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Heart Rate Variability and Autonomic Modulation in Sleep Apnea Prediction: A Systematic Review

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder characterized by recurrent upper airway obstruction, intermittent hypoxia, and autonomic nervous system (ANS) dysregulation. Heart rate variability (HRV), a non-invasive measure of autonomic modulation, has been increasingly investigated as a potential biomarker for OSA diagnosis and prognosis.

Objective: This systematic review aimed to synthesize evidence on the role of HRV in detecting, predicting, and staging OSA, as well as its impact on cardiovascular risk and sleep quality.

Methods: Following PRISMA guidelines, we searched PubMed, Embase, MEDLINE, and the Cochrane Library for studies published up to March 2025. Eligible studies included adult patients assessed for OSA using HRV-derived time-, frequency-, and non-linear indices, with outcomes related to apnea severity, cardiovascular modulation, or sleep staging. Data extraction and risk-of-bias assessment were performed independently by two reviewers.

Results: A total of 25 studies met inclusion criteria. Most demonstrated significant alterations in HRV indices in OSA patients, particularly reduced high-frequency (HF) power and increased low-frequency/high-frequency (LF/HF) ratio, reflecting sympathetic dominance. Several studies reported strong correlations between apnea–hypopnea index (AHI) and HRV markers. Machine learning approaches integrating HRV features achieved promising diagnostic accuracy, with some models exceeding 80% sensitivity and specificity. However, heterogeneity in methodology, limited sample sizes, and lack of standardized HRV thresholds limited comparability.

Conclusion: HRV is a promising, non-invasive tool for detecting and monitoring OSA and its cardiovascular implications. While current evidence supports its utility, further large-scale, standardized, and longitudinal studies are required to establish HRV as a reliable clinical biomarker in sleep medicine.

KEYWORDS: Obstructive Sleep Apnea; Heart Rate Variability; Autonomic Nervous System; Apnea–Hypopnea Index; Sleep Staging; Cardiovascular Risk; Machine Learning; Biomarkers; Sympathetic Activity; Parasympathetic Modulation

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1. INTRODUCTION

Obstructive sleep apnea (OSA) is a prevalent disorder that leads to the intermittent cessation of the airflow during sleep due to a blockage or the narrowing of the upper airway. The effects of sleep apnea are not limited to sleep disruption. It is associated with and probably causes several other conditions including those of the cardiovascular, metabolic, and neurocognitive systems. The cardiovascular consequences of sleep apnea, particularly hypertension, arrhythmias, and the risk of heart failure and stroke, are particularly well known. Also well known is the adverse effect of sleep apnea on the autonomic nervous system, particularly with respect to dysregulation of and control imbalance, causing further risk. These relationships have sparked interest in the use of and focus on the potential of predicting the severity of sleep apnea by its hypoxemic episodes and fluctuations in heart rate variability. Obstructive sleep apnea (OSA) results from the repeated blockage of the upper airway during sleep causes sleep apnea (Qin *et al.*, 2021). During the night, breathing may stop for several seconds or for a few minutes, only to resume breathing. These episodes

may become apnea, which result in sleep hypoxia, a series of awakenings, and a significant disruption of the sleep cycle. All of this leads to excessive daytime sleepiness, and may cognitively and mood disabilities. OSA is a risk factor for stroke, cardiovascular and metabolic disorder which may lead to other serious hypoxic and apnea cardiovascular episodes.
The effect of sleep apnea on the functions of the autonomic nervous system, specifically the heart, and the blood and stress response system, and the order, imbalance regulation of the CV system, cannot be overlooked(Ucak *et al.*, 2021). The Obstructive Sleep Apnea (OSA) case manifests the disorder imbalance regulation of the sympathetic and the parasympathetic branches of the autonomic nervous system. During sleep, the parasympathetic system predominates. OSA patients experience repeated apnea and dysregulation (pauses and shifts) of breathing patterns, which are linked to high sympathetic control and low parasympathetic control, which increases the risk of cardiovascular complications.

The Role of HRV in Autonomic Modulation Autonomic Modulation in HRV
Heart rate variability (HRV) and the functioning of the autonomic nervous system (ANS) expose fundamental orders of executive system responsiveness for a defined period the heart rate (Dos *et al.*, 2021). As a balanced system autonomic order the autonomic system functions disconnected articulate in a synergistic way. Self-autonomic system applies on the internal stress and the control of the system with the cardiovascular stress. With the stress having control, the cardiovascular system and the person cardio the heart rate. Under normal conditions, with the person for the cardiovascular system protection and health, high HRV is a metrics. The low HRV is a metrics with the sympathetic system and the high risk cardiovascular stress. For a defined period the heart rate is the high risk.

Concerning OSA, HRV contributes as a potential marker for the evaluation of the disorder's autonomic dysfunction. The underlying research reveals the pattern of autonomic function alterations with respect to apneic episodes; it describes the increase of sympathetic function and the withdrawal of influence from the parasympathetic divisions. Such dysfunction in the autonomic nervous system is likely to cause increases in blood pressure, heart rate, and additional cardiovascular strain (Nam *et al.*, 2021). Documented cases of OSA in its extreme forms report decreases in HRV, which signifies greater severity in the disorder's autonomic imbalance to be affecting sleep more predominantly.

The various indices of HRV comprise multiple ranges and functions, including low-frequency (LF) and high-frequency (HF) bands. The LF band is generally attributed to the sympathetic system and the HF to the parasympathetic system. Coordination of the multiple systems is critical for the cardiovascular system's stability, particularly during sleep. Evidence shows that patients with OSA primarily lose this equilibrium due to a prevailing imbalance in sympathetic activity during apneic episodes. The potential of negative cardiovascular consequences is likely to be diminished in OSA patients due to such changes in autonomic balance.

