

超声膈肌增厚率对重症肌无力危象机械通气患者撤机成功的预测价值

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【摘要】 目的 通过床旁超声评估重症肌无力危象机械通气患者的膈肌功能, 明确膈肌增厚率(DTF)对撤机成功的预测价值。**方法** 采用前瞻性研究方法, 选择 2015 年 3 月至 2017 年 2 月入住青岛大学附属医院重症医学科的重症肌无力危象且需行有创机械通气治疗的患者。所有患者采用低水平压力支持模式的自主呼吸试验(SBT), 并记录浅快呼吸指数(RSBI); 于 SBT 5 min 及 60 min 时采用床旁超声测量患者右侧膈肌呼气末膈肌厚度(DTee)、吸气末膈肌厚度(DTei), 并计算 DTF, 观察 SBT 过程中各项指标的变化。根据撤机结果将患者分为撤机成功组和撤机失败组, 比较两组患者各项指标的差异。采用受试者工作特征曲线(ROC)评价 SBT 60 min 时 DTF 及 RSBI 对撤机成功的预测价值。**结果** 共 37 例患者纳入最终分析, 共计完成 63 例次 SBT 5 min 时的超声测量和 50 例次 SBT 60 min 时的超声测量。SBT 5 min 时数据分析结果显示, 撤机成功组(33 例次)与失败组(30 例次)患者 RSBI、DTee、DTei 及 DTF 差异均无统计学意义(均 $P > 0.05$)。SBT 60 min 数据分析结果显示, 与撤机成功组(33 例次)比较, 撤机失败组(17 例次)患者 RSBI 明显升高(次·min⁻¹·L⁻¹: 80.41 ± 29.08 比 63.94 ± 23.84, $t = 2.146$, $P = 0.037$), DTee、DTei、DTF 均明显降低[DTee(mm): 22.00 ± 6.25 比 25.45 ± 4.99, $t = 2.127$, $P = 0.039$; DTei(mm): 27.94 ± 6.19 比 38.48 ± 6.15, $t = 5.731$, $P = 0.000$; DTF: (24.46 ± 14.11)% 比 (62.04 ± 30.21)%, $t = 4.845$, $P = 0.000$]。33 例次成功撤机患者 SBT 5 min 与 60 min 时 RSBI、DTee、DTei 及 DTF 差异无统计学意义(均 $P > 0.05$)。在 17 例次 SBT 超过 60 min 但撤机失败患者中, 与 SBT 5 min 比较, SBT 60 min RSBI 明显升高(次·min⁻¹·L⁻¹: 80.41 ± 29.08 比 57.29 ± 22.46, $t = 2.400$, $P = 0.029$), DTei 和 DTF 明显降低[DTei(mm): 27.94 ± 6.19 比 35.35 ± 6.84, $t = 3.024$, $P = 0.000$; DTF: (24.46 ± 14.11)% 比 (61.89 ± 23.97)%, $t = 5.810$, $P = 0.000$]; 但 DTee 在 SBT 过程中无明显变化。ROC 曲线分析显示: SBT 60 min 时 DTF 预测撤机成功的 ROC 曲线下面积(AUC)为 0.898; 以 DTF ≥ 27.90% 为截点, 敏感度为 93.9%, 特异度为 70.6%。SBT 60 min 时 RSBI 预测撤机成功的 AUC 为 0.669; 以 RSBI ≥ 86.50 次·min⁻¹·L⁻¹ 为截点, 敏感度为 81.8%, 特异度为 52.9%。**结论** SBT 60 min 时超声测量 DTF 是预测重症肌无力危象机械通气患者撤机成功的有效指标。

【关键词】 超声; 膈肌; 重症肌无力; 机械通气; 撤机

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Predictive value of ultrasonic diaphragm thickening fraction on successful weaning for patients with myasthenia gravis crisis Sun Qiang, Shan Feng, Dong Hai, Jiang Yan, Sun Yongmei, Sun Yunbo

