呼吸道治療建議與 COVID-19疫情防治

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2021/8/24 8:00-9:00

Pathophysiology of COVID-19

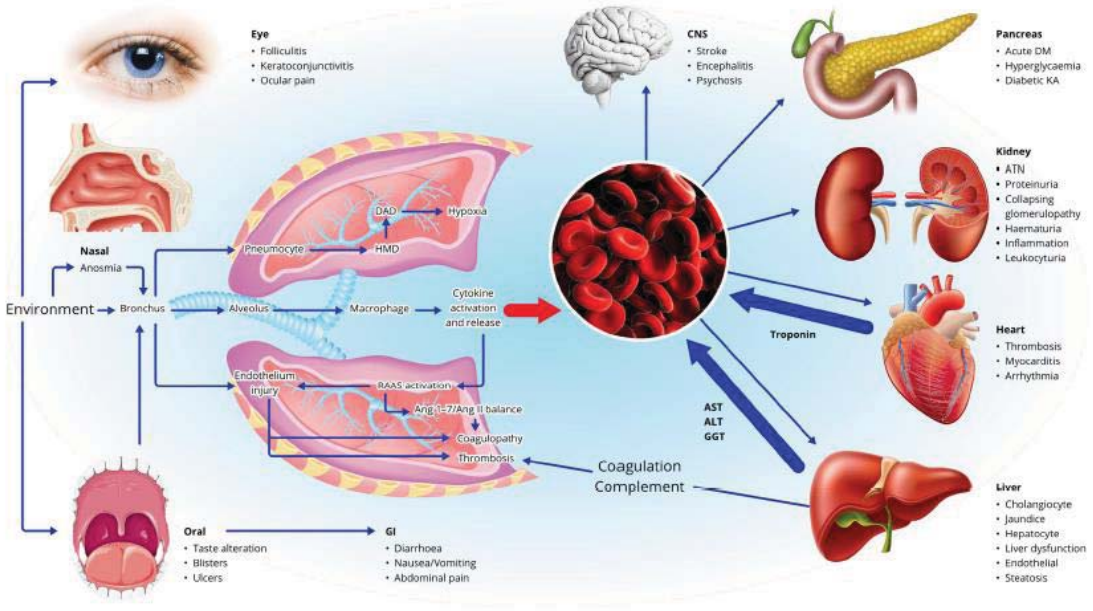
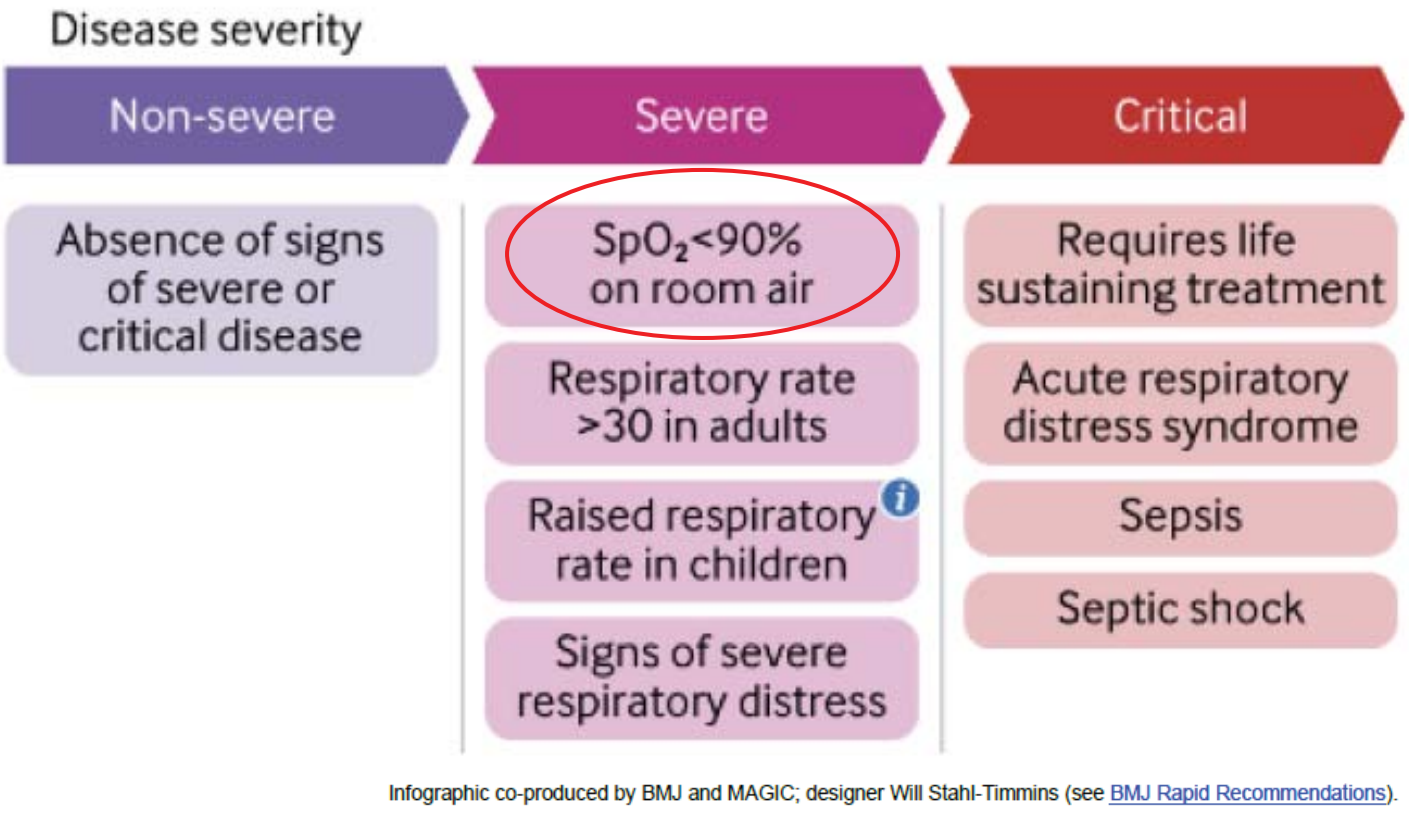


FIGURE 1 Simplified schematic of proposed pathological changes in severe acute respiratory syndrome coronavirus 2 infection. The three main portals of entry into the respiratory tract are through the eye, nasal cavity and oral route, with the latter also leading to infection of the gastrointestinal tract. In the respiratory tract, infection of pneumocytes leads to exudation of fibrinogen and hyaline membrane formation, followed by diffuse alveolar damage with hypoxia. Stimulation of macrophages and bronchiolar epithelial damage causes cytokine release into the alveolar spaces and into the blood. Either virus infection of endothelium or cytokine release activates the renin–angiotensin–aldosterone system, producing a pro-thrombotic tendency, with the formation of thrombi, mainly in the pulmonary vasculature. Either viraemia or cytokinaemia in the systemic circulation damages the brain, pancreas, kidneys, heart and liver producing a number of organ-specific changes, in addition to the increased thrombotic tendency. The multi-system damage is manifest by elevated troponin and liver enzymes in the blood, and the release of factors aggravates the pro-thrombotic tendency

Respirology 2021

COVID-19: 不同的疾病嚴重度



Infographic co-produced by BMJ and MAGIC; designer Will Stahl-Timmins (see BMJ Rapid Recommendations).

Non-severe disease (mild or moderate)

Mild disease		Symptomatic patients (Table 6.1) meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia. See the WHO website for most up-to-date case definitions *(1)*.
Moderate disease	**Pneumonia**	**Adolescent or adult** with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including SpO_2 ≥ 90% on room air *(86)*. **Child** with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest indrawing) and no signs of severe pneumonia. Fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 *(87)*. While the diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications. **Caution:** The oxygen saturation threshold of 90% to define severe COVID-19 was arbitrary and should be interpreted cautiously. For example, clinicians must use their judgment to determine whether a low oxygen

COVID 19 Clinical management, Living guidance 25 January 2021, WHO

表一、SARS-CoV-2 感染的相關臨床表現分類(參考 WHO, NIH 與 IDSA)

輕度	無併發症之輕症	沒有任何併發症的上呼吸道病毒性感染患者，可能出現非專一性的症狀，如發燒、咳嗽、喉嚨痛、鼻塞、倦怠、頭痛、肌肉痠痛等。少數患者出現腹瀉、噁心或嘔吐。年長或免疫力低下患者可能有比較不典型的症狀。孕婦因生理上產生的呼吸淺快或發燒等症狀，可能與感染症狀相同。
中度	肺炎	沒有嚴重肺炎徵候的肺炎患者，無氧氣設備輔助（room air）下血氧飽和度>94%。非嚴重肺炎的兒童患者會有咳嗽以及呼吸急促（fast breathing），但沒有嚴重肺炎的徵候。 呼吸急促定義：< 2 個月齡幼兒：≧ 60 下/分鐘；2–11 個月齡幼兒：≧50 下/分鐘；1–5 歲兒童：≧ 40 下/分鐘。
重度	嚴重肺炎	青少年或成人：發燒或呼吸道感染，合併下列任一項：呼吸速率 > 30 下/分鐘、嚴重呼吸窘迫（severe respiratory distress）PaO2/FiO2 <300、無氧氣設備輔助（room air）下血氧飽和度 ≦ 94%、或肺浸潤(infiltration)>50%。 兒童：咳嗽或呼吸困難，合併下列任一項：中樞性發紺（central cyanosis）或血氧飽和度 < 90%；嚴重呼吸窘迫（如呼吸呻吟聲[grunting]、極度嚴重之胸部凹陷）；肺炎合併危險徵候（如無法餵/進食、倦怠或意識喪失、抽搐等）。其他也可能會出現的肺炎徵候：胸部凹陷、呼吸急促（< 2 個月齡幼兒：≧ 60 下/分鐘；2–11 個月齡幼兒：≧ 50 下/分鐘；1–5 歲兒童：≧ 40 下/分鐘）。此為臨床性診斷，胸部 X 光可用於輔助排除併發症。

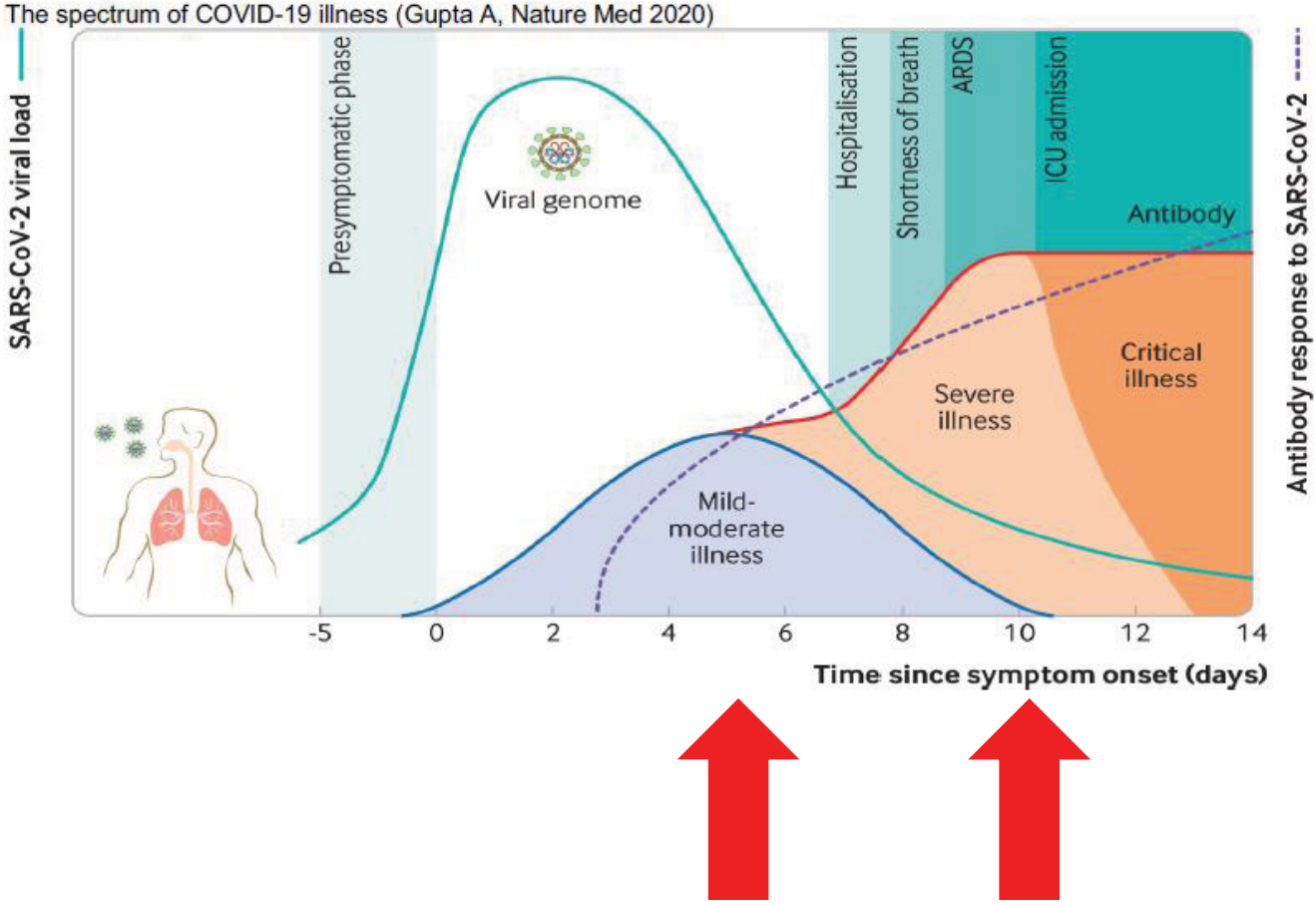
新型冠狀病毒（SARS-CoV-2）感染臨床處置暫行指引
行政院衛生福利部疾病管制署 編
2021年7月13日 第十三版

