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Effect on Quality of Life of Continuous Positive Airway Pressure in Patients with Obstructive Sleep Apnea Syndrome: A Meta-analysis

Jiyong Jing · Tiancha Huang · Wei Cui · Huahao Shen

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Abstract Continuous positive airway pressure (CPAP) is the standard treatment for obstructive sleep apnea syndrome (OSAS). However, the impact of CPAP on quality of life (QOL) is controversial. The aim of this study was to systematically review and determine whether CPAP improves QOL in patients with OSAS. We performed a comprehensive literature search to identify studies published between 1966 and 2007comparing values of CPAP with control. Weighted mean difference (WMD) was used to analyze the data. The pooled WMD was calculated by using a fixed or random-effect model. The outcomes for 1,256 patients from 16 studies, of whom 656 patients underwent CPAP and 600 were controls, were included. CPAP led to significant improvements in the Nottingham health profile part 2 (WMD = 1.657; 95% CI = 3.005, −0.308; $p = 0.016$), but there was no difference in other general QOL scores. Patients undergoing CPAP scored better in physical function (WMD = 3.457; 95% CI = 0.144, 6.771; $p = 0.041$), body pain (WMD = 4.017; 95% CI = −0.008, 8.042; $p = 0.05$), energy vitality (WMD = 6.984; 95% CI = 0.557, 13.411; $p = 0.033$) and physical component summary (PCS) (WMD = 2.040; 95% CI = 0.045, 4.035; $p = 0.045$) using the SF-36 tool. This meta-analysis shows that CPAP does not improve general QOL scores but does improve physical domains and vitality. Study design and QOL questionnaire tools are important to capture and evaluate information efficiently. However, generic QOL instruments may not be adequate in detecting important changes in quality of life in patients with OSAS.

Keywords Quality of life · Continuous positive airway pressure · Obstructive sleep apnea syndrome · Meta-analysis

Introduction

Obstructive sleep apnea affects nearly one in four men and one in ten women between the ages of 30 and 60 years in the United States [1]. OSAS (obstructive sleep apnea syndrome) is present when the number of apneic and hypopneic episodes, longer than 10 s, per hour of sleep (referred to as the apnea-hypopnea index, AHI) is five or more and the patient has excessive daytime sleepiness [2, 3]. Health consequences that may result from chronic sleep disruption or recurrent hypoxemia include neuropsychiatric and cardiovascular sequelae. Neuropsychiatric effects may include depression and cognitive dysfunction that can disrupt professional, family, and social life and increase risks for automobile and industrial accidents. Cardiovascular sequelae can include pulmonary and systemic hypertension, congestive heart failure, arrhythmia, myocardial infarction, and stroke [4–6].

The standard treatment for OSAS is continuous positive airway pressure (CPAP); it has become the treatment of first choice for patients with substantial disease. The effect of CPAP on quality of life (QOL) is unclear [7, 8]. The

Jiyong Jing and Tiancha Huang contributed equally to this work.

J. Jing · H. Shen (✉)
Department of Respiratory Disease, Second Affiliated Hospital of Zhejiang University Medical School, 88# Jefang Road, Hangzhou, Zhejiang Province 310009, China
e-mail: hshen@mail.hz.zj.cn

J. Jing
e-mail: jiyong_jing@163.com

T. Huang · W. Cui
Intensive Care Unit, Second Affiliated Hospital of Zhejiang University Medical School, Hangzhou, Zhejiang Province, China

present meta-analysis reviewed the available QOL evidence from CPAP randomized controlled trials to summarize the best evidence of the effect of CPAP in the treatment of OSAS on QOL.

Methods

Search Strategy and Selection Criteria

Randomized controlled clinical trials were identified via MEDLINE (source PubMed, 1966 to June 2007), EMBASE (1966 to June 2007), the Cochrane Controlled Clinical Trials Register Database (through 2nd quarter 2007), and the ClinicalTrials.gov website. All searches included the keywords and corresponding MeSH terms for Sleep Apnea Syndromes, "Sleep Apnea, Obstructive," "quality of life," "Continuous Positive Airway Pressure," and "randomized controlled trial." Manual reference checking of the bibliographies of all retrieved articles was also done.

Data Extraction

Data extraction was conducted independently by the two reviewers (J.Y. Jing and T.C. Huang). The following information was extracted from each study: first author, year of publication, study population characteristics, study design (parallel or pilot, crossover study), inclusion and exclusion criteria, number of subjects in each group [CPAP and control treatment including conservative treatment (CT), sham CPAP, oral placebo], quality of study, QOL tool used, domains of QOL, treatment duration, and severity of OSAS.

Inclusion Criteria

Prospective randomized controlled trials that were done in adults and published in English were considered for inclusion in this meta-analysis. The following criteria were used to select studies for analysis: (1) studies comparing CPAP treatment with control treatment, and (2) studies that used validated tools for QOL measurements.

Exclusion Criteria

Studies were excluded from the analysis for the following reasons: (1) outcomes of comparison were not reported or it was not possible to extract the data from the published results; (2) the study that did not use validated tools for QOL measures; and (3) more than one article reported outcomes on the same patient group (in that case either the more recent article or the one of higher quality was included).

Measures of Outcomes of Interest

The tools identified as providing validated measures of QOL following OSAS were Short Form 36 (SF-36), Nottingham Health Profile (NHF), Functional Outcomes of Sleep Questionnaire (FOSQ), European Quality of Life Questionnaire (EuroQOL), and Sleep Apnea Quality of Life Index (SAQLI) [9]. All five systems measure QOL within a range of domains and provide an overall indication of QOL.

SF-36

SF-36 was developed in the United States and is a generic measure of health status and can be used to measure health outcomes of clinical interventions [10]. It has been validated and tested for use in 13 countries [11]. The scoring method for SF-36 uses an algorithm to transform dichotomous and continuous variables into a scale from 0 to 100, with higher scores indicating best possible health.

