05$,^d $P < 0.01$;1 mm Hg=0.133 kPa,1 cm H₂O=0.098 kPa

P-V 曲线能够反映呼吸系统力学特征,对于指导 ARDS 治疗有重要的意义^[6]。ARDS 患者 P-V 曲线呈 S 型,通常由两点三段构成。低位平坦段是开放肺泡随压力变化时容积增大的结果,LIP 为陷闭肺泡的同时开放点,其后开放肺泡和开放的陷闭肺泡同时扩张,出现陡直段,肺容量接近肺总容量后,压力明显升高导致肺容量增加非常有限,称为高位平坦段,二者交点为 UIP,LIP 和 UIP 是肺损伤发生机会多少的分水岭。本研究结果显示,与 LPVS 组相比,LPVS+RM 组在实施以 P-V 曲线为导向的 RM 后, $\text{PaO}_2/\text{FiO}_2$ 和 Crs 有明显改善,气道压力下降;肺组织闭合区和充气不足区所占比例明显减少,正常充气区所占比例明显增加;Puls 等^[7]研究也得出相似的结果。在临床研究中,易丽和席修明^[8]将 RM 用于治疗 ARDS,可改善患者的 $\text{PaO}_2/\text{FiO}_2$ 。顾勤等^[9]的研究发现,对吸痰导致的 ARDS 患者氧分压下降,RM 治疗能较快地使氧分压恢复至吸痰前水平。郝东等^[10]在 ARDS 合并气胸患者中应用 RM 治疗,也取得了理想的效果。RM 改善氧合和肺 Crs 的机制可能包括:RM 是用较高的气道压使塌陷肺泡充分复张,功能残气量明显增加,肺 Crs 改善,有效增加肺容积^[11];邱海波等^[12]认为,RM 容积增加与 $\text{PaO}_2/\text{FiO}_2$ 的变化呈正相关。RM 使复张的肺泡保持在开放状态,导致 PIP、平均气道压明显降低。因此,以 P-V 曲线为导向的 RM 策略同以往选用一个固定压力的 RM 相比可能更为合理。

1998 年 Gattinoni 等^[13]发现,用 PEEP 治疗因肺炎导致的 ARDS 与因腹部疾病导致的 ARDS 在疗效方面有明显差异,并根据这一现象将 ARDS 分为 ARDSp 和 ARDSexp,结果显示,ARDSp 病理变化以肺泡腔内改变为主,如水肿、渗出和中性粒细胞聚集,导致肺的实变;ARDSexp 表现为小血管充血和肺间质水肿,肺泡腔的结构相对正常。本研究结果表明,在实施 RM 后,ARDSexp 模型 $\text{PaO}_2/\text{FiO}_2$ 、呼吸力学指标及 CT 形态学改变均明显好于 ARDSp 模型。国外学者的研究也得出过相似的结论^[14]。其原因为:ARDSp 早期的病理改变局限在肺泡腔内,肺部实变较明显,而 ARDSexp 肺间质水肿则更为明显。在呼吸力学方面,ARDSp 由于肺的实变,肺的弹性阻力要高于 ARDSexp;相反,ARDSexp 胸壁的弹性阻力比 ARDSp 要高 2 倍。由于存在着病理学和呼吸力学机制的差异,以肺间质水肿为主要改变的 ARDSexp 对 RM 的反应要比以肺实变为主要改变的 ARDSp 好^[15]。

综上,对于不同原因的 ARDS,以 P-V 曲线为导向的 RM 策略能较好地改善氧合和肺 Crs,改善肺通气,是一种有效的 RM 方法;且对 ARDSexp 的治疗效果优于 ARDSp。

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肺复张对肺内/外源性急性呼吸窘迫综合征模型犬呼吸生理和肺形态学影响的比较

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