SALA VIOLANTE/GINEVRA

URGENZE RESPIRATORIE

Moderatori: **Salvatore Maggiore – Giorgio Carbone**

Roberto Cosentini

La migliore sedazione per stati di agitazione nel paziente ventilato

XII congresso nazionale
simeu
RICCIONE 13-15 MAGGIO 2022

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SOCIETÀ ITALIANA MEDICINA D'EMERGENZA-URGENZA · SIMEU ·

Roberto Cosentini
EAS_Emergenza Alta Specializzazione

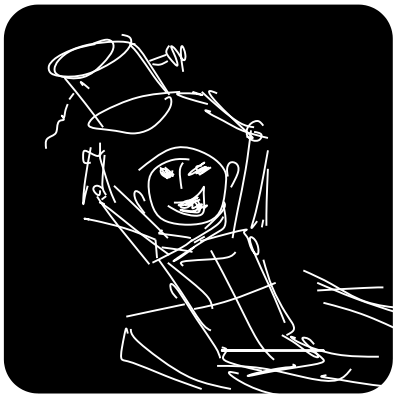
Ospedale di Bergamo
Regione Lombardia
ASST Papa Giovanni XXIII

COI

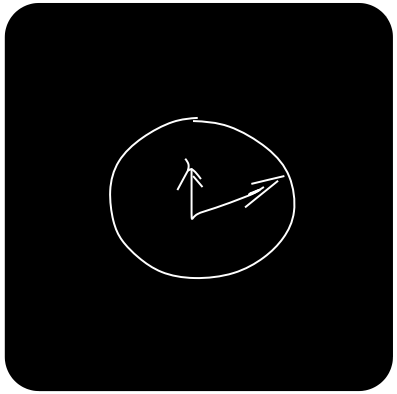
Fiammetta Pagnozzi

MIchelangelo Merisi

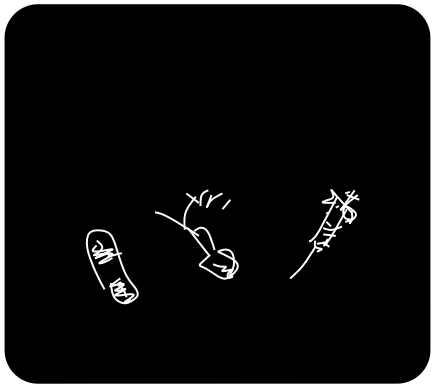
Sedation in NIV_4 key Q's



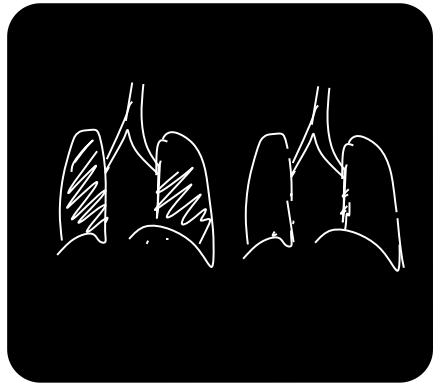
WHY



WHEN



WHAT



HOW

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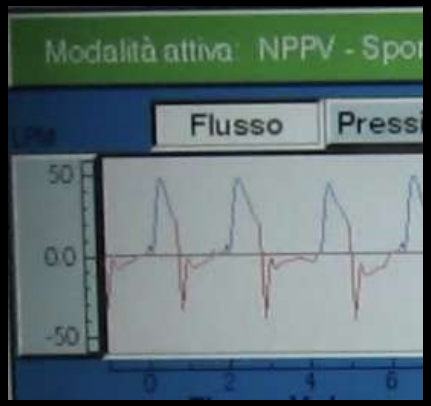
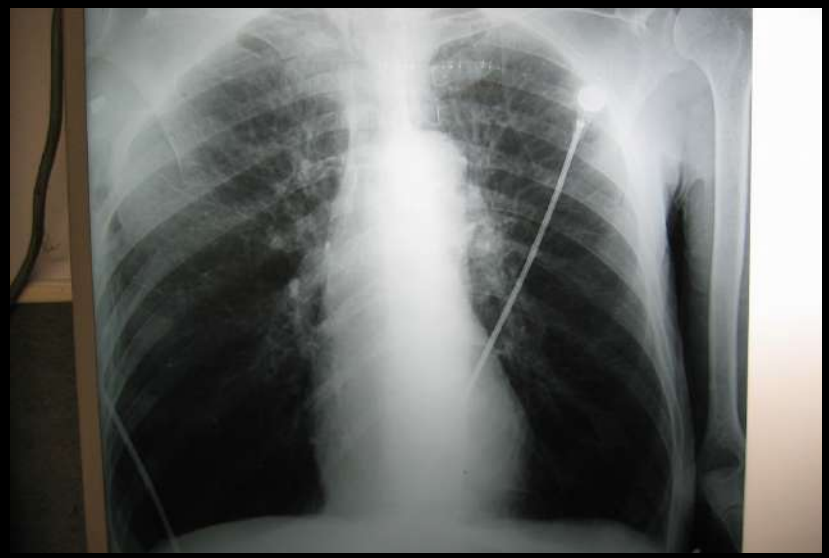
Case 1

