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CASE REPORT

Difficult weaning: Principles and practice of a structured diagnostic approach

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Abstract

Difficult weaning from mechanical ventilation is a major problem in critically ill patients. The pathophysiology of weaning failure is complex and multiple causes for difficult weaning may exist in any single patient. We have recently developed a structural framework ('ABCDE') for the assessment and treatment of difficult-to-wean patients. In this article, we present the case of a difficult-to-wean 68-year-old male with chronic obstructive pulmonary disease who had been on mechanical ventilation for three weeks. The patient was referred to our centre for assessment of the cause of weaning failure. During a spontaneous breathing trial at our centre an extensive physiological evaluation revealed diastolic dysfunction as the most important cause for weaning failure. It was advised to titrate continuous intravenous nitroglycerin to control systolic blood pressure during subsequent spontaneous breathing trials. In addition, oral antihypertensive drugs were added to control hypertension throughout the day. After treatment in the referring hospital, the patient was successfully weaned from mechanical ventilation within one week. This case report illustrates that a structured approach to weaning failure can unmask hidden pathology and help in the development of a tailored treatment strategy.

Introduction

In most patients, mechanical ventilation can be discontinued as soon as the underlying reason for acute respiratory failure has resolved. However, approximately one third of patients are considered difficult to wean from mechanical ventilation and six percent of patients still require mechanical ventilation more than seven days after the first weaning attempt.[1] The pathophysiology of weaning failure is complex and multiple causes for difficult weaning may exist in any single patient. Determining the primary reason for weaning failure requires an in-depth knowledge of the underlying pathophysiology. For this purpose, we have recently developed a diagnostic approach for difficult weaning.[2] Our 'weaning ABC' enables clinicians to systematically review the most likely causes for weaning failure. If we understand the barriers that impede successful weaning in some patients, then tailored treatment strategies can be developed to free patients from mechanical ventilation. The following topics should be included in any evaluation of a difficult-to-wean patient: airway / lung dysfunction, brain dysfunction, cardiac dysfunction, diaphragm / respiratory muscle dysfunction, and endocrine / metabolic dysfunction. In this article we demonstrate how the ABC approach can be used in clinical practice. This case report does not discuss the rationale for each individual diagnostic technique in depth, as this has recently been published elsewhere.[2]

Case report

A 68-year-old male, body weight 105 kg, height 1.84 m, was referred to our centre for evaluation of difficult weaning from mechanical ventilation. The patient's past medical history revealed chronic obstructive pulmonary disease (COPD) GOLD IV, paroxysmal atrial fibrillation, alcohol abuse and struma. Furthermore, the patient had a 53-pack-year history of smoking. Before hospital admission he lived independently with regard to daily activities, but had some help with housekeeping. The patient was admitted to hospital with an acute exacerbation of COPD due to pneumonia (pH 7.32, $PaCO_2$ 8.8 kPa, HCO_3^- 33 mmol/L). The following day the patient was admitted to the intensive care unit (ICU) with progressive respiratory failure (pH 7.29, $PaCO_2$ 9.6 kPa) and invasive ventilation was initiated. After three days he was successfully extubated. However, after two weeks, while still in hospital, he was readmitted to the ICU for invasive mechanical ventilation due to progressive respiratory failure. Despite multiple attempts, he could not be weaned from the ventilator during the next three weeks due to "exhaustion". On referral to our centre, he was able to sustain

a spontaneous breathing trial (SBT) through a tracheostomy tube for a few hours. The ABC approach for difficult weaning was used to identify the pathophysiology of weaning failure in this patient.[2]

In order to perform the measurements required for analysis of weaning failure, a pulmonary artery catheter was inserted through the patient's right jugular vein. Also, a nasogastric tube with oesophageal and gastric balloons and multiple electrodes for diaphragm electromyography were inserted. The patient could sustain the first SBT, disconnected from the ventilator and breathing through a T-tube with supplemental oxygen, in our centre for 18 hours.

