Management of Mechanical Ventilation in Patients with Obstructive Lung Disease

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胸腔內科暨重症系

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1. Non-invasive mechanical ventilation

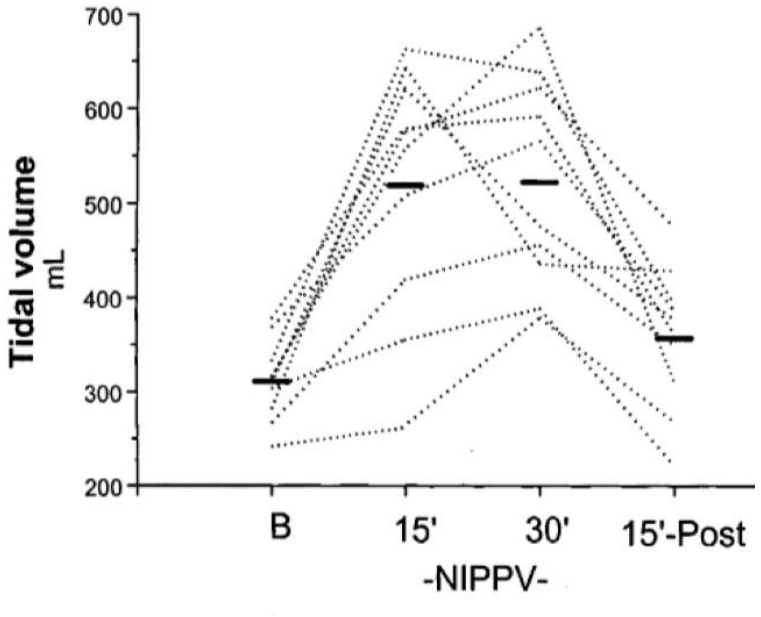
High-flow nasal cannula

2. Invasive Mechanical ventilation

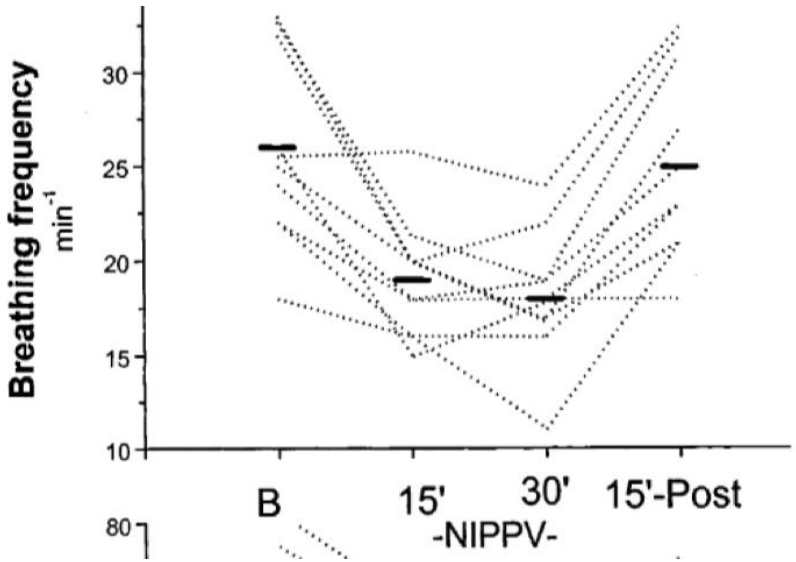
3. Aerosol therapy in MV

Effects of Noninvasive Ventilation on Pulmonary Gas Exchange and Hemodynamics during Acute Hypercapnic Exacerbations of Chronic Obstructive Pulmonary Disease

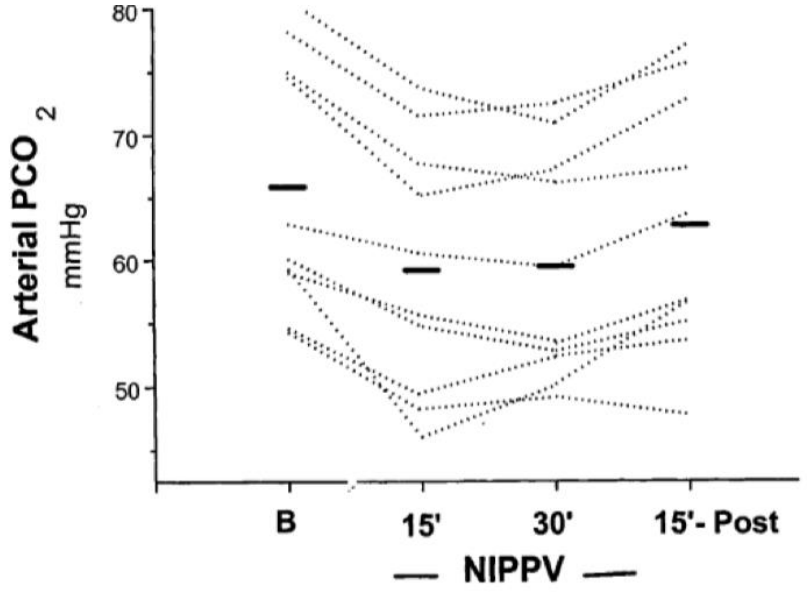
提升潮氣容積



減低呼吸次數



降低PCO2



Diaz et al. Am J Respir Crit Care Med. 1997 Dec;156(6):1840-5

[Intervention Review]

Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with usual care - Overall	Risk with NIV				
Mortality	183 per 1000	99 per 1000 (70 to 139)	RR 0.54 (0.38 to 0.76)	854 (12 RCTs)	⊕⊕⊕⊖ MODERATE[a]	Downgraded owing to risk of bias for some included studies
Need for endotracheal intubation	341 per 1000	123 per 1000 (95 to 157)	RR 0.36 (0.28 to 0.46)	1105 (17 RCTs)	⊕⊕⊕⊖ MODERATE[a]	Downgraded owing to risk of bias for some included studies
Length of hospital stay (days)	Mean length of hospital stay (days) was 17.5	MD 3.39 lower (5.93 lower to 0.85 lower)	-	888 (10 RCTs)	⊕⊕⊕⊖ MODERATE[a,b]	Downgraded owing to risk of bias and inconsistency of findings for some included studies

Osadnik CR, et al Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD004104.

Initiation of NIV

- Appropriately **monitored** location, **oximetry, respiratory impedance, vital signs** as clinically indicated
- Patient in bed or chair at >30-degree angle
- Select and fit **interface**
- Select **ventilator**
- Apply headgear; **avoid excessive strap tension** (one or two fingers under strap)
- Connect interface to ventilator tubing and turn on ventilaton

Mehta S, Hill NS. Noninvasive ventilation. Am J Respir Crit Care Med 2001; 163:540.

Initial setting of BiPAP

- Start with **low pressure** in **spontaneously triggered mode** with **backup rate**:
  - Inspiratory pressure at **8 to 12** cm H 2 O
  - Expiratory pressure at **3 to 5** cm H 2 O
- Gradually increase inspiratory pressure (10 to **20** cm H 2 O) as tolerated to achieve **alleviation of dyspnea**, **decreased respiratory rate**, **increased tidal volume** (if being monitored), and good patient-ventilator **synchrony**
- Provide O 2 supplementation as needed to keep **O 2 saturation >90%**

Mehta S, Hill NS. Noninvasive ventilation. Am J Respir Crit Care Med 2001; 163:540.

Comparison between nasal versus oronasal masks

Variables	Nasal	Oronasal	Full face
Comfort	+++	++	+
Claustrophobia	+	++	+++
Rebreathing	+	++	++
Lowers CO_2	+	++	++
Permits expectoration*	++	+	+
Permits speech¶	++	+	+
Permits eating$^{\Delta}$	+	–	–
Function if nose obstructed	–	+	+
Air leak	+++	+	+

Liesching T, Kwok H, Hill NS. Acute applications of noninvasive positive pressure ventilation. Chest 2003; 124:699.

A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation

Patients: COPD exacerbation and respiratory acidosis that were treated by NPPV

NPPV failure was defined as the **need for endotracheal intubation.**

- **Worsening of pH and PaCO2** in spite of correct NPPV administration
- The need **to protect the airways** (coma or seizure disorders) or to manage copious secretions
- **Hemodynamic instability** (heart rate<50 beats/min with loss of alertness, and/or systolic blood pressure <70 mmHg)
- **Agitation** and inability to tolerate the mask

Confalonieri et al. Eur Respir J 2005; 25: 348–355

A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation

TABLE 4 Logistic regression model used to build the risk chart

Variables	Admission			After 2 h		
	OR	p-value	95% CI	OR	p-value	95% CI
APACHE II score ⩾29	3.30	0.0001	1.81–6.01	4.79	0.0001	2.20–10.44
GCS 12–14	2.29	0.0008	1.41–3.72	1.93	0.0493	1.00–3.72
GCS ⩽11	4.40	<0.0001	2.59–7.49	5.16	<0.0001	2.54–10.50
pH <7.25	1.97	0.0046	1.23–3.15	21.02	<0.0001	10.07–43.87
pH 7.25–7.29	1.08	0.7511	0.68–1.72	2.92	0.0004	1.62–5.28
RR 30–34	1.83	0.0086	1.17–2.88	2.67	0.0021	1.43–4.99
RR ⩾35	2.66	<0.0001	1.66–4.25	4.95	<0.0001	2.64–9.29

OR: odds ratio; CI: confidence intervals; APACHE: acute physiology and chronic health evaluation; GCS: Glasgow Coma Scale; RR: respiratory rate.

Failure risk

- 疾病嚴重度 APACHE II ≥29
- GCS, esp ≤11
- pH <7.25; pH < 7.3 (2h)
- RR ≥30

Confalonieri et al. Eur Respir J 2005; 25: 348–355

Potential indicators of success in noninvasive ventilation

Younger age
Lower acuity of illness (APACHE score)
Able to cooperate, better neurologic score
Less air leaking, intact dentition
Moderate hypercarbia ($PaCO_2$ >45 mmHG, <92 mmHG)
Moderate acidemia (pH <7.35, >7.10)
Improvements in gas exchange and heart respiratory rates within first two hours

International Concensus Conferences in Intensive Care Medicine: Noninvasive positive pressure ventilation in acute respiratory failure. Am J Respir Crit Care Med 2001; 163:288

The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline

Rochwerg et al. Intensive Care Med (2020) 46:2226–2237

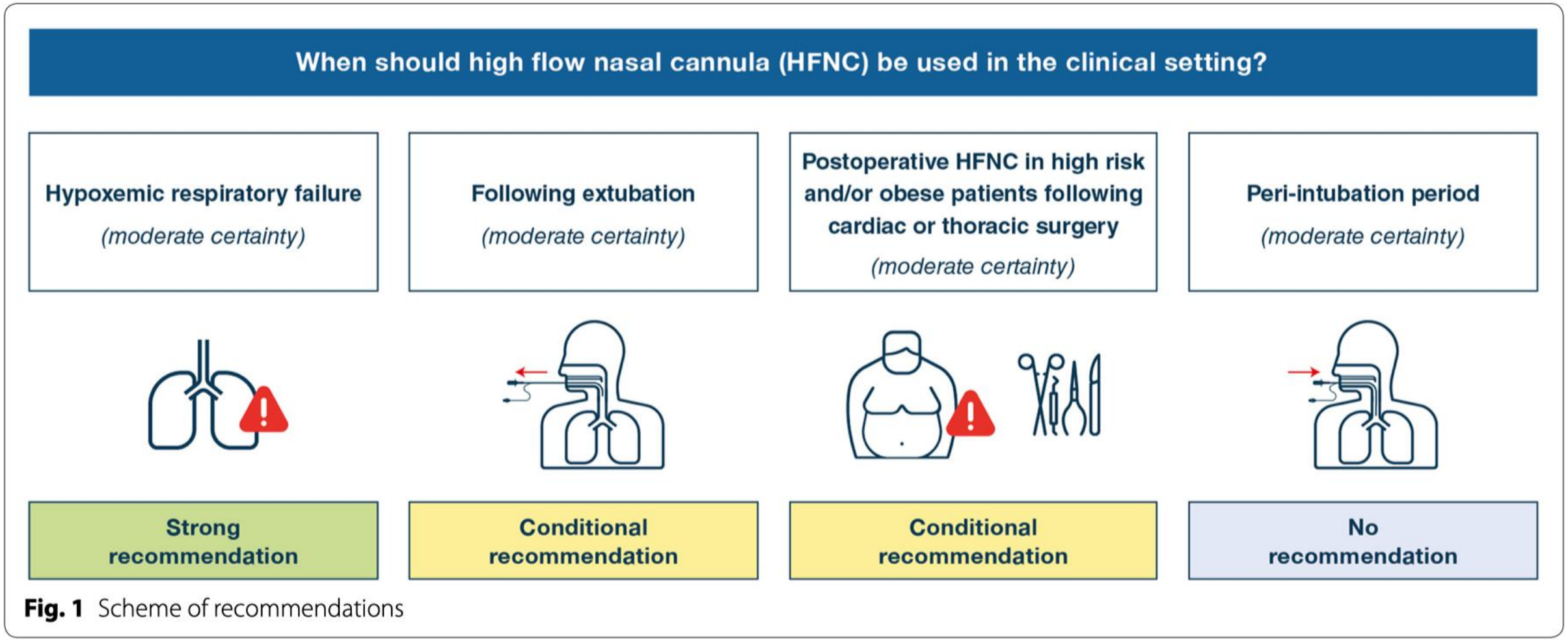


Fig. 1 Scheme of recommendations

ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure

Should HFNC or NIV be used in patients with **acute hypercapnic respiratory failure**?
Recommendation 8
We suggest **a trial of NIV** prior to use of HFNC in patients with COPD and acute hypercapnic respiratory failure (conditional recommendation, low certainty of evidence).

Five parallel-group RCTs and one crossover RCT

NOT reduce **mortality** or **intubation rate**

Length of stay in ICU are similar between HFNC and NIV.
HFNC may be more comfortable compared to, although **dyspnoea** is **similar.**
Gas exchange and **respiratory rate** were **similar** between HFNC and NIV.

