



## The Role of 2-Dimensional and 3-Dimensional Speckle Tracking Echocardiography in Detecting Early Myocardial Dysfunction in Obstructive Sleep Apnea Patients

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### Abstract

**Background:** Obstructive sleep apnea (OSA), a worldwide prevalent sleep-related breathing disorder, is associated with an increased rate of cardiovascular disease (CVD) incidence and higher all-cause mortality. Evidence demonstrates that OSA can contribute to subclinical cardiac damage and lead to a significantly higher risk of future heart failure. Speckle tracking echocardiography (STE) is a new technique that is useful for detecting subclinical dysfunction in patients without clinical manifestations of cardiac problems and who have normal conventional echocardiography. This review examines the application of STE for the early detection of subclinical dysfunction in all four heart chambers of individuals with OSA.

**Methods:** To provide an in-depth overview of the current evidence in this review study, we conducted a broad literature search across 4 major databases—PubMed, Scopus, Embase, and Web of Science—in July 2025. Keywords and combinations related to “speckle tracking echocardiography,” “global longitudinal strain,” “left atrium,” “left ventricle,” “right atrium,” “right ventricle,” and “obstructive sleep apnea” were used to identify relevant studies. We aimed to explore studies examining subtle functional alterations in cardiac chambers among patients with OSA using STE. Systematic reviews, meta-analyses, case reports, abstracts, letters, conference proceedings, and non-English publications were excluded to maintain focus on original research and clinical insights.

**Results:** After screening by title/abstract and full-text review, from a total of 145 studies, 29 were included based on the best match with our inclusion criteria. Our key finding in this systematic review were as follows: (1) left atrium (LA) subclinical systolic and early diastolic strain/strain rate decrease before alteration in conventional echocardiography indexes; (2) left ventricle (LV) early detectable strain/strain rate decrease in all its 3 contracting directions (longitudinal, circumferential, and radial); (3) subtle changes in LV myocardial work index (MWI); (4) valuable information about early strain changes in different directions of RV wall contraction despite its complex geometry.

**Conclusion:** Our study highlighted available studies describing subclinical strain and strain rate alterations in each cardiac chamber through speckle tracking echocardiography and addresses this method’s feasibility to detect early changes in myocardium as a result of OSA.

**Keywords:** Speckle Tracking Echocardiography, Obstructive Sleep Apnea, Strain Value, Strain Rate, Global Longitudinal Strain, Area Strain, Subclinical Dysfunction, LV Torsion

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### ↑What is “already known” in this topic:

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder globally associated with an increased risk of cardiovascular disease and all-cause mortality. Cardiac structural changes, such as left atrial enlargement, are typically detected at later stages using conventional imaging techniques.

### →What this article adds:

This systematic review compiles evidence demonstrating that speckle tracking echocardiography (STE) can detect subclinical strain and strain rate abnormalities in all 4 cardiac chambers in patients with OSA. The findings support the feasibility and utility of STE as a sensitive tool for identifying early myocardial dysfunction before conventional echocardiographic changes become apparent.

## Introduction

Affecting one-seventh of the world's adult population, obstructive sleep apnea (OSA) is a prevalent sleep-related breathing disorder. Obesity, age, and male sex are known as significant risk factors (1, 2). The disorder is characterized by recurrent upper-airway collapse during sleep, leading to intermittent hypoxemia, respiratory arousal, sympathetic activation, and highly negative intrathoracic pressure (3).

OSA is diagnosed by clinical manifestations (such as snoring, central sleep apnea, insomnia, and daytime sleeping), in addition to objective data from a home sleep apnea test (HSAT) or polysomnography study (gold standard) (3, 4). OSA confirms with the apnea-hypopnea index (AHI) or respiratory event index (REI) equal to  $\geq 5$  in the presence of symptoms, or  $\geq 15$  regardless of symptoms (3, 5). The severity of the disease is classified as mild, moderate, or severe when AHI is 5-14, 15-30, and  $>30$ , respectively (6).

A body of evidence indicates an elevated prevalence of cardiovascular disease (CVD) morbidity and mortality, as well as increased all-cause mortality, among patients with OSA. (2, 3). OSA is associated with various CVD complications (eg, systemic hypertension, arrhythmia, cardiac remodeling, pulmonary hypertension, myocardial dysfunction, heart failure, stroke, and sudden cardiac death) (3, 5, 7).

Speckle tracking echocardiography (STE) is a recent noninvasive method for evaluating myocardial function independent of the angle of intonation and translational movement, which is performed in 2-dimensional echocardiography (2DE) and 3-dimensional echocardiography (3DE). Speckles are natural acoustic markers resulting from the interaction between the ultrasound beam and myocardial fibres. The basis of STE is tracking the spatial dislocation of speckles that provides accurate, objective, and quantitative details about the myocardium, especially useful for spotting subclinical dysfunctions. (8, 9). The detection of subclinical myocardial dysfunction is achieved with greater sensitivity through STE than with traditional echocardiographic indices, most notably left ventricular ejection fraction. STE facilitates an objective and angle-independent evaluation of myocardial strain, thereby providing superior accuracy over conventional methods in the early detection of cardiac impairment (10).

Evidence indicates the role of OSA in subclinical cardiac impairment and the significantly higher risk of heart failure in the future (2). Abnormal strain values of cardiac chambers are useful markers for detecting subclinical dysfunction, even in patients with normal chamber volumes and preserved ejection fraction (6). Conventional echocardiography techniques, such as tissue Doppler imaging (TDI), 2DE, and M-mode, are not accurate enough for detecting early changes in strain values. Recently, emerging techniques such as 2D and 3D speckle tracking echocardiography (2DSTE and 3DSTE) have gained interest and are believed to be more sensitive in diagnosing subclinical dysfunction in OSA patients (4, 11-13).

This review aimed to investigate studies on the role of

STE in detecting early and subclinical systolic/diastolic dysfunction of the 4 chambers in patients with OSA.

## Methods

### Search Strategy

We did a broad comprehensive search in databases including, PubMed, Scopus, Embase and Web of Science using the Medical Subject Heading (Mesh) terms and Embase subject headings (Emtree), "speckle tracking echocardiography" OR "global longitudinal strain" AND "Heart Ventricles" OR "left atrium" OR "left ventricle" OR "right atrium" OR "right ventricle" AND "obstructive sleep apnea." A complete keyword list and search strategy are available in detail in the [Appendix 1](#).

