2024 수면호흡장애 연구회 & 집중치료 연구회 공동심포지엄

Sleep-disordered breathing and its impact in the ICU

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine
Seoul National University Bundang Hospital

Dong-Hyun Joo

Context

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- ✓ Why is sleep important in the ICU?
- ✓ Overview of Sleep-disordered breathing (SDB) in General or at-risk population
- ✓ Sleep-disordered breathing (SDB) in the ICU
  - ✓ Prevalence of SBD in the ICU
  - ✓ Risk factors for SDB in the ICU
  - ✓ Adverse outcomes of SDB in the ICU
  - ✓ Diagnostic approach to SDB in the ICU
- ✓ Summary

Why is sleep important in the ICU?

Sleep disruption are common in ICU patients

❖ Sleep disruption in the ICU

- Sleep deprivation, Sleep fragmentation, Abnormal circadian rhythms
- Abnormal sleep architecture
- Prevalence (variable): 25 ~75%

Crit Care Med. 2018 Sep;46(9); *J Sleep Med* 2021;18(2)

Critically ill *vs.* Healthy In sleep

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Question: How does sleep in critically ill adults differ from normal sleep in healthy adults?

Decrease	Normal	Increase
Deep sleep (stage N3 sleep and REM) Subjective sleep quality	Total sleep time (TST) Sleep efficiency (time asleep/time in bed)	Sleep fragmentation (arousals and awakenings/hour) Light sleep (stages N1 + N2) time spent sleeping during the day (*vs* night) 36~57%

Crit Care Med. 2018 Sep;46(9)

Risk factors for sleep disruption

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❖ Risk factor before ICU admission

- ➢ Consistent factors
  - ✓ Patients who report poor-quality sleep
  - ✓ Use of a pharmacologic sleep aid at home
- ➢ Inconsistent factors
  - ✓ female gender, older age
  - ✓ Premorbid medical conditions (e.g., hypertension, diabetes, cancer, and thyroid disease)

Patient-perceived, ICU-acquired factors

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TABLE 2. List of Factors That Patients Report as Disruptive to Sleep

Environmental	Physiologic and Pathophysiologic
Noise (447, 453, 454, 480, 483–488, 490, 491)	Pain (454, 483–486, 488, 490, 491)
Light (241, 453, 454, 480, 482–484, 486–488)	Discomfort (454, 483, 486, 488, 490)
Comfort of bed (483, 486–488)	Feeling too hot or too cold (484, 486, 488)
Activities at other bedsides (483, 486, 487)	Breathing difficulty (484, 491)
Visitors (clinician or family) (483)	Coughing (484, 491)
Room ventilation system (483)	Thirst (484, 486) and hunger (486, 488)
Hand washing by clinicians (483)	Nausea (484, 488)
Bad odor (486, 488)	Needing to use bedpan/urinal (486, 488)
Care Related	**Psychologic**
Nursing care (447, 453, 480, 482–484, 486, 488, 491)	Anxiety/worry/stress (483, 484, 486, 489–491)
Patient procedures (447, 453, 480, 482, 483, 487, 488)	Fear (485, 486, 489)
Vital sign measurement (442, 448, 475, 477, 481, 483)	Unfamiliar environment (485, 488, 491)
Diagnostic tests (447, 453, 480, 483)	Disorientation to time (454, 486)
Medication administration (447, 453, 480, 482)	Loneliness (488, 491)
Restricted mobility from lines/catheters (454, 486, 488)	Lack of privacy (485, 488)
Monitoring equipment (454, 486, 488)	Hospital attire (486, 488)
Oxygen mask (486, 488)	Missing bedtime routine (483)
Endotracheal tube (491)	Not knowing nurses' names (486)
Urinary catheters (486)	Not understanding medical terms (486)

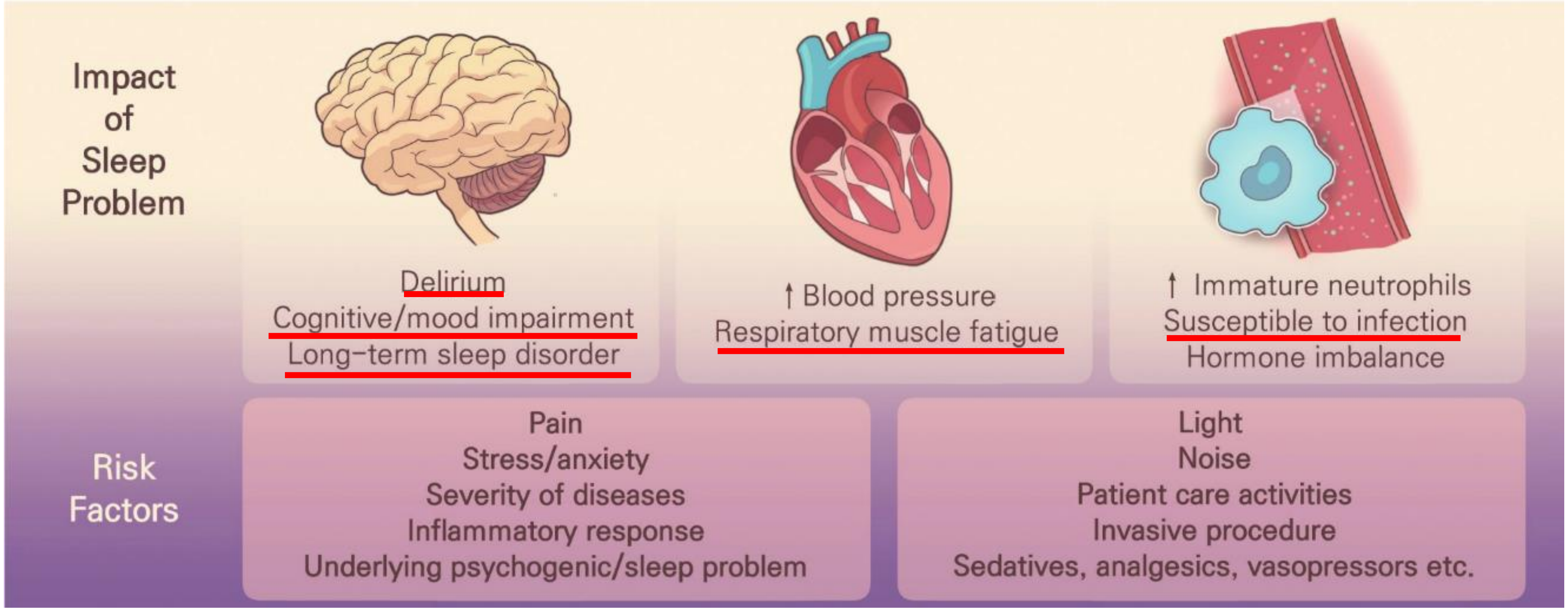
Crit Care Med. 2018 Sep;46(9)

Objectively measured ICU-acquired factors

- Polysomnography or actigraphy
- Risk factors
  - illness severity / Hypoxemia and alkalosis
  - Delirium
  - Receiving a benzodiazepine or propofol
  - patient-ventilator asynchrony
  - Spontaneous (*vs.* mechanically supported) breathing
  - Spontaneous mode of ventilation (*vs.* a controlled mode)

Crit Care Med. 2018 Sep;46(9)

Adverse outcomes with sleep disruption



- <u>Delirium occurrence</u>
- Duration of MV, ICU LOS, ICU mortality: Remain clear
- Outcomes after ICU discharge: Unknown

J Sleep Med 2021;18(2)

Adverse outcomes with sleep disruption

- Sleep as **a potentially modifiable risk factor** influencing recovery in critically ill adults

- 2013 PAD → 2018 PADIS guideline (Sleep disruption)

Crit Care Med. 2018 Sep;46(9)

Limitation of the guideline and current studies

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- **Relatively few studies** addressed sleep disruption in critically ill adult patients
- **<u>Not standardized, highly variable sleep measurements</u>**
  - Sleep quality assessment: exclude most ICU patients with sleep disruption (Delirium/Sedation)
  - PSG: highly abnormal and poor-quality EEG, No standard criteria
- **Limited clinically important outcomes**
  - Hard outcomes: Mortality, ICU LOS, and duration of mechanical ventilation.
  - Patient-centered outcomes
    - ✓ Long-term outcomes regarding sleep quality, psychologic health, Quality of life (ADL)
- **Future direction of studies**
  - **<u>Focus on improved methods for measuring sleep</u>**
  - Fine at-risk patients with sleep disruption
  - implementing interventions targeting patient-centered outcomes.

Sleep disordered breathing
- Overview

Classification of sleep disorder

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- The International Classification of Sleep Disorders – Third edition (ICSD-3)
  - Insomnia disorders
  - **Sleep-related breathing disorders (SDB)**
  - Hypersomnolence disorders
  - Circadian rhythm sleep-wake disorders
  - Parasomnias
  - Sleep-related movement disorders
  - Other sleep disorders

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Sleep-disordered breathing (SDB)

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- Abnormal breathing patterns during sleep
  - including apneas, hypopneas, and respiratory effort-related arousals

- Classification of SDB
  - **Obstructive Sleep Apnea (OSA) disorders: most common**
  - **Central Sleep Apnea (CSA) syndromes**
  - Sleep-Related **Hypoventilation** (SRHV) disorders
  - Sleep-Related **hypoxemia** (SRHO) disorders

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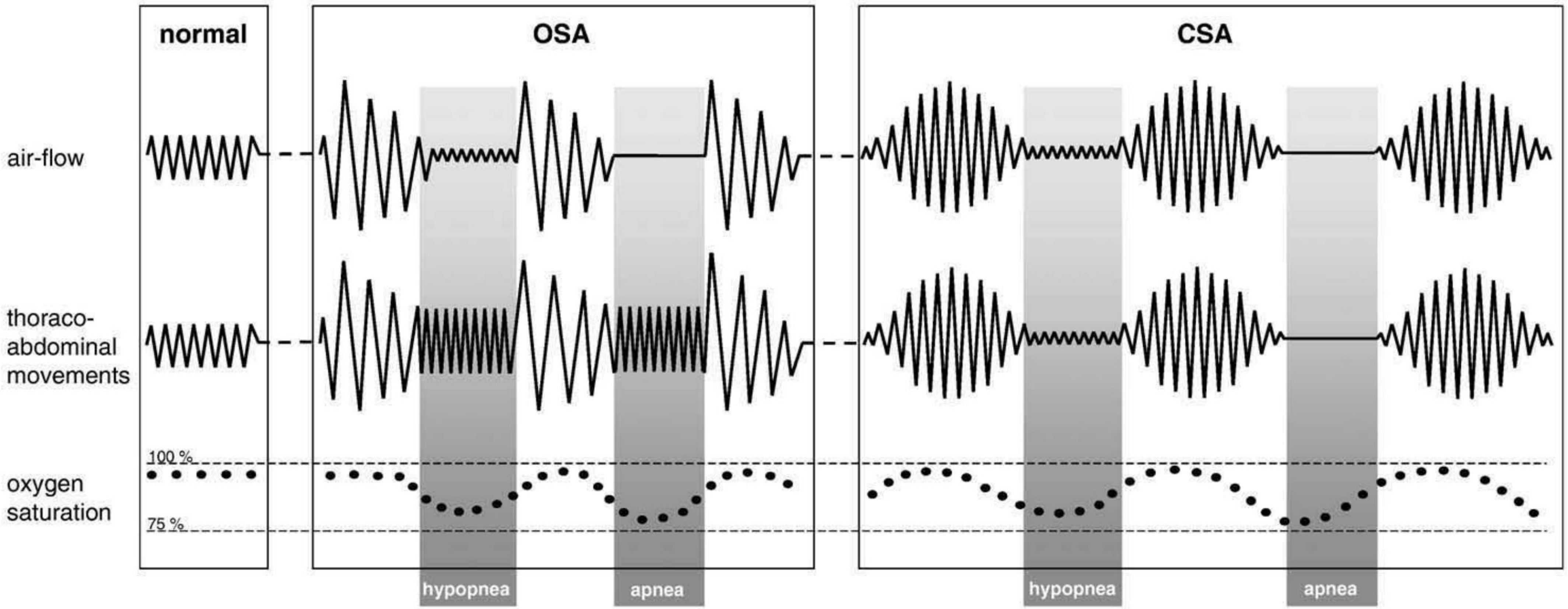
Diagnosis of SDB