危急 (Critical)

- ARDS
- Sepsis
- Septic shock
- Multisystem inflammatory syndrome in children (MIS-C)

新型冠狀病毒（SARS-CoV-2）感染臨床處置暫行指引
行政院衛生福利部疾病管制署 編
2021年7月13日 第十三版

1. The spectrum of COVID-19 illness (Gupta A, Nature Med 2020)



SARS-CoV-2

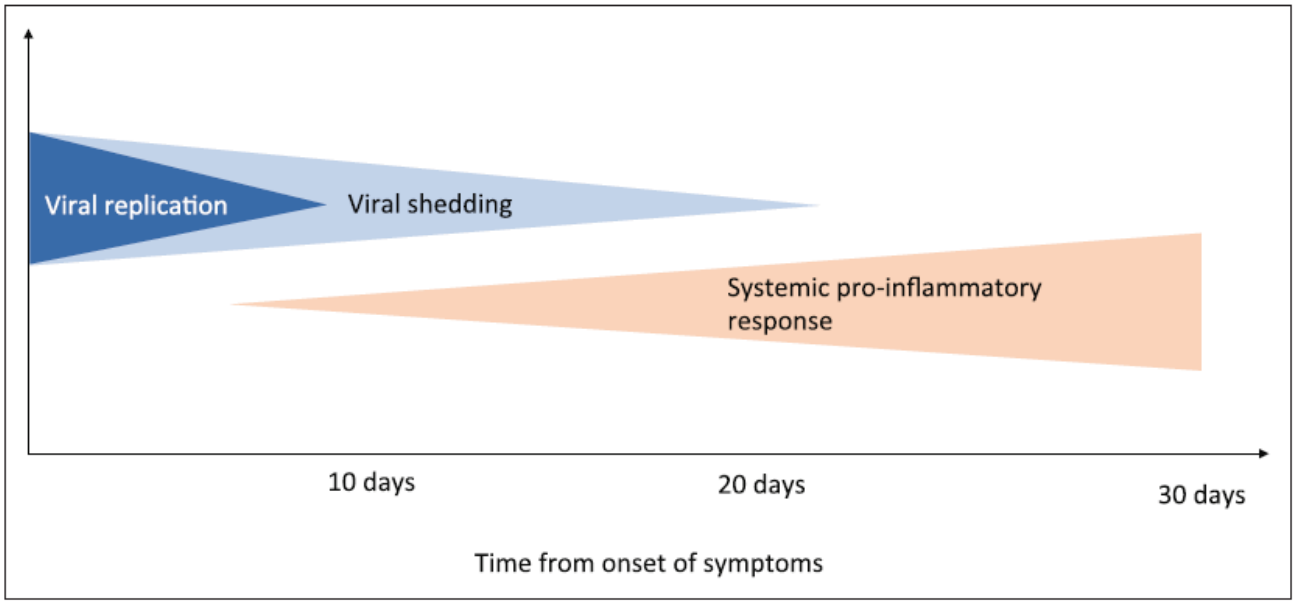
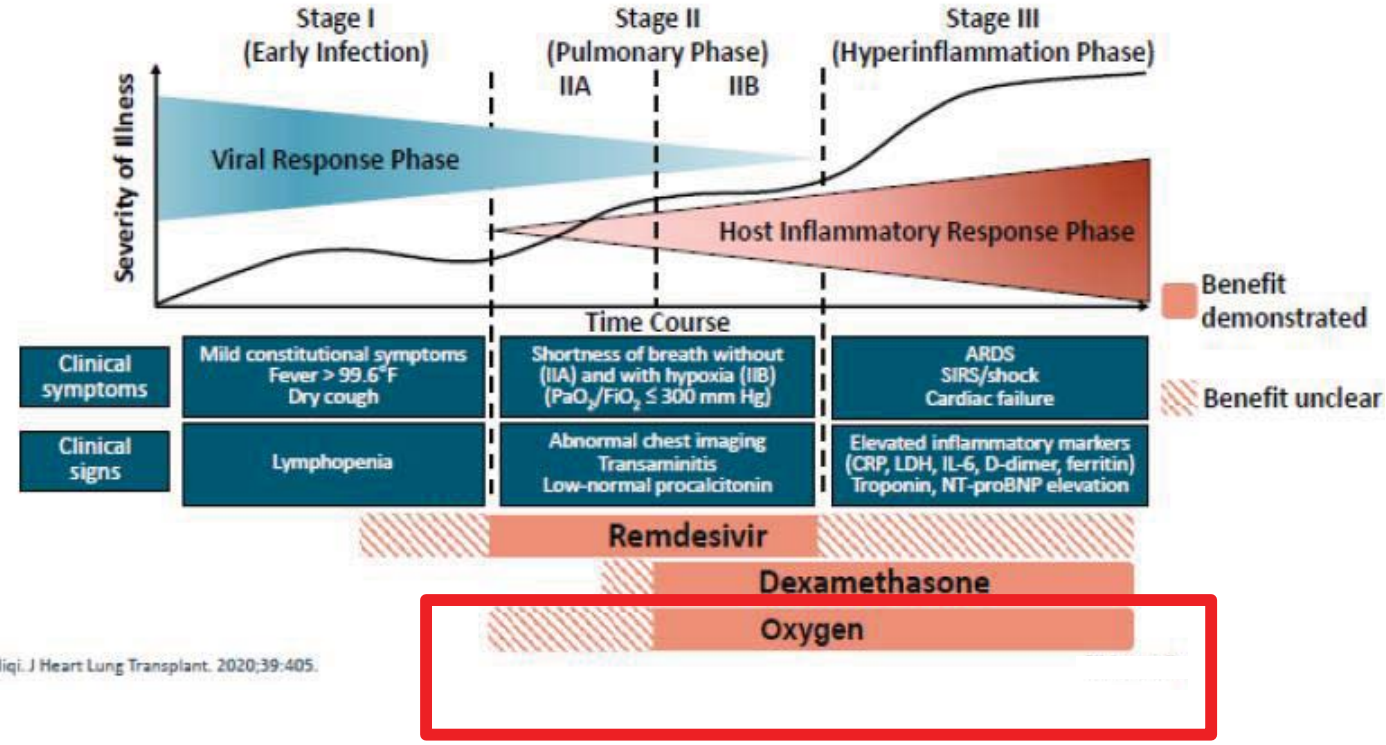


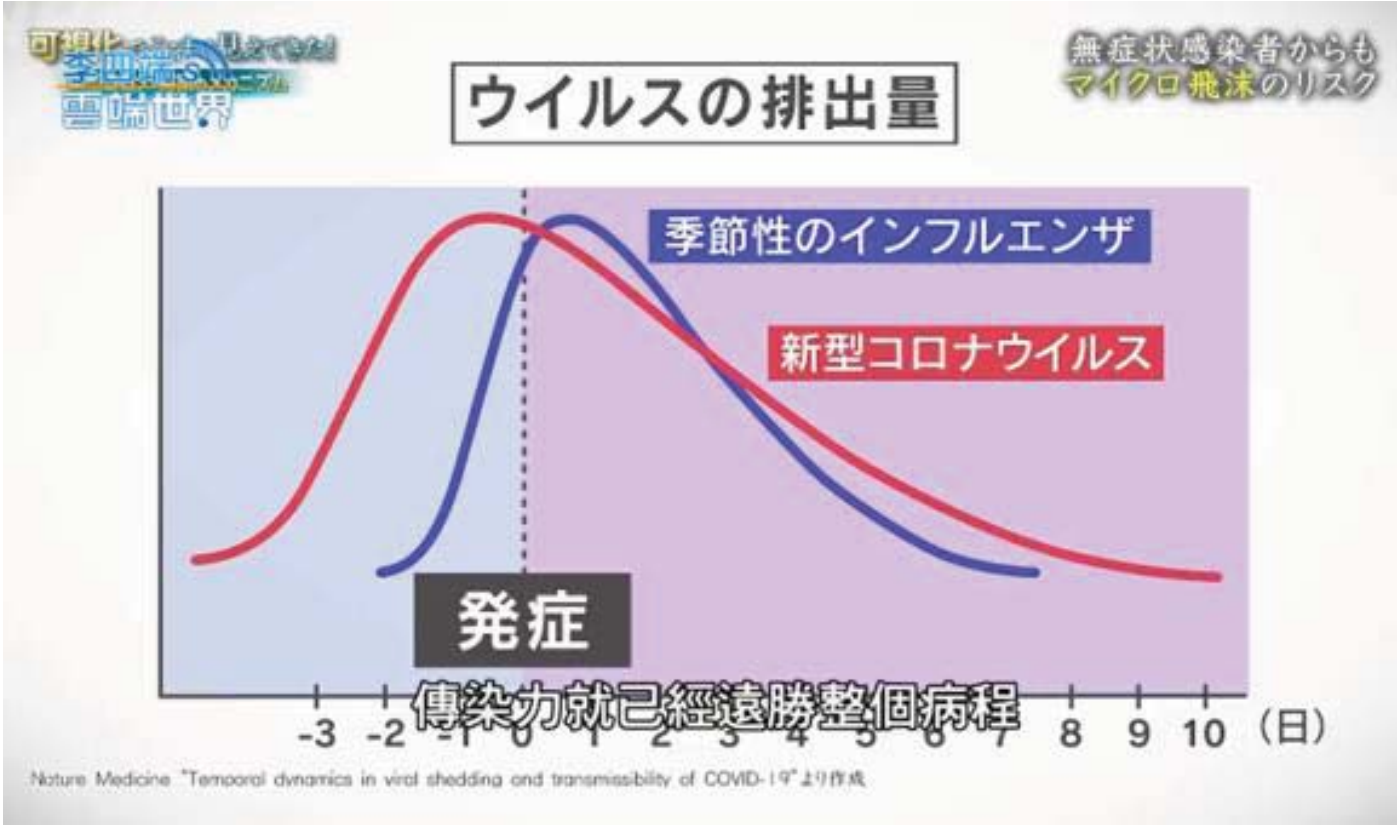
FIGURE 1. Viral replication begins prior to the onset of symptoms and continues for roughly 10 days after the onset of symptoms, although the duration may be longer among patients who are immunosuppressed or have severe illness. A systemic proinflammatory response may commence within 10 days of the onset of symptoms and can be progressive, causing the patient to become severely ill.

Curr Opin Pulm Med 2021, 27:169–175

病程與治療藥物的選擇



Siddiqi. J Heart Lung Transplant. 2020;39:405.

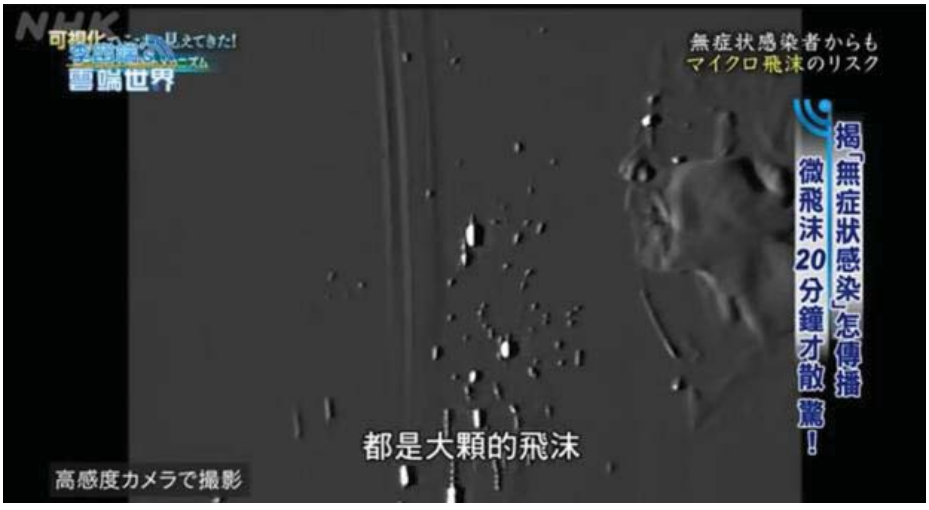


Aerosols (氣溶膠; 氣膠; 氣懸膠)

- 指氣體介質中懸浮的固體或液體顆粒
- 舉凡生活中常見的物質如粉塵、霧、煙、PM2.5、真菌孢子、飛沫，以及**臨床治療呼吸道疾病的吸入型藥物**等，均屬於氣溶膠
- 每個人在呼吸（平靜呼吸和深呼吸）、說話、**打噴嚏和咳嗽**的過程中，會產生許多肉眼可見或不可見的微粒，直徑大小介於0.01～500 μm
  - 當微粒直徑大於10 μm，可因重力而沉降於地面，稱之為「落塵」，而當微粒直徑≤10 μm時，可懸浮在空氣中，故稱為「懸浮微粒」。

飛沫（Droplet）

- 當人說話、打噴嚏或**咳嗽**等過程中產生大粒徑（大於5微米）的飛沫，一般來說，可飛行的距離約為1公尺（3英呎）；當飛沫中含有病毒等病原體時，近距離的接觸可增加人體感染的機會，稱為「飛沫傳染」。
- 人在說話或打噴嚏時產生的大粒徑飛沫會沉降於**地面或物體表面**，所以正確的洗手動作、經常清潔與消毒各種物品表面（如桌面、地板、儀器設備、玩具等），以及採取妥善食物覆蓋等措施，均可避免飛沫污染，