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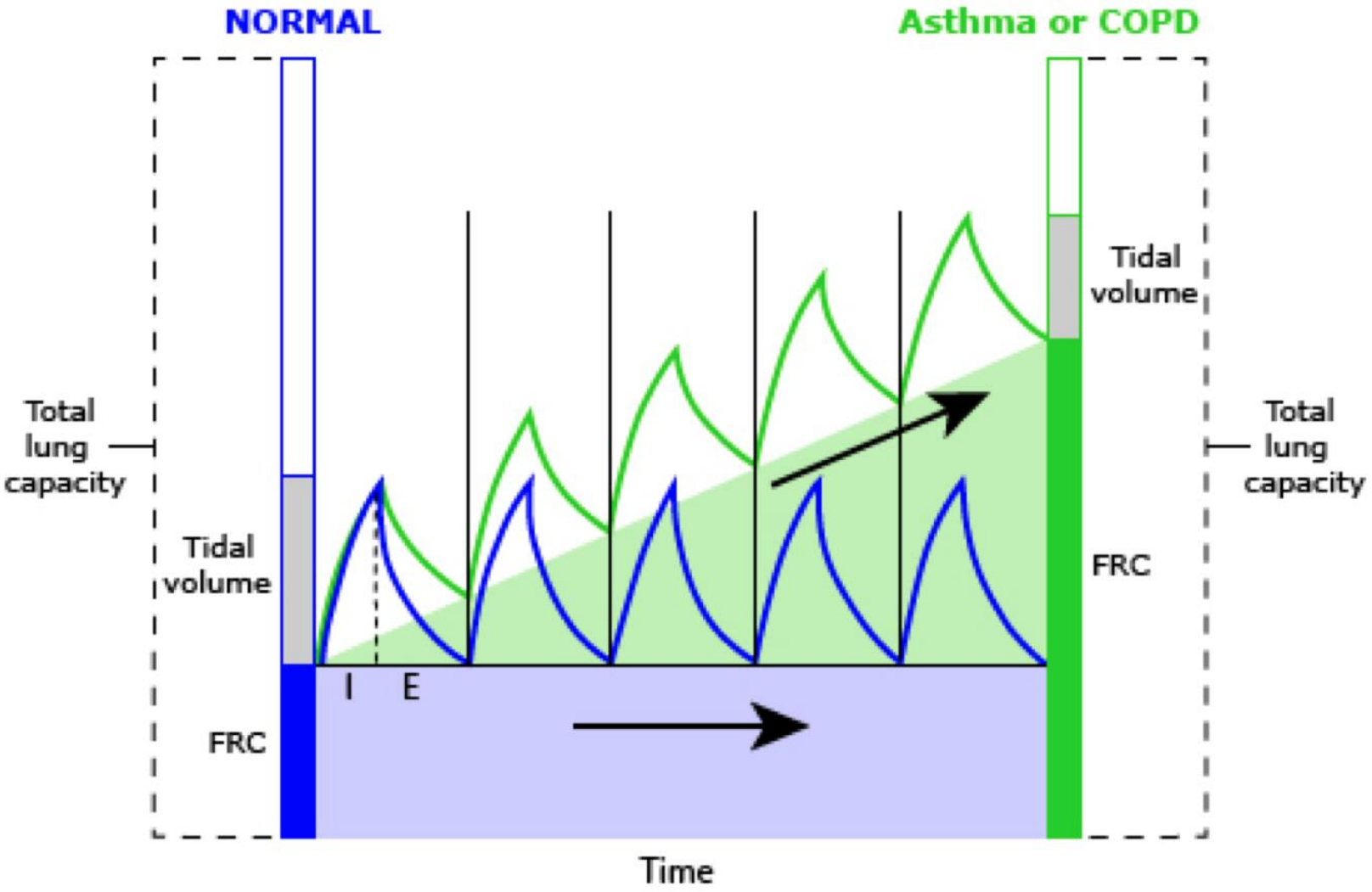
GOALS OF VENTILATOR MANAGEMENT in AE COPD

- Correct derangements in oxygenation and ventilation
- Reduce the work of breathing
- Prevent dynamic hyperinflation (DHI)

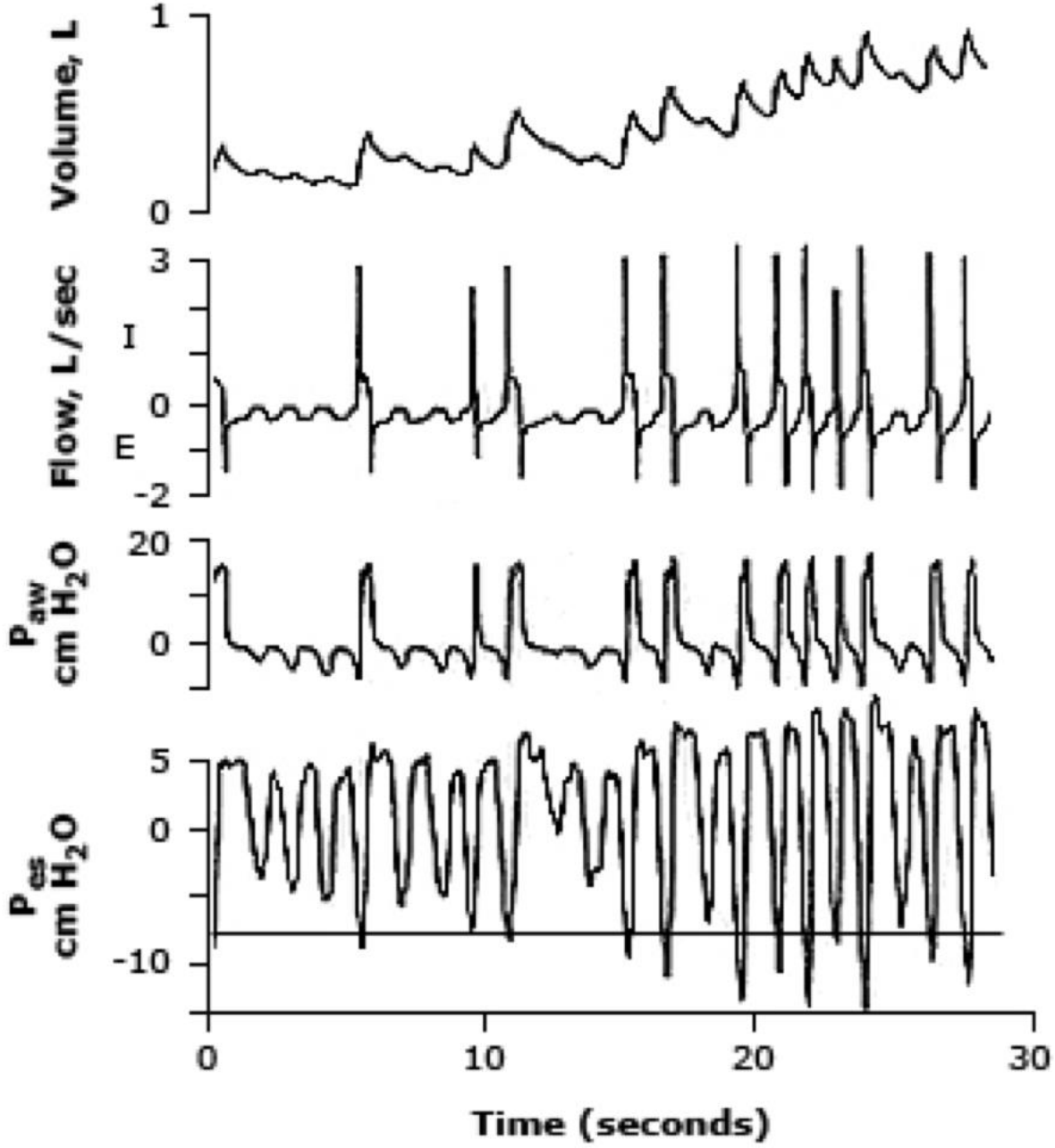
PC or VC or PSV
Vt 6-8ml/kg
RR 8-20
Inspiratory flow 60L/min
Trigger sensitivity – -1 to -2 cm H2O when pressure triggering is used or 2 L/min when flow triggering is used.

Dynamic hyperinflation during controlled ventilation in obstructive lung disease

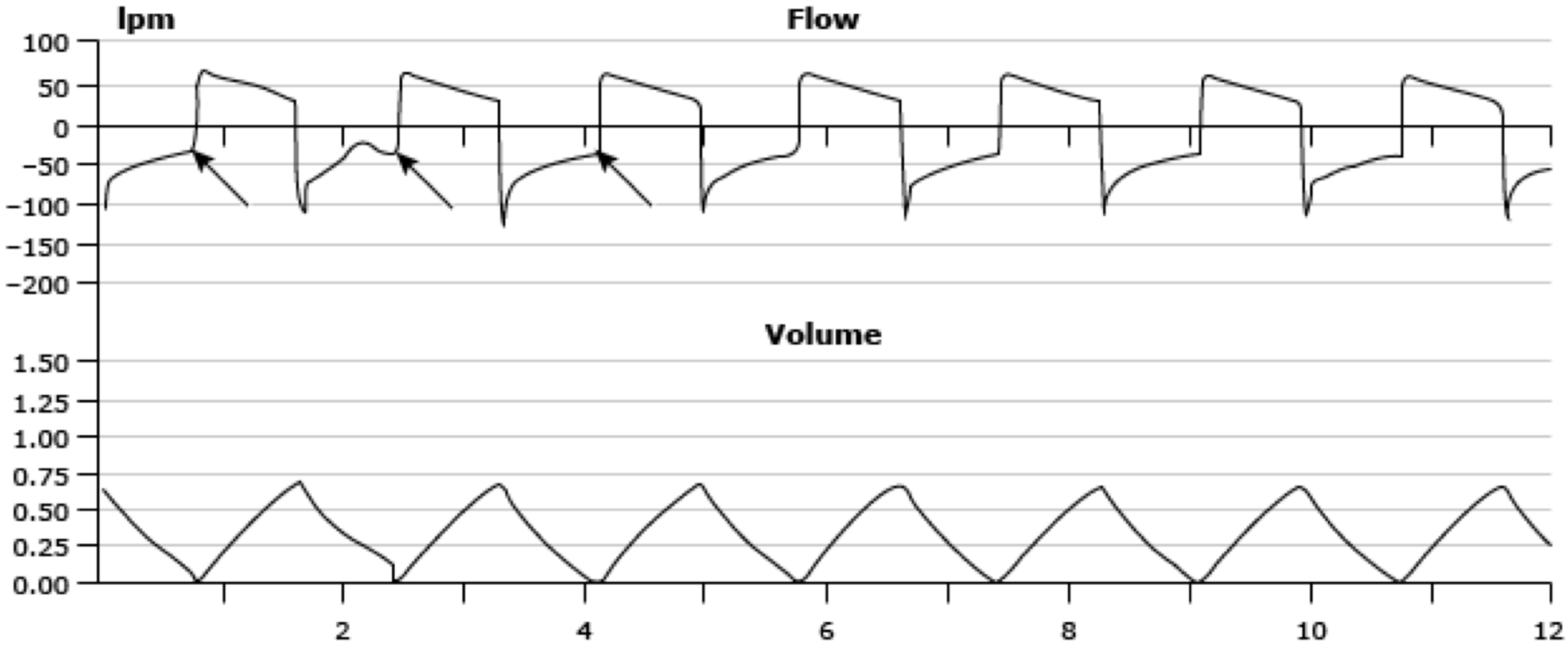


Tuxen DV. Permissive hypercapnic ventilation. Am J Respir Crit Care Med 1994; 150:870.

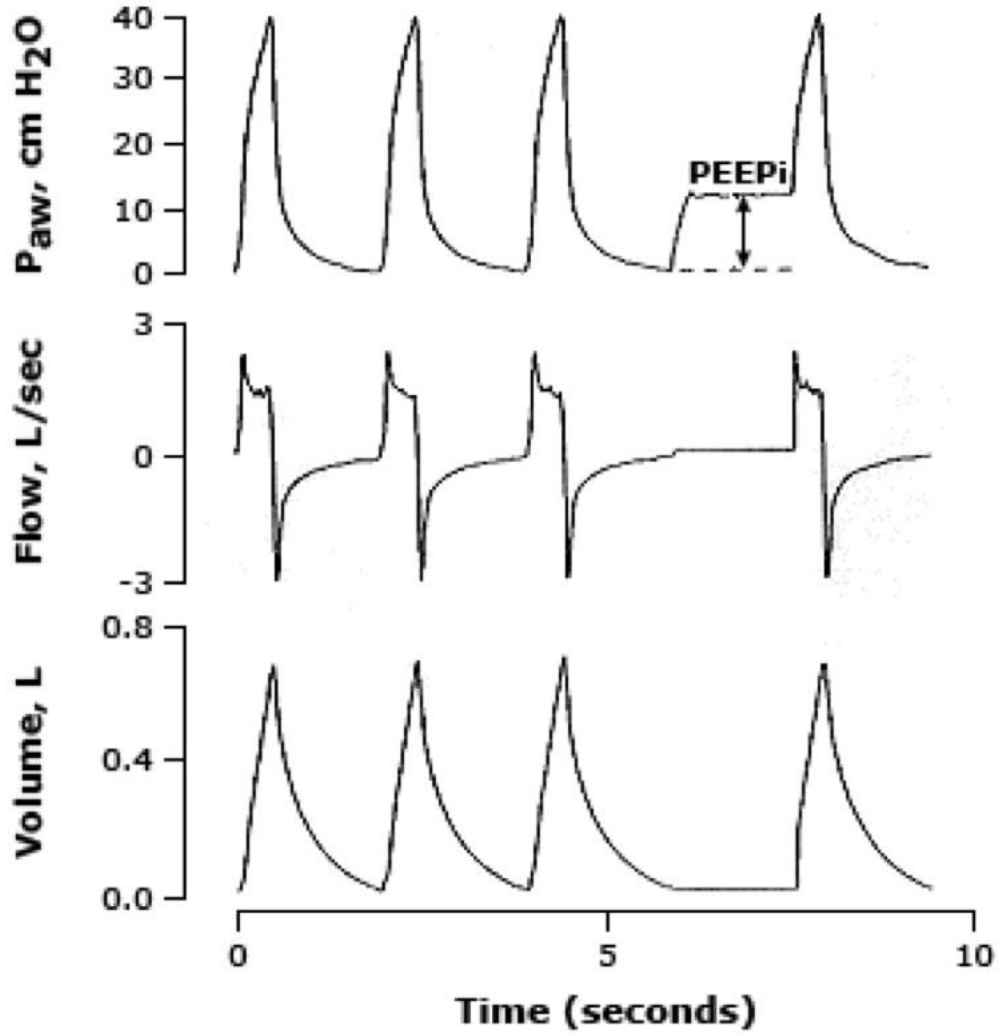
Increasing ventilator triggering in presence of intrinsic positive end-expiratory pressure (PEEPi)



