Centraal slaapapneu (CSA)

bij

Cardiaal lijden

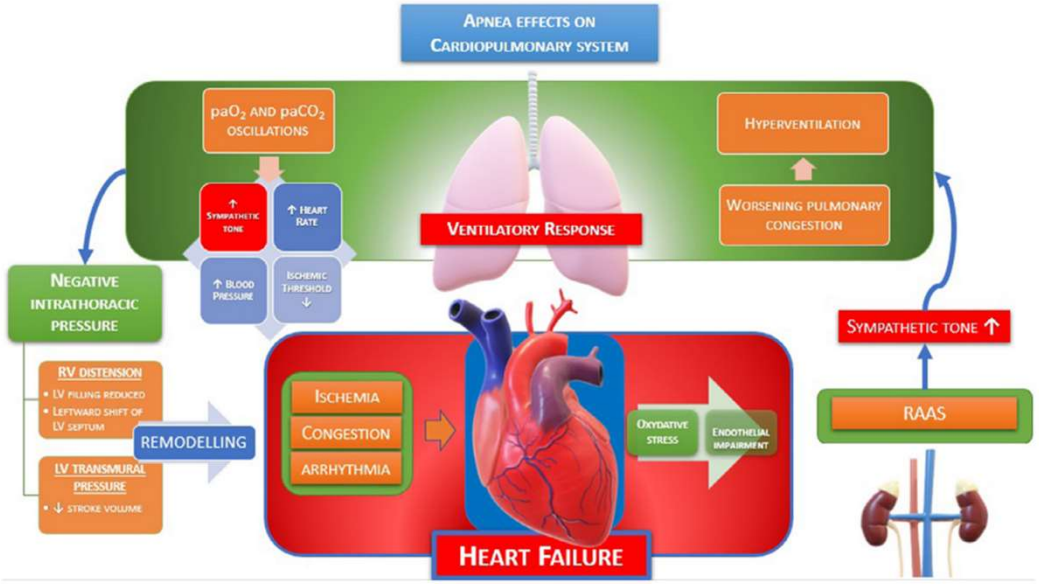
Dr. Hennie Janssen, longarts –somnoloog

Kempenhaeghe | Centrum voor Slaapgeneeskunde Kempenhaeghe

Alle kennis.
Alle aandacht.

Inhoud presentatie

- Hartfalen
- Ventilatie tijdens de slaap
- Casus
- Centraal slaapapneu
  - Prevalentie
  - Pathofysiologie
  - Fenotypen
  - Behandeling
- Take home message



Piccirillo, F. Am J Cardiol 2023

Hartfalen

ESC European Society of Cardiology
European Heart Journal (2021) 42, 3599–3726
doi:10.1093/eurheartj/ehab368
ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Table 3 Definition of heart failure with reduced ejection fraction, mildly reduced ejection fraction and preserved ejection fraction

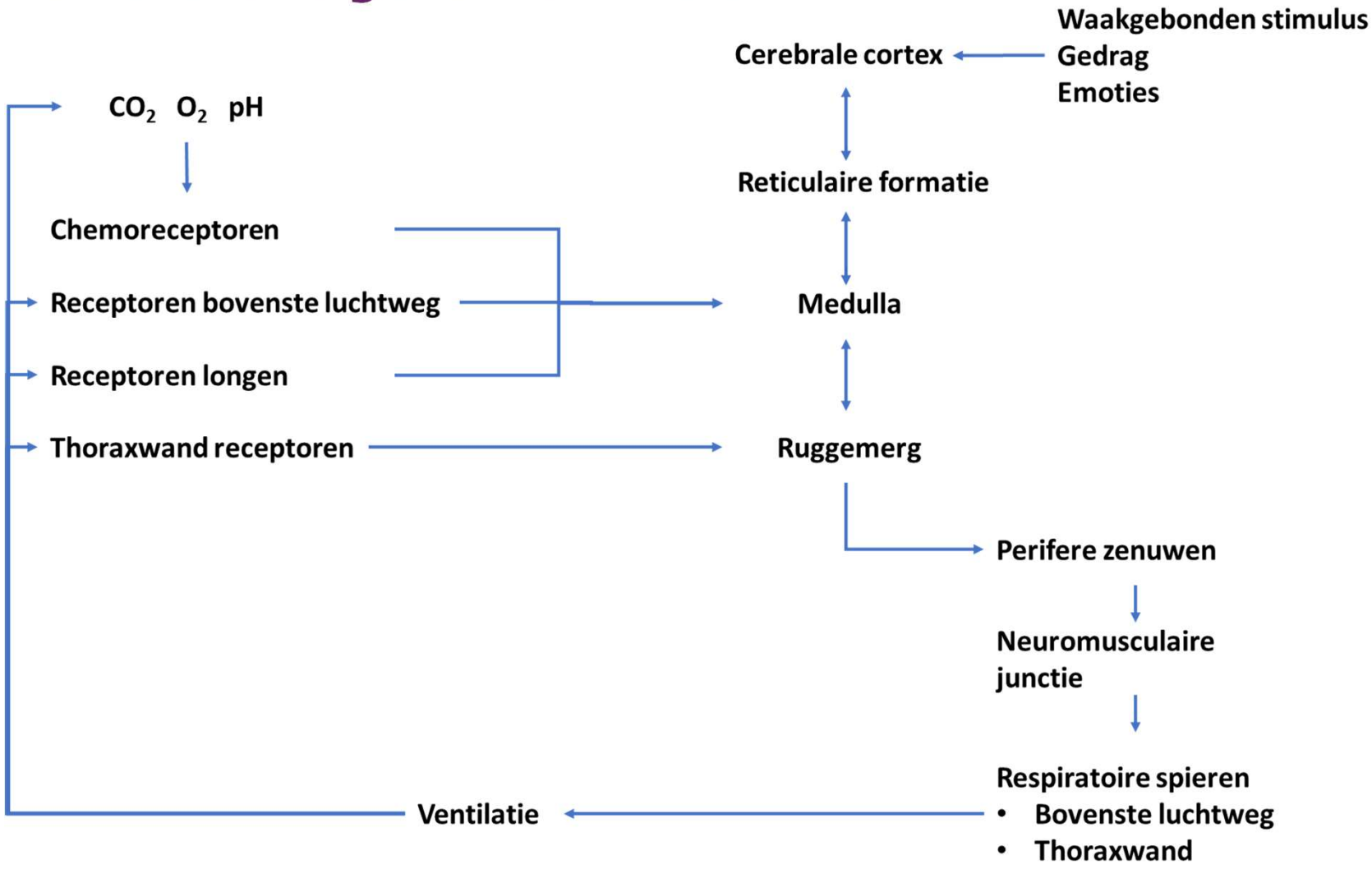
Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]

<u>Prevalentie hartfalen:</u>

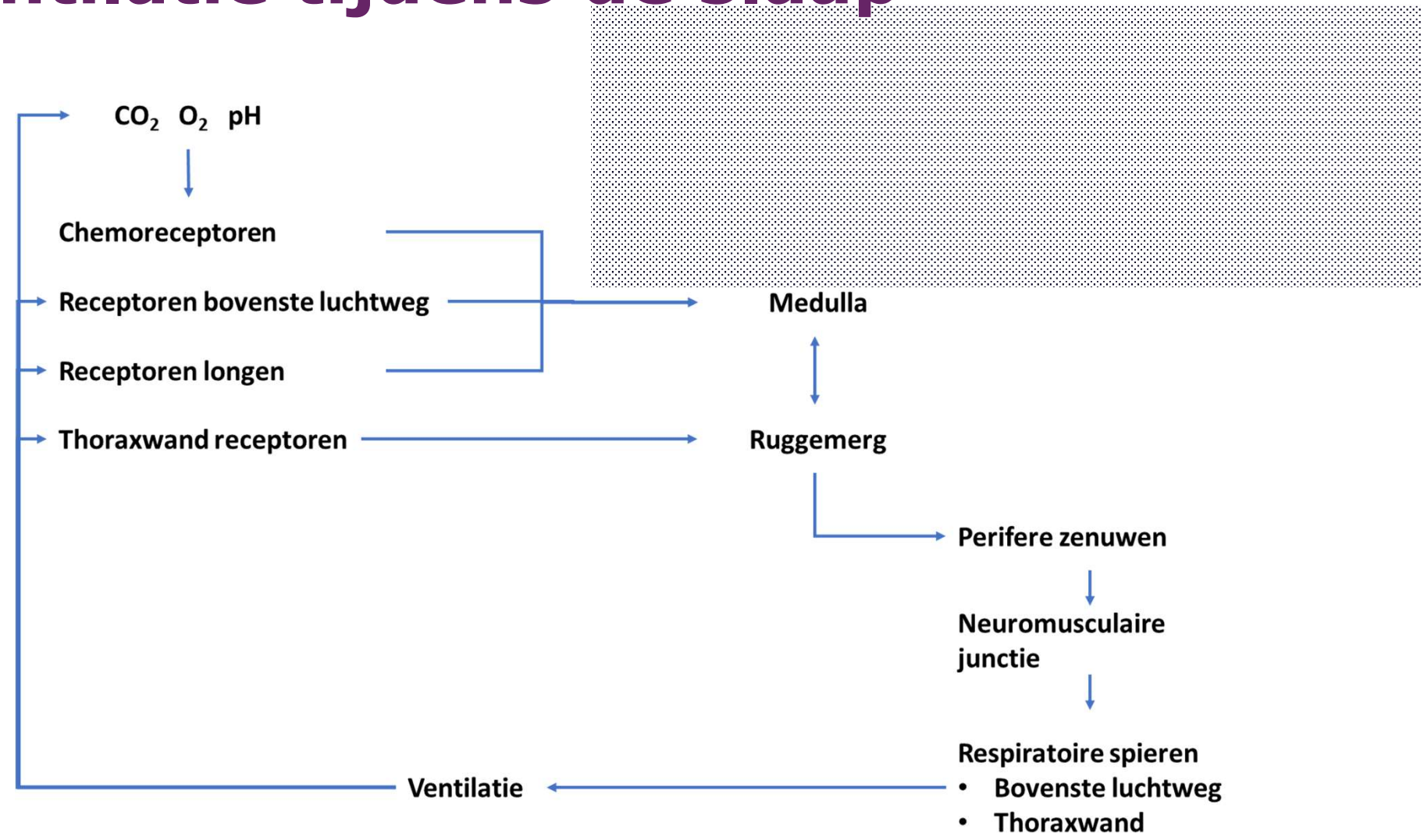
- > 70 jr >10%
- Op polikliniek cardiologie: HFrEF 60%, HFmrEF 24%, HFpEF 16%

<u>Mortaliteit:</u> Tot 67% < 5 jr na diagnose

Ventilatie tijdens waak



Ventilatie tijdens de slaap



Casus. Intake

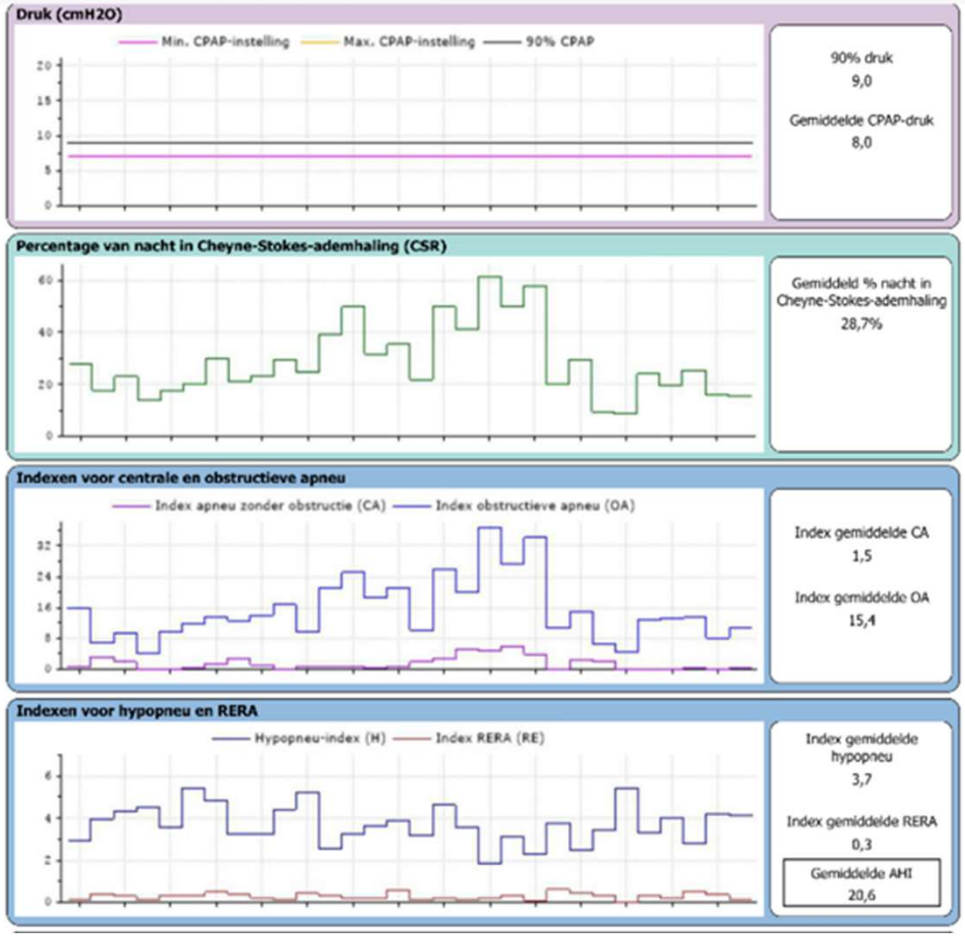
- Man 59 jaar
- VG:
  - 2016 ischemisch CVA,
  - 2016 Atriumfibrilleren waarvoor ECV en later ablatie (2019) nadien recidief atriumfibrilleren.
  - 2019 Echo cor: nl LVF/RVF, geen significant kleplijden, gedilateerde atria
  - Burn out

- RVK:
  2018 Gemengd slaapapneu (AHI 19/u) waarvoor CPAP. Blijft moe bij een wisselende maar nog verhoogde AHI onder CPAP (PSG met CPAP AHI 21/u, mn centraal, ODI 4% 11/u)

- Klachten:
  - Voor 2016 niets aan de hand. Doorslapen prima. Heel actief leven/sportief.
  - Sinds CVA Vermoeid++, soms snurken en ademstops ondanks CPAP, afgekeurd van werk

- LO: Lengte 187 cm. Gewicht 95 kg.

