

• 论著 •

ICU计划拔管患者撤机结局的影响因素分析

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【摘要】目的 分析通过自主呼吸试验(SBT)计划拔管患者撤机失败的危险因素及其对预后的影响。

方法 回顾性分析2018年11月至2019年11月秦皇岛市第一医院重症医学科收治的机械通气时间>24 h并通过SBT患者的临床资料。按照拔管后48 h内撤机结局分为撤机成功组和撤机失败组,收集两组患者基线资料、是否存在心肺基础疾病,撤机前24 h内B型钠尿肽(BNP)、液体平衡、白蛋白和血红蛋白,撤机前机械通气时间,SBT过程中浅快呼吸指数(RSBI),SBT结束时氧合指数、反射咳嗽峰流速以及预后等指标。以撤机结局为因变量,观察因素为自变量进行单因素分析,将单因素分析中差异存在统计学意义的因素进行二元Logistic回归分析,以确定撤机失败的影响因素。**结果** 纳入204例患者中有167例(81.9%)撤机成功,37例(18.1%)撤机失败。与撤机成功组比较,撤机失败组总机械通气时间和重症监护病房(ICU)住院时间明显延长〔d: 13.0(7.5, 23.5)比5.0(3.0, 8.0), 17.0(12.5, 31.0)比10.0(6.0, 15.0), 均 $P<0.01$ 〕,气管切开率和病死率明显升高(32.4%比0%, 51.4%比0%, 均 $P<0.01$)。单因素分析显示,撤机失败组与撤机成功组年龄、存在心肺基础疾病患者比例、BNP、反射咳嗽峰流速比较差异均有统计学意义〔年龄(岁): 70.65 ± 15.78 比 62.69 ± 15.82 , 存在心肺基础疾病: 62.2%比24.6%, BNP(ng/L): 416.87(32.70, 1225.80)比45.36(10.00, 273.60), 反射咳嗽峰流速(L/min): 59.89 ± 9.06 比 83.84 ± 16.52 , 均 $P<0.01$ 〕;而性别、入科时急性生理学与慢性健康状况评分Ⅱ(APACHEⅡ)、撤机前机械通气时间、白蛋白、血红蛋白、氧合指数、RSBI、撤机前24 h液体平衡差异无统计学意义〔男性: 51.4%比68.3%, APACHEⅡ(分): 16.70 ± 6.65 比 15.67 ± 6.28 , 撤机前机械通气时间(d): 6.0(2.5, 11.0)比5.0(3.0, 8.0), 白蛋白(g/L): 27.78 ± 4.15 比 27.76 ± 4.46 , 血红蛋白(g/L): 102.43 ± 15.80 比 100.61 ± 17.19 , 氧合指数(mmHg, 1 mmHg=0.133 kPa): 359.33 ± 79.83 比 365.75 ± 78.23 , RSBI(次·L⁻¹·min⁻¹): 50.73 ± 24.97 比 46.76 ± 15.53 , 液体正平衡: 70.3%比69.5%, 均 $P>0.05$ 〕。将单因素分析中差异有统计学意义的指标进行二元Logistic回归分析显示,年龄≥75岁〔优势比(OR)=3.099, 95%可信区间(95%CI)为1.003~9.574, $P=0.049$ 〕、存在心肺基础疾病($OR=3.599$, 95%CI为1.126~11.498, $P=0.031$)、撤机前24 h内BNP($OR=1.002$, 95%CI为1.000~1.003, $P=0.005$)是撤机失败的危险因素,而SBT结束时反射咳嗽峰流速是撤机失败的保护因素($OR=0.869$, 95%CI为0.823~0.917, $P=0.000$)。**结论** 对于通过SBT计划拔管患者,年龄≥75岁、存在心肺基础疾病、撤机前24 h内BNP升高,撤机失败风险较大; SBT结束时反射咳嗽峰流速升高,撤机失败风险较低。

【关键词】 机械通气; 自主呼吸试验; 撤机失败; 影响因素; 重症监护病房

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Influencing factors of weaning outcome of intensive care unit patients with planned extubation