A: airway and lung dysfunction

Impaired respiratory mechanics increase the work of breathing, and may contribute to a failed weaning trial. Respiratory mechanics were assessed using a technique applicable in awake patients. Briefly, the patient was ventilated in volume control mode overriding his respiratory drive . One must be careful not to increase intrinsic positive end-expiratory pressure (PEEPi) during this technique and thereby influence respiratory mechanics. Subsequently, end-inspiratory and end-expiratory occlusions were performed to calculate compliance and airway resistance (see *table 1*). Diaphragm electromyography was used to exclude activity of the respiratory muscles during volume control ventilation. The patient's static lung compliance (56 ml/cmH_2O), chest wall compliance (152 ml/cmH_2O), respiratory system compliance (41 ml/cmH_2O) and airway resistance (11.5 cmH_2O/L/s) were calculated. The work of breathing (WOB) was derived from the Campbell diagram (*figure 1*). WOB increased from 0.8 J/min to 1.38 J/min during the 18 hour SBT without an increase in PEEPi. An increase in PEEPi during spontaneous breathing, that is hyperinflation, is associated with weaning failure.[3]

Gas exchange remained adequate during the SBT, with only a slight increase in $PaCO_2$ (but normal pH), shunt and Aa-gradient (*table 2*). Formula derivations for shunt and Aa-gradient can be found in *table 1*.

Previous studies have shown that malposition of a tracheostomy tube can contribute to difficult weaning.[4] Videobronchoscopy was performed while the patient was disconnected from the ventilator and revealed granulation tissue at the distal end of the tracheostomy tube. This resulted in an approximately 50% obstruction of the cannula during expiration.

B: brain function (cognitive)

Among other cognitive disorders, delirium and depression have been associated with difficult weaning.[5] During admission to our centre, the patient was not found to be delirious according to the Confusion Assessment Method for the ICU. During the SBT the patient was very anxious for the development of hypercapnic coma and repeatedly requested to be reconnected to the ventilator. However, as blood gas analysis did not reveal any physiological reasons for failure, we were able to convince the patient to carry on with the SBT. Indeed, with verbal support he was able to sustain the weaning trial for 18 hours. The patient's fear of hypercapnic coma had resulted from a previous event, where he had developed severe hypercapnia at home. An evaluation by a psychiatrist did not reveal any evidence of depression.

C: cardiac function

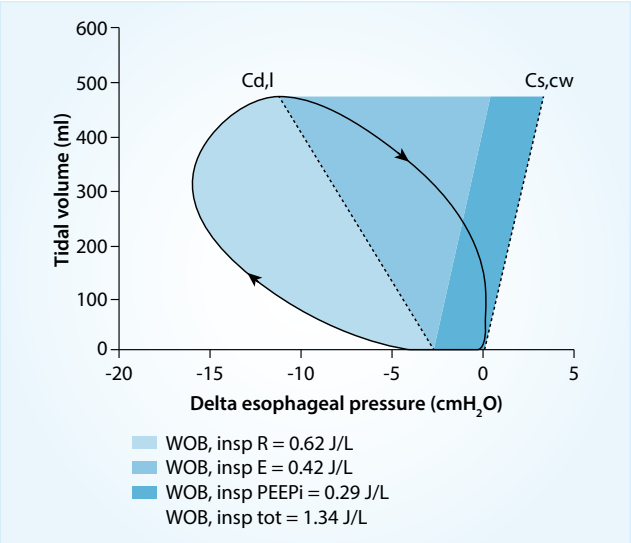
Evidence is accumulating in the literature that cardiac dysfunction, either systolic or diastolic, is a very common cause of weaning failure.[6-9] In our patient, transthoracic echocardiography during pressure support ventilation revealed

Table 1. Formula derivations for frequently used variables to calculate respiratory mechanics and gas exchange. Note: unit for pressure in the formulas for calculation of respiratory mechanics is cmH_2O. Unit for pressure in the formulas for calculation of gas exchange is mmHg, conversion factor from kPa to mmHg is 7.5. Unit for Hb is g/dL, conversion factor from mmol/L to g/dL is 1.6

Variable	Abbreviation	Derivation	Normal value
Static respiratory system compliance	Cs,rs (ml/cmH_2O)	ΔVt / (Paw,EIO – Paw,EEO) = $Cs,l^{-1} + Cs,cw^{-1}$	100
Static lung compliance	Cs,l (ml/cmH_2O)	ΔVt / (Ptp,EIO – Ptp,EEO)	200
Static chest wall compliance	Cs,cw (ml/cmH_2O)	ΔVt / (Ptt,EIO – Ptt,EEO)	200
Transpulmonary pressure	Ptp (cmH_2O)	Paw – Pes	
Transthoracic pressure	Ptt (cmH_2O)	Pes – Pb	
Airway resistance	Raw (cmH_2O/L/s)	(Paw,peak – Paw,EIO)/ Flow	< 5
Shunt	QS/QT (%)	(CcO_2 - CaO_2) / (CcO_2 - CvO_2)	< 5
Arterial oxygen content	CaO_2 (ml/dL)	1.34 x Hb x SaO_2 + (0.003 x PaO_2)	16 - 22
Mixed venous oxygen content	CvO_2 (ml/dL)	1.34 x Hb x SvO_2 +(0.003 x PvO_2)	12 - 17
Pulmonary capillary oxygen content	CcO_2 (ml/dL)	1.34 x Hb x 1 +(0.003 x PAO_2)	
Partial pressure of alveolar oxygen	PAO_2 (mmHg)	PiO_2 - ($PaCO_2$ / RQ)	
Partial pressure of inspired oxygen	PiO_2 (mmHg)	FiO_2 x (Pb – PH_2O)	
Oxygen delivery	DO_2 (ml/min)	CO x CaO_2	600 - 1200
Oxygen consumption	VO_2 (ml/min)	CO x (CaO_2 - CvO_2)	200 - 280
Oxygen extraction ratio	O_2ER	VO_2 / DO_2	0.23-0.32
Alveolar-arterial gradient	Aa-gradient (mmHg)	PAO_2 - PaO_2	7 - 14