A total of 29 studies were eligible for inclusion. We included studies that utilized speckle tracking echocardiography parameters, namely, strain and strain rate, to detect subtle regional myocardial remodeling in each cardiac chamber. Some studies have also investigated further variables, such as area strain and ventricular torsion, as early changes in OSA.

### Inclusion Criteria

(1) Studies that utilize speckle tracking echocardiography (2D/3D) to detect subclinical myocardial dysfunction in OSA patients; (2) studies that investigate each cardiac chamber, respectively, for speckle tracking assessment.

### Exclusion Criteria

(1) Studies that investigated volumetric/pressure/load echocardiographic parameters to detect OSA-related dysfunction, (2) studies with vague conclusions, (3) case reports, systematic reviews, meta-analyses, abstracts, letters, meetings, and non-English studies.

We defined PICO (population, intervention, control, and outcome) as follows:

(P): OSA patients

(I): Speckle tracking echocardiography study

(C): Conventional echocardiography (optional)

(O): Detecting early and subtle myocardial (each heart chamber) dysfunction

## Results

### Left Atrium

During the past decade, studying atrial function has been a hot topic of debate, and left atrial structural and functional remodeling is now a valuable clue in detecting patients prone to cardiovascular disease (14). Obstructive sleep apnea is one of many comorbidities targeting LA through its detrimental acute and chronic effects on myocytes that result in further complications, including atrial fibrillation, heart failure, stroke, and death (15).

Altekin et al demonstrated that the left atrial early diastolic strain rate decreases as OSA progresses to more advanced stages, and there is a significant difference between groups (categorized based on AHI) starting from

moderate OSA. Left atrium systolic strain, left atrium systolic strain rate, and left atrium early diastolic strain rate reduce as OSA gets more severe. Left atrium late diastolic strain and left atrium late diastolic strain rate values have an increasing trend until moderate OSA, and are lower in severe OSA in comparison with the moderate category (16). In a cohort study by Wan et al, including 50 healthy and 92 OSA patients, LA strain assessments showed subclinical changes before left ventricular hypertrophy (LVH) (17). The study cohort was categorized into 2 distinct groups based on left ventricular mass index (OSA with LVH & OSA without LVH). OSA patients exhibited lower systolic strain and early diastolic strain, but higher late diastolic strain, compared to healthy controls. Additionally, LVH aggravates these parameters, causing an extra decline in systolic strain and early diastolic strain in OSA patients (17). In another study, 49 obese patients (BMI  $\geq 25$  kg/m<sup>2</sup>) were examined, and 25 were diagnosed with OSA. Speckle tracking analysis revealed no significant difference in the mean peak late diastolic strain rate between OSA and non-OSA patients. However, the OSA cohort exhibited significantly reduced values for mean peak systolic strain, mean peak systolic strain rate, and early diastolic strain rate compared to the non-OSA group. ( $P = 0.001$ ,  $P = 0.002$  and  $P > 0.001$ , respectively) (18).

There are also studies investigating OSA-induced strain alteration in hypertensive patients and patients with stable cardiovascular disease with decreased ejection fraction. Medeiros et al evaluated speckle tracking indices in different phases of the cardiac cycle among 65 hypertensive patients with and without OSA. In a nutshell, left atrium strain in the reservoir and conduit phase, and also left atrium strain rate in the conduit phase, were lower in OSA patients (19).

Miskowicz et al categorize 32 patients with chronic coronary syndrome and EF < 50% into 2 groups regarding their AHI and measure their STE parameters. Similar to previous studies, the mean left atrial systolic strain rate, early diastolic strain rate, and late diastolic strain rate were significantly lower in the OSA group. Moreover, there was a remarkable correlation between AHI and LA systolic strain ( $r = -0.53$ ,  $P = 0.002$ ), LA systolic strain rate ( $r = -0.47$ ,  $P = 0.006$ ), LA early systolic strain rate ( $r = 0.67$ ,  $P < 0.001$ ), and late diastolic strain rate ( $r = 0.46$ ,  $P = 0.009$ ) (20).

Cetin et al. examined exercise capacity using a treadmill test in 55 OSA patients, divided into 2 groups based on AHI, more or less than 30. Both groups have a higher LA systolic strain rate and early diastolic strain rate after exercise, but exercise time was shorter in the AHI of >30. The strain and strain rate increase in group 2 was lower than in group 1 (AHI <30), and they (AHI >30) showed impaired exercise intolerance due to further diastolic dysfunction (21).

### Right Ventricle

The impact of OSA on RV has been less investigated than that of the LV.

The complex geometry of the right ventricle (RV) presents challenges for accurate measurements using echo-

cardiography (22). The retrosternal position and the unusual geometric shape of the RV, resembling a truncated pyramid, pose difficulties for straightforward geometric analysis or modeling (22). STE is now aiding physicians as an angle/load-independent tool to view this chamber (13, 23).

Buonauro et al demonstrated a significant decrease in RV global longitudinal strain (GLS) and lateral wall strain in patients with OSA compared with healthy controls, whereas other conventional echocardiographic indices of RV systolic function, such as TAPSE and 3D-derived RV ejection fraction, remained normal (24). In a study conducted by Aylin Tugcu et al, 27 patients with moderate to severe OSA were compared to 24 healthy controls in terms of several parameters, including strain and strain rate. The OSA group showed reduced regional long-axis shortening in both basal and mid segments, with a higher emphasis on the correlation of peak systolic strain and strain rate in mid segments with AHI than in basal parts (25). Right ventricular strain and systolic strain rate tend to be lower in moderate and severe OSA groups compared to healthy controls, with an earlier reduction in systolic strain rate value starting from moderate stages (26). On the other hand, a study showed that while there is no difference between regional RV strain and strain rate, apical measurements were substantially decreased in the OSA patients (27). Results of an investigation by Macek et al showed a correlation in which RV free-wall strain (average and mid) and RV septal strain (average, basal, mid, and apex) were significantly lower, along with the severity of the OSA (5). 2D-STE of OSA patients revealed that these patients have both LV and RV subclinical myocardial dysfunction, compared to matched controls (28). Consistent with the abovementioned studies, Vitarelli et al found reduced RVLS and 3D-RVEF and increased volumes along with changes in segmental dyssynchrony (29). As early detection of cardiac remodelling had gained significant attention, Li et al reported early diastolic strain rate deterioration in cases of OSA despite other normal echocardiographic features. They found that the RV peak early diastolic strain rate began to markedly decrease in moderate OSA, followed by a reduction in the peak late diastolic strain rate of RV in later stages (30).