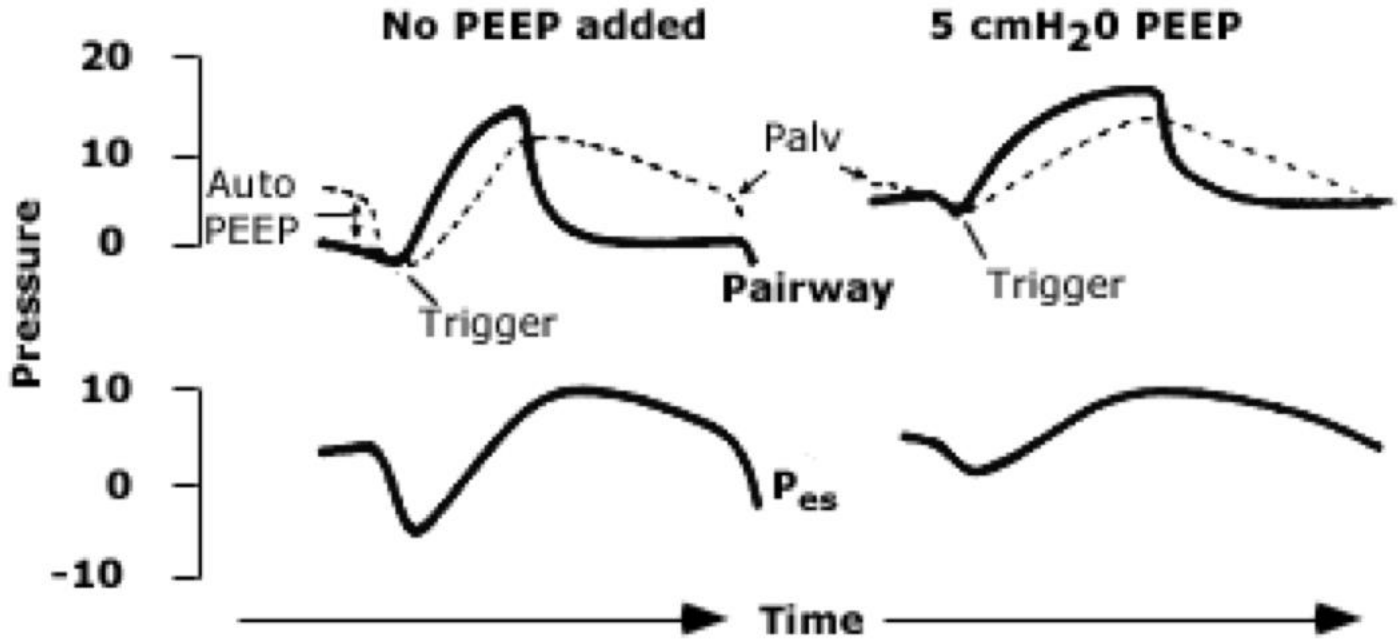
Detection Auto-PEEP: Time-flow graphic



Measurement of Intrinsic positive end-expiratory pressure (PEEPi)



PEEP use to improve the impact of auto-PEEP on trigger sensitivity and inspiratory effort



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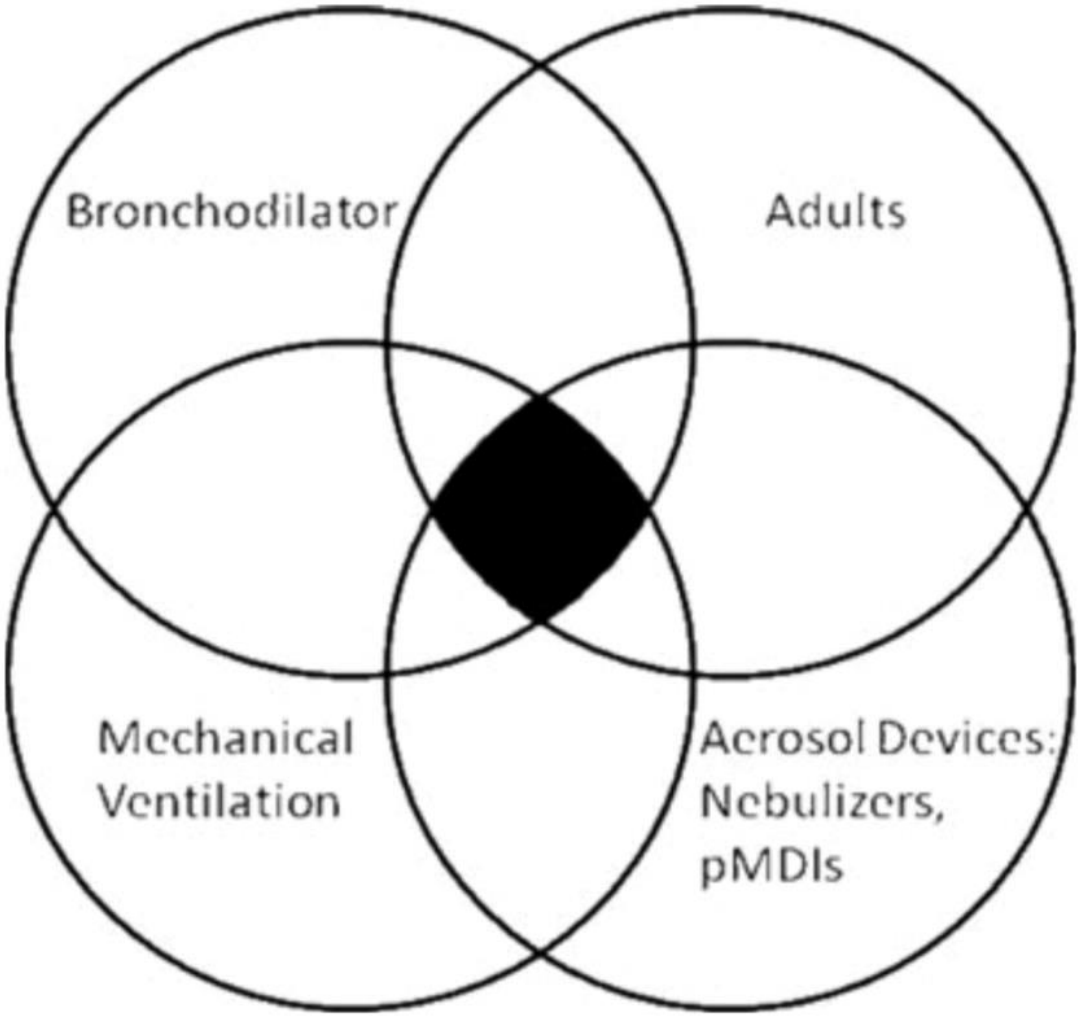
Aerosol therapy for patients with mechanical ventilator

Drugs

Bronchodilators
Short- v.s. long-acting

Ventilator settings

Location, Vt, rate…



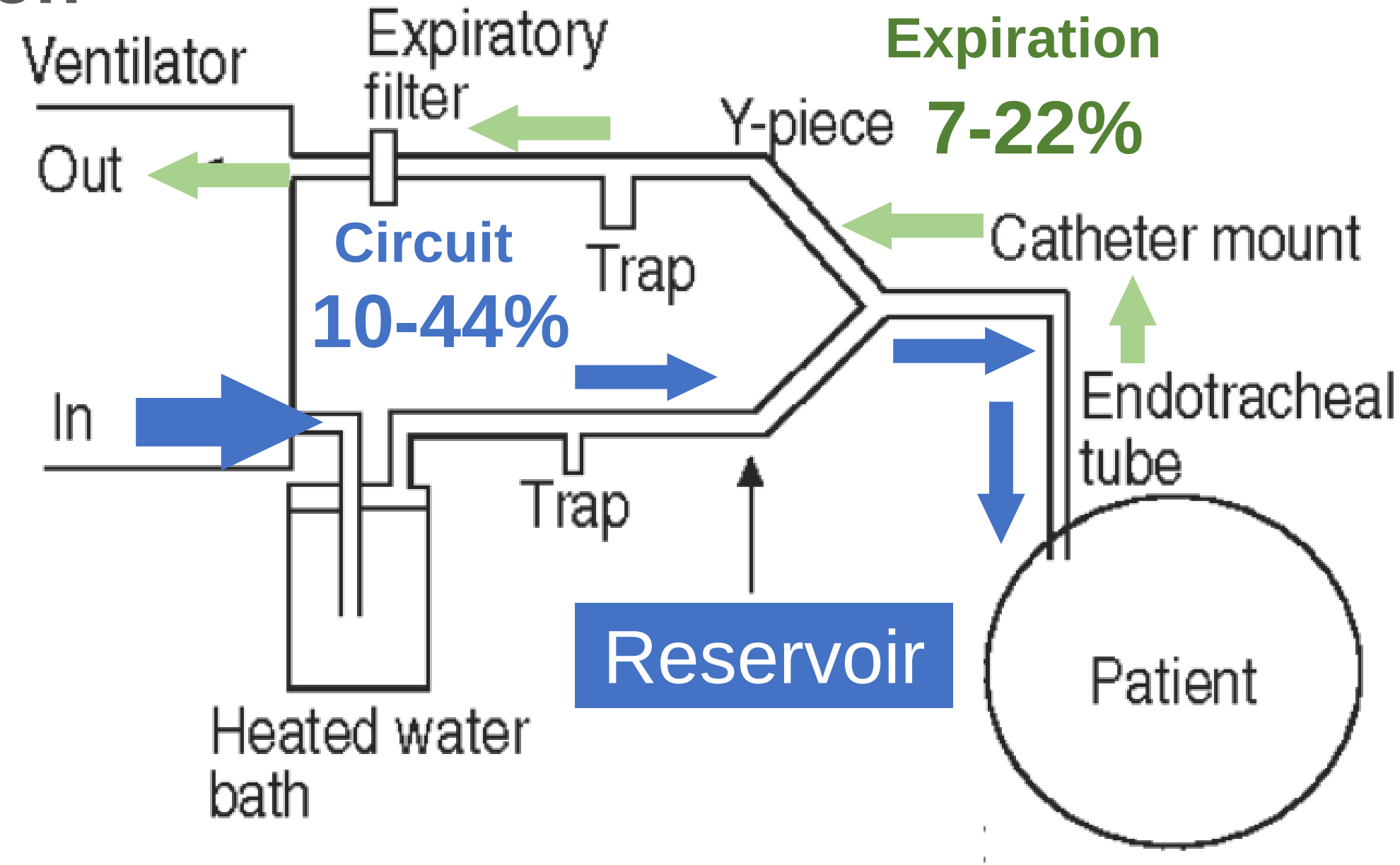
Devices

Nebulizer, MDI, SMI

Arzu et al, Nurs Crit Care 2012; 15(4): 192-203

Deposition

Before
Enter the lung



Acute exacerbation of COPD

Find the cause

Oxygenation

Bronchodilators

- **Short-acting** β_2 agonist: salbutamol
- **Short-acting** anti-cholinergic agents: ipratropium

Systemic corticosteroid

KEY POINTS FOR THE MANAGEMENT OF EXACERBATIONS

- Short-acting inhaled beta$_2$-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation **(Evidence C)**.
- Systemic corticosteroids can improve lung function (FEV_1), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not be more than 5-7 days **(Evidence A)**.
- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should be 5-7 days **(Evidence B)**.
- Methylxanthines are not recommended due to increased side effect profiles **(Evidence B)**.
- Non-invasive mechanical ventilation should be the first mode of ventilation used in COPD patients with acute respiratory failure who have no absolute contraindication because it improves gas exchange, reduces work of breathing and the need for intubation, decreases hospitalization duration and improves survival **(Evidence A)**.

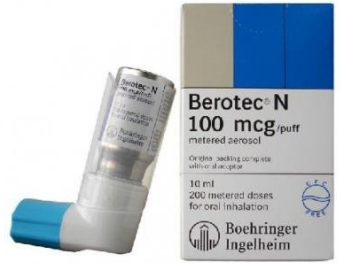
Short-acting bronchodilators Mechanical ventilated patients

Table 3. Investigations of Bronchodilator Therapy and Airway Response in Mechanically Ventilated Patients

Author, year (reference #)	Drug (dose, mg)	Aerosol device	Response
Gay, 1987[76]	Metaproterenol (1.8 mg)	Small-volume aerosol generator	Increase in expiratory flow at recoil pressure of 6 cm H_2O, and reduction in peak pressure and intrinsic PEEP
Wegener, 1987[77]	Ipratropium (0.2 mg)	pMDI and adapter	Decrease in inspiratory airway resistance and significant increase in paO_2
Fuller, 1990[21]	Fenoterol (0.8 mg) Fenoterol (1.75 mg)	pMDI-spacer Nebulizer	Decrease in peak airway pressure not significant with either device
	Albuterol (2.5, 5, 7.5 mg)	Nebulizer	
Yang, 1994[83]	Ipratropium (0.5 mg)	Nebulizer	Significant reduction in peak airway pressure, mean airway pressure and mean airway resistance
Fernandez, 1994[94]	Fenoterol (0.1 mg) + Ipratropium (0.04 mg)	pMDI and short catheter	Significant decrease in airway resistance with combination
Dhand, 1995[26]	Albuterol (1.0 mg)	pMDI-spacer	Significant reduction of airway resistance for up to 60 min
Manthous, 1993[82]	Albuterol (0.5, 1.5, 3.0 mg cumulative dose)	pMDI-spacer	Significant reduction in airway resistance with 1.5 and 3.0 mg albuterol
Dhand, 1996[29]	Albuterol (0.4, 1.2, 2.8 mg cumulative dose)	pMDI-spacer	Significant reduction in airway resistance with 0.4, 1.2 and 2.8 mg of albuterol
Mouloudi, 1998[84]	Albuterol (0.6 mg) with or without end-inspiratory pause	pMDI-spacer	Significant reduction in airway resistance. No effect of end-inspiratory pause
Waugh, 1998[85]	Albuterol (0.4, 0.8 mg)	pMDI and chamber spacers	Reduction in airway resistance with 4 puffs and 8 puffs. No difference in response between 2 chamber spacers
Mouloudi, 1999[87]	Albuterol (0.6 mg)	pMDI-spacer	Significant reduction in airway resistance. No effect of tidal volume 8 mL/kg versus 12 mL/kg body weight
Guerin, 1999[86]	Fenoterol (0.2 mg) + Ipratropium (0.4 mg) Fenoterol (1.25 mg) + Ipratropium (0.5 mg)	pMDI-spacer Nebulizer	Significant reduction in airway resistance with both pMDI and nebulizer
Duarte, 2000[88]	Albuterol (0.4, 1.0 mg) Albuterol 2.5 mg	pMDI-spacer Nebulizer	Significant reduction in airway resistance with both pMDI and nebulizer for up to 2 h