❖ Gold standard: In-lab Polysomnography (PSG)



Prevalence of OSA in general population

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❖ Prevalence

➢ AHI ≥ 5/hr: 9~38%

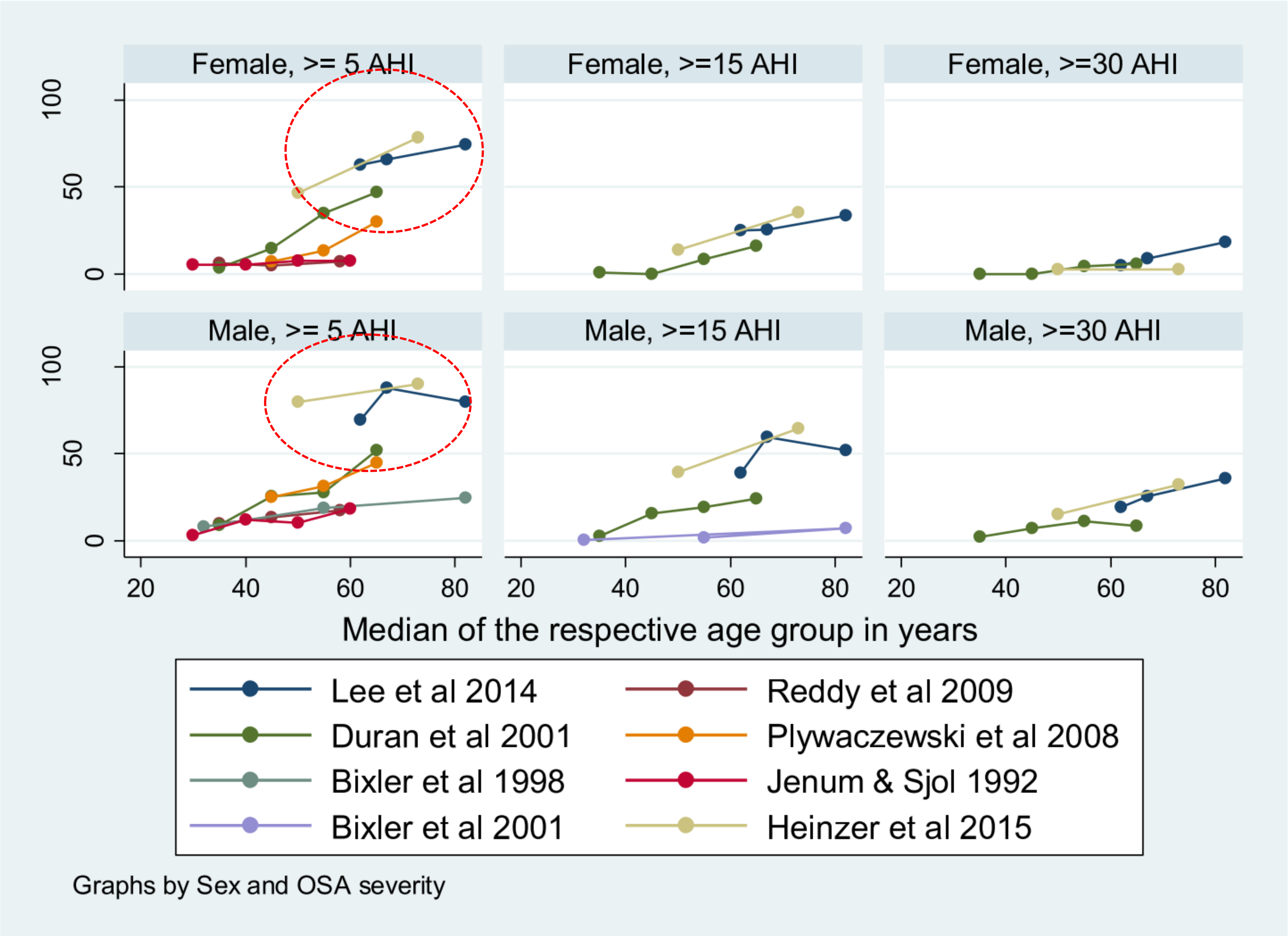
➢ AHI ≥ 15/hr: 6~17%

❖ Risk factors

➢ Older age

➢ Male sex

➢ BMI, obesity



Sleep Med Rev. 2017 Aug;34:70-81

Risk factors for OSA

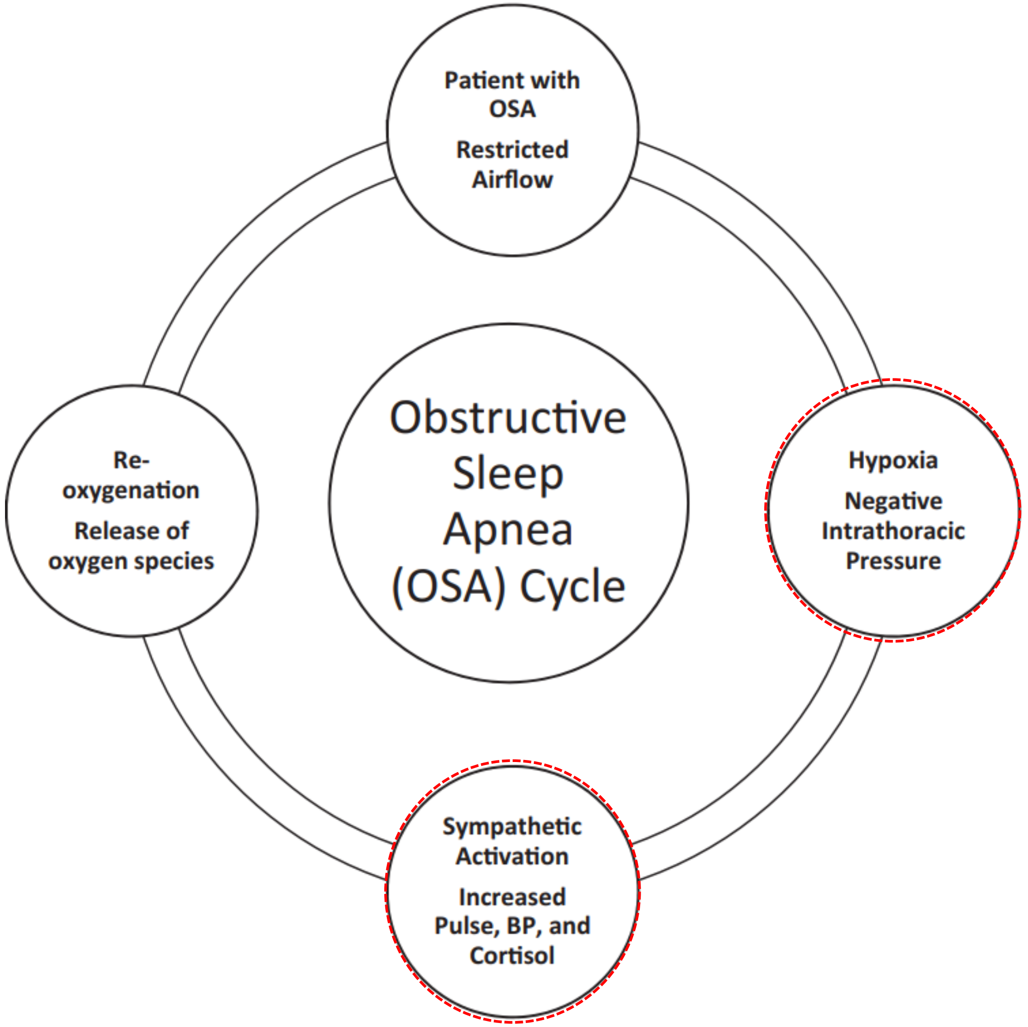
❖ Risk factors for OSA

- ➢ Older age / male sex / BMI, Obesity
- ➢ Smoking / Alcohol consumption / Physical inactivity / Chronic opioid use
- ➢ Comorbid medical condition
  - ✓ Cardiovascular disease (HTN, CAD, HF, AF, Stroke, etc.): ≈ 48%
  - ✓ Diabetes mellitus and metabolic syndrome: ≈ 54.5%
  - ✓ Respiratory disease (including COPD): ≈ 45.8 ~ 65.9%
  - ✓ Neuropsychiatric disorder (including depression, cognitive impairment)
  - ✓ COVID-19
  - ✓ Certain cancer (including H&N cancer, colorectal cancer)

Sleep Med Rev. 2017 Aug;34; *Ann Am Thorac Soc*. 2015 Aug;12(8); *Chest*. 2020 Sep;158(3); *J Clin Med.* 2020 Apr 2;9(4)

Adverse effect of OSA

- ❖ Cardiovascular and cerebrovascular outcomes
  - ➢ Major adverse cardiac events (MACEs)
    - ✓ Coronary heart disease, Cardiac death
    - ✓ Congestive heart failure
    - ✓ Stroke
    - ✓ All-cause mortality
- ❖ Cognitive and psychiatric complications
- ❖ Postoperative complications
  - ➢ Postop atrial fibrillation, delirium
  - ➢ Postop pulmonary complications



Curr Opin Pulm Med. 2019 Nov;25(6)

Curr Opin Pulm Med. 2019 Nov;25(6), BMJ Open. 2017 Dec 22;7(12), J Clin Anesth. 2020 Jun;62:109731, Anesth Analg. 2017 Dec;125(6)

Prevalence of CSA

- General population: < 1%
  - The Sleep Heart Health Study Cohort (n = 5804): 0.9%
- In-lab PSG in referral hospital: 2%
- In Specific populations
  - Cardiovascular disease (heart failure, AF, Stroke): 12 ~ 53%
  - OSA (Complex sleep apnea): 9.1 ~ 15%
  - Treatment-Emergent CSA (TE-CEA): 5 ~ 20.3%

Sleep. 2016 Jul 1;39(7); Sleep. 2022 Jun 25 45(1); Circulation. 2012 Sep 18;126(12); Sleep Mediicin 2013 Dec 14(1); Ann Thorac Med. 2016 Jul-Sep;11(3)

Risk factors for CSA

- ❖ Older Age / Male sex / BMI, obesity
- ❖ Comorbid medical conditions
  - ➢ Heart failure
  - ➢ Atrial fibrillation
  - ➢ DM, HTN, Dyslipidemia
  - ➢ Fluid retention
  - ➢ Stroke
  - ➢ Neuromuscular disorders
    - ✓ ALS, Spinal cord injuries, etc.
  - ➢ Chronic opioid use

