Recommended assessment and management of sleep disordered breathing in patients with atrial fibrillation, hypertension and heart failure: TSOC/TSSM/TSPCCM joint consensus statement

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指引發展重要日期

時間	會議
2021/12/26	TSOC 睡眠與心血管健康研討會
2022/3/2	TSSM調查睡眠及胸腔參與專家共識撰寫意願
2022/3/8	台灣胸腔暨重症加護醫學會「111年度睡眠醫學委員會第一次會議」討論三會專家共識撰寫事宜
2022/5/1	於線上召開「睡眠與心血管健康專家共識撰寫計畫第一次討論會議」
2022/6/19	於線上召開「睡眠與心血管健康專家共識撰寫計畫第二次專家討論會議」
2022/8/21	於君品酒店5樓笛卡爾廳召開「睡眠與心血管健康專家共識撰寫計畫第三次專家討論會議」
2023/2/25	於線上召開「睡眠與心血管健康專家共識撰寫計畫第四次專家討論會議」
2023/6/14	於線上召開「睡眠與心血管健康專家共識撰寫計畫專家討論會議_ revision」

Introduction: obstructive sleep apnea (OSA) overview

- Epidemiology
- Pathophysiology
- Clinical presentation
- Assessment
- Diagnostic testing
- Prognosis
- Treatment

Epidemiology

- Sleep disordered breathing: upper airway resistance syndrome, OSA, CSA, sleep related hypoventilation
- Characterized repeated partial or total collapse of the upper airway during sleep
- OSA ICSD 3 definition
  - AHI ≥5/h+ 1 OSA symptom
  - AHI ≥15/h
- Prevalence
  - General population
    - AHI ≥5/h: 9-38% ; AHI ≥15/h: 6-17%
    - Higher in man and elderly
  - Specific population
    - Bariatric surgery: 71-77%, TIA or stroke: 60-70%

Senaratna Sleep Medicine Reviews 2017; Peppard PE 2013 Am J Epidemiol *;* Ravesloot MJ Eur Arch Otorhinolaryngol 2012; Johnson KG J Clin Sleep Med. 2010; Heinzer M. Lancet Respiratory Medicine 2015

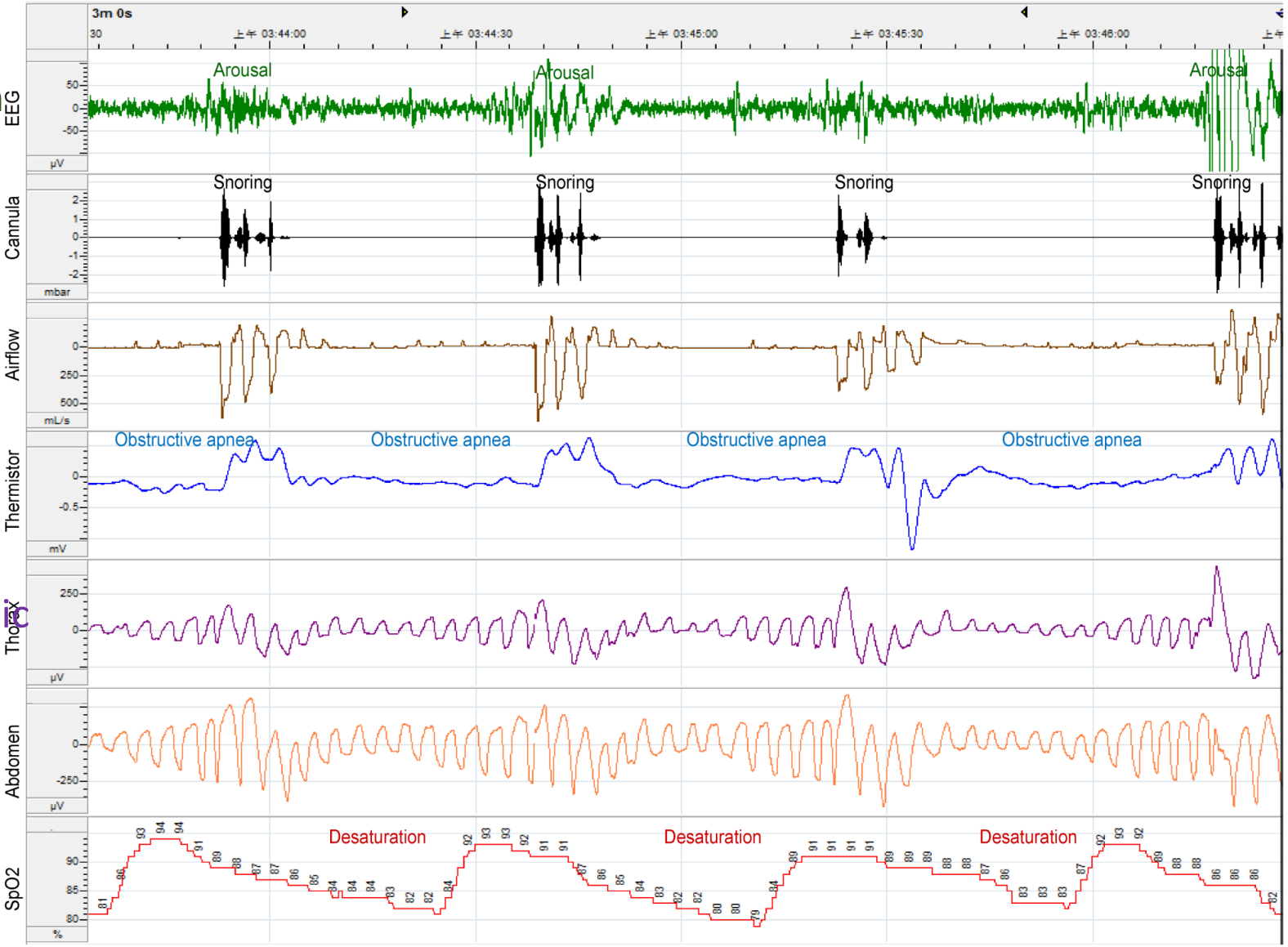
Pathophysiology (1): physiological changes on PSG