Oxygen support: 名詞定義

- 低流量氧氣 (Flow < 10 L/min)
  - 鼻導管 (Nasal cannula, NC)
  - 簡單型面罩 (simple face mask, SM)
  - 非再吸入性面罩 (Non-rebreathing mask, NRM)
- 高流量氧氣 (Flow >= 10 L/min)
  - Venturi mask
  - 高流量鼻導管 (High-flow nasal cannula, HFNC)
  - 非侵襲性呼吸器 (Non-invasive mechanical ventilation, NIV)
  - 侵襲性呼吸器 (Invasive mechanical ventilation, IMV)

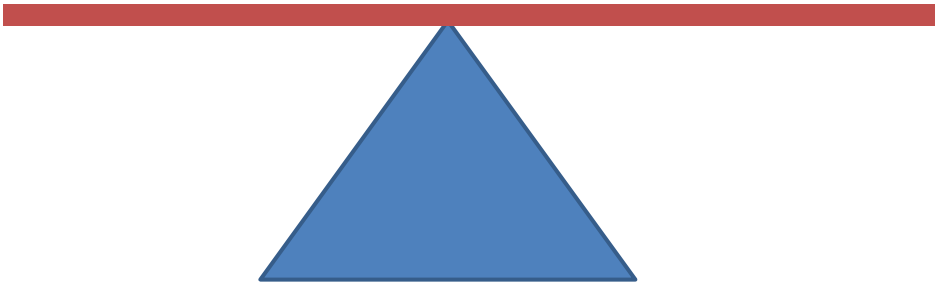
Clinical management of patients with COVID-19

- Improving patient outcomes e.g. by avoiding the need of tracheal intubation
- Maintaining HCW safety e.g. by avoiding an increased in widespread nosocomial transmission

HCW: Health Care Worker

Balance between Patient's outcome and HCW safety

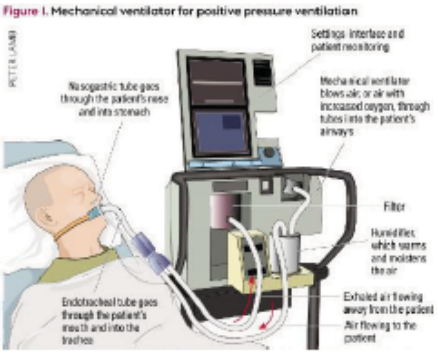
Patient's outcome HCW safety

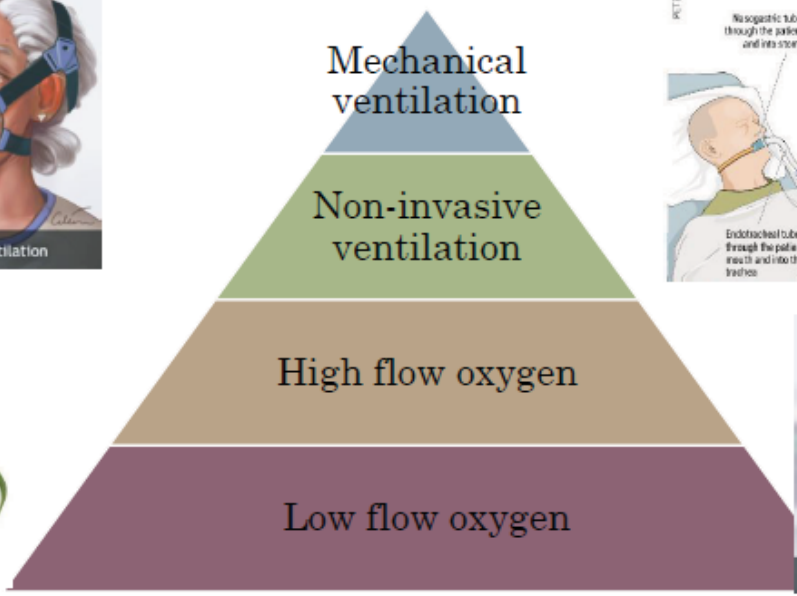


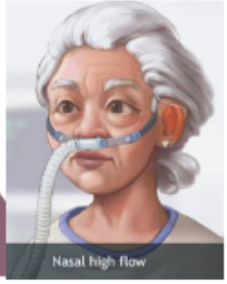
HCW: Health Care Worker

Management of COVID

- 20 % infected patients developed into hypothermia, and 10% of patient require intubation and mechanical ventilation support.





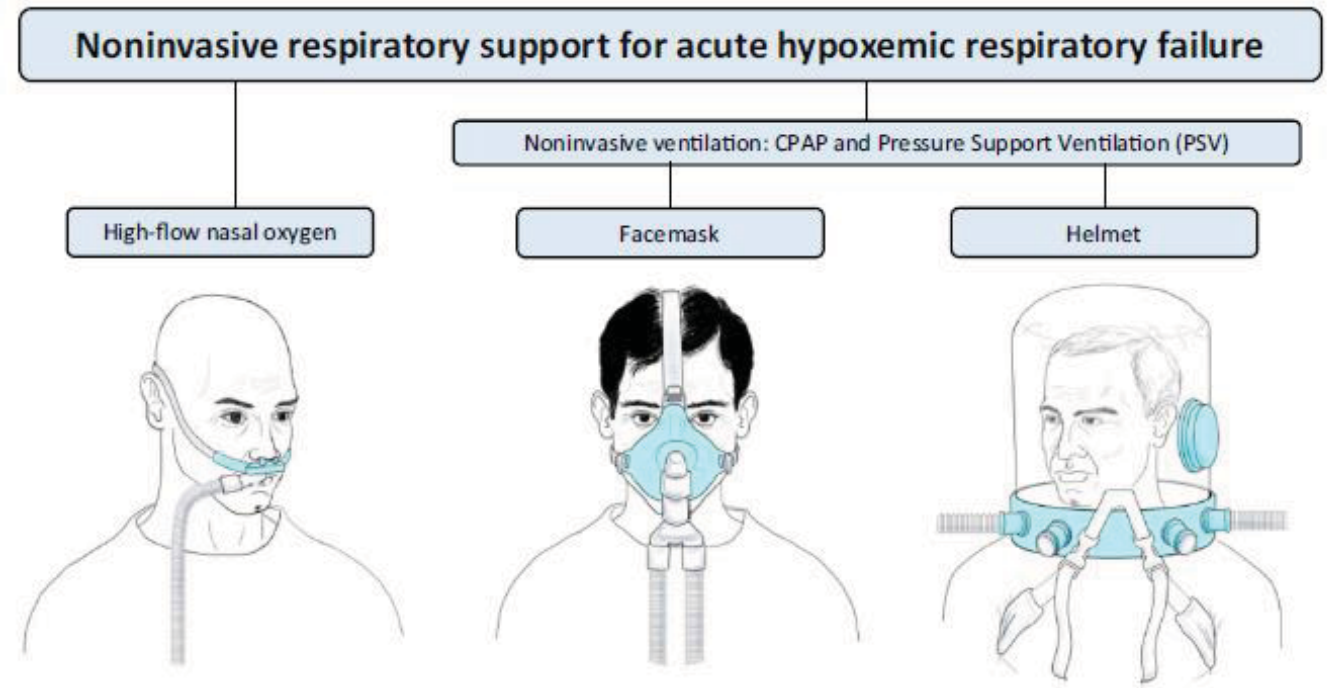


Oxygen support in COVID-19 AHRF

- Non-invasive oxygen support (NI-OS)
  - NIV (BiPAP, CPAP), HFNC, Non-rebreathing face mask
- Invasive oxygen support
  - Early IMV

AHRF: Acute Hypoxemic Respiratory Failure
NIV: Noninvasive ventilation
HFNC: High flow nasal canuula
IMV: Invasive mechanical ventilation

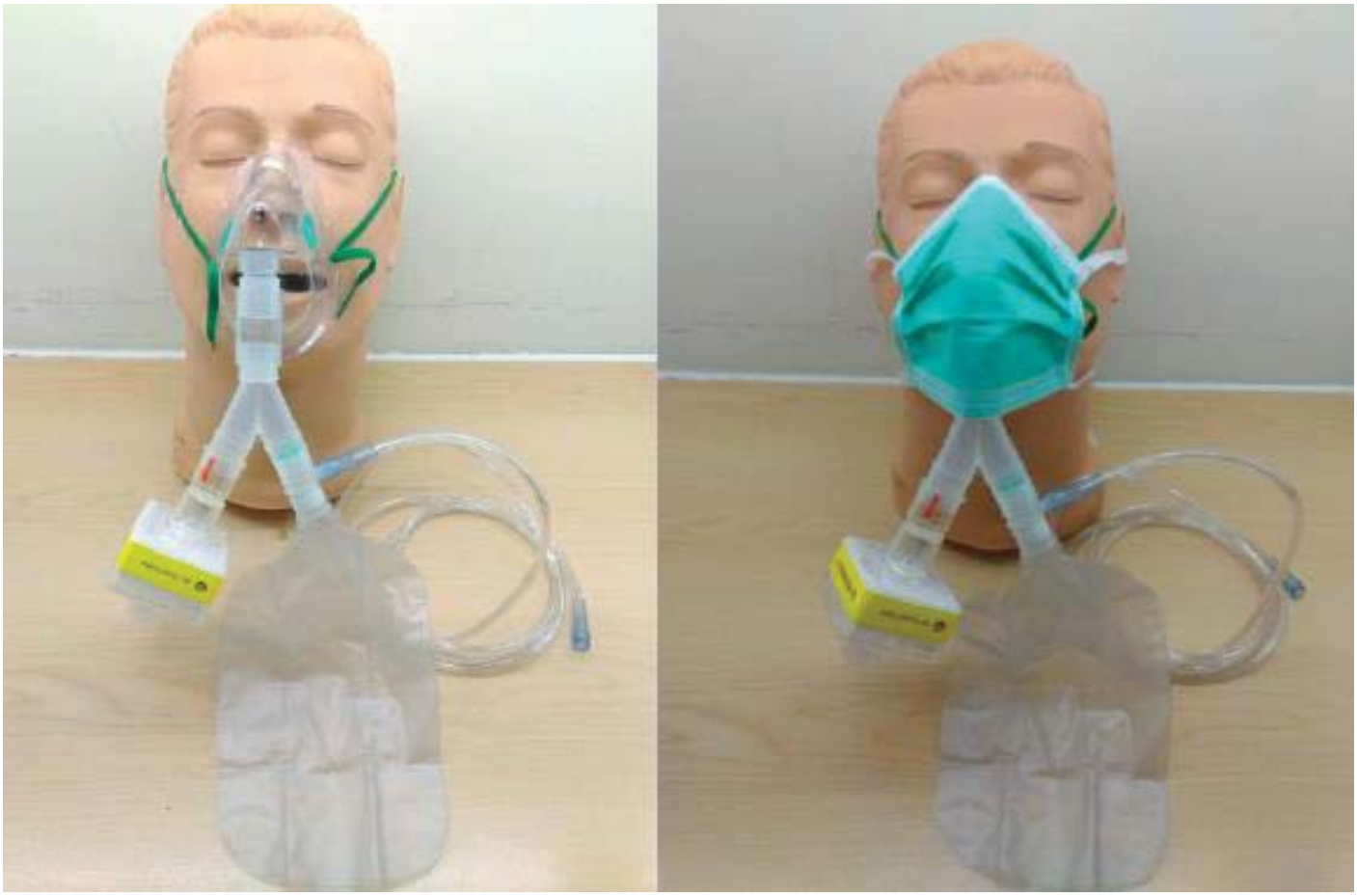
Noninvasive respiratory support for AHRF



Intensive Care Med (2021) 47:851–866

Low flow oxygen system

- Maximal flow : 15 L/min
- 給予O2的Flow並不保證大於病人的minute ventilation (MV)，因此若病人太喘會混入room air，造成給予的FiO2會變化不穩定
- 適用在較不喘的的病人，例如MV <10 L/min、RR<25 或 Tidal volume <700-800 ml
- Nasal cannula, Simple mask
- Non-rebreathing mask (10-15 L/min = FiO2 0.6 -0.95)



