1. 依據你對鬱血性心臟衰竭的瞭解，若你要進行『High Interval versus Moderate Intensity Exercise to Congestive Heart Failure: The Randomized Controlled Trial』的研究計劃，請說明你的研究設計，包括受試者選取標準（5 分），評估項目（10 分），以及運動介入內容（10 分）。（共計 25 分）

2. 請閱讀下列節錄文章後，說明睡眠呼吸中止症與心房震顫相關性的可能機制。（25 分）

Although the majority of evidence supports a strong association between sleep apnea and atrial fibrillation (AF), it remains unclear whether sleep-disordered breathing (SDB) is causal in the development of AF, as the two conditions share many of the same risk factors. Furthermore, the mechanism by which this may occur remains unclear. For example, obesity is a common risk factor for SDB and AF. But whether the link underlying the association is obesity itself or resulting effects on left atrial pressure and size, inflammatory and pro-fibrotic molecules, insulin resistance, or increased mean arterial blood pressure and atrial fibrosis is unknown. It has been suggested that the physiologic changes of SDB including intermittent hypoxia, hypercarbia, and intrathoracic pressure fluctuations predispose to arrhythmia through electrical and structural remodeling.

The proposed mechanism by which hypoxia promotes AF is via autonomic nervous system dysfunction and electrical remodeling. In a dog model of intermittent hypoxia, Lu and colleagues found that hypoxia initially resulted in parallel changes in heart rate variability (HRV) indices associated with sympathetic and parasympathetic activity such that the atrial effective refractory period (AERP) and AF vulnerability were not affected. However, with repeated hypoxic episodes, the parasympathetic indices of HRV were increased to a greater extent relative to sympathetic indices, and the AERP and AF vulnerability were also increased. This suggests that autonomic system imbalance may precipitate electrical changes in the atria that predispose to AF. Autonomic nervous system dysfunction is further supported in the development of AF based on studies of central sleep apnea (CSA) patients in whom increased concentrations of plasma and urinary norepinephrine and epinephrine have been documented, independent of left ventricular dysfunction.

Hypercarbia has also been implicated in electrical remodeling. In a sheep model, Stevenson et al found an inverse linear association between the effective refractory periods of the right and left atria and end-tidal CO_2 levels in hypercarbic sheep that was not present in the hypoxic or control sheep. In addition, atrial conduction times during pacing at a constant cycle length and during extra-stimulus testing were significantly prolonged during and after resolution of hypercapnia. In contrast, no

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corresponding changes in conduction times were observed in the hypoxic or control sheep during or after resolution of hypoxia. Interestingly, AF vulnerability was eliminated during hypercapnia but was significantly increased following resolution of hypercapnia and normalization of ERP. This suggests that hypercapnia may not promote AF acutely, but rather may promote electrical substrate remodeling over time after repeated exposure.

There is also data suggesting that hypercapnia can result in cardiac structural changes. In studies of ventricular myocytes isolated from rat hearts, White et al observed that exposure to medium with high levels of CO_2 resulted in decreased cell to cell conduction. Vorperian and colleagues exposed anesthesized dogs to an elevated mixture of inhaled CO_2 with resultant decrease in serum pH. They found that hypercarbia resulted in slowed propagation of impulses in the transverse direction, perhaps due to connexin (連接蛋白) dysfunction. However, it is unclear why these changes would occur selectively in the transverse rather than longitudinal direction and whether these structural changes occur in the atrium as well.

Fluctuations in intrathoracic pressure have also been implicated in electrical remodeling. Sympathetic stimulation during acute episodes of tracheal obstruction can produce increased intracellular calcium load, leading to shortening of action potential duration and initiation of AF. In a porcine model, Linz and colleagues simulated tracheal occlusion with and without the application of negative intrathoracic pressure (NTP). They found a significant decrease in the atrial effective refractory period (AERP) after two minutes of tracheal occlusion with -100mbar. In contrast, tracheal occlusion without NTP had no effect on AERP. The change in AERP was associated with increased inducibility of AF. Linz also investigated the effect of autonomic changes; atropine prevented AERP shortening in NTP, did not affect the AERP during normal breathing and decreased AF inducibility with NTP from 91% to 17%. These data suggest that negative intrathoracic pressure can precipitate electrophysiologic changes that increase the inducibility of AF, and that these changes may be mediated by an autonomic effect.

(以上摘要修改自Tung P, Anter E. Atrial fibrillation and sleep apnea: considerations for a dual epidemic. Journal of Atrial Fibrillation 2016;8(6):1283.)

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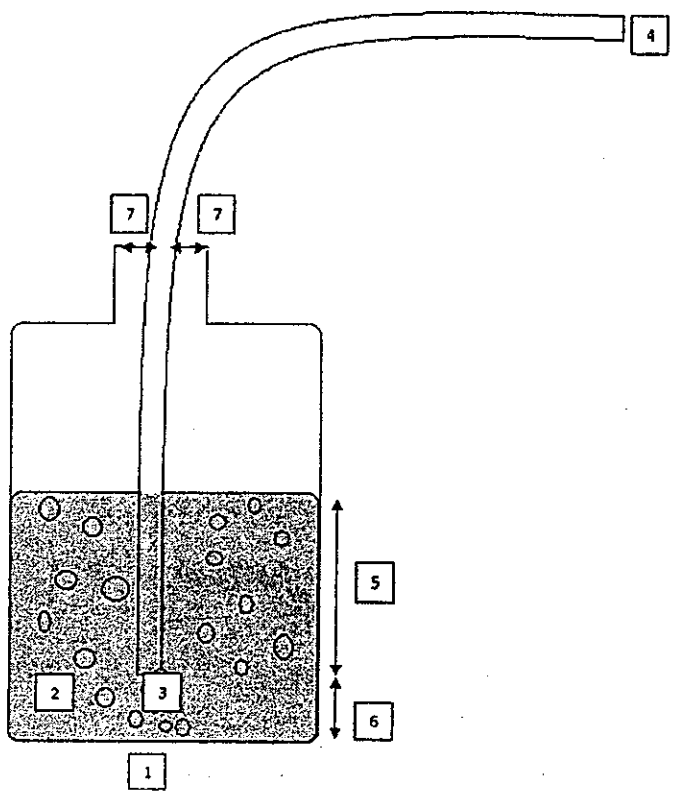
下圖摘自：Santos, M., Milross, M., Alison, J. (2016).Cardiopulmonary Physical Therapy Journal, 27(1), 3-10.