There are also conflicts between experts analyzing RV strain alteration among OSA patients. Hammerstingl et al reported that RV global and regional strain were notably reduced in patients with a higher AHI index. However, after regression analysis of all echocardiographic indices, only apical RV longitudinal strain was correlated with the severity of the disease (31). Additionally, the RV early diastolic strain rate declines as OSA progresses in later stages, while the RV late diastolic strain rate has significantly increased (26).

### Left Ventricle

Detecting subclinical left ventricular remodeling as a result of obstructive sleep apnea with speckle tracking echocardiography has been a highly controversial topic recently. Prior studies have mainly investigated obstructive sleep apnea's effects on left ventricular volumetric altera-

tion and have assessed its dysfunction through ejection fraction (23, 32). These conventional echocardiographic characteristics only highlight ventricular alteration at a point at which significant damage to the myocardium has been occurring, and the patient may not benefit much from available cardioprotective treatments (7).

Speckle tracking echocardiography has surpassed traditional echocardiographic methods in revealing subclinical ventricular changes due to the deleterious effects of OSA.

Altekin et al studied subclinical left ventricular myocardial impairment in a group of OSA patients with normal ejection fraction and without any confounding disease that would affect the myocardium. They utilize 2DSTE to assess systolic and diastolic strain and strain rate with longitudinal, circumferential, and radial parameters. They found that longitudinal, circumferential, and radial strain and strain rates were significantly lower in patients with severe OSA compared to other subgroups and healthy controls. Moreover, they spotted a correlation between the severity of diastolic dysfunction, using the SRE, SRA, and SRE/SRA values in all three directions, and the AHI index. Additionally, another valuable finding in this study was the early decrease in longitudinal strain in moderate OSA patients, despite normal LVEF, circumferential, and radial values (33).

In another study carried out by Altekin et al, the GLS value was assessed in OSA patients with normal ejection fraction, which showed a decreasing trend from moderate to severe OSA. They also evaluated segmental longitudinal strain in basal, mid, and apical segments, and the result showed a significant decrease in severe and moderate OSA groups compared to healthy controls (33).

The left ventricle has a nonhomogeneous wall, which consists of 3 layers of fibres oriented in different directions, and the coordinated contraction of these layers results in a healthy ventricular function. Zhou et al, by the use of 2DSTE, investigated peak systolic strain in 18 cardiac segments to illustrate the left ventricle's early systolic dysfunction in OSA patients despite normal LVEF. At each layer, endocardial strain was higher than mid and epicardial strain values, which is consistent with the fact that endocardial fibers are more prone to ischemia. In this study, 3-layer longitudinal and circumferential strain values were significantly lower in severe OSA patients compared with other groups, while they couldn't find any meaningful comparison between different groups (34).

Speckle tracking imaging can also assess left ventricular twisting motion. LV torsion, calculated by subtracting the maximal apical rotation from the maximal basal rotation, is a parameter that reveals possible diastolic dysfunction. Studies have shown that LVtor is increased in mild diastolic dysfunction as an initial compensation mechanism for the reduced longitudinal contraction, then is followed by LV untwisting in more severe diastolic impairment (35). Vitarelli et al have investigated this notion, along with longitudinal strain, as additional information to reveal early myocardial alterations in OSA. They concluded that severe OSA patients had reduced LV longitudinal strain and increased LVtor. They also demonstrated that peak diastolic untwisting velocity and untwisting rate

were elevated in severe OSAS, as well as the time-to-peak diastolic untwisting velocity (36).

Wang et al investigated subtle left ventricular dysfunction using 3DSTE, a novel echocardiographic method that has overcome the limitations of 2DSTE. What is more, they introduce "area strain" (AS), which reflects a composite of longitudinal and circumferential strain as a new parameter to assess subclinical LV remodelling in patients with OSA. Longitudinal strain and area strain were significantly lower in patients with moderate and severe OSA compared to mild OSA and healthy controls. In contrast, global circumferential and radial strain values were only decreased in severe OSA patients. This finding also highlights the vulnerability of endocardial fibres to ischemia, which includes longitudinal fibres (37).

Also, 2DSTE has been used in detecting overnight left ventricular regional and global mechanics changes. Haruki et al. have noted an acute significant reduction in left ventricular longitudinal strain in a group of 14 OSA patients, while there were no substantial changes in circumferential and radial strain values (12). Moreover, patients in the moderate and severe OSA groups showed a higher absolute change in myocardial strain (12). In a study carried out by Koshino and colleagues, 10 Mueller manoeuvres (MM) each for 12 seconds reduced global strain significantly, and then LV strain was improved immediately in the recovery phase. The aim was to simulate a negative intrathoracic pressure in healthy individuals, similar to what occurs in OSA, using MM, and to investigate possible deformations with 2DSTE. The global strain rate in the early LV filling phase was also significantly decreased during MM (S: baseline,  $-17.0 \pm 1.6\%$ ; MM,  $-14.5 \pm 2.2\%$ ;  $P < 0.0001$ , SR: baseline,  $1.09 \pm 0.20$  s<sup>-1</sup>; MM,  $0.92 \pm 0.21$  s<sup>-1</sup>;  $P = 0.01$ ) (38).

Impaired diastolic function is not uncommon among OSA patients. In a 2020 study by D'Andrea et al, they investigated possible myocardial subtle dysfunction during exercise in OSA patients with a normal ejection fraction. Not surprisingly, OSA patients had lower exercise tolerance and lower oxygen saturation. In addition, the LV global strain increase during physical activity was notably lower among OSA patients with an AHI of moderate and severe subgroups (39).

The potent diagnostic approach to detect early myocardial remodelling through strain and strain rate measurement has been investigated by several studies, as stated in prior paragraphs. Recently, the LV pressure-strain loop (PSL) technique, which is derived from speckle tracking echocardiography, has shown promising results in detecting slight changes in myocardial work indexes. PSL is not influenced by increased afterload and is a more accurate method to detect changes. Jin et al. assessed myocardial work indexes among 200 OSA patients divided by AHI with 2DSTE. They concluded that the assessed global work index (GWI), global constructive work (GCW), and global work efficiency (GWE) were lower in the severe OSA group compared with mild and moderate OSA, and global waste work (GWW) was markedly elevated in severe OSA (7). Moreover, a recent study conducted by Jun-Cheng Ni and colleagues investigated a similar hypothesis

in a group of 50 children with OSA, in which the GWI and GCW of children with OSA were significantly lower than those of healthy controls. Moreover, a negative correlation was observed between OAH1 and GWI ( $\beta = -32.87$ ; 95% CI,  $-53.47$  to  $-12.27$ ) and between OAH1 and GCW ( $\beta = -35.09$ ; 95% CI,  $-55.35$  to  $-14.84$ ) (40).