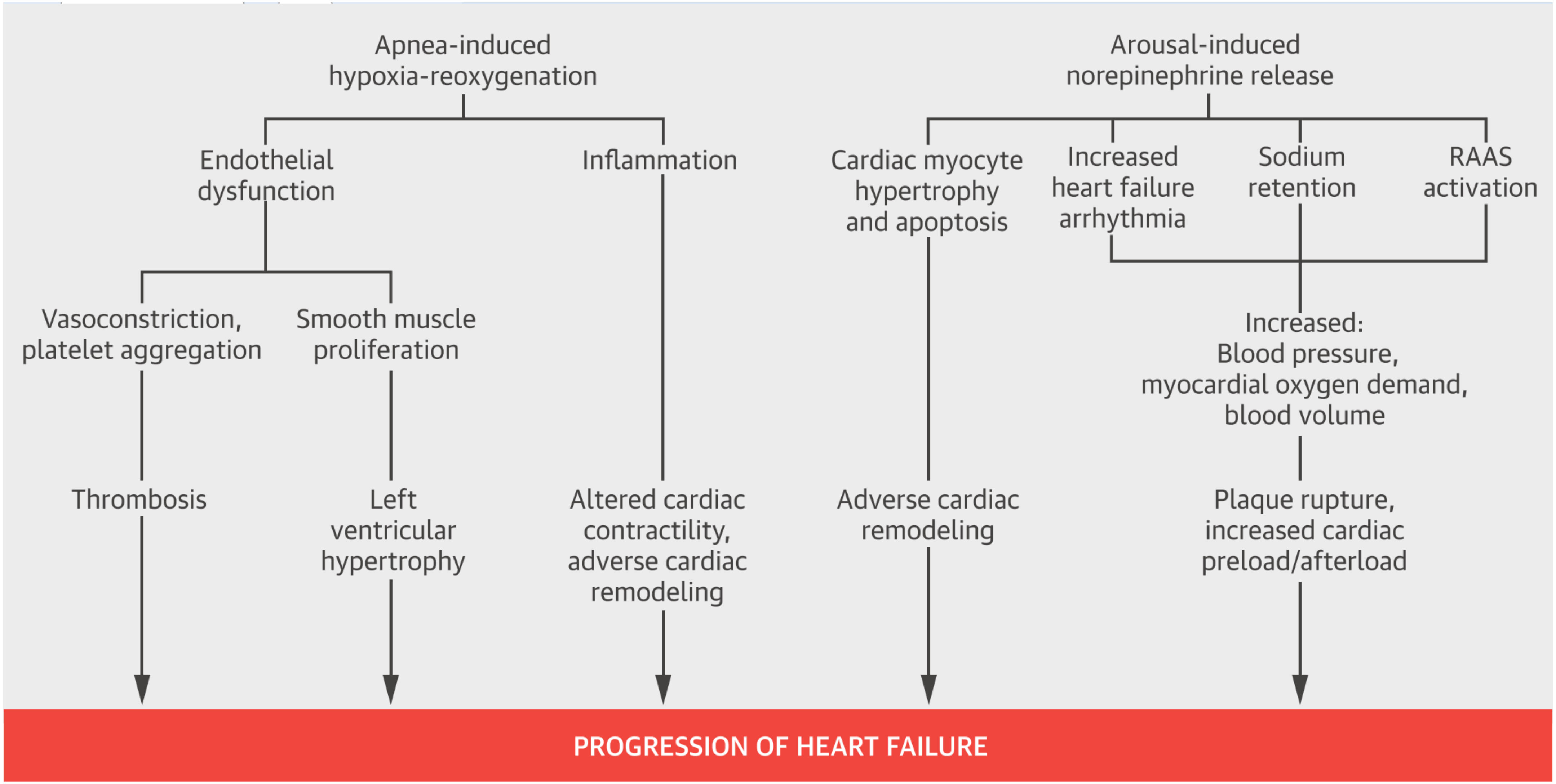
Table 3. Multilevel logistic regression results: predictors of CSA diagnosis among VA patients with a documented sleep test (N = 297,243)

Variable	OR	95% C.I.		P
Age (5 year increase)	1.13	1.11	1.14	<0.0001
Gender (male)	2.31	1.94	2.76	<0.0001
Heart failure	1.78	1.64	1.92	<0.0001
Ischemic heart disease	1.17	1.10	1.25	<0.0001
Cerebrovascular disease	1.65	1.50	1.82	<0.0001
Obese	1.11	1.05	1.17	<0.0001
Pulmonary hypertension	1.38	1.19	1.59	<0.0001
Arrhythmia	1.49	1.38	1.82	<0.0001
Atrial fibrillation	1.83	1.69	2.00	<0.0001
Chronic opioids	1.99	1.87	2.13	<0.0001
Chronic nonbenzo	2.22	1.95	2.53	<0.0001

Sleep Medicine. 2018 Sep;41(9)

Circulation. 2012 Sep 18;126(12); Eur J Heart Fail. 2016 Nov;18(11); Fed Pract. 2023 Mar;40(3); Sleep Medicine. 2018 Sep;41(9)

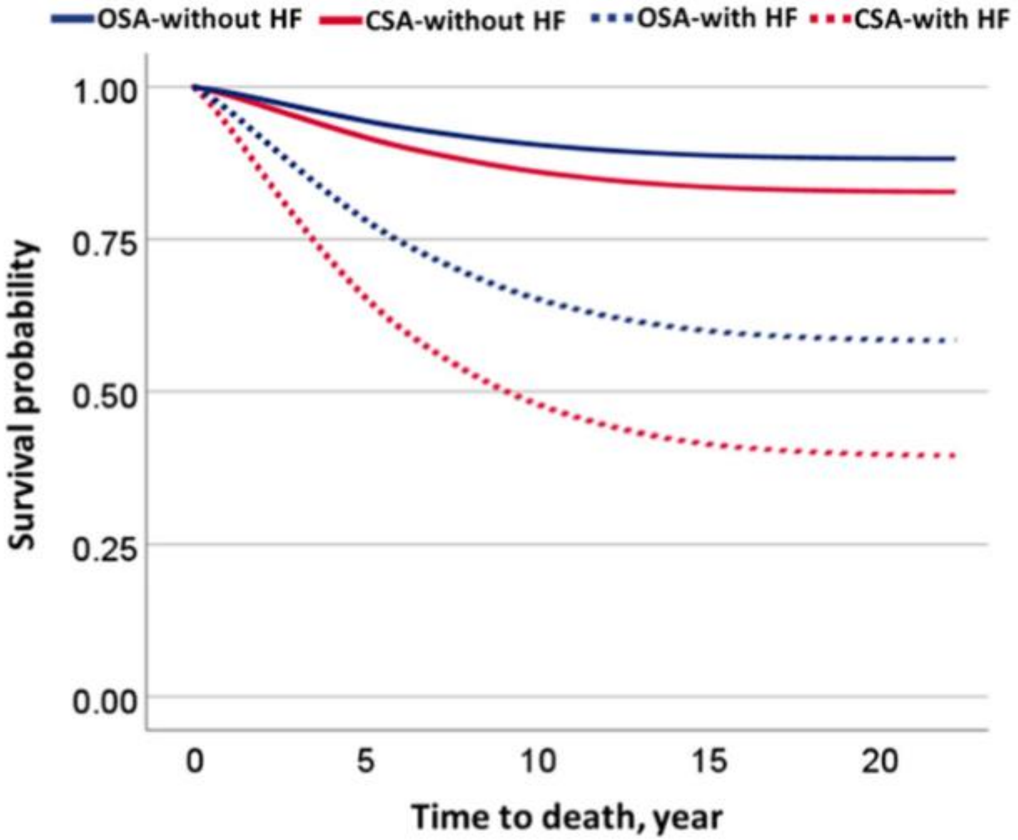
Adverse effect of CSA



J Am Coll Cardiol. 2015 Jan 6; 65(1)

Adverse effect of CSA

- Cardiovascular complications
- Cognitive and psychologic effects
- Postoperative complications
- All cause mortality
  - National Veterans Health Administration electronic medical records
  - CSA (n = 2,961) vs. OSA (n = 1,487,353)



	N	Death, N(%)	TtoD, M(IQR)	HR(95%CI) * unadjusted	aHR (95%CI) †
OSA-without HF	1,327,790	156,707 (11.8)	5.7 (3.1, 9.4)	Reference	Reference
CSA-without HF	2,308	388 (16.8)	3.2 (1.8, 5.8)	1.51(1.36,1.67)	1.41(1.28, 1.56)
OSA-with HF	159,563	64,749 (40.6)	3.9 (1.9, 6.9)	4.3(4.26,4.34)	2.20(2.18, 2.22)
CSA-with HF	653	355 (54.4)	1.9 (0.8, 4.0)	7.4(6.67,8.21)	3.66(3.30, 4.07)

J Am Coll Cardiol. 2015 Jan 6; 65(1); Ann Am Thorac Soc. 2023 Mar;20(3)

Sleep disordered breathing in the ICU

When is the SDB diagnosed in critically ill patients?

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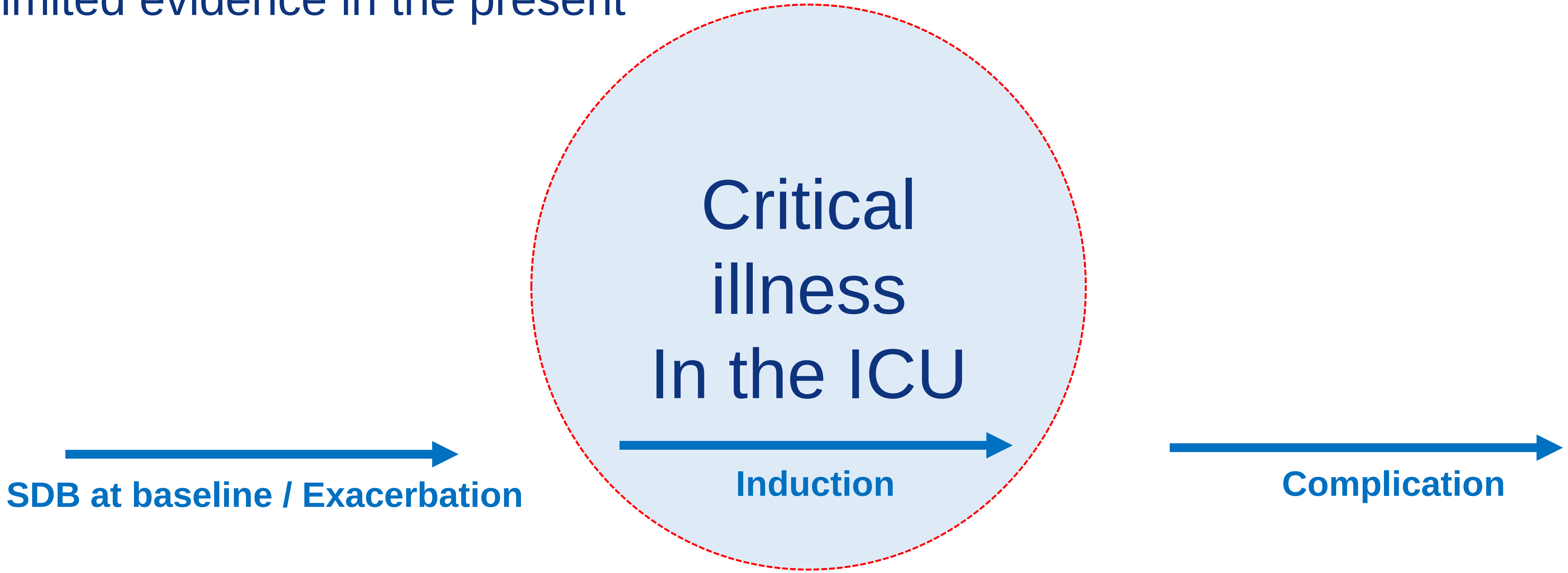
- Sleep-disordered breathing may be induced by, exacerbate, or complicate recovery from critical illness
- Limited evidence in the present



Sleep Breath. 2023 Jun;27(3)