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【Abstract】 Objective To confirm the predictive value of diaphragm thickening fraction (DTF) on successful weaning by bedside ultrasound in patients with myasthenia gravis crisis. **Methods** A prospective study was conducted. The patients with myasthenia gravis crisis undergoing mechanical ventilation admitted to Department of Critical Care Medicine of the Affiliated Hospital of Qingdao University from March 2015 to February 2017 were enrolled. All patients underwent a low level pressure support mode of spontaneous breathing test (SBT), and rapid shallow breathing index (RSBI) was recorded. The indicators of right diaphragm thickness at the end of inspiration (DTei) and expiration (DTee) were determined by bedside ultrasound at 5 minutes and 60 minutes of SBT, and DTF was calculated, the changes in above parameters were observed during SBT. The patients were divided into successful weaning group and failure weaning group, and the differences in above indexes were compared between the two groups. Receiver operating characteristic curve (ROC) was used to evaluate the predictive value of DTF and RSBI at 60 minutes of SBT on successful weaning. **Results** A total of 37 patients were enrolled in the study. Ultrasonic measurement data of 63 person-times at 5 minutes of SBT and 50 at 60 minutes of SBT were obtained. There were no statistical differences in RSBI, DTei, DTee, and DTF at 5 minutes of SBT between successful weaning group ($n = 33$) and failure weaning group ($n = 30$). At 60 minutes of SBT, compared with successful weaning group ($n = 33$), the patients in failure weaning group ($n = 17$) had a higher RSBI (times·min⁻¹·L⁻¹: 80.41 ± 29.08 vs. 63.94 ± 23.84, $t = 2.146$, $P = 0.037$), and lower DTee, DTei and DTF [DTee (mm): 22.00 ± 6.25 vs. 25.45 ± 4.99, $t = 2.127$, $P = 0.039$; DTei (mm): 27.94 ± 6.19 vs. 38.48 ± 6.15,

$t = 5.731, P = 0.000$; DTF: $(24.46 \pm 14.11)\%$ vs. $(62.04 \pm 30.21)\%$, $t = 4.845, P = 0.000$]. There were no statistical differences in RSBI, DTei, DTee, and DTF between 5 minutes and 60 minutes of SBT in 33 person-time successful weaning (all $P > 0.05$). In 17 person who had 60 minutes of SBT but failed weaning, the RSBI at 60 minutes of SBT was significantly higher than that at 5 minutes (times $\cdot \text{min}^{-1} \cdot \text{L}^{-1}$: 80.41 ± 29.08 vs. 57.29 ± 22.46 , $t = 2.400, P = 0.029$), and DTei and DTF were significantly decreased [DTei (mm): 27.94 ± 6.19 vs. 35.35 ± 6.84 , $t = 3.024, P = 0.000$; DTF: $(24.46 \pm 14.11)\%$ vs. $(61.89 \pm 23.97)\%$, $t = 5.810, P = 0.000$], but the change of DTee during SBT showed no statistical significance. ROC curve analysis showed that the area under ROC curve (AUC) of DTF at 60 minutes of SBT for predicting successful weaning was 0.898; when DTF $\geq 27.9\%$ as the cut-off point, the sensitivity was 93.9%, specificity was 70.6%. The AUC of RSBI for predicting successful weaning was 0.669; when RSBI ≥ 86.50 times $\cdot \text{min}^{-1} \cdot \text{L}^{-1}$ as the cut-off point, the sensitivity was 81.8%, specificity was 52.9%. **Conclusion** DTF at 60 minutes of SBT is the effective index of successful weaning prediction in mechanical ventilation patients with myasthenia gravis crisis.

【Key words】 Ultrasound; Diaphragm; Myasthenia gravis; Mechanical ventilation; Extubation

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重症肌无力是一种周围神经系统性疾病,随病情进展可诱发肌无力危象,导致呼吸衰竭(呼衰),必须使用机械通气治疗^[1-2]。膈肌作为主要的呼吸肌,其功能恢复程度对患者撤机成功与否起关键作用。有学者通过超声监测慢性阻塞性肺疾病(COPD)等危重病患者膈肌位移及厚度变化指导撤机,取得良好效果^[3-7]。本研究使用床旁超声监测重症肌无力危象机械通气患者撤机过程中膈肌增厚率(DTF),以明确其临床预测价值,对撤机时机进行准确判断。

1 资料与方法

1.1 研究对象:采用前瞻性研究方法,选择 2015 年 3 月至 2017 年 2 月入住青岛大学附属医院重症医学科的重症肌无力危象,并使用经口气管插管机械通气的患者。所有患者均为第 1 次因呼衰行机械通气治疗,在第 1 次拟撤机前 1 d 入组。