Sleep fragmentation

Flow cessation

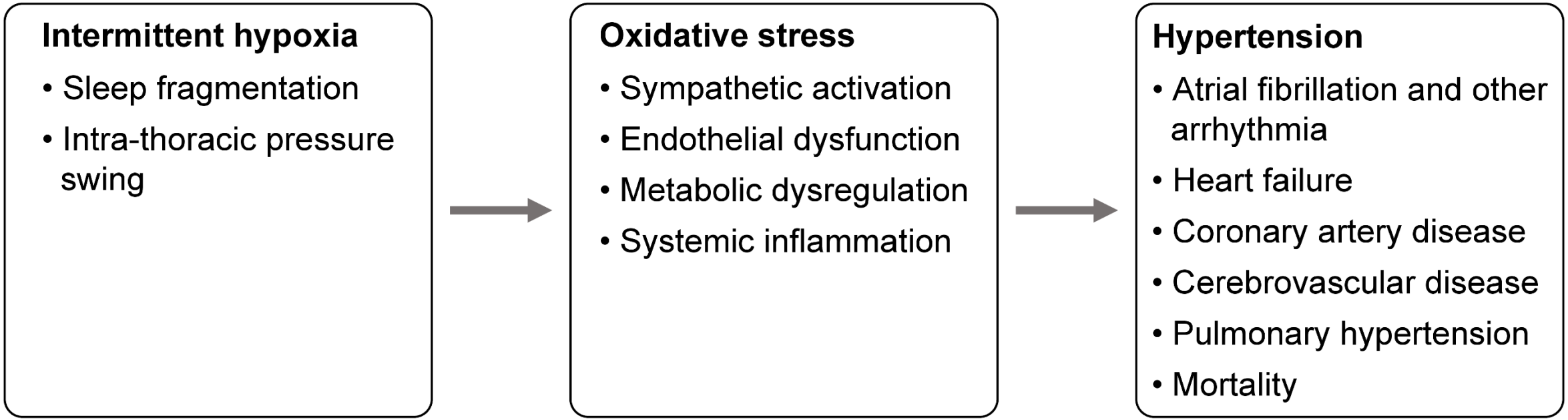
Increased intrathoracic pressure

Intermittent hypoxia



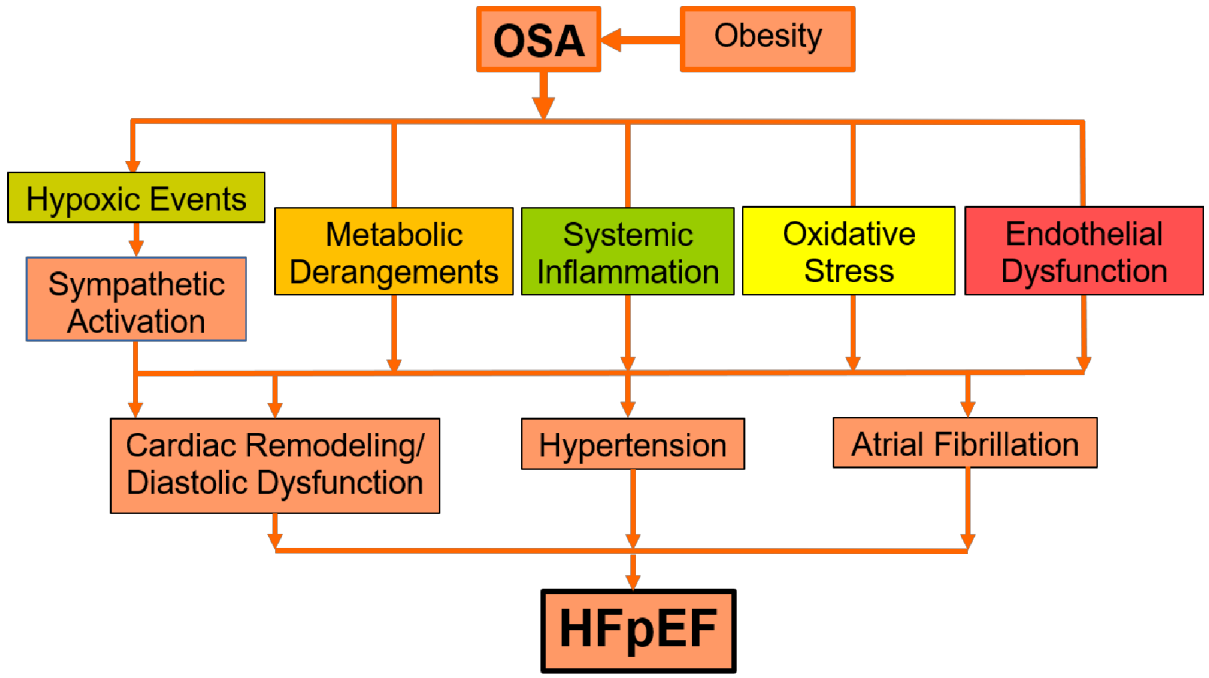
Pathophysiology (2): mechanism

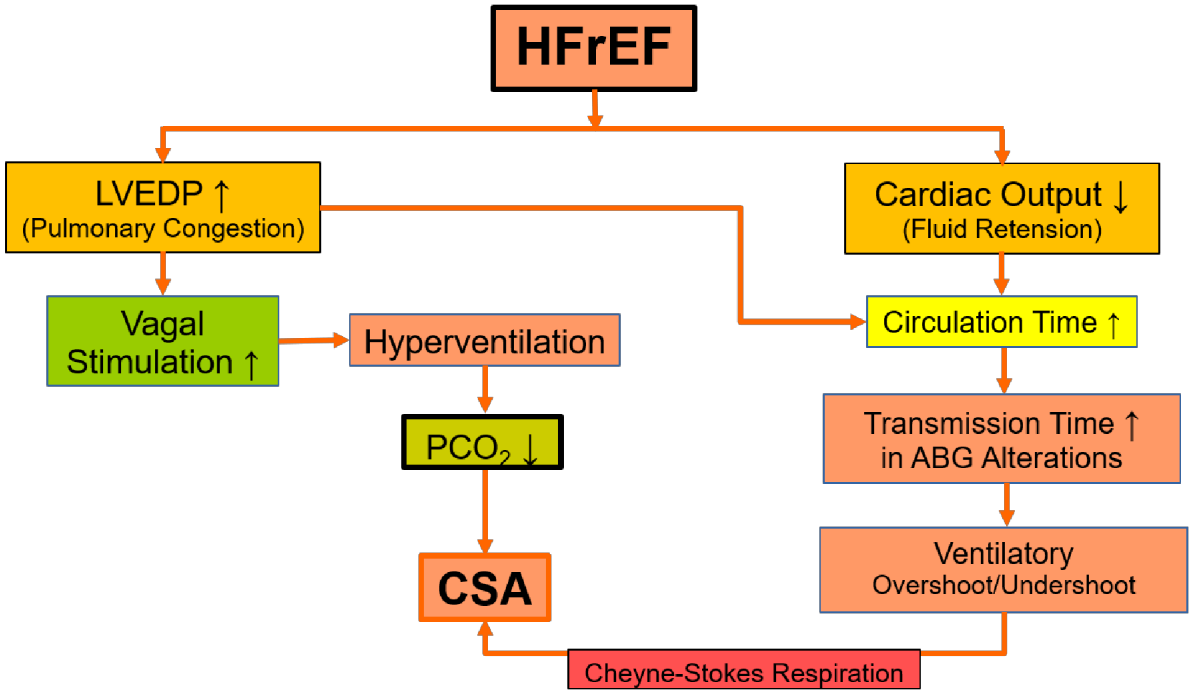
- Mechanism of obstructive sleep apnea (OSA) resulting cardiovascular disease and mortality



Gottlieb D. JAMA 20223; Yeghiazarians Y. Circulation 2021

Pathophysiology (3): mechanism between HF, OSA and CSA





Assessment (1): sleep history and PE

- The sleep history questionnaire
  - Habitual sleep pattern: time to bed and get off bed; sleep onset, sleep hour, WASO
  - Frequency and severity of breathing pauses at night
  - Gasping during sleep
  - Frequent awakening or sleep disruption
  - Daytime sleepiness and fatigue, particularly involuntary dozing off while driving
- Physical examination
  - Upper airway abnormalities revealed tonsillar hypertrophy
  - Macroglossia
  - Retrognathia
  - Mallampati score

Nuckton T. Sleep 2006

Assessment (2): questionnaire to identify OSA

AHI cutoff	Performance	**STOP-Bang[1]**	Berlin questionnaire[1]	NoSAS[2]	ESS[1]
≥5 (/h)	Sensitivity (%)	88 (83–91)	76 (71–81)	80 (75–83)	54 (45–63)
	Specificity (%)	42 (35–50)	59 (48–66)	58 (51–65)	65 (57–72)
≥15 (/h)	Sensitivity (%)	90 (86–93)	77 (73–81)	NA	47 (35–59)
	Specificity (%)	36 (29–44)	44 (38–51)	NA	62 (56–68)
≥30 (/h)	Sensitivity (%)	93 (89–95)	84 (79–88)	NA	58 (48-67)
	Specificity (%)	35 (28–44)	38 (31-56)	NA	60 (53–68)

[1] Chiu H. Sleep 2017; [2] Chen H. Sleep Breath 2022

Questionnaire to assess OSA risk

- Meta-analysis: STOP-Bang: the highest sensitivity; ESS: the lowest sensitivity
- STOP-Bang ≥3: excellent ability to identify moderate-severe OSA (sensitivity: 95%, negative predictive value: 77%) in a sleep clinic population.
