Obstructive sleep apnoea and left ventricular diastolic dysfunction among first responders to the 9/11 World Trade Center terrorist attack: A cross-sectional study

Author:

Iyengar-Kapuganti, RL; MacEda, CS; Croft, LB; Sawit, ST; Crowley, LE; Woodward, M; McLaughlin, MA

BMJ Open

Obstructive sleep apnoea and left ventricular diastolic dysfunction among first responders to the 9/11 World Trade Center terrorist attack: a cross-sectional study

Rupa Lakshmi Iyengar-Kapuganti [ORCID],[1] Cynara S Maceda,[1] Lori B Croft,[1] Simonette T Sawit,[2] Laura E Crowley,[3] Mark Woodward,[4,5] Mary Ann McLaughlin[1]

For numbered affiliations see end of article.

Correspondence to
Dr Rupa Lakshmi Iyengar-Kapuganti;
rupa.iyengar@mssm.edu

ABSTRACT

Objectives Obstructive sleep apnoea (OSA) is often linked to cardiovascular disease. A limited number of studies have reported an association between OSA and left ventricular diastolic dysfunction (LVDD). However, prior studies were performed on small patient populations. Studies have shown a high prevalence of OSA among first responders to the 9/11 World Trade Center (WTC) terrorist attack. We investigated the relationship between OSA and LVDD in a large population of WTC responders.

Design Cross-sectional study.

Setting One-time screening programme as part of the WTC-CHEST Study (NCT10466218), performed at a quaternary medical centre in New York City, from November 2011 to June 2014.

Participants A total of 1007 participants with mean age of 51 years of mostly non-Hispanic white men were evaluated. Patients from the WTC Health Program-Clinical Center of Excellence, who were over the age of 39 years, were eligible to participate.

Results Evaluation of those without OSA diagnosis showed no significant association with LVDD when comparing those screened (Berlin Questionnaire) as OSA high risk versus OSA low risk (p=0.101). Among those diagnosed with LVDD, there was a significant association when comparing those with and without patient-reported OSA (OR 1.50, 95% CI 1.13 to 2.00, p=0.005), but the significance was not maintained after adjusting for pertinent variables (OR 1.3, 0.94 to 1.75, p=0.119). Notably, comparing those with OSA diagnosis and those low risk of OSA, the OR for LVDD was significant (1.69, 1.24 to 2.31, p=0.001), and after adjusting for waist–hip ratio, diabetes and coronary artery calcium score percentile, the relationship remained significant (OR 1.45, 1.03 to 2.04, p=0.032).

Conclusion The strong association of OSA with LVDD in this population may inform future guidelines to recommend screening for LVDD in high-risk asymptomatic patients with OSA.

Strengths and limitations of this study

► This study investigated the relationship between obstructive sleep apnoea (OSA) and left ventricular diastolic dysfunction (LVDD), in a large, middle-aged population.
► It is focused on a single population that is largely male and Caucasian.
► The nature of the observational study design precludes the determination of a causal relationship between OSA and LVDD.

disease (CVD) and stroke, particularly cardiometabolic risk (insulin resistance, atherogenic dyslipidaemia).[1–5] Even in the presence of confounding factors, such as age, sex, obesity and dyslipidaemia, persuasive data associate OSA in the development of various CVDs, including hypertension, coronary artery disease (CAD), cerebrovascular disease, heart rhythm and conduction disorders.[6–9] Among those affected with sleep apnoea, there is a very high prevalence of untreated OSA.[10] Untreated OSA has a detrimental impact on health. The proposed pathophysiological mechanisms through which OSA can lead to cardiac dysfunction include increased sympathetic activity, endothelial dysfunction, systemic inflammation, oxidative stress and metabolic anomalies.[6 8] A shared feature of cardiac dysfunction among patients with OSA is diastolic dysfunction, a term that refers to anomalies in the physiological characteristics of the diastolic phase of the cardiac cycle. It has been suggested that diastolic dysfunction falls into a spectrum, from mild to moderate to severe, progressively leading to heart failure with preserved ejection fraction (HFpEF). HFpEF is defined as the presence of the triad of

INTRODUCTION

Obstructive sleep apnoea (OSA) is increasingly implicated in risk of cardiovascular

impaired diastolic dysfunction, normal systolic function and symptoms of heart failure (HF).[11] [12] Although it is well recognised that patients with HF regardless of left ventricular (LV) ejection fraction (EF) have a worsened prognosis, less is known about the risk of asymptomatic diastolic dysfunction.