Agitation in COPD exacerbation



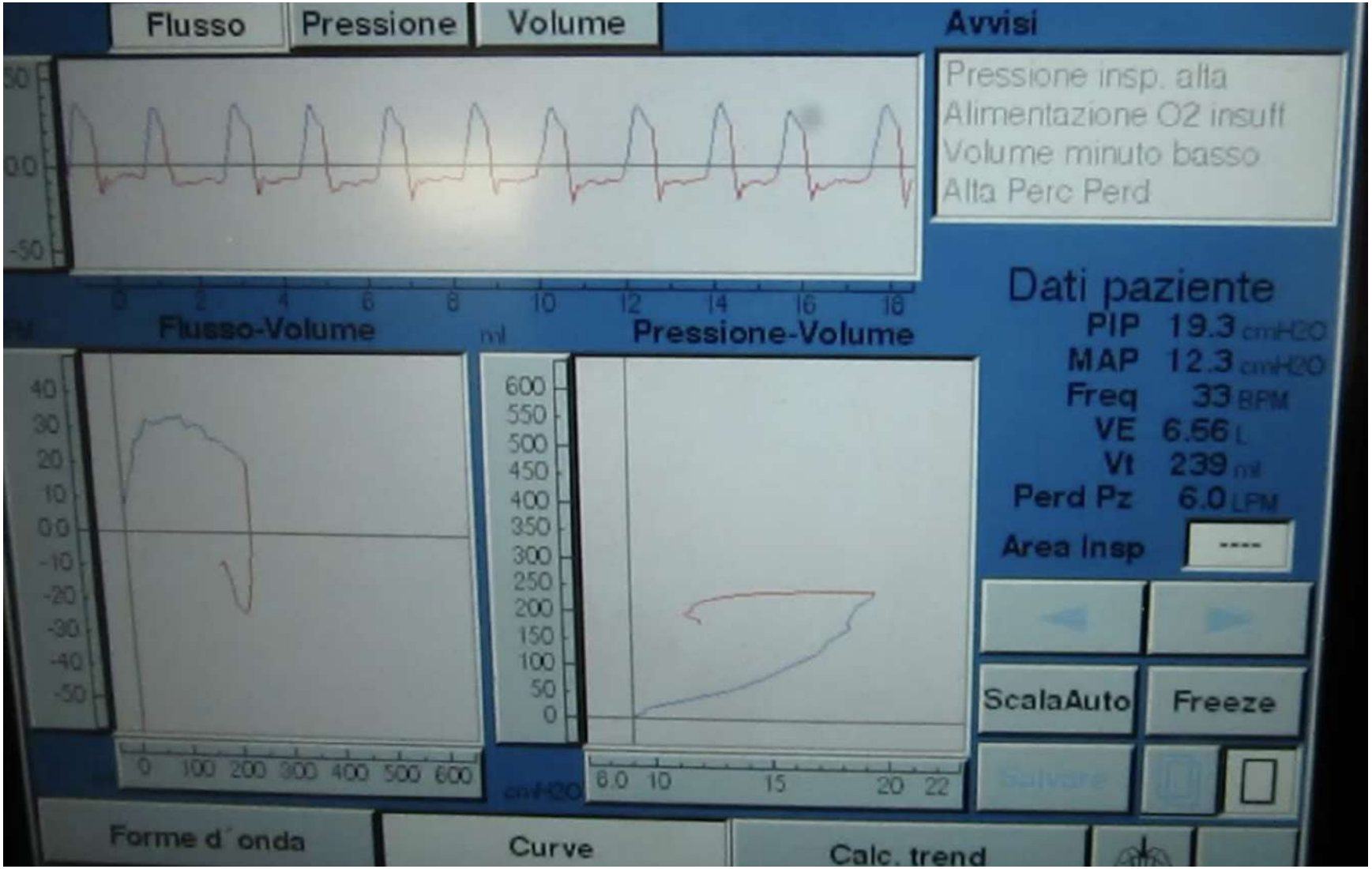
NIPPV
Just started



PIF = 42 L/min

cycl = 13 L/min

exp cycl = 13/42 = 31%



PIF = 42 L/min

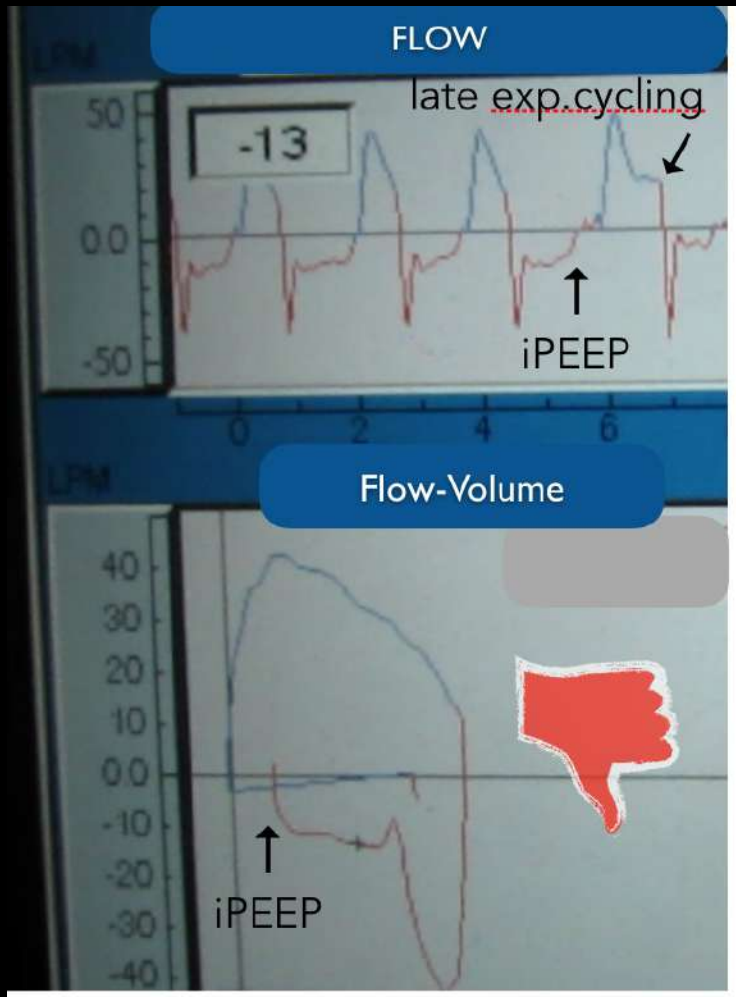
cycl = 13 L/min

exp cycl = 13/42 = 31%

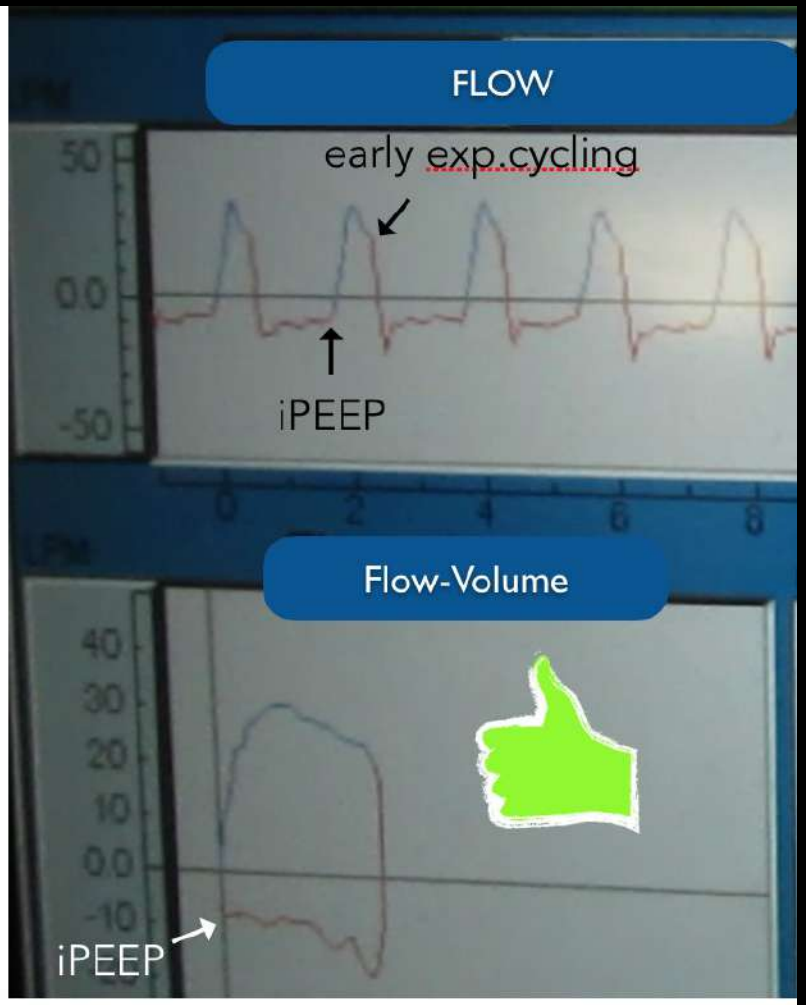
PIF = 34 L/min

cycl = 20 L/min

Exp cycl = 20/34 **= 60%**

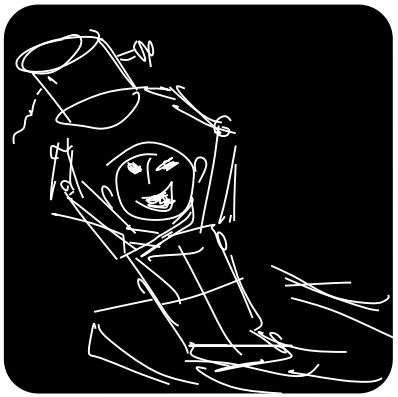


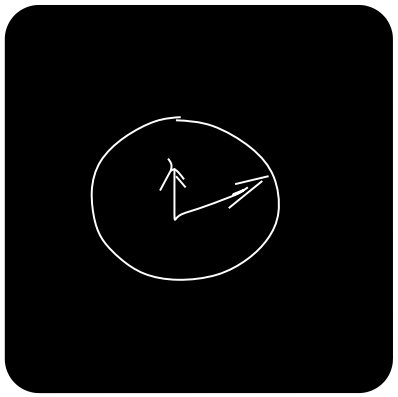
exp cycl = 13L/min/42
= **31%**



exp. cycl = 20 L/min/34
= **60%**

Sedation in NIV_4 key Q's





WHY WHEN WHAT HOW

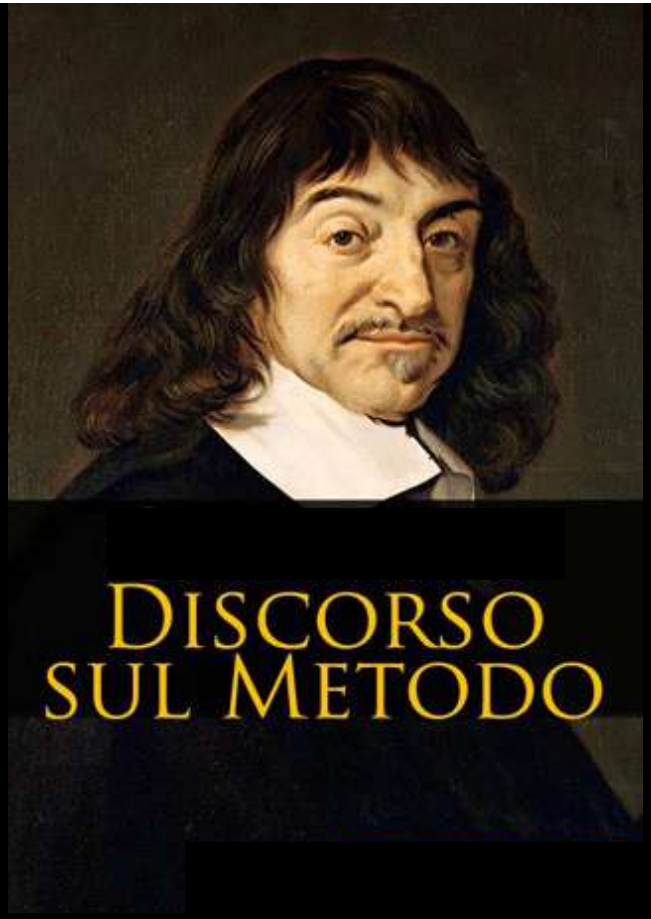
Dissynchrony

@rob_cosentini

Case 2

Agitation in COPD

BGA		BGA	
pH 7.33	→	pH 7.31	6 h
pCO2 54		pCO2 61	
pO2 64		pO2 57	
HOC3 28		HOC3 31	



My

Patient

does not improve

when my patient does not improve

when my patient does not improve

Treatment

DG

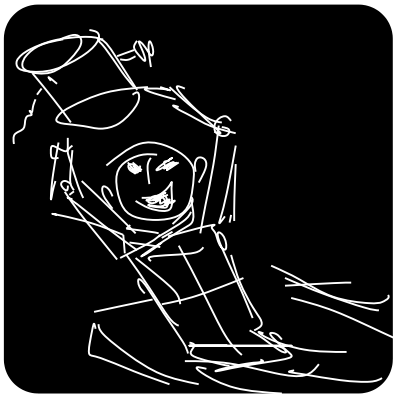
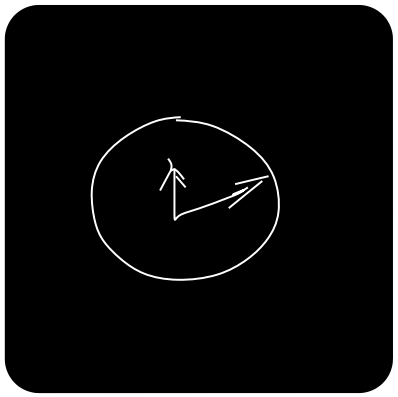
NO ZERO FLOW