- Regional Variation: Chinese people less symptomatic and obese, leading to lower diagnostic accuracy of questionnaire in East Asia compared to other regions (0.52 vs. 0.7–0.89).
- Patients with CVD have lower BMI, subjective sleepiness, less snoring

Chiu H. Sleep 2017; Chen H. Sleep Breath 2022

Questionnaire Title	Description of Questionnaire	Scoring Method
STOP-Bang	Eight-item questionnaire comprising snoring characteristics, tiredness, witnessed apnea, high blood pressure, BMI, age, neck circumference, and man	Score 0-2: Low risk of OSA Score 3-4: Intermediate risk of OSA Score 5-8: High risk of OSA STOP ≥2 + Male or BMI>35 or neck>40: High risk of OSA
NoSAS	Five-item questionnaire that includes neck circumference, BMI, snoring, age, and sex.	4 points allotted for neck circumference >40 cm, 3 for BMI 25-30 kg/m^2, 5 for BMI ≥30 kg/m^2, 2 for snoring, 4 for >55 y/o and 2 for male sex. A total score ≥ 8 indicates a high risk for OSA
Berlin questionnaire (BQ)	Three categories, namely, snoring, fatigue and hypertension, with each category including 2 to 5 questions for a total of 11 questions.	Positive responses to 2 or more categories indicate a high risk for OSA
Epworth Sleepiness Scale (ESS)	Eight-item questionnaire that asks respondents to rate their usual chances of dozing off or falling asleep during eight activities.	An ESS score ≥ 10 was defined as excessive daytime sleepiness

Assessment (3): Prediction model to assess OSA risk

- OSA prediction models based on symptoms, physical findings, or physiological measurements
- Most models aim for higher sensitivity and lower specificity.
- Goal: Promote early diagnosis of moderate-severe OSA.
- Potential challenge: High false-positive rate might lead to overprescription of polysomnography (PSG).