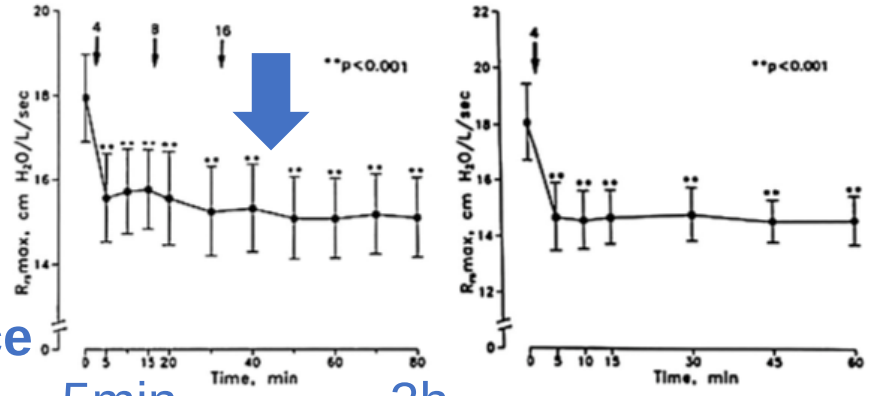
Table 3. (Continued)

Author, year (reference #)	Drug (dose, mg)	Aerosol device	
Mouloudi, 2000[89]	Albuterol (0.2, 0.6 mg)	pMDI-spacer	Sign d sq
Mouloudi, 2001[111]	Albuterol (0.6 mg)	pMDI-spacer	Sign bu ur
Mouloudi, 2001[90]	Albuterol (0.4 mg)	pMDI-spacer	Sign in
Malliotakis, 2008[93]	Salmeterol (0.1 mg)	pMDI-spacer	ventilation with similar tidal volumes Significant reduction in airway resistance for up to 8 h, but the duration of effect was variable and unpredictable in individual patients.
Kondili, 2011[109]	Albuterol (0.4 mg)	pMDI-spacer	Expiratory resistance of the respiratory system (expiratory Rrs) was several-fold higher than inspiratory resistance. After albuterol, there was significant reduction in expiratory Rrs with increase in the rate of lung emptying toward the end of expiration. Changes in expiratory Rrs did not correlate with changes in end-inspiratory inspiratory resistance after albuterol



Salbutamol, fenoterol, ipratropium **nebulizer** & **MDI**
Significant **decreased airway pressure and resistance**.

Airway resistance



5min 2h

Ari et al. J Aerosol Med Pulm Drug Deliv 2012; 25(6): 319-32.

Stable COPD

Pharmacologic Algorithm

Acute Exacerbation ≥ 2/y

C LAMA & LABA

D or + ICS **LAMA** & LABA

❶ **Bronchodilator**
❷ **Dual** bronchodilator LAMA+LABA
❸ **ICS**

Bronchodilators are important for stable **COPD** control

SABA

or LABA

➡ **LAMA & LABA**

More Symptoms

Acute exacerbation

- No clinical studies that have evaluated the use of inhaled long-acting bronchodilators (either beta2-agonists or anticholinergics or combinations) with or without inhaled corticosteroids during an exacerbation.

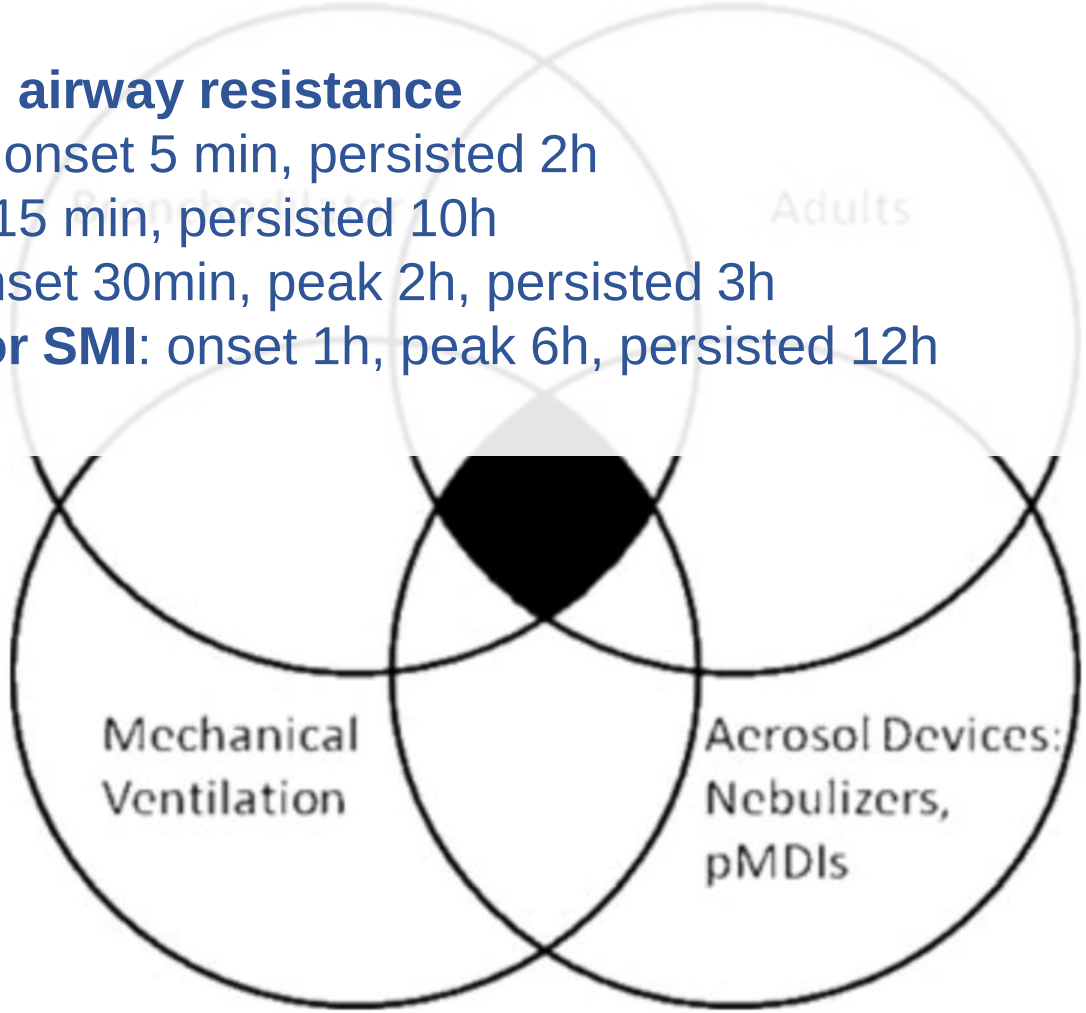
- We recommend to continue these treatments during the exacerbation or to start these medications **as soon as possible** **before hospital discharge.**

Inhalation therapy for patients with mechanical ventilator

1. Drugs

Bronchodilators **reduced airway resistance**
SABA nebulizer & MDI: onset 5 min, persisted 2h
LABA 4puff MDI: onset 15 min, persisted 10h
ICS/LABA 4puff MDI: onset 30min, peak 2h, persisted 3h
LAMA 2puff T-connector SMI: onset 1h, peak 6h, persisted 12h

Ventilator settings
Location, Vt, rate…



Devices
Nebulizer, MDI, SMI

Arzu et al, Nurs Crit Care 2012; 15(4): 192-203

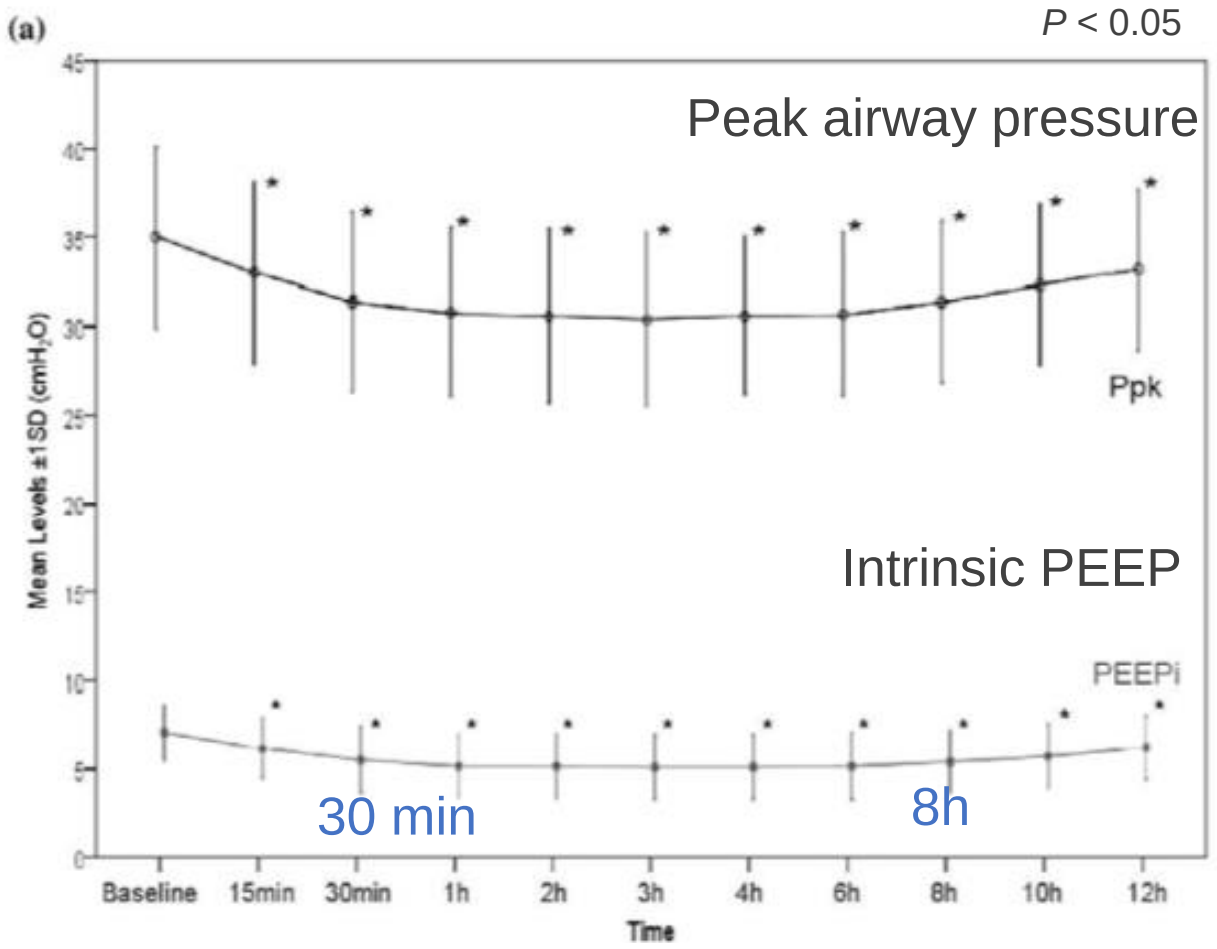
Long-acting β2-agonists

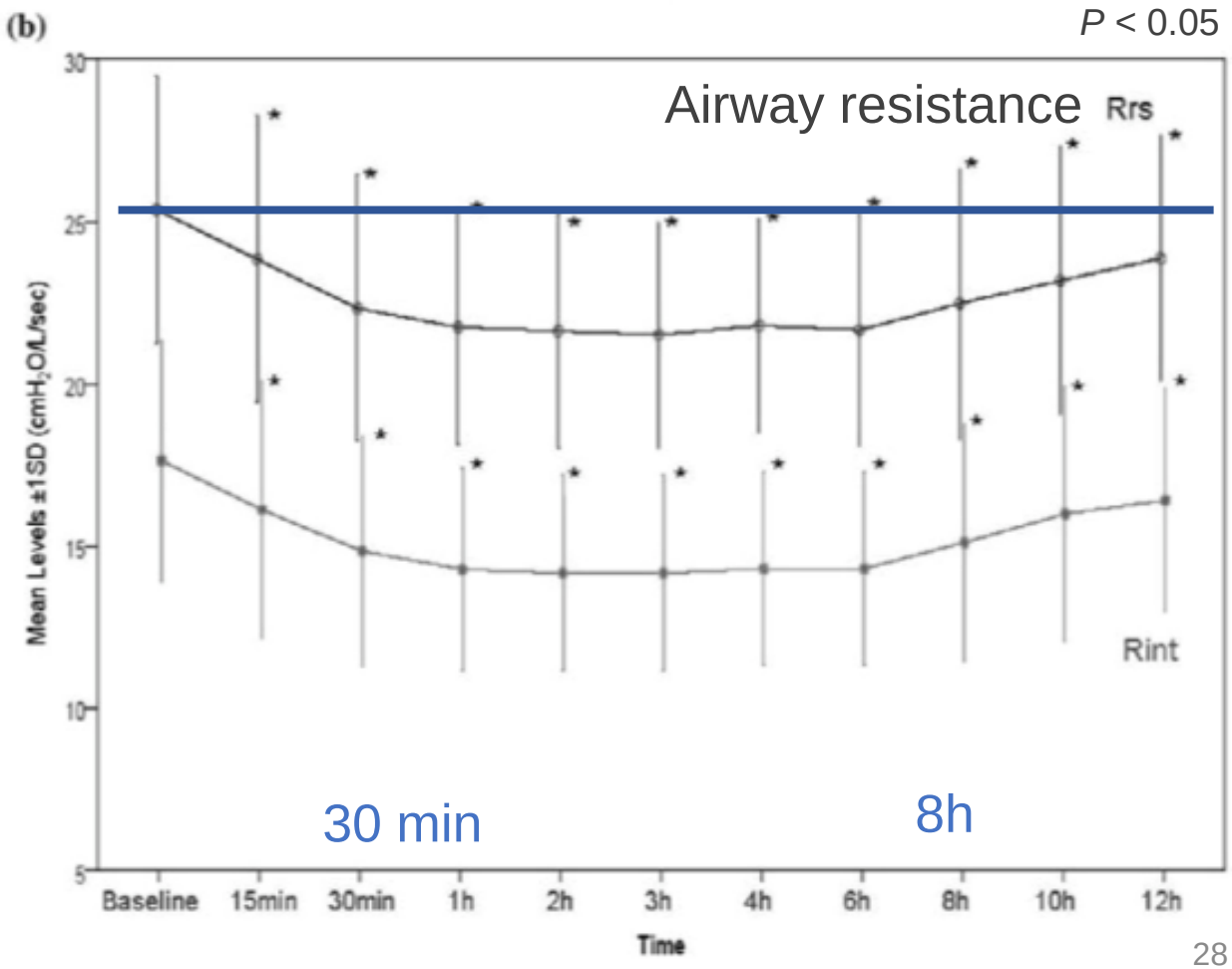
Malliotakis et al. Critical care 2008; 12(6): R140.