1.1.1 纳入标准:年龄 > 18 岁;意识清楚;氧合指数($\text{PaO}_2/\text{FiO}_2$) > 200 mmHg (1 mmHg = 0.133 kPa);血流动力学稳定。

1.1.2 排除标准:年龄 < 18 岁;3 个月内有胸腹腔手术史;合并腹腔高压或因严重肺部感染及 COPD 等其他疾病导致呼衰的患者。

1.1.3 剔除标准:中途放弃治疗或自愿退出研究者。

1.1.4 伦理学:本研究符合医学伦理学标准,获得医院伦理委员会批准(审批号:2015-01-16),所有患者家属均签署知情同意书。

1.2 观察指标及方法

1.2.1 呼吸功能指标:患者床头抬高 30° ,采用低水平压力支持模式的自主呼吸试验(SBT),支持压力设为 7 cmH₂O (1 cmH₂O = 0.098 kPa),吸入氧浓度(FiO_2)不超过 0.40。记录患者呼吸频率、潮气量,计算浅快呼吸指数(RSBI)。

1.2.2 床旁超声测量:于 SBT 5 min 及 60 min 应用美国 SonoSite 彩色多普勒超声诊断仪完成超声测量。

HFL38 型超声探头沿右侧腋中线寻找平静吸气末肺下界膈肌肋间水平,并标记为测量点。采用 B 超模式测量膈肌厚度^[8],取每个呼吸周期的最大值和最小值,分别作为吸气末膈肌厚度(DTei)和呼气末膈肌厚度(DTee),记录连续 3 个呼吸周期的数值,取均值,计算 DTF [$\text{DTF} = (\text{DTei} - \text{DTee}) / \text{DTee} \times 100\%$]。所有超声测量均由同一位超声科医生完成,测量结果对临床医生保密,测量目的对患者保密以减少患者的主观因素对测量结果的影响。研究结束后由临床医生查看超声结果并进行数据分析。

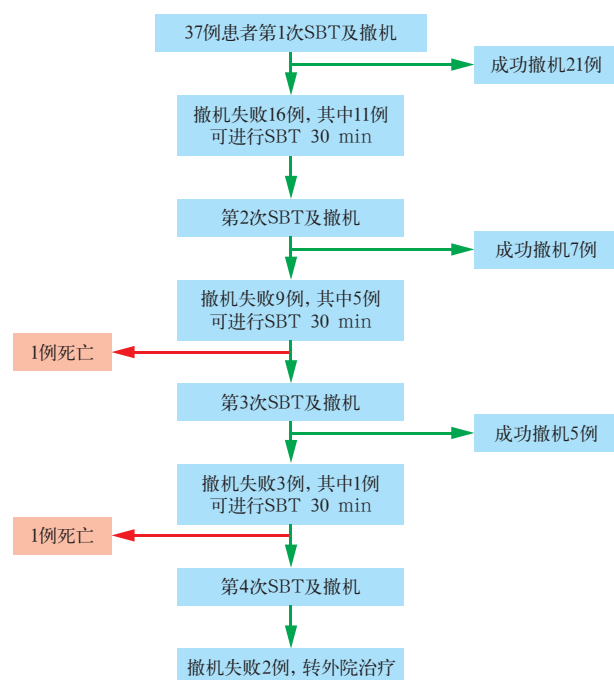
1.2.3 动脉血气分析:于每次超声测量结束 2 min 内抽取动脉血,进行血气分析。

1.3 撤机成功标准:SBT 2 h 后由临床医生根据患者耐受情况及气道廓清能力等指标拔管并撤机。以顺利撤机且 48 h 内不再需要使用有创或无创机械通气支持为撤机成功标准^[9]。对于初次撤机失败的患者,后续实施的撤机试验都纳入研究。根据撤机结果将患者分为撤机成功组和撤机失败组。

1.4 统计学方法:应用 SPSS 19.0 软件进行统计学分析。先对计量资料进行正态性检验,正态分布以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,用配对样本 t 检验和独立样本 t 检验;非正态分布以中位数(四分位数) [$M(Q_L, Q_U)$]表示,用 Mann-Whitney U 检验。采用受试者工作特征曲线(ROC)评价 DTF、RSBI 对撤机成功的预测价值。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 一般资料:共 37 例患者纳入分析,男性 16 例,女性 21 例;年龄 19 ~ 73 岁,平均 (43.4 ± 13.7) 岁;均行经口气管插管;所有患者均行 1 次或多次 SBT,其中 33 例撤机成功,2 例死亡,2 例转外院继续治疗(图 1);共计完成 63 例次 SBT 5 min 时的超声测量和 50 例次 SBT 60 min 时的超声测量,均得到清晰的超声膈肌图像。