High flow oxygen system

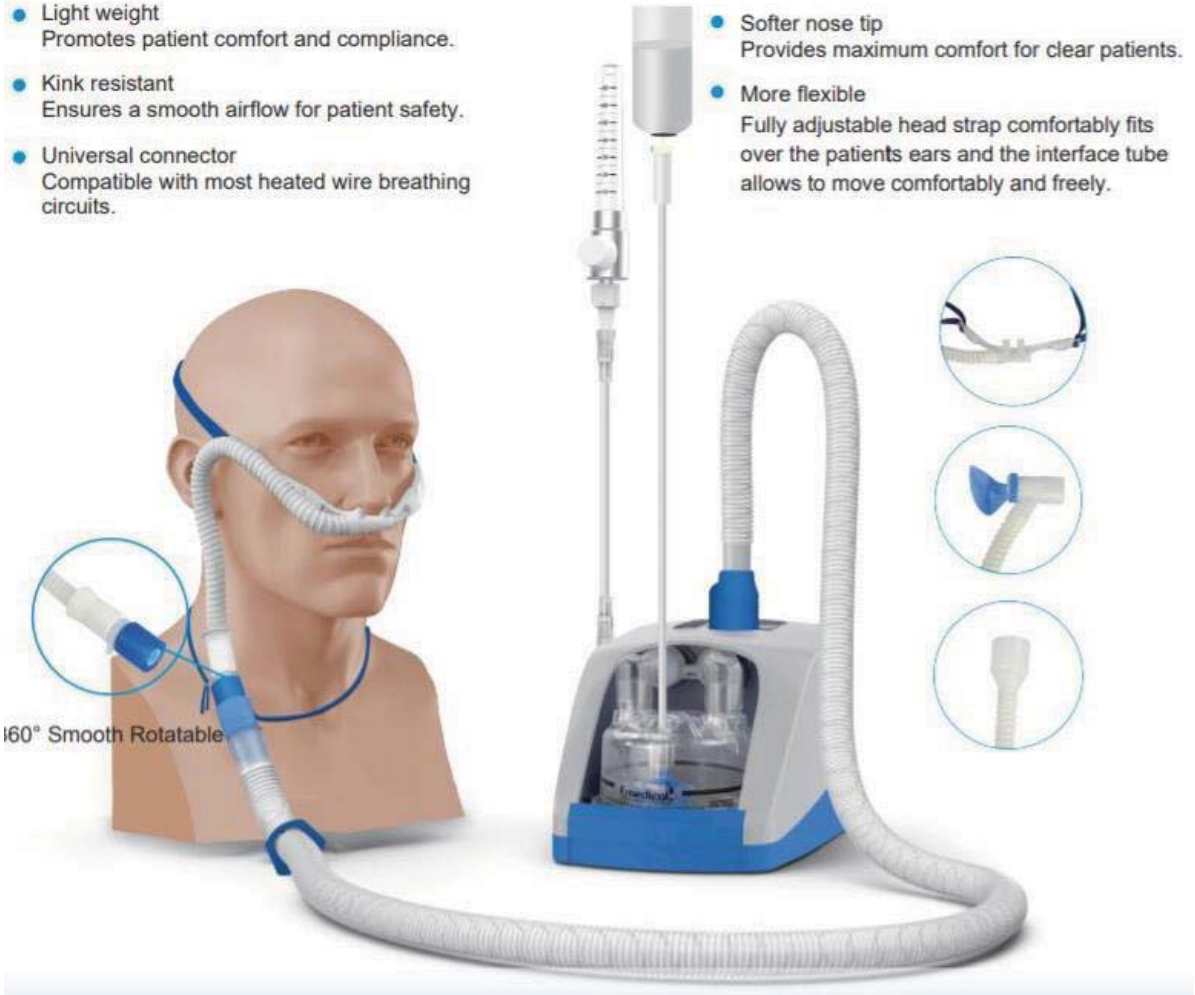
- 給予O2的flow > 3 倍的MV，因此不會吸入 room air 可以維持一定的FiO2
  - COPD 或 ARDS ?
- Venturi (air-entrainment) mask，High Flow Nasal Cannula (HFNC)
- Invasive mechanical ventilation (IMV)

Venturi mask

High Flow Nasal Cannula (HFNC)

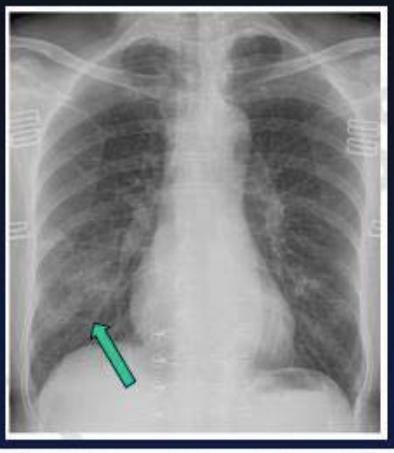
- Light weight
  Promotes patient comfort and compliance.
- Kink resistant
  Ensures a smooth airflow for patient safety.
- Universal connector
  Compatible with most heated wire breathing circuits.

- Softer nose tip
  Provides maximum comfort for clear patients.
- More flexible
  Fully adjustable head strap comfortably fits over the patients ears and the interface tube allows to move comfortably and freely.



肺炎(輕度或中重度)

- 早期識別出有嚴重臨床表現的患者，才可以及時對患者採取有效的支持性治療
- 若惡化可以病況依流程，快速、安全地轉入加護病房
- 肺炎的影像學表現
  - CXR
  - Chest CT



Radiology:cardiothoracic imaging Published Online:Feb 13 2020

臨床處置 (1)

- ✔ 儘早對呼吸窘迫，低血氧症或休克的患者給予氧氣治療
- 開始建議以5 L / min的速度給予氧氣治療，並適時調整流速，目標血氧飽和度為非懷孕之成年患者$SpO_2 \geq 90\%$和懷孕患者$SpO_2 \geq 92–95\%$
  - 對SARS-CoV-2患者進行照護的所有診療區域均應配備脈搏血氧儀、可用的供氧系統以及單次使用的供氧設備（如鼻導管，簡易供氧面罩、或非循環呼吸面罩等, NRM）。

臨床處置 (2)

- ✔ 若SARA-CoV-2患者無休克證據，則採取謹慎的輸液治療。
  - 患者應謹慎使用靜脈輸液，因為過度的輸液治療可能會使氧合情形惡化，尤其是呼吸器設備不足的醫療機構更需注意。
- ✔ 對臨床症狀較嚴重之患者，考慮給予經驗性抗生素/抗病毒藥物以治療其他可能的細菌/病毒感染。對於敗血症患者，建議在初次患者評估後給予適當的經驗性抗生素。有關肺炎經驗性治療可參考2018年「台灣肺炎診治指引」。

臨床處置 (3)

- ✔ 密切監測SARS-CoV-2患者是否出現症狀惡化的跡象，例如快速進展至呼吸衰竭和敗血症，並立即採取支持器官灌流治療措施。
- ! 治療疑似或確診SARS-CoV-2感染病患時，應避免使用Nebulizer等氣霧式治療，可使用Dry-powder inhaler (DPI)或Metered-dose inhaler(MDI)

When to intubate the critically ill COVID-19 patient

- Patients' tracheas may be intubated earlier in the course of their illness than in other settings
- A low threshold for intubation
- If SpO2 < 92% or unstable work of breathing (at: NRM at 12 LPM or Venturi mask at FiO2 60%)

Lancet Respir Med 2020 Published Online April 6, 2020
Brigham and Women's hospital protocol : COVID 19 clinical guideline
Surviving Sepsis Campaign guideline on management of COVID 19 Crit Care Med 2020

快速引導式插管 (Rapid sequence intubation) (1)

- 插管時會產生大量的病毒飛沫，因近距離接觸，使醫護人員暴露在非常高感染風險
- 務必要穿戴完整個人防護裝備後才能執行
- 執行插管者必須經完整插管訓練及具有實務經驗
- 插管必須在負壓隔離室進行

插管前準備事項 by SCC

病史詢問及家屬溝通	個人防護措施
取得插管同意書	拋棄式防水性連身型防護衣
NPO時間	雙層手套
過敏史	N95等級(含)以上之口罩
有無鬆動牙齒	拋棄式防護面罩
身高及體重	拋棄式防水長筒鞋套
全身健康狀況及過去病史	
呼吸窘迫治療概況	
身上點滴管路通順	

插管前準備物品

插管用具檢查
Video laryngoscope (3號或4號拋棄式葉片)
Endotracheal tube 7.0mm-7.5mm
Stylet放入Endotracheal tube 折成適當形狀，勿突出前端
20ml 空針檢查cuff
Oral Airway+Nasal Airway
固定用膠帶
HEPA filter 氣氣面罩
Laryngeal mask

疾病管制署 新型冠狀病毒(SARS-CoV-2)感染臨床處置暫行指引 2020年3月25日 第五版
Anesthesia 2020 Mar 27. doi: 10.1111/anae.15054. [Epub ahead of print]

From 張志華, 急重症繼續教育資訊平台

快速引導式插管 (Rapid sequence intubation) (2)

- 有臨床氧合或生命徵象不穩定而造成呼吸衰竭，應即刻進行插管處置，插管時須使用適當藥物來完成快速引導式插管(Rapid sequence intubation)。
- 若病人仍有自主呼吸時，可使用高流速氧氣設備進行5分鐘插管前給氧(Pre-oxygenation)，此時不建議使用甦醒球擠壓換氣(Ambu-bagging)。
- 執行插管時可藉助影像指引喉鏡(Video-assisted laryngoscope)來進行。
- 呼吸器進行機械通氣時，須使用密閉迴路系統的抽痰管(Closed system suction)。

Anesthesia 2020 Mar 27. doi: 10.1111/anae.15054. [Epub ahead of print]

機械通氣時避免飛沫噴濺

- X 避免中斷患者與呼吸機的連接管路，否則會導致PEEP消失和肺擴張不全
- 建議使用密閉式抽痰管並在需要斷開呼吸管路（例如，轉移呼吸管路至運送用呼吸機）時，須在氣管內管連結高效能氣體過濾器(例如HEPA、HMEF等)在遠端斷開，避免飛沫噴濺或使用無齒止血鉗套橡膠管夾住氣管導管。

指揮中心已採購
高流量氧氣鼻管系統500台

因應治療需求，指揮中心已採購高流量氧氣鼻管系統(HFNC)500台，其中200台今(6/13)日交貨，將由指揮中心與台灣胸腔暨重症醫學會協助分配至有需求的醫院，提供須高流量氧氣治療的COVID-19重症病患使用。

中央流行疫情指揮中心　2021/06/13

高流量氧氣鼻導管 (HFNC)

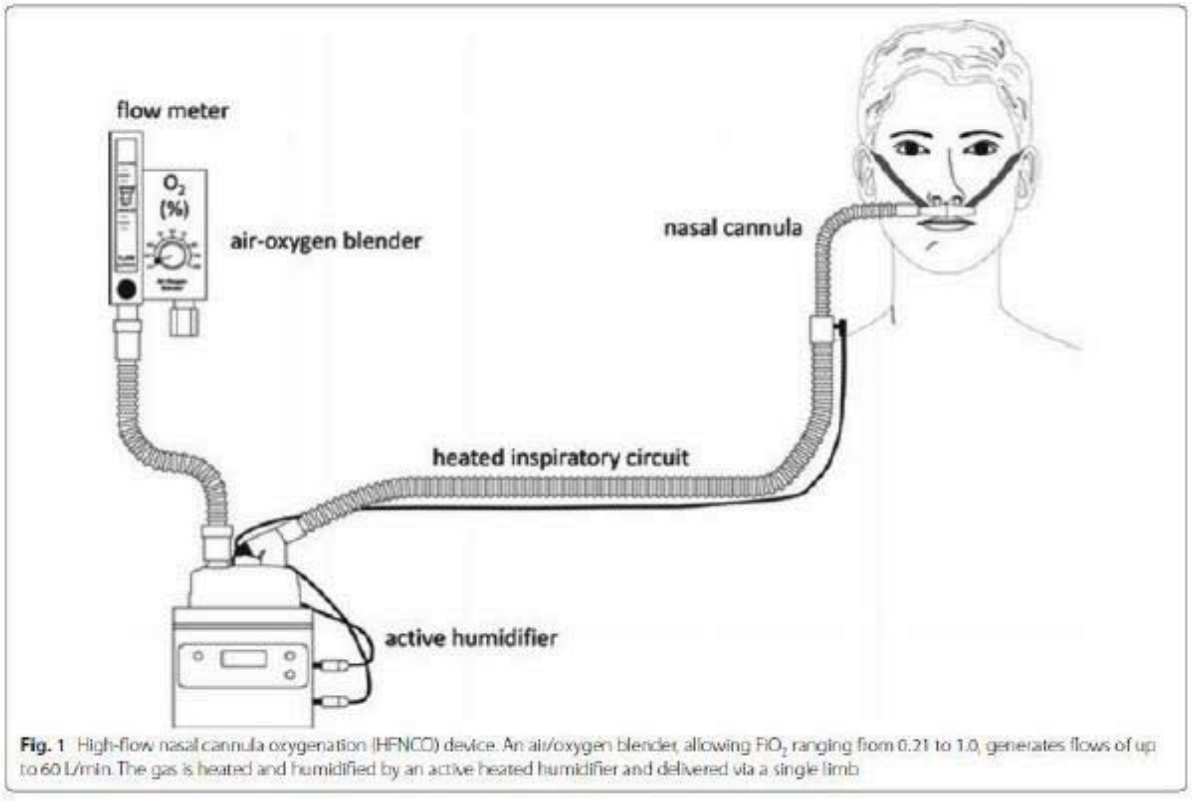
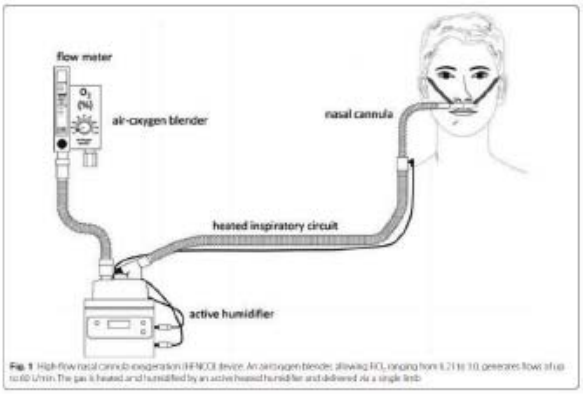