NHP

The NHP is another generic health-related QOL measure, widely used in Europe. It was designed to reflect the perceived effects of ill health on everyday life from the perspective of a layperson rather than that of the health professional. Part 1 includes 38 yes/no items in six domains: physical abilities, pain, sleep, social isolation, emotional reactions, and energy level. Part 2 includes seven aspects of life affected by health: occupation, ability to do jobs around the house, social life, home relationships, sexual life, hobbies, and holidays [12, 13].

FOSQ

The FOSQ is a sleep-specific questionnaire developed to reflect the impact of sleep disorders and excessive sleepiness on activities of daily life. FOSQ contains 30 items divided into five scales: activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcome. Scale scores were added to compute a global score ranging from 0 (maximal dysfunction) to 120 [14].

EuroQOL

The EuroQOL has been developed with cross-cultural applications in mind. The instrument was developed by the international European Quality of Life Group, which has since grown to include members from the United States, Canada, and Japan. The EuroQOL covers five dimensions of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.

SAQLI

The SAQLI was designed as a comprehensive health-related QOL measure for use in clinical trials with patients experiencing sleep apnea. It was based on broad-based input from sleep apnea patients and their partners as well as expert clinicians and the research literature. The first 35 questions measure four domains: daily function, social interactions, emotional functioning, and symptoms. The fifth domain on treatment-related symptoms is a unique feature, capturing the potential negative QOL impact of a treatment's side effects [15, 16].

Quality Assessment

The quality of each fully published trial was assessed by means of an established standard of methodologic quality [17, 18]. The quality of each study was evaluated by examining patient selection methods, comparability of the study groups, and assessment of outcome. Total methodologic quality scores were then used to rank the studies. Studies given six or more stars were considered to be of high quality. Methodologic quality assessment was independently performed by two independent reviewers (J.Y. Jing and W. Cui).

Statistical Analysis

The meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses (QUORUM) guidelines [19, 20]. Statistical analyses of continuous variables such as domain outcome for the QOL scores were analyzed using the weighted mean difference (WMD) and were reported with 95% confidence intervals (CI). The WMD summarizes the differences between the two groups with respect to continuous variables, accounting for sample size. For studies that presented continuous data as means and range values, the standard deviations (SD) were calculated using statistical algorithms and checked by using "bootstrap" resampling techniques. Thus, all continuous data were standardized for analysis. In the tabulation of results, squares indicate the point estimates of the effect of disease (WMD), with 95% confidence intervals indicated by horizontal bars. The diamond represents the summary estimate from pooled studies with 95% confidence intervals.

We used the χ^2 and Fisher exact tests to detect significant statistical heterogeneity. Heterogeneity was assessed using two methods. First, graphical exploration with funnel plots and the Egger test were used to evaluate publication bias [21]. Second, sensitivity analysis was undertaken for each of these groups of data. We also analyzed the effects of other covariates on the QOL (i.e., quality score, control type, time of treatment, study design, severity of OSAS). Meta-regression analyses were conducted to reveal potential sources of heterogeneity. The covariates in the regression analyses included study duration, quality score, mean AHI, and mean ESS. Analysis was conducted using STATA v8.2 (StataCorp., College Station, TX).

Literature Search

Of the original 237 studies identified, 216 were excluded because they did not compare QOL between CPAP and control treatment. We carefully read the full text of remaining 21 studies. Only 16 studies remained, published between 1994 and 2007, that matched the selection criteria and were included in this meta-analysis [7, 22–37]. Analysis was performed on a total of 1256 patients, which included 656 CPAP patients and 600 control patients. The characteristics of these studies are listed in Table 1.

Meta-analysis

General QOL Score

Seven studies gave a general (or global) health score for FOSQ (including 4 [28, 29, 31, 34] for absolute scores and 3 [7, 27, 35] for total score), five [7, 22–25] for NHP part 2 (energy domain only), one [27] for SF-36, one [30] for EuroQOL, and one [36] for SAQLI (Table 2). CPAP led to significant improvements in the Nottingham health profile part 2 (WMD = 1.657; 95% CI = −3.005, −0.308; p = 0.016) and in SAQLI (WMD = 0.900; 95% CI = 0.625, 1.175; p = 0.000), but there was no difference in general QOL scores when using other measurement tools. The general QOL score expresses the patient's personal health evaluation and is not a cumulative total of other domain scores.

Individual Domains and Subgroup Analysis

In eight studies [25, 28, 32–37], the SF-36 was used (Table 3). Patients undergoing CPAP scored better in physical function (WMD = 3.457; 95% CI = 0.144, 6.771; p = 0.041), body pain (WMD = 4.017; 95% CI = −0.008, 8.042; p = 0.05), energy vitality (WMD = 6.984; 95% CI = 0.557, 13.411; p = 0.033), and physical component score (PCS) (WMD = 2.040; 95% CI = 0.045, 4.035; p = 0.045) using the SF-36 tool.

In stratified analyses, the following were found: In parallel studies, physical function (WMD = 7.612; 95% CI = 2.573; 12.65; p = 0.003; four studies) physical problems (WMD = 13.906; 95% CI = 5.413, 22.40; p = 0.001; four studies), body pain (WMD = 7.174; 95% CI = 2.099 = 12.249; p = 0.006; four studies), general