Huang & Lee SLEEP 2020; Chiu H. Sleep 2017; Chen H. Sleep Breath 2022

Diagnostic testing (1)

	Physiological signal/channel	Diagnostic criteria	AHI cutoff for OSA severity	Accuracy in a high-risk population[1]
PSG	Sleep/wake status: EEG, EOG, chin EMG Air flows: nasal pressure, thermistor Respiratory effort: thoracic and abdominal Oxygen saturation: pulse oximetry Cardiac variable: pulse oximetry, ECG Others: body position, leg movement, snoring	**AHI** **RDI** (including RERA) **ODI** (3% or 4%)	Mild: 5/h ≤ AHI <15/h Moderate: 15/h ≤ AHI <30/h Severe: ≥30/h	Gold standard
HSAT	Type II–IV portable monitor OR SCOPER	**REI**	Presence of OSA: ≥5/h Moderate–severe: ≥15/h Severe: ≥30/h	Type II: AHI ≥5/h, 84–91%; AHI ≥15/h: 88% Type III: AHI ≥5/h, 84% - 91%; AHI ≥15/h: 65–91%; AHI ≥30/h, 88% Type IV (oximetry): AHI ≥5/h, 73% (95% CI, 68-78%); AHI ≥15/h: 86% (95% CI, 83–91%); AHI ≥30/h, 74% (95% CI, 71–76%)

PSG: polysomnography; HSAT: home sleep apnea testing

[1] Kapur V. J Clin Sleep Med 2017

Diagnostic testing (2)

- Diagnostic Testing: in-laboratory or home PSG and HSAT
- PSG
  - Gold standard for measuring various sleep-related parameters. Severity of OSA is determined by AHI or RDI.
    - ≥5/h with symptoms or ≥15/h regardless of symptoms.
  - OSA severity: Mild (5/h ≤ AHI <15/h), Moderate (15/h ≤ AHI <30/h), Severe (≥30/h)
- HSAT
  - Categorized into Portable Monitor type and SCOPER classification.
  - Adequate for diagnosing patients without complications and a high pretest probability for moderate-severe OSA.
  - If results are negative, inconclusive, or technically inadequate, PSG is necessary to confirm the diagnosis.

Kapur V. J Clin Sleep Med 2017

Diagnostic testing (3)
HSAT: portable monitor classification

- Type II: unattended polysomnography (≥7 channels)
- Type III: limited cardiopulmonary parameters (4–7 channels) including respiratory, oxygen saturation, and cardiac variable
- Type IV: 1-2 parameters including oximetry or ECG
- Technique adequacy
  - Under supervision of a board-certified sleep medicine physician
  - Incorporate minimum of nasal pressure, chest and abdominal respiratory inductance plethysmography, and oximetry (PAT with oximetry and actigraphy)
  - ≥4 hour of technically adequate oximetry and airflow data obtained during a recording attempt at habitual sleep period

Ferber R SLEEP 1994, Collop NA J Clin Sleep Med 2007, Kapur VK. J Clin Sleep Med 2017

Diagnostic testing (4)
HSAT: indication and contra-indication

- Indication: increased risk of moderate-severe OSA
    - Presence of excessive daytime sleepiness and ≥2 of 3 criteria (habitual loud snore, witnessed apnea or gasping or choking, or diagnosed hypertension)
- Conditions not suitable for HSAT
    - Comorbidity predisposing the non-obstructive SDB
        - Significant cardiopulmonary disease, neuromuscular disease, history of stroke, opiate
    - Non-respiratory sleep disorders
        - Central hypersomolence, parasomnia, sleep related movement disorder, severe insomnia, circadian rhythm disorders

Ferber R SLEEP 1994, Collop NA J Clin Sleep Med 2007, Kapur VK. J Clin Sleep Med 2017

Treatment

Modality	Indication	Effectiveness
CPAP	1. Mild OSA(15>AHI ≥5) with one of the following symptom (sleepiness, neurocognitive deficit, emotional disorder, insomnia, hypertension) or comorbidities 2. Moderate-severe OSA (AHI ≥15)	improve daytime sleepiness, neurocognition, blood pressure, dyslipidemia, and quality of life (QoL)
MAD	1. Mild-moderate OSA(30>AHI ≥15) with one of the following symptom (sleepiness, neurocognitive deficit, emotional disorder, insomnia, hypertension) or comorbidities 2. Moderate-severe OSA refuse or cannot tolerate CPAP therapy	improve daytime sleepiness, neurocognition, and QoL
Surgery	intolerant to or unaccepting CPAP 1. soft tissue surgery: BMI<40 kg/m^2 2. Bariatric surgery: BMI>35 $kg/m^{2:}$	improve daytime sleepiness and QoL