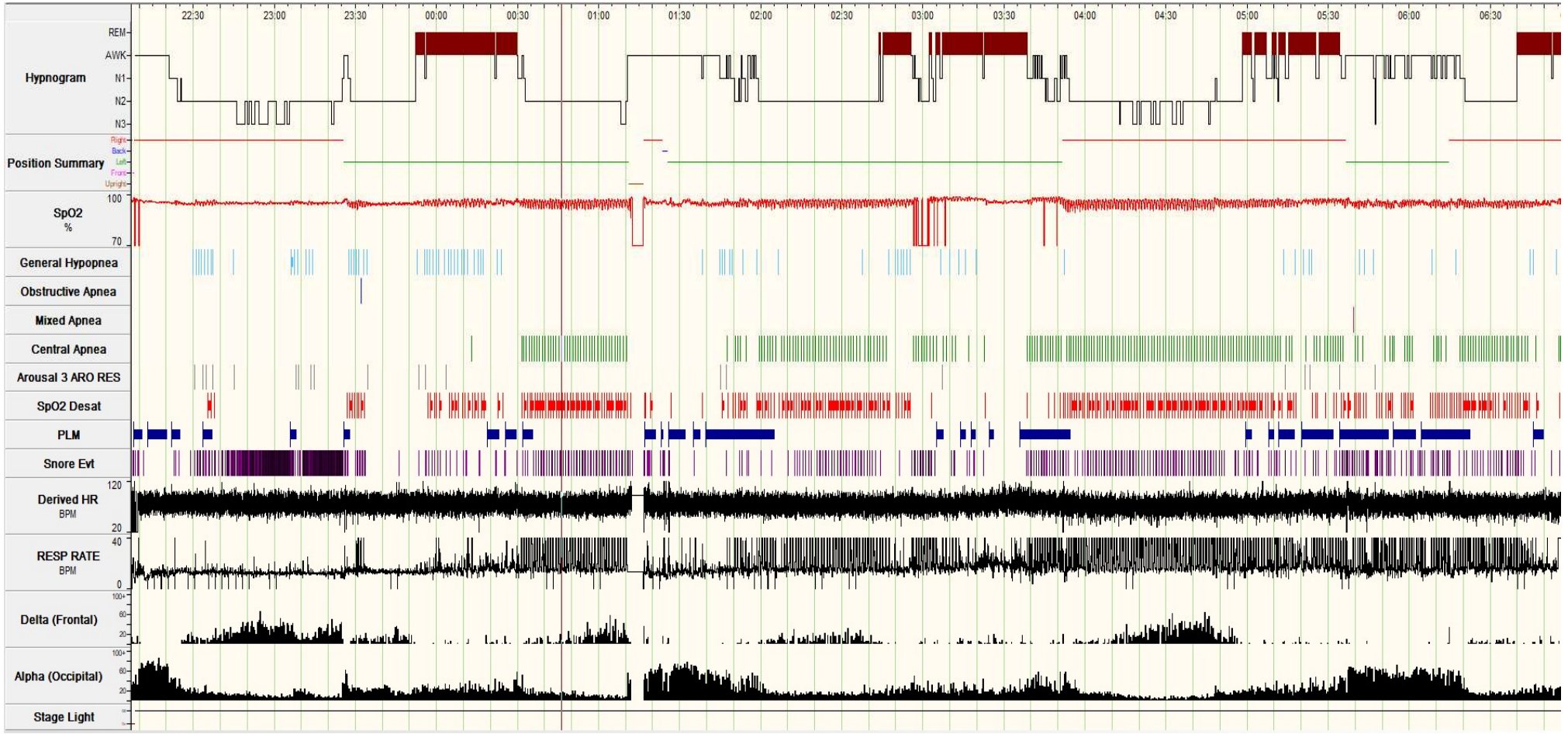
Casus. CPAP uitlezing bij intake



Q Is er nog iets dat je wil weten?

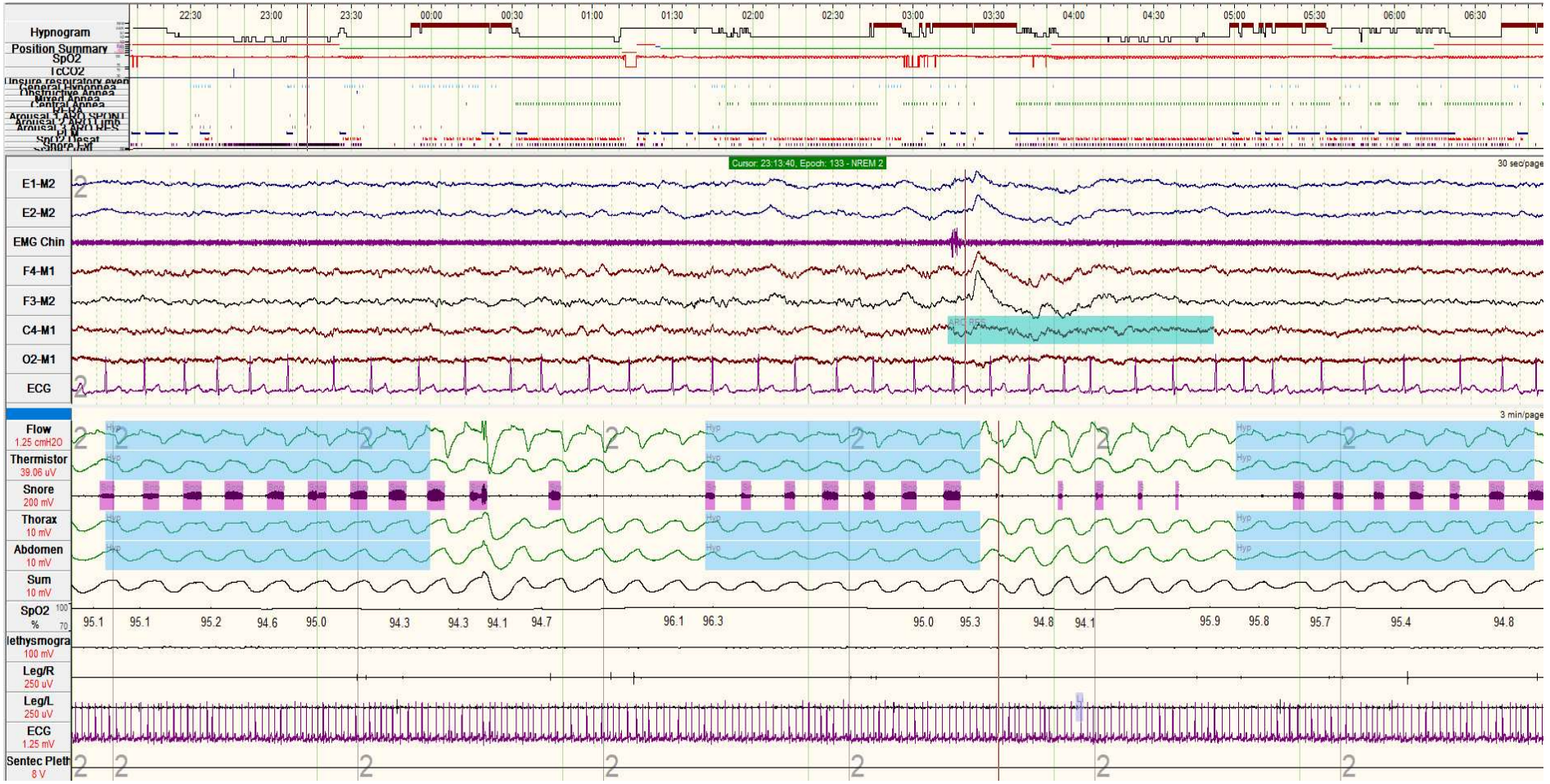
Q Wat wil je doen?

Casus. Klinische VideoPSG: Trend



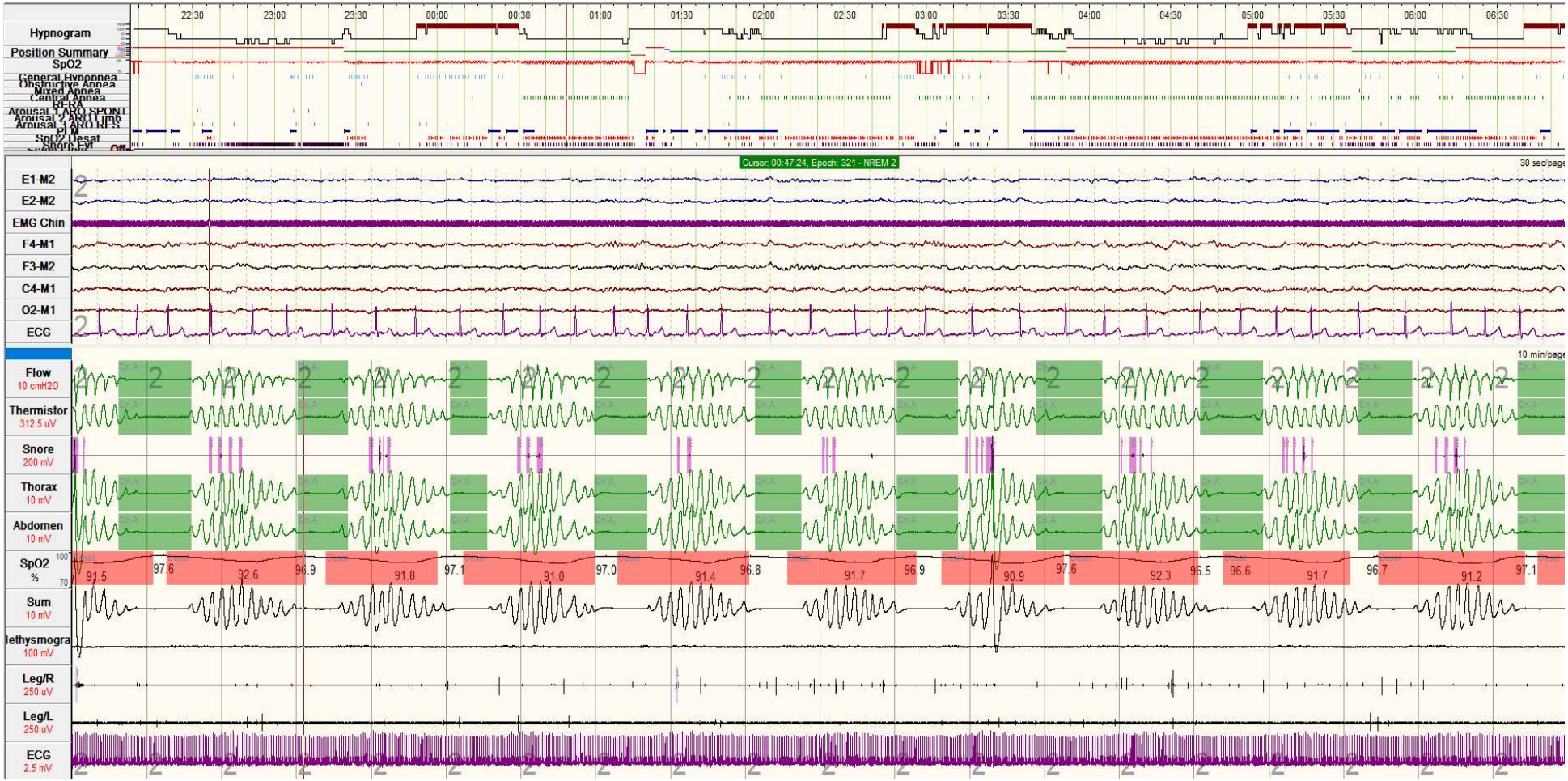
Q Wat valt je op?

Casus. Klinische videoPSG: begin van de nacht



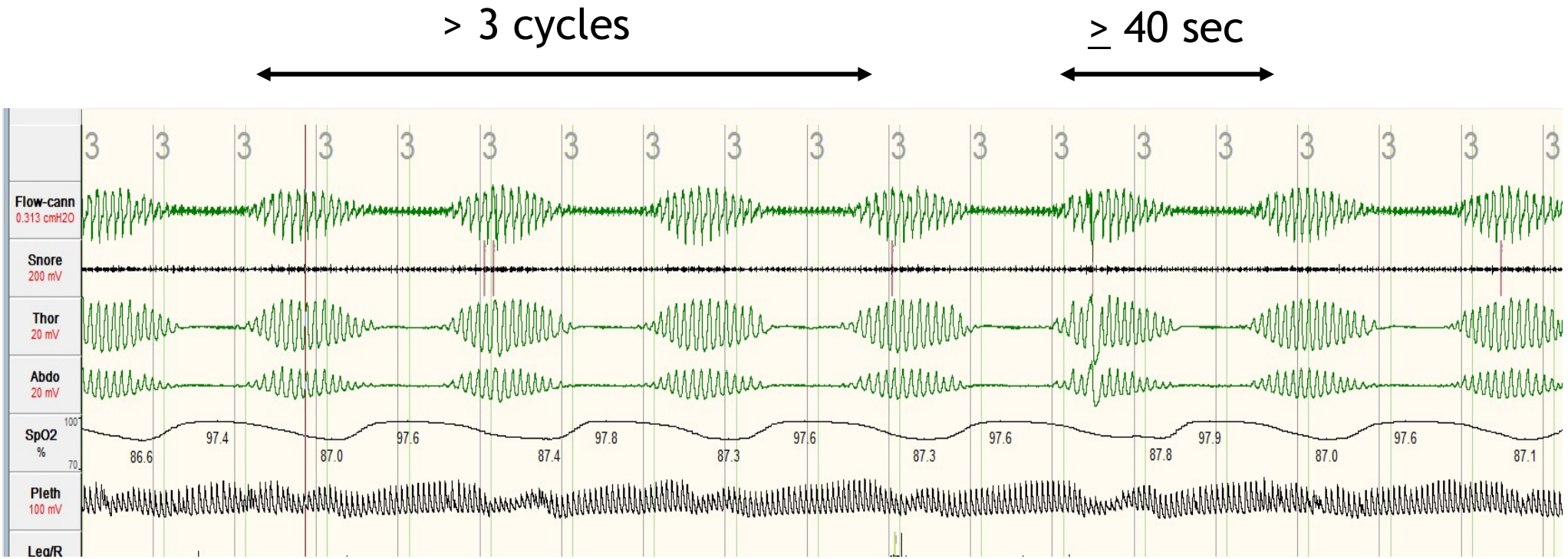
Q Wat zijn dit?

