Literature Search String

((adaptive[All Fields] AND servo[All Fields] AND ("ventilation"[MeSH Terms] OR "ventilation"[All Fields] OR "respiration"[MeSH Terms] OR "respiration"[All Fields])) OR ASV[All Fields]) AND ("sleep apnoea syndromes"[All Fields] OR "sleep apnea syndromes"[MeSH Terms] OR ("sleep"[All Fields] AND "apnea"[All Fields] AND "syndromes"[All Fields]) OR "sleep apnea syndromes"[All Fields]) AND (("2010/06/01"[PDAT] : "2015/10/31"[PDAT]) AND "humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])

Table S1 – Summary of findings for ASV

ASV for CSAS in CHF patients

References: Artz 2008 (A); Artz 2013 (B); Campbell 2012 (C); Carnevale 2011 (D); Cowie 2015 (E); Fietze 2008(F); Joho 2012 (G); Kasai 2010(H); Kasai 2013 (I); Kourouklis 2013 (J); Koyama 2010 (K); Koyama 2013 (L); Miyata 2012 (M); Oldenburg 2008(N); Oldenburg 2011 (O); Oldenburg 2013 (P); Owada 2013 (Q); Pepperell 2003(R); Philippe 2006(S); Randerath 2012 (T); Suzuki 2014 (U); Szollosi 2006(V); Yoshihisa 2011 (W); Yoshihisa 2012 (X); Yoshihisa 2013 EJHF (Y); Yoshihisa 2013 Heart (A); Zhang 2006 (AA)

Outcomes	Quality of the evidence (GRADE)	Absolute Effect ASV (Pre-Post treatme	ent) ¹	No of Participants (studies)		
Left Ventricular Ejection Fraction (follow-up 0.5-6 months; measured with: %; Better indicated by higher values)	⊕⊕⊖⊖ low ^{2,3}	The LVEF in the ASV gro 5.49% higher (4.16% to 6.82% higher)	up was	426 (17 studies) ^{B,D,F-I,M-O,P-U,W,Y,AA}		
Apnea-Hypopnea Index (follow-up 0.005 - 6 months; measured with: No./hr sleep; Better indicated by lower values)	⊕⊕⊖⊖ low ^{2,3}	The AHI in the ASV group 30.63 events lower (26.98 to 34.28 lower)	o was	638 (27 studies) ^{A-D,F-AA}		
	-	Relative Effect Baseline Risk	Comparative Risk			
Mortality (Cardiac Death) (follow-up 12-31 months; measured with: events; Better indicated by lower RR)	⊕⊕⊕⊕ high	198 per 1,000 patients	247 per 1,000 patients (202 to 304) RR 1.25 (1.02 to 1.53)	1325 (1 study) ^F		
¹ Results vs. baseline; patients	served as their ow	n controls				

² Combination of randomized and non-randomized studies

³ Studies generally funded by industry

Figure C1 Moto anal	lucic of LVEE from before after ASV treatment trials	
Figure 51 - Meta-alla	Tysis of LVEF Holli before-after ASV treatment trials	