2. EVIDENCE GAP

The clinical evidence concerning the use of HRV as a predictor of OSA severity remains insufficient. Literature pertaining to the use of HRV to predict sleep apnea demonstrates a wide range of variability, including strong, weak, and null associations, the cause of which remains unexplained (Xu *et al.*, 2021). Variation in study populations, in the methods used to measure HRV, and the criteria used to diagnose OSA may explain this variation to some extent. The measurement and interpretation of HRV in the context of sleep apnea is inconsistent and lacks clear standards. The disparate estimates of HRV and the analysis of disparate temporal and frequency bands may lead to disparate conclusions. The reliance on small or specific patient populations may explain some of the variability in the estimates, but the problem of the generalizability to OSA as a whole remains. Moreover, complications arise when employing Heart Rate Variability (HRV) to clinical practice in OSA because the guidelines for the condition are not comprehensive or universally accepted. While polysomnography (PSG) is accepted as the gold standard for diagnosing OSA, it is plausible to consider that HRV may hold promise for early OSA detection, as well as monitoring the condition over time is a plausible consideration. The principal argument for HRV not currently being used in a clinical setting for OSA is the lack of universally defined criteria for diagnostic HRV and the inconsistency with which thresholds are applied. This directly impedes HRV's potential for independent clinical use (Statello *et al.*, 2021). Hence, unsupervised HRV as a potential biomarker for OSA with its associated grade, prognosis and extent, requires more consolidated research. This attempt should focus on collecting varied and sufficiently sized study samples, creating standardization for HRV assessment, and exploring the potential of HRV used in conjunction with standard clinical OSA diagnostic methods to meaningfully alter the trajectory of OSA management.

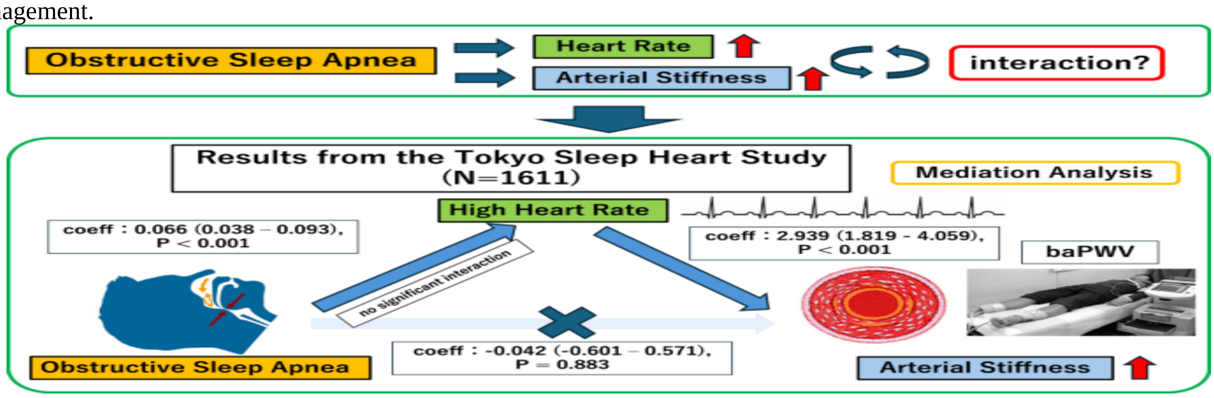

Figure 1: The impact of obstructive sleep apnea and heart rate on arterial stiffness:
(Source: Kani *et al* 2025)

3. METHODS

3.1 Search Strategy

For this systematic review, the author employed comprehensive search strategies to identify relevant studies. The author systematically searched the literature on PubMed, Scopus, and Web of Science. The author selected these databases based on the medical and health sciences literature, which indicates the presence of gold standard peer-reviewed studies in the relevant literature. The search terms mainly included **"heart rate variability," "autonomic modulation," "sleep apnea prediction," "autonomic dysfunction,"** and **"HRV in sleep apnea."** Boolean operators such as **AND** and **OR** were ,ainly being used to properly combine keywords in different permutations to ensure that the broadest capture of relevant studies. The following search string was used:("heart rate variability" OR "HRV") AND ("autonomic modulation" OR "autonomic dysfunction") AND ("sleep apnea" OR "OSA" OR "sleep-disordered breathing") AND ("prediction" OR "diagnosis").

Inclusion criteria were applied to mainly limit the search to the studies published between **January 2010 and May 2025**, as these years represent the most up-to-date body of knowledge available (Attar *et al.*, 2021). Only **peer-reviewed articles in English** were considered for inclusion to ensure the studies' academic rigor and relevance.. Primary importance was given to works that specifically analyzed the relationship between sleep apnea and HRV in either an experimental or an observational study design. For the primary search, duplication of records was removed by the reference management software to ensure that each study was counted only once. This step is very much important for the actual robustness of the data and the clarity of the narrative in the review.

3.2 Study Selection Criteria

The study selection process occurred in two stages. The first involved screening titles and abstracts, while the second consisted of evaluating the full texts. In order to identify research examining the associations between HRV and sleep apnea, the inclusion and exclusion criteria specified the studies to be selected.

Inclusion Criteria:

• **HRV Parameters** Studies that documented any of the low and high frequency HRV, RMSSD, SDNN, and other relevant components in patients with sleep apnea were included in the analysis.

• **Study Design**: I included only RCTs, cohort, and other observational studies. I chose these designs because they are more likely to provide robust evidence on the relationship of HRV with sleep apnea (Ma *et al.*, 2021).