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【Abstract】Objective To determine the risk factors of extubation failure and its effect on the prognosis of patients who had successfully passed a spontaneous breathing trial (SBT). **Methods** The clinical data of patients with mechanical ventilation more than 24 hours who passed SBT admitted to department of intensive care unit (ICU) of First Hospital of Qinhuangdao from November 2018 to November 2019 were retrospectively analyzed. According to the outcome of weaning within 48 hours after weaning, patients were divided into weaning success group and weaning failure group. The baseline data, the presence of basic cardiopulmonary diseases, B-type natriuretic peptide (BNP), fluid balance, albumin and hemoglobin within 24 hours before weaning, the time of mechanical ventilation before weaning, rapid shallow breathing index (RSBI) during SBT, oxygenation index, cough peak flow at the end of SBT, and prognostic indicators were collected. The outcome of weaning was taken as the dependent variable, and the observation factors were taken as the independent variable for univariate analysis. The factors with statistical significance in univariate analysis were analyzed by binary Logistic regression to determine the influencing factors of weaning failure. **Results** Of the 204 patients, 167 (81.9%) were successfully weaned, and 37 (18.1%) failed. Compared with the weaning success group, the total duration of mechanical ventilation and the length of ICU stay in the weaning failure group were significantly longer [days: 13.0 (7.5, 23.5) vs. 5.0 (3.0, 8.0), 17.0 (12.5, 31.0) vs. 10.0 (6.0, 15.0), both $P < 0.01$], and the tracheotomy rate and mortality were significantly higher (32.4% vs. 0%, 51.4% vs. 0%, both $P < 0.01$). Univariate analysis showed that there were significant differences in age, proportion of patients with cardiopulmonary diseases, BNP and cough

peak flow between weaning failure group and weaning success group [age (years old): 70.65 ± 15.78 vs. 62.69 ± 15.82 , cardiopulmonary diseases: 62.2% vs. 24.6%, BNP (ng/L): 416.87 (32.70, 1225.80) vs. 45.36 (10.00, 273.60), cough peak flow (L/min): 59.89 ± 9.06 vs. 83.84 ± 16.52 , all $P < 0.01$]. However, there were no significant differences in gender, acute physiology and chronic health evaluation II (APACHE II) at admission, mechanical ventilation time before weaning, albumin, hemoglobin, oxygenation index, RSBI and fluid balance 24 hours before weaning between weaning failure group and weaning success group [male: 51.4% vs. 68.3%, APACHE II: 16.70 ± 6.65 vs. 15.67 ± 6.28 , mechanical ventilation time before weaning (days): 6.0 (2.5, 11.0) vs. 5.0 (3.0, 8.0), albumin (g/L): 27.78 ± 4.15 vs. 27.76 ± 4.46 , hemoglobin (g/L): 102.43 ± 15.80 vs. 100.61 ± 17.19 , oxygenation index (mmHg, 1 mmHg = 0.133 kPa): 359.33 ± 79.83 vs. 365.75 ± 78.23 , RSBI (times $\cdot L^{-1} \cdot min^{-1}$): 50.73 ± 24.97 vs. 46.76 ± 15.53 , positive fluid balance: 70.3% vs. 69.5%, all $P > 0.05$]. The results of binary Logistic regression analysis showed that age ≥ 75 years old [odds ratio (*OR*) = 3.099, 95% confidence interval (95%CI) was 1.003–9.574, $P = 0.049$], presence of cardiopulmonary diseases (*OR* = 3.599, 95%CI was 1.126–11.498, $P = 0.031$), BNP within 24 hours before weaning (*OR* = 1.002, 95%CI was 1.000–1.003, $P = 0.005$) were the risk factors of extubation failure, while cough peak flow at the end of SBT was the protective factor (*OR* = 0.869, 95%CI was 0.823–0.917, $P = 0.000$). **Conclusions** For patients who had successfully passed SBT, age ≥ 75 years old, the presence of cardiopulmonary diseases and an increased level of BNP within 24 hours were the risk factors of extubation failure. In addition, the higher the cough peak flow at the end of SBT, the lower the risk of weaning failure will be.