Table 1 Characteristics of included studies

Study, Year	Design	SF-36	FOSQ	NHP	EuroQOL	SAQLI	No. of CPAP	No. of control	Mean age ± SD (years)	Control type	Time of treatment (weeks)	Mean ESS	Severity of OSAS	Mean or median AHI	Quality score
Ballester [26] 1999	Parallel RCT			√			68	37	53 ± 11/54 ± 9	CT	12	11.85	AHI ≥30	56	5
Barbe [27] 2001	Parallel RCT	√	√				29	25	54 ± 11/ 52 ± 10	Sham CPAP	6	7	AHI ≥30	55.4	6
Barnes [28] 2002	RC crossover trial	√	√				28	28	middle-aged	Sham CPAP	8	11.2	AHI 5–30	12.9	6
Barnes [29] 2004	RC crossover trial	√	√				80	80	46.4 ± 9	Oral placebo	12	10.7	AHI 5–30	21.3	6
Chakravorty [30] 2002	Parallel RCT				√		32	21	49 ± 11/ 52 ± 9.6	CT	12	14	AHI ≥15	49	5
Engleman [22] 1994	RC crossover trial			√[a]			32	32	49 ± 8	Oral placebo	4	NA	AHI 7–129	28	4
Engleman [23] 1997	RC crossover trial			√[a]			16	16	52 ± 8	Oral placebo	4	14	AHI 5–15	11	4
Engleman [24] 1998	RC crossover trial			√[a]			23	23	47 ± 12	Oral placebo	4	12	AHI ≥15	43	4
Engleman [25] 1999	RC crossover trial			√[a]			34	34	44 ± 8	Oral placebo	4	13	AHI 5–15	10	5
Faccenda [31] 2001	RC crossover trial		√				68	68	29–72	Oral placebo	4	15	AHI ≥15	35	5
Jenkinson [32] 1999	Double-blind parallel RCT	√					52	49	50 (33–71)/48 (36–68)	Sham CPAP	4	16.5	NA	NA	8
Lam [36] 2007	Parallel RCT	√				√	34	33	45 ± 6/47 ± 11	CT	10	12	AHI 5–40	21.6	5
Mansfield [33] 2004	Parallel RCT	√					19	21	57.2 ± 9/ 57.5 ± 8.3	CT	12	10	AHI ≥5 with CHF	28.2	5
Marshall [34] 2005	RC crossover trial	√	√				29	29	50.5 (25–67)	Sham CPAP	3	12.5	AHI 5–30	21.8	4
Monasterio [7] 2001	Parallel RCT		√	√			66	59	53 ± 9/54 ± 9	CT	24	12.6	AHI 10–30	20.5	5
Montserrat [35] 2001	Partial crossover RCT	√	√				23	22	55.65 ± 9.4/ 52.6 ± 10.9	Sham CPAP	6	16.5	AHI ≥15	53.8	6
Smith [37] 2007	RC crossover trial	√					23	23	61 ± 8	Sham CPAP	6	10	AHI ≥15 with CHF	36	6

[a] Nottingham health profile part 2

CT = conservative treatment; CHF = chronic heart failure; RCT = random control trial; ESS = Epworth Sleepiness Scale; NA = not available

Table 2 Meta-analyses of general QOL score for CPAP versus control

Questionnaire	No. of studies	WMD	95% CI	HG χ^2	HG p value	p value
FOSQ (absolute scores)	4	0.011	−0.040, 0.063	1.31	0.727	0.661
FOSQ (total score)	3	1.605	−2.421, 5.630	4.01	0.135	0.435
NHP	5	−1.657	−3.005, −0.308	2.11	0.716	0.016
SF-36	1	2.700	−0.913, 6.313	–	–	0.143
EuroQOL	1	2.000	−8.130, 12.130	–	–	0.699
SAQLI	1	0.900	0.625, 1.175			0.000

Table 3 Stratified meta-analyses on study quality, control type, time of treatment, study design, and severity of OSAS. Outcomes of QOL were measured using SF-36 for CPAP versus control

Outcome of questionnaire domain	Stratification	No. of studies	WMD	95% CI	HG χ^2	HG p value	p value	p*
General health	Overall	8	2.469	−0.738, 5.676	4.03	0.776	0.131	
Perception	Study quality							0.354
	High†	4	4.552	−0.893, 9.997	2.55	0.467	0.101	
	Low‡	4	1.363	−2.605, 5.331	0.63	0.89	0.501	
	Control type							0.970
	CT	2	3.243	−3.913, 10.400	0.11	0.738	0.374	
	Oral placebo	1	2.000	−7.273, 11.273	–	–	0.673	
	Sham CPAP	5	2.323	−1.567, 6.213	3.86	0.425	0.242	
	Time of treatment							0.940
	Long§	3	2.266	−3.914, 8.447	0.39	0.821	0.472	
	Short∫	5	2.544	−1.208, 6.295	3.63	0.458	0.184	
	Study design							0.095
	Parallel RCT	4	5.671	0.729, 10.614	0.98	0.806	0.025	
	Crossover trial	4	0.141	−4.073, 4.355	0.27	0.965	0.948	
	Severity of OSAS							0.488
	AHI 5–40	4	1.144	−2.816, 5.105	0.71	0.870	0.571	
	AHI >15	2	3.594	−4.776, 11.965	1.13	0.288	0.400	
	Unlimited	2	6.025	−1.187, 13.237	0.76	0.383	0.102	
Physical function	Overall	8	3.457	0.144, 6.771	5.73	0.571	0.041	
	Study quality							0.718
	High†	4	2.562	−3.327, 8.451	1.76	0.624	0.394	
	Low‡	4	3.872	−0.136, 7.881	3.84	0.279	0.058	
	Control type							0.148
	CT	2	9.456	2.578, 16.334	0.01	0.934	0.007	
	Oral placebo	1	1.00	−9.698, 11.698	–	–	0.855	
	Sham CPAP	5	1.736	−2.306, 5.778	1.90	0.754	0.400	
	Time of treatment							0.196
	Long§	3	6.706	0.772, 12.639	2.41	0.30	0.027	
	short∫	5	1.985	−2.009, 5.980	1.65	0.80	0.330	
	Study design							0.032
	Parallel RCT	4	7.612	2.573, 12.650	0.62	0.891	0.003	
	Crossover trial	4	0.291	−4.108, 4.690	0.51	0.917	0.897	
	Severity of OSAS							0.569
	AHI 5–40	4	2.846	−1.082, 6.775	3.65	0.302	0.156	
	AHI >15	2	0.865	−9.999, 11.730	0.72	0.395	0.876	
	Unlimited	2	6.912	−0.581, 14.404	0.23	0.628	0.071	