A limited number of small studies have consistently reported that patients with moderate-to-severe degree of OSA have a higher prevalence of left ventricular diastolic dysfunction (LVDD).[13–21] LVDD is the impairment of the relaxation ability of the myocardium and the impairment of the LV to fill appropriately without increasing filling pressures.[22] [23] Although LVDD results from alterations in the relaxation and filling of the LV, the EF generally stays within normal range. LVDD may be among the early cardiac alterations occurring in patients with OSA, even before the development of hypertension or CVD.[18]

On 11 September 2001, the destruction of the World Trade Center (WTC) resulted in inhalation of dust and chemicals to those at the site at the time of the disaster and for months following the incident. Now, two decades later, we are beginning to understand the long-term effects of this event on those who experienced it. Serious illness and injury following the attacks have affected thousands of responders who worked on the WTC rescue and recovery effort.[24] Multiple studies have shown significant associations between severe OSA and WTC exposure.[25–27] The high prevalence of OSA[26] among WTC responders makes this group a suitable population to assess the relationship between LVDD and OSA. To our knowledge, this is the first study to investigate the relationship between LVDD and OSA in a large population of WTC first responders.

METHODS
Study population
Participants of the Mount Sinai WTC Health Program-Clinical Center of Excellence, New York, New York, USA who were over the age of 39 years were eligible to participate in a one-time evaluation programme, WTC-CHEST (NCT10466218). Dissemination of the study was done by posting informational material at the WTC Health Program Clinics. A total of 1007 participants responded and were recruited from November 2011 to June 2014.

Patient and public involvement
Patients were not involved in the design, conduct, reporting or dissemination plans of this research.

Comprehensive cardiac evaluation
A one-time comprehensive cardiovascular evaluation of CVD risk, including the Framingham Risk Score,[2] was performed on each participant. The evaluation included several components: (1) demographics and medical history questionnaire to determine CVD risk consisting of hypertension, diabetes, smoking and family history of premature coronary heart disease (CHD) as well as

medication use and alcohol consumption; (2) exposure to the WTC cloud and subsequent clean up[24] [28]; (3) responses to validated questionnaires (Seattle Angina Questionnaire for chest pain, Dyspnea Questionnaire, Sexual Health Inventory for Men Questionnaire, Patient Health Questionnaire-9); (4) anthropometric measurements (waist circumference (WC), hip circumference, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP)); (5) laboratory blood analysis: fasting glucose, fasting lipid panel (total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), high-sensitivity C reactive protein (hs-CRP), haemoglobin A1c (HbA1c)), serum creatinine, complete blood count and vitamin D levels. Coronary artery calcium score (CACS), which is a quantitative estimate of cardiovascular risk, was measured in a subset of 907 of the 1007 participants. Based on the Multi-Ethnic Study of Atherosclerosis,[29] CACS percentile (CACS based on age, gender and race/ethnicity) greater than 75% was considered a CAD equivalent.

Sleep apnoea screening and assessment
Participants with no prior OSA diagnosis were screened for OSA risk. The Berlin Questionnaire (BQ) is the most widely used questionnaire to screen for OSA risk. High risk for OSA (OSA high risk) was defined as two or more positive categories on the BQ. Low risk for OSA (OSA low risk) was defined as those with less than two positive categories on the BQ.[30] [31] OSA diagnosis was defined as those who reported a physician diagnosis of OSA.

Echocardiography
Participants underwent comprehensive echocardiography including pulse-wave Doppler study to evaluate peak mitral inflow velocities at early (E) and late (A) diastole, transmitral E/A ratio and tissue Doppler imaging of the LV septum in the apical four-chamber view. Evaluation of LV diastolic function was performed according to the recommendations of the American Society of Echocardiography.[32] [33]

Statistical analysis
Analyses used SAS V.9.4, and p values of <0.05 were considered as significant. Continuous variables were summarised using their mean and SD, and analysed with either independent t-tests or analysis of variance, as appropriate. Variables with skewed distributions as determined by statistical testing underwent logarithmic transformation when warranted. Some continuous variables were dichotomised and/or categorised so as to analyse clinically meaningful differences. Dichotomous and categorical variables were analysed using X^2 or Fisher's exact tests, as appropriate, and represented as frequencies and percentages. For the primary outcome, LVDD, logistic regression was used to obtain estimated ORs, both unadjusted and adjusted for waist–hip ratio, diabetes and CACS percentile.