【Key words】 Mechanical ventilation; Spontaneous breathing trial; Failure of extubation; Influencing factor; Intensive care unit

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机械通气是呼吸衰竭患者重要的救治措施,在重症监护病房(intensive care unit, ICU)约有36%的患者接受机械通气^[1]。当前国际指南建议机械通气患者每日进行自主呼吸试验(spontaneous breathing trial, SBT)^[2],以早期识别能够自主呼吸的患者。然而,在符合脱机标准并成功完成SBT的计划拔管患者仍有12.40%~22.22%的拔管失败率^[3-4];拔管失败患者机械通气时间和住院时间延长,肺部并发症发生率升高,住院病死率增加,与不良预后显著相关^[3, 5]。拔管失败的病理生理原因包括呼吸能力与呼吸负荷的失衡、心功能障碍、上气道阻塞、脑病、咳嗽能力不足等^[6]。临床医生了解拔管结局的影响因素从而改进临床决策,将有助于改善患者的治疗效果。用于预测拔管结局的参数一般包括呼吸力学评估指标、心脏储备能力参数、气道通畅、气道保护能力等。研究表明,咳嗽能力、白蛋白^[7]、氧合指数、咳嗽强度、大量气道分泌物等^[8]均与拔管结局相关。其中,对于咳嗽能力的评价具有主观性,受患者主观努力影响,并且只适用于清醒合作患者^[7, 9]。诱发反射咳嗽测量反射咳嗽峰流速可扩大评价范围,包括不能和不愿配合进行自主咳嗽的患者。本研究通过回顾性分析本院机械通气患者资料,以确定撤机失败的影响因素及其对预后的影响。

1 资料与方法

1.1 研究对象:采用回顾性研究方法,选择2018年11月至2019年11月本院接受机械通气超过24 h且通过SBT的患者。所有患者在机械通气期间遵

循《中国成人医院获得性肺炎与呼吸机相关性肺炎诊断和治疗指南(2018年版)》标准^[10]实施护理,包括床头抬高30°~45°,每日2次使用洗必泰进行口腔护理,定时监测并维持气囊压力在25~30 cmH₂O(1 cmH₂O=0.098 kPa),对预期可能经历有创通气超过48 h或72 h的患者使用带气囊上分泌物吸引的气管导管,气囊放气前清除气囊上分泌物;插管期间尽量避免深镇静;积极采用呼吸训练、体位引流、翻身扣背或机械设备等方式实施呼吸道清除疗法。由医生决定是否拔除气管导管。拔管前测量血气分析并于气道内滴注2 mL生理盐水,使患者产生咳嗽动作,同时冻结呼吸机流速时间曲线,记录最大呼气峰流速值。

1.1.1 纳入标准:①年龄>18岁。②遵循指南建议^[2]通过筛查试验者,即引起呼吸衰竭的原发病得到控制;血流动力学稳定,未使用或小剂量使用血管升压药,限制药物剂量在5 μg·kg⁻¹·min⁻¹以内;氧合指数>200 mmHg(1 mmHg=0.133 kPa),呼气末正压≤5 cmH₂O,吸入氧浓度≤0.4,无明显电解质紊乱者。③通过SBT^[2]: SBT 30 min内患者无明显生命体征异常、无血流动力学异常、无通气换气功能异常、未出现主观不适。④浅快呼吸指数(rapid shallow breathing index, RSBI)<105 次·L⁻¹·min⁻¹。

1.1.2 排除标准:气管切开者;非计划拔管者。

1.1.3 伦理学:本研究符合医学伦理学标准,并经医院伦理委员会审批(审批号:2019H043),所有治疗及检测均获得过患者或家属知情同意。

1.2 研究方法

1.2.1 资料收集:建立资料收集表,内容包含患者年龄、性别、诊断;入ICU时急性生理学与慢性健康状况评分Ⅱ(acute physiology and chronic health evaluation II, APACHE II);是否潜在心肺基础疾病,包括慢性阻塞性肺疾病(chronic obstructive pulmonary diseases, COPD)、冠心病、瓣膜病、心房颤动等;撤机前24 h内B型钠尿肽(B-type natriuretic peptide, BNP)、液体平衡、白蛋白和血红蛋白;撤机前机械通气时间;SBT过程中RSBI;SBT结束时氧合指数、反射咳嗽峰流速;总机械通气时间、ICU住院时间、是否气管切开及预后。