Table 3 continued

Outcome of questionnaire domain	Stratification	No. of studies	WMD	95% CI	HG χ^2	HG p value	p value	p*
Physical problems	Overall	8	6.822	−2.193, 15.837	14.38	0.045	0.138	
	Study quality							0.940
	High†	4	5.737	−6.990, 18.463	6.25	0.100	0.377	
	Low‡	4	7.689	−7.443, 22.821	8.12	0.044	0.319	
	Control type							0.229
	CT	2	14.297	0.734, 27.86	0.0	0.98	0.039	
	Oral placebo	1	17.0	2.406, 31.594	–	–	0.022	
	Sham CPAP	5	1.098	−12.446, 14.64	11.42	0.022	0.874	
	Time of treatment							0.903
	Long§	3	9.308	–1.550, 20.167	1.45	0.485	0.093	
	Short∫	5	8.494	1.150, 15.838	12.91	0.012	0.502	
	Study design							0.062
	Parallel RCT	4	13.906	5.413, 22.40	3.14	0.370	0.001	
	Crossover trial	4	0.213	−14.655, 15.08	7.74	0.053	0.978	
	Severity of OSAS							0.062
	AHI 5–40	4	4.952	−9.261, 19.165	8.55	0.036	0.495	
	AHI >15	2	−2.275	−16.935, 12.385	0.09	0.766	0.761	
	Unlimited	2	18.943	7.717, 30.169	0.16	0.69	0.001	
Social functioning	Overall	8	2.575	−8.123, 13.274	1.39	0.986	0.637	
	Study quality							0.922
	High†	4	3.123	−12.21, 18.46	0.52	0.913	0.690	
	Low‡	4	2.055	−12.88, 16.99	0.86	0.835	0.787	
	Control type							0.761
	CT	2	−0.748	−23.34, 21.85	0.02	0.898	0.948	
	Oral placebo	1	11.0	−14.19, 36.19	–	–	0.392	
	Sham CPAP	5	1.275	−12.589, 15.14	0.83	0.934	0.857	
	Time of treatment							0.726
	Long§	3	3.912	−9.14, 16.965	0.02	0.988	0.986	
	Short∫	5	−0.162	−18.84, 18.514	1.25	0.87	0.557	
	Study design							0.953
	Parallel RCT	4	2.254	−12.82, 17.33	0.61	0.894	0.77	
	Crossover trial	4	2.901	−12.28, 18.084	0.78	0.855	0.708	
	Severity of OSAS							0.86
	AHI 5–40	4	2.054	−12.731, 16.84	0.86	0.835	0.785	
	AHI >15	2	−2.415	−27.85, 23.025	0.10	0.754	0.852	
	Unlimited	2	6.432	−13.116, 25.98	0.13	0.714	0.519	
Body pain	Overall	8	4.017	−0.008, 8.042	8.63	0.28	0.05	
	Study quality							0.679
	High†	4	4.808	−0.695, 10.312	2.34	0.505	0.087	
	Low‡	4	3.107	−2.794, 9.008	6.12	0.106	0.302	
	Control type							0.565
	CT	2	7.187	−1.414, 15.788	1.64	0.20	0.102	
	Oral placebo	1	7.0	−4.922, 18.922	–	–	0.250	
	Sham CPAP	5	2.467	−2.461, 7.395	5.85	0.211	0.327	
	Time of treatment							0.881
	Long§	3	4.496	−2.956, 11.949	3.15	0.207	0.237	
	Short∫	5	3.82	−0.962, 8.602	5.46	0.244	0.117	

Table 3 continued

Outcome of questionnaire domain	Stratification	No. of studies	WMD	95% CI	HG χ^2	HG p value	p value	p*
	Study design							0.045
	Parallel RCT	4	7.174	2.099, 12.249	1.65	0.649	0.006	
	Crossover trial	4	−1.333	−7.941, 5.274	2.98	0.395	0.692	
	Severity of OSAS							0.802
	AHI 5–40	4	2.646	−3.278, 8.57	6.64	0.084	0.381	
	AHI >15	2	4.196	−5.458, 13.85	0.68	0.410	0.394	
	Unlimited	2	5.667	−0.998, 12.333	0.87	0.351	0.096	
Mental health	Overall	8	2.026	−0.831, 4.882	12.93	0.074	0.165	
	Study quality							0.348
	High†	4	0.913	−7.223, 9.049	8.57	0.036	0.826	
	Low‡	4	0.867	−2.876, 4.609	3.48	0.324	0.650	
	Control type							0.631
	CT	2	4.136	−2.825, 11.097	0.08	0.782	0.244	
	Oral placebo	1	4.000	−3.372, 11.372	–	–	0.290	
	Sham CPAP	5	0.041	−6.456, 6.538	11.93	0.018	0.99	
	Time of treatment							0.753
	Long§	3	2.820	−2.894, 8.533	0.5	0.78	0.333	
	Short∫	5	0.922	−5.274, 7.119	12.33	0.015	0.77	
	Study design							0.026
	Parallel RCT	4	5.659	1.371, 9.946	5.21	0.157	0.01	
	Crossover trial	4	−0.873	−4.704, 2.957	2.76	0.43	0.655	
	Severity of OSAS							0.008
	AHI 5–40	4	0.602	−2.951, 4.155	3.16	0.406	0.74	
	AHI >15	2	−5.194	−13.538, 3.151	0.00	0.963	0.223	
	Unlimited	2	9.498	3.622, 15.374	0.06	0.813	0.002	
Emotional problems	Overall	8	0.525	−9.806, 10.857	18.88	0.009	0.921	
	Study quality							0.498
	High†	4	−1.005	−19.35, 17.34	14.40	0.003	0.914	
	Low‡	4	0.530	−8.800, 9.860	4.27	0.233	0.911	
	Control type							0.375
	CT	2	10.966	−3.324, 25.256	0.31	0.576	0.133	
	Oral placebo	1	−4.000	−19.94, 11.94	–	–	0.623	
	Sham CPAP	5	−3.018	−18.736, 12.70	16.60	0.002	0.707	
	Time of treatment							0.919
	Long§	3	2.482	−9.157, 14.122	4.34	0.114	0.676	
	Short∫	5	−0.937	−14.976, 13.1	14.53	0.006	0.896	
	Study design							0.002
	Parallel RCT	4	9.084	−5.208, 23.376	8.87	0.031	0.213	
	Crossover trial	4	−8.639	−18.257, 0.978	0.79	0.853	0.078	
	Severity of OSAS							0.001
	AHI 5–40	4	−4.041	−12.900, 4.819	3.89	0.274	0.371	
	AHI >15	2	−7.757	−20.779, 5.265	0.03	0.864	0.243	
	Unlimited	2	19.816	9.339, 30.293	0.02	0.893	0.000	
Energy vitality	Overall	8	6.984	0.557, 13.411	22.03	0.003	0.033	
	Study quality							0.082
	High†	4	7.191	−5.771, 20.154	15.58	0.001	0.277	
	Low‡	4	5.525	0.872, 10.178	3.43	0.330	0.020	

