Diagnostic capability of biological markers in assessment of obstructive sleep apnea: A systematic review and meta-analysis

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OBJECTIVE

To evaluate the diagnostic value of biological markers (exhaled breath condensate, blood, saliva and urina) for diagnosis of obstructive sleep apnea (OSA) compared to the gold standard full overnight polysomnography (nPSG).

METHODS

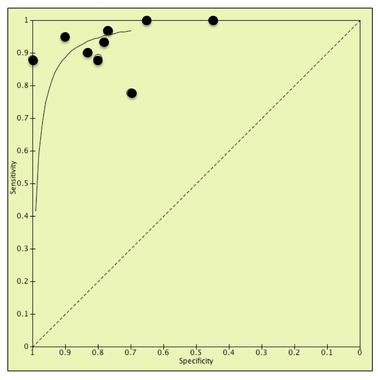
Eligibility Criteria. Retained articles included only those studies whose primary objective was to identify biomarkers in subjects with OSA confirmed by nPSG.
Search. Detailed individual search strategies for Cochrane, MEDLINE, EMBASE, PubMed, and LILACS were developed. The references lists from selected articles were also checked. A partial grey literature search was undertaken using Google Scholar.
Study Selection. Phase 1: Titles and abstracts for all identified citations were revised. **Phase 2:** Only studies that reported sensitivity and specificity or in which the data presented enabled these diagnostic assessments to be extrapolated were finally selected. At both stages a third author was involved when disagreements emerged among the two primary evaluators.
Data Collection Process and Data Items. One author collected the required information from the selected articles. A second author crosschecked all the retrieved information.
Risk of Bias in Individual Studies. The methodology of selected studies was evaluated using the 14- item Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS)[1].
Summary Measures. Sensitivity and specificity of biomarkers as diagnostic tests were considered as the main outcomes.
Synthesis of Results. The diagnostic capability of the biomarkers against nPSG was combined through a meta-analysis. Review Manager 5.2 (RevMan 5.2, The Nordic Cochrane Centre, Copenhagen, Denmark) was used to constructed receiver operating characteristic (ROC) graphs and forest plots.

RESULTS

Only 9 articles (4 in children/ 5 in adults) were finally included in the qualitative and quantitative synthesis. The studies were clustered in 3 groups, according to the sample and the index test: A, B, and C. The total sample for this meta-analysis was 1,716 subjects (258 children/1,458 adults).

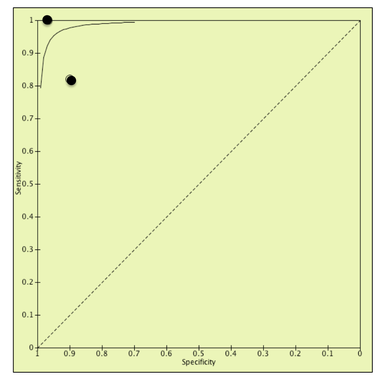
A. Studies in children that analyzed each biomarker individually.
Forest plot

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Benedek et al	14	3	4	7	0.78 [0.52, 0.94]	0.70 [0.35, 0.93]
Gozal et al (1)	58	14	2	46	0.97 [0.88, 1.00]	0.77 [0.64, 0.87]
Gozal et al (2)	53	12	7	48	0.88 [0.77, 0.95]	0.80 [0.68, 0.89]
Gozal et al (3)	56	13	4	47	0.93 [0.84, 0.98]	0.78 [0.66, 0.88]
Gozal et al (4)	54	10	6	50	0.90 [0.79, 0.96]	0.83 [0.71, 0.92]
Kheirandish-G et al (1)	50	11	0	9	1.00 [0.93, 1.00]	0.45 [0.23, 0.68]
Kheirandish-G et al (2)	50	7	0	13	1.00 [0.93, 1.00]	0.65 [0.41, 0.85]
Kheirandish-G et al (3)	44	0	6	20	0.88 [0.76, 0.95]	1.00 [0.83, 1.00]
Shah et al	19	2	1	18	0.95 [0.75, 1.00]	0.90 [0.68, 0.99]



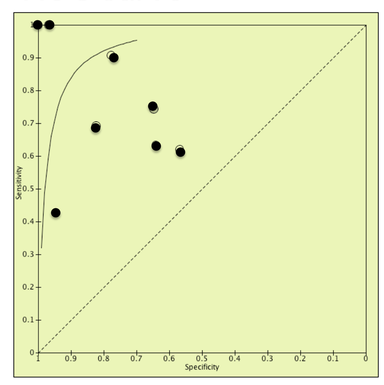
B. Studies in children that combined three or four biomarkers in one analysis.
Forest plot

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gozal et al	60	2	0	58	1.00 [0.94, 1.00]	0.97 [0.88, 1.00]
Kheirandish-Gozal	41	2	9	18	0.82 [0.69, 0.91]	0.90 [0.68, 0.99]



C. Studies in adults.
Forest plot

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Guo et al	49	2	5	7	0.91 [0.80, 0.97]	0.78 [0.40, 0.97]
Hiortsu et al (1)	119	114	73	150	0.62 [0.55, 0.69]	0.57 [0.51, 0.63]
Hirotsu et al (2)	93	150	54	268	0.63 [0.55, 0.71]	0.64 [0.59, 0.69]
Lentini et al	78	1	104	18	0.43 [0.36, 0.50]	0.95 [0.74, 1.00]
Li et al (1)	68	0	0	32	1.00 [0.95, 1.00]	1.00 [0.89, 1.00]
Li et al (2)	68	1	0	31	1.00 [0.95, 1.00]	0.97 [0.84, 1.00]
Ursavas et al (1)	27	6	12	28	0.69 [0.52, 0.83]	0.82 [0.65, 0.93]
Ursavas et al (2)	29	12	10	22	0.74 [0.58, 0.87]	0.65 [0.46, 0.80]



CONCLUSION

Kallikrein-1, uromodulin, urocortin-3 and orosomucoid-1 exhibit acceptable accuracy for use as an OSA diagnostic test in children when used in combination. Plasma IL-6 and IL-10 levels have potential to become a good biomarker aiming to identify adult individuals with and without OSA.

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