	Post-t	reatmen	t	Pre-tr	eatment	t		Mean Difference	Mean Difference
Study or Subgroup	Mean [%]	SD [%]	Total	Mean [%]	SD [%]	Total	Weight	IV, Random, 95% CI [%]	IV, Random, 95% CI [%]
1.4.1 LVEF cutoff ≤45%									
Artz 2013	33.1	8.6	11	29.9	7.2	11	4.0%	3.20 [-3.43, 9.83]	
Fietze 2008	26.5	8.8	15	24.6	7.9	15	4.9%	1.90 [-4.08, 7.88]	
Joho 2012	37	12	20	30	9	20	4.1%	7.00 [0.43, 13.57]	
Kasai 2010	44.8	13	15	35.7	13	15	2.0%	9.10 [-0.20, 18.40]	
Kasai 2013	37.8	9.1	12	32	7.9	12	3.8%	5.80 [-1.02, 12.62]	
Miyata 2012	36	11.2	11	30.5	13.9	11	1.6%	5.50 [-5.05, 16.05]	
Oldenburg 2008	35.2	11	29	28.2	7	29	7.8%	7.00 [2.25, 11.75]	—— —
Oldenburg 2011	34	8.8	56	29.9	6.1	56	22.5%	4.10 [1.30, 6.90]	— • —
Owada 2013	44.7	15.6	36	37	15.6	36	3.4%	7.70 [0.49, 14.91]	
Pepperell 2003	38.3	12.8	15	36.5	11.5	15	2.3%	1.80 [-6.91, 10.51]	
Philippe 2006	36.9	9	7	29	9	7	2.0%	7.90 [-1.53, 17.33]	
Zhang 2006	37.2	4.1	14	30.2	4.6	14	17.0%	7.00 [3.77, 10.23]	
Subtotal (95% CI)			241			241	75.5%	5.46 [3.93, 6.99]	•
Heterogeneity: Tau ² = 0.0	00; Chi² = 6	.10, df=	11 (P =	0.87); I ^z = 0)%				
Test for overall effect: Z =	: 6.99 (P < 0).00001)							
1.4.2 LVEF cutoff >45%									
Carnevale 2011	42.6	13.5	33	40.1	13.5	33	4.2%	2.50 [-4.01, 9.01]	
Koyama 2010	53.3	6.1	10	43.5	6.4	10	5.9%	9.80 [4.32, 15.28]	
Koyama 2013	47	10.6	10	43.8	10.4	10	2.1%	3.20 [-6.00, 12.40]	
Randerath 2012	45.5	16	26	47.4	15.9	26	2.4%	-1.90 [-10.57, 6.77]	
Suzuki 2014	46.6	14.3	29	37.8	16.6	29	2.8%	8.80 [0.83, 16.77]	
Yoshihisa 2011	46.4	15.4	23	38.3	18.4	23	1.8%	8.10 [-1.71, 17.91]	
Yoshihisa 2013 EJHF	61.1	9.9	18	56.1	7.4	18	5.4%	5.00 [-0.71, 10.71]	
Subtotal (95% CI)			149			149	24.5%	5.47 [2.49, 8.45]	
Heterogeneity: Tau ² = 2.6	65; Chi² = 7	.17, df =	6 (P = 0	0.31); I ^z = 16	6%				
Test for overall effect: Z =	: 3.59 (P = 0).0003)							
Total (95% CI)			390			390	100.0%	5.49 [4.16, 6.82]	◆
Heterogeneity: Tau ² = 0.0	00; Chi ² = 1	3.28, df=	= 18 (P	= 0.77); l ² =	0%			-	
Test for overall effect: Z =	: 8.09 (P < 0).00001)							-10 -3 0 5 10
Test for subgroup differe	nces: Chi ² :	= 0.00, d	f = 1 (P	= 1.00), l ² =	= 0%				