Prevalence of SDB in the ICU

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- ❖ Prevalence
  - ➢ AHI ≥5: 47 ~ 74%
- ❖ Limitations
  - ➢ Low sample size
  - ➢ Limited PSG driven data

Table 3 Literature review

Study	N	Method of OSA detection	Number of nights studied	Findings
[12]	64 male critical care unit patients	Polysomnography	1 night	AHI ≥ 5, 47% of patients Oxygen desaturation to ≤ 90%, 61% of sample
[13]	56 ICU patients	Polysomnography	1 night	AHI ≥ 5, 40 patients (71%)
[14]	73 patients admitted to the cardiac ICU	Cardiorespiratory sleep study and/or polysomnography	1 night	Positive sleep study (AHI > 5), 54 patients (74%) Confirmed diagnosis (from outpatient sleep study), 46 patients (63%) Mild OSA (AHI ≥ 5), 14 patients (30%) Moderate OSA (AHI ≥ 15), 11 patients (24%) Severe OSA (AHI ≥ 30), 21 patients (46%)
[15]	127 coronary care unit patients	Respiratory polygraphy	1 night	Non-OSA (AHI < 15), 38 patients OSA (AHI ≥ 15), 89 patients Median [IQR] oxygen desaturation index > 4%/h for non-OSA group, 4.7 [3.5–10.1] Median [IQR] oxygen desaturation index > 4%/h for OSA group, 20.2 [6.6–38.1] Median [IQR] time with SaO_2 < 90% for non-OSA group, 1.6 (0.2–10.0) Median [IQR] time with SaO_2 < 90% for OSA group, 4.20 (0.9–15.6)
[16]	14 patients admitted to an intermediate ICU	Portable polysomnography	1 night	Obstructive sleep apnea syndrome, 10 patients with mean respiratory disorder index h^{-1} (RDI) 60.1 (25.9) Central sleep apnea, 2 patients with mean RDI h^{-1} 45 (28.3) Obesity-hypoventilation syndrome (OHS), 2 patients with mean RDI h^{-1} 12.5 (3.5)
[17]	31 ICU patients	Respiratory polygraph	1 night	Mean obstructive apnea index (OAI) in patients with OAI > 5, 13 ± 6 New diagnosis of OSA in 14 patients (56%)

Sleep Breath. 2023 Jun;27(3)

Prevalence of SDB in the ICU

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- ❖ A single center study
  - ➢ 124 patients in 3 difference ICUs in MGH, non-intubated
  - ➢ AHI measurement using machine learning algorithm during up to 7 days
    - ✓ a thoracic respiratory effort belt
    - ✓ a standard ICU pulse oximeter
  - ➢ Reported prevalence
    - ✓ **68%** had an AHI ≥ 5
    - ✓ 40% an AHI > 15
    - ✓ 19% had an AHI > 30

Sleep Breath. 2023 Jun;27(3)

Prevalence of SDB in the ICU

- A single center study
  - Subgroup analysis
    - ✓ between patients with and without previous OSA diagnosis
      - median AHI 8.8 and 10.1, *p*-value = 0.37
    - ✓ baseline OSA diagnosis was not a strong predictor of AHI severity in the ICU
- Clinical implications
  - **A large burden of undiagnosed and untreated sleep-disordered breathing** in the ICU population.
  - Many factors in the ICU might **cause** or **worsen** sleep-disordered breathing

Sleep Breath. 2023 Jun;27(3)

Post COVID-19 SDB

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- A single-center prospective cohort study
  - Survivors of severe COVID-19 pneumonia requiring ICU care (n = 68)
  - Home polygraphy 3 month after the onset of symptom
  - Prevalence of sleep apnea using AHI ≥ 5
    - ✓ 13/68 (19.1%) with pre-existing sleep apnea
    - ✓ **62/68 (91%)** prevalence of sleep apnea with 85.5% OSA

Table 2 Prevalence and Characteristics of SA Based on Polygraph Results at 3 Months in Intensive Care Unit Survivors After SARS-CoV-2 Pneumonia

AHI value (Events/h)	SA (n=62)	Prevalence of Central Event Share (%)
SA	62 (91.2%)	Median, 5.15% [0.6–17.9%]
<15	18 (26.5%)	
15–30	22 (32.4%)	
>30	22 (32.4%)	

Notes: Values are presented as median [IQR=interquartile range] or number of patients or percentage.
Abbreviations: AHI, Apnea-hypopnea Index; SA, sleep apnea.

Post COVID-19 SDB

	Overall Population N = 68	AHI < 15 N = 24	AHI ≥ 15 N = 44	p-value
Intensive Care Unit				
Intubation	57 (83.8%)	18 (75.0%)	39 (88.6%)	0.1771
Curarization	57 (83.8%)	18 (75%)	39 (88.6%)	0.1771
Duration of curarization (d)	7 [2–11]	4 [0–9]	8 [3.5–14]	0.0261
Prone positioning treatment	49 (72.1%)	14 (58.3%)	35 (79.5%)	0.0900
Duration of prone positioning (d)	2.5 [0–7]	1 [0–4]	3 [1–9]	0.0453
Tracheostomy	8 (11.8%)	0 (0%)	8 (18.2%)	0.0434
Length of stay in the ICU (d)	16.5 [11–24]	12.5 [7.5–20.5]	17.5 [12–30]	0.0567
Length of stay in hospital (d)	44 [20–61]	41 [17–58.5]	45 [22–62]	0.4092
Weight loss at M3 (kg)	−3 [−6–1]	−1.3 [−5.5–4.5]	−3[−6—1]	0.1540

- Clinical implications
  - the importance of monitoring and treating Sleep Apnea in survivors after severe COVID-19
  - Sleep apnea as both **risk factors** and a **consequence** of severe infection (pneumonia)
    - ✓ Risk of untreated sleep apnea
    - ✓ Importance of F/U Sleep assessment in ICU survivors.

Nat Sci Sleep. 2022 Dec 22;14:

SDB in survivors of critical illness

- A single-center prospective cohort study
  - Survivor of critical illness with MV care (n = 36)
    - ✓ without hypercapnia and hypoxemia
    - ✓ Excluded pre-existing SDB
  - Full PSG + HRQoL questionnaires within 10 days (n = 36) and after 6 months (n = 29) of hospital discharge
  - SDB parameters
    - ✓ Prevalence: **22/36 (61%)** with SDB (AHI ≥15: 21 OSA, 1 CSA) in initial evaluation
    - ✓ AHI: decrease in AHI [**21.5** (6.5–29.4) vs. **12.8** (4.7–20.4)] during 6-month F/U
    - ✓ Sleep architecture: increase in N3 [**4.2%** (0–12.5) vs. **9.8%** (3.0–20.4)

Sleep Breath. 2019 Jun;23(2):463-471

SDB In patients with prolonged MV

- A single-center retrospective study
  - Difficult-to-wean patients for acute or postop respiratory failure (n = 63)
  - PSG after liberation from MV (time interval not described)
  - Prevalence of OSA
    - ✓ **43/63 (68.2%)** with OSA
    - ✓ Median AHI 35 events per hour
- No further published peer-reviewed article

Abstract presented at 2020 ERS: European Respiratory Journal 2020 56: 2550

Clinical implication of the previous studies

- Relative high prevalence of SDB during and after ICU mission
  - **Under-recognized/diagnosed SDB** in patients admitted to the ICU
  - **Under-treated SDB** in patients admitted to the ICU
  - Possible **induction of SBD** during ICU care
  - **SDB** as one of the important **complications** after ICU care

- Further large prospective studies are needed

Risk factors for SDB in the ICU patients

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- ❖ Absence of large-scale observational study

  → Absence of evidence regarding risk factors for SDB in the ICU patients

- ❖ Risk factors for OSA/CSA in general populations

OSA	CSA
Older age / male sex / BMI, Obesity Smoking / Alcohol consumption / Physical inactivity /	Older Age / Male sex / BMI, obesity
Chronic opioid use Cardiovascular disease Diabetes mellitus and metabolic syndrome Respiratory disease (including COPD) Neuropsychiatric disorder COVID-19	Chronic opioid use Heart failure, Atrial fibrillation DM, HTN, Dyslipidemia Fluid retention Stroke Neuromuscular disorders

Risk factors for SDB in the ICU patients

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- Possible factors for developing SDB during or after ICU admission
  - Frequent Medical Interventions (Opioid, Vasoactive drugs, etc.)
  - Mechanical ventilation
    - ✓ Endotracheal intubation: Change in upper airway structure
    - ✓ Tracheostomy: weaning failure due to unmasked OSA
  - ICU-Acquired Muscle Weakness
  - Altered Lung Volumes after severe infection

Fluid retention and sleep apnea

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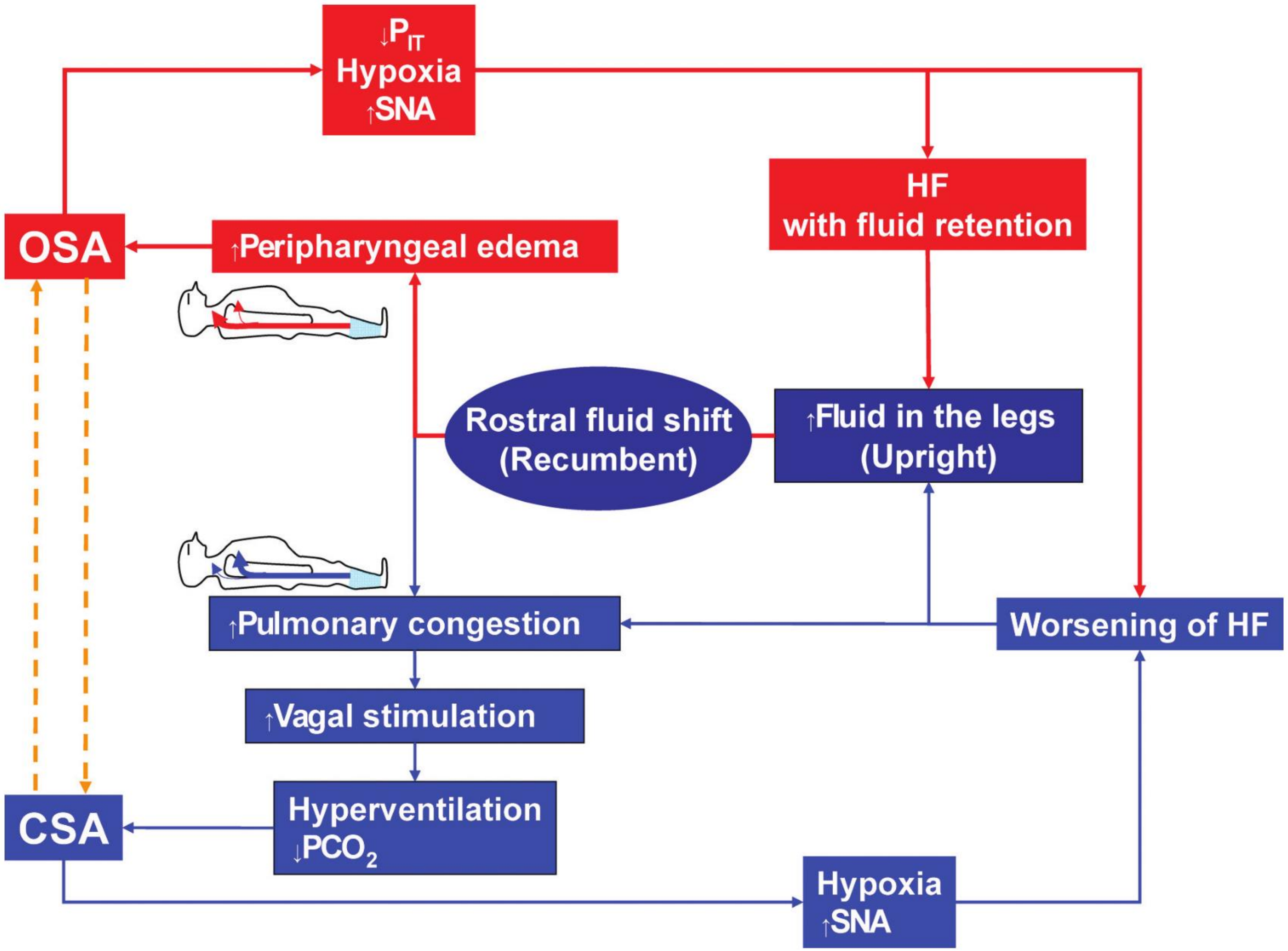