EXPIRATORY FLAT CURVE

salbutamol costs

4 h

Sedation in NIV_4 key Q's

WHY WHEN WHAT HOW

Dissynchrony

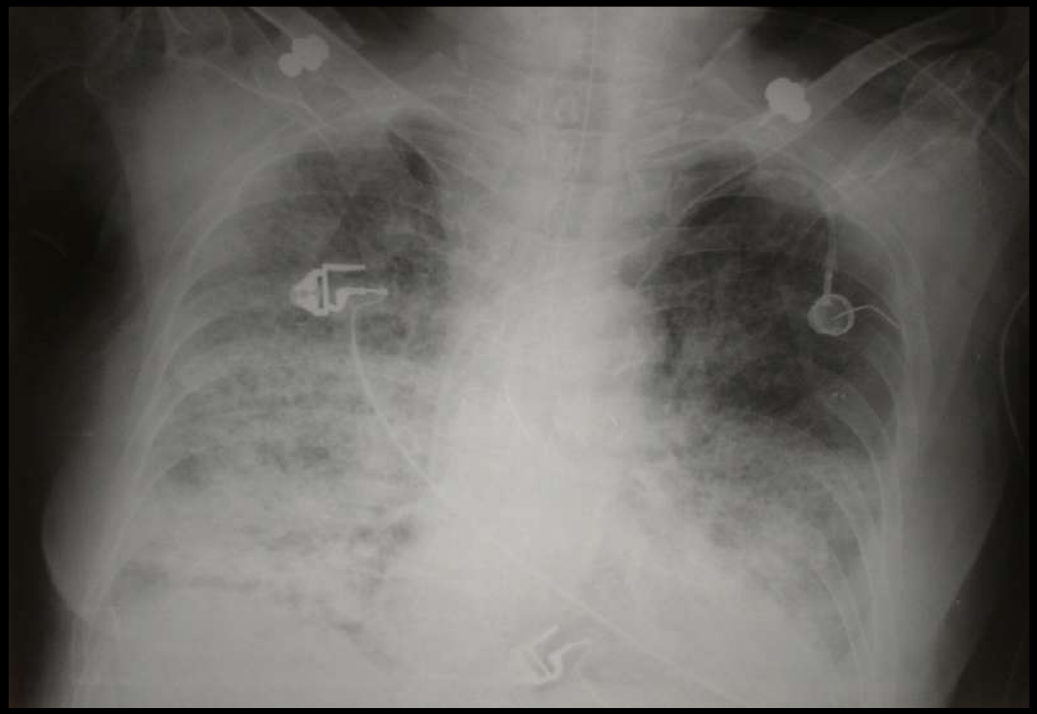
Treatment

@rob_cosentini

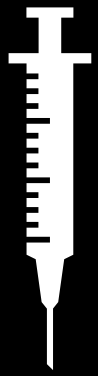
Case 3

Agitation in Pneumonia

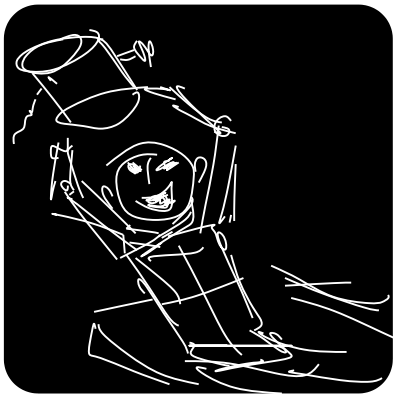
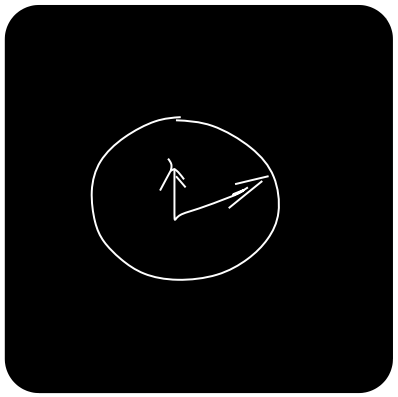
CPAP
FiO2 60%



RR 38'
SpO2 = 88%
pO2 54



Sedation in NIV_4 key Q's

WHY WHEN WHAT HOW

Dissynchrony

Treatment

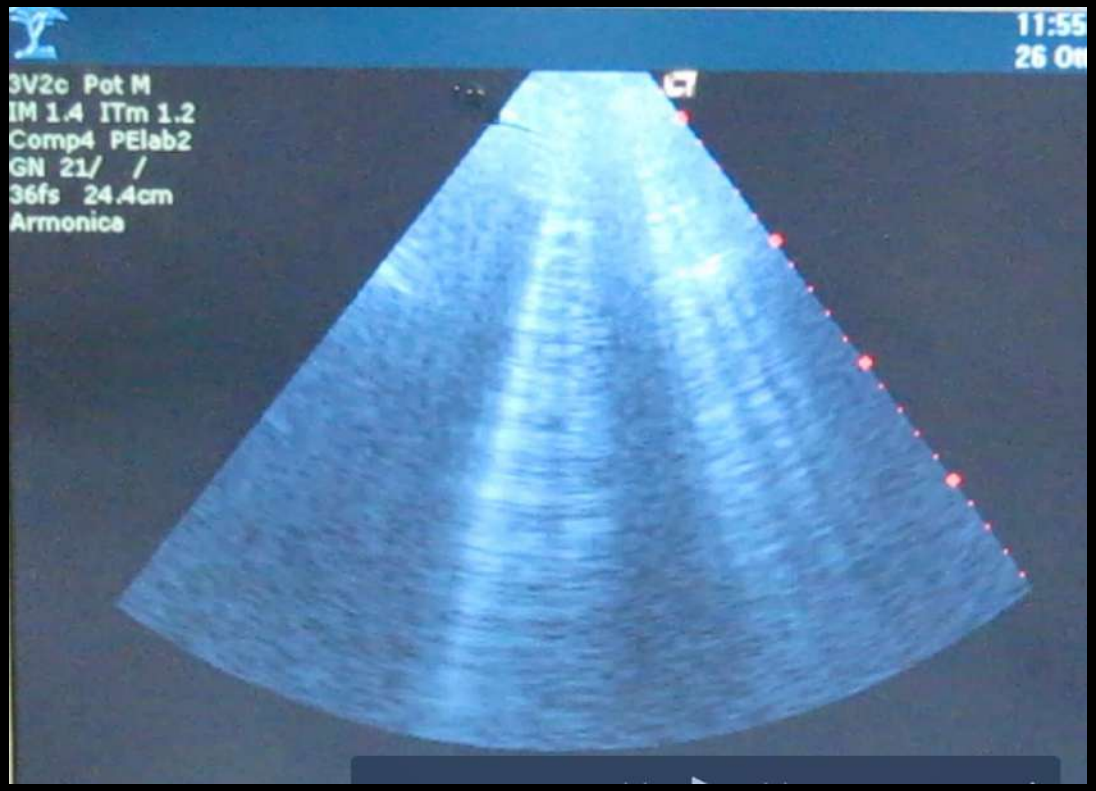
Failure

@rob_cosentini

Case 4

Agitation in ACPE

CPAP
FiO2 50%

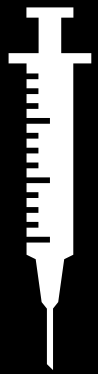


SpO2 98%
pCO2 31
pO2 145

Agitation in ACPE

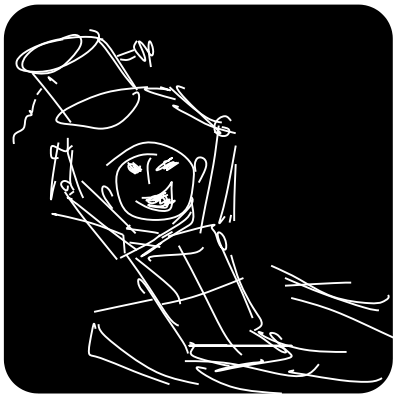
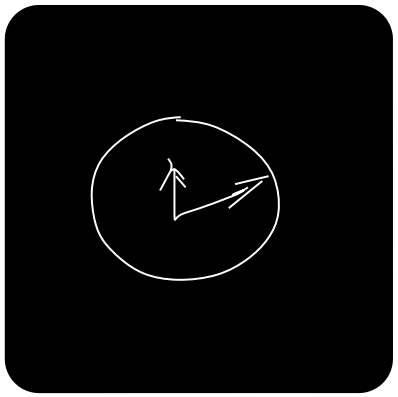
CPAP
FiO2 50%

SpO2 98%
pCO2 31
pO2 145




500 ml
480
460
440
420 400
380
360
340
320 300
280
260
240
220 200
180
160
B BRAUN
Ureofix® 500
150
140
130
120
110
100
90
80
70
60
50
40
35
30
25
20
15
10
5
2
2000 max.
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
Ureofix® 500
B BRAUN
PATIENT
Room
Bed
Ward
Date

Sedation in NIV_4 key Q's

WHY WHEN WHAT HOW

Dissynchrony

Treatment

Failure

Other

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Comfort During Non-invasive Ventilation

Gianmaria Cammarota†, Rachele Simonte† and Edoardo De Robertis*

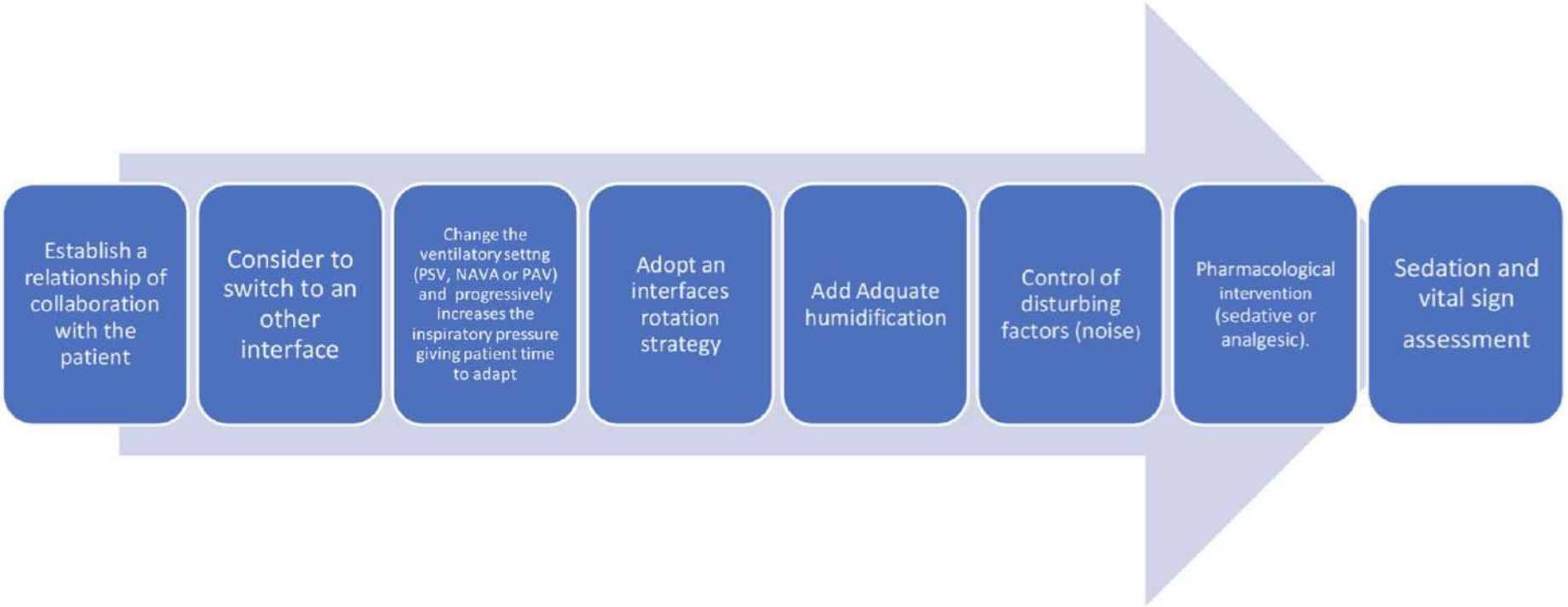
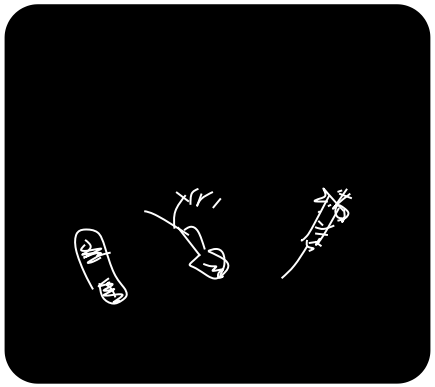


FIGURE 1 | Patient intolerance bundle of intervention.