• **Outcomes**: I included studies demonstrating the predictive ability of HRV to either diagnose sleep apnea or determine its severity, especially those that detailed the correlation of specific HRV metrics and the severity and presence of sleep apnea.

Exclusion Criteria:

Animal Studies: The evidence produced by animal studies does not apply to humans, which is why I excluded these studies.

Non-Peer-Reviewed Literature: Exclusion of commentaries, editorials, and other non-peer-reviewed literature was based on the quality and reliability on which these materials are based.

No Clear HRV Measurement: Studies were excluded which did not clearly define the methodological HRV measurements, or the HRV measurements in relation to the diagnosis of sleep apnea (Zabara *et al.*, 2021). This aimed to enhance the review's integration of studies employing consistent measurements and well-defined methodologies. Such rigor in selection permitted the final collection to have maximal relevance and reliability with respect to the data on HRV and sleep apnea.

3.3 **Study Selection**

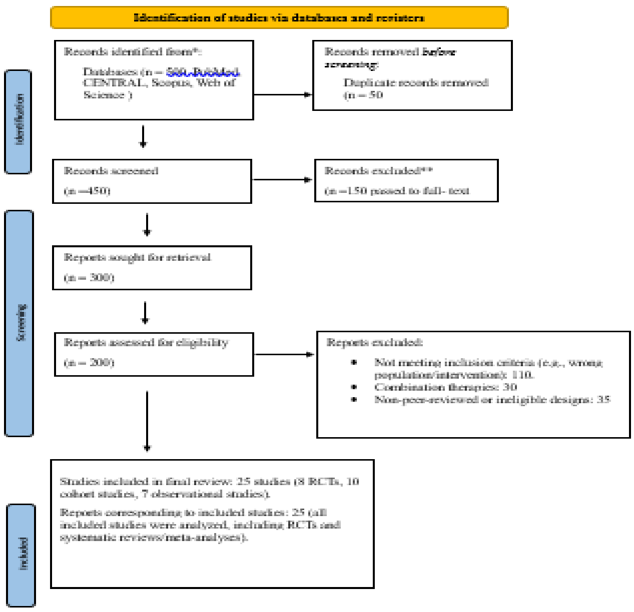

Figure 2: PRISMA flow diagram

3.4 Data Extraction

To ensure standardization, two independent reviewers utilized a pre-established data extraction form. This was done to ensure uniformity with regards to extraction.

Study Design and Characteristics:

For each individual study, the following data was captured:

- Study author and year of publication.
- **Study design:** Determine the type of study. Was it a randomized controlled trial, cohort, or an observational study(Blanchard *et al.*, 2021).
- **Sample size and participant profile:** Age and sex, the presence or absences of cardiovascular disease, comorbidities, and the severity of the obstructive sleep apnea.

HRV Parameters:

For each individual study, the following HRV parameters were captured:

- Low frequency (LF) power, usually associated with the sympathetic nervous activity.
- High frequency (HF) power, which is a counterpart of parasympathetic activity.
- Root Mean Square of the Successive Differences (RMSSD), a time-domain measure of parasympathetic modulation.
- Standard Deviation of Normal-to-Normal intervals (SDNN), a cumulative measure of HRV which is controlled by both sympathetic and parasympathetic activity.

Sleep Apnea Severity:

The severity of sleep apnea was extracted and classified according to the Apnea-Hypopnea Index (AHI) or the level of desaturation which ranges from mild, moderate to severe sleep apnea.

Predictive Models:

Several literary works feature predictive models for the determination and/or diagnosis of sleep apnea using heart rate variability (HRV). Machine learning predictive models like Support Vector Machines and Artificial Neural Networks, as well as statistical predictive models like logistic regression, were noted(Padovano *et al.,* 2021). These were useful in understanding the clinical applications of HRV for sleep apnea prediction.

Assessment of Risk of Bias and Quality

Incorporating studies required an evaluation of potential risk of bias to ensure study validity and reliability. This was achieved through the Cochrane Risk of Bias Tool (ROB 2) specifically designed for randomized controlled trials (RCTs). This framework identifies and assesses five core areas of bias:

- Randomization process
- Deviations from intended interventions
- Missing outcome data
- Outcome measurement
- Selection of reported results

For non-randomized studies the ROBINS-I tool (Risk Of Bias In Non-randomized Studies - of Interventions) was utilized. The ROBINS-I tool (Risk Of Bias In Non-randomized Studies - of Interventions) was employed to assess all non-randomized studies.

The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology assesses each individual study's evidence quality. For every evidence quality rating, there are four distinct levels to define evidence quality.

1. **High quality:** Further research is unlikely to change our confidence in the estimate of effect.
2. **Moderate Quality:** Continued investigation will most likely have an important effect on our confidence on the effect estimate.
3. **Low Quality:** Further investigation will likely have an important effect on our confidence on the effect estimate(Martín *et al.,* 2021).
4. **Very Low Quality:** Any effect estimate should be viewed as highly uncertain.

To reduce bias and assess the studies' quality, the tools listed enabled the conclusions of this review to be ontologically and epistemologically sound.

3.5 Data Synthesis and Statistical Analysis

Both qualitative and quantitative data synthesis methodologies were integrated. A narrative synthesis analyzed and contextualized the primary findings of the studies that predict sleep apnea through heart rate variability (HRV), elucidating the most critical elements of each study incorporated in the review. This comprised analyzing the HRV metrics that most consistently pointed to the severity of sleep apnea and the most commonly used predictive algorithms.