Table 3 continued

Outcome of questionnaire domain	Stratification	No. of studies	WMD	95% CI	HG χ^2	HG p value	p value	p*
	Control type							0.644
	CT	2	6.235	−0.541, 13.01	0.09	0.759	0.071	
	Oral placebo	1	12.0	1.972, 22.028	–	–	0.019	
	Sham CPAP	5	5.682	−5.075, 16.439	21.05	0.000	0.301	
	Time of treatment							0.115
	Long§	3	4.525	−1.281, 10.33	1.01	0.602	0.127	
	Short∫	5	8.242	−1.621, 18.105	18.53	0.001	0.100	
	Study design							0.017
	Parallel RCT	4	9.945	−0.301, 20.191	12.46	0.006	0.057	
	Crossover trial	4	3.564	−1.630, 8.758	3.86	0.277	0.179	
	Severity of OSAS							0.001
	AHI 5–40	4	4.295	−0.255, 8.845	4.01	0.26	0.067	
	AHI >15	2	1.942	−8.145, 12.03	0.04	0.841	0.706	
	Unlimited	2	18.741	12.309, 25.17	3.35	0.067	0.000	
MCS[a]	Overall	4	0.676	−5.357, 6.708	16.37	0.001	0.826	
	Study design							0.237
	Parallel RCT	3	1.098	−6.522, 8.719	14.97	0.001	0.778	
	Crossover trial	1	−1.0	−7.653, 5.653	–	–	0.768	
	Severity of OSAS							0.000
	AHI >15	3	−2.121	−5.530, 1.287	0.74	0.69	0.223	
	Unlimited	1	7.60	4.192, 11.008	–	–	0.000	
PCS[b]	Overall	4	2.040	0.045, 4.035	2.29	0.514	0.045	
	Study design							0.447
	Parallel RCT	3	2.237	0.178, 4.296	1.72	0.424	0.033	
	Crossover trial	1	−1.0	−9.091, 7.091	–	–	0.809	
	Severity of OSAS							0.293
	AHI >15	3	1.425	−0.877, 3.727	1.19	0.552	0.225	
	Unlimited	1	3.900	−0.102, 7.902	–	–	0.056	

†The study was scored by 6 or more

‡The study was scored by 5 or less

§The time of treatment was 8 weeks or more

∫The time of treatment was 7 weeks or less

* p values showed the difference between subgroups

[a] MCS was calculated in only four studies [27, 32, 35, 37]

[b] PCS was calculated in only four studies [27, 32, 35, 37]

health (WMD = 5.671; 95% CI = 0.729, 10.614; $p = 0.025$; four studies), mental health (WMD = 5.659; 95% CI = 1.371, 9.946; $p = 0.01$; four studies), and PCS (WMD = 2.237; 95% CI 0.178, 4.296; $p = 0.033$; three studies), components of SF-36, indicated consistent and significant improvements in health status in favor of CPAP. There was no difference in all domains in crossover studies. There was significant statistical heterogeneity between different study designs for physical function, body pain, vitality, physical problems, emotional problems, and mental health domains (Table 3, Fig. 1, 2). In long-term treatment studies, a significant improvement was demonstrated in physical function (WMD = 6.706; 95% CI = 2.573, 12.65; $p = 0.027$; three studies).

Meta-regression analyses showed that Epworth Sleepiness Scale (ESS), AHI, treatment duration, and study quality score were all not the sources of heterogeneity in most of the SF-36 domain. Only study design and AHI were the sources of heterogeneity in physical problems and body pain domain (Table 4).

Using the FOSQ tool, domain scores did not show differences between the CPAP group and the control group in four studies [28, 31, 34, 35]. There also was no significant statistical heterogeneity between subgroups (Table 5).

