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# A structural approach for diagnosing weaning failure

## A case from a specialised weaning centre

Using a case of a former patient we describe the structured approach of analysis of the cause of weaning failure with corresponding specific therapies used in our Centre for Expertise.

ing of intensive care nurses, residents, and intensivists. In the multidisciplinary team, physiotherapists and speech-language therapists (SLTs) play an important role besides other consultants (e.g. neurologist, psychiatrist, ENT specialist, rehabilitation medicine or pulmonologist). For mobilisation of our ventilated patients we use - besides regular training - our specialised gymnasium and our swimming pool (hydrotherapy), **Figure 1a** (Felten-Barentsz et al. 2015).

### Case

We describe the case of a 65 year old female referred to our unit from another hospital with prolonged mechanical ventilation of 13 days and multiple unsuccessful spontaneous breathing trials (SBTs).

She had a history of hypertension, cardiac failure (unclear aetiology) and peripheral and central vascular disease for which she had multiple times surgery (among others placement of an aortic bifurcation prosthesis with multiple revisions). She suffered from recurrent pleural and pericardial effusion.

The patient was admitted to the referring hospital 3 weeks previously with dyspnoea and signs of cardiac failure. A pleural centesis was complicated by haemothorax leading to haemodynamic instability and admission to the ICU. During the ICU admission in the referring hospital, she had recurrent pleural and pericardial effusion and acute-on-chronic kidney failure for which she needed renal replacement therapy. Intermittent hypertension appeared difficult to control.

In our unit, physical examination showed bilateral basal crackles with a regular heart rhythm and a systolic murmur. She had a

soft, nontender, distended abdomen. She had generalised oedema and a sacral decubitus wound. She was ventilated with pressure support mode (PS) 20 above 8 cmH<sub>2</sub>O positive end-expiratory pressure (PEEP), tidal volume ca. 420 mL, spontaneous respiratory rate 30/min, FiO<sub>2</sub> 0.50.

Our structured approach for the causes of weaning failure showed the following during a SBT using a T-piece trial:

### Airway and lung dysfunction

Factors increasing the work of breathing and thereby contributing to weaning failure, are increased airway resistance, decreased lung or chest wall compliance and impaired gas exchange.

Increased airway resistance may be due to the endotracheal tube and central or smaller airways. Sputum retention or plug can be a problem in the endotracheal tube or central airways, and tracheomalacia or tracheal stenosis can also cause obstruction in the central airways. Both can be visually inspected by performing a flexible bronchoscopy. Increased resistance of smaller airways can be a problem in patients with chronic obstructive pulmonary disease (COPD) and is associated with the development of intrinsic positive end-expiratory pressure (PEEPi). Increased airway resistance can also develop in patients failing during a T-piece trial (Jubran and Tobin 1997). Intrinsic PEEP is measured during controlled ventilation by performing an end-expiratory occlusion manoeuvre and during assisted ventilation by measuring the drop in oesophageal pressure (Pes) before inspiratory flow begins.

**Table 1** shows the results for these measure-

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Previously, we suggested a structural approach for diagnosing the cause of weaning failure (Heunks and van der Hoeven 2010; Schellekens et al. 2016). Here we discuss how we apply 'the ABC of weaning failure' at the Radboudumc Centre of Expertise for Weaning from Mechanical Ventilation using the case of a former patient. At our centre patients are admitted who failed previous weaning trials. Once a patient is admitted to the weaning centre, the first aim is to establish a firm diagnosis for the cause(s) of weaning failure. When the cause(s) are clarified, an individualised strategy for treating the patient is determined.

Our centre for expertise consists of 4 beds (expanding) and has a staff consist-



**Figure 1.** left, **a:** hydrotherapy with a ventilated patient. right, **b:** physiotherapy with family participation in a weaning patient.

Respiratory parameter	SBT duration (minutes)				
	5	30	60	120	180
Respiratory rate [breaths/minute]	32	31	32	31	32
Tidal volume [mL]	296	287	313	295	388
Minute ventilation [L/minute]	9.4	8.9	9.9	9.2	12.1
$\Delta$ Pes [cmH <sub>2</sub> O]	-15.9	-14.2	-16.0	-18.4	-21.4
$\Delta$ Pga [cmH <sub>2</sub> O]	5.5	4.9	3.6	1.6	4.2
$\Delta$ Pdi [cmH <sub>2</sub> O]	21.4	19.1	19.6	20.0	25.6
PEEPi [cmH <sub>2</sub> O]	3.5	2.7	2.6	2.9	3.5
$\Delta$ EAdi [ $\mu$ V]	10.9	10.3	13.3	16.4	20.8
Dynamic lung compliance [mL/cmH <sub>2</sub> O]	39.3	40.3	36.4	30.8	43.3
Airway resistance [cmH <sub>2</sub> O/L/s]	16	15	17	19	19
NMEx [cmH <sub>2</sub> O/ $\mu$ V]	2.0	1.9	1.5	1.2	1.2
NVE [mL/ $\mu$ V]	27.2	27.9	23.5	18.0	18.7
WOB [J/L]	1.3	1.2	1.3	1.5	1.8