CO = cardiac output, EEO = end-expiratory acclusion, EIO = end-inspiratory occlusion, Paw = airway pressure, Pb = barometric pressure, Pes = esophageal pressure, PH_2O = water vapour pressure, Hb = hemoglobin, RQ = respiratory coefficient , Vt = tidal volume.

Figure 1. Example of Campbell diagram to visualize work of breathing during spontaneous breathing. The two dashed lines represent the static chest wall compliance (Cs,cw) and dynamic lung compliance (Cd,l). The solid line with arrows represents the breathing cycle. Work of breathing is normally expressed in joules. One joule is the energy needed to move 1 liter of gas throught a 10 cmH_2O pressure gradient. Light blue area represents inspiratory work of breathing to overcome resistive forces (WOB, insp R). Medium blue area represents inspiratory work of breathing to overcome eleastic forces (WOB, insp E). Dark blue area represents inspiratory work of breathing to overcome intrinsic positive end-expiratory pressure (WOB, insp PEEPi). Normal total work of breathing (WOB, insp tot) in young healthy subjects is 0.47 ± 0.22 J/L



a reasonable systolic function (left ventricular ejection fraction 40%), but there was evidence of severe diastolic dysfunction (grade III; lateral E/e' = 13.3).[10]

Cardiac index and SvO_2 obtained from the pulmonary artery catheter, gradually increased during the SBT (*table 3*), indicating an adequate cardiac response to the increased WOB. NT-proBNP increased during the SBT (*table 3*). NT-proBNP is a hormone secreted by ventricular cardiomyocytes in response to increased ventricular wall stress. Also, pulmonary capillary wedge pressure increased during the SBT (*table 3*). Arterial blood pressure and pulmonary artery pressure were high from the start and increased during spontaneous breathing (*table 3*). ECG before and after 18 hours of spontaneous breathing did not reveal any signs of myocardial ischemia.

D: diaphragm / respiratory muscle dysfunction

Critical illness has profound effects on respiratory muscle structure and function.[11-13] Therefore, respiratory muscle weakness is a common cause of weaning failure. Maximal airway pressures were assessed using a handheld electronic manometer, by connecting the device to the tracheostoma via a swivel connector, to assess global respiratory muscle strength.[14] In our patient maximal inspiratory pressure was 60 cmH_2O (normal value ±100 cmH_2O) and maximal expiratory pressure 125 cmH_2O (normal value ±150 cmH_2O).[14]

Ultrasonography of the diaphragm revealed normal motion of the right hemidiaphragm during unassisted breathing and with sniffing (*figure 2*).[15] There was no adequate window to quantify movement of the left hemidiaphragm with ultrasound.

Measures of inspiratory effort, such as electrical activity of the diaphragm (EAdi) and transdiaphragmatic pressure swings (Δ Pdi = Δ gastric pressure – Δ oesophageal pressure) increased after disconnection from the ventilator, but reached a plateau after five hours of spontaneous breathing (*table 4*). The ratio between Pdi and EAdi, representing neuro-mechanical efficiency, remained stable during spontaneous breathing (*table 4*). This suggests that the capacity of the respiratory muscles was enough to counteract the increased load of breathing. In other words, there was no neuro-mechanical uncoupling or fatigue of the diaphragm. Also the ratio between tidal volume and EAdi, representing neuro-ventilatory efficiency (NVE), reached a plateau (*table 4*). NVE has been used to discriminate

Table 2. Gas exchange at different time points during 18 hours of spontaneous breathing. PSV level before SBT is 8 cmH_2O with 8 cmH_2O PEEP. During SBT patient is breathing through T-tube