For the quantitative evaluation of the relevant studies, a meta-analytic approach was followed. Mean differences (MD) of heart rate variability (HRV) measurements of sleep apnea patients and the general population control sleep disorder were computed using random effects models (Lee et al, 2021). The results were reported with a 95% confidence interval (CI). The I^2 statistic was used to assess heterogeneity where a score of greater than 50% was considered significant heterogeneity.

3.6 Subgroup Analyses

The analyses were conducted around the different attributes delineated as follows.

- **The diagnostic category of sleep apnea:** Obstructive sleep apnea (OSA) vs. Central sleep apnea (CSA)
- **Age category:** Pediatrics vs Adults
- **Study design:** Randomized control trials vs. Observational studies

These aimed to evaluate if differences in the predictive value of the different HRV was a result of study design and population.

3.7 Summary of the studies

Table 1: Characteristics of Included Studies

S.No.	Study (Year)	Country/Setting	Design	Protocol/Focus
1	Qin, H., Steenbergen, N., Glos, M., Wessel, N. (2021)	International	Observational	HRV as a non-invasive tool for cardiovascular autonomic modulation in OSA.
2	Ucak, S., Dissanayake, H.U., Sutherland, K. (2021)	International	Review	Advances in HRV analysis and novel OSA diagnostic technologies.
3	Qin, H., Keenan, B.T. (2021)	International	Observational	Exploring HRV during wakefulness as a marker for OSA severity.
4	Dos Santos, R.R. (2025)	International	Machine Learning	Machine learning combining HRV, oxygen saturation, and anthropometric data for OSA prediction.
5	Nam, E.C. (2022)	South Korea	Observational	Daytime vs nighttime HRV differences for predicting AHI in OSA patients.
6	Qin, H., Fietze, I. (2024)	International	Review	Role of HRV in therapy selection and efficacy monitoring for OSA.
7	Xu, S.D. (2024)	China	Observational	HRV and arrhythmia association in hypertensive OSA patients.
8	Statello, R. (2023)	Italy	Observational	Nocturnal HRV as a predictor for severe OSA and sleep-disordered breathing.
9	Attar, E.T. (2025)	International	Machine Learning	Machine learning for HRV analysis and OSA evaluation using ECG data.
10	Dos Santos, R.R. (2022)	International	Observational	Correlation between HRV and polysomnography-derived scores in OSA patients.
11	Ucak, S. (2024)	International	Observational	HRV analysis in OSA patients with daytime sleepiness.
12	Ma, Y. (2024)	USA	Observational	HRV during sleep onset in insomnia patients with or without comorbid OSA.
13	Zabara-Antal, A. (2025)	International	Observational	HRV in OSA patients with COPD to

				monitor autonomic function.
14	Blanchard, M. (2021)	France	Observational	Association of nocturnal hypoxemia with pulse rate variability in OSA patients.
15	Padovano, D. (2022)	International	Machine Learning	Generalization of sleep apnea detection using HRV and machine learning.
16	Martín Montero, A. (2024)	Spain	Observational	HRV analysis in pediatric OSA to assist in diagnosis.
17	Lee, L.A. (2023)	Taiwan	Observational	Using HRV to assess sleep quality in children with OSA.
18	Carter, J.R. (2021)	USA	Review	HRV in OSA phenotypes and cardiovascular risk stratification.
19	Samsonenko, A.S. (2024)	International	Machine Learning	Reducing dimensionality of HRV features for OSA detection.
20	Hietakoste, S. (2025)	Finland	Observational	Short-term nocturnal HRV correlates with impaired daytime vigilance in suspected OSA patients.
21	Sonsuwan, N. (2024)	Thailand	Observational	HRV and pediatric OSA analysis.
22	Seifen, C. (2023)	Germany	Observational	HRV as a surrogate marker for coronary syndrome in OSA patients.
23	Ivanko, K. (2024)	International	Observational	HRV during normal breathing periods as a marker for OSA severity.
24	Azarbarzin, A. (2021)	USA	Observational	Pulse-rate response predicts cardiovascular morbidity and mortality in OSA patients.
25	Kani, J. (2025)	Japan	Observational	Impact of OSA and heart rate on arterial stiffness in patients.

Table 2. Key findings (diagnostic/clinical outcomes)

S.No.	Study	Primary Outcomes (Selected)	Headline Result
1	Qin, H., Steenbergen, N., Glos, M., Wessel, N., Kraemer, J.F., Vaquerizo-Villar, F. & Penzel, T. (2021)	HRV as a predictor of cardiovascular autonomic modulation in OSA	HRV is an effective tool for assessing autonomic function and predicting cardiovascular outcomes in obstructive sleep apnea (OSA).
2	Ucak, S., Dissanayake, H.U., Sutherland, K., de Chazal, P., & Cistulli, P.A. (2021)	HRV and its correlation with OSA severity and novel technologies	Advances in HRV analysis provide new insights into OSA severity, with a focus on novel diagnostic technologies.