Mechanical ventilated patients

Salmeterol (25mcg/puff) 4 puff
MDI + spacer; inspiratory limb

Significant **decreased airway pressure and resistance**.
Evident at 30min; remained **8 hours** (6-10h)





International Journal of COPD

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ORIGINAL RESEARCH

Effect of salmeterol/fluticasone combination on the dynamic changes of lung mechanics in mechanically ventilated COPD patients: a prospective pilot study

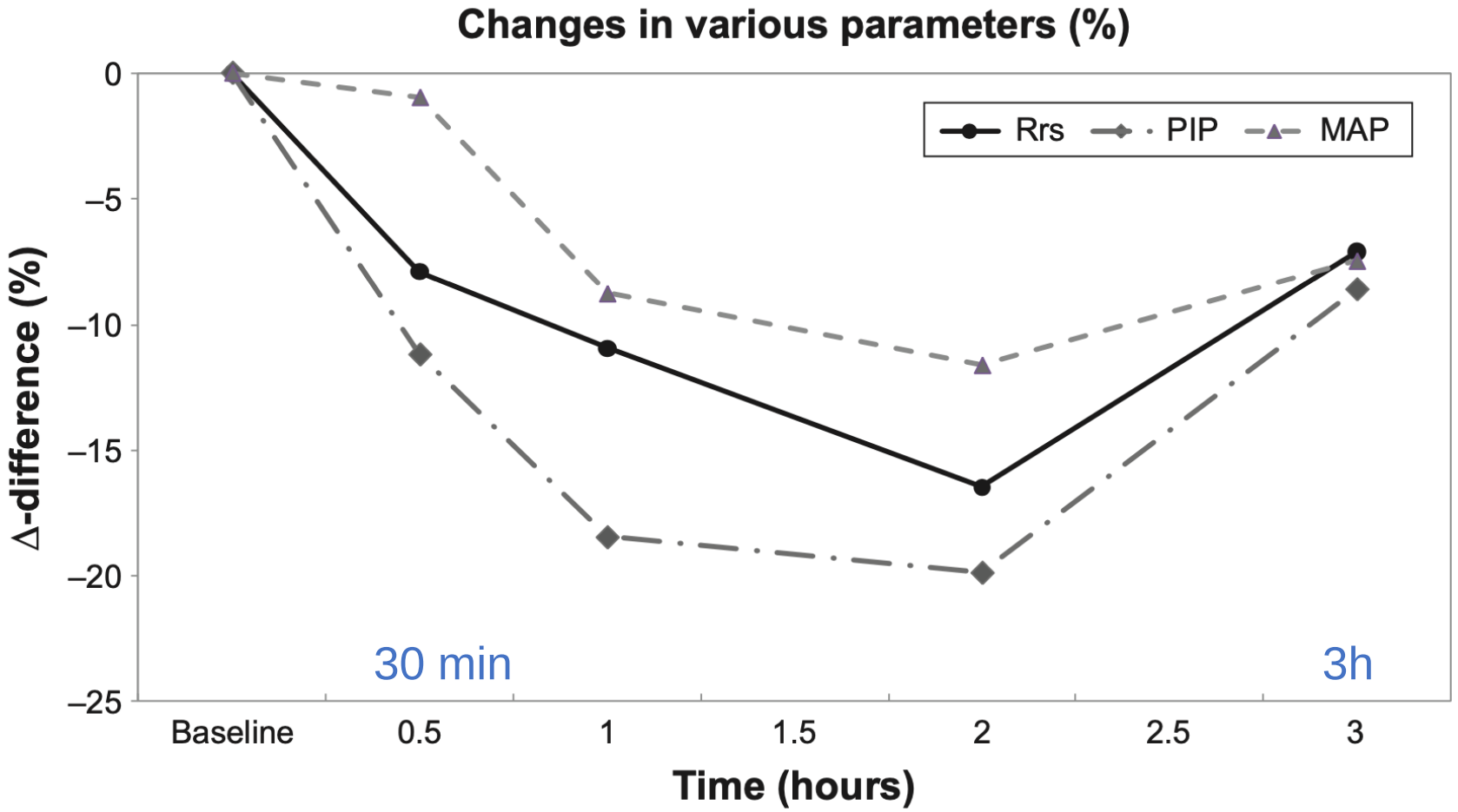
4 puffs of salmeterol 25 μg/fluticasone 125 μg combination therapy

ICS + LABA

Wei-Chih Chen[1,2]
Hung-Hsing Chen[2]
Chi-Huei Chiang[2]
Yu-Chin Lee[3]
Kuang-Yao Yang[1,2]

4 puffs of salmeterol 25 µg/fluticasone 125 µg combination therapy

ICS + LABA for AE COPD **decrease resistance and peak inspiratory pressure (30mins- 2 h - 3 h)**



2 puffs of tiotropium (2.5 µ g/puff) with T-adaptor connection

LAMA for stable COPD **decrease resistance and peak inspiratory pressure (1h - 6h – 12 h)**

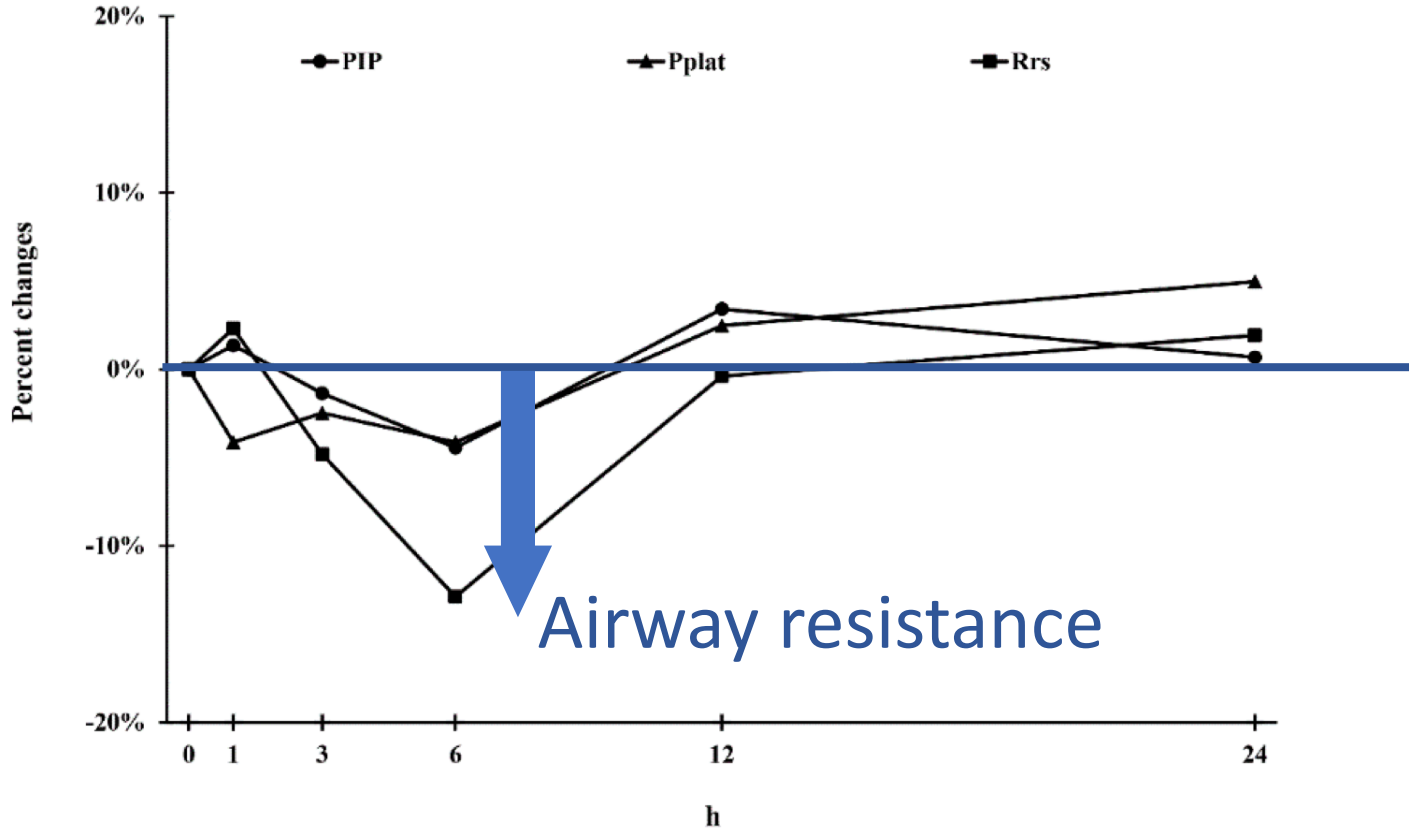


Figure 1. Percent changes (△-difference %) in Peak inspiratory pressure (PIP), mean airway pressure (Pmean), plateau pressure (Pplat), and maximum resistance of the respiratory system (Rrs).

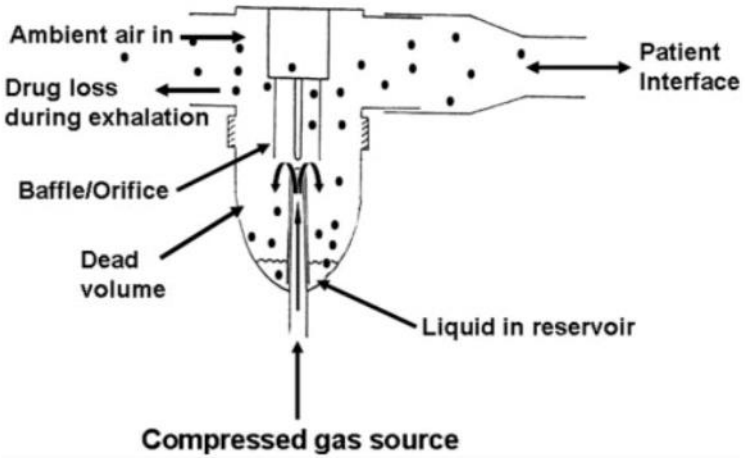
Fu et al. Pharmaceutics 2021, 13, 51.

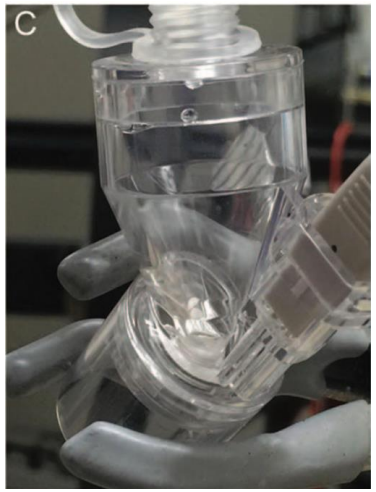
Deliver to lung

MDI+ chamber at Y-piece

38%

Jet Nebulizer	Ultrasonic Nebulizer	Vibrating mesh Nebulizer
3-7%	5%	10-15%





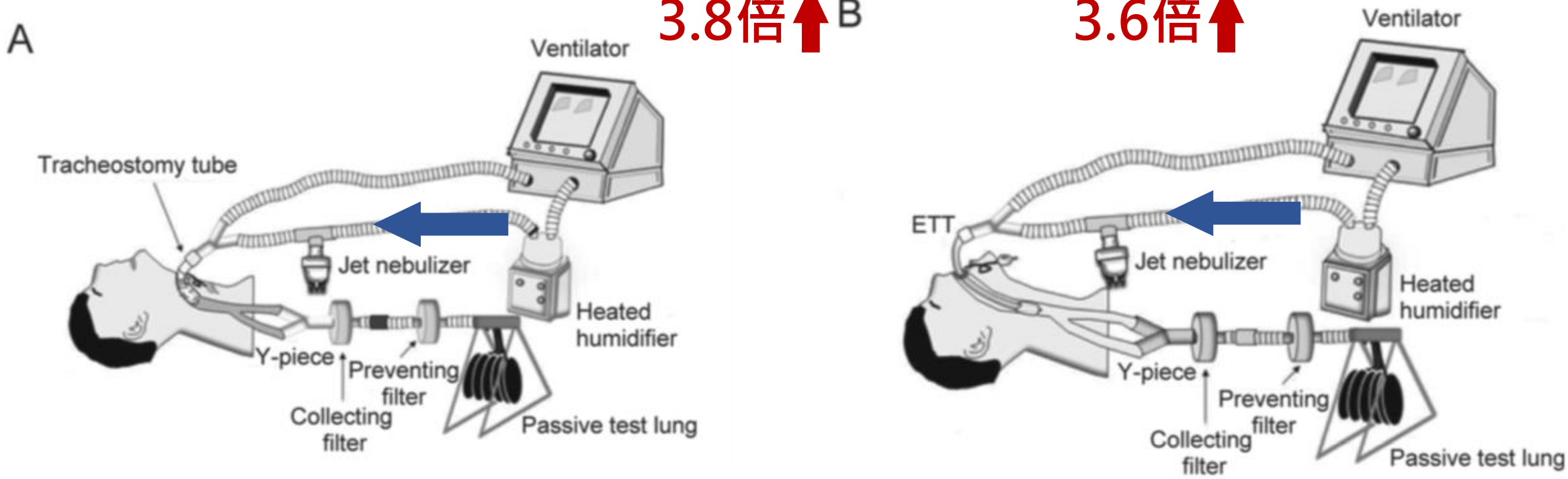
Mark et al. Chest. 1999;115(6):1653–7.