Casus. Klinische videoPSG: verder in de nacht



Q Wat is dit?

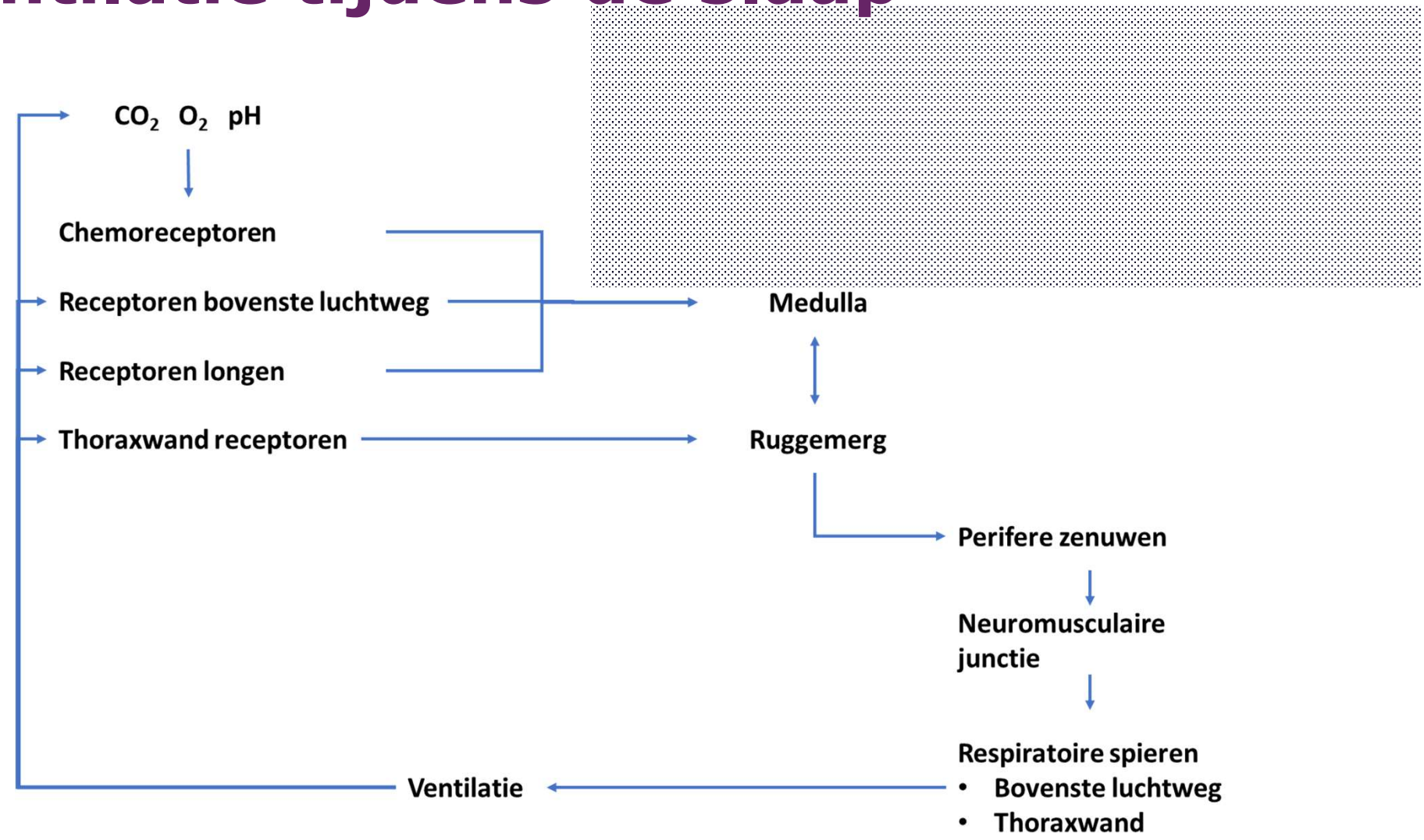
(Hunter) Cheyne Stokes breathing (CSB)/ Periodic breathing with central apnea