**Table 1.** Respiratory parameters during the course of a SBT.

SBT = spontaneous breathing trial; Pes = oesophageal pressure; Pga = gastric pressure; Pdi = transdiaphragmatic pressure; EAdi = electrical activity of the diaphragm; NMEx = neuromechanical efficiency; NVE = neuroventilatory efficiency; WOB = work of breathing

	Start SBT	1 hour SBT
pH	7.47	7.44
PaCO <sub>2</sub> [mmHg]	41	49
PaO <sub>2</sub> [mmHg]	117	67
HCO <sub>3</sub> <sup>-</sup> [mmol/L]	29.0	31.9
Base excess [mmol/L]	4.8	6.9
SaO <sub>2</sub> [%]	98	93
E [cm/s]	113	140
A [cm/s]	128	100
E/A	0.88	1.40
E' [cm/s]	7.00	6.59
E/E'	16.1	21.2

**Table 2.** Bloodgas and echocardiography results before and after a SBT.

Our patient was suffering from anxiety but did not show signs of *delirium* (CAM-ICU) or depression. She did have an acceptable *sleep quality* (NRS), (Rood et al. 2019). We regularly try to avoid benzodiazepines. Regarding management of anxiety interventions as cognitive behavioural therapy and the professional and patient attendance by our team of ICU nurses play an important role.

### Cardiac dysfunction

The conversion from mechanical ventilation to spontaneous breathing leads to changes in intrathoracic pressure affecting ventricular pre- and afterload and a necessary increase

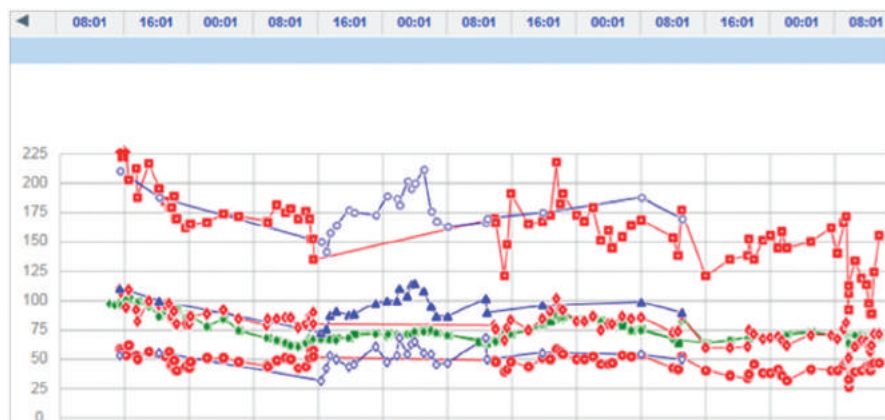
ments. Our patient had a low *dynamic lung compliance* of 30 to 44 (normal compliance range 60-100) mL/cmH<sub>2</sub>O, which remained constant during the SBT. A low lung compliance can have several causes, such as lung oedema, pneumonia or hyperinflation. We found a small amount of *PEEPi*, remaining constant during the SBT and therefore we could exclude hyperinflation. The *airway resistance*

was normal and remained constant during the SBT, therefore we concluded that this did not play a major role in the weaning problem.

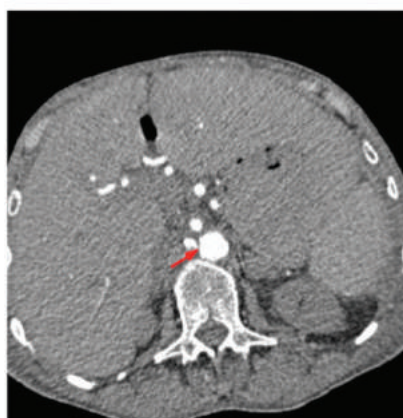
### Brain dysfunction

Brain dysfunction is associated with a higher risk of failed extubation and *anxiety* and *depression* may interfere with successful weaning (van den Boogard et al. 2012).