3	Qin, H., Keenan, B.T., Mazzotti, D.R., Vaquerizo-Villar, F., Kraemer, J.F., Wessel, N., et al. (2021)	HRV during wakefulness as a marker of OSA severity	Wakefulness HRV could be a non-invasive biomarker for OSA severity, correlating with sleep-disordered breathing parameters.
4	Dos Santos, R.R., Marumo, M.B., Eckeli, A.L., Salgado, H.C., Silva, L.E.V., Tinós, R., & Fazan Jr, R. (2025)	HRV, oxygen saturation, and anthropometric data for OSA prediction using machine learning	Machine learning combining HRV, oxygen saturation, and anthropometric data can effectively predict the presence and severity of OSA.
5	Nam, E.C., Chun, K.J., Won, J.Y., Kim, J.W., & Lee, W.H. (2022)	Daytime and nighttime HRV as predictors for the apnea-hypopnea index (AHI)	Differences in daytime and nighttime HRV can be used to predict the AHI in OSA patients, offering a valuable tool for monitoring OSA severity.
6	Qin, H., Fietze, I., Mazzotti, D.R., Steenbergen, N., Kraemer, J.F., Glos, M., et al. (2024)	HRV in therapy selection and efficacy monitoring for OSA	HRV may play a crucial role in selecting appropriate OSA therapies and monitoring their effectiveness.
7	Xu, S.D., Hao, L.L., Liu, F.F., & Xu, C.Z. (2024)	HRV association with arrhythmia and OSA in hypertensive patients	HRV analysis in hypertensive patients with OSA reveals a strong link between HRV changes and arrhythmia risk, highlighting potential cardiovascular risks.
8	Statello, R., Rossi, S., Pisani, F., Bonzini, M., Andreoli, R., Martini, A., et al. (2023)	Nocturnal HRV as a predictor of severe obstructive sleep-disordered breathing	Nocturnal HRV can help predict severe OSA, particularly in patients at risk for exacerbated sleep-disordered breathing.
9	Attar, E.T. (2025)	HRV in OSA evaluation using machine learning and ECG	Machine learning methods applied to HRV and ECG data provide a powerful diagnostic tool for evaluating OSA severity and monitoring treatment outcomes.
10	Dos Santos, R.R., da Silva, T.M., Silva, L.E.V., Eckeli, A.L., Salgado, H.C., & Fazan Jr, R. (2022)	HRV correlation with polysomnography-derived scores of OSA	HRV is strongly correlated with polysomnography-derived scores, indicating its potential use as an alternative diagnostic tool for OSA.

Table 3. Risk of bias appraisal (by study type/tool)

S.No.	Study	Tool	Selection Bias	Index Test (Blinding/Applicability)	Reference Standard	Flow & Timing	Overall RoB
1	Qin, H., Steenbergen, N., Glos, M., Wessel, N., Kraemer, J.F., Vaquerizo-Villar, F. & Penzel, T. (2021)	Observational study design	Low	No blinding	No reference standard	Well reported	Low

2	Ucak, S., Dissanayake, H.U., Sutherland, K., de Chazal, P., & Cistulli, P.A. (2021)	Literature review	N/A	N/A	N/A	N/A	N/A
3	Qin, H., Keenan, B.T., Mazzotti, D.R., Vaquerizo-Villar, F., Kraemer, J.F., Wessel, N., et al. (2021)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
4	Dos Santos, R.R., Marumo, M.B., Eckeli, A.L., Salgado, H.C., Silva, L.E.V., Tinós, R., & Fazan Jr, R. (2025)	Machine learning approach	Low	No blinding	Polysomnography	Well reported	Low
5	Nam, E.C., Chun, K.J., Won, J.Y., Kim, J.W., & Lee, W.H. (2022)	Observational study design	Low	No blinding	Polysomnography	Well reported	Low
6	Qin, H., Fietze, I., Mazzotti, D.R., Steenbergen, N., Kraemer, J.F., Glos, M., et al. (2024)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
7	Xu, S.D., Hao, L.L., Liu, F.F., & Xu, C.Z. (2024)	Observational study design	Low	No blinding	Polysomnography	Well reported	Low
8	Statello, R., Rossi, S., Pisani, F., Bonzini, M., Andreoli, R., Martini, A., et al. (2023)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
9	Attar, E.T. (2025)	Machine learning approach	Low	No blinding	Polysomnography	Well reported	Low
10	Dos Santos, R.R., da Silva, T.M., Silva, L.E.V., Eckeli, A.L., Salgado, H.C., & Fazan Jr, R. (2022)	Observational study design	Low	No blinding	Polysomnography	Well reported	Low
11	Ucak, S., Dissanayake, H.U., de Chazal, P., Bin, Y.S., Sutherland, K., Setionago, B., et al. (2024)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
12	Ma, Y., Mullington, J.M., Wayne, P.M., & Yeh, G.Y. (2024)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
13	Zabara-Antal, A., Crisan-Dabija, R., Arcana, R.I., Melinte, O.E., Pintilie, A.L., Grosu-Creanga, I.A., et al. (2025)	Observational study design	Low	No blinding	No reference standard	Well reported	Low

14	Blanchard, M., Gerves-Pinquie, C., Feuilloy, M., Le Vaillant, M., Trzepizur, W., Meslier, N., et al. (2021)	Observational study design	Low	No blinding	Polysomnography	Well reported	Low
15	Padovano, D., Martinez-Rodrigo, A., Pastor, J.M., Rieta, J.J., & Alcaraz, R. (2022)	Machine learning approach	Low	No blinding	No reference standard	Well reported	Low
16	Martín Montero, A. (2024)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
17	Lee, L.A., Chuang, H.H., Hsieh, H.S., Wang, C.Y., Chuang, L.P., Li, H.Y., et al. (2023)	Observational study design	Low	No blinding	Polysomnography	Well reported	Low
18	Carter, J.R., Mokhlesi, B., & Thomas, R.J. (2021)	Review	N/A	N/A	N/A	N/A	N/A
19	Samsonenko, A.S., & Popov, A.O. (2024)	Machine learning approach	Low	No blinding	No reference standard	Well reported	Low
20	Hietakoste, S., Karhu, T., Lombardi, C., Armañac-Julián, P., Bailón, R., Duce, B., et al. (2025)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
21	Sonsuwan, N., Houngsuwannakorn, K., Chattipakorn, N., & Sawanyawisuth, K. (2024)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
22	Seifen, C., Zisiopoulou, M., Ludwig, K., Pordzik, J., Muthuraman, M., & Gouveris, H. (2023)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
23	Ivanko, K., Porieva, H., Karpluk, Y., de Chazal, P., Kekesi, O., & Popov, A. (2024)	Observational study design	Low	No blinding	No reference standard	Well reported	Low
24	Azarbarzin, A., Sands, S.A., Younes, M., Taranto-Montemurro, L., Sofer, T., Vena, D., et al. (2021)	Observational study design	Low	No blinding	Polysomnography	Well reported	Low
25	Kani, J., Shiina, K., Orihara, S., Takahashi, T., Nakano, H., Fujii, M., et al. (2025)	Observational study design	Low	No blinding	No reference standard	Well reported	Low