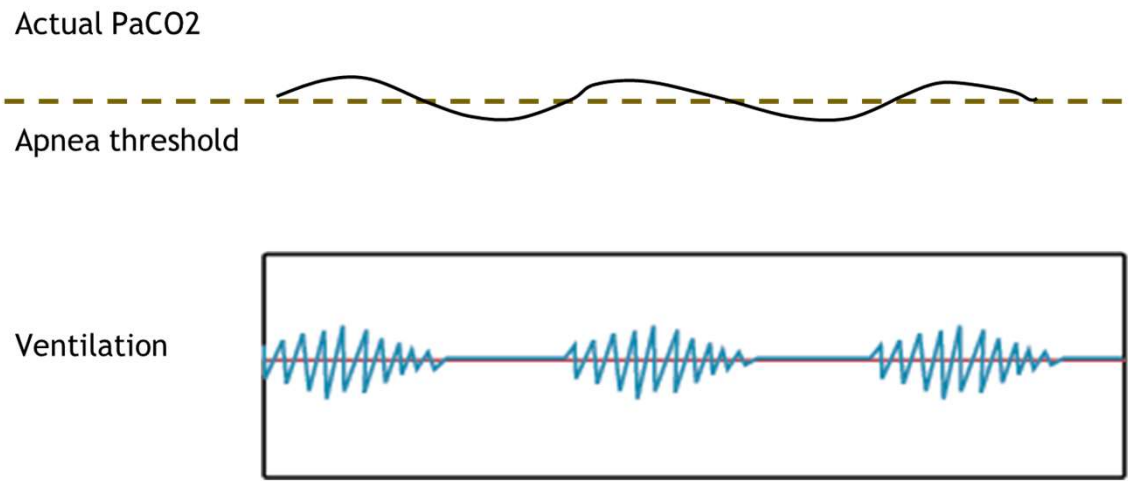
AHI ≥ 5/h, Registered sleep ≥ 2 hours

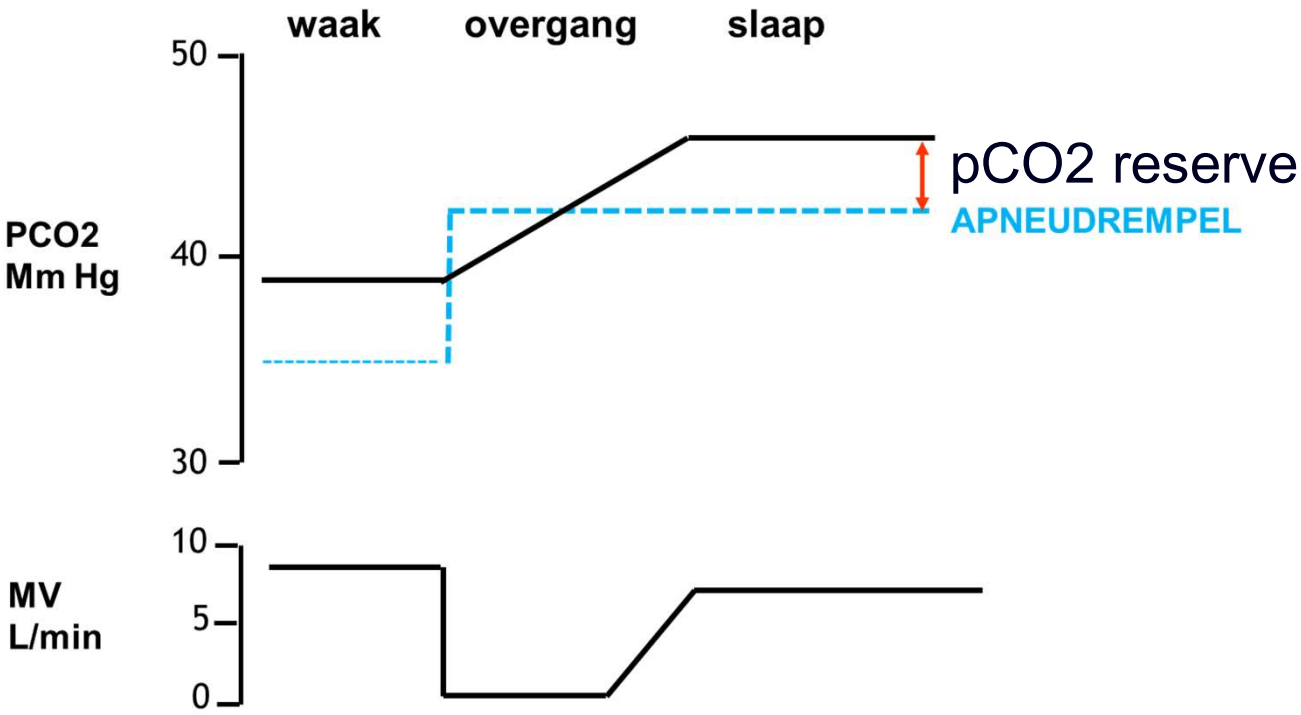
Bron: AASM scoringsmanual

Ventilatie tijdens de slaap



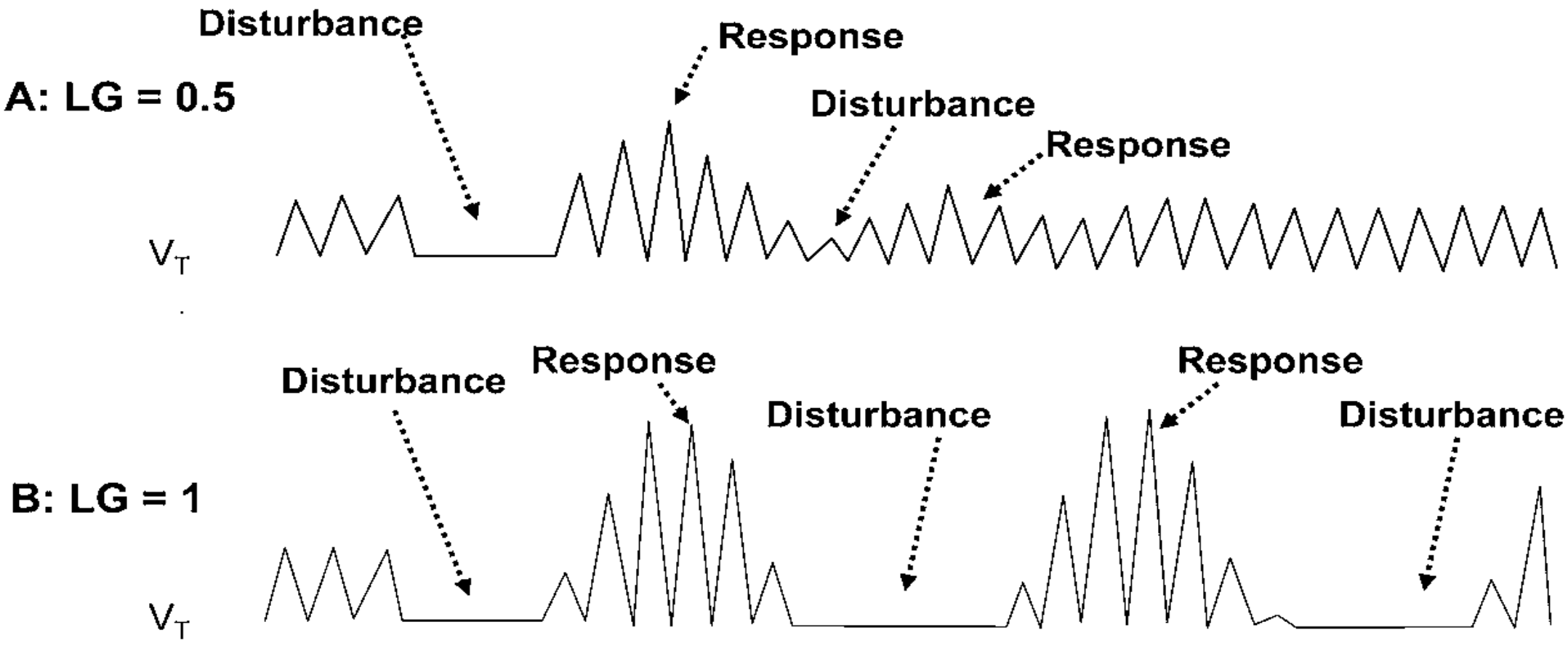
Apneudrempel





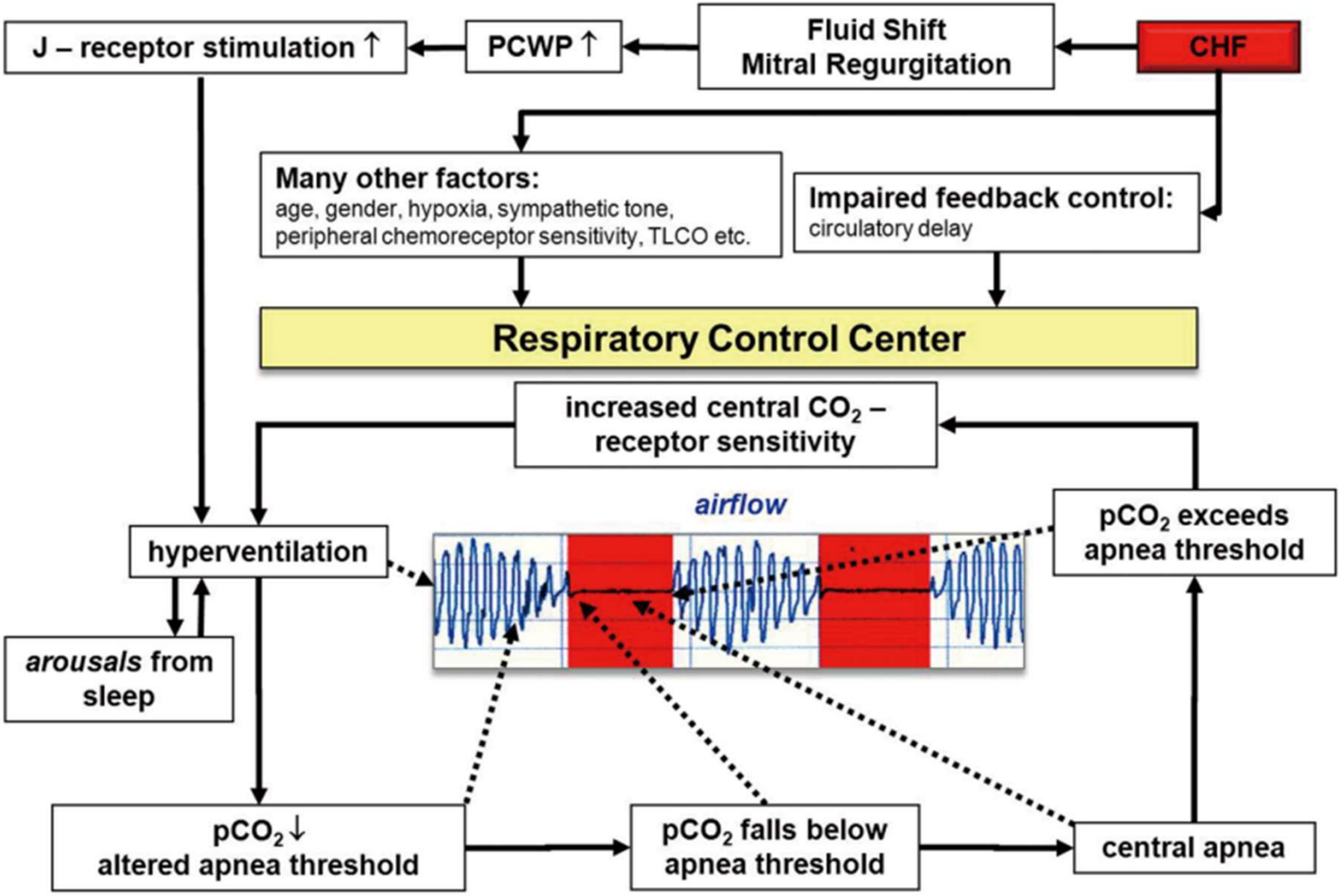
Adapted from Randerath, WJ.
Sleep Medicine Textbook. 2021

Loop gain



White DP, Am J Respir Crit Care Med 2005

Pathofysiologie



Oldenburg O.
Circ. J. 2012

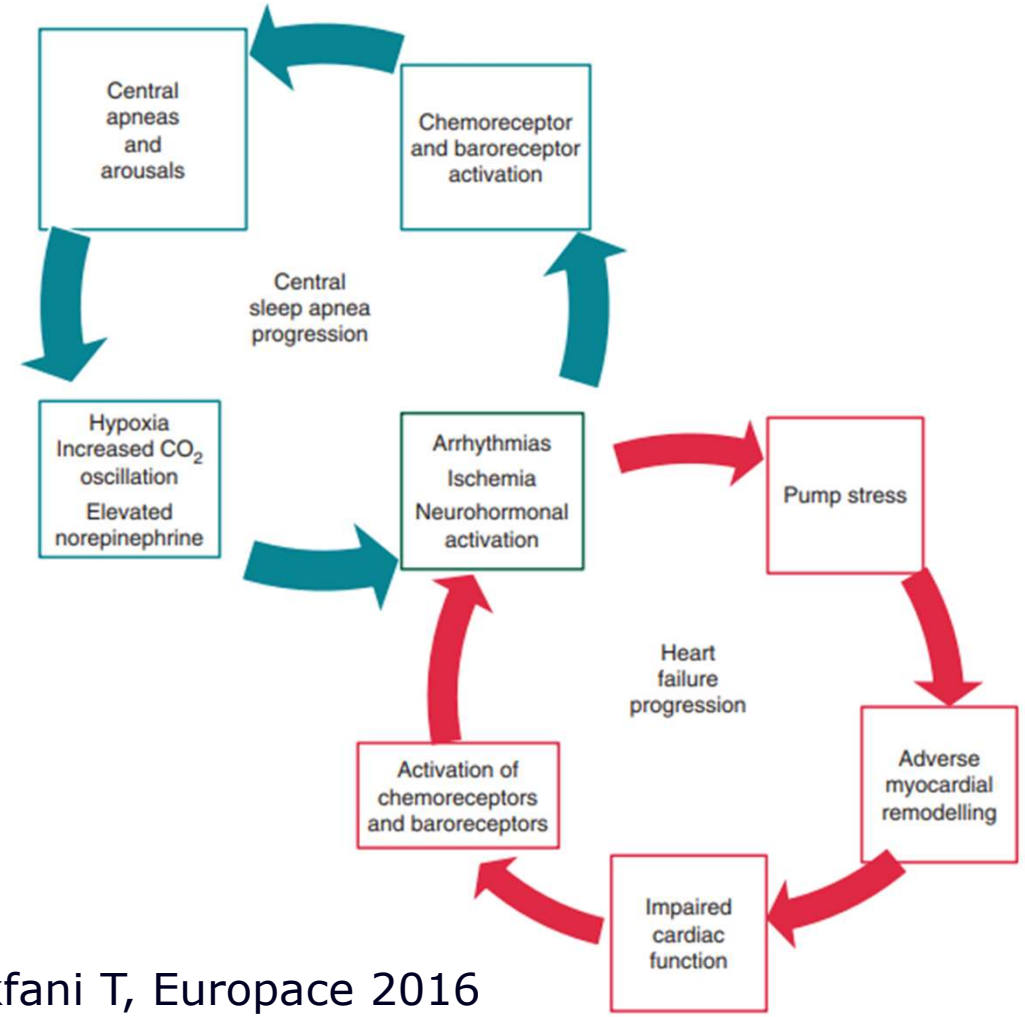
CSA en hartfalen: interactie

Q

Wat is de prevalentie van CSA In hartfalen?

Prevalentie CSA in HF

- HFrEF 25-40%
- HFpEF 18-30%



Bekfani T, Europace 2016

Casus. Conclusie

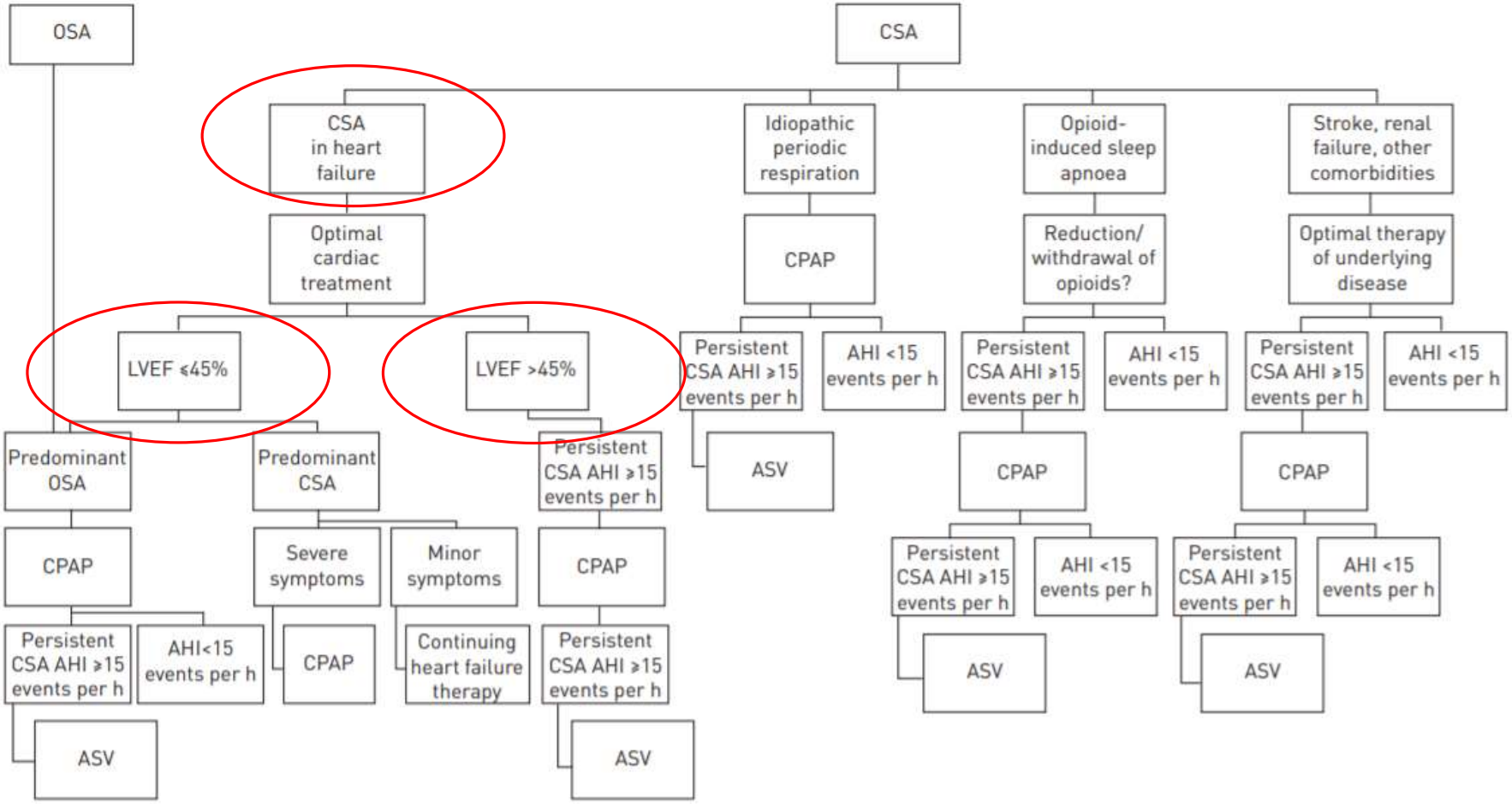
59 jarige patiënt met in de voorgeschiedenis o.a. een ischemisch CVA en permanent atriumfibrilleren, komt met persisterende en toenemende vermoeidheid sinds het CVA.

- Gemengd slaapapneu met een AHI van 45/u, ODI 4% 28/u, saturatie 0.2 min < 90%. in zijligging. Patiënt slaapt niet op de rug. Bij onderliggend atriumfibrilleren en na een doorgemaakt CVA. CPAP gaf ook bij een lage AHI eerder geen verbetering op de moeheid. Ondanks het slaapapneubeeld wordt er een goede cyclische slaapstructuur gezien.

- Gezien de goede slaapstructuur ondanks het slaapapneu, is het de vraag of de moeheid ook niet (deels) door de comorbiditeit veroorzaakt wordt.

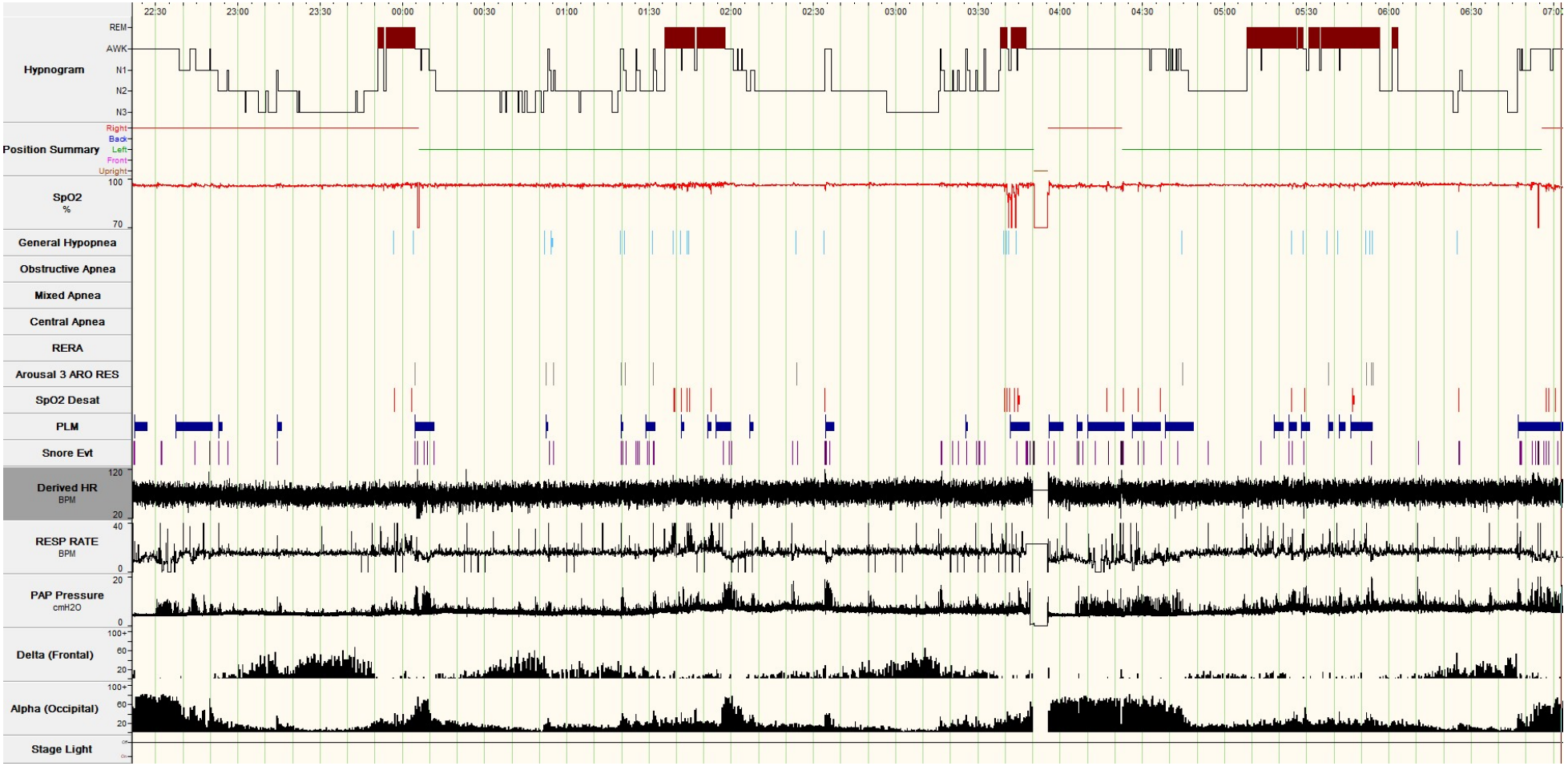
Q ga je behandelen? En zo ja, hoe?