### Right Atrium

The RA has basic functions such as reservoir role for storing blood while the RV is in contraction, transferring blood from veins to the RV as a conduit in the diastolic phase, filling the RV actively by atrial contraction in the late diastolic phase (about 15% to 25% of the total RV filling volume), and containing sinus node and its importance in the electrical conduction system (40, 41). Recently, studies have put the accent on the predictive value of the RA morphology for clinical events, in advance of the RV (41).

OSA effects on the RA have not been explicated yet, but available data support the possible adverse sequelae in this chamber as a result of OSA (42). OSA is associated with an increased risk of atrial fibrillation, a relationship potentially explained by pro-fibrotic myocardial changes and autonomic dysregulation affecting the atrioventricular node (43-45). Moreover, studies have demonstrated the challenges of rhythm control approaches in patients with both AF and OSA. (46).

Kondratavičienė et al observations of moderate-to-severe OSA patients revealed that the RA diameter was markedly higher compared to the control group (11). RA dilation following increased RV end-diastolic pressure will eventually end in right heart failure. There are limited studies investigating strain changes in the RA of OSA patients through STE (47). A study conducted by Li et al showed RA-global strain and early diastolic RA-strain rate decrease in moderate OSA versus the control group, and these parameters were reduced even further in the severe group. The right atrial strain rate in the ventricular systolic phase (RA-SRs) and right atrial strain rate in the ventricular late diastolic phase (RA-SRa) were lower in severe OSA than those in the control group (RA-SRs: vs control group,  $P = 0.004$ ; vs mild OSAS group,  $P = 0.008$ ; RA-SRa: vs control group,  $P = 0.034$ ) (47). **Figure 1** illustrates the subtle changes in four cardiac chambers detected by STE and the adverse cardiovascular effects in OSA patients who are diagnosed late or poorly managed.

### Discussion

As a disorder involving recurrent hypopnea and apnea during sleep, obstructive sleep apnea contributes significantly to increased cardiovascular disease and mortality rates (48). Repetitive episodes of hypoxia induce apnea-related myocardial alterations due to the imbalance between oxygen supply and demand (28). In the cellular aspect, this hypoxemic, hypercapnic state, along with the ensuing acidosis, will activate the sympathetic nervous system, which has negative multisystemic impacts (16). Deleterious inflammatory, neurohumoral, and mechanical mechanisms cause myocardial fibrosis, resulting in com-

plications such as atrial fibrillation or worsening of heart failure (5, 45).

Considering all the destructive effects of OSA on healthy individuals or those with preexisting comorbidities, early detection of subtle myocardial remodeling is now gaining special attention among experts. Conventional echocardiography could detect flawed systolic or diastolic cardiac function in a stage where the heart has been through volumetric and overt functional conversion, and researchers have shown that a normal ejection fraction does not provide convincing data to rule out cardiac damage (6). Recently, experts have been seeking novel noninvasive imaging methods to identify early changes. This issue has substantial importance as early intervention could benefit patients to an appreciable degree, and also detecting minimal changes could help to estimate treatment efficacy (28). In this regard, speckle tracking echocardiography has shown promising results by assessing the strain and strain rate of each chamber in distinct cardiac cycles(49). With this angle-independent, easily reproduced, and sensitive cardiac imaging tool, a layer-specific evaluation of exquisite changes in myocardial fibres arranged as longitudinal, circumferential, and radial patterns could be performed (6). Moreover, left ventricular twisting motion assessment and recently investigated myocardial work parameters could all be measured with STE (36).

Limited information is available about OSA's influence on the right atrium. RA's irregular shape can best be studied via the STE technique, enabling regional assessment of this chamber. The global strain rate and early diastolic longitudinal strain rate of RA are reduced in moderate OSA, representing initial dysfunction in the reservoir and conduit phases of the right atrium. Further decrease in RA-GLS and RA-SRe happens in severe OSA, plus a reduction in systolic longitudinal strain rate and late diastolic longitudinal strain rate of the right atrium. Moreover, RA-GLS and RA-SRe were established as independent determinants of OSAS severity (47). RA reservoir and conduit functions progressively declined while booster pump function increased from normal to concentric hypertrophy, with speckle-tracking confirming that altered left ventricular geometry significantly impacts RA phasic function in OSA patients (50).

The anterior position of the right ventricle in the chest, its complex geometry, and also its combined myocardial fibres with the left ventricle in the interventricular septum make it hard to assess this chamber with reliable measures, which is why the right ventricle is being recalled as "forgotten chamber" (13). Combining quantitative and qualitative estimates using STE is now becoming the gold standard in assessing RV subtle changes in OSA. The RV dysfunction could be due to increased systolic pulmonary arterial pressure and rapid changes in preload during apnea/hypopnea episodes (29). Other mechanisms involved could be oxidative stress, increased sympathetic nervous activity, elevated blood pressure leading to increased afterload, and higher preload due to increased end-diastolic volume (6, 30). Moreover, while the effect of OSA on RV dysfunction was primarily attributed to