Circulation. 2012 Sep 18;126(12)

Adverse outcomes of SDB in the ICU

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- ❖ Not proven robust long-term ICU outcomes with sleep disruption
- ❖ Possible adverse outcomes related to SBD in the ICU
  - ➢ Increased cardiovascular risks
  - ➢ ICU delirium
  - ➢ Impaired quality of life during and after ICU admission
  - ➢ Decrease in physical performance
  - ➢ Prolonged mechanical ventilation
  - ➢ Impaired immune function, poor outcomes with sepsis?
  - ➢ Disrupted glucose metabolism (Impaired insulin sensitivity)

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Diagnostic approach to SDB in the ICU

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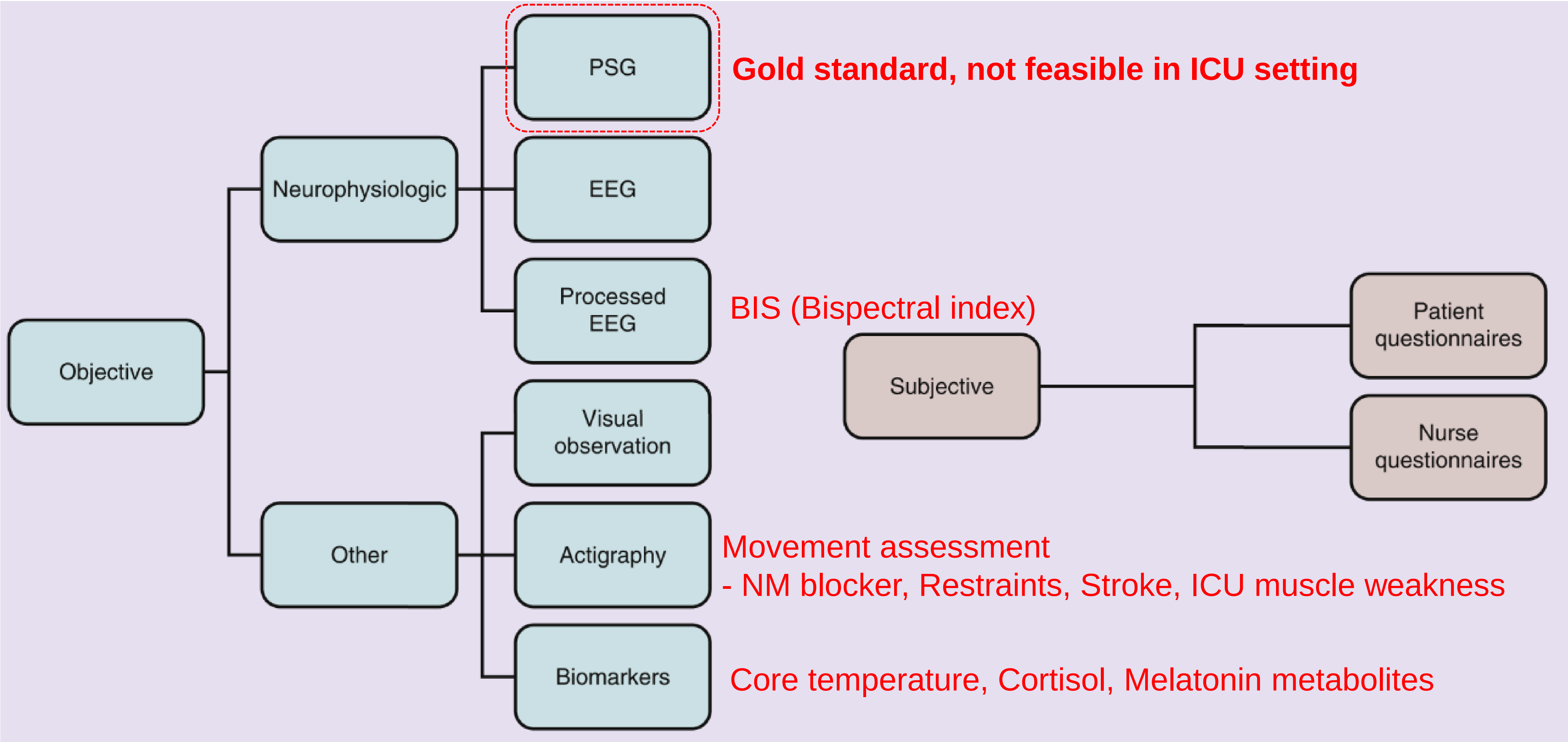

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Richards-Campbell Sleep Questionnaire (RCSQ)

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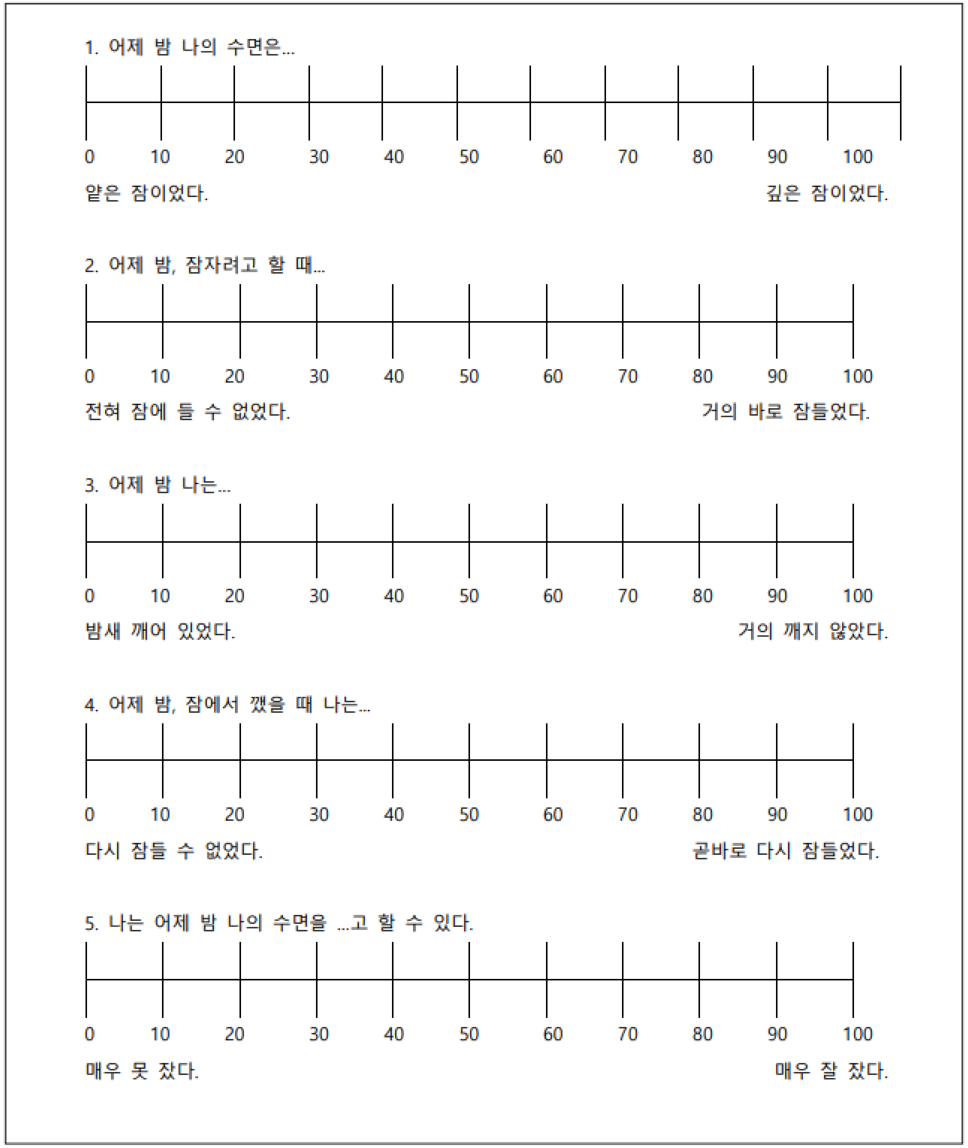
- ❖ Developed for use in critically ill patients
  - ➢ Five-to-six visual analogue scales
  - ➢ K-RCSQ (Validation, 2020)

- ❖ Limitations
  - ➢ Impaired consciousness (Sedation, delirium)
  - ➢ Inadequate memory recall



1. 어제 밤 나의 수면은...

0 10 20 30 40 50 60 70 80 90 100

얕은 잠이었다. — 깊은 잠이었다.

2. 어제 밤, 잠자려고 할 때...

0 10 20 30 40 50 60 70 80 90 100

전혀 잠에 들 수 없었다. — 거의 바로 잠들었다.

3. 어제 밤 나는...

0 10 20 30 40 50 60 70 80 90 100

밤새 깨어 있었다. — 거의 깨지 않았다.

4. 어제 밤, 잠에서 깼을 때 나는...

0 10 20 30 40 50 60 70 80 90 100

다시 잠들 수 없었다. — 곧바로 다시 잠들었다.

5. 나는 어제 밤 나의 수면을 ...고 할 수 있다.

0 10 20 30 40 50 60 70 80 90 100

매우 못 잤다. — 매우 잘 잤다.