1.2.2 分组:根据拔管后48 h内是否再插管或死亡将患者分为撤机成功组和撤机失败组。

再插管标准^[11]:呼吸频率持续>35次/min,或<8次/min,呼吸节律异常;动脉血氧分压(arterial partial pressure of oxygen, PaO₂)<50 mmHg;不能纠正的高碳酸血症;上气道梗阻症状;出现明显血流动力学异常。

1.3 统计学方法:将病历数据资料录入Excel表,使用SPSS 23.0软件进行统计学分析。计数资料以例数、百分比表示,组间比较采用 χ^2 检验或Fisher确切概率法;符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,组间比较采用独立样本t检验;不符合正态分布的计量资料以中位数(四分位数)[$M(Q_L, Q_U)$]表示,采用非参数秩和检验。将单因素分析中可能影响撤机结局的因素作为自变量进行二元Logistic回归分析。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 ICU机械通气患者拔管结果:共纳入204例机械通气时间>24 h的患者,其中外科术后30例,脓毒症48例,外伤18例,存在心肺基础疾病58例,神经肌肉疾病3例,颅脑损伤41例,脊髓损伤4例,其他2例。204例患者中167例撤机成功,37例撤机失败,撤机失败率为18.1%;死亡19例,均为撤机失败患者,撤机失败患者病死率为51.4%。与撤机成功组比较,撤机失败组总机械通气时间和ICU住院时间明显延长,气管切开率和病死率明显增加,差异均有统计学意义(均 $P<0.05$;表1)。

2.2 ICU机械通气患者发生撤机失败的单因素分析(表2):撤机成功组与失败组组间年龄、是否存在心肺基础疾病、BNP、反射咳嗽峰流速差异有统计学意义(均 $P<0.01$);而两组间性别、撤机前机械

通气时间、入科时APACHE II评分、血红蛋白、白蛋白、氧合指数、SBT过程中RSBI、撤机前24 h液体平衡差异均无统计学意义(均 $P>0.05$)。

表1 ICU机械通气患者预后指标在撤机成功与失败两组间对比

指标	撤机成功组 (n=167)	撤机失败组 (n=37)	Z值	P值
总机械通气时间 [d, M(Q _L , Q _U)]	5.0(3.0, 8.0)	13.0(7.5, 23.5)	-6.458	0.000
ICU住院时间 [d, M(Q _L , Q _U)]	10.0(6.0, 15.0)	17.0(12.5, 31.0)	-4.752	0.000
气管切开[例(%)]	0(0)	12(32.4)	Fisher	0.000
死亡[例(%)]	0(0)	19(51.4)	Fisher	0.000

注:ICU为重症监护病房

表2 ICU机械通气患者基线资料及临床指标在撤机成功与失败两组间对比

指标	撤机成功组 (n=167)	撤机失败组 (n=37)	t/ χ^2 / Z值	P值
年龄(岁, $\bar{x} \pm s$)	62.69±15.82	70.65±15.78	-2.768	0.006
性别[例(%)]			3.818	0.051
男性	114(68.3)	19(51.4)		
女性	53(31.7)	18(48.6)		
入科时APACHE II (分, $\bar{x} \pm s$)	15.67±6.28	16.70±6.65	-0.849	0.397
撤机前机械通气时间 [d, M(Q _L , Q _U)]	5.0(3.0, 8.0)	6.0(2.5, 11.0)	-0.867	0.386
心肺疾病史[例(%)]			19.901	0.000
有	41(24.6)	23(62.2)		
无	126(75.4)	14(37.8)		
白蛋白(g/L, $\bar{x} \pm s$)	27.76±4.46	27.78±4.15	-0.021	0.983
血红蛋白(g/L, $\bar{x} \pm s$)	100.61±17.19	102.43±15.80	-0.576	0.565
氧合指数(mmHg, $\bar{x} \pm s$)	365.75±78.23	359.33±79.83	0.433	0.666
RSBI(次·L ⁻¹ ·min ⁻¹ , $\bar{x} \pm s$)	46.76±15.53	50.73±24.97	-0.562	0.578
液体平衡[例(%)]			0.009	0.923
正平衡	116(69.5)	26(70.3)		
负平衡	51(30.5)	11(29.7)		
BNP[ng/L, M(Q _L , Q _U)]	45.36 (10.00, 273.60)	416.87 (32.70, 1 225.80)	-4.571	0.000
反射咳嗽峰流速 (L/min, $\bar{x} \pm s$)	83.84±16.52	59.89±9.06	12.203	0.000