Table 1 Baseline characteristics of the WTC-CHEST Study population by OSA status

| | | No OSA diagnosis | | | |
| | Total population | OSA low risk* | OSA high risk* | OSA diagnosis† | |
	(n=1007)	(n=451)	(n=274)	(n=282)	P value‡
Age (years)	51.37±6.03	51.36±6.31	50.86±5.50	51.83±6.06	0.1671
Gender–male (n (%))	841 (83.10)	346 (76.72)	239 (87.23)	251 (89.01)	<0.0001
Race (n (%))					0.5736
1=white	717 (70.85)	321 (71.18)	202 (73.72)	192 (68.09)	
2=African American	114 (11.26)	49 (10.86)	31 (11.31)	33 (11.70)	
3=other§	181 (17.89)	81 (17.96)	41 (14.96)	57 (20.21)	
Ethnicity–Hispanic (n (%))	754 (74.73)	114 (25.28)	59 (21.53)	82 (29.18)	0.1170
Ever smoked (n (%))	291 (28.93)	120 (26.67)	83 (30.40)	88 (31.43)	0.3243
Cigarette use (n (%))					0.4533
0=never smoked	715 (71.07)	330 (73.33)	190 (69.60)	192 (68.57)	
1=social smoker	23 (2.29)	11 (2.44)	3 (1.10)	9 (3.21)	
2=current smoker	31 (3.08)	13 (2.89)	8 (2.93)	10 (3.57)	
3=ex-smoker	237 (23.56)	96 (21.33)	72 (26.37)	69 (24.64)	
Family history of premature CHD	178 (17.62%)	89 (19.73%)	43 (15.69%)	45 (15.96%)	0.2685
Hypertension¶	335 (33.17%)	84 (18.63%)	122 (44.53%)	128 (45.39%)	<0.0001
Hyperlipidaemia¶	379 (37.60%)	141 (31.26%)	116 (42.65%)	122 (43.26%)	0.0007
Diabetes mellitus¶	85 (8.42%)	27 (5.99%)	25 (9.12%)	33 (11.74%)	0.0219
Metabolic syndrome¶	341 (33.70%)	85 (18.85%)	113 (41.24%)	143 (50.71%)	<0.0001
GORD¶	462 (45.79%)	159 (35.25%)	115 (42.12%)	168 (66.67%)	<0.0001
Sinusitis¶	405 (40.10%)	136 (30.16%)	101 (36.86%)	168 (59.57%)	<0.0001
Asthma¶	250 (24.75%)	88 (19.41%)	58 (21.17%)	104 (36.88%)	<0.0001
RADS¶	81 (8.05%)	22 (4.88%)	16 (5.86%)	43 (15.41%)	<0.0001
Chronic bronchitis¶	101 (10.02%)	29 (6.44%)	21 (7.66%)	51 (18.15%)	<0.0001
Emphysema¶	12 (1.19%)	7 (1.55%)	1 (0.37%)	4 (1.42%)	0.0241
COPD¶	106 (10.50%)	32 (7.10%)	21 (7.66%)	53 (18.79%)	<0.0001
CACS percentile >75% (n=907)	242/907 (26.68%)	89/443 (22.08%)	52/196 (26.53%)	101/308 (32.79%)	0.0060
WTC exposure (n (%))					0.0905
Low	175 (17.34)	96 (21.29)	31 (14.49)	48 (13.95)	
Intermediate	498 (49.36)	210 (46.56)	113 (52.80)	175 (50.87)	
High	242 (23.98)	105 (23.28)	54 (25.23)	83 (24.13)	
Very high	94 (9.32)	40 (8.87)	16 (7.48)	38 (11.05)	

Continuous variables presented as mean. Categorical variables presented as number of patients (%).
*As defined by the Berlin Questionnaire.
†Patient-reported physician diagnosis.
‡Comparing the three OSA groups.
§Asian, American Indian/Alaska Native, Hawaiian/Pacific Islander.
¶Self-reported, on medication or medical chart documentation.
CACS, coronary artery calcium score; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; GERD, gastro-oesophageal reflux disease; OSA, obstructive sleep apnoea; RADS, reactive airway dysfunction syndrome; WTC, World Trade Center.