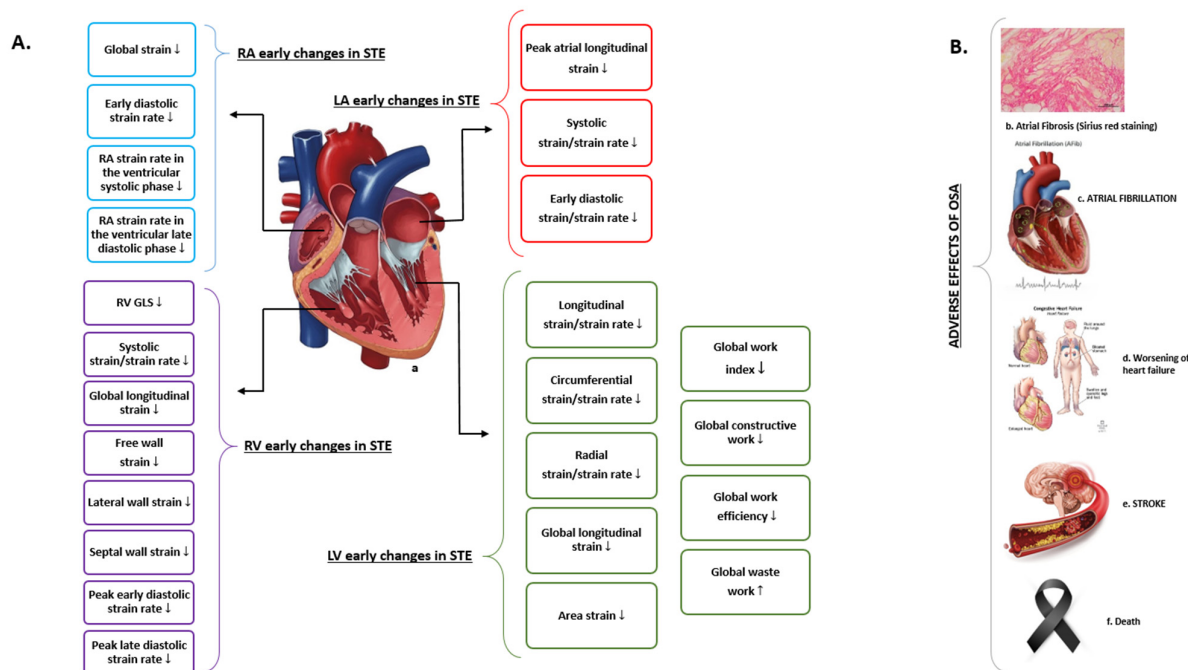


Figure 1. A. Schematic illustration summarizing OSA subtle changes in each cardiac chamber detected via speckle tracking echocardiography. B. OSA has debilitating consequences if diagnosed late and not managed properly

hypoxemia during the daytime because of the lung disease (31), it has been recently found that the difference remained even after adjusting for hypoxemia (32). Heart failure, pulmonary hypertension, and increased cardiovascular morbidity and mortality are common side effects of OSA on the RV(24, 48). Several studies concluded that RV longitudinal strain and strain rate have a predictive value in identifying subtle changes. An essential issue while evaluating RV mechanics is to know the indispensable effect of LV dysfunction on interventricular septum fibres, and consider free wall fibres as our target (4, 15).

Almost all studies demonstrated that RV GLS and RV free wall strain significantly decreased as OSA progressed, and this was before noticeable alterations of other echocardiographic parameters (51). Chetan et al found an independent association between RV GLS with systolic pulmonary arterial pressure and OSA severity, while other RV function qualifying parameters were in a normal range (4). Hammerstingl states the same conclusion, that RV GLS is significantly impaired in severe OSA (31). However, there is also a controversy with Altekin's study, where they didn't find a meaningful correlation between RV GLS and CPAP (24, 26). RV diastolic function is influenced at earlier stages, causing an early diastolic strain rate decrease in moderate OSA, followed by a decrease in peak late diastolic strain rate at later stages (30).

Left ventricular remodelling as a result of OSA side effects eventually causes left atrial damage(17, 18). Peak atrial longitudinal strain in the left atrium is usually impaired in OSA patients (52). LA remodelling due to altered filling pressures causes a reduction in LA passive function, LA longitudinal stretching (reduction in mean

peak systolic strain and strain rate), and passive contraction compliance (reduction in mean peak early diastolic strain rate) (18).

Assessing left ventricular strain and strain rate via STE has shown promising results in identifying subtle LV changes even in patients with normal ejection fraction and volumetric indexes. The layer-specific myocardial evaluation showed earlier destruction of longitudinal fibres located in the endocardial layer being most sensitive to ischemia during apnea episodes in OSA (34). Providing precise measurement of both regional and global strain and strain rates of about 18 segments of the left ventricle in a single beat, qualitative and quantitative evaluation of longitudinal, circumferential, radial and area strains and also left ventricle's twisting motions are all distinctive elements of STE (34, 36) Altekin et al demonstrated a decreasing trend of longitudinal strain and strain rate values as OSA progresses. Moreover, the late diastolic strain rate of circumferential and radial fibres started to increase from moderate disease stages (53). Other studies confirm a global longitudinal decrease as OSA progresses, starting in moderate stages (33). Area strain was a new parameter indicating longitudinal and circumferential strain as a compound, which was demonstrated to be lower in moderate and severe OSA in comparison with mild OSA and healthy controls (37). STE was also able to show acute strain changes during MM, which resemble negative intrathoracic pressure. Global left ventricular longitudinal strain in systole and strain rate in early filling were markedly reduced during the MM (38). Recent studies are now investigating the possible role of myocardial work indexes in detecting early myocardial remodelling. A study con-

ducted in a group of 34 children with OSA, compared with healthy controls, reported significantly lower GLS, GWI, and GCW in the OSA group. A significant inverse relationship was observed between disease severity and both GWI and GCW in the multiple linear regression model, indicating a deterioration in myocardial efficiency with advancing disease (54).

Despite its clinical value, the widespread application of STE is confronted by several obstacles. These include variability in strain measurements across various vendors, the need for high-quality images, operator expertise, and limited availability in some centers. Additionally, the cost of advanced software and equipment may restrict routine use in resource-limited settings (55).

A notable limitation of this review is the clinical and methodological heterogeneity across the included studies. Differences in OSA severity classification (e.g., varying AHI thresholds), patient comorbidities, echocardiographic modalities (2D vs 3D STE), software platforms, and the specific strain parameters assessed (longitudinal, circumferential, radial, area strain, myocardial work indices) may affect the consistency and comparability of results. While a formal heterogeneity analysis was not performed due to the narrative nature of this review, these variations have been acknowledged and qualitatively addressed in each section. This highlights the need for future studies to use standardized imaging protocols and uniform strain measurement criteria, thereby enhancing reproducibility and clinical applicability.

All in all, despite limitations and several confounding comorbidities affecting OSA prognosis, speckle tracking echocardiography showed promising diagnostic ability to detect subtle myocardial changes in OSA patients. With this method, patients will hopefully be able to receive available treatments for OSA earlier. This will benefit both patients and the healthcare system to a considerable extent, resulting in a significant decrease in cardiovascular morbidity and mortality.

### Conclusion

This review highlights the value of STE in detecting subclinical myocardial changes across OSA stages, often preceding structural cardiac alterations. The observed correlation between OSA severity and strain parameters supports STE as a promising tool for early diagnosis and intervention. Additional studies are needed to standardize its clinical application.

### Authors' Contributions

Conception and design: M.B; Collection and assembly of data: Y.M.K. and A.H.M; Data interpretation: Y.M.K., A.H.M., and M.B; Manuscript writing: Y.M.K. and A.H.M; Reviewing and commenting on manuscript: M.B. and S.E. Final approval of manuscript: All authors.