Time	Resp. freq.	Tidal volume (mL)	pH	PaO_2 (kPa)	$PaCO_2$ (kPa)	HCO_3-(mmol/L)	Base Excess (mmol/L)	SpO_2 (%)
PSV	25	339	7.45	10.9	6.6	33.9	8.7	100
SBT 10 min	22	354	7.44	19.1	6.8	34.1	8.7	98
SBT 12 hr	23	374	7.41	15.5	7.3	34.1	8.2	99
SBT 18 hr	22	382	7.40	14.2	7.7	34.9	8.6	99

Time	Shunt (%)	DO_2 (mL/min)	VO_2 (mL/min)	O_2 extraction ratio	Aa-gradient (mmHg)
PSV	9	772	245	0.32	142
SBT 10 min	17	834	210	0.25	150
SBT 12 hr	15	986	266	0.27	172
SBT 18 hr	19	1132	238	0.21	178

DO_2 = oxygen delivery, PEEP = positive end-expiratory pressure, PSV = pressure support ventilation, SBT = spontaneous breathing trial, VO_2 = oxygen consumption.

Table 3. Cardiac function at different time points during 18 hours of spontaneous breathing. PSV level before SBT is 8 cmH_2O with 8 cmH_2O PEEP. During SBT patient is breathing through T-tube

Time	PCWP (mmHg)	PAP (mmHg)	ABP (mmHg)	CVP (mmHg)	HR (bpm)	CI ($L/min/m^2$)	SvO_2 (%)	BNP (pg/mL)	Lactate (mmol/L)
PSV	5	39/24 (30)	150/70 (97)	5	79	2.5	69	74	0.9
SBT 10 min	7	42/24 (31)	139/83 (107)	7	70	2.7	74	-	-
SBT 12 hr	12	45/27 (31)	171/68 (95)	8	84	3.2	73	-	1.1
SBT 18 hr	17	49/28 (34)	169/68 (101)	4	89	3.6	79	2113	0.7

ABP = arterial blood pressure, NT-proBNP = n-terminal pro b-type natriuretic peptide, CVP = central venous pressure; CI = cardiac index; HR = heart rate; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure, SBT = spontaneous breathing trial.

Figure 2. Ultrasonographic M-mode images from the right hemidiaphragm. Left: normal breathing, the diaphragm moves 1.8 cm cephalad during inspiration. Right: sniff procedure, the diaphragm moves 2.4 cm cephalad

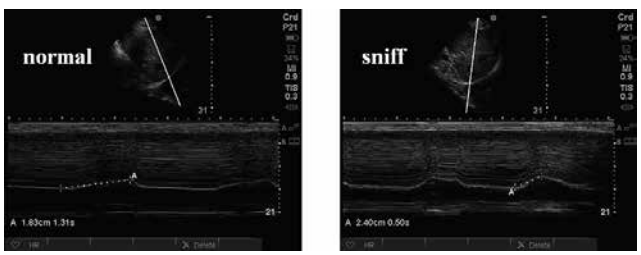
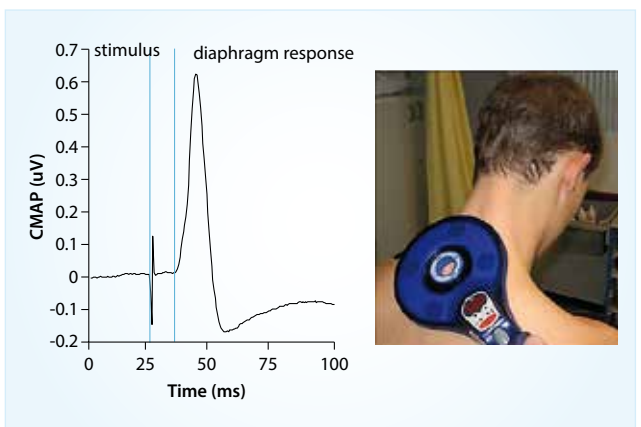


Figure 3. Left: Compound muscle action potential (CMAP) of the diaphragm in response to magnetic phrenic nerve stimulation. Right: Positioning of the magnetic coil around the spinous process of C7 to stimulate the phrenic nerves



between extubation failure and success in patients weaning from mechanical ventilation.[16]

Magnetic phrenic nerve stimulation was performed to evaluate the integrity of the phrenic nerve (*figure 3*). Phrenic nerve conduction time was slightly increased to 9 ms (normal value 7.1±0.7 ms). A mechanical response (transdiaphragmatic twitch pressure) could not be measured accurately in this patient.

