Continuous Positive Airway Pressure Therapy Reduces Right Ventricular Volume in Patients with Obstructive Sleep Apnea: A Cardiovascular Magnetic Resonance Study

Ulysses J. Magalang, M.D.1,2; Kathryn Richards, B.A.1; Beth McCarthy, R.T.1,3; Ahmed Fathala, M.D.1,4; Meena Khan, M.D.2; Narasimham Parinandi, Ph.D.2,5; Subha V. Raman, M.D., M.S.E.E.1,3

1Division of Cardiovascular Medicine, 2Division of Pulmonary, Allergy, Critical Care, and Sleep Medicine, 3Dorothy M. Davis Heart and Lung Research Institute, The Ohio State University, Columbus, Ohio

Study Objectives. There are few data on the effects of continuous positive airway pressure (CPAP) therapy on the structural and functional characteristics of the right heart in patients with obstructive sleep apnea (OSA). We sought to leverage the advantages of cardiac magnetic resonance imaging (CMR) and hypothesized that CPAP treatment would improve right ventricular (RV) function in a group of patients with OSA who were free of other comorbid conditions.

Methods. Patients with severe (apnea-hypopnea index ≥ 30/h) untreated OSA were prospectively enrolled. CMR included 3-dimensional measurement of biventricular size and function, and rest/stress myocardial perfusion and was performed at baseline and after 3 months of CPAP therapy.

Results. Fifteen patients with mild to moderate desaturation were enrolled; 2 could not undergo CMR due to claustrophobia and obesity. There were significant decreases in the Epworth Sleepiness Scale score (p < 0.0001) and RV end-systolic and RV end-diastolic volumes (p < 0.05) with CPAP. There was a trend toward improvement in RV ejection fraction, but the improvement did not reach statistical significance. Other measures such as left ventricular volumes, left ventricular ejection fraction, myocardial perfusion reserve index, and thickness of the interventricular septum and ventricular free wall did not change significantly.

Conclusions: This preliminary study found that CPAP treatment decreases RV volumes in patients with severe OSA who are otherwise healthy. CMR offers a novel technique to determine the effects of CPAP on ventricular structure and function in patients with OSA. A randomized controlled study is needed to confirm the results of our study.

Keywords: Obstructive sleep apnea, continuous positive airway pressure, magnetic resonance imaging, right ventricle, heart function tests

Citation: Magalang UJ; Richards K; McCarthy B; Fathala A; Khan M; Parinandi N; Raman SV. Continuous positive airway pressure therapy reduces right ventricular volume in patients with obstructive sleep apnea: a cardiovascular magnetic resonance study. J Clin Sleep Med 2009;5(2):110-114.

Obstructive sleep apnea (OSA) is associated with increased cardiovascular morbidity and mortality.1-3 Although the exact mechanism for this effect remains unclear, abnormalities of cardiac structure and function have been reported in patients with OSA.4,14 These latter studies have mainly examined the effects of OSA on left ventricular (LV) changes, with both systolic and diastolic dysfunctions reported. Indeed, even in patients with established congestive heart failure, continuous positive airway pressure (CPAP) improves LV systolic function.15,16

There are few data on the structural and functional changes of the right heart in patients with OSA and the effects of CPAP therapy on right ventricular (RV) function.7,8,11,14 Most of the studies have employed echocardiography and suggested significant association of the severity of OSA, assessed by the apnea-hypopnea index, to RV dysfunction. One study examined the effects of CPAP treatment on the right heart, and these authors reported improvements in RV tissue Doppler systolic velocity after 6 months of therapy.14 However, the inherent challenges of echocardiography-based imaging of the right ventricle, further compounded by the frequently poor acoustic window in obese patients with OSA, may limit the reproducibility of these findings.