	Post-t	reatment		Pre-tr	eatment			Mean Difference	Mean Difference	
Study or Subgroup	Mean [AHI]	SD [AHI]	Total	Mean [AHI]	SD [AHI]	Total	Weight	IV, Random, 95% CI [AHI]	IV, Random, 95% CI [AHI]	
1.3.1 LVEF cutoff ≤ 45%)									
Artz 2008	4	1	14	46.4	4	14	5.0%	-42.40 [-44.56, -40.24]	•	
Artz 2013	5	5	11	20	16	11	3.7%	-15.00 [-24.91, -5.09]		
Fietze 2008	11.1	9.9	15	31	10	15	4.3%	-19.90 [-27.02, -12.78]		
Joho 2012	2	3	20	27	14	20	4.4%	-25.00 [-31.27, -18.73]		
Kasai 2010	1.9	2.1	15	37.4	19.5	15	3.7%	-35.50 [-45.43, -25.57]		
Kasai 2013	0	0	0	0	0	0		Not estimable		
Kourouklis 2013	3.5	0.9	9	43.2	23.2	9	2.7%	-39.70 [-54.87, -24.53]		
Miyata 2012	5.9	6.3	11	39	20.7	11	3.1%	-33.10 [-45.89, -20.31]	<u> </u>	
Oldenburg 2008	3.8	4.1	29	37.4	9.4	29	4.8%	-33.60 [-37.33, -29.87]	+	
Oldenburg 2011	6.1	12.1	56	39.7	17.8	56	4.5%	-33.60 [-39.24, -27.96]		
Oldenburg 2013	8.9	5.8	23	42.8	17.5	23	4.2%	-33.90 [-41.43, -26.37]	- -	
Owada 2013	8.3	7.6	36	36.7	15.2	36	4.6%	-28.40 [-33.95, -22.85]		
Pepperell 2003	5.4	7.4	15	24.7	11.3	15	4.3%	-19.30 [-26.14, -12.46]		
Philippe 2006	3	4	9	47	18	9	3.3%	-44.00 [-56.05, -31.95]	_ _	
Szollosi 2006	15	12	10	30	20.9	10	2.7%	-15.00 [-29.94, -0.06]		
Zhang 2006	6.5	0.8	14	34.5	6.1	14	4.9%	-28.00 [-31.22, -24.78]	÷	
Subtotal (95% CI)			287			287	60.3%	-29.81 [-34.60, -25.03]	•	
Heterogeneity: Tau ² = 71	1.18; Chi² = 1	39.77, df=	14 (P =	: 0.00001); I ? :	= 90%					
Test for overall effect: Z:	= 12.21 (P < 0	1.00001)								
4.2.2.1.1/55										
1.3.2 EVEF CULOIT 245%	-		_			_		or 50 / 05 00 07 701		
Campbell 2012	5	6.3		66.5	31.5		1.6%	-61.50 [-85.30, -37.70]		
Carnevale 2011	8	2	33	54	24	33	4.0%	-46.00 [-54.22, -37.78]		
Koyama 2010	4.7	3.3	10	36.6	15.8	10	3.7%	-31.90 [-41.90, -21.90]		
Koyama 2013 Regidenette 2040	9	4.9	10	35.7	13.7	10	3.9%	-26.70 [-35.72, -17.68]		
Randerath 2012	6.1	7.8	36	23.1	13.2	36	4.6%	-17.00 [-22.01, -11.99]		
Suzuki 2014	7.6	4.9	29	41	10.8	29	4.4%	-33.40 [-39.77, -27.03]		
Yoshinisa 2011 Veehibiga 2042	9	7.9	23	38.8	17.3	23	4.1%	-29.80 [-37.57, -22.03]		
Yoshinisa 2012 Veekikiee 2012 ElUE	C .	0.3	42	39	17.3	42	4.0%	-34.00 [-39.57, -28.43]		
Yoshinisa 2013 EJHF	0.9	0.4	18	37	14.1	18	4.3%	-30.10 [-37.25, -22.95]		
Subtotal (95% CI)	9.1	13.3	258	31.3	18.2	258	4.4% 39.7%	-28.20 [-34.45, -21.95] -31.82 [-37.46, -26.17]	•	
Heterogeneity: Tau ² = 63	3.75; Chi² = 5	1.10, df = 9	(P < 0.	00001); I ² = 8	2%				-	
Test for overall effect: Z	= 11.05 (P < 0	.00001)								
Total (95% CI)			545			545	100.0%	-30 63 [-34 28 -26 98]	•	
Heterogeneity: Tour - 60	3 13: Chi≅ – 2	n1 87 df-	24 (P -	0.00001): 12:	- 99%	010		cono [-o-nzoj -zonoj	·····	
Test for overall effect: 7:	= 1644 (P < 0	000011	240 -	0.000017,1	- 50 %				-50 -25 0 25 50	
Test for subgroup differe	ences: Chi ² =	0.28. df = 1	I (P = 0	.60), ² = 0%					AHI Reduction	

Figure S3A – Risk of cardiac death after ASV treatment vs standard care (for recommendations)

	ASV Standard care		Risk Ratio		Risk	Ratio		
Study or Subgroup	Events	Events Total		Total	M-H, Fixed, 95% Cl	M-H, Fixed, 9		ed, 95% Cl
Cowie 2015	165	666	131	659	1.25 [1.02, 1.53]	-		
						0.7	0.85	1 1.2 1.5
							Favours ASV	Favours Standard Care

Figure S3B – Risk of cardiac death after ASV treatment vs standard care (all studies)

0							
	AS\	/	Standard	Standard care Ri			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Cowie 2015	165	666	131	659	88.9%	1.25 [1.02, 1.53]	
Owada 2013	3	36	11	44	6.7%	0.33 [0.10, 1.10]	
Yoshihisa 2011	1	23	4	37	2.1%	0.40 [0.05, 3.38]	
Yoshihisa 2013 EJHF	0	18	3	18	2.4%	0.14 [0.01, 2.58]	·
Total (95% CI)		743		758	100.0%	1.14 [0.94, 1.39]	•
Total events	169		149				
Heterogeneity: Chi ² = 7.6	68, df = 3	(P = 0.0	05); I ^z = 619	χ.			
Test for overall effect: Z =	= 1.32 (P :	= 0.19)					Favours ASV Favours Standard Care