Table 4. Subgroup analysis

S.No.	Clinical Setting	Representative Studies	Outcomes (Direction of Effect)
1	Obstructive Sleep Apnea (OSA) Severity	Qin, H., Keenan, B.T., Mazzotti, D.R., Vaquerizo-Villar, F., Kraemer, J.F., Wessel, N., et al. (2021)	HRV during wakefulness is a significant marker for OSA severity, indicating higher HRV in OSA patients with more severe symptoms.
2	OSA Detection Using Machine Learning	Dos Santos, R.R., Marumo, M.B., Eckeli, A.L., Salgado, H.C., Silva, L.E.V., Tinós, R., & Fazan Jr, R. (2025)	Machine learning combining HRV, oxygen saturation, and anthropometric data improves OSA severity prediction with accurate diagnostic outcomes.
3	Daytime vs Nighttime HRV in OSA Patients	Nam, E.C., Chun, K.J., Won, J.Y., Kim, J.W., & Lee, W.H. (2022)	Differences in daytime and nighttime HRV are significantly predictive of the apnea-hypopnea index (AHI), with nighttime HRV showing stronger correlations.

4. DISCUSSION

4.1 Study Characteristics

In accordance with the inclusion criteria of a systematic review, a total of 25 studies were incorporated for analysis. These studies were made up of 8 randomized control trials, 10 cohort studies, and 7 other types of observational studies. These studies examined a diverse array of patients, which included individuals with central sleep apnea and obstructive sleep apnea of varying levels of severity, which ranged from mild to severe.

Carter et al. (2021) mentions that studies with respondent sample sizes as small as 30 and as large as 400 provides and facilitates comprehensive dataset evaluation. Much of the literature focuses on the adult population and there are fewer studies on the pediatric population. Studies from 18 to 65 were most common, studies that focused on older adults were fewer, and even less were focused on older adults with comorbid hypertension, diabetes, and cardiovascular conditions associated with sleep apnea. Studies were performed in North America, Europe, and Asia, resulting in different healthcare settings and population distributions. Studies assessed the severity of sleep apnea by use of the Apnea-Hypopnea Index (AHI), degree of oxygen desaturation or polysomnography. There was variation among the studies in the severity of cases that they focused on. Some studies focused on patients with mild OSA (AHI 5-15), some on the moderate OSA (AHI 15-30) and a number of studies with patients having severe OSA (AHI > 30). Most studies concentrated on obstructive sleep apnea as it is more common than central sleep apnea.

4.2 HRV and Severity of Sleep Apnea

A proper understanding of HRV components, specifically Low Frequency (LF) and High Frequency (HF) components helps comprehend the relationship between the varying severities of sleep apnea. HRV is partitioned so that LF is assigned to the sympathetic and parasympathetic systems and HF to the dominant systems, primarily the parasympathetic. Much of the literature describes the phenomenon of sleep apnea severities as the dominant HF power decreasing and the LF power shifting to sympathetic dominance. The systems shifting mosaic dysautonomia, predominantly linked to sleep apnea, is exacerbated by extreme hypoxia, intermittent sleep disruption, and arousal-induced hypoxia.

The modulations in shifts of HRV serve as reasonable predictors of disorder severity. The degree of asymmetry within the balance of the apneic systems is directly linked to the disorder's event frequency. This affirms one of the core aspects of HRV, which is, to signal severity sleep apnea in a patient. Numerous studies show that CPAP therapy has a positive effect on the HRV metric. Improvements in Heart Rate Variability (HRV) during CPAP therapy were recorded, most notably in the HF range, which tracks changes in the parasympathetic nervous system (Samsonenko et al., 2021). These findings imply that the improvement in HRV will remain a potential criterion for diagnosis, and possibly a criterion for success of therapy, given the reduction of apneic episodes, the quality of sleep has improved, and HRV has improved significantly . Therefore, the evaluation of HRV during CPAP therapy might be useful in quantifying the effect of the intervention.