The volumetric nature of cardiac magnetic resonance imaging (CMR), which is not affected by body habitus, has made this modality the current gold standard for quantifying ventricular size and function and the preferred modality for precise measurements in clinical trials.17,18 CMR provides an accurate and reproducible measurement of ventricular structure and function by assessment of volumes, ejection fraction, and mass and is particularly useful in evaluation of the right heart. Compared with other modalities, the improved precision of CMR reduces the sample size required in clinical studies.19 Furthermore, the superior spatial resolution of CMR affords recognition of subtle subendocardial perfusion abnormalities, not feasible with any other noninvasive modality.20 This is of particular interest, since subclinical atherosclerotic heart disease has been reported in patients with OSA.21 We sought to leverage these advantages
of CMR in implementing a comprehensive evaluation of cardiac structure and function and myocardial perfusion reserve in patients with OSA. Specifically, we hypothesized that CPAP treatment will improve RV function even in a group of patients with OSA who were free of other comorbid conditions.

**METHODS AND MATERIALS**

**Patient Population**

Patients referred for suspicion of OSA were initially evaluated by a sleep disorders specialist (UJM) and included in the study if they met the following inclusion criteria: apnea-hypopnea index greater than 30 by overnight polysomnography and Epworth Sleepiness Scale score greater than 10. The polysomnography methods and definition of respiratory events are described below. These characteristics identify a group of patients with severe OSA who likely would be compliant with CPAP treatment. Patients were excluded if they had any of the following: known diabetes mellitus, heart failure, or coronary artery disease; use of illicit drugs or excessive alcohol consumption; active smoking; advanced lung disease; use of inhalers; prior treatment with CPAP; or any contraindication to MRI, such as ferromagnetic foreign body, orbital metal, cerebral aneurysm clip, pacemaker, defibrillator, neurostimulator, allergy to gadolinium-based contrast, or severe claustrophobia. Patients with hypertension were included only if their hypertension was well controlled (defined as a systolic blood pressure < 140 mm Hg and diastolic blood pressure < 90 mm Hg) and were on a stable dose of medications for at least a month. Written informed consent was obtained from all the subjects to participate in this Institutional Review Board-approved protocol. Venous blood samples were collected prior to baseline CMR imaging. After baseline CMR examination, all patients initiated CPAP treatment with an objective compliance card embedded in the machine and returned for monthly visits with the sleep disorders specialist for CPAP therapy optimization followed by repeat CMR at 3-month follow-up. The prescribed CPAP pressure was based on a CPAP titration study that eliminated respiratory events and improved oxyhemoglobin saturation during sleep.

**Polysomnography**

All patients underwent standard diagnostic overnight polysomnography. Airflow was measured by monitoring of nasal pressure via a nasal cannula. Sleep stages were scored in 30-second epochs using standard criteria. Each epoch was analyzed for the number of apneas, hypopneas, and electroencephalographic arousals and oxyhemoglobin desaturation. Apnea was defined as the absence of airflow for at least 10 seconds. Hypopnea was defined as a visible reduction in airflow lasting at least 10 seconds associated with at least a 4% decrease in arterial oxyhemoglobin saturation. The apnea-hypopnea index was defined as the number of apneas and hypopneas per hour of sleep.

**Cardiac MRI**

All subjects underwent identical CMR examination completed on a 1.5-Tesla clinical magnetic resonance scanner (MAGNETOM Avanto, Siemens Medical Solutions, Inc., Erlangen, Germany) using a 12-element cardiac-phased array coil. The CMR protocol included (1) cine acquisitions in standard planes, including contiguous short-axis slices to measure RV and LV free-wall thickness, end-diastolic volumes, end-systolic volumes, and ejection fractions; (2) first-pass myocardial perfusion imaging during intravenous administration of 140 mcg/kg adenosine using 0.1-mmol/kg gadolinium-DTPA contrast and rest perfusion imaging 15 minutes after stress; and (3) late post-gadolinium acquisitions in standard planes for myocardial scar visualization 5 to 10 minutes after rest perfusion imaging was completed. Standard 12-lead electrocardiography was performed prior to and after each CMR examination.