Stepped care behandeling

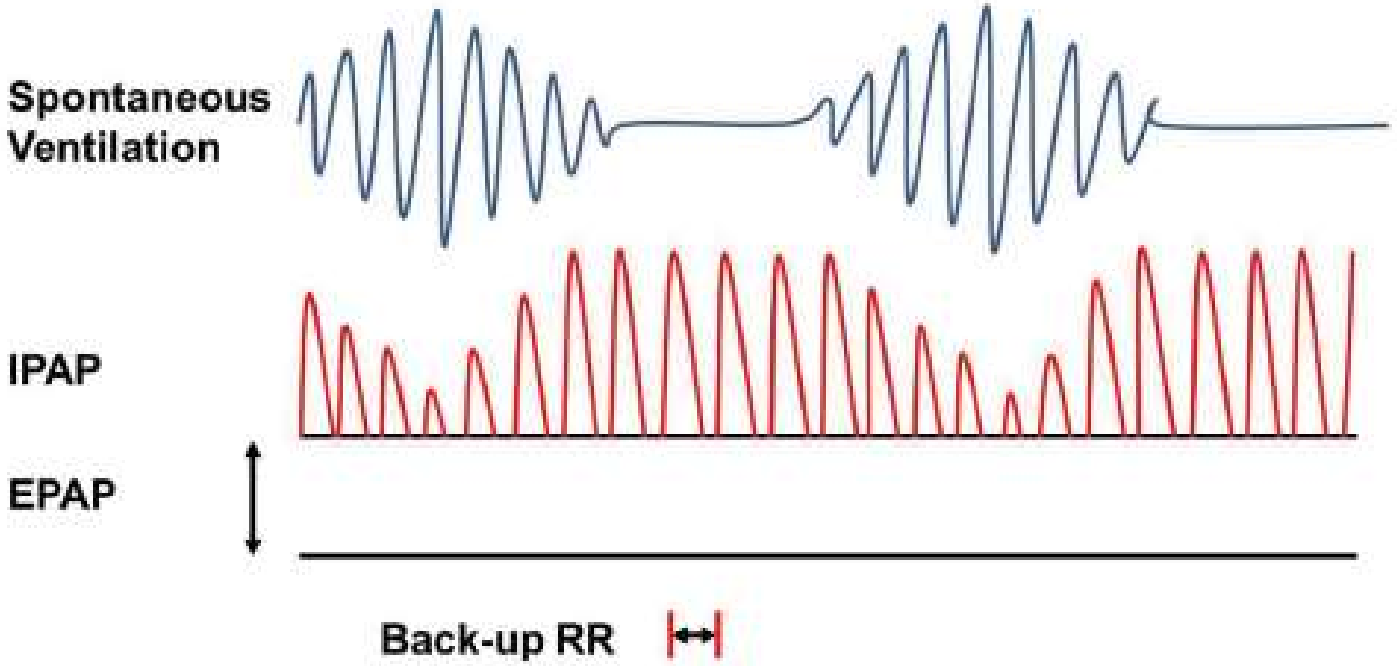


Randerath W. Eur Respir J 2017

Casus. Adaptive Servo ventilation



Adaptive Servo Ventilation (ASV)



Oldenburg O, Circulation J 2012

Casus. Adaptive Servo ventilation

Instell. apparaat		
Therapiemodus: **ASVauto**	Aanloop inschakelen: **RAMP_ON**	Aanlooptijd: **17,5 Minuten**
Basisinstellingen: **PLUS**	Max EPAP: **7,0 cmH20**	Min EPAP: **4,0 cmH20**
Max PS: **10,0 cmH20**	Min PS: **0,0 cmH20**	
IPAP - cmH20		
Mediaan: **5,3**	95e percentiel: **8,3**	Maximum: **12,2**
EPAP - cmH20		
Mediaan: **4,5**	95e percentiel: **6,0**	Maximum: **6,8**
Lek - L/min		
Mediaan: **0,0**	95e percentiel: **0,0**	Maximum: **1,2**
Doel-minuutventilatie - L/min		
Mediaan: **7,4**	95e percentiel: **8,4**	Maximum: **9,4**
Teugvolume - mL		
Mediaan: **500**	95e percentiel: **720**	Maximum: **1330**
Minuutventilatie - L/min		
Mediaan: **7,9**	95e percentiel: **10,2**	Maximum: **15,8**
Ademhalingsfrequentie - ademhalingen/min		
Mediaan: **15**	95e percentiel: **17**	Maximum: **23**
Ademhalingsindices - gebeurtenissen/u		
Apneu-index: **0,0**	Hypopneu-index: **1,3**	AHI: **1,3**
Totaal gebruik		
Gebruikte dagen >= 4 uren : **16**	Gebruikte dagen < 4 uren : **0**	% Gebruikte dagen >= 4 uren : **100**
Dagen niet gebruikt: **0**	Totaal dagen: **16**	Totaal gebruikte uren: **138:49**
Mediaan dagelijks gebr.: **8:38**	Gemidd. dagelijks gebr.: **8:40**	

Klinisch:

- Slaapt goed,
- Gewend aan druk
- Meer energie, sport
- Vrolijker

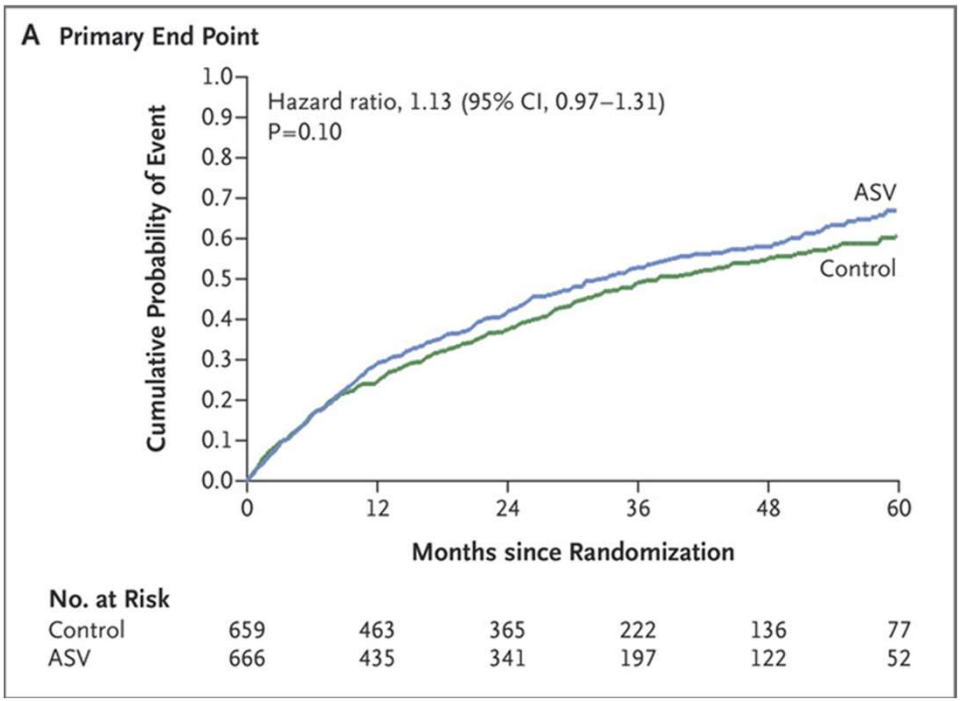
Q

Ben je tevreden?

Wat als LVEF≤45%?

SERVE-HF studie

- Multicenter (91) RCT
- 1325 HF ptn met CSA
  - NYHA II – IV, LVEF ≤ 45%
  - CSA AHI ≥ 15/u
  - ASV/usual care vs usual care

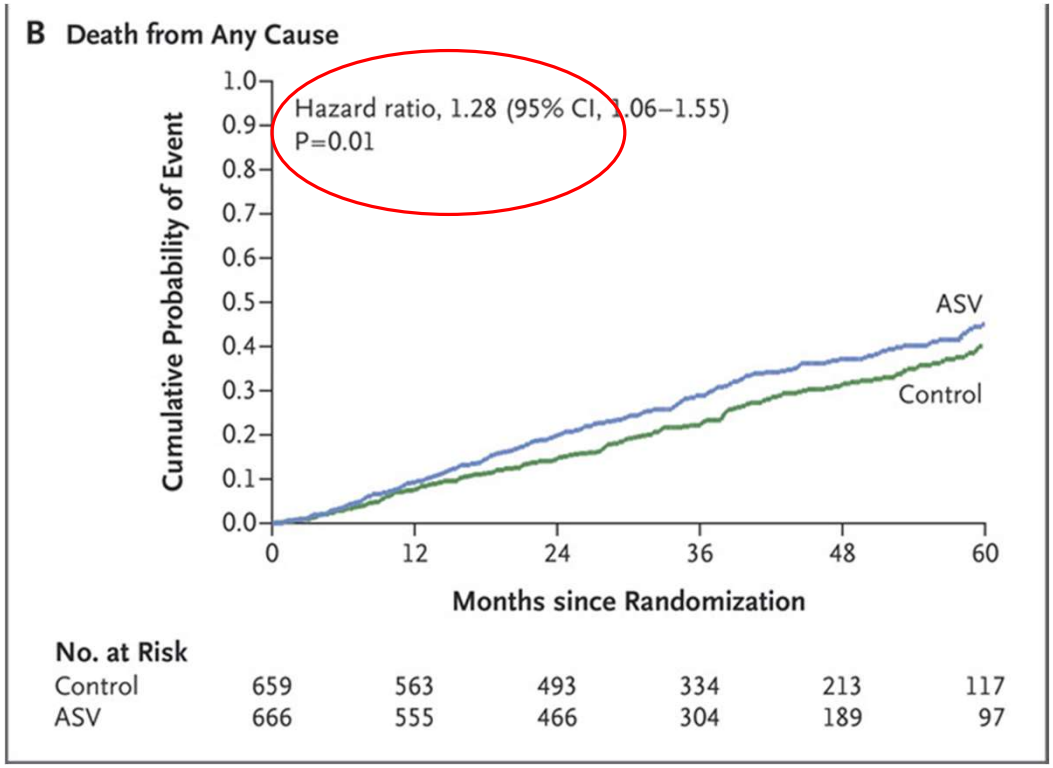


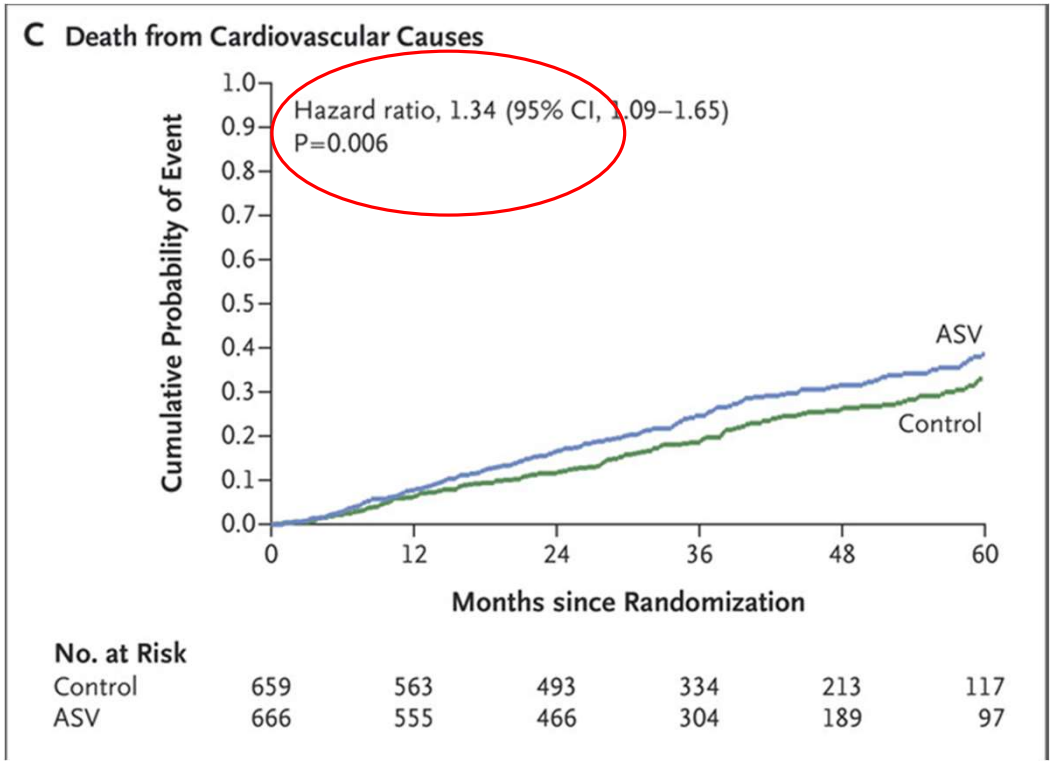
- Conclusie:

Intention to treat analysis: geen verschil op het primaire eindpunt (composite death form any cause, lifesaving cardiovasculaire intervention, or unplanned hospitalization for HF)

Cowie MR et al. N Engl J Med 2015

SERVE-HF studie: secundaire eindpunten





Cowie MR et al. N Engl J Med 2015

AASM guideline update

JCSM
Journal of Clinical Sleep Medicine

SPECIAL ARTICLES

Updated Adaptive Servo-Ventilation Recommendations for the 2012 AASM Guideline: "The Treatment of Central Sleep Apnea Syndromes in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses"

R. Nisha Aurora, MD, MHS[1]; Sabin R. Bista, MD[2]; Kenneth R. Casey, MD, MPH[3]; Susmita Chowdhuri, MD[4]; David A. Kristo, MD[5]; Jorge M. Mallea, MD[6]; Kannan Ramar, MD[7]; James A. Rowley, MD[8]; Rochelle S. Zak, MD[9]; Jonathan L. Heald, MA[10]

RECOMMENDATIONS

Adaptive Servo-Ventilation for the Treatment of Central Sleep Apnea Syndrome Related to Congestive Heart Failure

Recommendation 1: Adaptive servo-ventilation (ASV) targeted to normalize the apnea-hypopnea index (AHI) should not be used for the treatment of CSAS related to CHF in adults with an ejection fraction ≤ 45% and moderate or severe CSA predominant, sleep-disordered breathing. (STANDARD AGAINST)

"In afwachting van publicatie ADVENT-HF trial.."