MDI: greater delivery efficiency than jet nebulizer

Table 1. Mean Inhaled Mass and Lung Dose as Percent of Nominal Dose Delivered Distal to the Trachea With Each Aerosol Device

Salbutamol (SABA)	2.5mg/3ml TT			¼的劑量 ETT		
	Jet Nebulizer	0.1mg x 4 puff pMDI	*P*	Jet Nebulizer	pMDI	*P*
Inhaled mass, mean ± SD μg	97.3 ± 14.0*	63.6 ± 0.4†	.01	79.6 ± 3.8	50.1 ± 8.2	.005
Lung dose, mean ± SD %	3.9 ± 0.5‡	14.7 ± 0.1§	.001	3.2 ± 0.1	11.6 ± 1.9	.002

3.8倍 3.6倍



Arzu et al. Respir Care. 2015;60(11):1570–1574.

Procedure	*Metered-dose inhaler*	*Nebulizer*
Adjust ventilator settings	a. V_T 500 mL: make sure that plateau pressure if measurable ≤32 cm H_2O b. Duty cycle ≥0.30 and/or inspiratory flow 30–50 L/min: make sure that intrinsic PEEP does not rise c. No change in applied PEEP and F_IO_2	

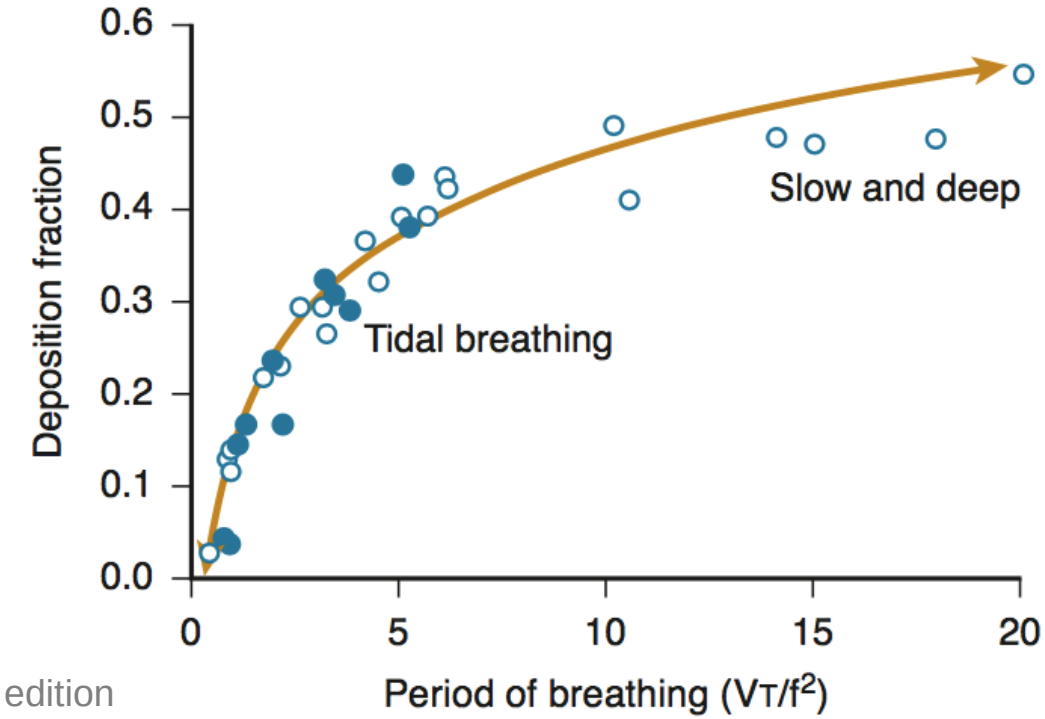
4. Ventilator settings

Deep Vt 500ml

Slow

↑Vt/f^2

1. ↑Vt 越深
2. ↓f 越慢

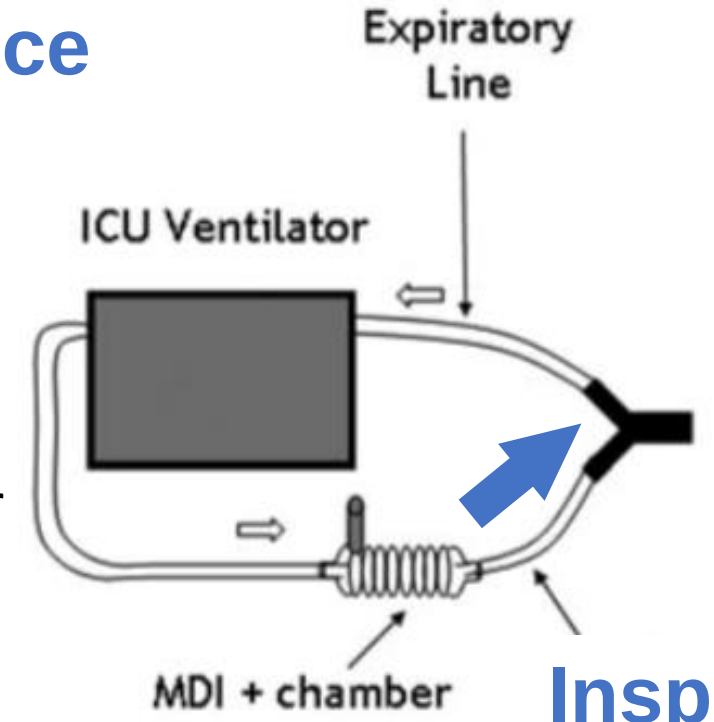


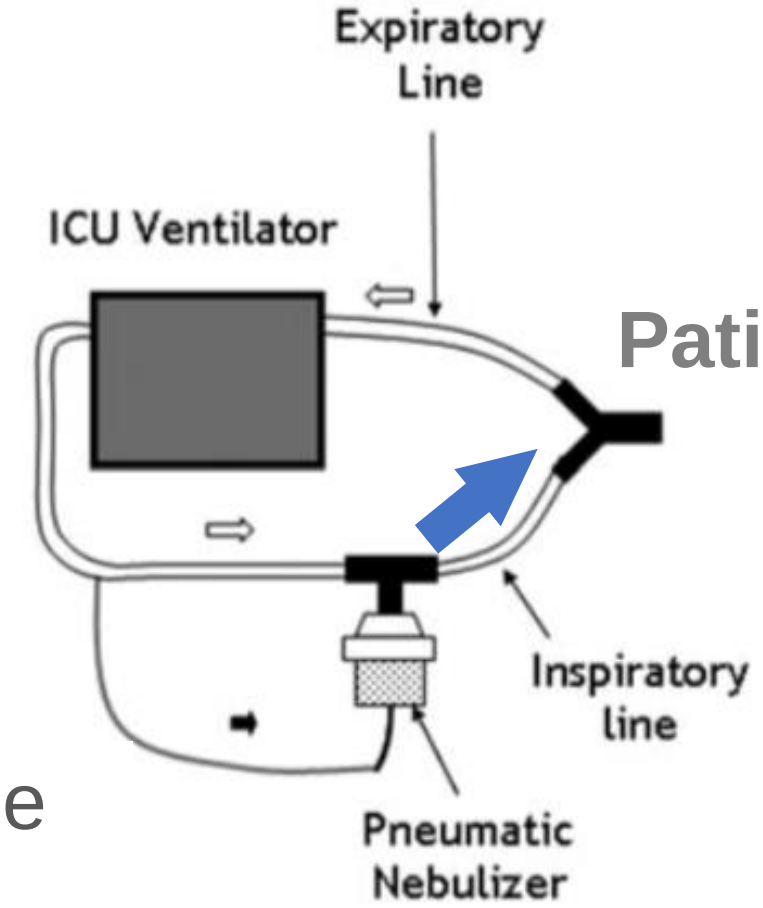
Murray & Nadels et al, Textbook of Respiratory Medicine, 6th edition

Guerin. J Aerosol Med Pulm Drug Deliv. 2008 Mar;21(1):85-96

Procedure	Metered-dose inhaler	Nebulizer
Choose the device	MDI plus a cylinder chamber	Small volume nebulizer
Locate the device	In the inspiratory line between 10 to 30 cm from the Y piece	
	Bottom-up in the chamber	Horizontal

1. Locate the device





Metered dose inhaler

MDI

Inspiratory limb

15cm from Y piece

MDI+ **Spacer**

In Vitro Evaluation of Aerosol Performance and Delivery Efficiency During Mechanical Ventilation Between Soft Mist Inhaler and Pressurized Metered-Dose Inhaler

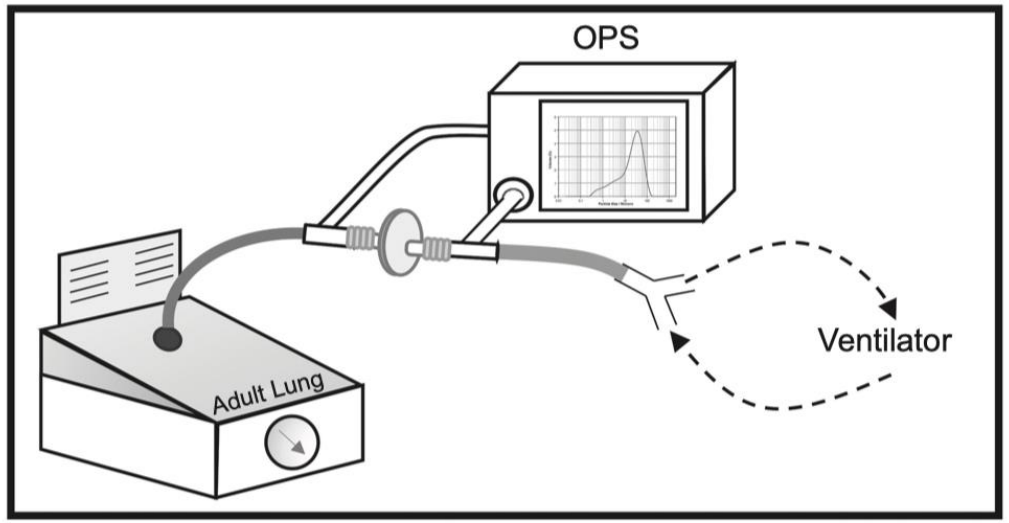
Wei-Ren Ke, Wei-Jhen Wang, Tzu-Hsuan Lin, Chao-Ling Wu, Sheng-Hsiu Huang, Huey-Dong Wu, and Chih-Chieh Chen