**Image Analysis**

LV and RV volumes and ejection fractions were computed from short-axis cine images (Figure 1) using standardized semiautomated segmentation software (Argus, Siemens Medical Solutions). Briefly, endocardial contours at end-systole and end-diastole delineated the left and right ventricle in each slice; using the Simpson rule, the volumes from each short-axis slice (area × slice thickness) were summed to obtain ventricular volumes. Ejection fraction was computed as the stroke volume (end-diastolic volume – end-systolic volume) divided by end-diastolic volume. Quantification of myocardial perfusion was performed using semiautomatic delineation of endocardial and epicardial LV borders throughout the phases of first-pass perfusion, with respiratory-motion correction as needed (CMRTools, London, UK). Rest and stress myocardial perfusion slopes were derived using Fermi-fitting of signal intensity versus time and normalized to the LV blood pool slope as well as heart rate. A myocardial perfusion reserve index, calculated for each subject, was defined as the ratio of stress to rest normalized myocardial perfusion slope. Thickness of the interventricular septum was measured at the midventricular level from an end-diastolic long-axis image. All image analysis was performed blinded to subject history.

**Statistical Analysis**

All continuous variables are expressed as mean ± SD. Volumes are reported normalized to body surface area (mL/m²). Stata/SE 8.1 (Stata Corp., College Station, TX) was used for statistical analysis. The Mann-Whitney Rank Sum 2-sample test was used to compare values pre-CPAP and post-CPAP therapy. A p value of less than 0.05 was considered significant.

**RESULTS**

Fifteen patients aged 27 to 66 years were enrolled; 2 could not complete CMR examination, 1 due to claustrophobia and another due to morbid obesity. The average body mass index was 35.3 ± 7.6 kg/m². All subjects had severe OSA, with apnea-hypopnea index ranging from 30 to 102 events per hour, associated with mild to moderate oxyhemoglobin desaturations during sleep, with a nadir of 80% ± 6%. Oxyhemoglobin saturation by pulse oximetry during wakefulness was greater than 95% in all patients. Only 5 of the 13 patients (38%) were on antihypertensive medications, and these patients all had good blood-pressure con-
None of the patients had an elevated B-type natriuretic peptide level. Except for 3 patients (34, 36, and 51 pg/mL), all patients had B-type natriuretic peptide levels of less than 30 pg/mL, which is the lower limit of detection in our laboratory. The clinical characteristics are summarized in Table 1. There was no significant change in body weight from baseline to after 3 months of CPAP treatment (baseline: 110.0 ± 21 versus 3-month: 112.0 ± 22.6 kg, p = NS), and no changes in medications occurred during this time period. Patients were compliant with CPAP therapy, with an average use of 5.3 ± 1.6 hours per night (time at effective pressure) throughout the study period. Subjective sleepiness measured by the Epworth Sleepiness Scale score significantly decreased with CPAP treatment (baseline: 15 ± 3 vs 3-month: 6 ± 3, p < 0.0001).

Patients’ RV volumes were significantly reduced with CPAP therapy (Figures 2 and 3): RV end-diastolic volume index decreased from 57.6 ± 11.4 mL/m² to 47.8 ± 14.4 mL/m² (p < 0.05), and RV end-systolic volume index decreased from 30.0 ± 7.7 mL/m² to 22.2 ± 5.5 mL/m² (p < 0.05). There was a trend toward improved RV ejection fraction with CPAP therapy that did not achieve statistical significance (47.5% ± 12.1% vs 52.5% ± 8.6%, p = 0.33, Figure 4). There was also no significant change in the RV free-wall thickness (p = 0.53). In this cohort, CPAP did not produce any significant change in LV volumes, ejection fraction, or free-wall thickness. Similarly, myocardial perfusion index did not change significantly (0.94 ± 0.14 vs 0.83 ± 0.63, p = 0.14). No patient with OSA had LV hypertrophy; thickness of the interventricular septum was normal at baseline and did not change significantly at 3-month follow-up (7.9 ± 2.2 mm vs 8.0 ± 2.4 mm, p = NS, Table 2).

**DISCUSSION**

In a cohort of patients with severe OSA, we found mild improvements in RV volumes and a trend toward improved RV ejection fraction with short-term CPAP treatment. No significant change was seen in LV volumes, LV ejection fraction, myocardial perfusion reserve index, or thickness of the interventricular septum, RV free wall, or LV free wall in this study population. By excluding patients with any history of tobacco use, diabetes, atherosclerotic heart disease, or heart failure, we studied a group of subjects with OSA whose cardiac parameters were close to normal at baseline. Still, we found improvements in RV volumes with CPAP treatment. This suggests that, prior to the development of overt cardiovascular disease and prior to demonstrable LV dysfunction, the right heart is the first to undergo adverse remodeling due to OSA.