注: SBT 为自主呼吸试验

图1 超声测量膈肌增厚率(DTF)预测重症肌无力危象机械通气患者撤机成功的临床研究入选病例流程

2.2 SBT 5 min 时的数据分析(表1):在 63 例次 SBT 5 min 时的超声测量数据中,撤机成功组 33 例次,撤机失败组 30 例次;两组年龄、急性生理学与慢性健康状况评分系统 II (APACHE II) 评分、机械通气时间、 $\text{PaO}_2/\text{FiO}_2$ 无明显差异 (均 $P>0.05$),说明两组一般资料均衡,有可比性。两组 RSBI、DTee、DTei 及 DTF 差异均无统计学意义 (均 $P>0.05$)。

2.3 SBT 60 min 时的数据分析(表1):在 50 例次 SBT 60 min 时超声测量数据中,撤机成功组 33 例次,

撤机失败组 17 例次;两组年龄、APACHE II 评分、机械通气时间、 $\text{PaO}_2/\text{FiO}_2$ 无明显差异 (均 $P>0.05$),说明两组一般资料均衡,有可比性。与撤机成功组比较,撤机失败组患者 RSBI 明显升高,DTee、DTei、DTF 均明显降低 (均 $P<0.05$)。

2.4 成功撤机患者测量数据分析(表2):33 例次成功撤机患者 SBT 5 min 与 60 min 时的 RSBI、DTee、DTei 及 DTF 差异无统计学意义 (均 $P>0.05$)。

2.5 SBT 超过 60 min 但撤机失败患者测量数据分析(表2):在 17 例次 SBT 超过 60 min 但撤机失败患者中,与 SBT 5 min 比较,SBT 60 min 时 RSBI 明显升高,DTei 和 DTF 明显降低 (均 $P<0.05$);但 DTee 在 SBT 过程中无明显变化。

表2 撤机成功和撤机失败的重症肌无力危象患者 SBT 5 min 与 60 min 时超声测量数据比较 ($\bar{x} \pm s$)

撤机成功					
时间	例次	RSBI (次·min ⁻¹ ·L ⁻¹)	DTee (mm)	DTei (mm)	DTF (%)
SBT 5 min	33	60.67 ± 19.40	23.76 ± 5.04	36.36 ± 5.53	57.66 ± 31.15
SBT 60 min	33	63.94 ± 23.84	25.52 ± 4.99	38.48 ± 6.15	62.04 ± 30.21
t 值		1.552	1.752	1.84	0.582
P 值		0.131	0.089	0.075	0.565
SBT 超过 60 min 但撤机失败					
时间	例次	RSBI (次·min ⁻¹ ·L ⁻¹)	DTee (mm)	DTei (mm)	DTF (%)
SBT 5 min	17	57.29 ± 22.46	22.18 ± 4.99	35.35 ± 6.84	61.89 ± 23.97
SBT 60 min	17	80.41 ± 29.08	22.00 ± 6.25	27.94 ± 6.19	24.46 ± 14.11
t 值		2.400	0.089	3.024	5.810
P 值		0.029	0.930	0.000	0.000

注: SBT 为自主呼吸试验, RSBI 为浅快呼吸指数, DTee 为呼气末膈肌厚度, DTei 为吸气末膈肌厚度, DTF 为膈肌增厚率

表1 完成 SBT 5 min (63 例次) 和 60 min (50 例次) 撤机成功与失败两组重症肌无力危象患者临床资料比较 ($\bar{x} \pm s$)