### Ethical Considerations

Not applicable.

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### Conflict of Interests

The authors declare that they have no competing interests.

### References

1. Lyons MM, Bhatt NY, Pack AI, Magalang UJ. Global burden of sleep-disordered breathing and its implications. *Respirology*. 2020;25(7):690-702.
2. Tadic M, Gherbesi E, Faggiano A, Sala C, Carugo S, Cuspidi C. Obstructive sleep apnea and right ventricular function: A meta-analysis of speckle tracking echocardiographic studies. *J Clin Hypertens (Greenwich)*. 2022;24(10):1247-54.
3. Redline S, Azarbarzin A, Peker Y. Obstructive sleep apnoea heterogeneity and cardiovascular disease. *Nat Rev Cardiol*. 2023;20(8):560-73.
4. Chetan IM, Gergely-Domokos B, Beyer R, Tomoaia R, Cabau G, Vulturar D, et al. The role of 3D speckle tracking echocardiography in the diagnosis of obstructive sleep apnea and its severity. *Sci Rep*. 2022;12(1):22347.
5. Macek P, Poręba M, Stachurska A, Martynowicz H, Mazur G, Gać P, et al. Obstructive Sleep Apnea and Sleep Structure Assessed in Polysomnography and Right Ventricular Strain Parameters. *Brain Sci*. 2022;12(3).
6. Sascău R, Zota IM, Stătescu C, Boișteanu D, Roca M, Maștaleru A, et al. Review of Echocardiographic Findings in Patients with Obstructive Sleep Apnea. *Can Respir J*. 2018;2018:1206217.
7. Jin S, Ding X, Guo D, Qin Y, Zhu W, Zhao Z, et al. Subclinical left ventricular myocardial dysfunction in patients with obstructive sleep apnea syndrome: insights from noninvasive left ventricular myocardial work analysis. *BMC Cardiovasc Disord*. 2022;22(1):552.
8. Bansal M, Kasliwal RR. How do I do it? Speckle-tracking echocardiography. *Indian Heart J*. 2013;65(1):117-23.
9. Mondillo S, Galderisi M, Mele D, Cameli M, Lomoriello VS, Zaca V, et al. Speckle-tracking echocardiography: a new technique for assessing myocardial function. *J Ultrasound Med*. 2011;30(1):71-83.
10. Mor-Avi V, Lang RM, Badano LP, Belohlavek M, Cardim NM, Derumeaux G, et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. *J Am Soc Echocardiogr*. 2011;24(3):277-313.
11. Kondratavičienė L, Tamulėnaitė E, Vasylyė E, Januškevičius A, Ereminienė E, Malakauskas K, et al. Changes in Left Heart Geometry, Function, and Blood Serum Biomarkers in Patients with Obstructive Sleep Apnea after Treatment with Continuous Positive Airway Pressure. *Medicina (Kaunas)*. 2022;58(11).
12. Haruki N, Takeuchi M, Kanazawa Y, Tsubota N, Shintome R, Nakai H, et al. Continuous positive airway pressure ameliorates sleep-induced subclinical left ventricular systolic dysfunction: demonstration by two-dimensional speckle-tracking echocardiography. *Eur J Echocardiogr*. 2010;11(4):352-8.
13. Chetan IM, Domokos Gergely B, Albu A, Tomoaia R, Todea DA. Understanding the role of echocardiography in patients with obstructive sleep apnea and right ventricular subclinical myocardial dysfunction - comparison with other conditions affecting RV deformation. *Med Ultrason*. 2021;23(2):213-9.
14. Inciardi RM, Rossi A. Left atrium: a forgotten biomarker and a potential target in cardiovascular medicine. *Journal of Cardiovascular Medicine*. 2019;20(12).
15. Mandoli GE, Borrelli C, Cameli M, Mondillo S, Ghiadoni L, Taddei C, et al. Speckle tracking echocardiography in heart failure development and progression in patients with apneas. *Heart Failure Reviews*. 2022;27(5):1869-81.
16. Altekin RE, Yanikoglu A, Karakas MS, Ozel D, Kucuk M, Yilmaz H, et al. Assessment of left atrial dysfunction in obstructive sleep apnea patients with the two dimensional