Fig. 1 High-flow nasal cannula oxygenation (HFNCO) device. An air/oxygen blender, allowing FiO_2 ranging from 0.21 to 1.0, generates flows of up to 60 L/min. The gas is heated and humidified by an active heated humidifier and delivered via a single limb

High flow nasal cannula (HFNC)

- capable of delivering high flow of 30–60L/min
- precise fraction of inspired oxygen (FiO_2)
- heated and humidified gas
- enhancing patients' comfort
- better outcomes



Intensive Care Med (2016)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

106 Were assigned to high-flow–oxygen group

96 Were assigned to standard-oxygen group

111 Were assigned to non-invasive-ventilation group

2 Withdrew consent

1 Withdrew consent

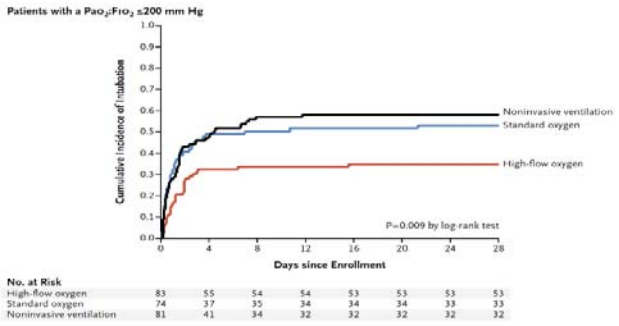
310 Were included in the analysis and in the 90-day follow-up
106 Were in the high-flow–oxygen group
94 Were in the standard-oxygen group
110 Were in the noninvasive-ventilation group

Exclusion criteria: COPD or asthma AE; Acute pulmonary edema; PaCO2 > 45 mmHg

N Engl J Med 2015

Reduce intubation and mortality

Reduced intubation rate



90 Day survival

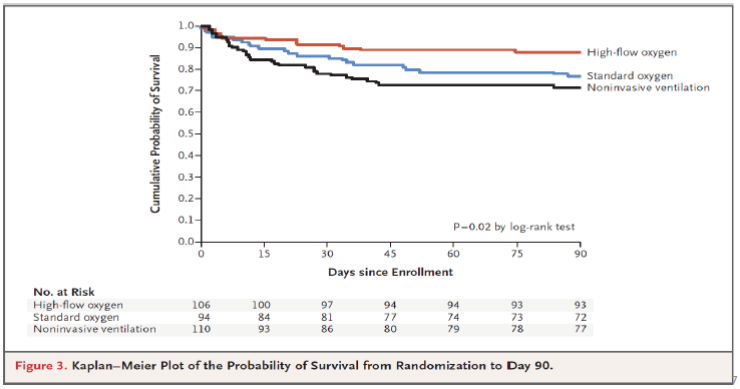


Figure 3. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.

NEJM 2015

SYSTEMATIC REVIEW

High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: a systematic review and meta-analysis

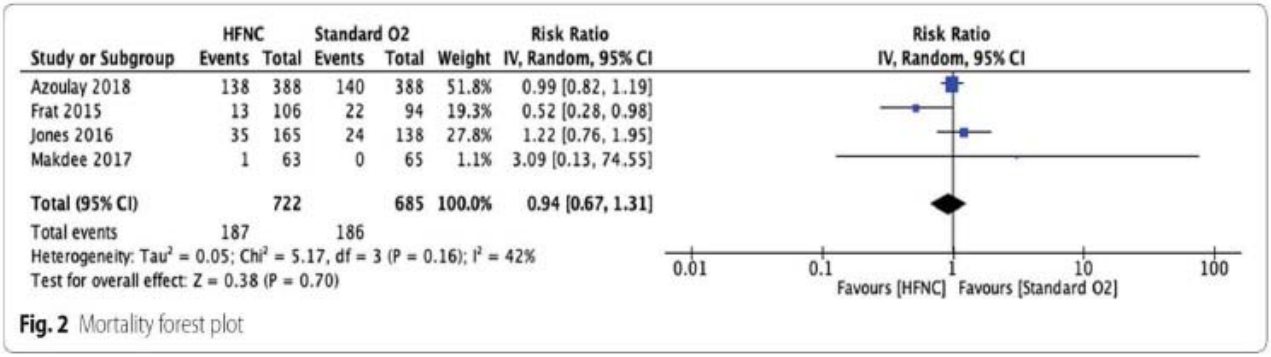


Fig. 2 Mortality forest plot

HFNC does not decrease mortality in acute hypoxemic respiratory failure patients

Intensive Care Med (2019) 45[8]

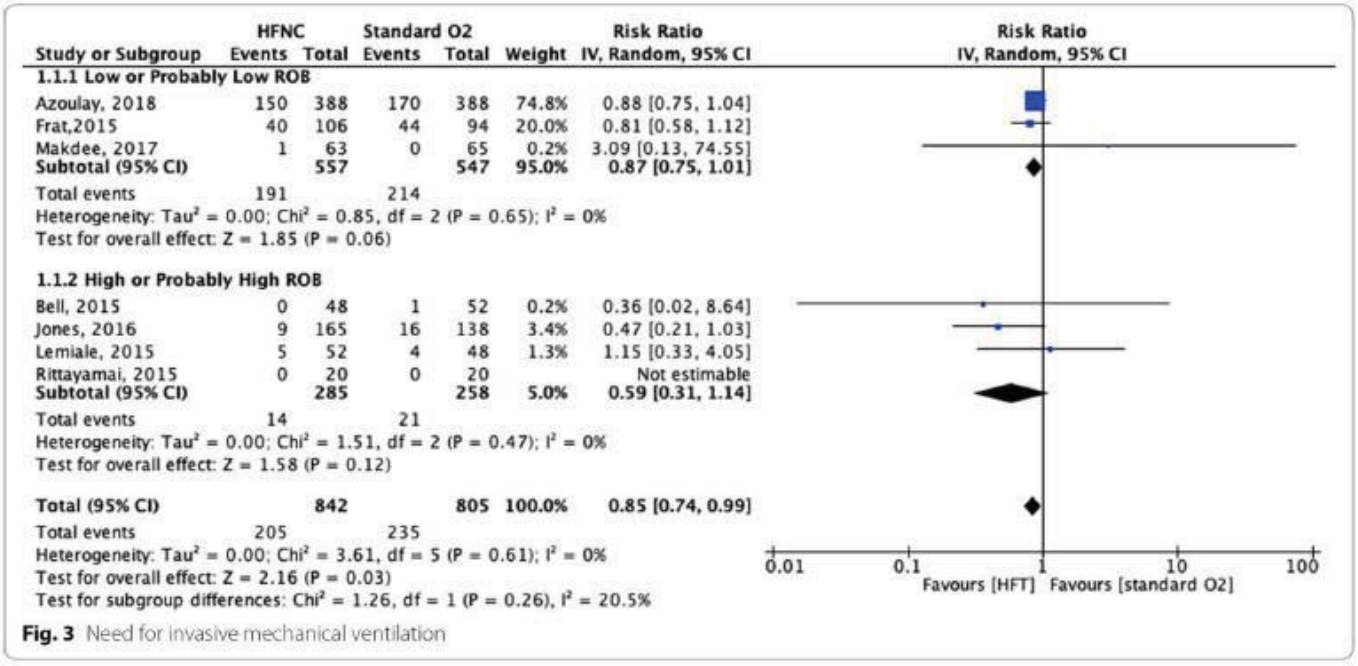


Fig. 3 Need for invasive mechanical ventilation

May decrease the need for intubation; 4.4% absolute reduction

Clinical application of HFNC

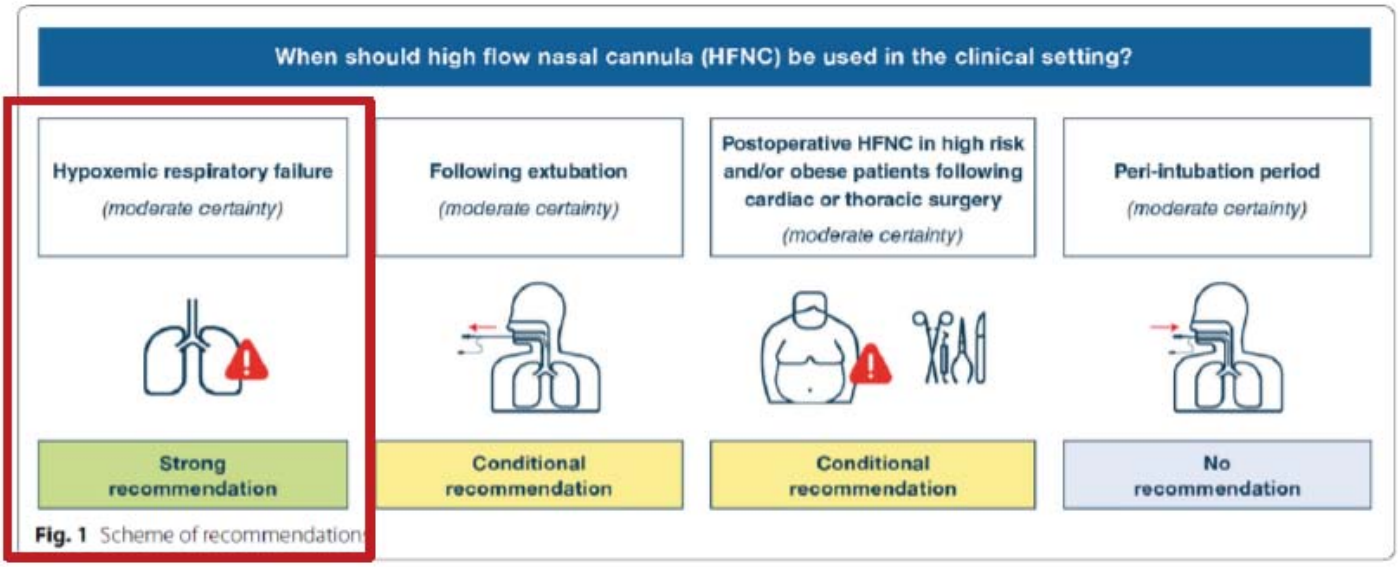


Fig. 1 Scheme of recommendations

Intensive Care Med (2020)

ORIGINAL ARTICLE

An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy

Oriol Roca[1,2], Berta Caralt[1,3], Jonathan Messika[4,5,6], Manuel Samper[7], Benjamin Sztrymf[8,9], Gonzalo Hernández[10], Marina García-de-Acilu[1], Jean-Pierre Frat[11,12,13], Joan R. Masclans[2,3,7], and Jean-Damien Ricard[4,5,6]

ROX Index = $\frac{SpO_2/FiO_2}{RR}$				
Time post intervention	2 hours	6 hours	12 hours	All times
ROX Index	< 2.85	< 3.47	< 3.85	> 4.88
Decision	Intubate	Intubate	Intubate	Observe

only for patients with pneumonia-related AHRF

Am J Respir Crit Care Med 2019

Oxygen therapy – WHO recommendation

The following recommendations pertain to adult and paediatric patients with ARDS who are treated with non-invasive or high-flow oxygen systems.

- **High-flow nasal oxygen (HFNO) should be used only in selected patients with hypoxemic respiratory failure.**
- **Non-invasive ventilation (NIV) should be used only in selected patients with hypoxemic respiratory failure.**
- **Patients treated with either HFNO or NIV should be closely monitored for clinical deterioration.**

Remark 1: Adult HFNO systems can deliver 60 L/min of gas flow and FiO_2 up to 1.0. Paediatric circuits generally only handle up to 25 L/min, and many children will require an adult circuit to deliver adequate flow.

Remark 2: Because of uncertainty around the potential for aerosolization, HFO, NIV, including bubble CPAP, should be used with airborne precautions until further evaluation of safety can be completed.

Remark 3: Compared with standard oxygen therapy, HFNO reduces the need for intubation *(42)*. Patients with hypercapnia (exacerbation of obstructive lung disease, cardiogenic pulmonary oedema), hemodynamic instability, multiorgan failure, or abnormal mental status should generally not receive HFNO, although emerging data suggest that HFNO may be safe in patients with mild-moderate and non-worsening hypercapnia *(42, 43, 44)*. Patients receiving HFNO should be in a monitored setting and cared for by experienced personnel capable of performing endotracheal intubation in case the patient acutely deteriorates or does not improve after a short trial (about 1 hour). Evidence-based guidelines on HFNO do not exist, and reports on HFNO in patients infected with other coronaviruses are limited *(44)*.