Method
Procedure

Order	Task	Definition
1	Expert Task Force	
2	Raise research question and category	
3	Formulate PECO/PICO	PECO: specify population/Exposure/Comparison/Outcome PICO: specify patient/population, intervention, comparator, critical and important outcome
4	Systematic search and data extraction	
5	Summary of findings	Relative and absolute effect
6	Decide on overall quality of evidence	Level: high, moderate, low, very low
7	Decide GRADE domain	Quality of evidence, benefits/harms, patient preference and value, resource use
8	Decide direction and strength of recommendation	Strong For, Weak For, Weak Against, Strong Against

- Result: 12 Question, 15 PICO, 11 recommendation

Quality of overall evidence

Level	Definition[67]
High	Very confident that the true effect lies close to that of the estimate of the effect
Moderate	Moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect
Very low	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

Benefit vs. Harms/Burdens

Assessment of Benefit vs. Harms/Burdens	Overall quality of evidence			
	High	Moderate	Low	Very low
High certainty that benefits outweigh harms/burdens	Strong For	Strong For	Weak For	Weak For
Low certainty that benefits outweigh harms/burdens	Weak For	Weak For	Weak For	Weak For
Low certainty that harms/burdens outweigh benefits	Weak Against	Weak Against	Weak Against	Weak Against
High certainty that harms/burdens outweigh benefits	Strong Against	Strong Against	Strong Against	Strong Against

Recommendation and implication

Direction strength	Final recommendation	Implication
Strong For	We recommend….	Almost all patients should receive the recommended action
Weak For	We suggest …	Most patients should receive the recommended action
Weak Against	We suggest against….	Most patients should not receive the recommended action
Strong Against	We recommend against ….	Almost all patients should not receive the recommended action

Method
Systematic search (1): AF and OSA

1	sleep apnea
2	sleep apnoea
3	sleep disordered breathing
4	OSA
5	OSAS
6	SDB
7	Sleep Apnea, Obstructive[MeSH]
8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
9	atrial fibrillation
10	atrial fibrillations
11	#9 OR #10
12	continuous positive airway
13	auto-cpap
14	CPAP
15	nCPAP
16	aPAP
17	Continuous Positive Airway Pressure [MeSH]
18	#12 OR #13 OR #14 OR #15 OR#16 OR #17
19	meta-analysis* [title/abstract]
20	1. #8 AND #11 AND #19 2. #8 AND #11 AND #18 AND #19

Systematic search (2): OSA and Hypertension

1.sleep Apnea Syndromes	13.Hypertension	25.high blood pressure	35.positive airway pressure [MeSH]
2.sleep apnea, obstructive	14.white-coat hypertension [MeSH]	26.resistant hypertension [MeSH]	38.mandible-advanced device [MeSH]
3.obstructive sleep apnea	15.blood pressure	27.malignant hypertension [MeSH]	39 surgical intervention
4.sleep apnea syndrome	16.in-office BP [MeSH]	28.refractory hypertension [MeSH]	#12 AND #35 AND #39 #12 AND #35 AND #38 AND #39
5.Apnea	17.out-of-office BP monitoring [MeSH]	29.nocturnal hypertension [MeSH]	
6.sleep disorder	18.masked hypertension	30.isolated nocturnal hypertension [MeSH]	
7.Sleep Apnea, Obstructive[MeSH]	19.isolated home hypertension [MeSH]	31.nighttime hypertension [MeSH]	
8.(Sleep Apnea Syndromes [MeSH]	20.isolated ambulatory hypertension [MeSH]	32.nighttime BP [MeSH]	
9.obstructive sleep apnea [MeSH])	21.reverse white-coat effect [MeSH]	33."Hypertension" [MeSH]	
10.apnea [MeSH]	22.reverse white-coat hypertension [MeSH]	34.high blood pressure [MeSH]	
11.sleep disorder [MeSH])	23.white-coat normotension [MeSH]	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR#24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34	
#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	24.sustained hypertension [MeSH]		

Systematic search (3): OSA and HFrEF

1	sleep apnea syndrome (s)
2	sleep apnea
3	obstructive sleep apnea
4	sleep disorder (SD)
5	apnea
6	obstructive sleep apnea syndrome (OSAS)
7	central sleep apnea
8	sleep disordered breathing (SDB)
9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
10	heart failure
11	chronic heart failure
12	acute heart failure
13	heart failure hospitalization
14	incident heart failure
15	prevalent heart failure
16	#10 OR #11 OR #12 OR #13 OR #14 OR #15
17	heart failure with reduced ejection fraction
18	reduced ejection fraction heart failure
19	systolic heart failure
20	#17 OR #18 OR #19

21	heart failure with preserved ejection fraction
22	preserved ejection fraction heart failure
23	diastolic heart failure
24	#21 OR #22 OR #23
25	Non-invasive ventilation
26	sleep apnea treatments
27	positive airway pressure
28	continuous positive airway pressure (CPAP)
29	ventilation therapy
30	adaptive servo ventilation (ASV)
31	randomized controlled trial
32	acute heart failure
33	#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32
34	meta-analysis* [title/abstract]

Result

PECO 1:P: population-based cohort; E: OSA, C: no OSA; O: incidence, prevalence, and severity of AF

- One meta-analysis (13 trials comprising 2,660 participants) showed the prevalence of OSA among AF patients was higher than general population[1]
  - AHI ≥5/h: 78% (95% CI, 70%-86%) vs. 9-38%; AHI ≥15/h: 40% (95% CI, 32%-48%) vs. 6-17%
- Prevalence of AF in OSA patient was higher than genera population[2]: 4.8% vs 1%
- OSA was a risk factor for AF burden

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
AF	OSA	no OSA	risk of AF	Φ12	528300	⊕⊕◯◯ Low	OR 2.54 (2.2-2.92)[3]
AF post catheter ablation	OSA	no OSA	risk of AF recurrence	$ 6	4483	⊕⊕⊕◯ Moderate	*RR: 1.31 (1.16-1.48)[4]

Φ: OSA was detected by PSG or HSAT in only six studies; $ only studies in which OSA was detected by PSG or HSAT

[1]Kadhim K. Can J Cardiol 2021;[2] Mehra R. Am J Respir Crit Care Med 2006; [3]Zhang D. Medicine (Baltimore) 2022; [4]Li L. Europace 2014

PICO 2: In adult patients with OSA, does 24-48-h continuous ECG monitor accurately identify patients with AF compared to history and physical examination?