RESULTS

Baseline characteristics of the study population (n=1007) are shown in table 1. Overall, the mean age was 51 years, mostly non-Hispanic white men. Twenty-eight per cent (282) were diagnosed with OSA, 27% (274) were OSA high risk and 45% (451) were OSA low risk. Those with OSA diagnosis and OSA high risk were more likely to be male and had a significantly higher prevalence of comorbidities compared with those who were OSA low risk. There were no significant differences in age, race/ethnicity, smoking, alcohol use and family history of premature CHD among the three groups. No significant valvular disease was seen in the cohort: one

Table 2 Anthropometric and laboratory analyses of the WTC-CHEST Study population by OSA status

| | No OSA diagnosis | | | |
| | OSA low risk* | OSA high risk* | OSA diagnosis† | |
	(N=451)	(N=274)	(N=282)	P value
Waist circumference (cm)	96.27±12.60	105.84±11.63	107.85±13.61	<0.0001‡ <0.0001§
Hip circumference (cm)	101.88±9.32	108.79±9.98	110.52±12.04	<0.0001‡ <0.0001§
Waist:hip circumference ratio	0.94±0.079	0.97±0.059	0.98±0.064	<0.0001‡ <0.0001§
Body mass index (kg/m^2)	27.84±3.91	31.54±4.30	32.45±5.27	<0.0001‡ <0.0001§ 0.0480¶
Systolic blood pressure (mm Hg)	116.15±12.05	120.32±10.37	119.47±11.01	<0.0001‡ 0.0004§
Diastolic blood pressure (mm Hg)	74.51±7.92	76.36±6.95	76.12±8.16	0.0055‡ 0.0182§
Total cholesterol (mg/dL)	193.42±35.40	193.45±35.74	188.01±35.57	0.0952
HDL-C (mg/dL)	58.94±17.72	52.58±12.87	50.39±13.18	<0.0001‡ <0.0001§
LDL-C (mg/dL)	111.90±32.02	115.46±32.80	110.57±30.86	0.1696
Triglyceride level (mg/dL)	112.92±67.26	130.79±81.72	137.82±80.71	0.0060‡ <0.0001§
Blood glucose (mg/dL)	78.53±15.50	79.32±17.08	80.54±13.90	0.2354
HbA1c (%)	5.63±0.77	5.74±0.77	5.83±0.83	0.0023§
hs-CRP (mg/L)	2.21±4.05	2.89±3.63	3.01±3.45	0.0169§

Continuous variables presented as mean. Categorical variables presented as number of patients (%).
*As defined by the Berlin Questionnaire.
†Patient-reported physician diagnosis.
‡Comparing OSA low risk and OSA high risk.
§Comparing OSA low risk and OSA diagnosis.
¶Comparing OSA high risk and OSA diagnosis.
HbA1c, haemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C reactive protein; LDL-C, low-density lipoprotein cholesterol; OSA, obstructive sleep apnoea; WTC, World Trade Center.

patient had aortic stenosis and another had bicuspid aortic valve. Based on published WTC exposure scores,[24] there was no significant difference in WTC dust exposure among all OSA groups.

Mean values of SBP, DBP and WC were significantly higher in OSA diagnosis and OSA high risk groups compared with OSA low risk group. Mean BMI was significantly higher in those diagnosed with OSA compared with those not diagnosed with OSA. Mean HDL-C was significantly higher in OSA low risk group separately compared with OSA high risk and OSA diagnosis groups. Mean value of TG was significantly lower in OSA low risk group separately compared with OSA high risk and OSA diagnosis groups. Mean HbA1c and hs-CRP were significantly higher in OSA diagnosis compared with OSA low risk group (table 2). SBP, DBP, WC and BMI as well as mean TG and blood glucose were significantly higher in

those with LVDD compared with those without LVDD. Mean HDL-C was significantly higher in those without LVDD. There was no significant difference in mean total cholesterol, LDL-C, HbA1c and hs-CRP between those with and without LVDD (table 3).