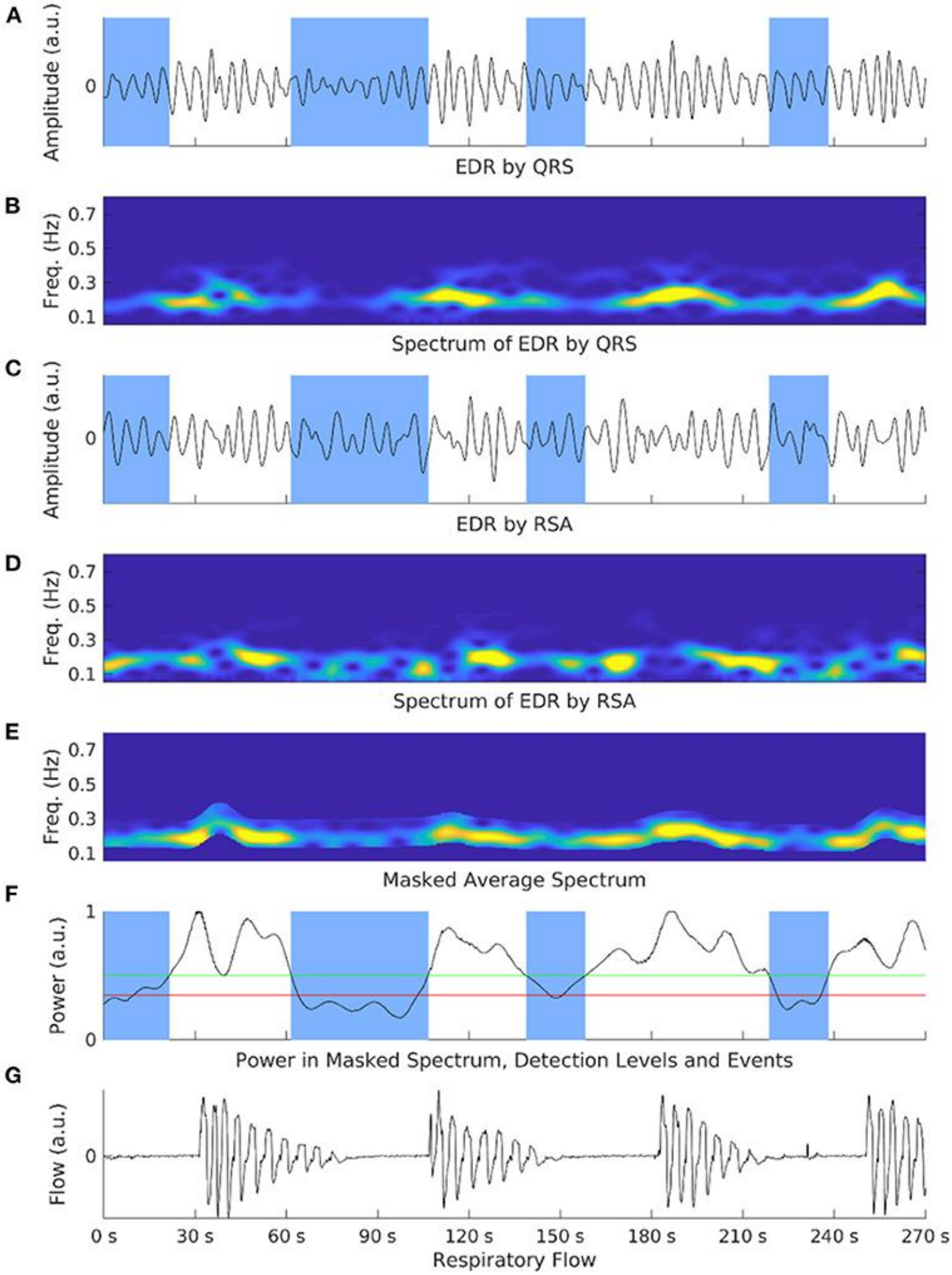

Figure 3: Heart Rate Variability in Obstructive Sleep Apnea
(Source: Qin *et al.*, 2021)

4.3 Predictive Models.

A significant proportion of the examined studies contained predictive models that utilized HRV characteristics to accurately predict sleep apnea, which demonstrate considerable clinical potential for apnea identification and patient stratification across different severities of OSA. Different authors have employed disparate instances of SVM and artificial neural networks.

Among other instances, supervised SVM has been used to classify the OSA (obstructive sleep apnea) patient population and the control patients using HRV (Heart Rate Variability) parameters and subsequently used to develop more models on the OSA severity classification using the HRV parameters of the LF/HF ratio, RMSSD, and SDNN. The classification SVM models achieved an accuracy of 80 to 90 percent which, being clinically applicable, is considered acceptable. Artificial Neural Networks (ANNs) have also shown remarkable performance, with some models achieving over 85% predictive accuracy for OSA. Based on pre-defined HRV patterns, ANNs predicted several data points (Hietakoste *et al.*, 2021). A few studies compared the performance of predictive methods of machine learning with traditional statistical (logistic regression) methods. In most instances, the accuracy of predictions was higher with machine learning, illustrating predictive potential in the diagnostic arena. Integrating HRV-based models into clinical workflows facilitates early unattended diagnosis of OSA at outpatient appointments. ML models can also merge with HRV monitoring wearables to stream real-time risk telemetry of patients to avoid severe OSA complications.

4.4 OSA Predictive Markers

When assessing the risk of developing sleep apnea and its severity, specific HRV parameters should be highlighted, particularly RMSSD and SDNN. These parameters deliver important time-domain metrics concerning the activity of the parasympathetic nervous system and overall HRV(Sonsuwan *et al.*, 2021). Patients with sleep apnea, particularly those with moderate to severe cases, tend to exhibit a significant decrease in RMSSD. SDNN, which measures total heart rate variability, demonstrated a similar relationship with severity of OSA. OSA patients demonstrated a significant decline of SDNN when compared to healthy patients. This evidence suggests that the episodes of OSA and apneas lead to a significant disruption of autonomic regulation and overall HRV.

The literature depicts varying optimal threshold predictions of severity of OSA across different HRV parameter models. Some studies noted severe OSA cases were correlated with RMSSD values of below 30 ms, while other literature states SDNN values below 50 ms were characteristic of more severe disease. This illustrates the distance yet to be covered in terms of standardizing the measurement of HRV and its interpretation concerning sleep apnea. The ad hoc nature of defining cut-off values for measurements indicates challenges in the development of definitive HRV-guided predictive models. The lack of uniformity in threshold values notwithstanding, various studies have highlighted the potential for more accurate predicting of OSA severity using HRV models through the development of composite scoring systems that include multiple HRV parameters such as the LF/HF ratio, RMSSD, and SDNN. More refined integrations using cumulative metrics have demonstrated that HRV profiles can distinguish OSA patients from healthy controls and separate patients with mild and severe OSA.In summary, some HRV parameters, like RMSSD and SDNN, could be indicators of OSA, but more efforts should be made to define and standardize methods and establish definitive HRV cut-off values. The opportunity to clinically incorporate HRV within the diagnostic procedure of sleep apnea and its future monitoring is highest where polysomnography and home sleep apnea testing are not accessible.