WHO/2019-nCoV/clinical/2020.4

Taiwan guideline

高流量鼻導管（HFNC, high flow nasal cannula）

感染臨床診療指引第十版（2021 年 5 月 14 日），建議可考慮使用高流量鼻導管，防護措施等同於執行可能產生飛沫微粒之醫療處置，並且應密切監視病患臨床變化 [5]。在中國大陸及歐美指引也建議可以選擇性使用，或許可以部分減少插管之機會。[2, 3, 4]

- 強烈建議：在負壓隔離病房使用，醫護人員要有適當的防護，病人需於高流量鼻導管外加戴外科口罩，盡量減少飛沫微粒外漏。[1, 3, 4, 10]
- 因為一般鼻導管以及面罩加貯氧袋無法精準控制給予之氧氣濃度，在危急病人不適用，此時應使用可以控制氧氣濃度的設備。[3]

非侵襲式呼吸器

- 使用時機：
  - 因為會有飛沫微粒產生，可能造成環境受染，及高失敗率，目前使用也有爭議。依台灣疾管署新冠病毒感染臨床診療指引第十版（2021 年 5 月 14 日），建議由醫師判斷，依臨床狀況使用非侵襲式呼吸器 [5]。在中國大陸及歐美也建議可以嘗試使用，或許可以部分減少插管之機會。[1, 2, 6]

Organization/country	Recommendation	Comment
AAMR, Argentina [33]	HFNC	Pro
ANZICS (Australia/New Zealand) [35]	HFNC	Suggest
AIPO (Italy) [36]	Helmet CPAP	-
CTS (China) [37]	HFNC	Pro
ESICM/SCCM (EU/US) [38]	HFNC	Pro
German recommendations for critically ill patients with COVID-19 (Germany) [39]	Helmet NIV	Restricted
Irish Thoracic Society, (Ireland) [33]	HFNC	Pro
National Healthcare System Guidelines, (UK) [40]	CPAP	HFNC contra indicated, no benefit but risk
SEPAR (Spain) [41]	HFNC	Maintain > 2-m distance
SPP (Portugal) [42]	HFNC	Pro
US Department of Defense COVID management guidelines [33]	HFNC	Pro
US Surviving Sepsis Campaign/SCCM [33]	HFNC	HFNC next modality for patient's not tolerating supplemental O_2
WHO [43••]	HFNC	Not for: COPD, cardiopulmonary edema, hemodynamic instability

Difficult to draw a conclusion

- At present, no definitive evidence on whether noninvasive respiratory support is beneficial or harmful for patients with COVID-19
  - evolving nature of the pandemic
  - paucity of data
  - no controlled prospective trials inform the respiratory management of severe covid-19 pneumonia

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Research Paper

The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: A multi-centre prospective observational study

- 293 hypoxemic respiratory failure patients enrolled; 137 (47%) patients success
- median duration of HFNC use
  - success vs. failure : 6 vs. 2 days ($p<0.001$)
- ROX-6 $\geqq$ 3.7 : 80% predictive of success
- ROX-6 $\leqq$ 2.2 was 74% predictive of failure

Oxygen requirement and respiratory parameters after 6 h on HFNO.

	Total (n = 293)	Failure (n = 156)	Success (n = 137)	P-value
SpO_2 (%)				
Median (IQR)	90 (86–94)	89 (83–92)	91 (89–94)	<0.001
FiO_2 (%)				
Median (IQR)	90 (85–95)	90 (90–95)	90 (80–93)	<0.001
Respiratory rate (breaths/mins)				
Median (IQR)	37 (30–43)	40 (34–46)	32 (28–40)	<0.001
Heart rate (beats/mins)				
Median (IQR)	101 (90–108)	104 (92–110)	97 (88–105)	<0.001
SpO_2/FiO_2 ratio				
Median (IQR)	100 (93–107	98 (89–103)	104 (98–115)	<0.001
ROX index at 6 h (ROX-6)				
Median (IQR)	2.78 (2.25–3.62)	2.41 (2.06–3.05)	3.26 (2.72–4.10)	<0.001
Modified ROX index at 6 h (mROX-6)				
Median (IQR)	2.90 (2.16–3.74)	2.33 (1.92–3.12)	3.44 (2.67–4.20)	<0.001

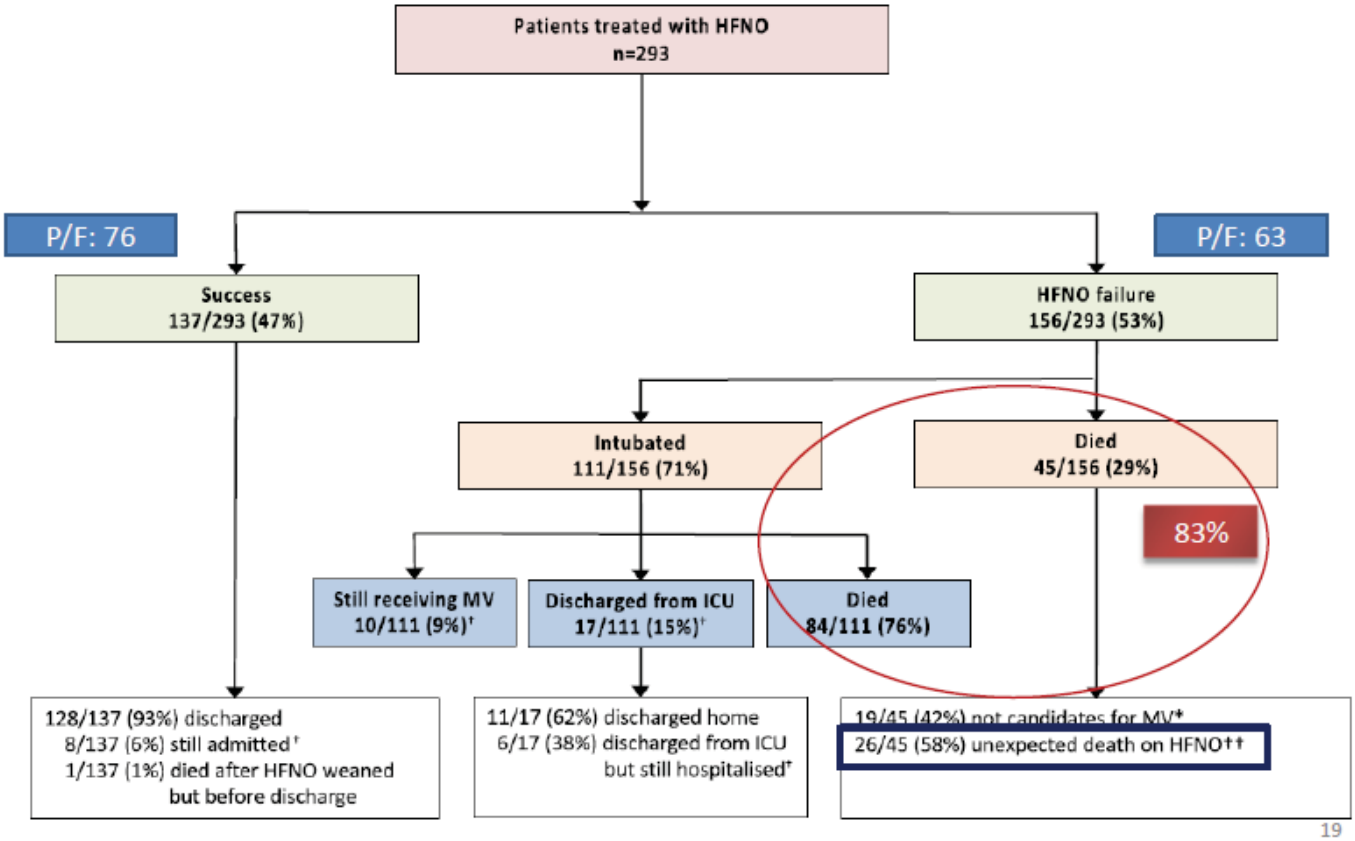


Table 3
Predictors of HFNO failure.

Variable	N	Estimated HR* (95% CI)	P-value	Adjusted HR† (95% CI)	P-value
Age (per year increase)	293	1.00 (0.99–1.02)	0.795		
Male (vs. females)	293	0.95 (0.70–129/)	0.749		
HIV status (vs. negative)					
Positive	45	0.75 (0.48–1.19)	0.224		
Hypertension	131	0.99 (0.73–1.34)	0.930		
Diabetes*					
Well-controlled (vs. no diabetes)	55	0.97 (0.63–1.50)	0.883	1.27 (0.81–2.00)	0.301
Poorly controlled (vs. no diabetes)	79	1.31 (0.93–1.88)	0.143	1.56 (1.06–2.28)	0.023
Obesity (BMI ≥30 kg/m^2 vs. <30 kg/m^2)	153	0.80 (0.58–1.09)	0.158		
mSOFA (per 1 point increase)	290	1.18 (1.04–1.36)	0.054		
Duration of symptoms (per 1 day increase)	293	1.02 (0.98–1.06)	0.313		
Treatment with steroids	221	0.31 (0.22–0.44)	0.001	0.25 (0.18–0.37)	<0.001
ICU setting (vs. medical ward)	105	0.68 (0.48–0.97)	0.032		
ROX-6 score (per 1 point increase)	279	0.46 (0.37–0.58)	<0.001	0.42 (0.33–0.53)	<0.001
mROX-6 score (per 1 point increase)	277	0.51 (0.42–0.61)	<0.001		
Lymphocyte count (per 1 × 10^9 increase)	249	1.19 (0.92–1.52)	0.181		
CRP (vs. <100 mg/L)	38				
100–199	66	0.71 (0.38–1.30)	0.269		
200–299	50	0.88 0.46–1.70)	0.712		
300–399	31	1.14 (0.59–2.20)	0.701		
400–499	15	1.54 (0.70–3.38)	0.280		
≥500	7	2.99 (1.23–7.25)	0.015		
D-dimer (vs. <1.5 mg/L)	150				
1.51–5.0	39	1.48 (0.93–2.36)	0.097		
≥5	42	1.99 (1.28–3.12)	0.002		

LETTER

Prediction of outcome of nasal high flow use during COVID-19-related acute hypoxemic respiratory failure

Noémie Zucman[1], Jimmy Mullaert[2], Damien Roux[3], Oriol Roca[4], Jean-Damien Ricard[1*] and Contributors

- 62 patients enrolled, median age was 55
- profound hypoxemia at HFNC initiation: under FiO2 0.8, SpO2 96%
- **Results:**
  - 34% (21/62) succeeded
  - ICU mortality was 17%

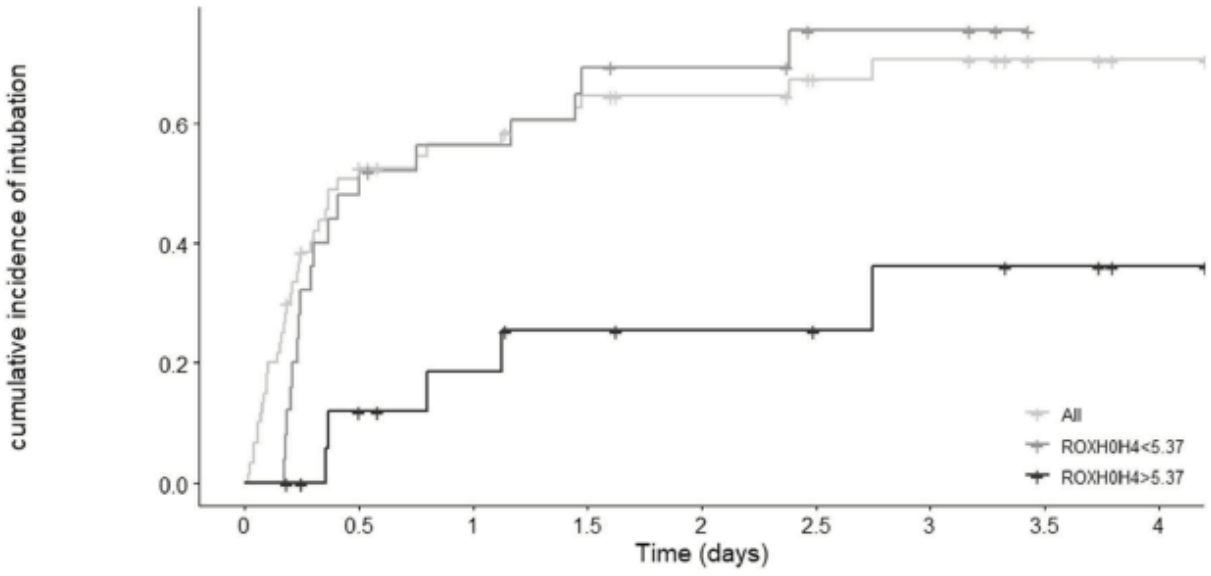


Fig. 1 Cumulative incidence of orotracheal intubation for all at-risk patients ($N=60$) and after 4 h of NHF ($N=45$) stratified on ROX-H0H4 (landmark at H4). NHF, nasal high flow. ROX-H0H4 was defined as the latest value of the ROX index within the first 4 h after NHF initiation

median time to intubation was 10 h

High-Flow Nasal Cannula in Critically Ill Patients with Severe COVID-19

- A retrospective study in France
- Hypoxemic respiratory failure:
  - respiratory rate >25
  - bilateral pulmonary infiltrates on chest X-ray or CT
  - need oxygen >3 L/min to maintain SpO_2>92%
- 146 (39%, n=379) patients used HFNC