**Figure 2.** Blood pressure [arterial, red and non-invasive, blue (mmHg)]; heart rate [green (/min)] over time showing better blood pressure control with intensified therapy [AT2-agonist, nitroglycerin, and intensive fluid removal]



**Figure 3.** CT angiogram: severe stenosis at the origin of the left (a) and right (b) renal artery

in cardiac output due to increased oxygen consumption by respiratory muscles (Dres et al. 2014).

Cardiac function can be investigated non-invasively by electrocardiography (ECG) and echocardiography. An increase in brain natriuretic peptide (BNP, increase of  $\geq 48$  ng/L or  $\geq 12\%$ ) during weaning is also a reliable sign of a cardiac cause of weaning failure. If this does not clarify the problem, a pulmonary arterial catheter can be inserted to measure pulmonary arterial occlusion pressure and cardiac index. Transpulmonary thermodilution may be used to determine extravascular lung water (increased when  $\geq 14\%$ ) (Lemaire et al. 1988; Dres et al. 2014).

NT-proBNP level of our patient was  $>35000$  (normal  $<300$ ) pg/mL before and after a SBT. Although we could not determine an increase during weaning, a cardiac cause for weaning failure was suspected.

Her ECG did not show signs of ischaemia before and after a SBT. Thus cardiac ischaemia as a cause of weaning failure was deemed to be unlikely.

Echocardiography showed an enlarged left atrium with a hypertrophic left ventricle with good contractility without segmental wall motion abnormalities and a good right ventricular function. The aortic annulus showed calcification without stenosis, a minimal tricuspid insufficiency was seen with an estimated pulmonary systolic pressure of 50–55 mmHg. There was an increase in E/A and E/E' after the SBT compared to before consistent with congestive heart failure with preserved ejection fraction (diastolic dysfunction, Table 2). Treatment consisted of afterload reduction by blood pressure control and intensive fluid removal via haemofiltration.

Our patient had a decrease in  $\text{PaO}_2$  after 1 hour SBT (Table 2). At this point haemofiltration

with fluid removal was initiated (more than 3 L) which led to improvement of  $\text{SpO}_2$ , thus the SBT could eventually be continued until the evening (7 hours). This course was consistent with our final conclusions.

Our patient suffered from a difficult to treat hypertension (Figure 2). Regarding the difficulty of blood pressure control also in the referring hospital, we felt the need to exclude a renal cause of hypertension by means of a contrast CT scan, which showed severe stenosis at the origin of the left and the right renal artery (Figure 3). After consulting the nephrologist and the interventional radiologist, we concluded that there was no invasive treatment possible due to atherosclerosis and risk of complications and that the patient would need chronic haemodialysis. We focussed on medical treatment of hypertension with an AT2-antagonist (allergy for ACE inhibitor), nitroglycerin during SBTs (Routsi et al. 2010) and on fluid removal using haemodialysis.

### Diaphragm/respiratory muscle function

During mechanical ventilation respiratory muscle dysfunction rapidly develops and is associated with difficult weaning (Jaber et al. 2011; Hooijman et al. 2015; Goligher et al. 2018). Importantly, diaphragm weakness is not the same as intensive care unit acquired weakness (Dres et al. 2017), in other words, the diaphragm can be weak without peripheral muscle weakness and vice versa. Therefore, respiratory muscle function itself should be monitored (Doorduyn et al. 2013). It can be monitored using different techniques; here we will focus on measuring the electrical activity of the diaphragm (EAdi) and transdiaphragmatic pressure (Pdi; computed as gastric (Pga) minus oesophageal (Pes) pressure).

In our patient, a T-piece trial was performed while measuring flow, EAdi, Pes, and Pga. She had a relatively high respiratory rate with low tidal volumes (Table 1). EAdi varied between 10–21  $\mu\text{V}$ , which can be considered normal. The inspiratory decrease in Pes was moderate to high (13–19  $\text{cmH}_2\text{O}$ ), while the inspiratory increase in Pga was also high (3.3–7.0  $\text{cmH}_2\text{O}$ ), resulting in a Pdi (18–25  $\text{cmH}_2\text{O}$ ) higher than cut-off values defining diaphragm weakness (i.e. 11  $\text{cmH}_2\text{O}$ ) (American Thoracic Society/European Respiratory Society 2002). In addition, neuromechanical efficiency (NME; i.e.