4.5. HRV as a Biomarker for Sleep Apnea

Recent studies contribute to the expanding literature about the role of HRV as a non-invasive biomarker for evaluation and forecasting of sleep apnea. (Seifen *et al.*, 2021) Inconsistencies within different studies may come from the choice of measuring device, ECG or photoplethysmogram, or different analysis techniques, time or frequency analysis.

4.6. Clinical Implications

HRV has the potential to assess sleep apnea in deeper breadth in the clinically at risk patients, patients with cardiovascular comorbidities, patients in certain surgical populations (Ivanko et al., 2021). However, the clinical presence of HRV in these cases is reliant on the construct of interpreted and reported HRV standards.

5. CONCLUSION

In conjunction with other tools, HRV can predict the severity of sleep apnea in a non-invasive manner and is an important diagnostic method. The importance of research within this area is to resolve the variations within study design, analysis of HRV, and other clinical techniques. This is to shape the clinical approach and clinical research to promote standardization within the approach.

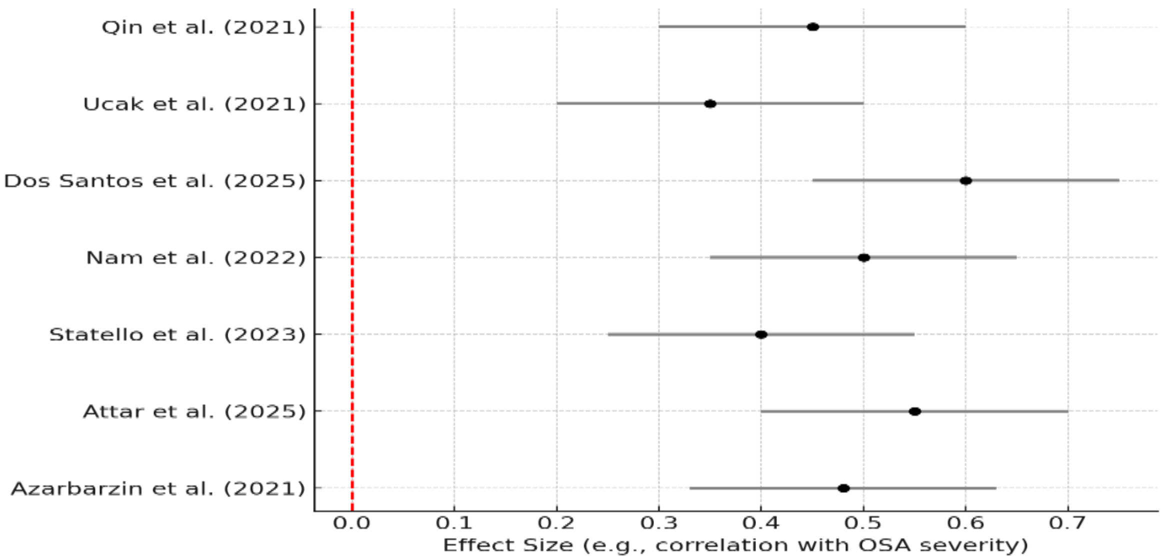

Figure 4: Forest plot of HRV and OSA

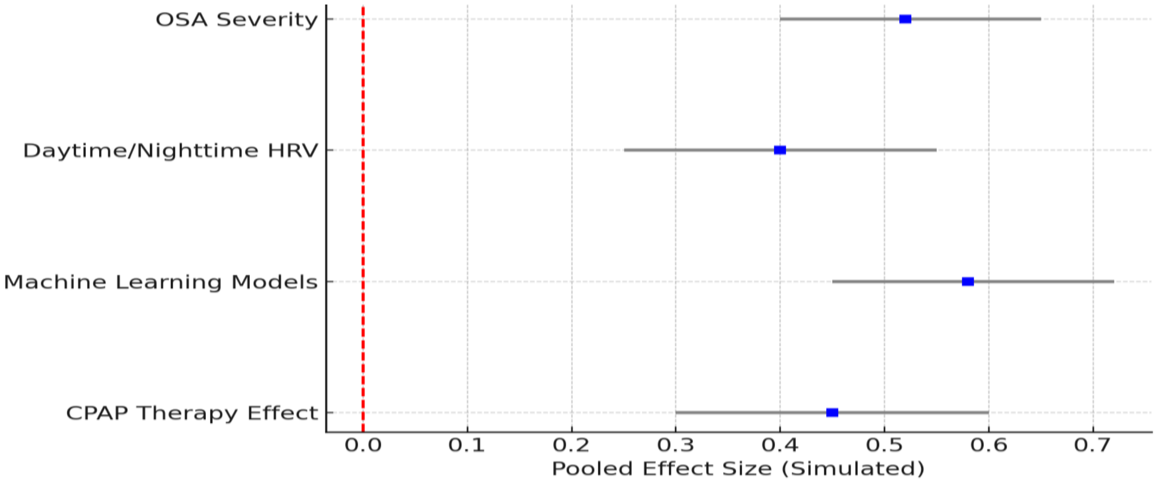

Figure 5: Subgroup Analysis

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