ADVENT-HF studie

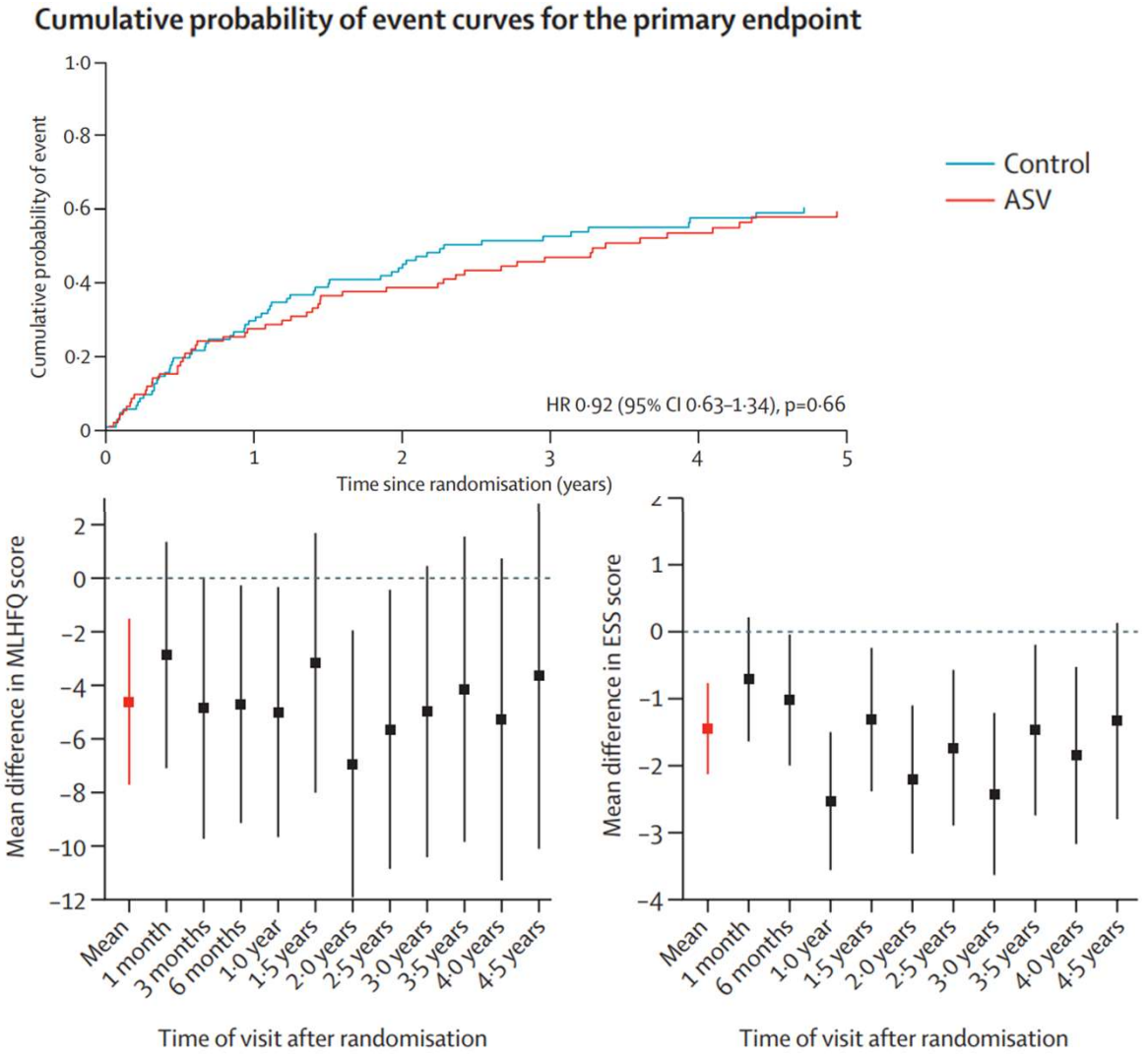
Adaptive servo-ventilation for sleep-disordered breathing in patients with heart failure with reduced ejection fraction (ADVENT-HF): a multicentre, multinational, parallel-group, open-label, phase 3 randomised controlled trial

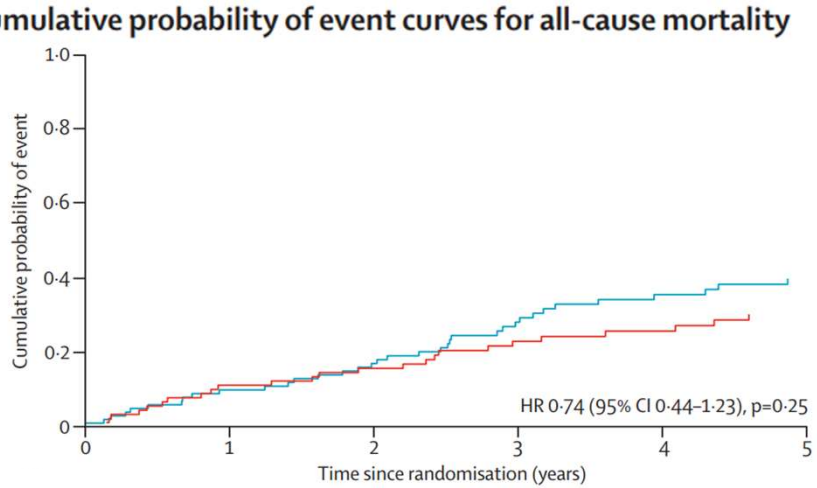
T Douglas Bradley, Alexander G Logan, Geraldo Lorenzi Filho, R John Kimoff, Joaquin Durán Cantolla, Michael Arzt, Stefania Redolfi, Gianfranco Parati, Takatoshi Kasai, Mark E Dunlap, Diego Delgado, Shoichiro Yatsu, Adriana Bertolami, Rodrigo Pedrosa, George Tomlinson, Jose M Marin Trigo, Claudio Tantucci, John S Floras, on behalf of the ADVENT-HF Investigators

- N= 731
  - LVEF $\leq$ 45%
  - AHI $\geq$ 15/u: 533 OSA and 198 CSA
- ASV/standard optimal treatment vs optimal treatment
- Primairy Endpoint: cumulative incidence of the composite of all-cause mortality, first admission to hospital for CV reason, new onset atrial fibrillation of flutter, and delivery of an appropriate cardioverter-defibrillator shock
- Secundary endpoint: o.a all-cause mortality, sleep structure, QOL, ESS

Bradley TD et al. Lancet Respir Med 2023

ADVENT-HF studie: CSA ptn





<u>Conclusie</u>

- 198/430 (46%) CSA pts geïncludeerd
- Geen effect op primair eindpunt
- Geen effect op mortaliteit
- Verbetering QOL en ESS en NYHA

Te lage power dus geen definitieve conclusie tav behandeling CSA in HFrEF en mortaliteit

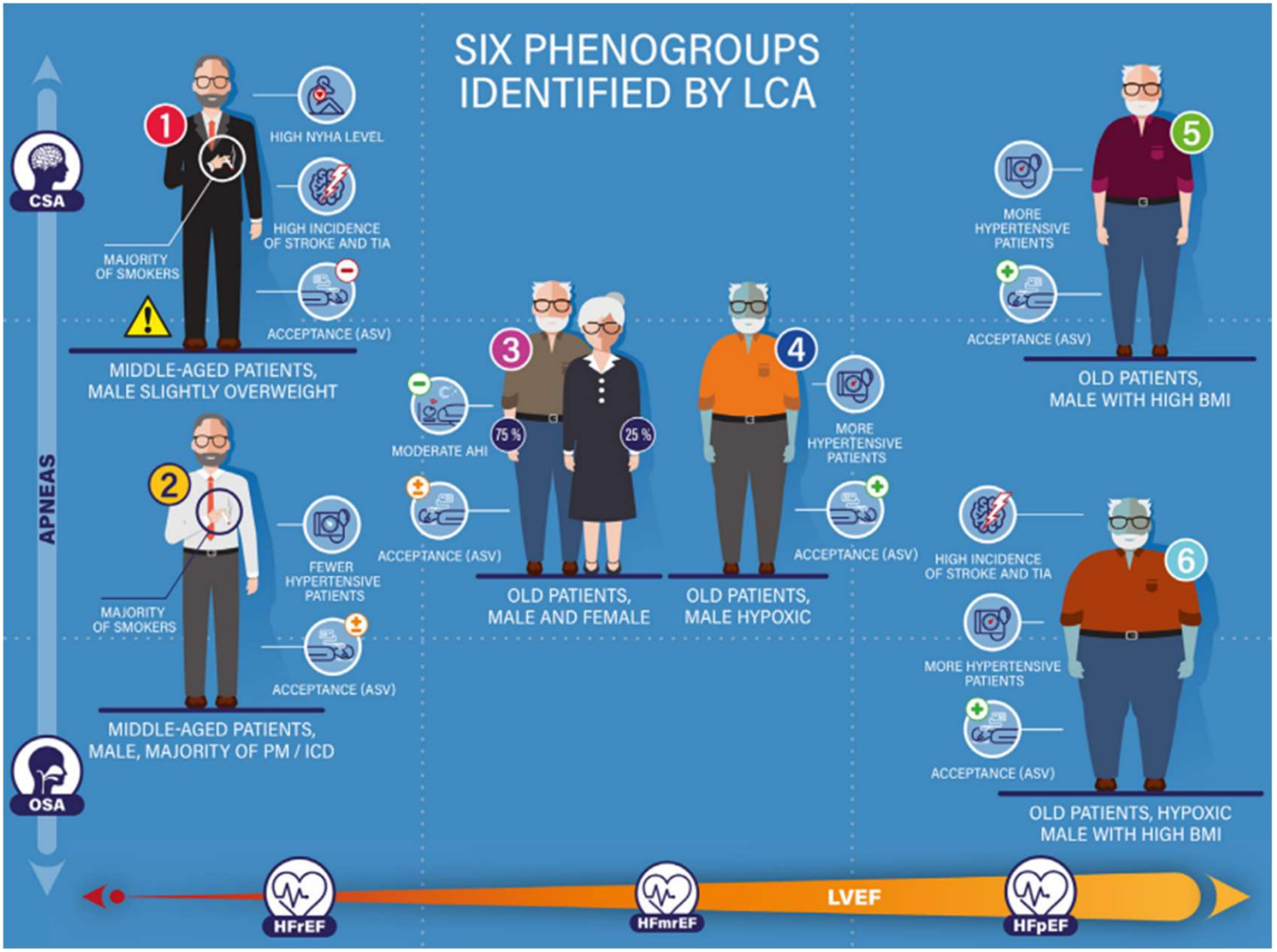
Bradley TD et al. Lancet Respir Med 2023

CSA fenotypen: FACE studie

- Multicenter prospective observational cohort trial
- 503 HF ptn met predominant CSA ± OSA component
- ASV vs controlegroep
- Inclusie 2009-2018
- Primaire eindpunt: tijd tot composite first event (all cause death, lifesaving CV intervention or unplanned hospitalisation for worsening of chronic HF.
- 6 onderscheidende clusters

Tamisier R, Thorax 2022
Tamisier R, Sleep Medicine 2023

CSA fenotypen: FACE studie



- Multicenter
- Prospectief cohort
- Inclusie 2009-2018
- 503 HF ptn met CSA
- ASV vs controle
- Primair eindpunt:

  Tijd tot composite

  first event:

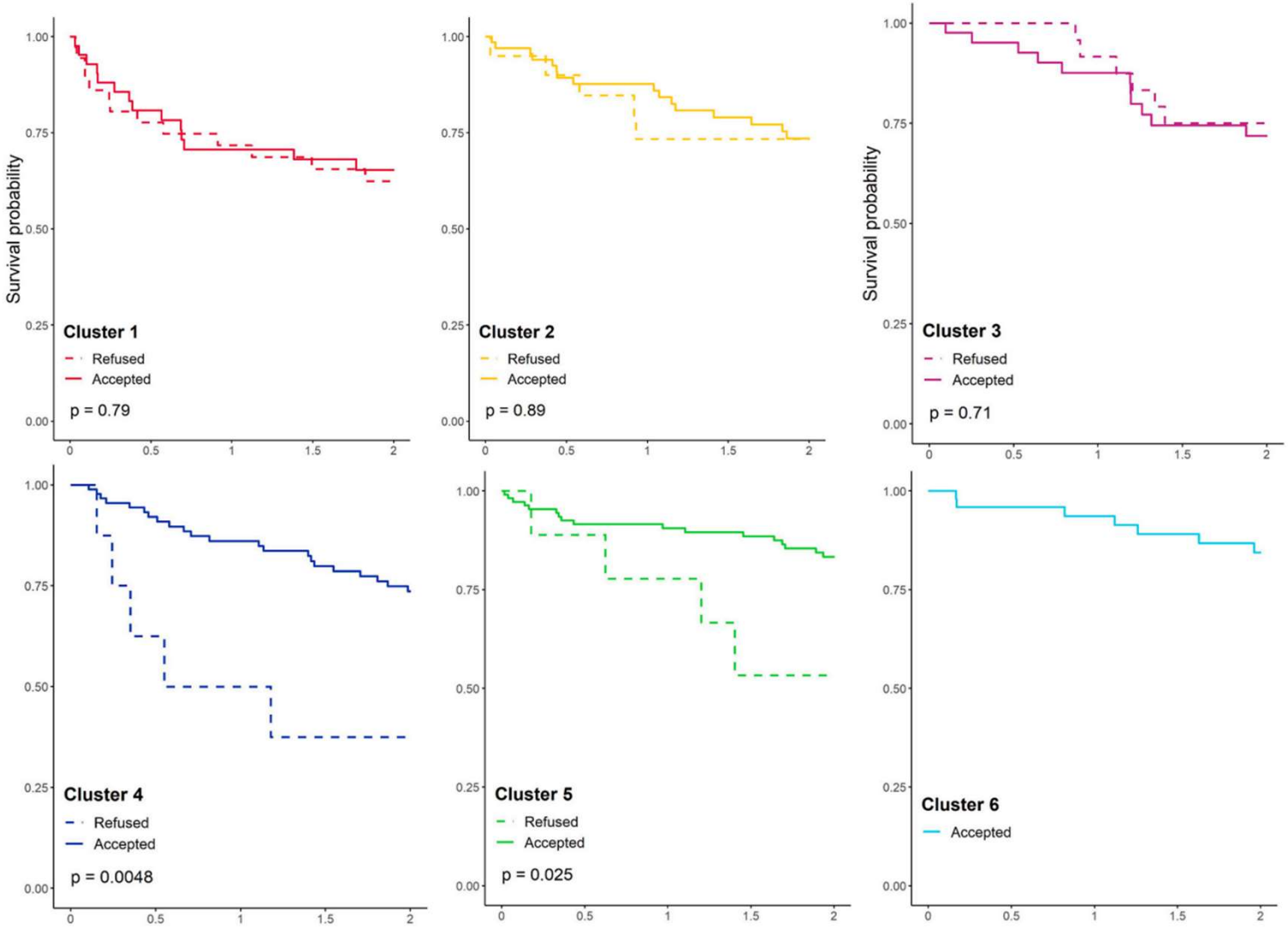
  All cause death

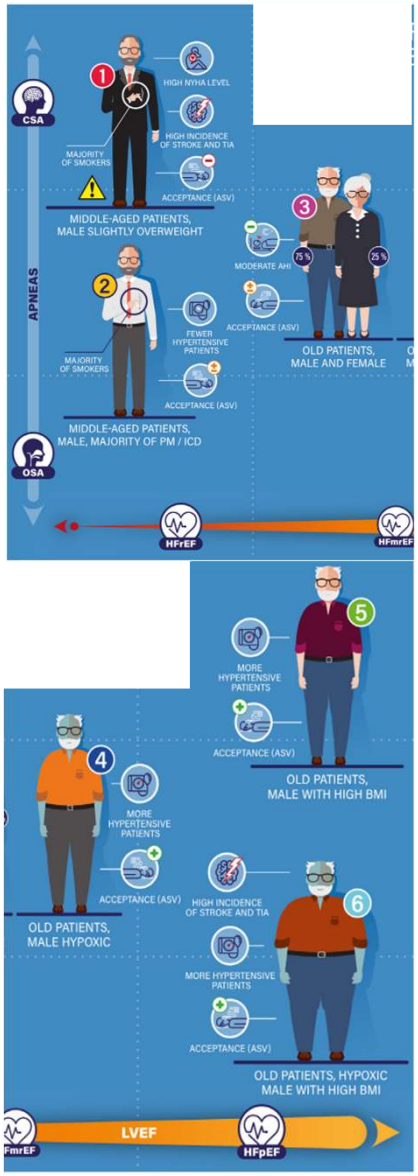
  Life saving CV intervention

  Unplanned hospitalisation for HF

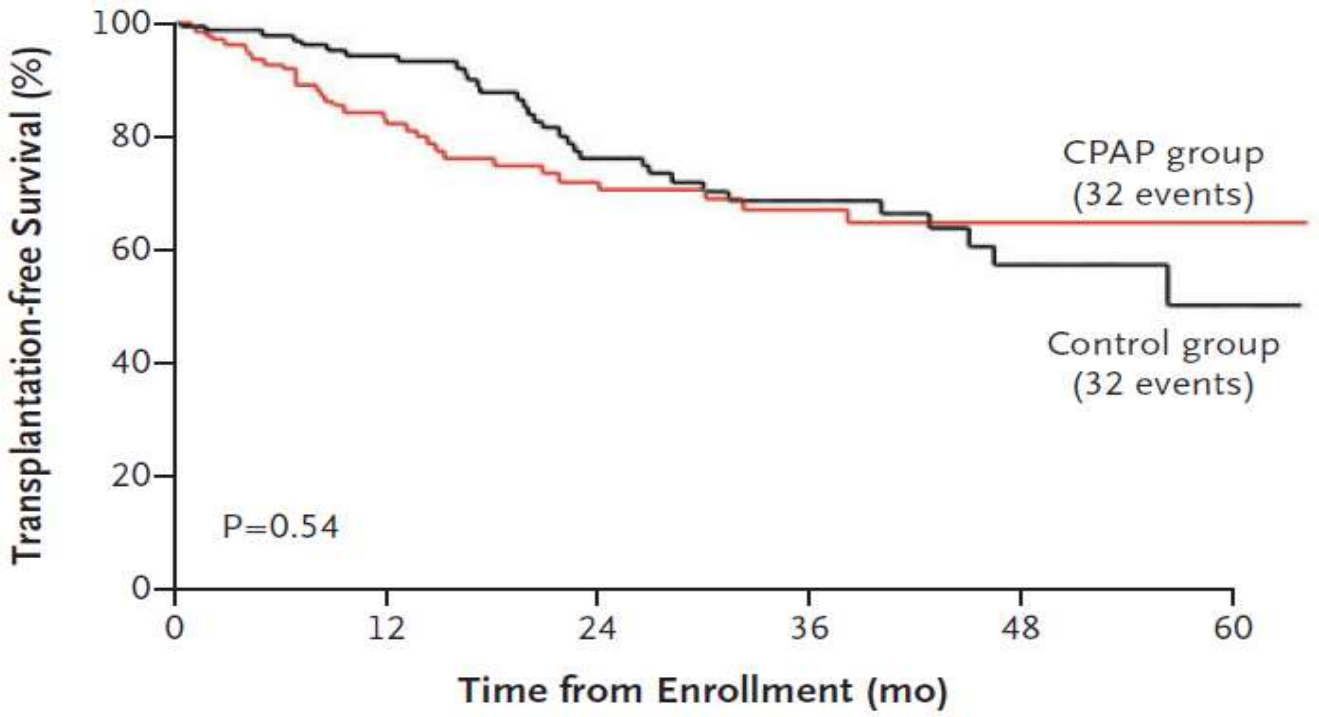
Tamisier R, Thorax 2022

FACE study: 2 jaar follow up





CPAP



No. at Risk

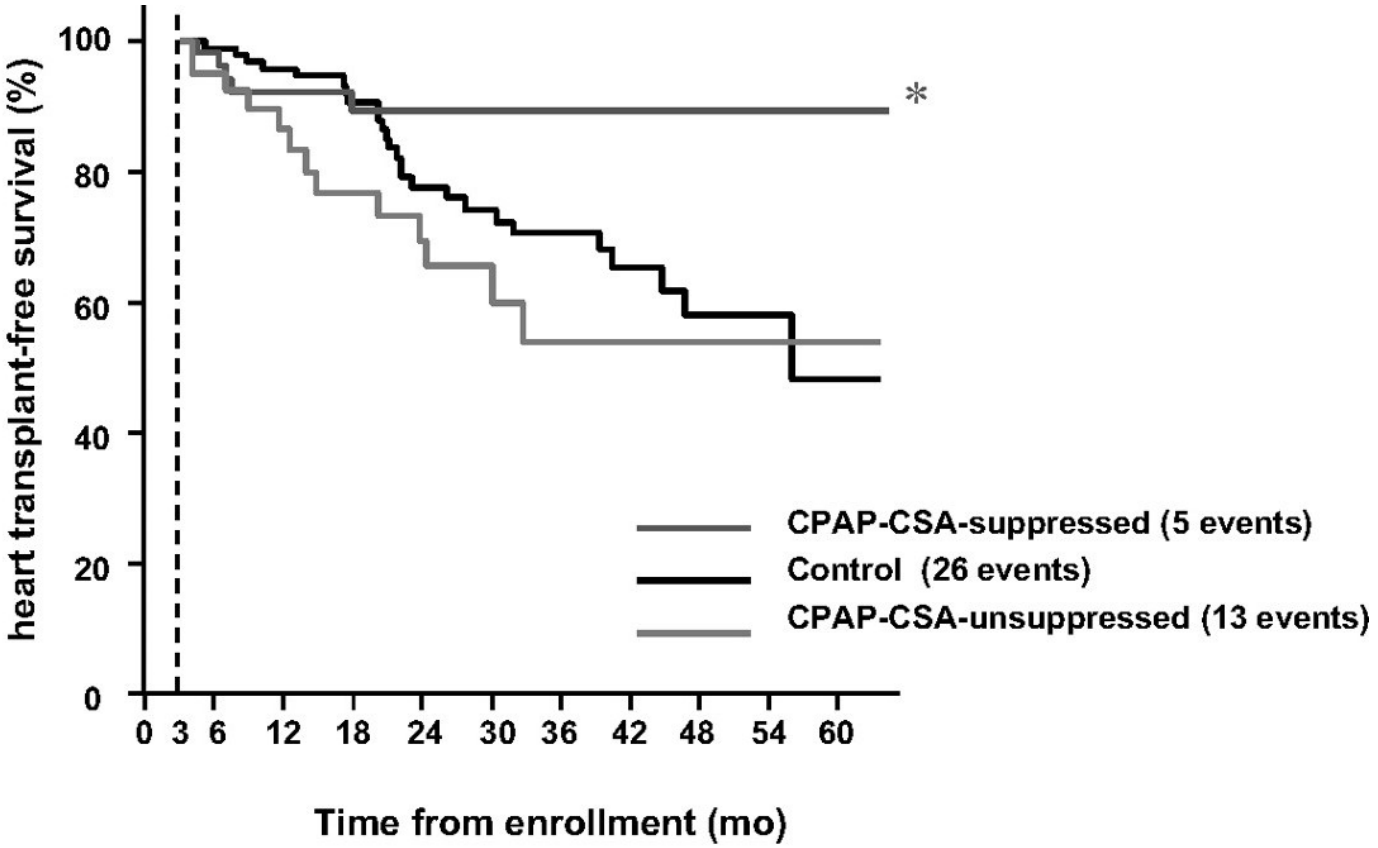
CPAP group	128	104	79	59	49	42	33	24	20	12	6
Control group	130	117	96	79	59	46	37	27	19	12	4

<u>CANPAP trial</u>

- N= 258
  - •HF NYHA II - IV
  - •LVEF < 40%
- CPAP vs controle
- AHI ⇓ 53%
- Voortijdig gestopt

Bradley TD et al. N Engl J Med 2005

CPAP



CANPAP

- PostHoc, 3mnd
- 57% AHI < 15/u
  - Betere LVEF
  - Betere survival

Conclusie

- Respons in ~ 50%
- AHI ⇓ ~50%

Arzt M et al. Circulation 2007

Zuurstof

Study	Pts	NOT		AHI (events/h)		
Author, year	N	Duration	L/min	Baseline	NOT	*p*
Hanly 1989 [23	9	One night	2–3	30.0 ± 4.7	18.9 ± 2.4 (−37%)	<0.01
Walsch 1995 [24	7	One night	2	32 ± 7	23 ± 4 (−28%)	<0.05
Franklin 1997 [25	16	One night	1–5	37.1 ± 0	8.6 ± 0 (−77%)	<0.01
Krachman 1999 [26	9	One night	2	44 ± 9	18 ± 5 (−59%)	<0.001
Javaheri 1999 [27	36	One night	2–4	49 ± 19	29 ± 29 (−41%)	0.0001
Teschler 2001 [28	14	One night	2	44.5 ± 3.4	28.2 ± 3.4 (−37%)	<0.001
Krachman 2005 [30	10	One night	2	57 ± 61	9 ± 11 (−84%)	<0.05
Suzuki 2006 [32	15	One night	3	20 ± 5	6.4 ± 2.1 (−68%)	<0.05
Bordier 2014 [37	19	One night	3	40.5 ± 10.7	26.4 ± 1.6 (−35%)	<0.0001
Andreas 1996 [38	22	One week	4	26 ± 24	10 ± 9 (−62%)	<0.001
Staniforth 1998 [39	11	One month ("long term")	2	37.8 ± 3.9	24.9 ± 3.7 (−34%)	0.01
Krachman 2005 [30	10	One month	2	57 ± 61	12 ± 17 (−79%)	<0.05
Campbell 2012 [36	7	Two months	2	63 ± 30	19.4 ± 15.7 (−79%)	<0.05
Arzt 2005 [29	10	Three months	2	28.8 ± 3.2	8.7 ± 4.1 (−70%)	0.02
Sasayama 2006 [31	25	Three months	3	21.0 ± 10.8	10.0 ± 10.6 (−52%)	<0.001
Toyoma 2009 [34	10	Three months	3	26.1 ± 9.1	5.1 ± 3.4 (−80%)	<0.01
Shigemitsu 2007 [33	18	Four months	2–3	33.1 ± 11.3	6.23 ± 3.16 (−81%)	0.0004
Bordier 2014 [37	16	Six months	3	36.8 ± 2.6	18.3 ± 2.4 (−50%)	<0.0001
Sasayama 2009 [35	21	12 months	3	19.0 ± 12.3	9.0 ± 8.4 (−53%)	<0.01