J Nurs Meas. 2000 Fall-Winter;8(2); *Acute and Critical Care* 2020 August 35(3)

Infeasibility of PSG in the ICU

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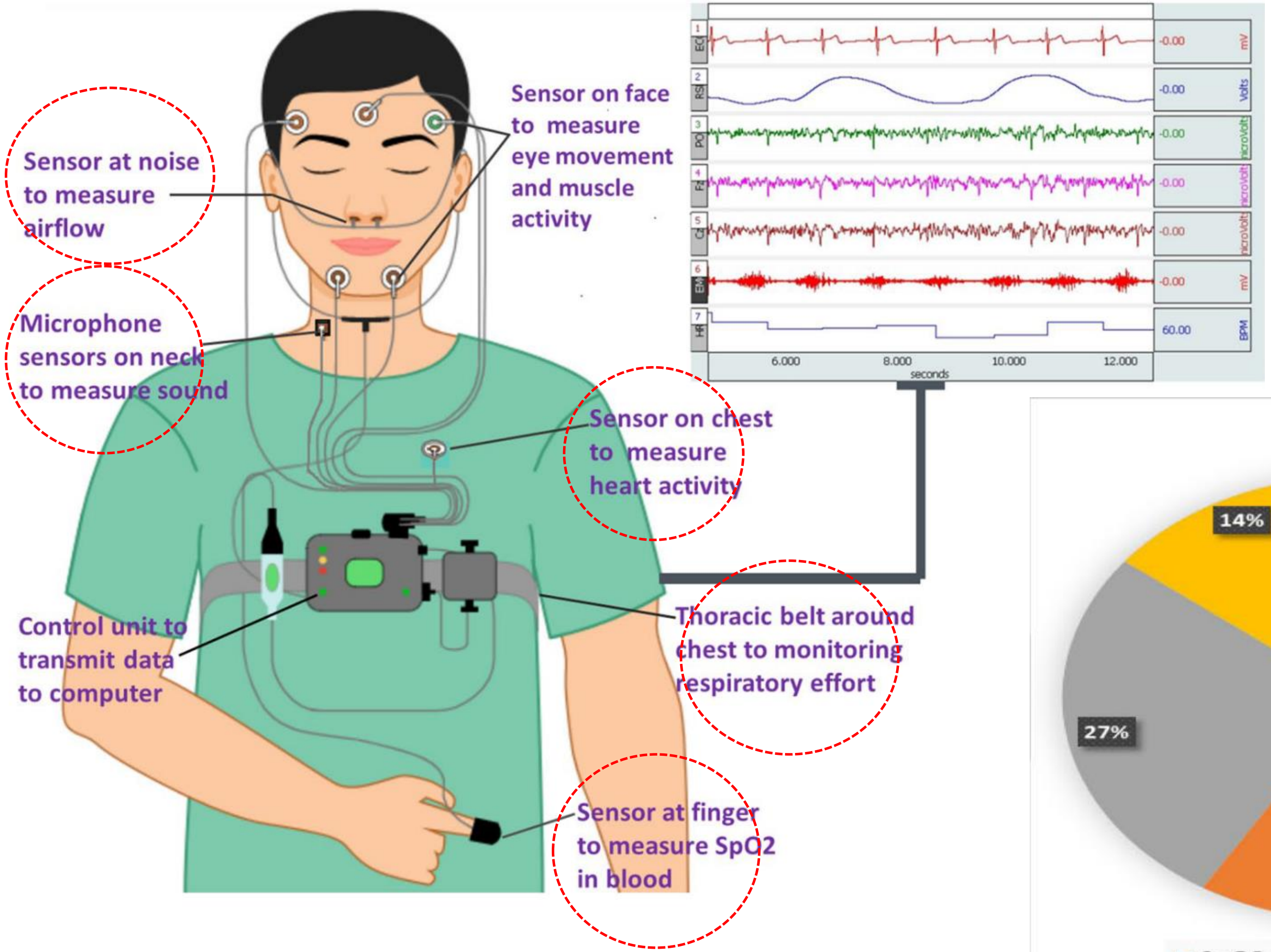
- ❖ Expensive, time consuming, requiring trained personnel
- ❖ Higher daytime sleep in ICU patients, requiring 24-hour recording
- ❖ Atypical sleep pattern in ICU patients
  - ➢ Influence by numerous medication and underlying illness
  - ➢ Standard scoring system is not reliable

→ <u>Need alternative diagnostic strategies</u>

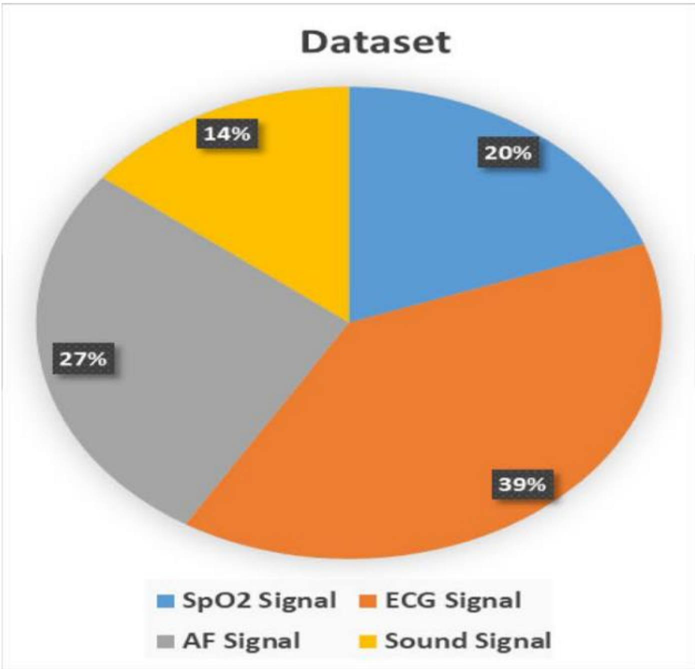
→ <u>No standardized approach in assessing sleep in the ICU</u>

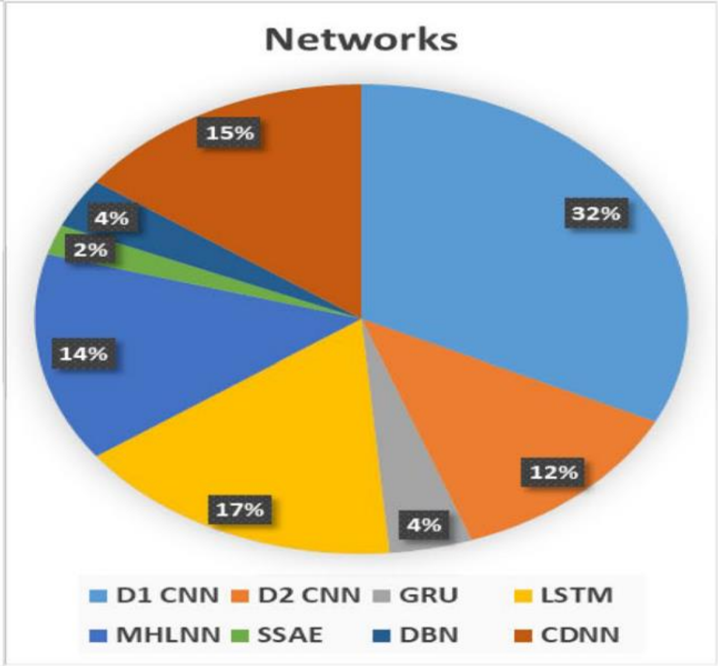
Principles and Practice of Sleep Medicine, 7th ed

Machine learning algorithm to detect sleep apnea



+ Wrist-worn watch



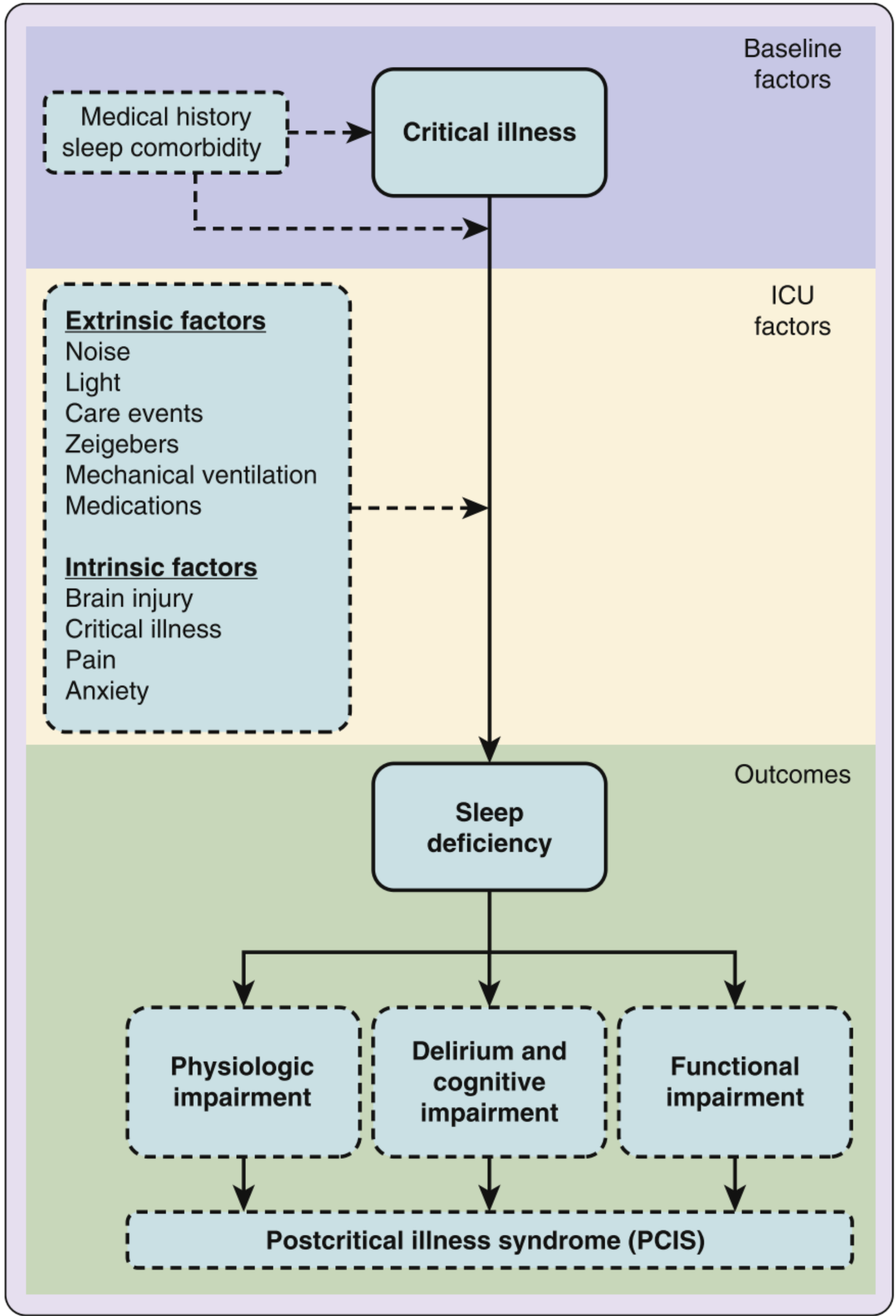


Biomed Eng Lett. 2023 Jul 5;13(3); *IEEE Trans Biomed Eng.* 2024 Mar 18

Summary

Sleep disruption in the ICU

- Sleep disruption is **common** in critically ill patients
- **Predisposing factors and intrinsic/extrinsic ICU-acquired factors** is associated with increased risk of Sleep disruption
- Sleep disruption is **hypothesized to contribute to poor clinical outcomes** in critically ill patients admitted to the ICU
- Future studies should focus on the **improved method for assess sleep** in the ICU



Sleep-disordered breathing in the ICU

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- **Relatively few studies** addressed **SDB** in critically ill adult patients

- Limited data suggested that SDB is **common** and is **expected to contribute to poor clinical outcomes** in ICU patients.

- **Standardized approach in assessing sleep in the ICU** and **Further Large-scale prospective studies** are needed to evaluate the prevalence of SDB and to find at-risk population of SDB patient **during** and **after** ICU admission

Thank you for your attention

jdhyun2000@gmail.com

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Celebrating 20 years of excellence
We continue to lead the way in healthcare innovation and patient-centered care

Overview of Sleep disruption in the ICU, based on 2018 PADIS guideline

Delirium *vs.* No Delirium.

Question: Is sleep different in critically ill adults if delirium

(vs no delirium) is present?

❖ Patients with delirium

- ➢ TST, sleep efficiency, or sleep fragmentation: No change
- ➢ time spent in light (N1 + N2) *vs.* deeper (N3) sleep: Unknown
- ➢ REM sleep: decreased
- ➢ Circadian sleep-cycle disruption, Daytime sleep: Increased
- ➢ Subjective sleep quality: Unclear

Crit Care Med. 2018 Sep;46(9)

Mechanical Ventilation (MV) *vs.* No MV

Question: Is sleep different in critically ill adults who are mechanically ventilated (vs not mechanically ventilated)?