Am J Respir Crit Care Med 2020

	No HFNC ($n=233$)	HFNC ($n=146$)	*P* Value
Patients characteristics			
Age, yr	63 (53–69)	60 (53–67)	0.249
Sex, F	57 (25)	31 (21)	0.549
Body mass index, kg/m^{-2}	28 (25–32)	27 (25–30)	0.213
Comorbidities			
COPD	13 (6)	7 (5)	0.923
Asthma	12 (5)	11 (8)	0.468
Diabetes	72 (31)	42 (29)	0.745
High blood pressure	121 (52)	67 (46)	0.299
Chronic heart failure	22 (10)	10 (7)	0.488
Immunosuppression	49 (21)	19 (13)	0.060
On ICU admission			
Time since disease onset, d	8 (5–10)	10 (7–12)	<0.001
Time since hospital admission, d	1 (0–3)	1 (0–3)	0.599
Body temperature, °C	37.9 (37.0–38.7)	38.0 (37.4–38.7)	0.146
Oxygen flow, L/min^{-1}	15 (8–15)	15 (9–15)	0.045
Number of quadrants involved on chest X-ray	4 (2–4)	4 (2–4)	0.658
Pa_{O_2}/Fi_{O_2} at Day 1 (worst value), mm Hg	130 (97–195)	126 (86–189)	0.433
Leukocytes, G/L^{-1}	8.08 (5.49–11.30)	8.09 (5.70–10.79)	0.537
Lymphocytes, G/L^{-1}	0.80 (0.59–1.16)	0.70 (0.54–1.03)	0.056
D-dimer, IU	1,908 (830–3,968)	1,500 (920–2,770)	0.194
Lactate, mmol/L^{-1}	1.2 (1.0–1.8)	1.4 (1.0–1.7)	0.292
SOFA at Day 1	6 (3–9)	4 (3–5)	<0.001
Oxygenation/ventilation strategy			
CPAP	3 (1)	3 (2)	0.873
NIV	18 (8)	9 (6)	0.703
Duration of HFNC therapy, d	0	4 (2–6)	—
Before intubation*			
Respiratory rate, min^{-1}	33 (26–36)	30 (25–32)	0.089
Sp_{O_2}, %	94 (88–97)	97 (95–100)	0.010
Fi_{O_2}, %	66 (49–66)	100 (90–100)	0.008
Organ failure and support during ICU stay			
Vasopressors	123 (53)	42 (29)	<0.001
Acute kidney injury	139 (60)	56 (40)	<0.001
Renal replacement therapy	57 (25)	17 (12)	0.003
Outcome variables			
Invasive mechanical ventilation at Day 28	175 (75)	82 (56)	<0.001
ICU mortality	68 (34)	30 (25)	0.117
Mortality at Day 28	70 (30)	30 (21)	0.055
Mortality at Day 60	72 (31)	31 (21)	0.052

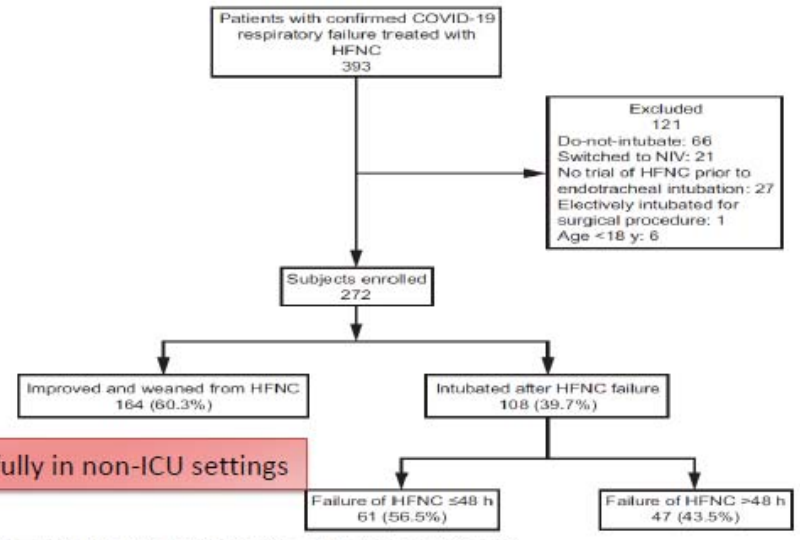
Significantly reduce intubation

No effect on fatality

24

High-Flow Nasal Cannula Therapy in COVID-19: Using the ROX Index to Predict Success

Abhimanyu Chandel, Saloni Patolia, A Whitney Brown, A Claire Collins, Dhwani Sahjwani, Vikramjit Khangoora, Paula C Cameron, Mehul Desai, Aditya Kasarabada, Jack K Kilcullen, Steven D Nathan, and Christopher S King



111 managed successfully in non-ICU settings

Figure 1. Flow chart. HFNC = high-flow nasal cannula, NIV = noninvasive ventilation.

Respir Care 2021;66

Predict of failure

	All Subjects ($n = 272$)	Weaned from HFNC ($n = 164$)	HFNC Failure ($n = 108$)	P
Age, y	57 ± 13	54 ± 14	60 ± 13	< .001
Female	92 (33.8)	60 (36.6)	32 (29.6)	.24
Race, non-White	248 (91.2)	154 (93.9)	94 (87.0)	.08
Body mass index, kg/m^2	28.7 (25.2–33.4)	28.6 (25.5–33.2)	28.7 (24.9–33.6)	.90
HFNC duration, d	3 (1–6)	4 (2–7)	2 (1–4)	< .001
Comorbid diseases				
No comorbid disease	83 (3.5)	60 (36.6)	23 (21.3)	.01
Hypertension	116 (42.6)	64 (39.0)	52 (48.1)	.17
Diabetes mellitus	101 (37.1)	56 (34.1)	45 (41.7)	.25
Chronic kidney disease	20 (7.4)	8 (4.9)	12 (11.1)	.061
End-stage renal disease	8 (2.9)	4 (2.4)	4 (3.7)	.72
Coronary artery disease	9 (3.3)	5 (3.0)	4 (3.7)	.74
Hyperlipidemia	74 (27.2)	40 (24.4)	34 (31.5)	.21
Asthma	13 (4.8)	9 (5.5)	4 (3.7)	.57
COPD	2 (0.7)	1 (0.6)	1 (0.9)	> .99
Active cancer	7 (2.6)	1 (0.6)	6 (5.6)	.02
HFrEF	4 (1.5)	2 (1.2)	2 (1.9)	.65
Systemic anticoagulation	9 (3.3)	8 (4.9)	1 (0.9)	.09
Clinical data at HFNC initiation				
Heart rate, beats/min	93 (80–104)	89 (80–103)	95 (82–104)	.19
Mean arterial pressure, mm Hg	89.7 ± 13.0	89.3 ± 12.9	9.3 ± 13.2	.57
Breathing frequency, breaths/min	29 (24–36)	28 (24–36)	30 (26–37)	.059
Oxygen saturation	93 (90–96)	93 (90–96)	93 (89–95)	.22
SOFA score	3 (1–5)	2 (1–4)	4 (2–7)	< .001
White blood cells, $\times 10^9$ per mL	8.3 (6.0–11.4)	8.0 (6.0–1.9)	8.9 (6.1–11.6)	.40
Neutrophil to lymphocyte ratio	6.5 (4.2–11.7)	6.1 (3.9–1.6)	8.1 (4.9–12.0)	.02
Lactate, mmol/L	1.7 (1.3–2.3)	1.5 (1.3–2.1)	1.9 (1.4–2.8)	< .005
C-reactive protein, mg/L	16.8 (10.0–24.2)	16.7 (9.8–23.6)	17.2 (1.8–26.3)	.51
D-dimer, μg/mL	1.3 (0.9–2.5)	1.3 (0.8–2.2)	1.3 (0.9–2.7)	.25
Procalcitonin, ng/mL	0.3 (0.1–0.6)	0.2 (0.1–0.5)	0.3 (0.1–1.0)	.033
ROX index				
2 h after HFNC	4.5 (3.3–6.0)	4.9 (3.7–6.7)	3.6 (2.8–4.8)	< .001
6 h after HFNC	4.6 (3.6–6.3)	5.1 (4.1–6.9)	3.9 (3.0–4.8)	< .001
12 h after HFNC	4.7 (3.4–6.2)	5.3 (4.3–6.9)	3.8 (2.6–4.5)	< .001

Age

SOFA

Lactate

ROX index

RESEARCH Open Access

High-flow nasal oxygen in patients with COVID-19-associated acute respiratory failure

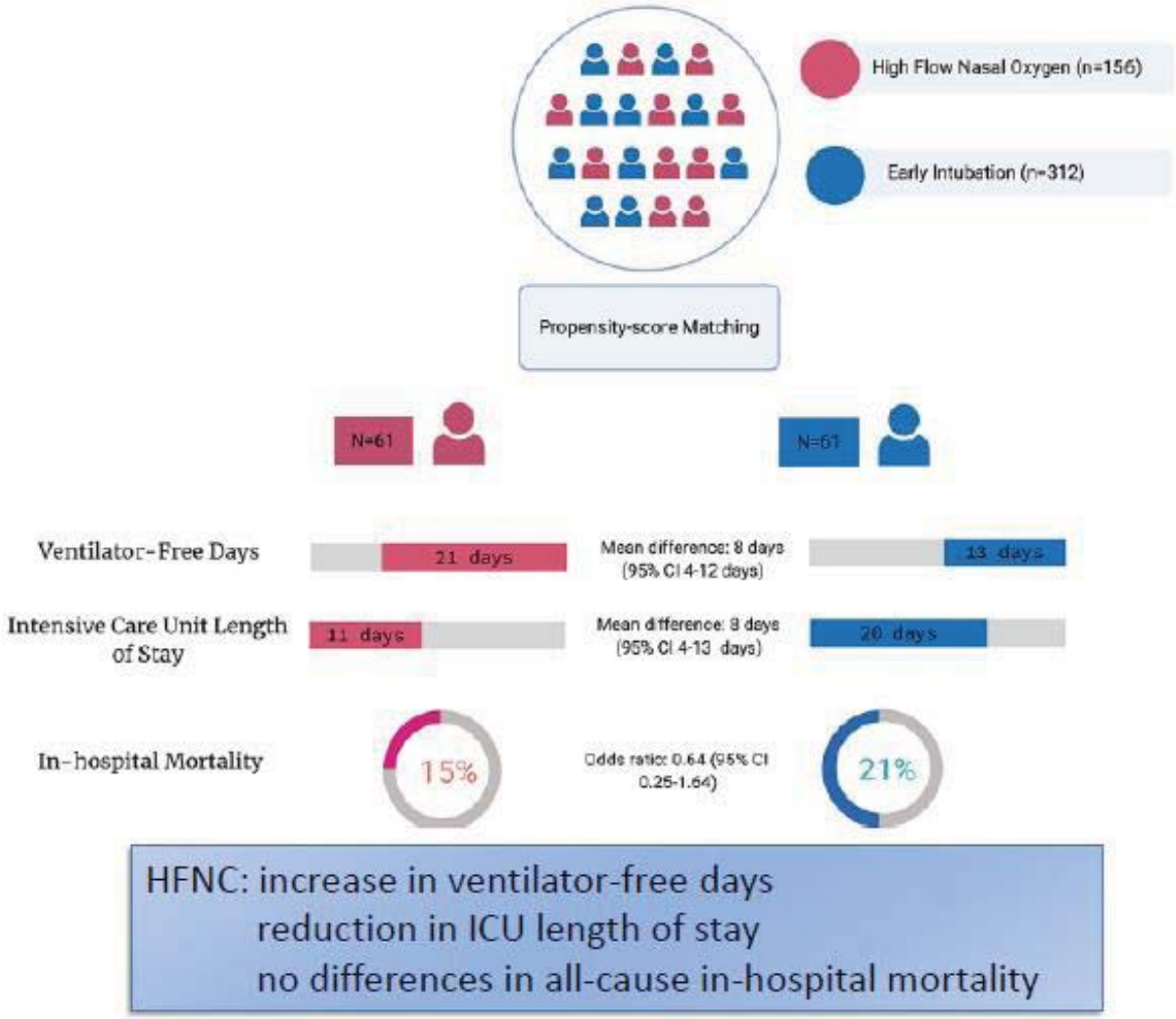
Ricard Mellado-Artigas[1*], Bruno L. Ferreyro[2,3], Federico Angriman[3,4], María Hernández-Sanz[5], Egoitz Arruti[6], Antoni Torres[7,8,9], Jesús Villar[8,10,11], Laurent Brochard[3,11] and Carlos Ferrando[1,8] for the COVID-19 Spanish ICU Network

- A multicentre cohort study using a prospectively collected database
- Propensity score matching
  - high-flow nasal oxygen v.s. early intubation
- Out of 468 eligible patients, 122 matched (61 for each group)

Crit Care (2021)

Table 1 Baseline characteristics of the matched sample of adult patients with COVID-19 related acute respiratory failure

Covariate	Early intubation (N = 61)	HFNO (N = 61)	SMD
Demographic characteristics			
Age, *years*—mean (SD)	61 (11)	62 (11)	0.06
Female gender, n (%)	36 (48)	27 (40)	0.14
BMI, *kg/m2* – mean (SD)	28.8 (4.3)	28.8 (5.5)	0.01
Time to ICU admission, *days* – median [IQR]	2 [1–4]	2 [1–4]	0.11
Baseline comorbid disease			
Number of comorbidities – median [IQR]	1 [0–1]	1 [0–2]	0.00
Immunosupression, (n, %)	2 (3.3)	4 (6.6)	0.15
Active cancer, (n, %)	0 (0)	6 (9.8)	0.47
Initial severity of disease			
SOFA score—median [IQR]	5 [3–7]	4 [4–7]	0.00
Glasgow coma score—median [IQR]	15 [15]	15 [15]	0.41
APACHE II score—median [IQR]	11 [9–14]	10 [9–113]	0.11
PaO_2:FIO_2 ratio—mean (SD)	117 (51)	121 (49)	0.09
Respiratory rate, *rpm*—mean (SD)	25 (5)	25 (5)	0.04
Oxygen saturation, %—mean (SD)	88 (7)	89 (6)	0.09
ROX index—median [IQR]	4.4 [3.4–6.4]	5 [4–6.2]	0.25
$PaCO_2$, *mmHg*—mean (SD)	37 (8)	38 (12)	0.02
Gas flow, L/min—mean (SD)	–	55 (12)	–
FIO_2, %—mean (SD)	79 (18)	72 (16)	0.45
Heart rate (bpm)—mean (SD)	81 (18)	82 (15)	0.03
Systolic blood pressure (mmHg)—mean (SD)	128 (21)	124 (18)	0.21
Use of steroids, n (%)	47 (77)	45 (73.8)	0.08
Laboratory values			
pH—mean (SD)	7.4 (0.1)	7.44 (0.06)	0.66
Creatinine, *mg/dl*—mean (SD)	1.0 (0.8)	1.0 (0.7)	0.01
Bilirubin, *mg/dl*—mean (SD)	0.7 (0.5)	0.7 (0.3)	0.01
Lactate, *mmol/l*—mean (SD)	0.3 (0.6)	0.4 (0.7)	0.13
D-dimer, *U/l*—mean (SD)	4025 (11,944)	2235 (4724)	0.19
Leucocyte count, *10^9/l*—mean (SD)	8.1 (3.6)	8.3 (4.8)	0.04
Lymphocyte count, *10^9/l*—mean (SD)	0.7 (1.0)	0.7 (0.5)	0.09
Platelet count, *10^12/l*—mean (SD)	223 (88)	241 (126)	0.16