- Although it may be rational to screen OSA patients for AF due to its high prevalence, evidence to support a recommendation of routine screening is low.
- The clinical use of patient-triggered ECG recorders should be cautiously interpreted since 30% of AF patients are asymptomatic.
- For commercially available photoplethysmography-based wearables, the quality and functionality vary and warrant careful physician review and interpretation.

P	I	C	O	Study No.	Participant No.	Evidence quality	Absolute effects (95% CI)
AF with OSA	add on 24-48-hour continuous ECG monitor	history, pulse taking, and auscultation	detection of new-onset AF	111[1-6] (6 RCT)	98574	⨁◯◯◯ Very low	Incidence of newly detected AF 1.5% (0.4–3.8%)[1]

1. Karregat EPM *et al*. Int J Cardiol 2021.
2. Hanke T *et al*. Circulation 2009.
3. Yeung C *et al*. Am J Cardiol 2018.
4. Noubiap JJ *et al*. Int J Cardiol Heart Vasc 2021.
5. Al Qurashi AA *et al*. J Electrocardiol 2022.
6. Petryszyn P *et al*. PLoS One 2019.

Recommendation 1

We suggest that a 24- to 48-h ECG monitor, in addition to history, pulse taking, and auscultation, be used to detect AF in patients with OSA

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Weak	Low	Low certainty that benefits outweigh harms	The majority of well- informed patients would most likely choose the ECG monitor as a patient-care strategy

PICO 3: In adult patients with AF, does the questionnaire accurately identify patients with OSA?

- A couple of questionnaires, including the ESS, Berlin Questionnaire, STOP-Bang, and NoSAS Score have been applied to identify patients with high a risk of OSA.
- Most patients with AF were non- sleepy and snored less, so the sensitivity and specificity of these questionnaires to identify moderate-severe OSA were low.

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
AF	Screening questionnaire	PSG	accuracy of OSA detection	2	218	⨁⨁◯◯ Low	AUC (detection AHI ≥ 15/h)[1] • ESS: 0.50 (95% CI, 0.41-0.58) • STOP-Bang: 0.65 (95% CI, 0.58-0.73) • NoSAS: 0.68 (95% CI, 0.60-0.75)

[1] Starkey SY. CJC Open 2021

Recommendation 2. We suggest using a screening questionnaire to identify OSA in patients with AF. Patients who are identified as having a high risk of OSA or a low risk with clinical concern should undergo diagnostic testing to confirm the diagnosis of OSA

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Weak	Low	Low certainty that benefits outweigh harms	The majority of well-informed patients would most likely choose the questionnaire to identify OSA

PICO 4: In adult patients with AF and suspect OSA, does HSAT accurately diagnose OSA compared to PSG?

- One study tested six Type III portable devices, and the rate of successful execution was 72-79% while the AUC for identifying moderate-severe OSA ranged from 0.76-0.80[1]

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
AF	HSAT	PSG	accuracy of OSA diagnosis	3	646	⨁⨁◯◯ Low	AUC (detection AHI ≥ 15/h): 0.89 (0.84-0.96) [1]

[1] Mohammadieh A. J Clin Sleep Med 2021

Recommendation 3: We suggest that HSAT be used for the diagnosis of OSA in patients with AF

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Weak	Low	Low certainty that benefits outweigh harms	The majority of well-informed patients with AF undergoing cardiac ablation would most likely choose PSG or HSAT to diagnose OSA

PICO 5: Does CPAP treatment, compared to no therapy, reduce AF recurrence after interventional AF treatment?

- One meta-analysis (5 trials comprising 3,763 participants) showed untreated OSA was associated with a higher risk of AF recurrence (RR, 1.57; 95% CI, 1.36-1.81)[1]
- 7 observational trials investigated the CPAP effect on the risk of AF recurrence
  - 6 catheter ablation, 1 cardioversion, 1 medication

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
AF with OSA	CPAP	inactive control	Risk of AF recurrence after catheter ablation	6	4483	⨁⨁⨁◯ Moderate	RR: 0.58 (0.50-0.67)[1]

[1]Shukla JACC Clin Electrophysiol 2015

Recommendation 4

We recommend that clinicians use CPAP to treat OSA in AF patients to reduce AF recurrence after catheter ablation

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Strong	Moderate	High certainty that benefits outweigh harms	The vast majority of well-informed patients would most likely choose CPAP over no treatment

PECO 6: Is OSA an independent risk factor for hypertension?

- In a systematic review and meta-analysis of 26 observational studies with 51,623 participants, a dose-dependent relationship between OSA and hypertension was shown, with pooled ORs of 1.184 (95% CI = 1.093-1.274, P < 0.05), 1.316 (1.197-1.433, P < 0.05), and 1.561 (1.287-1.835, P < 0.05) for mild, moderate, and severe OSA, respectively
- There are also studies that further found a significant correlation between OSA and specific phenotypes of hypertension (essential hypertension, resistant hypertension)

P	E	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
population-based cohort	OSA	no OSA	risk of essential hypertension	16	45973	⊕⊕⊕◯ Moderate	OR 1.80 (1.54-2.06) [1]
population-based cohort	OSA	no OSA	risk of resistant hypertension	6	1465	⊕⊕⊕◯ moderate	OR 2.84 (1.70-3.98) [1]

[1]Hou H. J Glob Health 2018. [2]Maier LE.Hypertension 2022

PICO 7: Do adult patients with OSA have a higher prevalence of hypertension than those without OSA?