- Have not yet been fully investigated, limited data
  - MV may worsen sleep fragmentation, architecture, and circadian rhythm (daytime sleep)
    - ✓ Excessive pressure support, ventilator asynchronies, or ventilator alarms
  - MV with respiratory failure may improve sleep efficiency and reduce fragmentation

Crit Care Med. 2018 Sep;46(9)

Considerable variability in sleep parameters

- Several factors
  - total recording time
  - quality of the recordings
  - experience of the scorer (awareness of atypical sleep)
  - the criteria used to analyze sleep
  - disease severity
  - LOS on the day of polysomnography evaluation
  - both sedative type and depth of sedation
  - and whether delirium
- Harmonization in scoring rules and recording practices (e.g., systematic recording of noise levels and mental status) and studying homogeneous groups of patients might help to assess the prevalence of sleep alterations in critically ill patients

Prevalence of Unusual/Dissociated Sleep

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Question: What is the prevalence of unusual or dissociative sleep patterns in critically ill adults?

- The prevalence of unusual or dissociated sleep patterns is highly variable and depends on patient characteristics.
  - Atypical sleep and pathologic wakefulness
    - ✓ Absence of K complexes and sleep spindles
    - ✓ Dissociation between EEG rhythms and behavioral wakefulness
    - ✓ not included in conventional R&K EEG scoring rules
  - Prevalence: 23 ~ 31 % / 60~97%(non-sedated or lightly sedated / Sedated ICU patients)
  - Contributing factors: sedative/opioids, delirium, sepsis, etc.

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Risk factors for sleep disruption

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❖ Limitations

- ➢ Patient-centered using questionnaires and interviews
  - ✓ subject to recall bias
  - ✓ exclude patients who are not able to self-report due to sedation, delirium, dementia, or acute brain injury
  - ✓ Underestimate microarousals with severe sleep fragmentation
- ➢ Studies using polysomnography
  - ✓ highly abnormal and poor-quality EEG, No standard criteria
  - ✓ causation, only association, **not causation**

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Sleep disturbance and outcomes

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- In healthy individuals
  - Poor sleep may adversely affect the immune system, glycemic control, and the psychologic well-being
- In critically ill patients
  - Delirium occurrence:
    - ✓ Association, but not sure for causation.
    - ✓ a potentially modifiable risk factor for ICU delirium?
    - ✓ No single interventions to be proved except for a multicomponent delirium prevention protocol or multidisciplinary bundles
  - Duration of MV, ICU LOS, ICU mortality: Remain clear
  - Outcomes after ICU discharge: Unknown

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Routine sleep monitoring in the ICU

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Recommendation: We suggest not routinely using physiologic sleep monitoring clinically in critically ill adults (conditional recommendation, very low quality of evidence)

- Physiologic monitoring To determine if a patient is asleep or awake
  - Use of actigraphy, bispectral analysis (BIS), EEG, and PSG
- "not" include monitoring of patients' perceived sleep by either validated assessment (e.g., the Richards Campbell Sleep Questionnaire)
  - No studies evaluate the effect of routine monitoring in critical outcomes
    - ✓ delirium occurrence, duration of mechanical ventilation, ICU LOS, ICU mortality, and patient satisfaction
  - very costly and labor-intensive
  - Uncertain benefit in broad ICU population (limited generalizability)
    - ✓ Patients with acute coronary syndrome

Nonpharmacologic Interventions to Improve Sleep

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❖ Ventilation mode

Recommendation: We suggest using assist-control ventilation at night (vs pressure support ventilation) for improving sleep in critically ill adults (conditional recommendation, low quality of evidence).

Recommendation: We make no recommendation regarding

the use of an adaptive mode of ventilation at night (vs pressure support ventilation) for improving sleep in critically ill adults

- Automatically adjusted pressure support, proportional assist ventilation, proportional assist ventilation with load-adjustable gain factors, and neutrally adj.usted ventilator assist

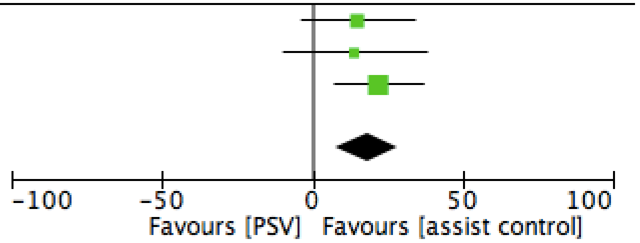
AC *vs.* PSV

❖ Sleep efficiency

Study or Subgroup	Control Ventilation Mean	Control Ventilation SD	Control Ventilation Total	PSV Mean	PSV SD	PSV Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Toublanc 2007	65	25	20	50	35	20	30.6%	15.00 [-3.85, 33.85]	2007
Cabello 2008	58	28.2	15	44	37.8	15	19.1%	14.00 [-9.87, 37.87]	2008
Andrejak 2013	61	25	26	39	29	26	50.3%	22.00 [7.28, 36.72]	2013
Total (95% CI)			**61**			**61**	**100.0%**	**18.33 [7.89, 28.76]**	

Heterogeneity: $Chi^2 = 0.49$, df = 2 (P = 0.78); $I^2 = 0\%$
Test for overall effect: Z = 3.44 (P = 0.0006)

Mean Difference IV, Fixed, 95% CI

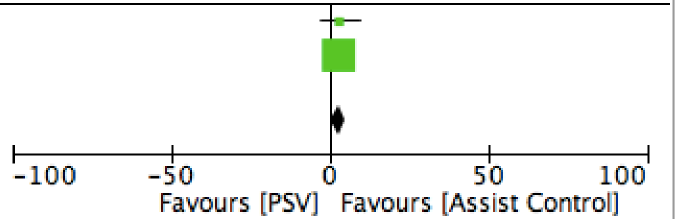


❖ REM sleep

Study or Subgroup	Control Mode Mean	Control Mode SD	Control Mode Total	PSV Mean	PSV SD	PSV Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Cabello 2008	7	9.6	15	4	7.4	15	13.6%	3.00 [-3.13, 9.13]	2008
Andrejak 2013	3.46	6	26	0.7	2	26	86.4%	2.76 [0.33, 5.19]	2013
Total (95% CI)			**41**			**41**	**100.0%**	**2.79 [0.53, 5.05]**	

Heterogeneity: $Chi^2 = 0.01$, df = 1 (P = 0.94); $I^2 = 0\%$
Test for overall effect: Z = 2.42 (P = 0.02)

Mean Difference IV, Fixed, 95% CI



Adaptive ventilation strategy *vs.* PSV

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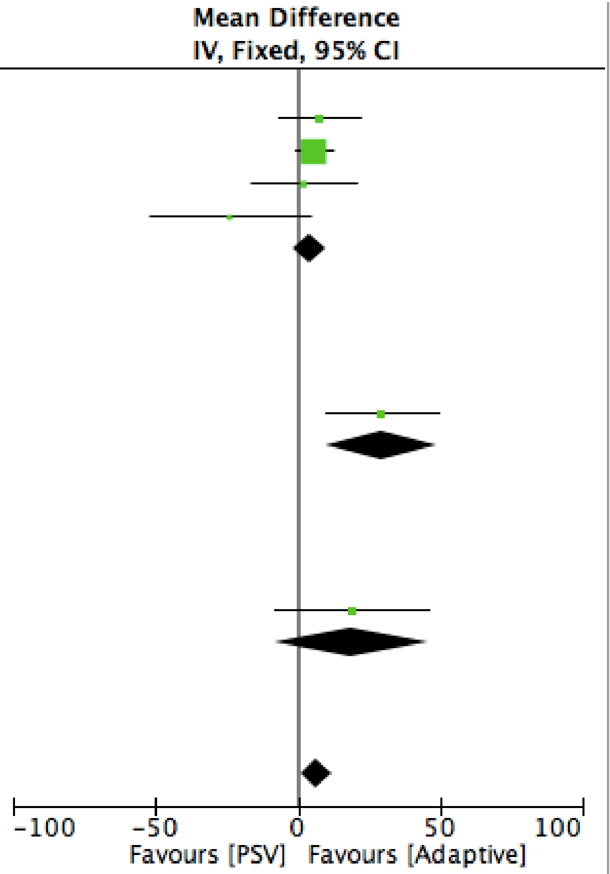
❖ Sleep efficiency

Study or Subgroup	Adaptive Vent Mean	Adaptive Vent SD	Adaptive Vent Total	PS Mean	PS SD	PS Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
1.1.1 PAV									
Alexopoulou 2007 NonSed	75.6	10.8	9	68.1	19.2	9	13.2%	7.50 [-6.89, 21.89]	
Alexopoulou 2007 Sed	98.9	2.3	11	93.3	10.8	11	64.4%	5.60 [-0.93, 12.13]	2007
Bosma 2007	60	23	13	58	25	13	8.0%	2.00 [-16.47, 20.47]	2007
Alexopoulou 2013	26.9	36.3	14	50.8	39.6	14	3.5%	-23.90 [-52.04, 4.24]	2013
Subtotal (95% CI)			**47**			**47**	**89.2%**	**4.41 [-1.13, 9.96]**	
Heterogeneity: $Chi^2 = 4.26$, df = 3 (P = 0.23); $I^2 = 30\%$									
Test for overall effect: Z = 1.56 (P = 0.12)									
1.1.2 NAVA									
Delisle 2011	73.5	18.2	14	44	33	14	7.0%	29.50 [9.76, 49.24]	2011
Subtotal (95% CI)			**14**			**14**	**7.0%**	**29.50 [9.76, 49.24]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.93 (P = 0.003)									
1.1.3 Adj PSV									
Cabello 2008	63	37.8	15	44	37.8	15	3.7%	19.00 [-8.05, 46.05]	2008
Subtotal (95% CI)			**15**			**15**	**3.7%**	**19.00 [-8.05, 46.05]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.38 (P = 0.17)									
Total (95% CI)			**76**			**76**	**100.0%**	**6.73 [1.49, 11.96]**	
Heterogeneity: $Chi^2 = 10.83$, df = 5 (P = 0.05); $I^2 = 54\%$									
Test for overall effect: Z = 2.52 (P = 0.01)									
Test for subgroup differences: $Chi^2 = 6.57$, df = 2 (P = 0.04), $I^2 = 69.6\%$									



Nonpharmacologic Interventions to Improve Sleep

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- Noise and Light Reduction: Use of earplugs and eye shade
  - 2 RCTs, 2 Observational studies evaluated use of earplugs +/- eye shades
    - ✓ Improved patient-reported sleep quality
    - ✓ Reduced delirium
    - ✓ Increase proportion of ≥ 4 hours of sleep
  - Inclusion of not-sedated ICU patients (not severely ill patients)
  - But little risk and low cost

Recommendation: We suggest using noise and light reduction strategies to improve sleep in critically ill adults (conditional recommendation, low quality of evidence).

Pharmacologic Interventions to Improve Sleep

❖ Melatonin

- ➢ 3 RCTs (n = 60) evaluated efficiency of night-time melatonin in
  - ✓ Sleep quality and Sleep quantity (as evaluated by BIS)
  - ✓ Sleep using actigraphy
  - ✓ Duration of "observed nocturnal sleep" by bedside nurse assessment
- ➢ No definite improvement in sleep assessments

Recommendation: We make no recommendation regarding the use of melatonin to improve sleep in critically ill adults (no recommendation, very low quality of evidence).