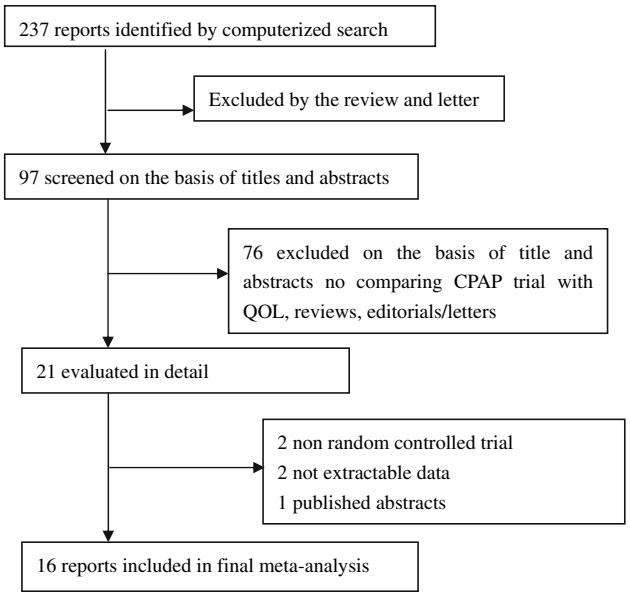

Fig. 1 Study selection process for meta-analysis

Ballester [26] reported no difference using NHP. Lam [36] reported CPAP patients had a significantly better score in the symptoms, emotional, and daily function than the control patients using the SAQLI (Table 6). Further studies using these tools could help to derive a more reliable overview.

Discussion

According to Schipper et al. [38, 39], "Quality of life (QOL) in clinical medicine represents the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient." Improving the quality of life of the OSAS patient is one of the main targets of treatment [40–44]. When comparing CPAP treatment with control, there was no difference in general health perception and total QOL score, except for Nottingham health profile part 2 (energy domain only).

In individual domains, the results of the present meta-analysis found that there was no difference between CPAP and CT or placebo in improving emotional function, MCS, or mental health domain. However, CPAP improves physical function, energy vitality, and PCS domains of the SF-36. Pichel et al. found that the QOL score and symptom improvement of long-term treatment were better than short-term one [7, 44], and there was significant statistical heterogeneity in physical function improvement between study designs. The decrease in physical function was influenced by objective indices of sleep discontinuity and subjective sleepiness. The physical function and the physical role were related to nocturnal parameters indicating sleep disruption, i.e., amount of stage 1 and slow wave sleep, with additional

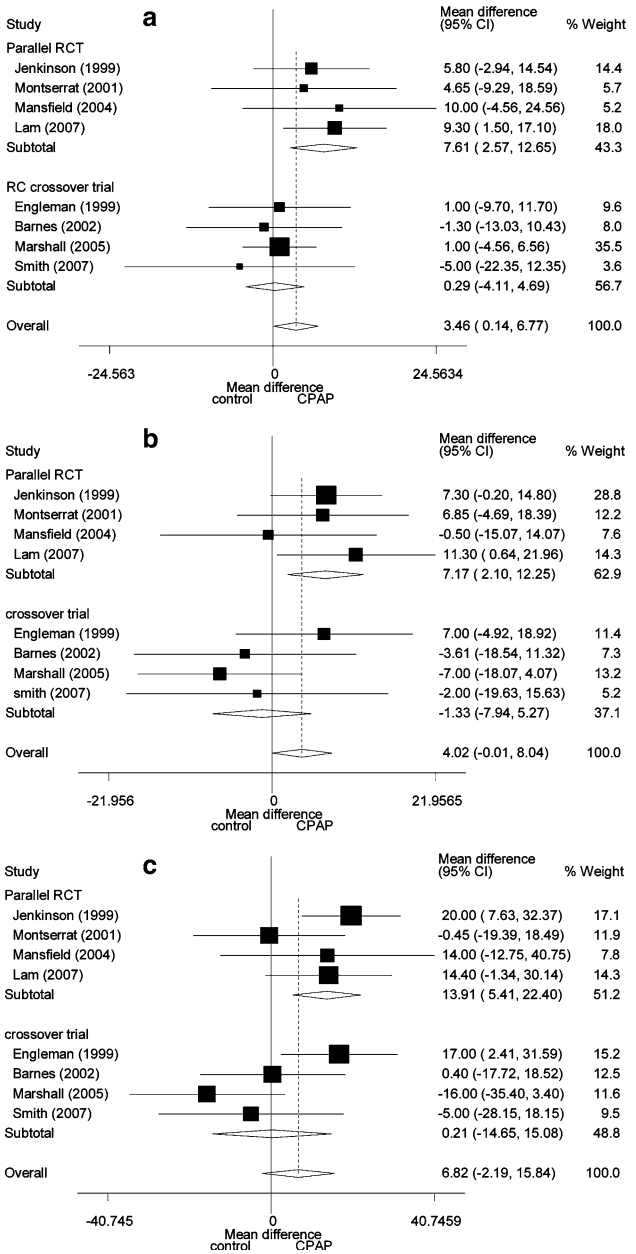

Fig. 2 Forrest plot of outcomes of SF-36 of physical function (**a**), body pain (**b**), and physical problems (**c**) for CPAP versus control, stratified meta-analysis with study design

influence from indices of daytime sleepiness and BMI [45]. Vitality improvement also could be found using NHP part 2 and was not related with control types or the length of treatment period. There was significant statistical heterogeneity in improvement of energy vitality and severity of OSAS between study designs. Hypoxemia, AHI, sleep disruption, and sleep fragmentation appeared to have an impact on physical function and energy vitality.

The improvement in physical scores, especially energy vitality, with CPAP is consistent with studies demonstrating significant improvements in sleepiness with CPAP.