- Hypertension is a major risk factor for CVD and mortality, and the risk is mitigated after blood pressure reduction.
- One Canadian cluster RCT (n=140,642 aged residents ≥65 years): a multicomponent intervention including hypertension screening lowered annual hospital admissions for CVD (MI: RR: 0.87, 95% CI: 0.79-0.97, p = 0.008] and CHF [RR: 0.90, 95% CI: 0.81-0.99, p = 0.029]).
- No high-quality studies confirming the benefit of screening OSA patients for hypertension

P	E	O	Study No.	Participant No.	Evidence quality	Absolute effects (95% CI)
OSA	Home BP measurement	accuracy of hypertension detection	1	2215	⨁⨁◯◯ Low	AUC: 0.85 (0.82-0.88)[1]

[1]Karnjanapiboonwong A. BMC Cardiovasc Disord. 2020

Recommendation 5

- We suggest that clinicians screen OSA patients for hypertension by home blood-pressure monitoring following the “722” protocol (preferred method), ambulatory blood pressure monitoring or office blood pressure monitoring.

Strength of Recommendation	**Evidence Quality**	**Benefits vs. Harms**	**Patient Values and Preferences**
Strong	Moderate	High certainty that benefits outweigh harms	The vast majority of well-informed patients would most likely choose CPAP over no treatment

PICO 8: Do adult hypertension patients benefit from identification of OSA?

- Hypertension often coexists with OSA, which may have a significant impact on blood pressure control and pose a risk of concomitant or impending CVD other than hypertension.
- No high-quality studies have prospectively evaluated the clinical benefit/cost-effectiveness of screening for OSA among hypertensive patients
- The use of a simple and inexpensive tool, such as the STOP-bang questionnaire, to identify patients with OSA in need of aggressive treatment seems cost-effective
- In cases of resistant and refractory hypertension, the benefit is likely further increased with the identification of OSA

P	I	C	O	Study No.	Participant No.	Evidence quality	Absolute effects (95% CI)
Hypertension	STOP-Bang questionnaire	PSG	accuracy of OSA detection	1	303	⊕⊕◯◯ Low	AUC (detection AHI ≥15/h): 0.724 (0.678-0.768)[1]

[1]Zheng Z. Clin Cardiol 2021;44:1526-34.

Recommendation 6

- We suggest that clinicians screen for OSA among hypertensive patients, especially those with resistant hypertension. Initial screening could be performed with STOP-Bang questionnaire and subsequent confirmation could be attained by PSG.

Strength of Recommendation	**Evidence Quality**	**Benefits vs. Harms**	**Patient Values and Preferences**
Strong	Moderate	High certainty that benefits outweigh harms	The vast majority of well-informed patients would most likely choose CPAP over no treatment

PICO 9: In adult patients with OSA and hypertension, what is the choice of modality for OSA treatment?

- A randomized, controlled trial of 318 patients with OSA and AHI >15 combined with cardiovascular disease who underwent 12 weeks of PAP, oxygen or sleep education revealed that the treatment of OSA with PAP resulted in a significant reduction in both daytime and nighttime BP.[1]
- 26 clinical trials investigated the CPAP effect on the reduction of blood pressure in OSA with hypertension.

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
OSA with hypertension	modality for OSA treatment	no OSA treatment	hypertension severity	26 (19RCT)	2826	⊕⊕⊕⊕ High	2.4 mmHg (0.1-4.7)[1]

[1] Gottlieb DJ. N Engl J Med 2014

Recommendation 7

We recommend that clinicians treat hypertensive OSA patients with CPAP, which can reduce blood pressure by 2 to 4 mm Hg. Notably, there is a significant association between CPAP compliance and the magnitude of blood pressure reduction.

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Strong	High	High certainty that benefits outweigh harms	The vast majority of well-informed patients would most likely choose CPAP over no treatment

PICO 10: Does PAP/MAD/surgery versus no therapy improve the control of hypertension?

- One meta-analysis that included 51 studies revealed that compared with an inactive control, MADs were associated with a reduction in SBP and DBP, and there was no significant difference between PAP and MADs in their association with changes in SBP or DBP.[1]
- 8 clinical trials investigated the non-CPAP effect on the reduction of blood pressure in OSA with hypertension.

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
OSA with hypertension	PAP/MAD/surgery	no treatment	control rate of hypertension	8 RTC	528	⊕⊕⊕◯ Moderate	2.1 mmHg (0.8-3.4)[1]

[1] Bratton DJ. JAMA 2015

Recommendation 8

We suggest that clinicians use non-CPAP therapies, such as oral appliances, as an alternative treatment to CPAP for selected patients

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Week	Moderate	Low certainty that benefits outweigh harms	The majority of well-informed patients would most likely choose non-CPAP therapy over no Treatment

PECO 3: *P: population-based cohort; E: OSA, CSA; C: no OSA or CAS; O: incidence, prevalence, and severity of HF

- The prevalence of moderate or severe sleep apnea in patients with HFrEF is between 47% and 66%.
- The proportion of CSA among HFrEF was equal to or higher than that of OSA compared to those in the general population, whose sleep apnea is almost exclusively OSA. On the other hand, the overall prevalence of CSA and OSA may be comparable among HFpEF patients.
- The diagnosis of sleep apnea provides prognostic information for patients with HF, as either untreated OSA or CSA increased the adjusted risk of mortality two-fold.