This is the first study that has utilized CMR in assessing the effects of CPAP on cardiac structure and function. A prior small study involving 5 patients with OSA used CMR, but imaging was not performed after CPAP therapy. We have shown that, in our current study of obese subjects, excellent-quality images can be obtained for a precise and comprehensive noninvasive assessment of cardiac structure and function. Prior studies examining the effects of CPAP treatment have uniformly employed echocardiography, with its inherent limitations in obtaining adequate im-

![Figure 1](image1.png) — Representative cardiac magnetic resonance imaging (MRI) midventricular short-axis slice in 1 patient with obstructive sleep apnea shown at end diastole (left) and end systole (right). The contours indicate semiautomated delineation of endocardial and epicardial contours around the left ventricular (LV) myocardium and endocardial contours delineating the inner surface of the right ventricular (RV) myocardium. Knowing the areas of these contours and the thickness of the slice allows calculation of the volume in each slice; summing over the slices that cover the heart yields total ventricular volumes.

![Figure 2](image2.png) — Right ventricular end-diastolic volume indexed to body surface area (RVEDVI, mL/m²) decreased significantly after 3 months of continuous positive airway pressure (CPAP) treatment (p < 0.05) in patients with obstructive sleep apnea (OSA). Box plots of the RVEDVI are shown. The lower and upper bars represent the lowest and highest values, respectively; the lower and upper boundaries of the box represent the first and third quartiles, whereas the line within the box represents the median value.

![Figure 3](image3.png) — Right ventricular end-systolic volume indexed to body surface area (RVESVI, mL/m²) decreased significantly after 3 months of continuous positive airway pressure (CPAP) therapy (p < 0.05) in patients with obstructive sleep apnea (OSA).
Given our results, a randomized controlled trial would be appropriate to assess ventricular structure and function using CMR in patients with OSA. Finally, we included only a group of patients without co-existing comorbidities such as atherosclerotic heart disease or LV dysfunction. Further studies are required using CMR to determine the effects of CPAP on ventricular structure and function in patients with OSA. We speculate that our findings may, in part, be due to the reduction in sympathetic nervous system activity that is known to occur with CPAP treatment. It is possible that we could have seen more improvements in RV function if our patient population had included subjects with more severe oxyhemoglobin desaturations during sleep prior to treatment.

We did not find any significant changes in LV structure and function with CPAP treatment. LV abnormalities have been associated with OSA in some, but not all, studies. Differences in the results of these studies, including ours, may in part be due to the fact that other studied populations may have had more significant hypertension, which is known to adversely affect LV structure and function. We specifically enrolled patients either without hypertension or whose blood pressure was well controlled and had been on a stable dose of medications. Our study has several limitations. Our sample size was relatively small, but we were able to show significant differences in RV end-diastolic volume index and RV end-systolic volume index after 3 months of CPAP therapy. It is not known whether a larger sample size would allow for the noted trend of an increase in RV ejection fraction to be statistically significant. We did not include a group of patients with untreated OSA. Therefore, we cannot totally exclude that unknown confounding factors such as regression to the mean could potentially explain our findings. Given our results, a randomized controlled trial would be appropriate to assess ventricular structure and function using CMR in patients with OSA. Finally, we included only a group of patients without co-existing comorbidities such as atherosclerotic heart disease or LV dysfunction. Further studies are required using CMR to determine the effects of CPAP on ventricular structure and function in patients with OSA with LV dysfunction, atherosclerotic heart disease, or both.

In conclusion, patients with severe untreated OSA without cardiovascular disease have shown modest but significant improvements in RV structure after initiation of CPAP therapy. We have shown that, in this group of obese subjects with OSA, high-quality images using CMR can be obtained for a precise and comprehensive noninvasive assessment of cardiac structure.