完成 SBT 5 min									
组别	例次	年龄 (岁)	APACHE II (分)	MV 时间 (d)	$\text{PaO}_2/\text{FiO}_2$ (mmHg)	RSBI (次·min ⁻¹ ·L ⁻¹)	DTee (mm)	DTei (mm)	DTF (%)
撤机成功组	33	44.21 ± 14.75	12.33 ± 3.25	11.09 ± 3.95	328.90 ± 45.47	60.67 ± 19.40	23.76 ± 5.04	36.36 ± 5.53	57.66 ± 31.15
撤机失败组	30	45.17 ± 12.16	13.60 ± 2.84	13.03 ± 5.61	316.30 ± 58.85	67.60 ± 21.89	21.97 ± 5.99	33.27 ± 7.80	55.94 ± 30.84
t 值		0.279	1.642	1.601	0.961	1.333	1.228	1.831	0.220
P 值		0.781	0.106	0.115	0.340	0.187	0.203	0.072	0.827
完成 SBT 60 min									
组别	例次	年龄 (岁)	APACHE II (分)	MV 时间 (d)	$\text{PaO}_2/\text{FiO}_2$ (mmHg)	RSBI (次·min ⁻¹ ·L ⁻¹)	DTee (mm)	DTei (mm)	DTF (%)
撤机成功组	33	44.21 ± 14.75	12.33 ± 3.25	11.09 ± 3.95	341.51 ± 63.50	63.94 ± 23.84	25.45 ± 4.99	38.48 ± 6.15	62.04 ± 30.21
撤机失败组	17	46.35 ± 13.53	13.12 ± 3.08	12.94 ± 6.11	325.24 ± 61.06	80.41 ± 29.08	22.00 ± 6.25	27.94 ± 6.19	24.46 ± 14.11
t 值		0.499	0.823	1.297	0.870	2.146	2.127	5.731	4.845
P 值		0.620	0.415	0.201	0.389	0.037	0.039	0.000	0.000

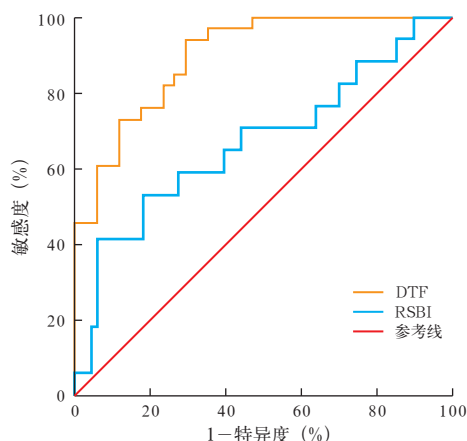
注: SBT 为自主呼吸试验, APACHE II 为急性生理学与慢性健康状况评分系统 II, MV 为机械通气, $\text{PaO}_2/\text{FiO}_2$ 为氧合指数, RSBI 为浅快呼吸指数, DTee 为呼气末膈肌厚度, DTei 为吸气末膈肌厚度, DTF 为膈肌增厚率; 1 mmHg=0.133 kPa

2.6 SBT 60 min 时各指标预测撤机成功的 ROC 曲线分析(表 3; 图 2): SBT 60 min 时超声测量 DTF 预测撤机成功的 ROC 曲线下面积(AUC)为 0.898; 以 $DTF \geq 27.90\%$ 为截点, 敏感度为 93.9%, 特异度为 70.6%。SBT 60 min 时的 RSBI 预测撤机成功的 AUC 为 0.669; 以 $RSBI \geq 86.50$ 次 $\cdot \text{min}^{-1} \cdot \text{L}^{-1}$ 为截点, 敏感度为 81.8%, 特异度为 52.9%。

表 3 SBT 60 min 时超声测量 DTF 和 RSBI 对重症肌无力危象患者撤机成功的预测价值

参数	AUC	95%CI	敏感度 (%)	特异度 (%)	阳性预测值 (%)	阴性预测值 (%)
DTF	0.898	0.807 ~ 0.988	93.9	70.6	86.1	85.7
RSBI	0.669	0.502 ~ 0.837	81.8	52.9	77.1	60.0