TABLE 1 | Principal causes of discomfort in non-invasive ventilation (NIV).

Interface
Anchor system
Ventilatory setting
Humidification
Noise
Position of the patient
Psychological distress
Anxiety
Fear
Pain

Sedation in NIV_4 key Q's



WHY WHEN WHAT HOW

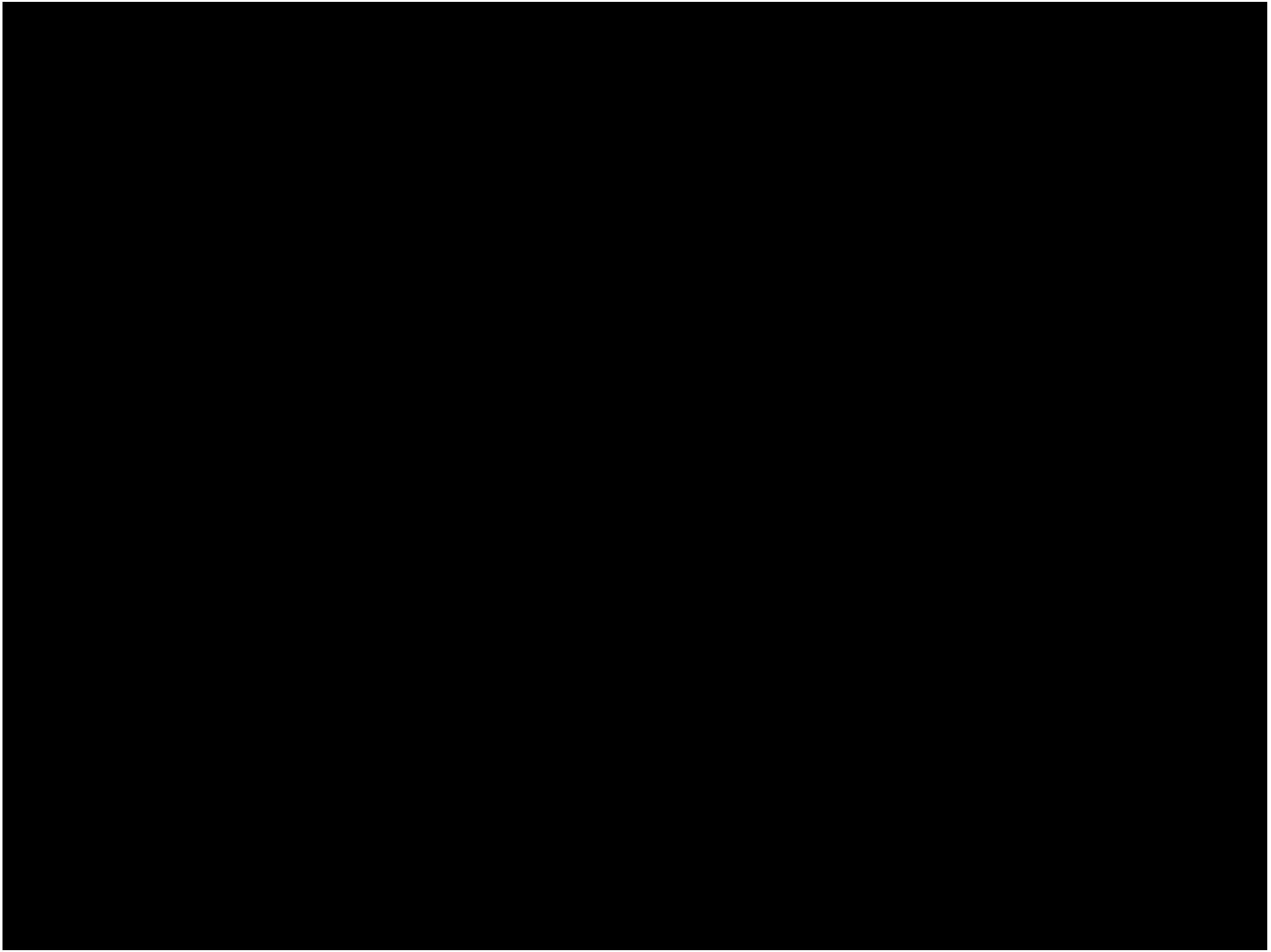
Dissynchrony

Treatment

Failure

Other

@rob_cosentini



Non-Invasive Ventilation and sedation: Evidence to support and practical advice

Article *in* Giornale Italiano di Cardiologia · June 2017

Battistoni I et al.

Tabella 1. Studi sull'utilizzo della sedazione durante ventilazione non invasiva.

Studio	N. pazienti	Indicazioni	Interfaccia utilizzata	Tipo di sedazione	Inizio della sedazione
Rocker et al.[12]	10	ARF	FFM	Morfina	All'inizio della NIV
Constantin et al.[13]	13	ARF (n=10) AHRF (n=3)	FFM	Remifentanil Midazolam[a]	Scarsa tolleranza alla NIV
Rocco et al.[14]	36	ARF	FFM, helmet	Remifentanil	Scarsa tolleranza alla NIV
Akada et al.[15]	10	ARF	FFM	Dexmedetomidina[b]	Scarsa tolleranza alla NIV
Takasaki et al.[16]	2	SAA	FFM	Dexmedetomidina	Scarsa tolleranza alla NIV
Clouzeau et al.[17]	10	ARF (n=7) AHRF (n=3)	FFM	Propofol	Scarsa tolleranza alla NIV
Senoglu et al.[18]	40	COPD	FFM	Dexmedetomidina vs Midazolam RCT	All'inizio della NIV
Huang et al.[19]	62	ACPO	FFM	Dexmedetomidina vs Midazolam RCT	Scarsa tolleranza alla NIV

Tabella 2. Meccanismo d'azione e dosaggio dei principali farmaci utilizzati per la sedazione durante ventilazione non invasiva.

Farmaco	Meccanismo d'azione	Insorgenza di effetto	Emivita di eliminazione	Dosaggio intermittente	Dosaggio di mantenimento
Propofol	Potenziamento del sistema GABAergico a livello del SNC, blocco dei canali del Na^+	1-2 min	Uso breve: 3-12h Uso prolungato: fino a 50h	5 µg/kg/min in 5 min	5-50 µg/kg/min
Midazolam	Potenziamento del sistema GABAergico a livello del SNC	2-5 min	3-11h	0.01-0.05/kg	0.02-0.1 mg/kg/h
Morfina	Agonista del recettore per gli oppioidi a livello centrale e periferico	5-10 min	3-4h	2-4 mg e.v.	2-30 mg/h
Remifentanil	Agonista del recettore per gli oppioidi a livello centrale e periferico	1-3 min	3-10 min	N/A	Carico 1.5 µg/kg Mantenimento: 0.5-15 µg/kg/h
Dexmedetomidina	Agonista selettivo del recettore α_2-adrenergico	5-10 min	2-3h	1 µg/kg in 10 min	0.2-0.7 µg/kg/h
Ketamina	Antagonista dei recettori post-sinaptici NMDA	30 s	2-3h	1-2 mg/kg	0.5-1 mg/kg

Matsumoto *et al. BMC Pulmonary Medicine* (2015) 15:71

Role of sedation for agitated patients undergoing noninvasive ventilation: clinical practice in a tertiary referral hospital

Dexmedetomidine	0.2 μg/kg/h by continuous intravenous infusion
Midazolam	0.03 mg/kg/h by continuous intravenous infusion
Propofol	0.3 mg/kg/h by continuous intravenous infusion
Morphine	0.02 mg/kg/h by continuous subcutaneous infusion
Fentanyl	0.05–0.1 μg/kg/h by continuous subcutaneous infusion
*Ketamine	0.1–0.2 mcg/kg/h