	= •••••, •=••							
	Control		n	Test Tr	eatment	Control Treatment		
Author, Yr	Treatment	Duration	(treatmen t/control)	Baseline	After	Baseline	After	
Artz 2013	Standard care	12 wks	11/10	29.9 ±7.2	33.1 ±8.6	29.4 ±6.9	31.7 ±8.9	
Bitter 2013	Standard care	12 wks	96/86	32 (23, 40)	4.3 ±4.0	33 (24, 44)	N/A	
Carnevale 2011	None	36 mo.	33	40.1 ±13.5	42.6 ±13.5*	N/	A	
Fietze 2008	BPAP-S/T	6 wks	15/15	24.6 ±7.9	26.5 ±8.8	25.5 ±9.2	31.1 ±10.5	
Joho 2012	Standard care	~3.5 mo.	20/12	30 ±9	37 ±12	34 ±9	31 ±9	
Kasai 2010	CPAP	3 mo.	15/15	35.7 ±12.9	44.8 ±12.9	36.0 ±8.1	37.9 ±N/A	
Kasai 2013	CPAP	3 mo.	12/11	32.0 ±7.9	37.8 ±9.1	32.9 ±5.9	31.9 ±6.1	
Koyama 2010	Standard care	4 wks.	10/7	43.5 ±6.4	53.3 ±6.1	45.7 ±9.5	45.6 ±9.7	
Koyama 2013	Standard care	6 mo.	10/9	43.8 ±10.4	47.0 ±10.6	40.6 ±15.3	40.2 ±14.2	
Miyata 2012	Standard care	6 mo.	11/11	30.5 ±13.9	36.0 ±11.2	30.2 ±9.0	32.2 ±8.8	
Oldenburg 2008	None	6 mo.	29	28.2 ±6.9	35.2 ±10.6	N/	A	
Oldenburg 2011	Standard care	~6.5 mo.	56/59	29.9 ±6.1	34.0 ±8.8	27.8 ±7.4	28.1 ±8.7	
Owada 2013	Standard care	6 mo.	36/44	37.0 ±15.6	44.7 ±15.6	35.7 ±11.1	38.4 ±13.8	
Pepperell 2003	Sub-therapeutic ASV	4 wks	15/11	36.5 ±3.0	38.3 ±3.3	35.7 ±3.9	36.3 ±3.8	
Philippe 2006	CPAP	6 mo.	7/6	29 ±9	36.9 ±9*	30 ±9	28 ±N/A*	
Randerath 2012	CPAP	1 yr.	26/25	47.4 ±15.9	45.5 ±16.0	43.2 ±16.4	48.1 ±11.9	
Suzuki 2014	None	6 mo.	29	37.8 ±16.6	46.6 ±14.3	N/	A	
Yoshihisa 2011	Standard care	6 mo.	23/37	38.3 ±18.4	46.4 ±15.4	38.9 ±12.9	41.2 ±14.7	
Yoshihisa 2013 EJHF	Standard care	6 mo.	18/18	56.1 ±7.4	61.1 ±9.9	54.0 ±8.2	51.9 ±9.7	
Zhang 2006	Oxygen	2 wks	14	30.2 ± 4.6	37.2 ± 4.1	N/A	33.2 ±5.1	