注: SBT 为自主呼吸试验, DTF 为膈肌增厚率, RSBI 为浅快呼吸指数, AUC 为受试者工作特征曲线下面积, 95%CI 为 95% 可信区间



注: SBT 为自主呼吸试验, DTF 为膈肌增厚率, RSBI 为浅快呼吸指数, ROC 曲线为受试者工作特征曲线

图 2 SBT 60 min 时超声测量 DTF 和 RSBI 预测重症肌无力危象患者撤机成功的 ROC 曲线

3 讨论

对于重症肌无力危象行机械通气治疗的患者, 准确判断撤机时机非常重要。及早成功撤机可有效缩短重症加强治疗病房(ICU)住院时间、降低治疗费用、减少呼吸机相关性肺炎(VAP)等并发症的发生率^[10-12]; 而撤机失败则导致患者病情反复甚至加重。目前临床上没有针对重症肌无力危象患者撤机的“金标准”, 普遍参考 COPD 等的指导意见, 采用 SBT 结合多项指标来指导撤机, 失败率较高^[13-15]。因此, 寻找更合理的撤机预测指标成为重症肌无力危象患者治疗的关键。重症肌无力危象患者往往膈肌受累而不得不使用呼吸机辅助呼吸, 同时膈肌是最主要的呼吸肌, 主导正常通气过程中 70% 以上的工作量^[16], 膈肌功能的恢复程度决定着重症肌无力

危象伴呼吸衰竭患者的预后, 所以评价膈肌功能并指导撤机是一个确切可行的方法^[17]。目前监测膈肌功能的方法主要有超声、电生理、CT 和膈肌力学等^[18], 其中应用床旁超声评价膈肌功能可无创、实时、准确地提供高质量的膈肌图像, 适合临床应用^[19-20]。

鉴于正压通气对膈肌运动的影响, 对机械通气患者采用收缩幅度来评价膈肌功能可能比运动幅度更为合理^[21]; 同时, 超声观察右侧膈肌较左侧操作简便可靠、图像清晰、有利于测量^[22], 所以本研究通过床旁超声评价重症肌无力危象患者呼吸过程中右侧 DTF 来预测撤机结果。研究显示, 撤机失败者 SBT 60 min 时 DTF 明显低于成功者, 且 ROC 曲线提示 DTF 对撤机成功的预测价值较高; 虽然 SBT 60 min 时两组 DTei 和 DTee 也有明显差异, 但由于膈肌厚度的个体差异较大, 部分健康人群膈肌厚度可低至 1.5 mm 以下^[23-25], 不建议使用膈肌的绝对厚度来指导撤机, 所以 DTF 是更可靠的预测指标。

本研究对比了 SBT 5 min 时各项指标, 发现撤机成功组与失败组间差异无统计学意义, 可能是 SBT 初始阶段, 重症肌无力患者的膈肌力量储备尚充足, 收缩力没有明显下降, 尚能维持呼吸功能需要, 而随着 SBT 的进行, 部分患者逐渐出现膈肌疲劳, 表现为收缩能力下降, 呼吸费力, 导致撤机失败^[26]。本研究结果显示, 成功撤机患者 SBT 60 min 时的 DTF 与 5 min 时无明显差异; 而 SBT 超过 60 min 但撤机失败的患者, 其 SBT 60 min 时的 DTF 明显低于 5 min 时, 所以对于重症肌无力患者, 膈肌收缩的耐力可能更重要, 并提示 SBT 60 min 时膈肌状态较 5 min 时对撤机更有意义。这种随 SBT 时间延长的膈肌收缩力下降是重症肌无力患者的特殊性^[27], 也提示我们对于重症肌无力患者, 要采用较长时间 SBT 的 DTF 来提高对撤机结果的预测价值。

本研究分析了 SBT 60 min 时 RSBI 和 DTF 对撤机结果的预测价值, 结果显示, DTF 的敏感度和特异度均高于 RSBI。可能是 DTF 直接反映了膈肌本身的功能变化^[28-29], 能体现重症肌无力患者的呼吸能力, 敏感度和特异度相对较高, 而 SBT 患者努力吸气时肋间肌、腹肌等辅助呼吸肌做功, 掩盖了膈肌收缩力下降的表现, 导致 RSBI 特异度不高^[30]。因此, 对于重症肌无力患者, DTF 预测撤机成功的价值较 RSBI 更有意义。

有研究表明, 影响撤机结果的因素还包括患者的气道廓清能力^[31]。咳嗽作为患者主动进行气道

廓清的重要手段,在预防拔管后再插管中起到重要作用,对于重症肌无力危象患者,膈肌的力量储备是影响其主动咳嗽能力的重要因素。DTF 为膈肌功能的直接体现,在咳嗽中的临床意义还有待研究。

综上所述,SBT 60 min 时超声测量 DTF 是预测重症肌无力危象机械通气患者撤机成功的有效指标,适于临床应用。

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