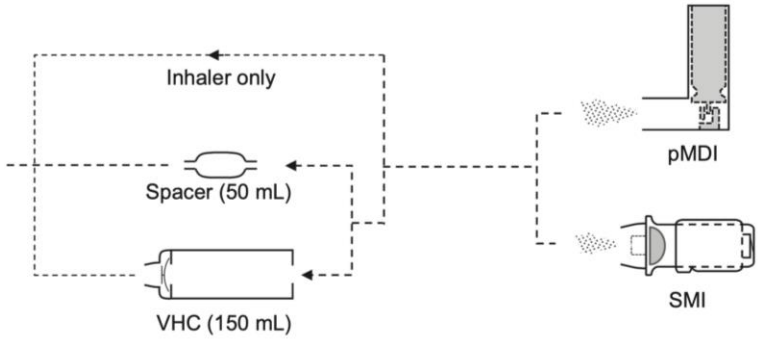
Respimate

Soft moisture inhaler

SMI

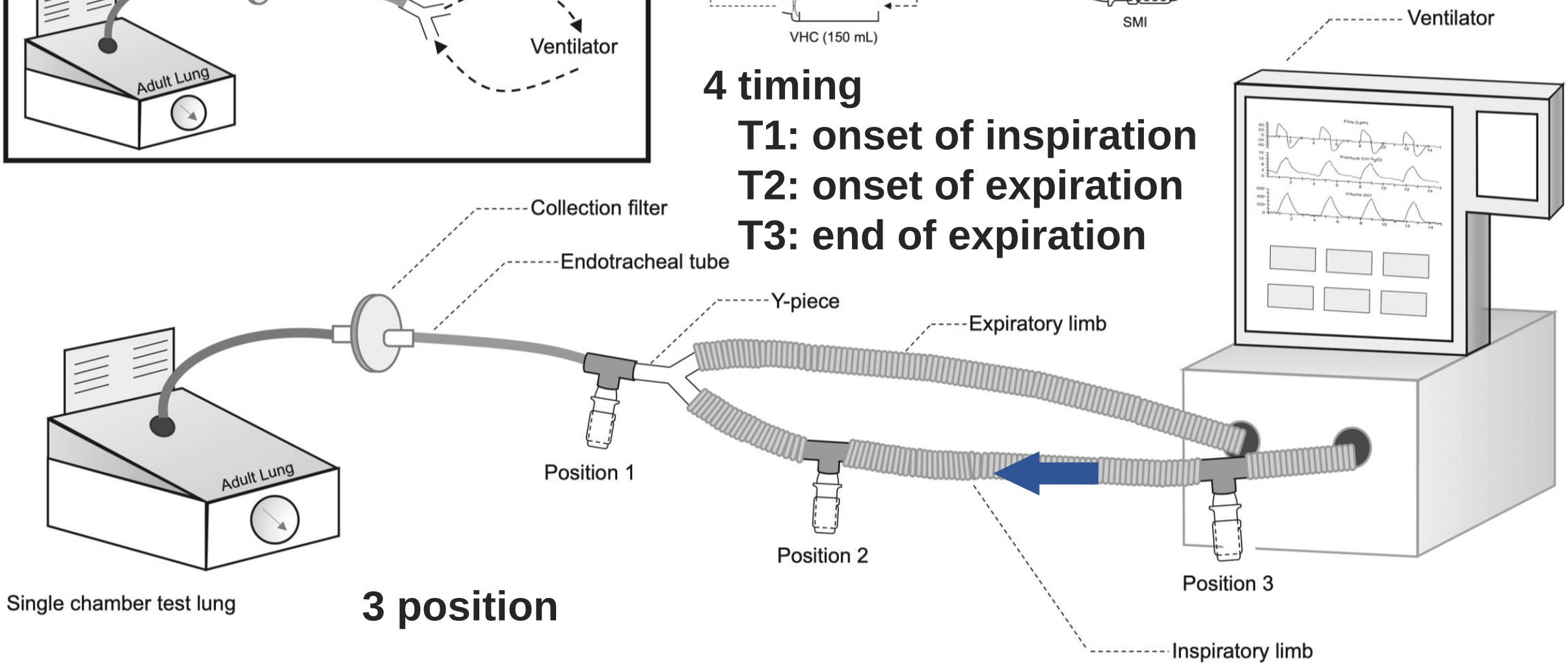
2 inhaler, spacer, VHC 1 pMDI vs SMI





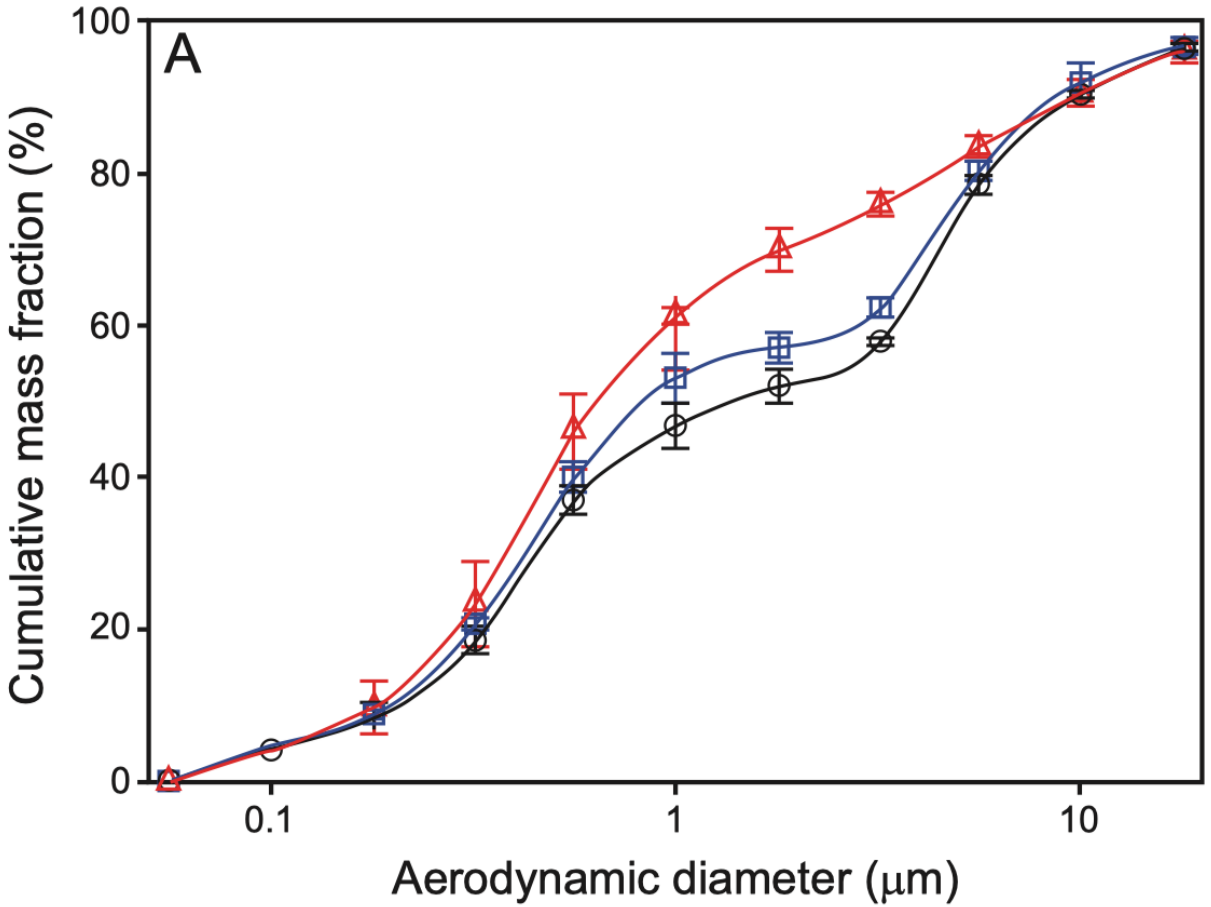
4 timing

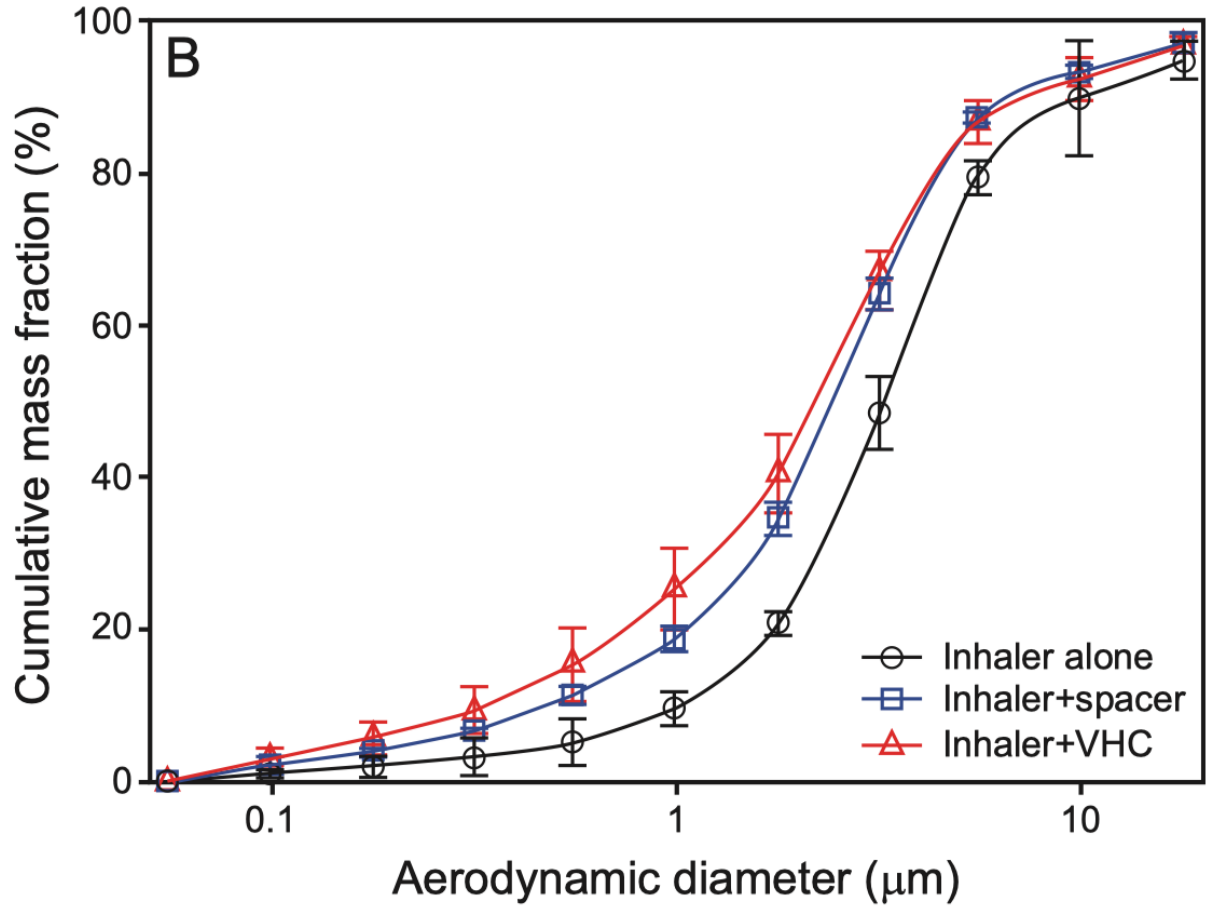
- T1: onset of inspiration
- T2: onset of expiration
- T3: end of expiration