E: endocrine and metabolic function

Very few studies have evaluated the contribution of endocrine dysfunction to difficult weaning. However, one remarkable paper by Huang & Lin reported that adrenal dysfunction may play a role in difficult weaning from mechanical ventilation.[17] In our patient, thyroid-stimulating hormone was slightly reduced (0.25 mE/L). Adrenal function could not be assessed due to the patient's chronic use of dexamethasone for COPD.

The patient's nutritional requirements were assessed during CPAP with a metabolic monitor and calculated at approximately 2300 kcal/24 hr. The caloric intake was adjusted accordingly.

Discussion

Difficult weaning from mechanical ventilation is a major challenge, even for the experienced clinician. At a first glance, one would expect that COPD (airway resistance, respiratory muscle weakness) would be the major determinant of difficult weaning in a patient in this vignette. However, extensive physiological evaluation during a spontaneous breathing

Table 4. Diaphragm function at different time points during 18 hours of spontaneous breathing. PSV level before SBT is 8 cmH_2O with 8 cmH_2O PEEP. During SBT patient is breathing through T-tube

Time	EADi (µV)	Pga (cmH_2O)	Pes (cmH_2O)	Pdi (cmH_2O)	PEEPi (cmH_2O)	NVE (ml/µV)	NME (cmH_2O/µV)
PSV	13	1	-4	5	2	29	0.38
SBT 10 min	23	1	-8	9	2	15	0.39
SBT 5 hr	37	1	-14	15	3	11	0.40
SBT 12 hr	35	1	-12	13	3	11	0.37
SBT 18 hr	37	1	-14	15	3	10	0.40

EAdi = electrical activity of the diaphragm, NME = neuro-mechanical efficiency, NVE = neuro-ventilatory efficiency, Pdi = transdiaphragmatic pressure, PEEPi = intrinsic positive end-expiratory pressure, Pes = esophageal pressure, Pga = gastric pressure, PSV = pressure support ventilation, SBT = spontaneous breathing trial.

trial revealed several remarkable findings. Both pulmonary capillary wedge pressure and NT-proBNP increased during the spontaneous breathing trial. This response is consistent with the development of heart failure.[18] Indeed, transthoracic echocardiography revealed severe diastolic dysfunction. How could diastolic heart failure explain failed weaning? Interstitial pulmonary oedema may develop with diastolic heart failure and has been shown to stimulate irritant receptors in the pulmonary interstitium. Activation of these irritant receptors contributes to sensation of dyspnoea.[19] Indeed, in our patient the increase in Aa-gradient (*table 2*) and elastic work of breathing is consistent with the development of pulmonary oedema. Therefore, the major cause of weaning failure in this patient was diastolic dysfunction.

Other factors contributing to weaning failure included the anxiety for hypercapnic coma and partial tracheostomy obstruction due to granulation tissue (thereby increasing airway resistance). Even though the patient received mechanical ventilation for more than three weeks, respiratory muscle strength and endurance were only slightly affected and not primarily responsible for weaning failure. Nevertheless, in many cases of failure to wean, respiratory muscle dysfunction plays an important role, therefore respiratory muscle function should be monitored effectively in critically ill patients.[20]

Based on the findings of the ABC analysis we formulated the following tailored treatment strategy: 1) Optimal treatment of diastolic dysfunction. During subsequent SBT's it was recommended to titrate continuous intravenous nitroglycerin to maintain systolic blood pressure well below 140 mmHg.[21] In addition, it has recently been shown that in patients with elevated BNP, a BNP driven fluid management strategy decreases the duration of weaning.[22] Furthermore, oral antihypertensive drugs were added to control hypertension throughout the day. 2) Consultation from a psychiatrist or psychologist to reduce anxiety. 3) Canula change and removal of granulation tissue. 4) Replacement of dexamethasone by prednisone to prevent a (further) reduction in respiratory muscle function. Fluorinated steroids may have a higher risk of inducing myopathies than non-fluorinated steroids.[23] This treatment strategy resulted in successful weaning from the ventilator within one week after analysis in the referring hospital.

In conclusion, this case report illustrates that a structured approach to weaning failure may unmask hidden pathology and help in the development of a tailored treatment strategy. We realize that some of the techniques used in this case report are not available in many centres, such as diaphragm electromyography, magnetic stimulation of the phrenic nerves and detailed analysis of respiratory mechanics. In addition, the interpretation of these measures requires expertise. Therefore, if routine assessment, as defined in our previous paper, does not reveal an obvious cause for weaning failure or first line treatment fails, then consultation with a centre of expertise such as ours should be considered.

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