*non-included in the study

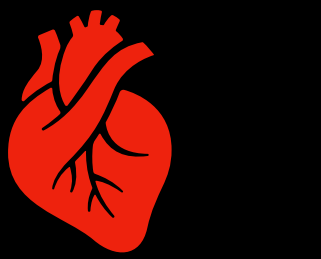

Propofol
Injectable Emulsion, USP
200 mg per 20 mL

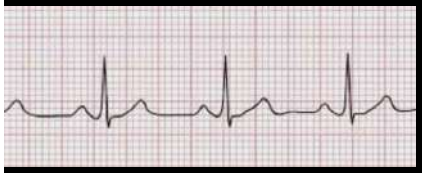

Midazolam
Injection, USP
5 mg/5 mL
FOR IM OR IV USE


Morphine
Sulfate Inj., USP
5 mg/mL

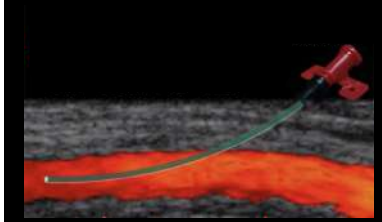

dexdor
Dexmedetomidin
400 Mikrogramm/4 ml

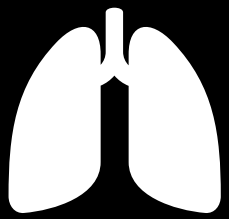

NDC 42023-138-10
Ketamine HCl
Injection, USP
500 mg/10 mL
(50 mg/mL)
10 mL

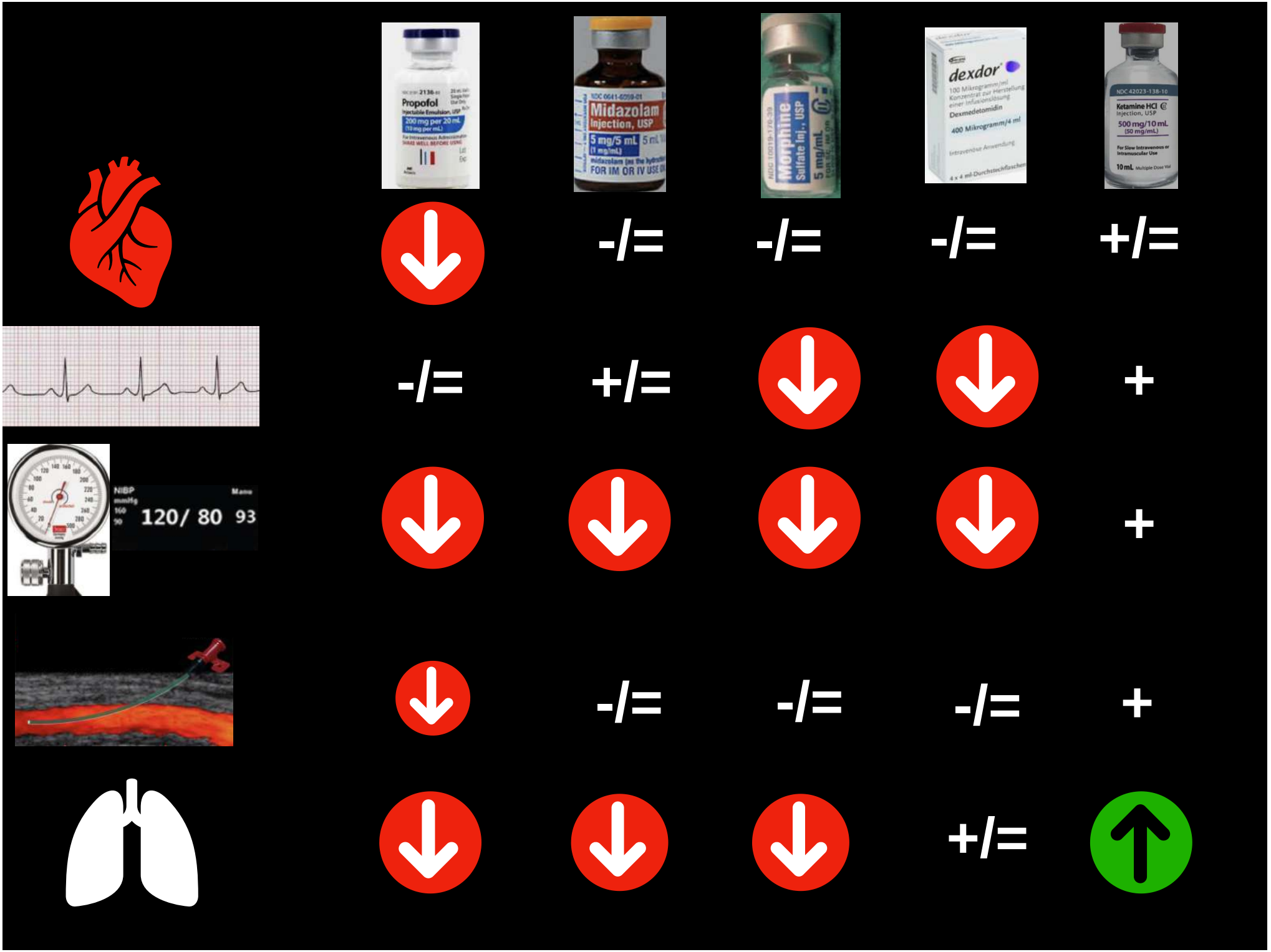




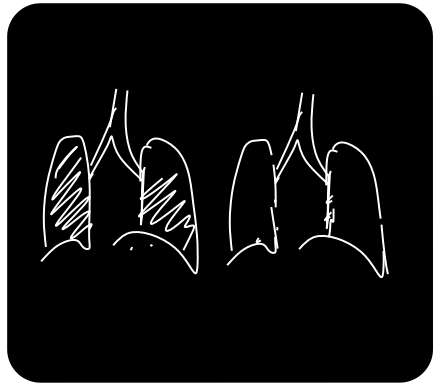

NIBP
mmHg
120/ 80
93






Propofol
Midazolam
Injection, USP
5 mg/5 mL
FOR IM OR IV USE
Morphine
Sulfate Inj., USP
5 mg/mL
dexdor
Dexmedetomidin
400 Mikrogramm/4 ml
Ketamine HCl
Injection, USP
500 mg/10 mL
(50 mg/mL)
10 mL
NIBP
120/ 80 93
-/=
-/=
-/=
+/=
-/=
+/=
+
+
-/=
-/=
-/=
+
+/=

Sedation in NIV_4 key Q's



WHY WHEN WHAT **HOW**

Dissynchrony

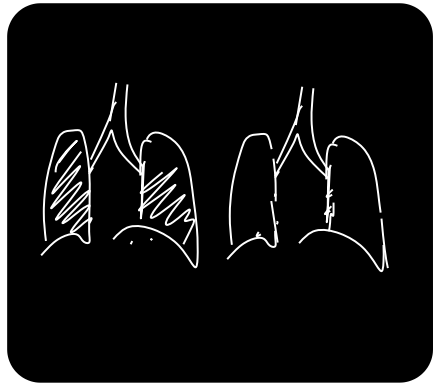
Treatment

Failure

Other

@rob_cosentini

Sedation in NIV_4 key Q's



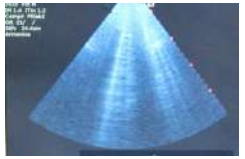
ACPE

COPD & ASTHMA

How

@rob_cosentini

Morphine in ACPE



- Odds ratios for **intubation and ICU admission** for pulmonary edema patients
- Morphine — **5:1** (Sacchetti, et al. Am J Emerg Med, 1999)

ODDS RATIO

5.0

- Based on ADHERE registry of patients admitted with decompensated CHF
- Compared use of morphine vs. no morphine (Peacock, et al. Emerg Med J, 2008)

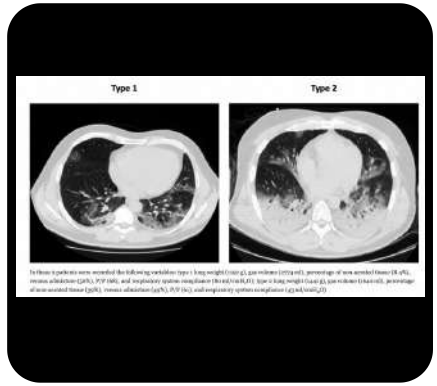
- **Morphine** was an **independent predictor of mortality**, odds ratio **4.84**

ODDS RATIO

4.84

- **Benzodiazepine/Dexmeto**

Sedation in NIV_4 key Q's



ACPE

COPD & ASTHMA

Covid-19

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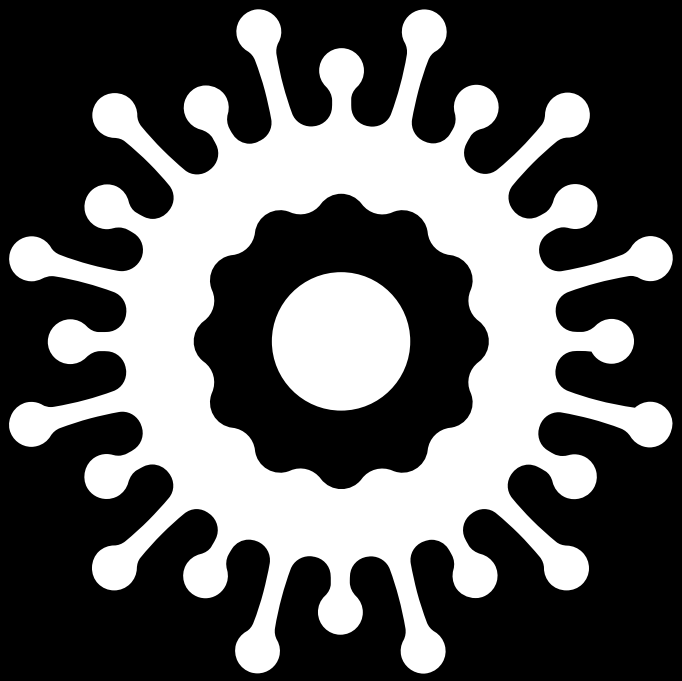
Conclusioni

“ A few observation and much reasoning lead to error;
many observations and little reasoning to truth”

Alexis Carrel, *Reflections On Life*

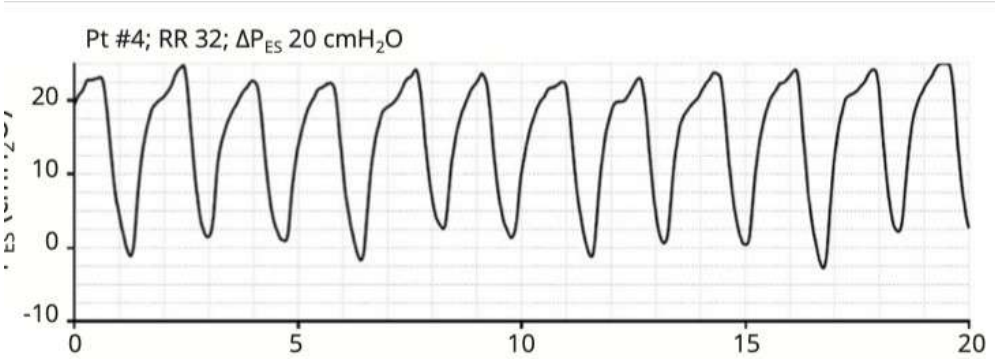
COVID19



Case 4

Barbara, 69 ys

Treated with hCPAP



☐ Tpulm Press

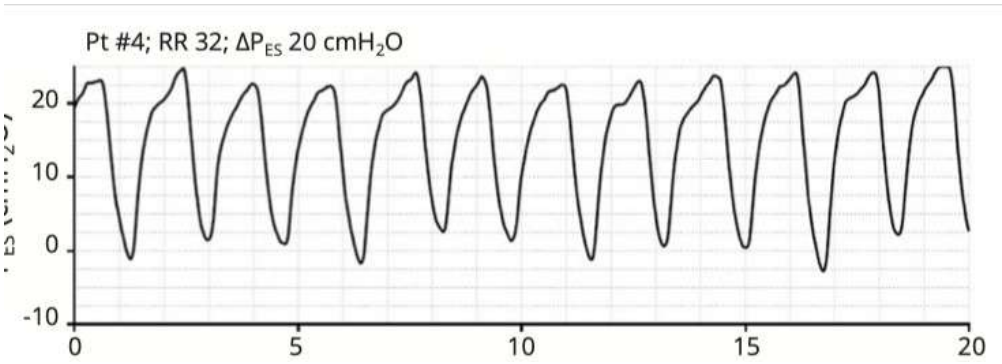
pH 7.49
pCO_2 29
pO_2 62
SpO_2 94%
FiO2 60%

RR 30

ure and ARDS patients on non-invasive support. Minerva Anestesiol 2019;85:1014-23. DOI: 10.23736/S0375-9393.19.13418-9)
ssessment by esophageal manometry predicts noninvasive ventilation outcome in De Novo respiratory failure. a pilot study. Am J Respir Crit Care Med. 2020;202:558–567. doi: 10.1164/rccm.201912-2512OC
rasso S, Chiumello D, Guérin C, Patroniti N, Ranieri VM, Gattinoni L, Nava S, Terragni PP, Pesenti A, Tobin M, Mancebo J, Brochard L; The application of esophageal pressure measurement in patients with respiratory failure. Am J Re
n Acute Respiratory Failure. Am J Respir Crit Care Med. 2017 Feb 15;195(4):438-442. doi: 10.1164/rccm.201605-1081CP. PMID: 27626833.