注:ICU为重症监护病房,APACHE II为急性生理学与慢性健康状况评分Ⅱ,RSBI为浅快呼吸指数,BNP为B型钠尿肽;1 mmHg=0.133 kPa

2.3 通过SBT的ICU机械通气患者发生撤机失败的二元Logistic回归分析(表3):以撤机结局为因变量,将单因素分析中差异有统计学意义的指标作为自变量进行二元Logistic回归分析,结果显示,年龄≥75岁、存在心肺基础疾病、BNP是撤机失败的独立危险因素,而反射咳嗽峰流速是撤机失败的保护因素(均 $P<0.05$)。

表3 ICU 机械通气患者撤机结局影响因素的二元 Logistic 回归分析

因素	β 值	s_{β}	χ^2 值	df	P 值	OR 值	95%CI
存在心肺基础疾病	1.281	0.593	4.669	1	0.031	3.599	1.126~11.498
反射咳嗽峰流速	-0.141	0.027	26.269	1	0.000	0.869	0.823~0.917
BNP	0.002	0.001	8.062	1	0.005	1.002	1.000~1.003
年龄≥75岁	1.131	0.576	3.861	1	0.049	3.099	1.003~9.574

注:ICU 为重症监护病房, BNP 为 B 型钠尿肽, df 为自由度, OR 为优势比, 95%CI 为 95% 可信区间

3 讨 论

本研究中 204 例 ICU 计划撤机患者中,有 18.1% 撤机失败,其中 51.4% 死亡。与撤机成功患者相比,撤机失败患者总机械通气时间、ICU 住院时间均明显延长,气管切开率增加,病死率增加,与先前的研究结果基本一致^[3, 5]。大型随机对照试验结果显示,普通 ICU 患者 5%~20% 撤机失败率是合理的^[2],虽然本研究中撤机失败率在此范围内,但在 64 例存在心肺基础疾病的高危人群中,有 23 例(35.9%)撤机失败,而在撤机失败患者中死亡 13 例(56.5%),再插管风险和撤机失败后病死率均较高。当机械通气转为自然通气,吸气时胸腔压力由正压转为负压,中心静脉与右心房压力梯度增加,回心血量及右心前负荷增加,胸膜腔内压力的改变以同样的方式影响左心前负荷,同时增加左室跨壁收缩压及左室后负荷,加重心脏负担,诱发心力衰竭。此外,当机械通气转变为自主呼吸时患者呼吸功增加,可能加重心血管的功能障碍。除心源性撤机失败外,呼吸泵衰竭和呼吸肌力与负荷的失衡也是撤机失败的主要原因。慢性呼吸系统疾病通常伴呼吸肌肉超负荷、气体交换异常、全身炎症和肌肉萎缩或肌肉无力,以上因素均可能增加撤机失败的风险^[12]。国外研究证实,无创机械通气能降低撤机失败高风险患者的撤机失败率^[13-14],但使用无创通气的指征和时机尚不清楚。临幊上发现无创通气无效时尽早进行有创通气,而不是挽救性治疗,可能会改变患者的临床结局。

随着年龄的增长,呼吸系统逐渐退化,老年人会出现胸廓僵硬,功能残气量增加,膈肌和呼吸肌力量减弱,大脑咳嗽中枢敏感性降低,对缺氧和高碳酸血症的通气反应减弱^[15]。有报道显示,老年患者在撤机后 48~72 h 内有 20%~35% 需要重新插管^[16-17],撤机失败率高于一般人群。本研究中年龄≥75 岁患者撤机失败率是<75 岁者的 3.099 倍。咳嗽是一种生理防御机制,能够预防误吸和清除气