Table 4 Meta-regression analysis to identify sources of heterogeneity

Questionnaire domain	Covariates	Coefficient	SE	*Z*	*p*	95% CI
General health	ESS	−0.09	0.98	−0.09	0.925	−2.01, 1.82
Perception	AHI	−0.12	0.25	−0.48	0.632	−0.62, 0.377
	Treatment duration	−1.25	1.76	−0.71	0.476	−4.69, 2.19
	Study quality score	1.90	4.25	0.45	0.654	−6.42, 10.22
	Study design	11.17	10.38	1.08	0.282	−9.18, 31.52
Physical function	ESS	0.91	1.096	0.84	0.404	−1.23, 3.06
	AHI	−0.07	0.28	−0.24	0.807	−0.63, 0.49
	Treatment duration	0.92	2.04	0.45	0.652	−3.08, 4.92
	Study quality score	−2.9	4.76	−0.61	0.542	−12.23, 6.42
	Study design	5.37	11.64	0.46	0.645	−17.44, 28.17
Physical problems	ESS	−2.86	2.64	−1.08	0.279	−8.05, 2.32
	AHI	−1.32	0.53	−2.53	0.012	−2.37, −0.30
	Treatment duration	−5.78	4.02	−1.44	0.151	−13.66, 2.1
	Study quality score	17.14	10.72	1.60	0.110	−3.87, 38.15
	Study design	52.39	25.43	2.06	0.039	2.55, 102.22
Social functioning	ESS	−1.39	1.95	−0.72	0.472	−5.21, 2.41
	AHI	−0.57	0.38	−1.51	0.132	−1.30, 0.17
	Treatment duration	−2.36	2.78	−0.85	0.396	−7.82, 3.09
	Study quality score	8.05	7.69	1.05	0.296	−7.04, 23.13
	Study design	12.83	18.07	0.71	0.478	−22.59, 48.26
Body pain	ESS	−1.63	1.61	−1.02	0.31	−4.79, 1.52
	AHI	−0.698	0.35	−1.99	0.047	−1.39, −0.01
	Treatment duration	−4.37	2.41	−1.81	0.07	−9.09, 0.36
	Study quality score	10.36	6.49	1.6	0.111	−2.36, 23.09
	Study design	36.54	15.28	2.39	0.017	6.60, 66.49
Mental health	ESS	−0.03	0.94	−0.03	0.973	−1.88, 1.81
	AHI	−0.38	0.23	−1.63	0.104	−0.83, 0.08
	Treatment duration	−0.42	1.89	−0.22	0.825	−4.13, 3.29
	Study quality score	1.76	4.24	0.41	0.679	−6.56, 10.07
	Study design	8.15	10.53	0.77	0.439	−12.49, 28.80
Emotional problems	ESS	−0.35	2.65	−0.13	0.895	−5.54, 4.84
	AHI	−0.22	0.54	−0.40	0.689	−1.29, 0.85
	Treatment duration	1.27	4.03	0.32	0.751	−6.62, 9.17
	Study quality score	−1.41	10.8	−0.13	0.896	−22.58, 19.76
	Study design	11.98	25.29	0.47	0.636	−37.59, 61.56
Energy vitality	ESS	−0.14	1.59	−0.09	0.927	−3.26, 2.97
	AHI	−0.33	0.35	−0.92	0.355	−1.02, 0.36
	Treatment duration	−1.02	2.58	−0.40	0.692	−6.09, 4.04
	Study quality score	3.25	6.615	0.49	0.623	−9.71, 16.22
	Study design	9.865	16.1	0.61	0.54	−21.70, 41.43

The present meta-analysis facilitated the aggregation of data from a variety of sources using standardized QOL assessment tools, the results of which provided greater statistical power to detect significant differences, with subsequent sensitivity analysis demonstrating the robustness of the pooled analysis. The heterogeneity of the studies was analyzed and the results can be seen in Tables 2–5 and in the funnel plot in Figure 2. There was significant heterogeneity in some of the outcomes of the overall analysis. Sensitivity and publication bias were analyzed and the results are shown in the funnel plots in Figures 3 and 4. The results show that the design of the study affects the result of QOL significantly, as does the control type. However, ESS, the severity of OSAS, the

Table 5 Stratified meta-analyses of study quality and severity of OSAS

Outcome of questionnaire domain	Stratification	No. of studies	WMD	95% CI	HG χ^2	HG p value	p value	p*
Active level	Overall	4	0.104	−0.084, 0.291	3.64	0.303	0.279	
	Study quality							0.809
	High†	2	0.134	−0.177, 0.445	2.30	0.13	0.398	
	Low‡	2	0.086	−0.149, 0.321	1.29	0.257	0.472	
	Severity of OSAS							0.198
	AHI 5–40	2	0.044	−0.164, 0.252	0.22	0.64	0.68	
	AHI >15	2	0.358	−0.072, 0.787	1.76	0.184	0.103	
General productivity	Overall	4	0.181	−0.236, 0.599	9.75	0.021	0.395	
	Study quality							0.689
	High†	2	1.093	−1.267, 3.454	9.49	0.002	0.364	
	Low‡	2	0.020	−0.228, 0.269	0.10	0.752	0.874	
	Severity of OSAS							0.188
	AHI 5–40	2	0.000	−0.208, 0.208	0.0	1	1	
	AHI >15	2	1.150	−1.114, 3.413	8.01	0.005	0.319	
Intimacy and sexual activity[a]	Overall	2	0.262	−0.411, 0.935	0.52	0.471	0.446	
General productivity	Overall	4	0.214	0.001, 0.427	0.70	0.874	0.049	
	Study quality							0.767
	High†	2	0.144	−0.365, 0.652	0.47	0.494	0.579	
	Low‡	2	0.229	−0.006, 0.463	0.14	0.706	0.056	
	Severity of OSAS							0.565
	AHI 5–40	2	0.178	−0.067, 0.424	0.11	0.741	0.155	
	AHI >15	2	0.323	−0.106, 0.752	0.26	0.611	0.140	
Vigilance	Overall	4	0.283	−0.198, 0.765	12.45	0.006	0.249	
	Study quality							0.761
	High†	2	2.160	−2.207, 6.527	12.21	0.00	0.332	
	Low‡	2	0.129	−0.106, 0.363	0.14	0.706	0.282	
	Severity of OSAS							0.348
	AHI 5–40	2	0.10	−0.122, 0.322	0.00	1	0.376	
	AHI >15	2	2.208	−2.061, 6.476	11.57	0.001	0.311	

[a] Intimacy and sexual activity were calculated in only two studies [28, 35]

QOL outcomes measured using FOSQ for CPAP versus control

†The study was scored by 6 or more

‡The study was scored by 5 or less

* p values showed the difference between subgroups

Table 6 Meta-analyses of quality-of-life domain outcomes measured using NHP and SAQLI for CPAP versus control