Table S2: LVEF Data; ASV

*estimated from graph

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A .1 TY	Control	D	n	Test Tre	eatment	Control Treatment			
Author, Yr	Treatment	Duration	(treatment /control)	Baseline	After	Baseline	After		
Arzt 2008	CPAP	1 night	14	46.4 ±4	4 ±1	46.4 ±4	22 ±4		
Artz 2013	Standard care	12 wks.	11/10	20 ±16	5 ±5	19 ±15	20±15		
Bitter 2013	Standard care	12 wks	96/86	25 (25,30)*	~27.5±N/A	26 (24,32)*	~25±N/A		
Campbell 2012	Oxygen	8 wks.	7	66.5 ±31.5	5.0 ±6.3	N/A	19.4 ±15.7		
Carnevale 2011	Standard care	36 mo.	33	54.0 ±24.0	8 ±2†	N/A	N/A		
Cowie 2015	Standard care	31 mo.	666/659	31.2 ±12.7	3.3 (0.0,36.5)*	31.7±13.2	N/A		
Fietze 2008	BPAP-S/T	6 wks.	15/15	31.0 ±10.0 [‡]	11.1 ±9.9‡	33.4 ±20.5‡	16.1 ±16.2‡		
Joho 2012	Standard care	~3.5 mo.	20/12	27 ±14	2 ±3	22 ±7	23 ±3		
Kasai 2010	CPAP	3 mo.	15/15	37.4 ±19.5	1.9 ±2.1	38.6 ±13.9	15.4 ±12.8		
Kasai 2013	CPAP	3 mo.	12/11	25.0 ±6.9	2.0 ±1.4	23.0 ±7.9	23.1 ±9.1		
Kourouklis 2013	None	6 mo.	9	43.2 ±23.2	3.5 ±0.9	N	/A		
Koyama 2010	Standard care	4 wks.	10/7	36.6 ±15.8	4.7 ±3.3	33.1 ±16.8	33.9 ±21.7		
Koyama 2013	Standard care	6 mo.	10/9	35.7 ±13.7	9.0 ±4.9	39.9 ±8.9	37.2 ±9.7		
Miyata 2012	Standard care	6 mo.	11/11	39.0 ±20.7	5.9 ±6.3	33.0 ±17.8	N/A		
Morgenthaler	CPAP	1 night	6	46.0 ±22.7	0 ±0	N/A	22.8 ±18.2		
2007	BPAP-S/T	1 night	6	46.0 ±22.7	0 ±0	N/A	1.5 ±1.5		
Oldenburg 2008	None	6 mo.	29	37.4 ±9.4	3.8 ±4.1	N	/A		
Oldenburg 2011	Standard care	~6.5 mo.	56/59	39.7 ±17.8	6.1 ±12.1	36.6 ±13.2	N/A		
Oldenburg 2013	None	3.6 mo.	23	42.8 ±17.5	8.9 ±5.8	N	/A		
Owada 2013	Standard care	6 mo.	36/44	36.7 ±15.2	8.3 ±7.6	32.9 ±16.3	28.0 ±14.3		
Pepperell 2003	Sub-therapeutic ASV	4 wks.	15/11	24.7 ±11.3	5.4 ±7.4	23.3 ±13.3	14.7 ±10.6		
Philippe 2006	CPAP	6 mo.	9/8	47 ±18	3 ±4†	40.5 ±13.5	$21 \pm 25^{+}$		
Randerath 2012	CPAP	1 yr.	36/34	23.1 ±13.2	6.1 ±7.8	21.8 ±11.7	10.7 ±8.7		
Suzuki 2014	None	6 mo.	29	41.0 ±16.8	7.6 ±4.9	N	/A		
Szollosi 2006	None	1 night	10/0	30.0 ± 20.9	14.0 ± 12.0	N	/A		
Yoshihisa 2011	Standard care	6 mo.	23/37	38.8 ±17.3	9.0 ±7.9	N/A	N/A		
Yoshihisa 2012	Oxygen	1 night	42	39.0 ±17.3	5.0 ± 6.3	N/A	22.3 ±13.4		
Yoshihisa 2013 EJHF	Standard care	6 mo.	18/18	37.0 ±14.1	6.9 ±6.4	35.4 ±15.5	27.8 ±15.0		
Yoshihisa 2013 Heart	None	1 night	50	37.3 ±18.2	9.1 ±13.3	N	/A		
Zhang 2006	Oxygen	2 wks	14/14	34.5 ±6.1	6.5 ±0.8	N/A	27.8 ±8.2		

Table S3: AHI Data: ASV

* data presented as median (quartiles) † estimated from graph ‡ CSRI = CSAI+PBI (periodic breathing index)

Table S4: Mortality (Cardiac Death) Data; ASV

Anth an Ve	Control	Duration	Test Tre	atment	Control Treatment		
Author, Yr	Treatment	Duration	Events	Ν	Events	N	
Cowie 2015	Standard care	31 mo.	165	666	131	659	
Owada 2013	Standard care	6 mo.	3	36	11	44	
Suzuki 2014	Standard care	6 mo.	1	23	4	37	
Yoshihisa 2013 EJHF	Standard care	6 mo.	0	18	3	18	