- speckle-tracking echocardiography. *Clin Res Cardiol.* 2012;101(6):403-13.
17. Wan Q, Xiang G, Xing Y, Hao S, Shu X, Pan C, et al. Left atrial dysfunction in patients with obstructive sleep apnea: a combined assessment by speckle tracking and real-time three-dimensional echocardiography. *Ann Palliat Med.* 2021;10(3):2668-78.
  18. Kim SM, Cho KI, Kwon JH, Lee HG, Kim TI. Impact of obstructive sleep apnea on left atrial functional and structural remodeling beyond obesity. *Journal of Cardiology.* 2012;60(6):475-83.
  19. Medeiros MA, Lins-Filho OL, Patriota T, Del Castillo JM, Silveira CAM, de Albuquerque ES, et al. Abnormal atrial function in hypertensive patients with obstructive sleep apnea assessed by speckle tracking echocardiography. *Hypertens Res.* 2020;43(8):841-4.
  20. Miśkowiec D, Karolina K, Michalski BW, Uznańska-Loch B, Kurpesa M, Kasprzak JD, et al. Left Atrial Dysfunction Assessed by Two-Dimensional Speckle Tracking Echocardiography in Patients with Impaired Left Ventricular Ejection Fraction and Sleep-Disordered Breathing. *Echocardiography.* 2016;33(1):38-45.
  21. Çetin S, Vural M, Akdemir R, Fırat H. Left atrial remodelling may predict exercise capacity in obstructive sleep apnoea patients. *Acta Cardiologica.* 2018;73(5):471-8.
  22. Kosiborod M, Th Wackers FJ. Assessment of Right Ventricular Morphology and Function. *Semin Respir Crit Care Med.* 2003;24(03):245-62.
  23. Tadic M, Cuspidi C, Grassi G, Mancina G. Obstructive sleep apnea and cardiac mechanics: how strain could help us? *Heart Fail Rev.* 2021;26(4):937-45.
  24. Buonauro A, Galderisi M, Santoro C, Canora A, Bocchino ML, Lo Iudice F, et al. Obstructive sleep apnoea and right ventricular function: A combined assessment by speckle tracking and three-dimensional echocardiography. *Int J Cardiol.* 2017;243:544-9.
  25. Tugcu A, Yildirimtürk O, Tayyareci Y, Demiroglu C, Aytekin S. Evaluation of subclinical right ventricular dysfunction in obstructive sleep apnea patients using velocity vector imaging. *Circ J.* 2010;74(2):312-9.
  26. Altekin RE, Karakas MS, Yanikoglu A, Ozel D, Ozbudak O, Demir I, et al. Determination of right ventricular dysfunction using the speckle tracking echocardiography method in patients with obstructive sleep apnea. *Cardiol J.* 2012;19(2):130-9.
  27. Güvenç TS, Hüseyinoğlu N, Özben S, Kul Ş, Çetin R, Özen K, et al. Right ventricular geometry and mechanics in patients with obstructive sleep apnea living at high altitude. *Sleep Breath.* 2016;20(1):5-13.
  28. D'Andrea A, Martone F, Liccardo B, Mazza M, Annunziata A, Di Palma E, et al. Acute and Chronic Effects of Noninvasive Ventilation on Left and Right Myocardial Function in Patients with Obstructive Sleep Apnea Syndrome: A Speckle Tracking Echocardiographic Study. *Echocardiography.* 2016;33(8):1144-55.
  29. Vitarelli A, Terzano C, Saponara M, Gaudio C, Mangieri E, Capotosto L, et al. Assessment of Right Ventricular Function in Obstructive Sleep Apnea Syndrome and Effects of Continuous Positive Airway Pressure Therapy: A Pilot Study. *Can J Cardiol.* 2015;31(7):823-31.
  30. Li J, Lin X, Li H, Lu C, Li R, Liu W, et al. Right ventricular diastolic dysfunction in patients with obstructive sleep apnea syndrome. *Echocardiography.* 2020;37(2):317-22.
  31. Hammerstingl C, Schueler R, Wiesen M, Momcilovic D, Pabst S, Nickenig G, et al. Impact of untreated obstructive sleep apnea on left and right ventricular myocardial function and effects of CPAP therapy. *PLoS One.* 2013;8(10):e76352.
  32. Cuspidi C, Tadic M. Obstructive sleep apnea and left ventricular strain: Useful tool or fancy gadget? *J Clin Hypertens (Greenwich).* 2020;22(1):120-2.
  33. Altekin RE, Yanikoglu A, Karakas MS, Ozel D, Yıldırım AB, Kabukçu M. Evaluation of subclinical left ventricular systolic dysfunction in patients with obstructive sleep apnea by automated function imaging method; an observational study. *Anadolu Kardiyol Derg.* 2012;12(4):320-30.
  34. Zhou NW, Shu XH, Liu YL, Shen H, Li WJ, Gong X, et al. A Novel Method for Sensitive Determination of Subclinical Left-Ventricular Systolic Dysfunction in Subjects With Obstructive Sleep Apnea. *Respir Care.* 2016;61(3):366-75.
  35. van Dalen BM, Soliman OI, Vletter WB, ten Cate FJ, Geleijnse ML. Age-related changes in the biomechanics of left ventricular twist measured by speckle tracking echocardiography. *Am J Physiol Heart Circ Physiol.* 2008;295(4):H1705-11.
  36. Vitarelli A, D'Orazio S, Caranci F, Capotosto L, Rucos R, Iannucci G, et al. Left ventricular torsion abnormalities in patients with obstructive sleep apnea syndrome: an early sign of subclinical dysfunction. *Int J Cardiol.* 2013;165(3):512-8.
  37. Wang D, Ma GS, Wang XY, Lu QQ, Wang Y, Liu NF. Left ventricular subclinical dysfunction associated with myocardial deformation changes in obstructive sleep apnea patients estimated by real-time 3D speckle-tracking echocardiography. *Sleep Breath.* 2016;20(1):135-44.
  38. Koshino Y, Villarraga HR, Orban M, Bruce CJ, Pressman GS, Leinveber P, et al. Changes in left and right ventricular mechanics during the Mueller maneuver in healthy adults: a possible mechanism for abnormal cardiac function in patients with obstructive sleep apnea. *Circ Cardiovasc Imaging.* 2010;3(3):282-9.
  39. D'Andrea A, Canora A, Sperlongano S, Galati D, Zanotta S, Polistina GE, et al. Subclinical impairment of dynamic left ventricular systolic and diastolic function in patients with obstructive sleep apnea and preserved left ventricular ejection fraction. *BMC Pulm Med.* 2020;20(1):76.
  40. D'Alto M, D'Andrea A, Di Salvo G, Scognamiglio G, Argiento P, Romeo E, et al. Right atrial function and prognosis in idiopathic pulmonary arterial hypertension. *Int J Cardiol.* 2017;248:320-5.
  41. Li J, Lu C, Wang W, Gong K, Zhao L, Wang Z. Assessment of right atrium dysfunction in patients with obstructive sleep apnea syndrome using velocity vector imaging. *Cardiovascular Ultrasound.* 2018;16(1).
  42. Dimitri H, Ng M, Brooks AG, Kuklik P, Stiles MK, Lau DH, et al. Atrial remodeling in obstructive sleep apnea: implications for atrial fibrillation. *Heart Rhythm.* 2012;9(3):321-7.
  43. Leung RS, Bowman ME, Diep TM, Lorenzi-Filho G, Floras JS, Bradley TD. Influence of Cheyne-Stokes respiration on ventricular response to atrial fibrillation in heart failure. *J Appl Physiol (1985).* 2005;99(5):1689-96.
  44. Sin DD, Fitzgerald F, Parker JD, Newton G, Floras JS, Bradley TD. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. *Am J Respir Crit Care Med.* 1999;160(4):1101-6.
  45. Cameli M, Lisi M, Righini FM, Massoni A, Natali BM, Focardi M, et al. Usefulness of atrial deformation analysis to predict left atrial fibrosis and endocardial thickness in patients undergoing mitral valve operations for severe mitral regurgitation secondary to mitral valve prolapse. *Am J Cardiol.* 2013;111(4):595-601.
  46. Ng CY, Liu T, Shehata M, Stevens S, Chugh SS, Wang X. Meta-analysis of obstructive sleep apnea as predictor of atrial fibrillation recurrence after catheter ablation. *Am J Cardiol.* 2011;108(1):47-51.
  47. Li J, Lu C, Wang W, Gong K, Zhao L, Wang Z. Assessment of right atrium dysfunction in patients with obstructive sleep apnea syndrome using velocity vector imaging. *Cardiovasc Ultrasound.* 2018;16(1):32.
  48. Tadic M, Cuspidi C. Obstructive Sleep Apnea and Right Ventricular Remodeling: Do We Have All the Answers? *J Clin Med.* 2023;12(6).
  49. Hunt TEF, Traaen GM, Aakerøy L, Massey RJ, Bendz C, Øverland B, et al. Cardiac remodelling in patients with atrial fibrillation and obstructive sleep apnoea. *Open Heart.* 2024;11(2).
  50. Zhang Y, Xing XQ, Zhang ZX, Li J, Wang J. Multimodal echocardiography for assessing whether left ventricular geometry affects right atrial phasic function in patients with obstructive sleep apnea syndrome: A cross-sectional observational study. *J Clin Ultrasound.* 2024;52(7):883-96.
  51. Tadic M, Gherbesi E, Faggiano A, Sala C, Carugo S, Cuspidi C. Obstructive sleep apnea and right ventricular function: A meta-analysis of speckle tracking echocardiographic studies. *J Clin Hypertens.* 2022;24(10):1247-54.
  52. Mandoli GE, Borrelli C, Cameli M, Mondillo S, Ghiadoni L,