Conclusie

- Respons in ~ 50%
- AHI ⇓ ~50%

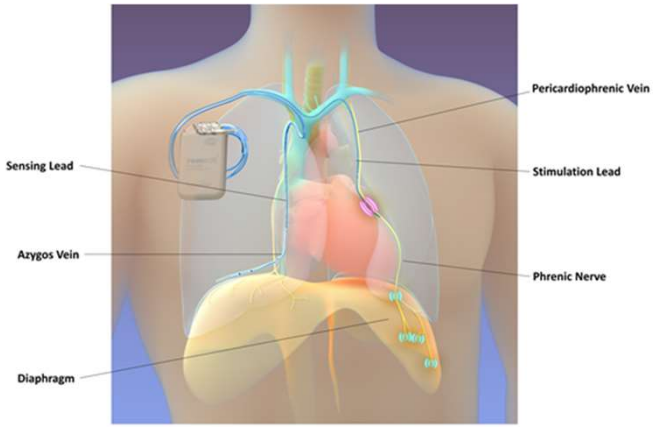
RCT 3 jr: LOFT-HF

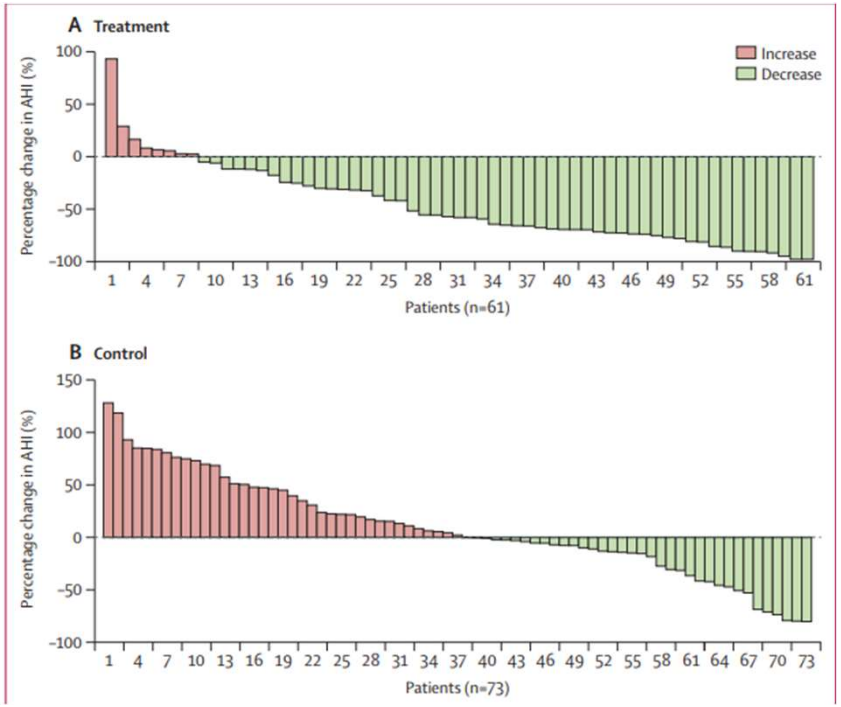
- Zuurstof vs Sham
- Eindpunt: Mortality, lifesaving CV intervention, unplanned hospitalization for HF

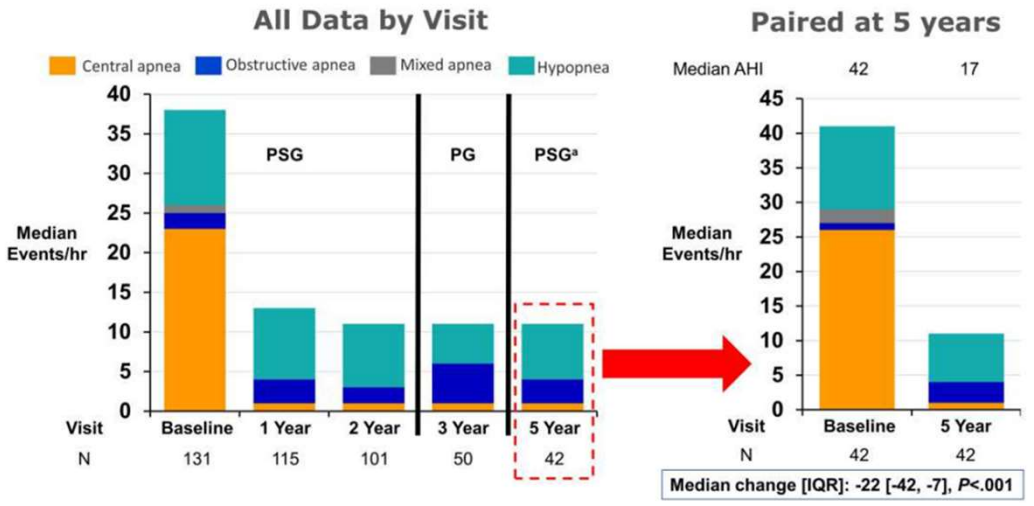
Bordier P, et al. Sleep Medicine 2016

N. Phrenicus stimulatie

- 151 CSA ptn, 31 centra
- AHI ≥ 20/u, OAI < 20% AHI







Costanzo MR. Lancet 2016 en Nature and science of sleep 2021

Medicatie

- Cardiale medicatie
- Stabilisatie van de ademhaling
  - 5 RCT (4 HF patienten)
  - N= 68 in totaal (!)
  - Acetazolamide, buspirone, theophylline, triazolam
  - Interventieperiode : 3 dagen- 1 week

Cochrane Library

Cochrane Database of Systematic Reviews

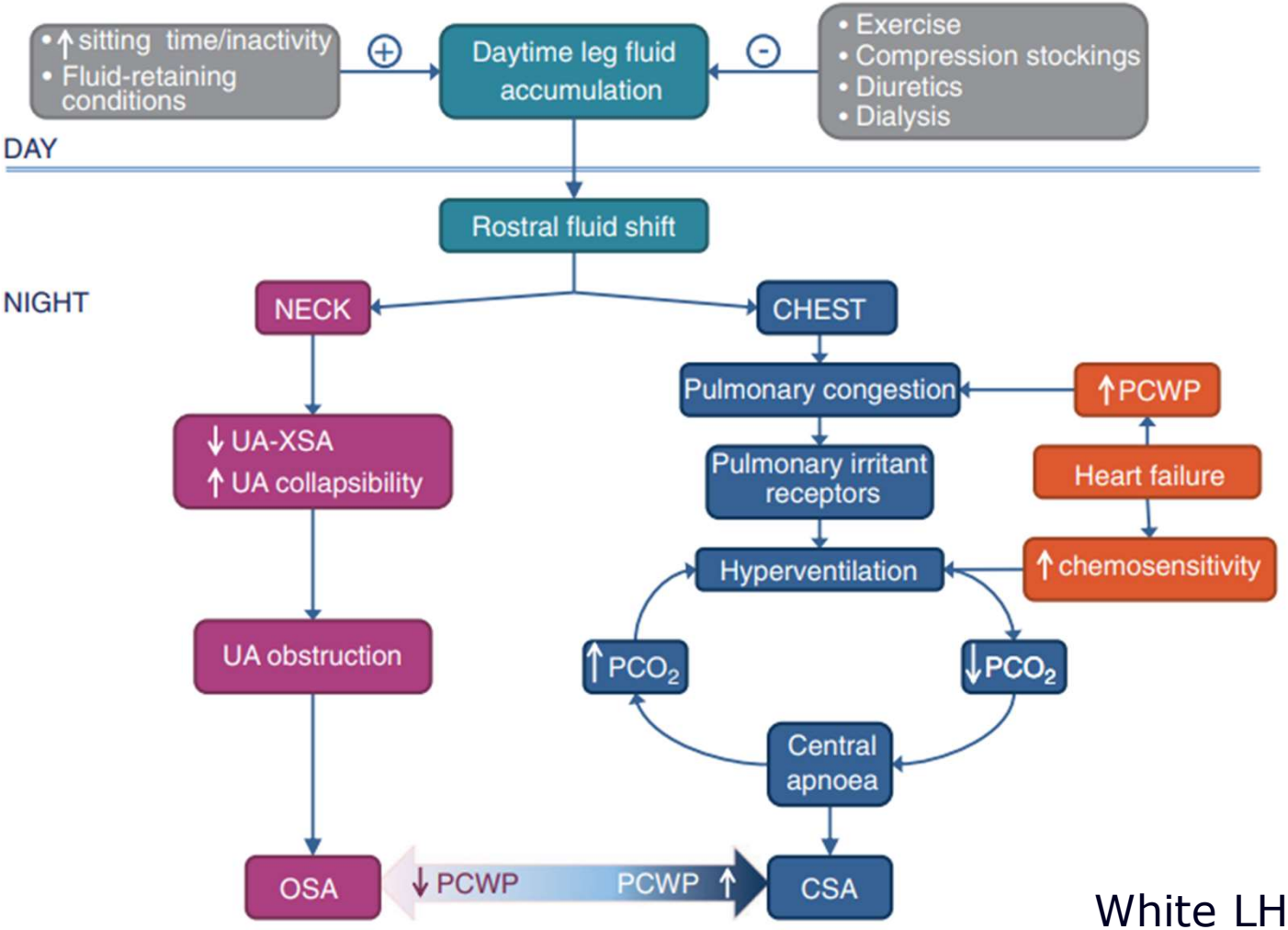
Pharmacological treatment for central sleep apnoea in adults (Review)

Authors' conclusions

There is insufficient evidence to support the use of pharmacological therapy in the treatment of CSA. Although small studies have reported positive effects of certain agents for CSA associated with heart failure in reducing the number of respiratory events during sleep, we were unable to assess whether this reduction may impact the quality of life of people with CSA, owing to scarce reporting of important clinical outcomes such as sleep quality or subjective impression of daytime sleepiness. Furthermore, the trials mostly had short-term follow-up. There is a need for high-quality trials that evaluate longer-term effects of pharmacological interventions.

Rocha A. Cochrane Database of Systematic Reviews 2023

Voorkomen fluid shift



White LH, Bradley TD. J Physiol 2013

Positie therapie in PCSA met SPT

Table 2 Respiratory indices during baseline and after 1 month and 6 months of follow-up

	Baseline $N=16$	$T=1$ month $N=16$	$T=6$ months $N=13$	p value[a]	p value[b]
Total AHI, events/h	23.4 [12.9–31.2]	11.5 [7.2–24.5]	9.7 [3.4–27.6]	0.044*	0.075
Total AI, events/h	14.4 [8.6–29.7]	6.2 [1.5–17.9]	5.0 [0.7–23.7]	0.041*	0.087
Total central AI, events/h	9.4 [6.4–11.8]	2.5 [1.0–5.4]	0.9 [0.1–11.9]	0.008*	0.152
Oxygen Desaturation Index, events/h	16.3 [5.5–23.8]	6.9 [3.5–17.6]	7.1 [2.0–18.1]	0.041*	0.182
Supine AHI, events/h	59.8 [42.2–76.5]	62.2 [15.0–79.5]	20.2 [0.0–36.2]	0.807	0.013*
Non-supine AHI, events/h	7.3 [2.1–11.8]	7.6 [4.1–15.2]	5.2 [1.9–21.8]	0.163	0.124
Supine central AI, events/h	21.0 [12.9–36.9]	9.6 [0.5–22.0]	0.0 [0.0–18.1]	0.079	0.081
Non-supine central AI, events/h	1.4 [0.9–3.1]	1.2 [0.1–3.8]	0.7 [0.0–5.1]	0.363	0.937
Percentage supine sleep	37.6 [17.2–51.8]	6.7 [0.7–22.8]	6.8 [0.7–22.1]	<0.001*	0.001*
Total sleep time, h	6.7 [6.3–7.5]	6.9 [5.7–7.7]	7.0 [5.5–7.6]	0.717	0.600
Sleep efficiency, %	87.7 [72.3–92.4]	89.6 [79.6–94.0]	91.4 [78.1–95.0]	0.326	0.382
% REM	19.8 [16.1–23.1]	20.0 [12.7–22.4]	16.9 [11.8–26.4]	0.836	0.173
% Stage N1	5.7 [3.2–12.3]	7.4 [5.1–10.8]	6.9 [4.1–8.9]	0.918	0.917
% Stage N2	53.3 [45.0–58.0]	53.4 [44.9–59.7]	52.7 [49.7–60.3]	0.776	0.279
% Stage N3	19.3 [14.7–24.1]	20.7 [15.1–25.0]	21.3 [13.8–27.1]	0.717	0.917
Microarousal index, #/h	13.9 [3.1–35.9]	10.5 [5.4–16.5]	11.3 [5.6–15.9]	0.073	0.084
Positional change index, #/h	2.6 [1.9–3.7]	3.1 [1.8–5.7]	2.2 [1.2–4.8]	0.959	0.263
Minimal SpO_2 (%)	87.0 [84.3–88.0]	88.5 [86.3–91.0]	88.0 [86.5–90.5]	0.047*	0.062
Mean SpO_2	95.0 [93.5–96.0]	95.5 [95.0–96.0]	95.0 [94.0–96.0]	0.068	0.248
SpO2 < 90% (%TIB)	0.4 [0.03–2.03]	0.01 [0.00–0.28]	0.1 [0.0–0.3]	0.028*	0.171

N= 16 mannen
Positioneel CSA

Benoist LBL et al. Eur Arch Otorhinolaryngol. 2019

Take home message

- Cardiaal/hartfalen is de meest voorkomende oorzaak van CSA
- CSA is een onafhankelijke prognostische merker in hartfalen
- Fenotypen CSA in hartfalen
- Behandeling van CSA in hartfalen: onduidelijk effect op mortaliteit
- Meerdere behandelingsmogelijkheden, ‘stepped care’
  - Vooralsnog geen ASV bij LVEF $\leq$45%
  - Soms kleine studies
  - Grijpen aan op een bepaald aspect in de pathofysiologie
  - Partieel effect op uitkomstmaten
  - Belangrijk: klachten bespreken in relatie tot bevinding PSG
  - ‘Personalized Medicine’