Echocardiographic indices of LV function according to OSA group are shown in table 4. Those with OSA diagnosis and OSA high risk were more likely to have increased LV mass (p<0.0001), and LV hypertrophy compared with those with OSA low risk (p<0.0001). Those with OSA diagnosis had significantly increased LV index compared with those with OSA low risk (p=0.0247). There was no significant difference in LV EF among the three groups. Diastolic function could not be evaluated in 64 of 1007 participants (6.3%) because of incomplete echocardiographic data. Of the remaining 943 participants, 52.7% (138 of 262) with OSA diagnosis had LVDD compared with 46.1% (119 of 258)

Table 3 Anthropometric and laboratory analyses of the WTC-CHEST Study population by LVDD status

	LVDD–no	LVDD–yes	
	(N=519)	(N=426)	P value
Waist circumference (cm)	39.66±5.81	40.93±4.89	0.0003
Hip circumference (cm)	41.51±4.46	42.24±4.26	0.0106
Waist:hip circumference ratio	0.95±0.07	0.97±0.07	<0.0001
Body mass index (kg/m^2)	29.82±5.09	30.68±4.73	0.0078
Systolic blood pressure (mm Hg)	116.8±11.15	120.1±11.5	<0.0001
Diastolic blood pressure (mm Hg)	74.43±7.82	76.86±7.55	<0.0001
Total cholesterol (mg/dL)	192.2±34.34	192.4±36.27	0.9260
HDL-C (mg/dL)	56.38±17.25	52.47±13.12	<0.0001
LDL-C (mg/dL)	122.7±31.38	133.2±32.13	0.8138
Triglyceride level (mg/dL)	117.0±71.11	135.6±81.05	0.0002
Blood glucose (mg/dL)	78.22±14.66	80.79±16.81	0.0136
HbA1c (%)	5.68±0.80	5.76±0.80	0.1223
hs-CRP (mg/L)	2.49±3.78	2.86±3.93	0.1411

Continuous variables presented as mean. Categorical variables presented as number of patients (%).
HbA1c, haemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C reactive protein; LDL-C, low-density lipoprotein cholesterol; LVDD, left ventricular diastolic dysfunction; WTC, World Trade Center.

among OSA high risk, and 39.7% (168 of 423) among OSA low risk groups. There was a higher prevalence of LVDD in those with OSA diagnosis and OSA high risk compared with OSA low risk group (p=0.0038).

The associations of OSA diagnosis and OSA risk with LVDD are summarised in table 5. Those with OSA diagnosis had 1.50 times odds of having LVDD compared with those without OSA (p=0.0055). However, the association only trended towards significance after adjusting for confounding variables. Among those without OSA diagnosis, there was no significant association with LVDD when comparing OSA high risk and OSA low risk. Notably, the odds of having LVDD for those with OSA diagnosis were 1.69 times that of those who were OSA low risk (p=0.0010). Additionally, after adjusting for waist–hip ratio, diabetes and CACS percentile, the relationship remained significant (OR 1.45, 95% CI 1.03 to 2.04, p=0.0325). These results indicate a clear association between OSA and LVDD, independent of CAD.

DISCUSSION

There is still some degree of uncertainty about whether or not the association between OSA and LVDD is an independent one. Some of the most common risk factors for diastolic dysfunction, such as hypertension, ageing and diabetes, are also common features of patients with OSA. Notwithstanding differing results,[34] most of the studies of patients with different cardiovascular profiles have found this association to be independent from other confounding factors, such as age, gender, BP, hypertension and BMI.[13–17] However, a majority of these studies were carried out on small patient populations. The results of our study build up the evidence that

OSA carries the risk of developing LVDD independent of these risk factors. Additionally, it was not known if the relationship between OSA and LVDD is dependent on CAD. In this study, the association remained significant after adjusting for CACS, which demonstrates that OSA is independently associated with LVDD irrespective of CAD status.