Questionnaire	Domain	No. of studies	WMD	95% CI	HG χ^2	HG p value	p value
NHP	Emotional reactions	1	−9.40	−20.0, 1.20	–	–	0.082
	Energy	1	−9.50	−21.24, 2.24	–	–	0.113
	Pain	1	−0.30	−10.063, 9.463	–	–	0.952
	Physical	1	−6.00	−13.487, 1.487	–	–	0.116
	Sleep	1	2.100	−7.700, 11.90	–	–	0.674
	Social isolation	1	−2.700	−10.23, 4.831	–	–	0.482
SAQLI	Daily functioning	1	0.700	0.144, 1.256	–	–	0.014
	Emotional	1	0.700	0.262, 1.138	–	–	0.002
	Social interactions	1	0.30	−0.138, 0.738	–	–	0.180
	Symptoms	1	1.700	1.144, 2.256	–	–	0.000

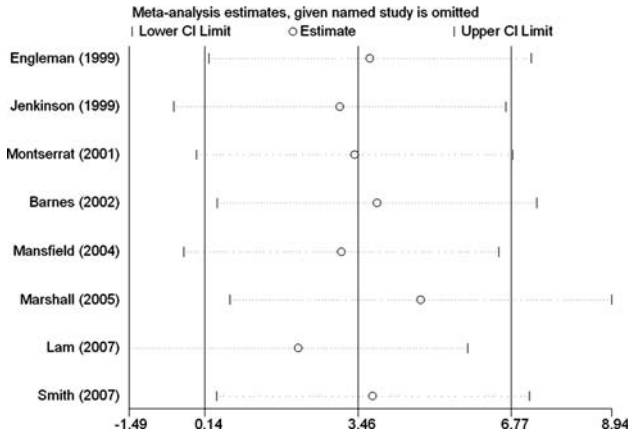

Fig. 3 The influence of individual studies on the summary WMD. The vertical axis at 3.46 indicates the overall WMD and the two vertical axes at 0.14 and 6.77 indicate its 95% confidence interval (CI). Every open circle indicates the pooled WMD when the left study was omitted in a meta-analysis with a random model. The two ends of every broken line represent the respective 95% CI

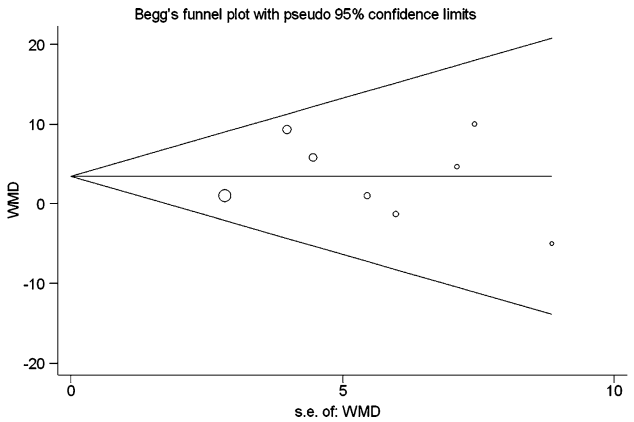

Fig. 4 Funnel graph for the assessment of potential publication bias in physical function for CPAP compared with control. This is a scatterplot of the incidence estimated from individual studies plotted on the horizontal line (SE of the WMD) and the vertical axis (WMD). The result of the Egger test for publication bias was not significant ($p = 0.805$)

quality of score, and the duration of treatment do not affect the QOL scores, except that the physical function of SF-36 indicated significant improvements in long-term trials but not in short-term ones and mean AHI was the source of heterogeneity in physical problems and body pain.

Study design is important in understanding the relationship between patient characteristics and adherence [46]. The crossover study design reduces the efficiency of capturing the QOL effects of CPAP because the washout period is too short to eliminate the effects of pretreatment. In the included studies [22–25, 28, 29, 31, 34, 37] the washout period ranged from 0 to 2 weeks. Long-term parallel-group trials may be more efficient at capturing the important information regarding the persistence of benefits from CPAP treatment, convenience of continued usage, loss to follow-up, and cardiovascular outcome of CPAP treatment.

Control types include CT, oral placebo, and sham CPAP. The selection of control type is controversial. Engleman et al. [22–25] deemed sham CPAP therapy is not possible because a nasal mask without effective CPAP would make both sleep and gas exchange worse. However, the meta-analysis results do not demonstrate that.

The present meta-analysis results demonstrate that there are some different results among QOL questionnaire tools. As a generic measure, SF-36 does not include questions specific for OSAS. The vitality dimension is the closest proxy for sleep-related disturbances [47]. Thus, SF-36 may successfully discriminate between patients with and without OSAS and be sensitive to treatment-induced changes, but it should be accompanied by an OSAS-specific instrument if the researcher is interested in more besides the eight dimensions and two subscales included in SF-36. For specific health-related QOL instruments, preliminary evidence suggests that the SAQLI and the FOSQ are both potentially useful [9].

Although generic questionnaires are designed to measure all important aspects of QOL, they are less likely to detect change in QOL than a disease-specific questionnaire that focuses on specific areas of QOL [48]. Such a disease-specific questionnaire is clearly needed in OSAS research [49], but the number of randomized controlled trial studies that used the disease-specific questionnaire such as SAQLI was small, so further studies are needed to confirm.

In conclusion, when comparing CPAP with control treatment, our meta-analysis shows little impact of CPAP on general QOL. However, CPAP improves physical domains and vitality. Study designs and validated QOL questionnaire tools are important to capture and evaluate information efficiently. However, generic QOL instruments may not be adequate to detect important changes in the quality of life in patients with OSAS. Future randomized controlled trials in this area should concentrate on a disease-specific questionnaire or on large long-term parallel-group trials.

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