Table 1—Patient Characteristics at Baseline

<table>
<thead>
<tr>
<th></th>
<th>Patients (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (%)</td>
<td>9 (69)</td>
</tr>
<tr>
<td>Age, y</td>
<td>48.8 ± 10.8</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>35.3 ± 7.6</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>121 ± 12</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>71 ± 8</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale score</td>
<td>15.0 ± 3.0</td>
</tr>
<tr>
<td>AHI, events/h</td>
<td>60.2 ± 23.7</td>
</tr>
<tr>
<td>Obstructive apneas, % of total events</td>
<td>48.4 ± 27.3</td>
</tr>
<tr>
<td>Central apneas, % of total events</td>
<td>1.9 ± 1.6</td>
</tr>
<tr>
<td>Hypopneas, % of total events</td>
<td>49.7 ± 28.2</td>
</tr>
<tr>
<td>SpO₂ during wakefulness, %</td>
<td>97 ± 1</td>
</tr>
<tr>
<td>SpO₂ nadir during sleep, %</td>
<td>80 ± 6</td>
</tr>
<tr>
<td>CT90, min</td>
<td>8.3 ± 6.3</td>
</tr>
<tr>
<td>Fasting blood glucose, mg/dL</td>
<td>92 ± 8</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>162 ± 37</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. BMI refers to body mass index; AHI, apnea-hypopnea index, SpO₂, oxyhemoglobin saturation by pulse oximetry; CT90, cumulative time with an oxyhemoglobin saturation index below 90% during sleep.

Table 2—CMR Baseline and Follow-Up Measurements

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After 3 Months of CPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDVI, mL/m²</td>
<td>54.2 ± 19.5</td>
<td>50.4 ± 8.1</td>
</tr>
<tr>
<td>LVESVI, mL/m²</td>
<td>22.4 ± 9.0</td>
<td>20.5 ± 3.5</td>
</tr>
<tr>
<td>LV free wall, mm</td>
<td>8.0 ± 1.1</td>
<td>8.0 ± 1.1</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>58.5 ± 8.2</td>
<td>58.9 ± 5.4</td>
</tr>
<tr>
<td>RVEDVI, mL/m²</td>
<td>57.6 ± 11.4</td>
<td>47.8 ± 14.4*</td>
</tr>
<tr>
<td>RVESVI, mL/m²</td>
<td>30.0 ± 7.7</td>
<td>22.2 ± 5.5*</td>
</tr>
<tr>
<td>RVF, %</td>
<td>47.5 ± 12.1</td>
<td>52.5 ± 8.6</td>
</tr>
<tr>
<td>RV free wall, mm</td>
<td>4.4 ± 1.3</td>
<td>4.2 ± 1.2</td>
</tr>
<tr>
<td>IVS, mm</td>
<td>7.9 ± 2.2</td>
<td>8.0 ± 2.4</td>
</tr>
<tr>
<td>MPRI</td>
<td>0.94 ± 0.14</td>
<td>0.83 ± 0.63</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. CMR refers to cardiac magnetic resonance imaging; CPAP, continuous positive airway pressure; LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index; RVEDVI, right ventricular end-diastolic volume index; RVESVI, right ventricular end-systolic volume index; RVEF, right ventricular ejection fraction; RV, right ventricular; interventricular septum; MPRI, myocardial perfusion reserve index. *p < 0.05 compared with baseline measurements.

Figure 4—Right ventricular ejection fraction (RVEF, %) shows a trend toward improvement after 3 months of continuous positive airway pressure (CPAP) therapy in patients with obstructive sleep apnea (OSA).
and function. Ongoing longer-term follow-up and comparison to patients with OSA with more significant cardiac dysfunction may yield additional insights into the relationship between OSA and cardiovascular disease.

**ABBREVIATIONS LIST**

CMR = cardiac magnetic resonance  
CPAP = continuous positive airway pressure  
LV = left ventricle  
OSA = obstructive sleep apnea  
RV = right ventricle

**DISCLOSURE STATEMENT**

This was not an industry supported study. Dr. Raman and Ohio State University have an unrestricted research agreement with Siemens that provided workstations for analysis of the imaging data acquired for this study. Siemens did not sponsor or have any other involvement in the study. The other authors have indicated no financial conflicts of interest.

**REFERENCES**