Barbara, 69 ys

Treated with hCPAP



pH 7.49
pCO_2 29
pO_2 62
SpO_2 94%
FiO2 60%

□ Tpul… Press

□ Lung Injury

□Vascular Leakage

RR 30

patient-SILI

ure and ARDS patients on non-invasive support. Minerva Anestesiol 2019;85:1014-23. DOI: 10.23736/S0375-9393.19.13418-9)
ssessment by esophageal manometry predicts noninvasive ventilation outcome in De Novo respiratory failure. a pilot study. Am J Respir Crit Care Med. 2020;202:558–567. doi: 10.1164/rccm.201912-2512OC
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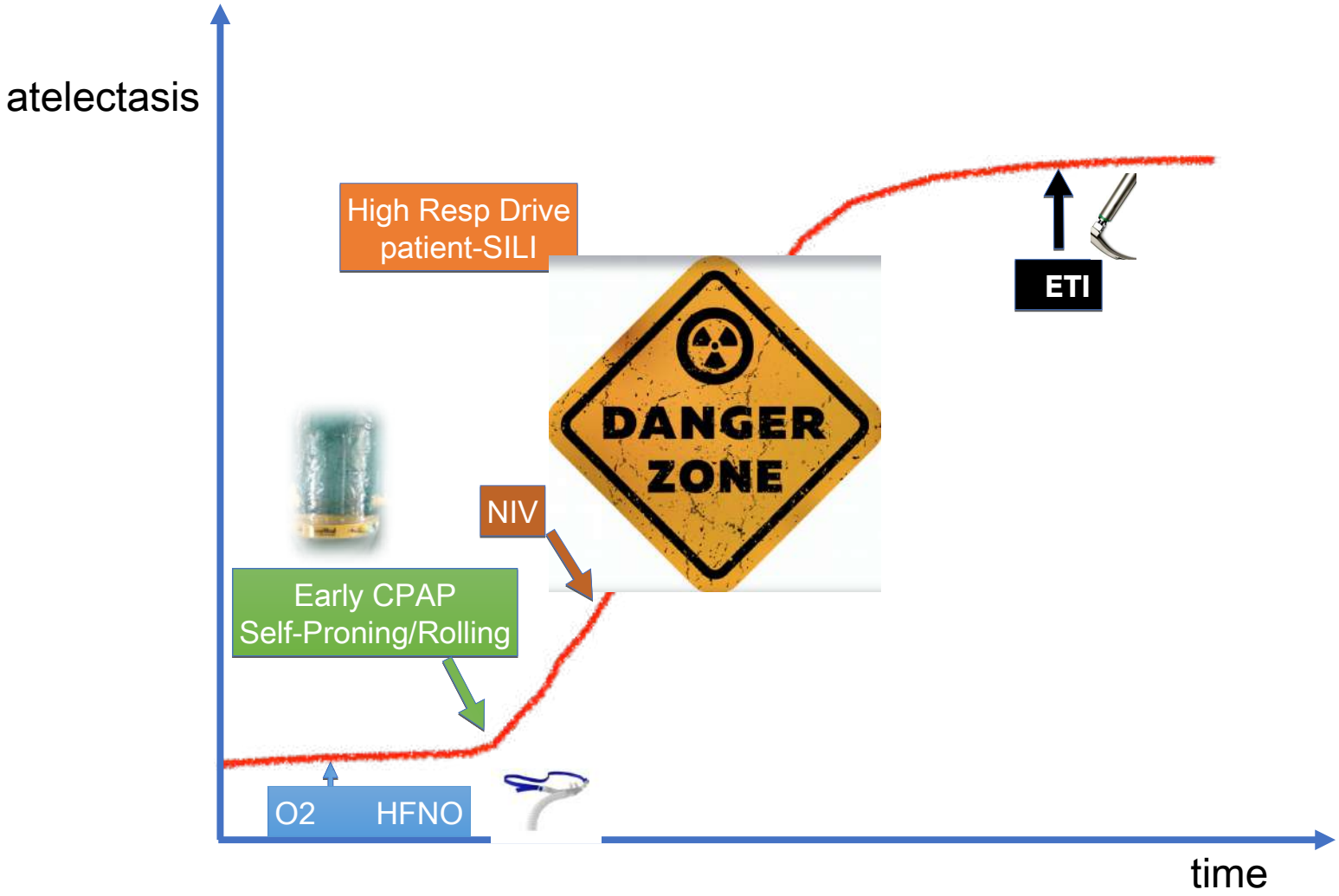
RESPIRATORY


RESPIRATORY
EFFORT

hypoxia according to atelectasis



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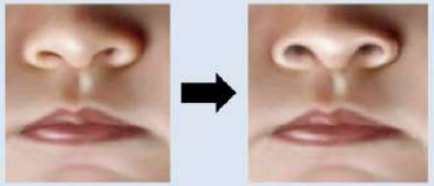
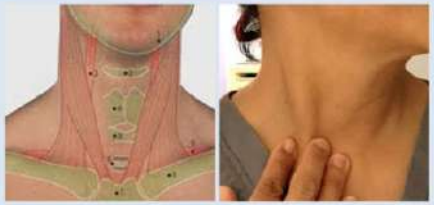
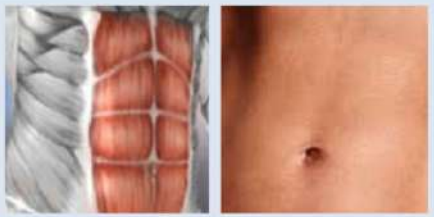
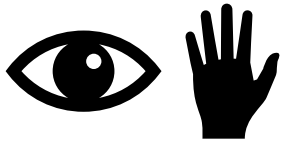
Critical Care

RESEARCH LETTER Open Access

Development of a work of breathing scale and monitoring need of intubation in COVID-19 pneumonia

ELEMENT	METHOD	POINTS
 Respiratory Rate	By Counting (bpm)	≤ 20 = 1 21-25 = 2 26-30 = 3 > 30 = 4
 Nasal Flaring (inspiration)	By Observation	1
 Sternocleido-mastoid Use (inspiration)	By Palpation	1
 Abdominal Muscles Use (expiration)	By Palpation	1

monitor WOB



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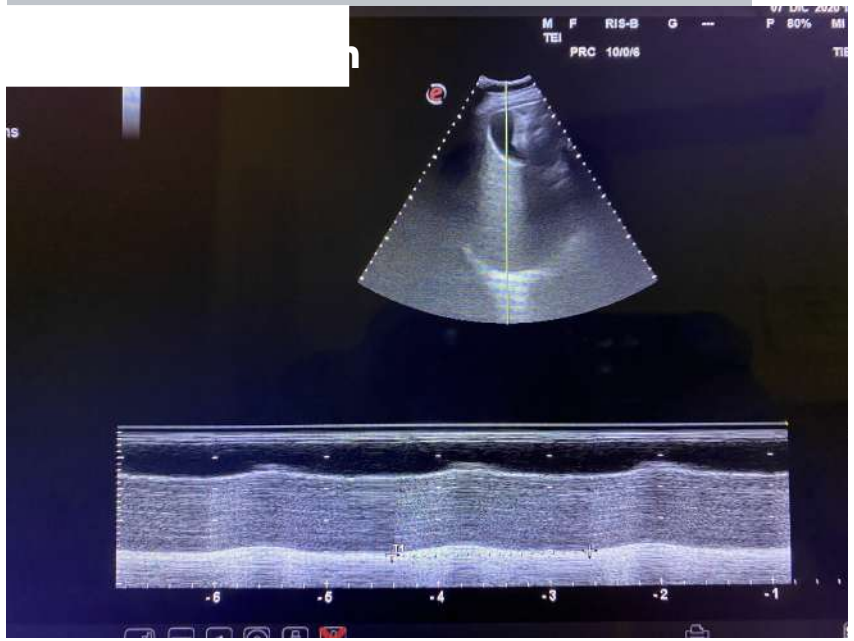