Predictor of failure

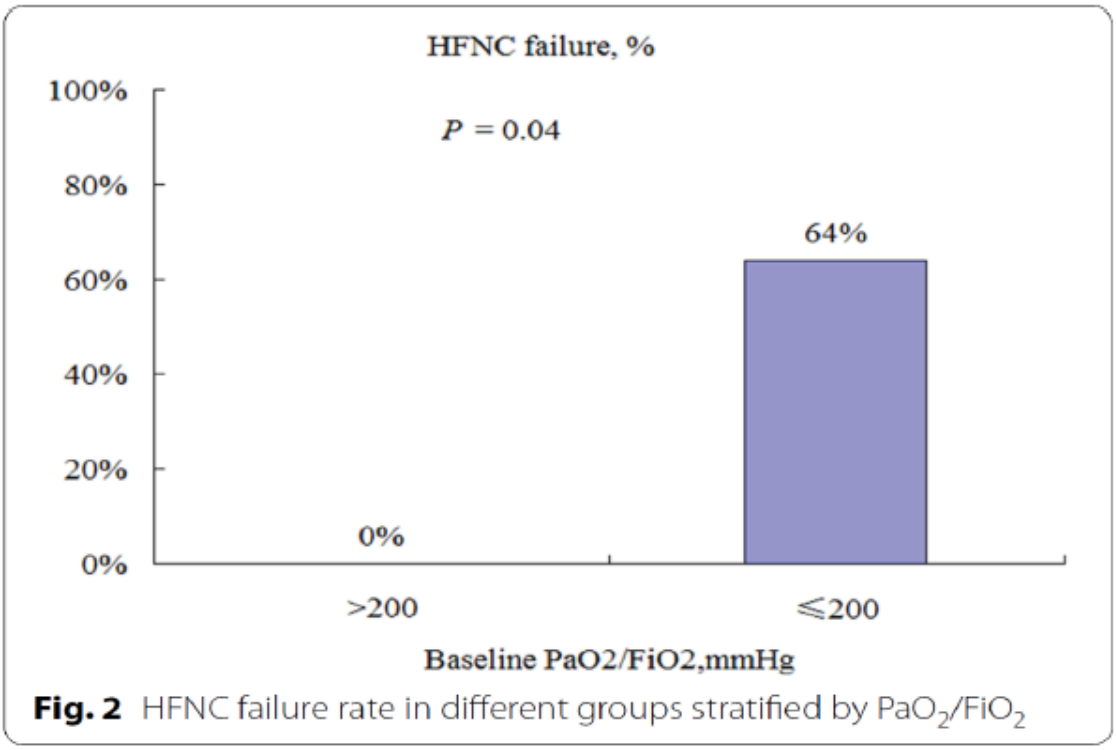
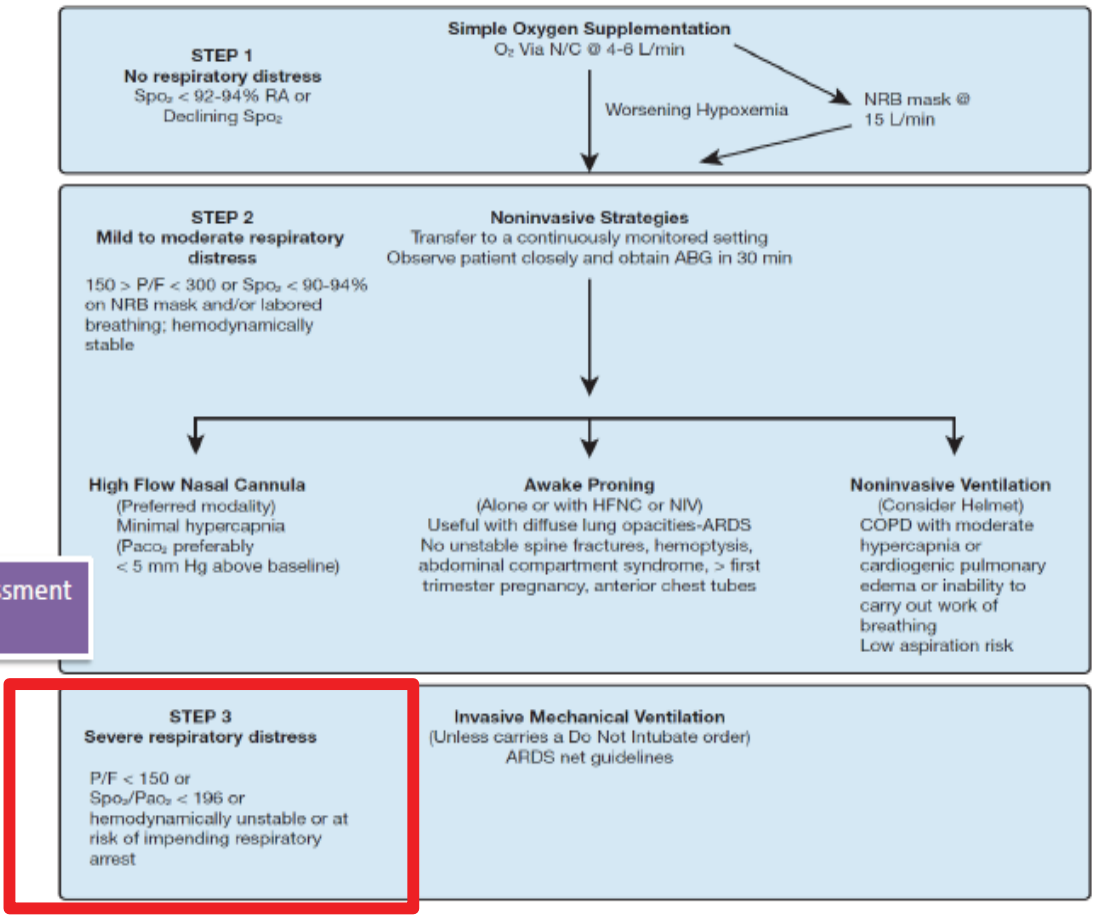


Fig. 2 HFNC failure rate in different groups stratified by PaO_2/FiO_2

Wang et al. Ann. Intensive Care (2020)

Oxygen therapy for severe COVID 19 pneumonia



Clinical assessment
ROX index

CHEST 2020

Clinical application of HFNC

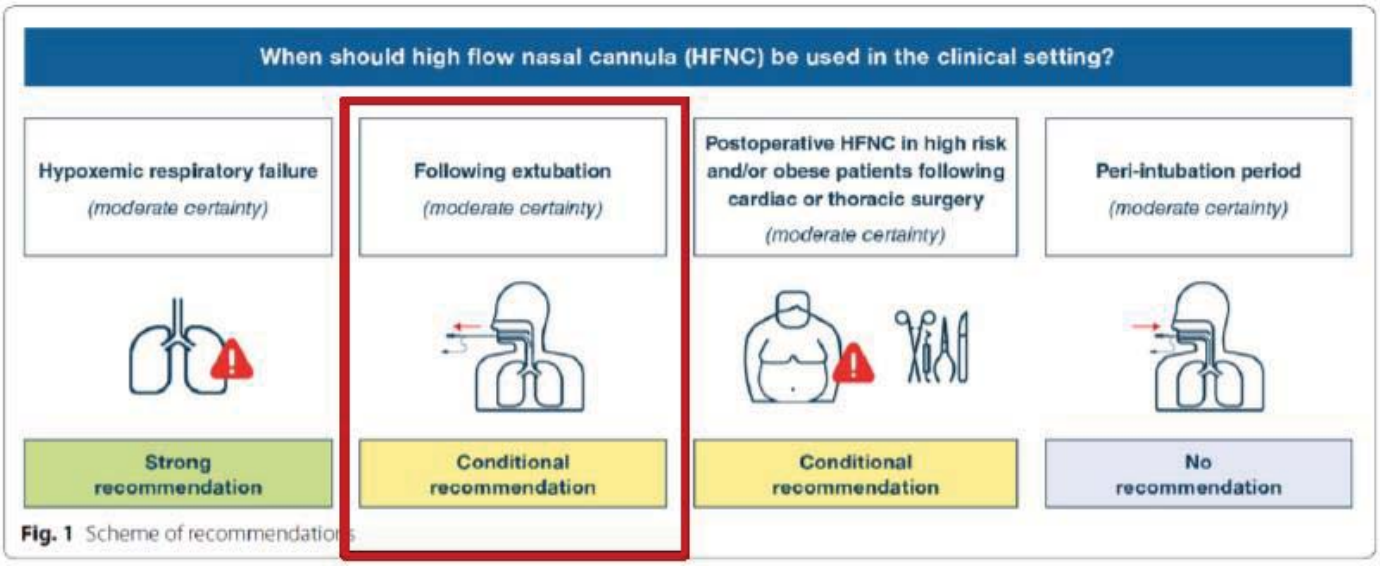


Fig. 1 Scheme of recommendations

Intensive Care Med (2020)

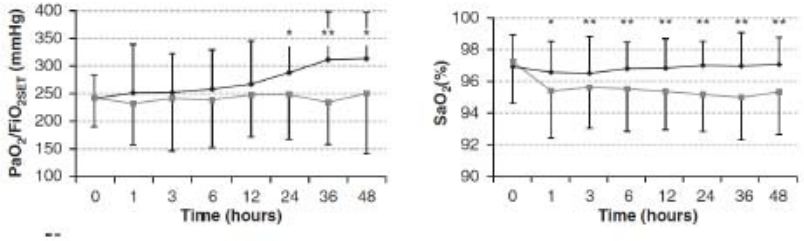
ORIGINAL ARTICLE

Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation

Effects on Oxygenation, Comfort, and Clinical Outcome

Salvatore Maurizio Maggiore[1], Francesco Antonio Idone[1], Rosanna Vaschetto[2], Rossano Festa[1], Andrea Cataldo[1], Federica Antonicelli[1], Luca Montini[1], Andrea De Gaetano[3], Paolo Navalesi[4,5,6], and Massimo Antonelli[1]

- Compared with the Venturi mask, HFNC has
  - fewer desaturations (40% vs. 75%; $P < 0.001$)
  - lower reintubation rate (4% vs. 21%; $P = 0.01$)



Am J Respir Crit Care Med 2014

Clinical outcomes of high-flow nasal cannula in COVID-19 associated postextubation respiratory failure. A single-centre case series

Francesca Simioli, Anna Annunziata, Gerardo Langella, Giorgio E. Polistina, Maria Martino, Giuseppe Fiorentino

Department of Respiratory Pathophysiology, Monaldi-Cotugno Hospital, Naples, Italy

- 9 patients were de-escalated to HFNC(5 Helmet CPAP, 4 invasive mechanical ventilation)
- HFNC (2 hours)
  - PaO_2/FiO_2 : 254 ± 69.3 mm Hg
  - Mean ROX index :11.17 (range: 7.38–14.4)
- HFNC (day 3), PaO_2/FiO_2 increased to 396 ± 83.5 mm Hg

Anaesthesiol Intensive Ther[38] 2020

High-flow nasal cannula oxygen therapy to treat patients with hypoxemic acute respiratory failure consequent to SARS-CoV-2 infection

Andrea Vianello ,[1] Giovanna Arcaro,[2] Beatrice Molena,[2] Cristian Turato,[3] Andi Sukthi,[2] Gabriella Guarnieri,[2] Francesca Lugato,[2] Gianenrico Senna,[4] Paolo Navalesi[5]

- In a RICU of Italy
- 73 healthcare workers (HCWs) (20 physicians, including residents, 40 nurses and 13 healthcare assistants) were exposed
- Exposure duration was 48 (44–52) hours
- All HCWs underwent nasopharyngeal swab on a weekly basis

Thorax[39] 2020

Results

- COVID-19 PCR testing were negative in all staff during the study period and the following 14 days.
  - wore appropriate personal protective equipment
  - gowns, hair covers, gloves, eye and face shields, and filtering face-piece respirator class 2
  - applied a surgical mask over the nose and mouth of patients

結論

- 嚴重COVID-19肺炎，是指在未使用氧氣下，SPO2<= 94%，此時建議氧氣治療。
- 氧氣治療一般分成低流量、高流量系統。
- HFNC屬高流量系統，通常用於較嚴重的COVID-19肺炎。
  - 可以ROX index來評估初始的治療效果，但不能延遲有需要插管的病人。
- 目前不建議於較嚴重COVID-19肺炎，使用非侵襲性呼吸器

感謝古世基醫師、胡漢忠醫師提供部分資料