道内分泌物,是成功撤机的重要条件。本研究中,撤机失败组中 13 例(35.1%)因咳嗽能力不足而再次插管。咳嗽峰流速是用力呼气期间产生的最大流速,能够反映呼吸肌肉力量,与半定量咳嗽强度评分(semiquantitative cough strength score, SCSS)呈正相关,具有与 SCSS 同样预测撤机结局的准确性^[18]。自主咳嗽峰流速是通过 SBT 机械通气患者撤机结局的重要预测因子,但受主观努力程度影响^[7, 9]。反射咳嗽是由于机械或化学刺激,引起胸腹、喉部肌肉迅速收缩,产生强大气流的过程^[19]。与自主咳嗽峰流速相比,反射咳嗽峰流速不受主观努力影响,并且能够扩大可评价患者范围,包括不能配合进行自主咳嗽的患者,对于意识障碍的机械通气患者尤为重要^[20-21]。

BNP 和 N 末端脑钠肽前体(N-terminal pro-brain natriuretic peptide, NT-proBNP)是心脏容积与功能状态的生物标志物,是由心肌细胞为响应不同的刺激而分泌的。本研究中撤机成功组与失败组之间撤机当日基线 BNP 差异存在统计学意义;先前的研究也证实,高基础 BNP 水平与撤机失败风险增加有关^[22-23]。刘莲等^[24]将 159 例 ICU 即将脱机患者脉搏指示连续心排血量监测(pulse indicator continuous cardiac output, PiCCO)的血流动力学参数、BNP、尿量、液体平衡量等因素进行回归分析,证实以 PiCCO 监测指标联合中心静脉压、液体平衡量等指标建立脱机失败预测模型对预测脱机结局有指导意义。另外,有研究表明,SBT 结束时 BNP 或 SBT 期间 BNP 增加可能也与撤机失败或撤机后呼吸窘迫相关^[25-26]。与半衰期为 20 min 的 BNP 相比,NT-proBNP 半衰期更长,约 120 min。而 SBT 时间一般为 30~60 min, SBT 期间左心室后负荷和前负荷增加,可能会刺激 BNP 分泌,NT-proBNP 峰值却出现较晚,这也许是 BNP 预测撤机相关心力衰竭准确性高于 NT-proBNP 的原因^[23]。在一项关于脱机患者液体管理的研究中,研究者对比了 BNP 驱动液体管理策略与临床医生经验性液体管理策略对撤机成功时间的影响,应用 BNP 驱动液体管理策略组液体负平衡比例、使用利尿剂的频率和剂量较高,尤其缩短了左室功能不全患者撤机成功时间;但 COPD 患者、不存在左室功能不全及 COPD 的其他患者撤机成功时间差异无统计学意义^[26]。可能非心功能不全患者能够耐受拔管时急性血流动力学变化,且拔管失败的原因为呼吸衰竭或气道等因素。本研究

中两组间液体平衡差异无统计学意义。RSBI 为呼吸频率与潮气量的比值,其阈值>105 次·min⁻¹·L⁻¹高度预测撤机失败^[27]。针对不同群体的患者,RSBI 预测撤机成功与否的价值存在差异^[28],例如:对于缺乏气道保护能力而不是呼吸能力的患者,RSBI 并不是很好的预测成功撤机的指标。虽然以往的研究证实白蛋白、血红蛋白以及氧合指数是撤机失败的预测因子^[7-8],但在本研究中两组间差异并无统计学意义。

综上,ICU 患者病情危重、复杂,撤机失败的影响因素众多。本研究显示,年龄≥75岁、存在心肺基础疾病、BNP 是撤机失败的危险因素,反射咳嗽峰流速是撤机失败的保护因素。撤机失败患者总机械通气时间和 ICU 住院时间较撤机成功患者明显延长,气管切开率增加,ICU 病死率增加,尤其是伴有心肺基础疾病患者撤机失败率和病死率更高,临幊上应重点关注此类患者,利用多种手段进行精细化机械通气管理、撤机前的评估以及撤机后患者管理,以降低撤机失败率和病死率。本研究为单中心研究,且撤机失败患者较少,需扩大样本并进行前瞻性多中心研究进一步研究撤机失败的影响因素。

利益冲突 所有作者均声明不存在利益冲突

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