(1) Container; (2) water in container; (3) tubing end in container; (4) tubing end in mouth; (5) water column height; (6) space between end of tubing and base of container; (7) air escape orifice.

使用說明：患者嘴巴含住(4)，以鼻子吸氣，吐氣時，把氣經(4)吐至水瓶內。

3. 試述： 臨床上，物理治療師可以用此簡單設備來？（10 分）
4. 呈上題：其作用原理為？（10 分）

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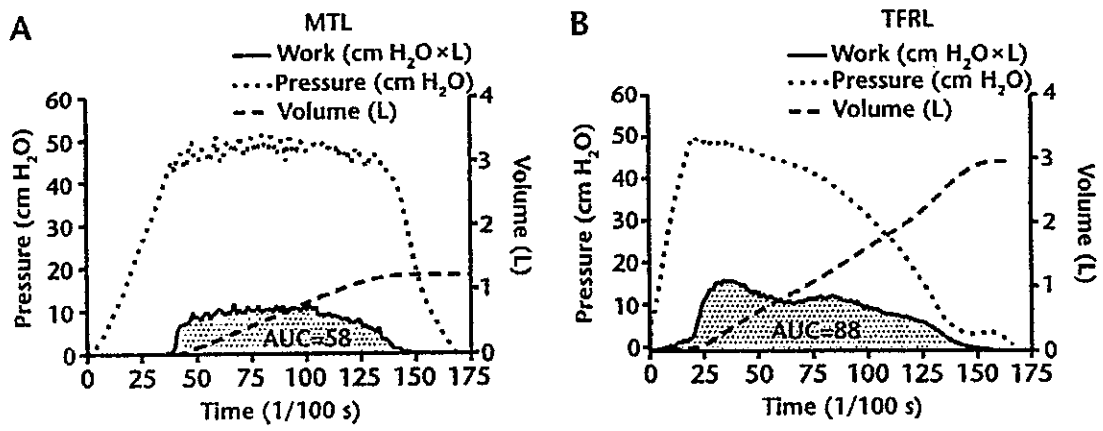
下圖及文摘自：Langer D, Charususin N, Jácome C, Hoffman M, McConnell A, Decramer M, Gosselink R. Efficacy of a Novel Method for Inspiratory Muscle Training in People With Chronic Obstructive Pulmonary Disease. Phys Ther. 2015;95(9):1264-73.



圖說明：Comparison between 2 training devices during a typical inhalation against a resistance corresponding to 60% of baseline maximal inspiratory pressure (50 cm H_2O): (A) MTL: mechanical threshold loading, (B) TFRL; tapered flow resistive loading. AUC: area under the curve for total external inspiratory work as integrated from mouth pressure (cm H_2O) and volume (L) signals over time.

Above figure illustrates the comparison of a single inhalation undertaken by a patient during MTL and a single inhalation undertaken by the same patient during TFRL. The TFRL device applies a tapered resistance provided by an electronically controlled, dynamically adjusted valve, which contrasts to the constant load applied by the MTL device. After flow-independently overcoming an initial threshold load (in this case, 50 cm H_2O, corresponding to 60% of the individual's PImax on both devices), pressure remained constant during MTL, whereas pressure was volume-dependently tapered during TFRL. This reduction of the absolute load during inhalation against the TFRL accommodates the pressure-volume relationship of the inspiratory muscles and thereby helps to maintain resistance at the same relative intensity throughout inhalation. This application of a tapered load allows end-inspiratory volume to approach total lung capacity, even at high training intensities. It is apparent from the example shown in Figure that this patient with COPD, training at 60% of his PImax, was able to achieve an inspiratory volume during TFRL that was twice that achieved during MTL. Furthermore, due to this higher inspiratory tidal volume, more external work was performed per breath (see Fig., area under the curve), despite a lower mean inspiratory pressure during inhalation. These observations confirm limitations to the intensity of pressure threshold loading that were recently identified in healthy people. In that study, the authors found that the amount of external mechanical work

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undertaken during loading 60% of PImax decreased considerably due to impairment of tidal volume expansions and premature termination of inhalation. In this way, high intensity TFRL (in contrast to MTL) provides a training stimulus to the inspiratory muscles at shorter lengths that corresponds to operating lengths of these muscles during exercise (especially in patients with COPD who dynamically hyperinflate).

從圖、文所提供的資訊，回答下列問題：

5. 簡述臨床上 COPD 患者進行吸氣肌訓練的困難（限制）為？（5 分）
6. 試述 TFRL 訓練的特性及其與 MTL 的不同。（10 分）
7. 請問若要回答「TFRL 或 MTL 對 COPD 患者吸氣肌的訓練，何者較佳」的研究問題，實驗應該要如何設計？（15 分）

試題隨卷繳回