P	E	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
HFrEF	OSA	no OSA	risk of mortality	5[1, 2-6]	32,459	⊕⊕⊕◯ Moderate	HR 1.53 (1.1-2.2)[5]

[1]Oldenburg O. Eur J Heart Fail 2007;[2]Javaheri S. J Am Coll Cardiol 2007; [3]Wang H. J Am Coll Cardiol 2007; [4]Javaheri S. Am J Respir Crit Care Med 2011; [5]Khayat R. Eur Heart J 2015; [6]Oldenburg O. European heart journal 2016.

PICO 12: Does fixed pressure-CPAP treatment improve LVEF in patients with OSA and HFrEF when compared to no therapy?

- Currently, high quality RCTs for clinically meaningful endpoints such as mortality and hospital readmission for patients with HF and OSA are lacking.
- Two nonrandomized observational studies with small number of patients investigating the effect of CPAP on patients with HFrEF and OSA showed a trend toward reduced mortality and a hospitalization-free survival benefit in the CPAP group, respectively.

P	I	C	O	Study No.	Participant No.	Evidence quality	Absolute effects (95% CI)
HFrEF with OSA	Fixed-pressure-CPAP	Usual care	Improvement of LVEF	5 RCT[1-5]	173	⊕⊕⊕◯ Moderate	5.18% (3.27%–7.08)[6]

[1]Kaneko Y. N Engl J Med 2003; [2]Mansfield DR. Am J Respir Crit Care Med 2004; [3]Egea CJ. Sleep Med 2008; [4]Gilman MP. Clin Sci (Lond) 2008; [5]Hall AB. Circulation 2014; [6]Sun H. PLoS One 2013.

Recommendation 9

We recommend that clinicians use fixed pressure-CPAP to treat patients with OSA and HFrEF to improve LVEF

- The first randomized controlled trial showed a significant increase of LVEF in CPAP group than in the control group (8.8 vs 1.5 percent, p=0.009) [1].
- The majority of subsequent RCTs using fixed pressure-CPAP showed consistent results [2-4].

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Strong	Moderate	High certainty that benefits outweigh harms	The vast majority of well-informed patients would most likely choose CPAP over no treatment

[1] Kaneko NEJM 2003. [2]Mansfield AJRCCM 2004 [3]Usui JACC 2005 [4] Egea 2008 Sleep Med

PICO 14: Does fixed pressure-CPAP treatment improve LVEF in patients with CSA and HFrEF when compared to no therapy?

- Theoretically, CPAP could generate increases in lung volume and cardiac output, both of which can help to diminish the ventilatory instability in CSA.
- Early RCTs showed an approximately 50% decrease in AHI after 4e12 weeks of CPAP treatment.

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
HFrEF with CSA	Fixed-pressure-CPAP	Usual care	Improvement of LVEF	4 RCT[1-4]	322	⊕⊕◯◯ Low	CPAP 2.2% vs. control 0.4% (P=0.02)[4]

[1]Naughton MT. Am J Respir Crit Care Med 1995; [2]Naughton MT. Am J Respir Crit Care Med 1995; [3]Tkacova R. J Am Coll Cardiol 1997; [4]Bradley TD. N Engl J Med 2005.

Recommendation 10

We suggest that clinicians use fixed-pressure CPAP to treat patients with CSA and HFrEF to improve LVEF

- The Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Herat Failure (CANPAP) Trial demonstrated an increase in LVEF in fixed-pressure CPAP group comparing to control group (2.2% vs 0.4% p=0.02).[1]

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Weak	Low	Low certainty that benefits outweigh harms	The majority of well-informed patients would most likely choose CPAP over no treatment

[1] Bradley 2005 NEJM

PICO 15: Should minute ventilation triggered-ASV be applied in patients with CSA and HFrEF when compared to no therapy?

- The effectiveness of adaptive servo-ventilation (ASV), which is more effective than CPAP in completely eradicating CSA respiratory events, was further explored.

P	I	C	O	Study No.	Participant No.	Evidence quality	Relative effects (95% CI)
HFrEF with CSA	mv-ASV	Usual care	Mortality	1 RCT[1]	1325	⊕⊕⊕◯ Moderate	all-cause mortality HR: 1.28 (1.06–1.55); CV mortality HR 1.34 (1.09 to 1.65)[1]

[1]Cowie MR. N Engl J Med 2015.

Recommendation 11

We recommend against minute ventilation-triggered ASV in patients with CSA and HFrEF

- The Treatment of Sleep-Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Serve Ventilation in Patients wit Herat Failure (SERVE-HF) revealed a both higher all cause (HR, 1.28; 95% CI, 1.06 to 1.55) and cardiovascular mortality (HR, 1.34% CI, 1.09 to 1.65) in the ASV group than in the control group. [1]

Strength of Recommendation	Evidence Quality	Benefits vs. Harms	Patient Values and Preferences
Strong	Moderate	High certainty that harms outweigh benefits	The vast majority of well-informed patients would most likely not choose mv-ASV over no treatment

[1] Cowie N Engl J Med 2015

Future direction

- Several recommendations supported by low-quality evidence, including
  - Identification of OSA using clinical tools such as questionnaires for patients with AF and hypertension
  - Identification of AF using 24 to 48-h ECG monitoring in patients with OSA
  - Identification of hypertension using home BP measurement for patients with OSA
  - Effect of non-CPAP treatments on BP reduction in patients with coexisting OSA and hypertension
  - This can be attributed to the indirect nature of the observational studies
- To generate high-quality evidence, it is essential to conduct
  - RCTs with representative participants to address patient-centered outcomes
  - Large-scale case control studies with participants propensity-score-matched for important confounders as an alternative to RCT