*P<sub>di</sub>/EAdi*) was relatively high (Doorduyn et al. 2018). These respiratory parameters indicate that there was no sign of *diaphragm weakness*. Furthermore, the patient had a *high breathing effort* (normal range work of breathing (WOB) 0.2–0.9 J/L) mainly due to a low *dynamic lung compliance* (Table 1). In this patient, there was no need for inspiratory muscle training (Martin et al. 2002).

### Endocrine and metabolic dysfunction

Adrenal insufficiency (Huang and Lin 2006) and hypothyroidism (Datta and Scalise 2004) have been described as possible reasons for weaning failure accompanied by successful treatments though the literature is scarce. Our patient had a normal TSH 1.76 (normal range 0.27–4.2) mE/L. Aldosterone level was elevated 0.87 (normal range 0.08 – 0.69) nmol/L. Renin level was increased as well 120 (normal range 4.4 – 85) mU/L matching with the diagnosis of renal artery stenosis. A short ACTH test showed an adequate reaction (baseline 0.65, 30 min 0.89 and 60 min 0.97 µmol/L).

### Feeding and dysphagia

*Malnutrition* frequently occurs in critically ill patients and is associated with higher mortality (Mogensen et al. 2015) and reduced muscle mass contributing to difficult weaning. During spontaneous ventilation patients have an increased energy expenditure compared to controlled ventilation (Hoher et al. 2008). Patients ventilated more than 48 hours have a high risk of dysphagia (Skoretz et al. 2010), which has a relation with duration of intubation, age, muscle weakness, and neurological diseases. Screening for *dysphagia* after extubation by ICU nurses or SLTs improves oral intake (See et al. 2016). Fiberoptic endoscopic

evaluation of swallowing (FEES) can help in the work-up (Scheel et al. 2016).

We use indirect calorimetry to estimate individual necessary intake of calories (our patient 1894 kCal/day) and an estimate for targeted protein intake (1.2–1.5 g/kg/d). Our patient was fed via a nasogastric tube. She did not have signs of dysphagia after extubation, and oral intake could be increased.

### Conclusion

In our opinion, an individualised structural evaluation of weaning failure helps to find the underlying causes of weaning failure and to prescribe an individualised treatment plan. We think that our patients benefit from separating our more acute care ICUs from this specialised unit, being able to focus on a different kind of patient with a dedicated staff (Figure 1b). We recently showed that difficult to wean patients treated at our unit had a high rate of successful weaning (79%) (Frenzel 2018). Our patients were vulnerable before admission with an increase of their frailty at discharge improving modestly after 3 months (clinical frailty score), while mental health was comparable to the situation before admission (SF 36). However, we do not know yet what the relevance of this approach is regarding the whole population of patients with prolonged mechanical ventilation and weaning failure in terms of outcome parameters such as ventilator-free days, mortality or quality of life. Currently, the MONITOR-IC study is investigating the effects and consequences of ICU admission on quality of life during five years after ICU admission (Geense et al. 2017). Also, patients admitted to our weaning centre are included in this study, and we hope to be able to report these results soon.

The identified factors for weaning failure that played a role in our described patient were:

- CHF with preserved ejection fraction (diastolic dysfunction)
- Acute-on-chronic kidney failure
- Difficult to treat hypertension due to renal artery stenosis
  - Leading altogether to peripheral and lung oedema

She was treated with:

- No angiographic/surgical intervention due to severe atherosclerosis with increased risk of complications
- Intensive fluid removal with haemodialysis (total negative fluid balance 9.6 L)
- Nitroglycerin during SBT (systolic blood pressure < 150 mmHg) to prevent CHF due to increased afterload
- Treatment of hypertension with AT2 antagonist

Our patient could be successfully weaned from the ventilator and extubated within 4 days. ■

### Key points

- Factors increasing the work of breathing and thereby contributing to weaning failure, are increased airway resistance, decreased lung or chest wall compliance and impaired gas exchange.
- Brain dysfunction is associated with a higher risk of failed extubation and anxiety, sleep disturbances and depression may interfere with successful weaning.
- During mechanical ventilation respiratory muscle dysfunction rapidly develops and is associated with difficult weaning, but not with peripheral muscle weakness.
- Adrenal insufficiency and hypothyroidism have been described as possible reasons for weaning failure accompanied by successful treatments.
- Malnutrition frequently occurs in critically ill patients and is associated with higher mortality and reduced muscle mass contributing to difficult weaning.
- An individualised structural evaluation of weaning failure helps to find the underlying causes of weaning failure and to prescribe an individualised treatment plan.

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