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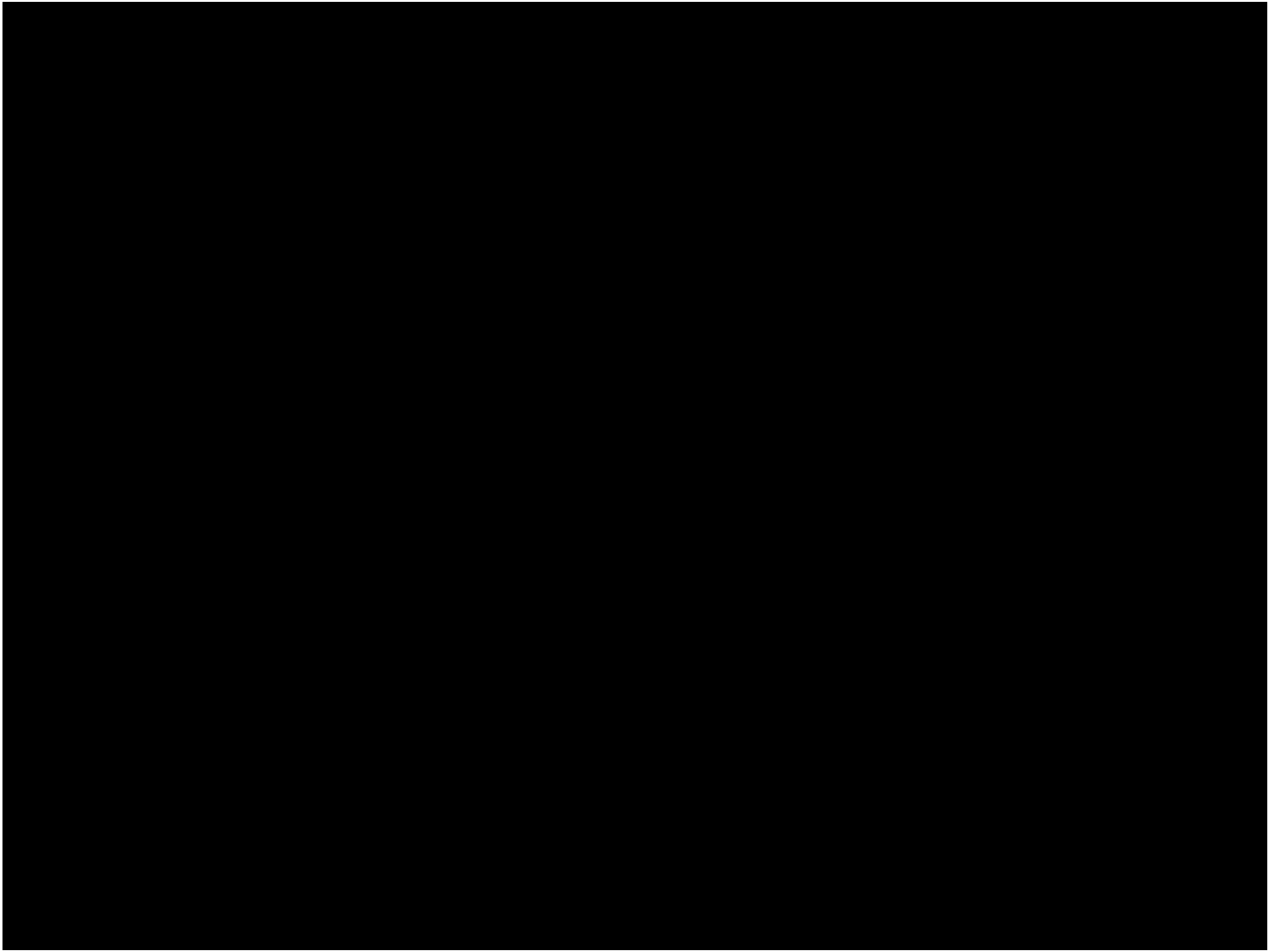

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REVIEW Open Access

Sedation in non-invasive ventilation: do we know what to do (and why)?

Dan Longrois[1*], Giorgio Conti[2], Jean Mantz[3], Andreas Faltlhauser[4], Riku Aantaa[5] and Peter Tonner[6]

Abstract

This review examines some of the issues encountered in the use of sedation in patients receiving respiratory support from non-invasive ventilation (NIV). This is an area of critical and intensive care medicine where there are limited (if any) robust data to guide the development of best practice and where local custom appears to exert a strong influence on patterns of care.

We examine aspects of sedation for NIV where the current lack of structure may be contributing to missed opportunities to improve standards of care and examine the existing sedative armamentarium. No single sedative agent is currently available that fulfils the criteria for an ideal agent but we offer some observations on the relative merits of different agents as they relate to considerations such as effects on respiratory drive and timing, and airways patency. The significance of agitation and delirium and the affective aspect(s) of dyspnoea are also considered.

We outline an agenda for placing the use of sedation in NIV on a more systematic footing, including clearly expressed criteria and conditions for terminating NIV and structural and organizational conditions for prospective multicentre trials.

Keywords: Agitation, Benzodiazepines, Delirium, Dexmedetomidine, Dyspnoea, Ketamine, Non-invasive ventilation, Opioids, Propofol, Sedation

Table 4 Properties of sedative drug classes relevant to delivery of sedation in NIV

Sedative	Haemodynamic stability	Analgesia	Amnesia	Anxiolysis	PVD	Avoidance of PONV	Promotion of natural sleep	Suitability for use after extubation	Delirium avoidance	Total
Propofol	2	2	2	2	2	4	2	2	1	20
Midazolam	3	2	4	2	2	2	2	1	1	19
Opioids	4	4	1	2	1	1	1	2	1	20
Dexmedetomidine	3	2	2	4	4	2	4	4	3	28
Ketamine	4	3	2	1	4	1	1	4	1	21

Larger numbers indicate a more satisfactory impact on the nominated property. This is primarily a qualitative and relative assessment of the features and benefits of different drugs and drug classes, framed in general terms. Hence, the individual category scores and in particular scores shown in the 'Total' column are crude summaries that should not be over-interpreted and which do not necessarily reflect the net merits or demerits of particular agents in the circumstances of a particular patient.

PONV, postoperative nausea and vomiting; PVD, preservation of ventilatory drive.

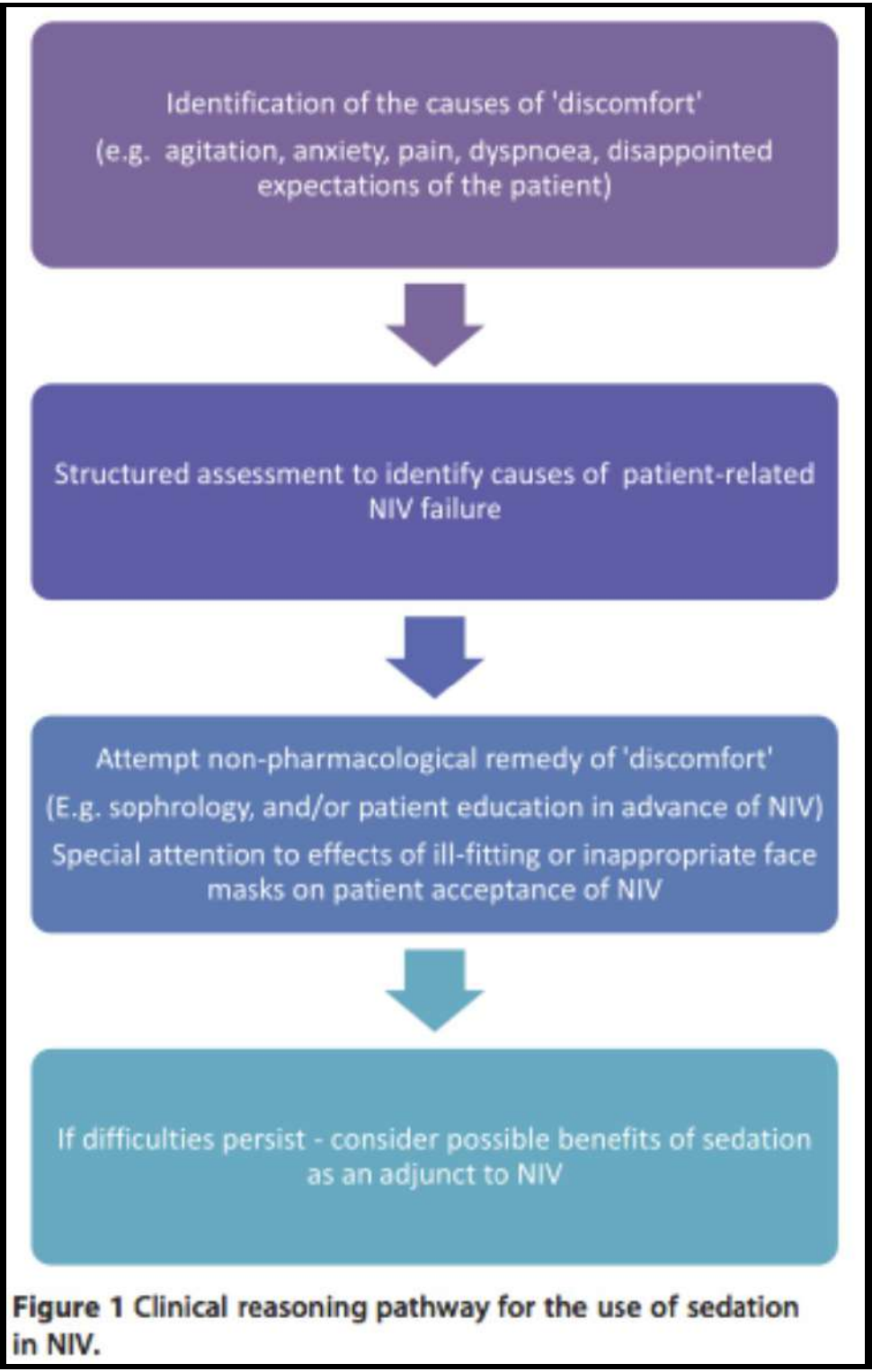


Figure 1 Clinical reasoning pathway for the use of sedation in NIV.

Sedatives considered in mechanically ventilated COVID-19 patients.

Sedatives	Current use	Potential benefits in COVID-19	Potential adverse effects	Any COVID-19 study	Findings related to COVID-19	Recommendation
Etomidate	Induction agent	- Hemodynamic stability - Minimal respiratory depression - Reduced risk of histamine release	- Adrenocortical suppression - Hypercarbia - Cardiovascular instability in elderly patients with HTN	No	N/A	May be used for induction in young patients
Ketamine	- Induction agent - Maintenance at low doses - Analgesia in ICU	- Reduces inflammatory markers such as IL-6 - Minimal respiratory depression	- Hallucinations	Yes	- Potential for immune modulation - Neuropsychiatric benefits	Primary choice for induction of sedation of COVID patients, particularly those that are hemodynamically unstable
Propofol	- Induction agent - Maintenance at low doses	- Rapid onset, rapid recovery - Anti-inflammatory/ immunomodulatory effects	- Diminished cardiac output, hypotension - Propofol infusion syndrome	Yes	- Myotoxicity - Propofol infusion syndrome	Should not be used for prolonged deep sedation
Dexmedetomidine	Light sedation in mechanically ventilated patients	- Minimal risk of delirium - Hemodynamic stability - Reduced time requiring ventilation - Reduced peri--intubation agitation (lower risk of aerosolizing particles)	- Bradycardia and hypotension with initial bolus - Withdrawal when used in high doses >24 h	Yes	- Combination of Dexmedetomidine and midazolam is effective dual therapy for long term sedation with limited side effects	Primary choice for long-term sedation when used in conjunction with benzodiazepines
Benzodiazepines	Continuous sedation in the setting of anxiety and agitation	- Treatment of acute agitation - Short-term break--through sedation	- Hypotension - Reduced respiratory drive - Longer ventilator times - delirium	Yes		Should not be used as monotherapy for long term sedation due to increased risk of aspiration causing refractory hypoxemia and longer ventilation times
Inhalational Volatile Sedatives	- Pediatric patients - Ambulatory surgeries	- Reduced need for hemodynamic support - Reduced need for opioids - Shorter ventilation times	- Malignant hyperthermia	No	N/A	Use for prolonged sedation is experimental and not FDA approved

Table II. Most widely used sedatives in pediatric non-invasive ventilation

DRUG IV DOSE (MG/KG) INDICATIONS & COMMENTS

Midazolam 0.1 to 0.2 **Sedative,** anxiolytic, amnesiac and non-analgesic
Minimal effects on hemodynamics
Rapid administration leads to respiratory arrest
Effects are reversible with flumazenile

Fentanyl 0.002 **Very strong analgesic**; sedative
Minimal effects on hemodynamics
High dose or rapid administration leads to chest wall rigidity
Effects are reversible with naloxone

Ketamine 0.5 to 2 **Strong analgesic**; **amnesiac and hallucinogen**
Bronchodilator (indicated for asthmatics), induces sialorrhea and bronchorrhea (preventable with atropine), hallucinations (preventable with benzodiazepines) and laryngospasm (highly problematic in NIV)

Propofol 1-2 **Potent hypnotic**
Minimal effects on hemodynamics or respiratory efforts at this dose
Not recommended for children under 3 years

Remifentanilo Remifentanil **Bolus delivery not recommended**.