Pharmacologic Interventions to Improve Sleep

- ❖ Dexmedetomidine
  - ➢ 2 RCTs (n = 74) including MV and non-MV patients
    - ✓ increased stage 2 sleep (MD, 47.85% min; 95% CI, 24.05–71.64; moderate quality)
    - ✓ decreased in stage 1 sleep (MD, –30.37%; 95% CI, –50.01 to –10.73; moderate quality)
    - ✓ No effect on sleep fragmentation, REM sleep
  - ➢ Clinical concern: High cost, hemodynamic side effects, limited generalizability of the studies to all ICU patients for the sole purpose of sleep promotion

Recommendation: We make no recommendation regarding the use of dexmedetomidine at night to improve sleep (no recommendation, low quality of evidence).

Pharmacologic Interventions to Improve Sleep

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- ❖ Propofol
  - ➢ 3 RCTs compared propofol vs BDZ or placebo (n = 76)
    - ✓ No improvement in sleep, Decreased REM sleep
  - ➢ Hemodynamic effect, respiratory depression

Recommendation: We suggest not using propofol to improve sleep in critically ill adults (conditional recommendation, low quality of evidence).

- ❖ TCA, Atypical antipsychotics, other hyponitcs
  - ➢ Insufficient evidence regarding sleep promotion in the critically ill

Sleep-Promoting Protocol

First author, year	Study design	Population	Intervention components	Results
Hu 2015	RCT	Heart surgery patients in ICU	Earplugs and eye shades, relaxing music	Better self-perceived sleep quality
Kamdar 2013	Observational pre- postintervention	Medical ICU	Earplugs and eye shades, relaxing music + Zolpidem or Antipsychotics	No improvement in sleep quality
Li 2011	Observational pre- postintervention	Med-surg ICU	Earplugs and eye shades, relaxing music	No improvement in self-reported sleep
Patel 2014	Observational pre- postintervention	Med-surg ICU	Earplugs and eye shades + Removal of medication known to worsen sleep	Better self-perceived sleep quality

Sleep-Promoting Protocol

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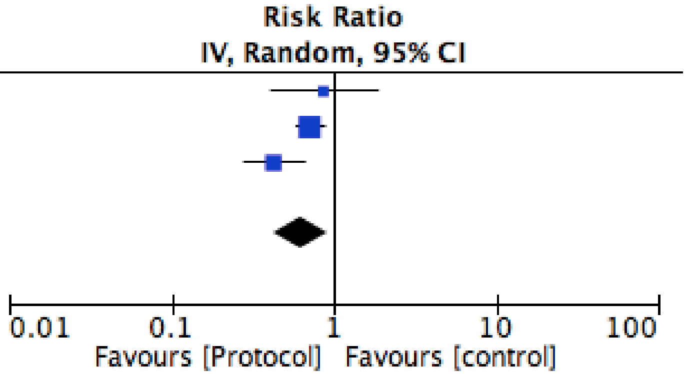
❖ Multicomponent Sleep Protocol

- ➢ Earplugs, eye shades, music +/- medication adjustment
- ➢ Low or very low qualities of included studies
- ➢ But with potential benefits in delirium reduction, with minimal risk

Study or Subgroup	Protocol Events	Protocol Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI	Year
Lee 2012	6	13	8	15	17.6%	0.87 [0.41, 1.84]	2012
Kamdar 2013	86	175	76	110	49.3%	0.71 [0.58, 0.87]	2013
Patel 2014	24	171	55	167	33.0%	0.43 [0.28, 0.65]	2014
Total (95% CI)		**359**		**292**	**100.0%**	**0.62 [0.42, 0.91]**	
Total events	116		139				

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 5.04$, df = 2 (P = 0.08); $I^2 = 60\%$
Test for overall effect: Z = 2.44 (P = 0.01)



Recommendation: We suggest using a sleep-promoting, multi -component protocol in critically ill adults (conditional recommendation, very low quality of evidence.)

2010 → 2021 KSCCM PADIS guideline

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Treatment

KSCCM Recommendation

- Sleep disturbance is a common risk factor for delirium in the ICU. Appropriate control of sleep disturbance can prevent delirium. (Grade B) [Update]
- A sleep-promoting protocol (offering earplugs and eye-shades, avoiding unnecessary examinations) should be used to improve the sleep of critically ill patients. (Grade A) [Update]

Table 11. Description of a sleep-promoting protocol

	Description
Noise	Close all doors
	Reduction of call and machine alarm sounds (24:00–06:00)
	Medical staff talk quietly
	Use of earplugs
Light	Turn off central lighting in the intensive care unit (24:00–06:00)
	Application of eyeshades
	Use of dim bedside lighting for patient care
Patient care	Prohibition of unnecessary tests and blood collection (24:00–06:00)
	Maintaining adequate sedation
	Assessment of pain and use of appropriate analgesics
	Use of the assist-control ventilation mode during the night (24:00–06:00)

Small sized studies reporting sleep disruption

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Table 3. Studies using objective measures of sleep

Study (No. of Patients)	Measure Time from Hospital Discharge	TST (*h*)	Sleep Efficiency (%)	Arousal Index	Sleep Onset Latency (*min*)	SWS (%)	REM (%)	AHI
Skinner, 2005 (43)	Portable sleep study admission							22.4 ± 20.3
n = 18 CCU patients with ACS or LV failure	Portable sleep study >6 wk							13.3 ± 12.8
BaHammam, 2005 (48)	PSG 3 d	4.5 ± 0.3	62.3 ± 4.6	40.3 ± 3.7				41.5 ± 4.2
n = 21 ACS CCU patients with AHI>10 on first PSG*	PSG 6 mo	5.7 ± 0.3	80.9 ± 4.2	21.9 ± 2.1				30.3 ± 4.7
BaHammam, 2006 (28)	PSG 3 d	4.6 ± 0.4	61	44.8 ± 4.5	24.9 ± 3.8	10	10	
n = 20 First time ACS CCU patients*	PSG 6 mo	5.7 ± 0.4	82	25.3 ± 3.9	19.6 ± 4.8	8	16	
Lee, 2009 (39)	PSG >6 mo	5.8	80.2	16.2	14.9	23.5	19.7	1.8
n = 7 patients with ARDS with self-reported sleep disturbance†								
Schiza, 2010 (44)	PSG 3 d	3.9 ± 0.7	59.8 ± 10.1	26.6 ± 11.9	52.5 ± 13.4	5.4 ± 2.1	3.1 ± 3.9	4.9 ± 1.9
n = 22 First-time ACS CCU patients‡	PSG 1 mo	5.0 ± 0.7	74.5 ± 6.1	13.4 ± 6	35.7 ± 10.8	10.3 ± 2.6	10.9 ± 3.5	4.1 ± 1.5
	PSG 6 mo	5.5 ± 0.4	82.6 ± 5.9	3.9 ± 1.9	21.7 ± 7.9	12.8 ± 2.5	13.1 ± 2.8	2.1 ± 1.0
Schiza, 2012 (47)	PSG 3 d	3.9 ± 0.7	62.3 ± 9.6	26.9 ± 10.9		5.5 ± 2.1	2.4 ± 2.9	19.7 ± 6.9
n = 28 First time ACS CCU patients with AHI>10 on first PSG‡	PSG 1 mo	5.0 ± 1.0	75.9 ± 7.9	12.9 ± 3.8		10.7 ± 2.1	11.0 ± 1.3	13.9 ± 5.9
	PSG 6 mo	5.7 ± 0.4	83.8 ± 5.6	4.3 ± 3.5		13.7 ± 3.2	13.6 ± 3.7	7.5 ± 4.6
Dhooria, 2016 (31)	PSG	4.64 (3.6–6.4)	54 (32.3–65.4)		21.5 (8.4–61.0)	15.9 (8.4–24.1)	5.5 (2.3–15.1)	1.9 (0.7–2.7)
n = 20 patients with ARDS§	1 mo post-ICU							
Solverson, 2016 (40)	Actigraphy 3 mo	6.2 ± 3.4	78 ± 18	11 ± 5 awakenings per night	12 ± 11			
n = 11 MICU/SICU patients								

Ann Am Thorac Soc. 2017 Sep;14(9)

Effect of common-used medicine in sleep

Table 158.1 Effect of Commonly Used Intensive Care Unit Medications on Sleep

Sedatives/Hypnotics	
Benzodiazepines	↓W, REM, SWS, SL ↑TST, Stg II
Propofol	↓W, SL ↑TST
Alpha$_2$ agonists (dexmedetomidine)	↓SL, REM ↑SWS
Analgesics	
Opioids	↓TST, REM, SWS ↑W, Stg II
NSAIDs	↓TST, SE
Antipsychotics	
Typical (haloperidol)	↓W, SL ↑SE, Stg II
Atypical (olanzapine)	↓W, SL ↑TST, SE, SWS
Antidepressants	
Tricyclics	↓W, REM ↑TST
SSRIs	↓TST, SE, REM ↑W
Trazodone	↓W, SL, REM ↑TST, ±SWS
Cardiovascular	
Antihypertensives	
Beta antagonists	↑W, SL ↓REM (variable, depends on lipid solubility)
Alpha$_2$ agonists	↓REM
Calcium antagonists	NA
ACE inhibitors	No effect on sleep
Diuretics	NA
Amiodarone	Nightmares
Antihypotensives	
Epinephrine/ norepinephrine	↓SWS, REM
Dopamine	↓SWS, REM
Respiratory	
Xanthines (theophylline)	↓TST, SE, REM, SWS ↑W
Antiepileptics	
Phenytoin	↓SL ↑SWS
Barbiturates	↓W, SL, REM ↑TST
Carbamazepine	↓SL, REM ↑SWS
Valproic acid	↓W ↑TST
Gabapentin	↓W ↑TST, REM, SWS
H_2 Antagonists	
Cimetidine?	↑SWS
Corticosteroids	↓REM, SWS ↑W, Stg II
Substances of Abuse	
Ethanol	↓SL, REM (first half of the night) ↑REM (second half of the night), nightmares
Cannabis	↓REM ↑SWS (if acute use; tolerance if long-term use)
Nicotine	↓TST, REM ↑SL

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Sleep assessments in ICU patients

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Measurement Tool	Outcome Measured	Advantages	Disadvantages
Traditional			
Subjective[a]	Patients' or surrogate's subjective assessment of their sleep	Most accessible, least costly	Recall bias. Altered recall due to delirium or sedation. Variable relationship with results of polysomnography
Actigraphy	Motion detector	Simple, not intrusive, little cost	Measures only motion so the effects of sedation and ICU care on motion not considered
Electroencephalogram-focused			
Processed electroencephalogram	Analysis of electroencephalogram waveform as surrogate for depth of sedation	Easy to use and available	Not validated against polysomnography as a measure of sleep
Polysomnography	Electroencephalogram Electrooculogram Electromyogram	Gold standard for measuring sleep in all patient settings	Limited by cost, requires skilled personnel to apply, interpretation difficult in the ICU, very intrusive
Single-channel electroencephalogram	Mostly delta power Frontal electrode	Uses delta waves to detect acute encephalopathy and/or ICU "depth of sleep" Mildly intrusive, easily applied. Real-time data	Crude assessment of level of consciousness. Likely cannot distinguish between different states of altered consciousness
Multichannel electroencephalogram	Several channel electroencephalogram (frontal) and also capable of collecting electrooculogram and electromyogram	Includes electroencephalogram but also with ability to do sleep staging Mildly intrusive, easily applied. Real-time data	Not as good as polysomnography for sleep staging
Newer physiologic-based methods of sleep assessment: not yet tested in the critically ill			
Functional imaging	CNS blood flow (functional MRI) CNS metabolism (positron emission tomography)	Records very specific physiologic measurements	Costly. Difficult/even risky to transport critically ill adults to conduct these studies. Studied in the critically ill for disorders of consciousness but not specifically sleep
MicroRNA	Experimental use for detecting or predicting poor sleep quality	Could become available serum biomarker	Currently untested for clinical use and in the critically ill