- Taddei C, et al. Speckle tracking echocardiography in heart failure development and progression in patients with apneas. *Heart Fail Rev.* 2022;27(5):1869-81.
53. Altekin RE, Yanikoglu A, Baktir AO, Karakas MS, Ozel D, Cilli A, et al. Assessment of subclinical left ventricular dysfunction in obstructive sleep apnea patients with speckle tracking echocardiography. *Int J Cardiovasc Imaging.* 2012;28(8):1917-30.
54. Ni JC, Zhang F, Xu WQ, Hu XL, Zhao XY, Sun YW, et al. Role of automated functional imaging and myocardial work in assessment of cardiac function in children with obstructive sleep apnea. *Int J Cardiovasc Imaging.* 2024.
55. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging.* 2015;16(1):1-11.

## Echocardiography in Detecting Early Myocardial Dysfunction in Obstructive Sleep Apnea Patients

### Appendix 1. Search details (3/30/2024)

PUBMED	QUERY	RESULTS
#1	("Global Longitudinal Strain"[mesh] OR speckle tracking echocardiography[tiab] OR strain[tiab] OR strain rate[tiab] OR global longitudinal strain*[tiab] OR circumferential strain*[tiab] OR horizontal strain*[tiab])	564,179
#2	("Heart Ventricles"[mesh] OR "Heart atria"[mesh] OR "Right ventricle"[mesh] OR "Left ventricle"[mesh] OR "Right atrium"[mesh] OR "Left atrium"[mesh] OR "Myocardium"[mesh] OR Heart Ventricles[tiab] OR Right ventricle[tiab] OR Left ventricle[tiab] OR Right atrium [tiab] OR Left atrium[tiab] OR Cardiac ventricle[tiab] OR Myocardium[tiab] OR Heart muscle[tiab])	425,232
#3	("Sleep Apnea, Obstructive"[mesh] OR obstructive apnea syndrome[tiab] OR obstructive apnea* during sleep[tiab] OR obstructive sleep apnea hypopnea syndrome[tiab] OR obstructive sleep disordered breathing[tiab] OR OSAHS[tiab] OR Upper Airway Resistance Sleep Apnea Syndrome[tiab])	33,322
#1 AND #2 AND #3		34
EMBASE	QUERY	RESULTS
#1	('speckle tracking echocardiography'/exp OR 'global longitudinal strain'/exp OR 'speckle tracking echocardiography':ab,ti OR 'strain':ab,ti OR 'strain rate':ab,ti OR 'global longitudinal strain*':ab,ti OR 'circumferential strain*':ab,ti OR 'horizontal strain*':ab,ti)	632,792
#2	('Right ventricle'/exp OR 'Left ventricle'/exp OR 'Right atrium '/exp OR 'Left atrium'/exp OR 'Heart Ventricles':ab,ti OR 'Right ventricle':ab,ti OR 'Left ventricle':ab,ti OR 'Right atrium ':ab,ti OR 'Left atrium':ab,ti OR 'Cardiac ventricle':ab,ti OR 'Myocardium':ab,ti OR 'Heart muscle':ab,ti)	361,430
#3	('obstructive sleep apnea'/exp OR 'obstructive apnea syndrome':ab,ti OR 'obstructive apnea* during sleep':ab,ti OR 'obstructive sleep apnea hypopnea syndrome':ab,ti OR 'obstructive sleep disordered breathing':ab,ti OR 'OSAHS':ab,ti OR 'Upper Airway Resistance Sleep Apnea Syndrome':ab,ti)	20,205
#1 AND #2 AND #3		47
Scopus	QUERY	RESULTS
#1	(TITLE-ABS ("speckle tracking echocardiography" OR "strain" OR "strain rate" OR "global longitudinal strain*" OR "circumferential strain*" OR "horizontal strain*"))	1,926,378
#2	(TITLE-ABS ("Heart Ventricles" OR "Heart atria" OR "Right ventricle" OR "Left ventricle" OR "Right atrium" OR "Left atrium" OR "Cardiac ventricle" OR "Myocardium" OR "Heart muscle"))	221,720
#3	(TITLE-ABS ("Sleep Apnea, Obstructive" OR "obstructive sleep apnea" OR "obstructive apnea syndrome" OR "obstructive apnea* during sleep" OR "obstructive sleep apnea hypopnea syndrome" OR "obstructive sleep disordered breathing" OR "OSAHS" OR "Upper Airway Resistance Sleep Apnea Syndrome"))	47,817
#1 AND #2 AND #3		28
Web of sciences	QUERY	RESULTS
#1	(TS= ("speckle tracking echocardiography" OR "strain" OR "strain rate" OR "global longitudinal strain*" OR "circumferential strain*" OR "horizontal strain*"))	1,265,660
#2	(TS= ("Heart Ventricles" OR "Heart atria" OR "Right ventricle" OR "Left ventricle" OR "Right atrium" OR "Left atrium" OR "Cardiac ventricle" OR "Myocardium" OR "Heart muscle"))	196,413
#3	(TS= ("Sleep Apnea, Obstructive" OR "obstructive sleep apnea" OR "obstructive apnea syndrome" OR "obstructive apnea* during sleep" OR "obstructive sleep apnea hypopnea syndrome" OR "obstructive sleep disordered breathing" OR "OSAHS" OR "Upper Airway Resistance Sleep Apnea Syndrome"))	52,130
#1 AND #2 AND #3		36