NON INVASIVE VENTILATION IN PEDRIATICS (2009). Medina, Pons, Martinòn-Torres

Agonisti recettori GABA

BDZ

- molto usate, facilità di impiego, antidoto
- breve emivita se usate a boli. Possibile ic
- **delirogene**, agitazione paradossa 1%, amnesia e disorientamento
- riduzione diametro VA, ipotensione
- eliminazione renale

PROPOFOL

- rapido inizio e rapido offset.
- ipotensione marcata, solo ambiente anestesiologico

analgesia variabile (tolleranza, metabolismo epatico, capacità individuale di eliminazione)

OPPIOIDI

- **RAMIFENTANIL**: di sintesi. Azione potente, breve durata, selettivo su recettori M.

Non metabolismo epatico né renale ma esterasi plasmatiche e tissutali in metaboliti inattivi.

Emivita 10 minuti indipendentemente dalla durata infusione. Inizio azione 1 min e raggiunge rapidamente steady state —> facilmente titolabile, non rischio accumulo.

Indicato per induzione e mantenimento anestesia generale e analgesia in MV

- **SUFENTANIL**: riduzione disconfort, buona sedazione vigile, azione non significativa su drive

Dexdetomidina

~~Agonista A2 centrale (inibisce rilascio~~ NA) con proprietà sedativa ed ansiolitica (recettori locus ceruleo) ed analgesica tramite recettori midollari.

- si ottiene sedazione cosciente: pazienti facilmente risvegliabili e reattivi

- rapido onset ed off. Non agisce sulla collassabilità delle via aeree

- iper/ipotensione o bradicardia (dose dipendente)

KETAMINA

- NON RIDUCE dinamica respiratoria ALLE DOSI ANALGO-SEDATIVE

- RIDUCE RESISTENZA VA ed è broncodilatatrice

- AUMENTA COMPLIANCE CARDIOVA SCOLARE E LA VENTILAZIONE MINUTO. Produce stimolazione cardiovascolare per eccitazione del sistema nervoso simpatico centrale e probabilmente per inibizione della ricaptazione della noradrenalina a livello delle terminazioni nervose simpatiche

- MANTIENE RIFLESSI LARINGO-FARINGEI

MA ipersalivazione, reazioni allergiche ed azione sul sistema

Clonidina

E’ un alfa agonista centrale ed antagonista alfa periferico, caratteristica che lo rende utilizzabile negli stati ipertensivi e come sedativo-ansiolitico.

Agisce a livello del sistema nervoso centrale riducendo l'attivazione del sistema simpatico, del ritmo cardiaco e della pressione arteriosa grazie alla sua capacità di attivare selettivamente i recettori alfa-2 presinaptici del sistema nervoso centrale.

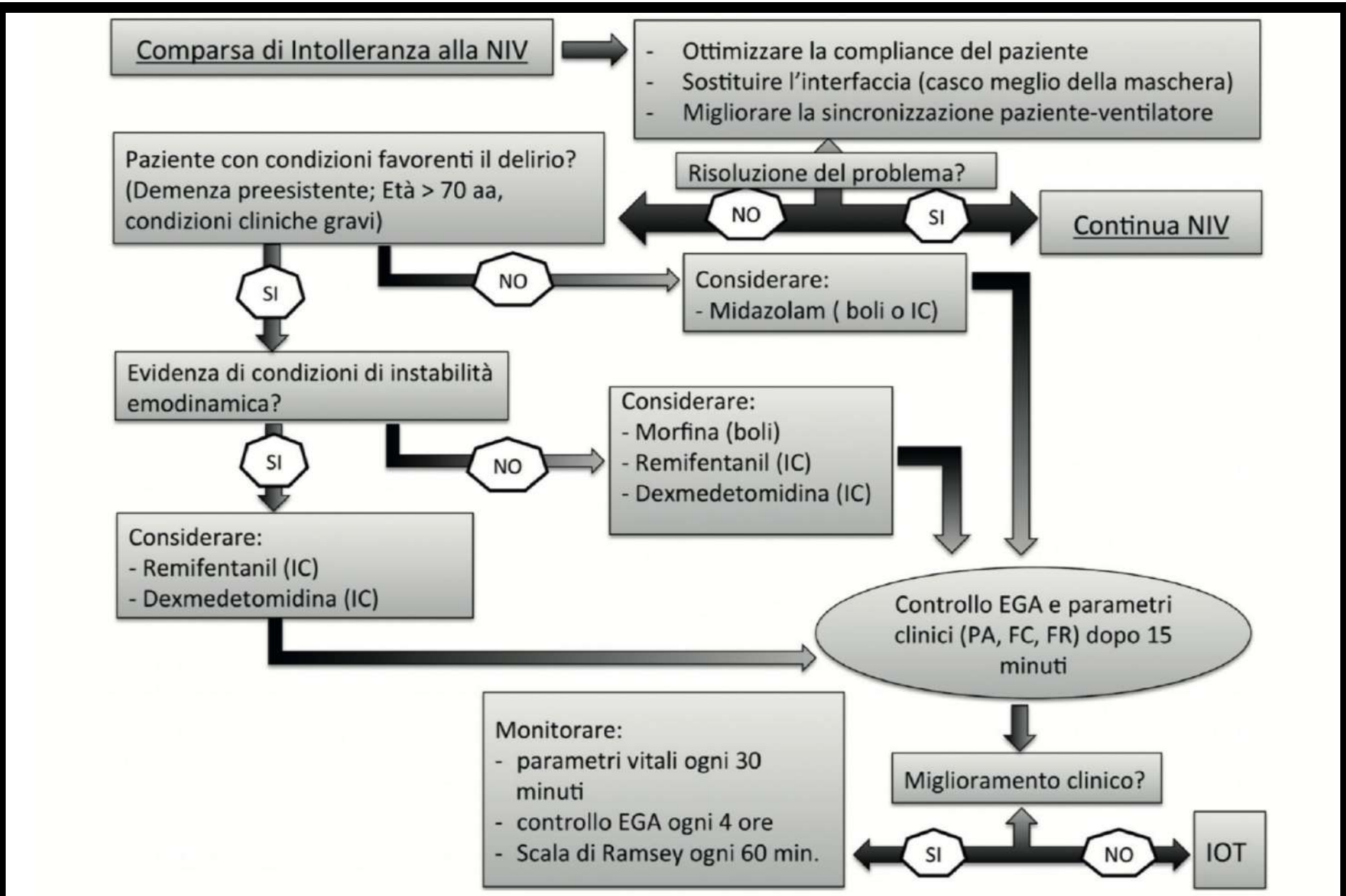
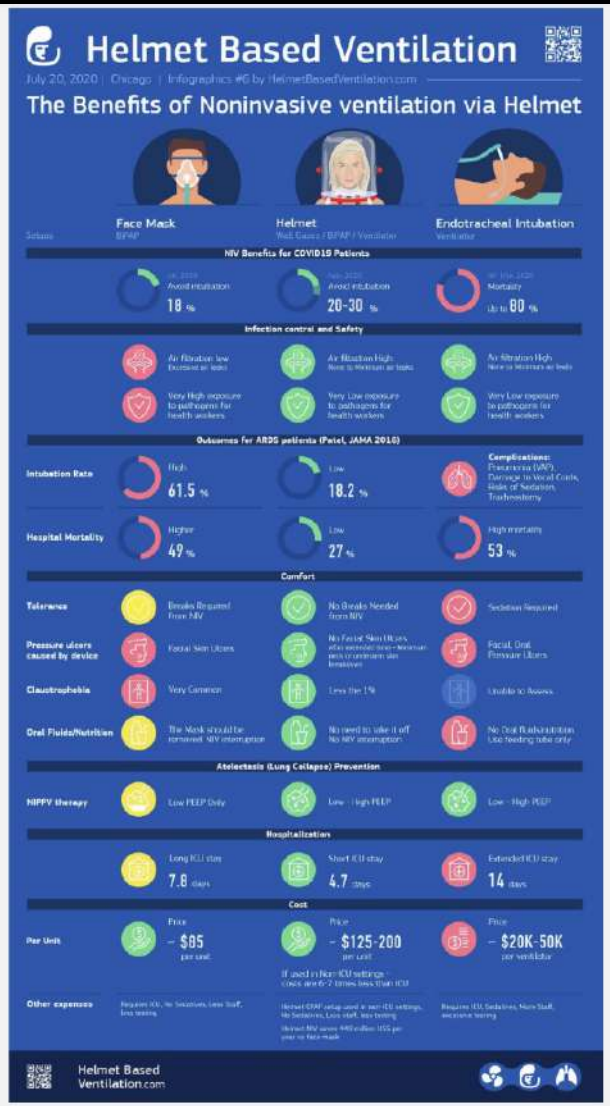


Figura 1. Algoritmo per la gestione dell'intolleranza alla ventilazione non invasiva (NIV).
EGA, emogasanalisi; FC, frequenza cardiaca; FR, frequenza respiratoria; IC, infusione continua; IOT, intubazione orotracheale; PA, pressione arteriosa.



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