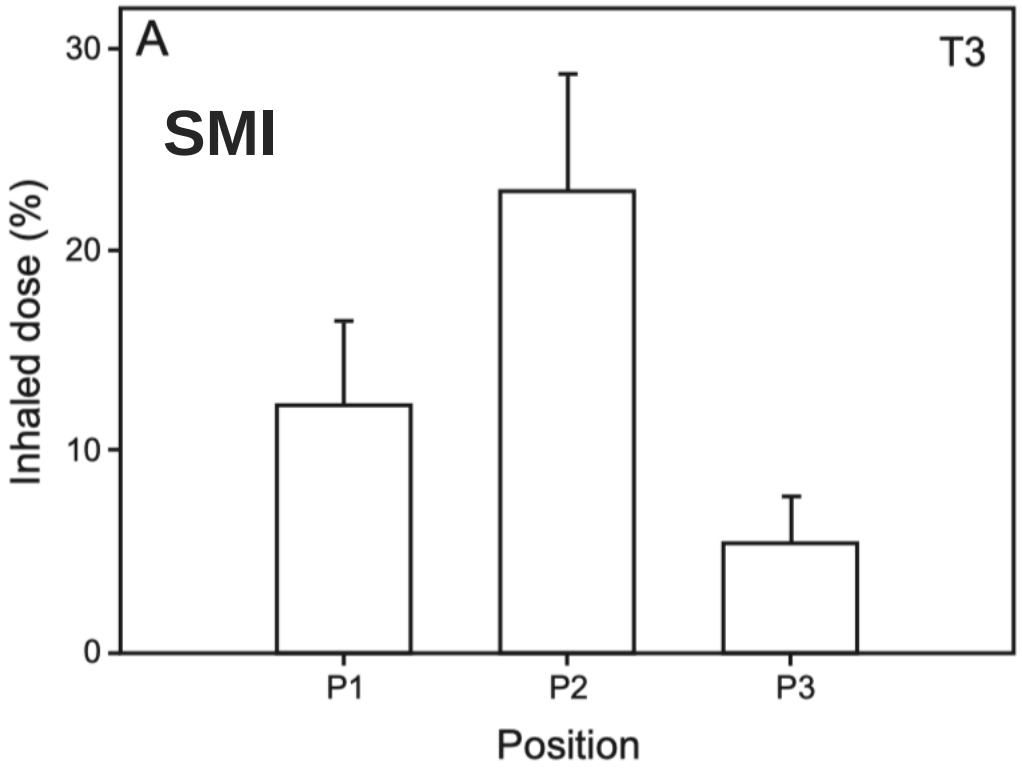


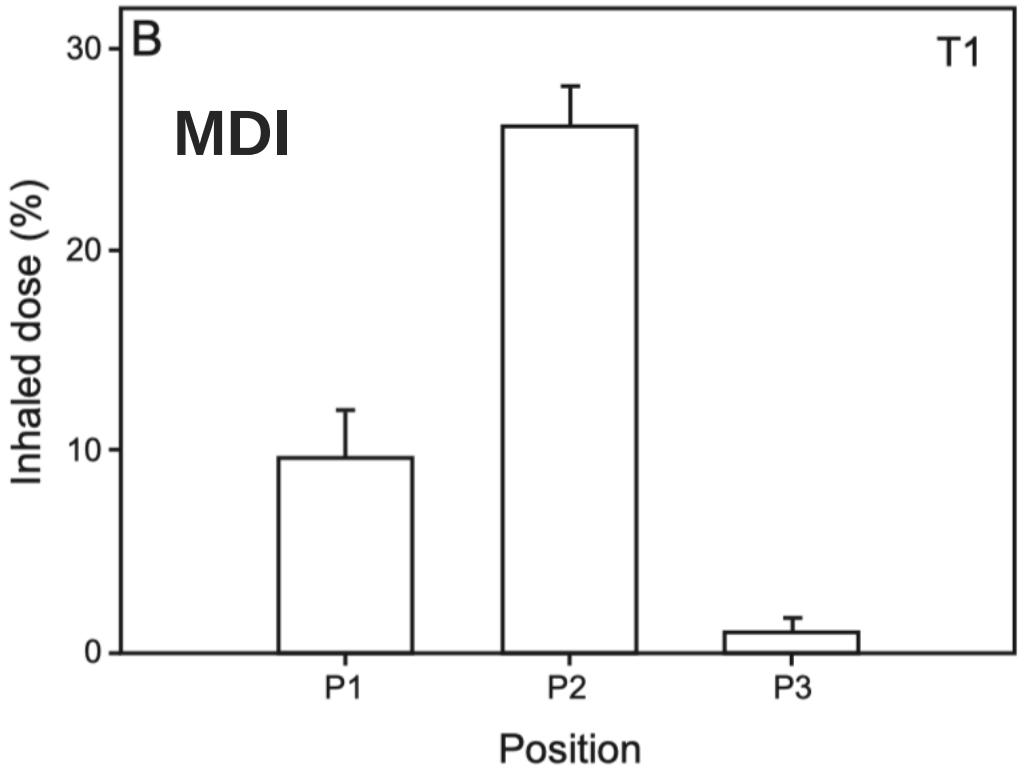
3 position

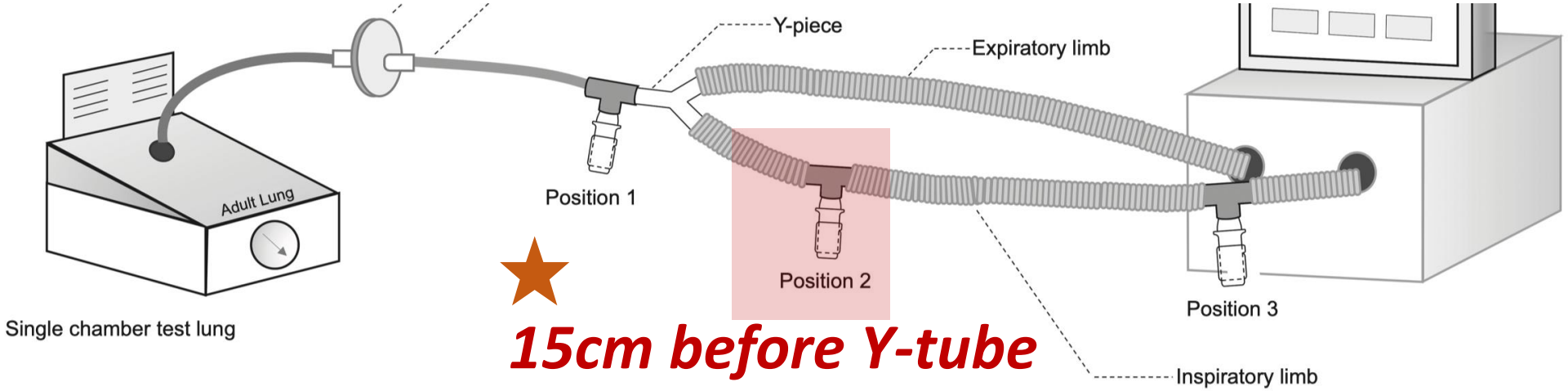
VHC > spacer > inhaler only











15cm before Y-tube

4 timing

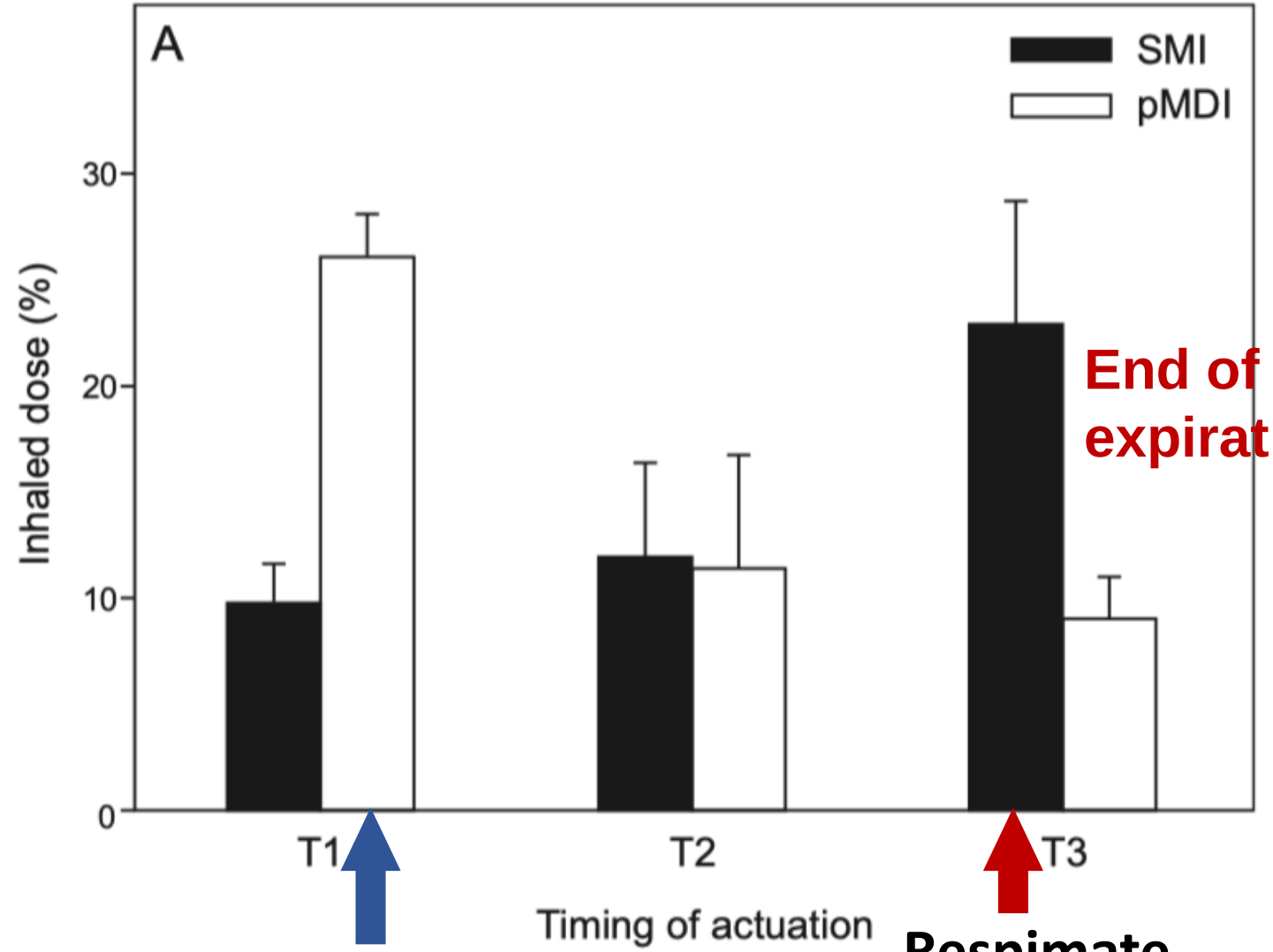
- **T1: onset of inspiration**
- **T2: onset of expiration**
- **T3: end of expiration**

SMI: end of expiration

pMDI: onset of inspiration

The spray duration
SMI : **1.43** ± 0.12 s
pMDI: **0.17** ± 0.03 s

Ti: 0.9 s



End of expiration

Metered dose inhaler

MDI

Respimate

Soft moisture inhaler

SMI

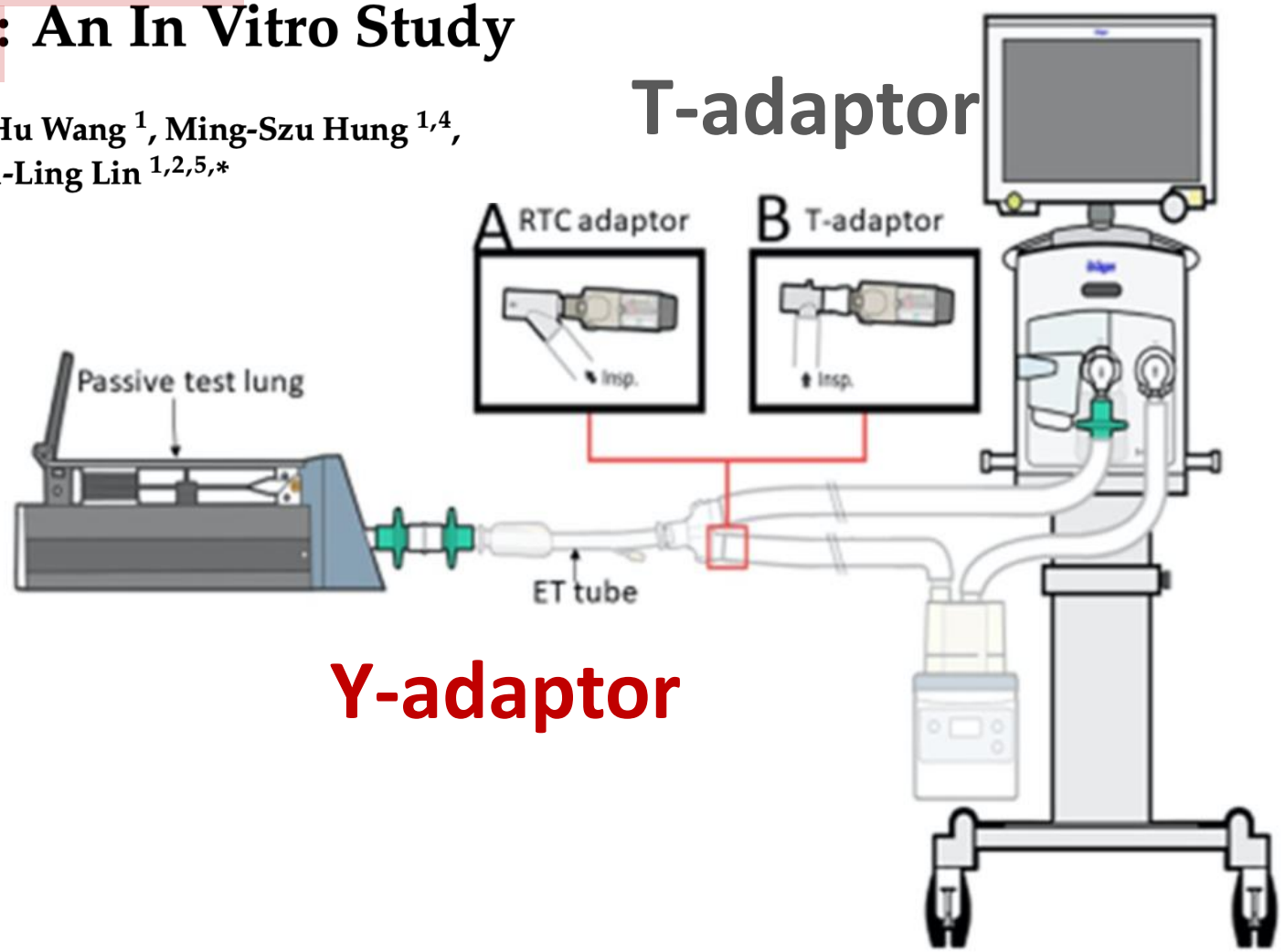
pharmaceutics

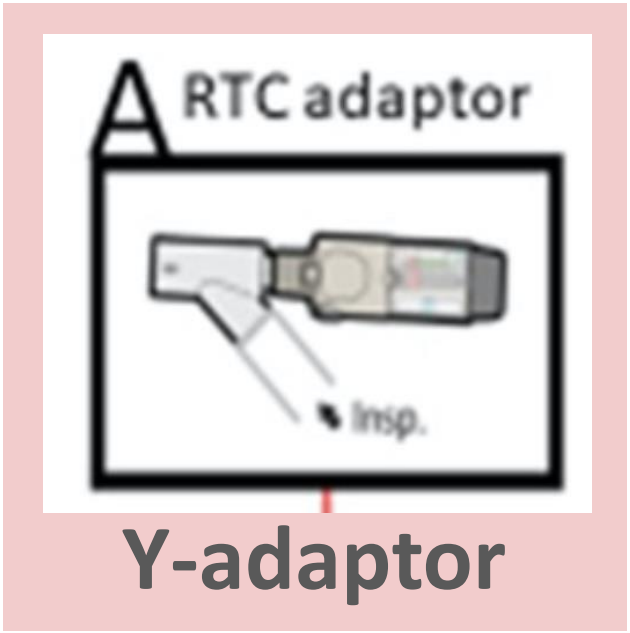
MDPI

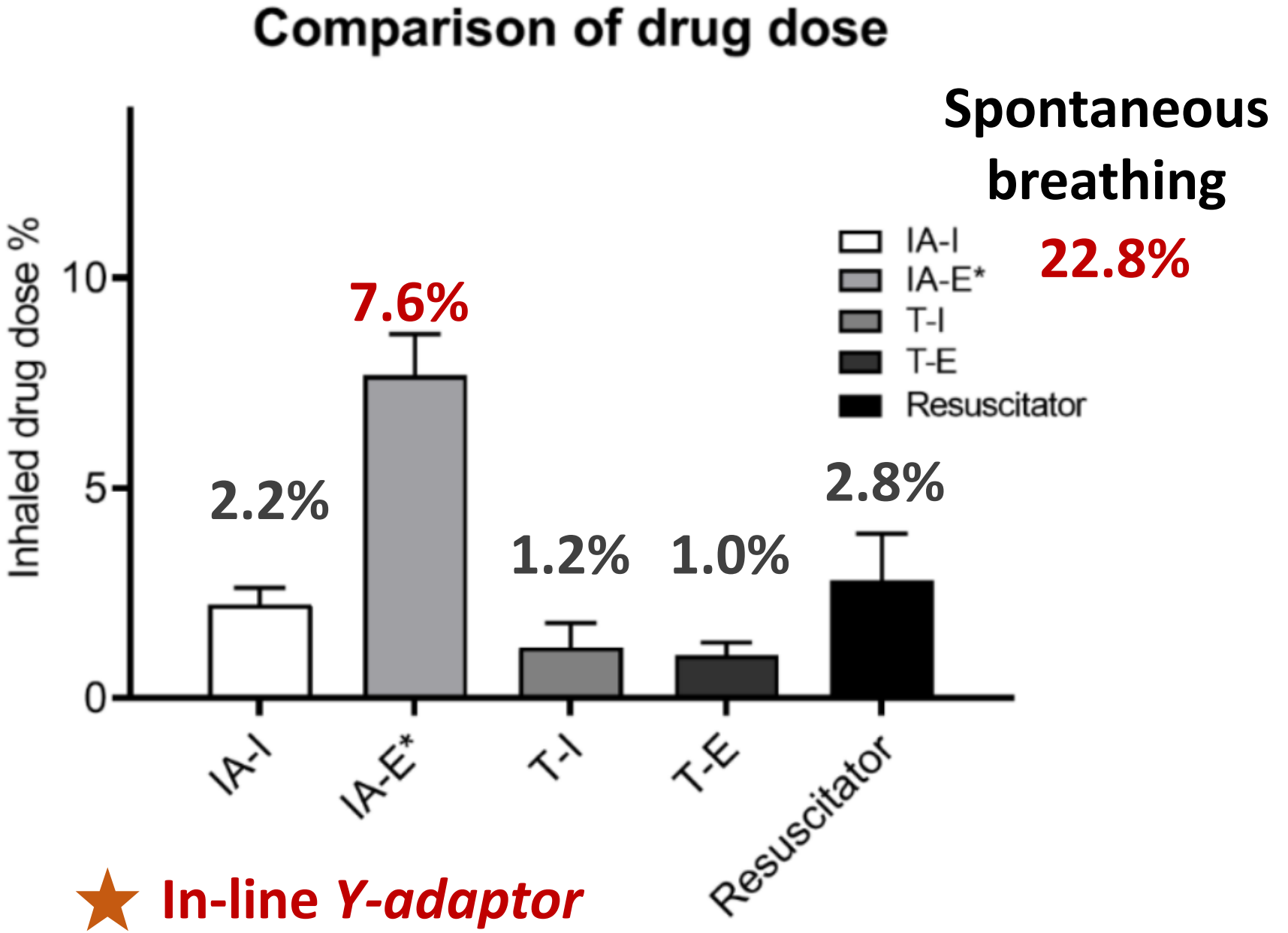
Article

Optimal Connection for Tiotropium SMI Delivery through Mechanical Ventilation: An In Vitro Study

Tien-Pei Fang [1,2], Yu-Ju Chen [3], Tsung-Ming Yang [4], Szu-Hu Wang [1], Ming-Szu Hung [1,4], Shu-Hua Chiu [1], Hsin-Hsien Li [5], James B. Fink [6] and Hui-Ling Lin [1,2,5,*]







Spontaneous breathing

22.8%

★ **In-line *Y-adaptor***

Actuation during *Expiration*


3. 吐氣期給藥
2. Y型接頭
1. 進氣端，Y型接管前15 cm

Summary

Prevalence

BD, ICS, Abx
Nebulizer most
Different MV settings

Drugs

AE: Short-acting, Nebulizer
May add long-acting BD when condition is stable

Devices

MDI / SMI+ spacer/Chamber > VMN > JN

Deposition

of the aerosol therapy

Central airway
Limited by secretion and atelectasis

Ventilator settings

MDI / SMI: **Inspiratory limbs,15cm from Y piece**
Stop heated humidifier
Vt ↑, RR ↓
MDI: inspiration, SMI: **Y-connector, expiration**
30-60s interval, ↑ dose

Management of Mechanical Ventilation in Patients with Obstructive Lung Disease

1. Non-invasive mechanical ventilation

High-flow nasal cannula

2. Invasive Mechanical ventilation

3. Aerosol therapy in MV

中國醫藥大學附設醫院

胸腔內科暨重症系

陳韋成醫師