Recent studies have reported the increasing prevalence of OSA in men up to 30% and women 15% in North America.[10 35] The prevalence and awareness of OSA risk have increased since the landmark study of the Wisconsin Sleep Cohort,[36 37] and recently, the American Heart Association recommended OSA screening for patients with high-risk CVD (eg, those with poorly controlled hypertension, pulmonary hypertension and recurrent atrial fibrillation).[38] However, routine screening for OSA is not part of general healthcare from the guidelines released by US Preventive Services Task Force (USPTF) of 2017. The USPTF group stated there is insufficient evidence to give guidelines for recommendations for OSA screening in asymptomatic adults.[39] Results of this study may inform future guidelines to recommend OSA screening in high-risk asymptomatic patients and more importantly, screening for LVDD in patients with OSA. Diastolic dysfunction can be identified through routine echocardiography. Knowing the relationship between OSA and LVDD, it will be important to establish whether screening patients who are identified as high risk of OSA or those diagnosed with OSA would benefit from evaluation of LV function in order to initiate early intervention that can prevent the long-term consequences of CVD.[40] This is particularly important as the prevalence of high-risk OSA in WTC responders is 36.6%.[25]

Table 4 Echocardiographic indices of LV function according to OSA group

| | No OSA diagnosis | | | |
	OSA low risk*	OSA high risk*	OSA diagnosis†	P value
N	451 (423‡)	274 (258‡)	282 (262‡)	
EF (%)	61.28±5.23	61.64±5.34	61.76±5.61	0.4515
E/A (continuous)	1.11±0.35	1.10±0.52	1.04±0.60	0.2141
E/e' (continuous)	7.63±2.39	8.76±5.53	8.42±2.84	0.0033§
				0.0177¶
e'/a' (continuous)	0.87±0.59	0.77±0.25	0.78±0.40	0.0361§
				0.0512¶
LV mass	184.69±149.92	171.08±39.70	153.84±38.44	0.0263§
				<0.0001¶
LV index	76.12±16.19	79.16±16.31	84.72±74.05	0.0197¶
LVPW thickness–abnormal (n (%))‡	86 (19.07)	80 (29.20)	105 (37.23)	<0.0001
LV septal thickness–abnormal (n (%))‡	188 (41.68)	156 (56.93)	167 (59.22)	<0.0001
RWT–abnormal (n (%))‡	151 (33.48)	112 (40.88)	147 (52.13)	<0.0001
LV geometry (n (%))‡				<0.0001 (FE)
0=normal geometry	292 (64.75)	156 (56.93)	132 (46.81)	
1=concentric remodelling	148 (32.82)	107 (39.05)	139 (49.29)	
2=eccentric hypertrophy	8 (1.77)	6 (2.19)	3 (1.06)	
3=concentric hypertrophy	3 (0.67)	5 (1.82)	8 (2.84)	
Diastolic dysfunction–yes (n (%))‡	168 (39.72)	119 (46.12)	138 (52.67)	0.0038

Continuous variables presented as means. Categorical variables presented as number of patients (%).
*As defined by the Berlin Questionnaire.
†Patient-reported physician diagnosis.
‡Sixty-four participants with missing echocardiographic indices for diastolic function.
§Comparing OSA low risk and OSA high risk.
¶Comparing OSA low risk and OSA diagnosis.
EF, ejection fraction; FE, Fisher's exact; LV, left ventricular; LVPW, LV posterior wall; OSA, obstructive sleep apnoea; RWT, relative wall thickness.

Limitations of the study include use of self-reported OSA diagnosis and use of BQ to assess for OSA risk. However, these methods were based on previous studies done in this cohort.[25] Since the BQ takes into account BMI and history of hypertension, we did not adjust for it in our analysis but used waist–hip ratio that has been shown to have a strong association with sleep apnoea.[41]

The findings would be more robust if sleep study data were available to provide evaluation of OSA severity and LVDD. Moreover, this study is focused on a single population that is largely male and Caucasian, and the relationships we find here between OSA and LVDD may not be generalisable to a more diverse population. Additionally, this population was exposed to environmental factors in

Table 5 Association of OSA diagnosis and OSA risk with left ventricular diastolic dysfunction

		OR	95% CI	P value
OSA diagnosis vs no OSA diagnosis*	Unadjusted	1.499	1.126 to 1.996	0.0055
	Adjusted†	1.281	0.938 to 1.749	0.1191
OSA high risk vs OSA low risk on the BQ‡	Unadjusted	1.299	0.950 to 1.777	0.1007
	Adjusted†	1.272	0.910 to 1.779	0.1596
OSA diagnosis* vs low risk on the BQ‡	Unadjusted	1.689	1.238 to 2.306	0.0010
	Adjusted†	1.452	1.032 to 2.044	0.0325

*Patient-reported physician diagnosis.
†Adjusted ORs were obtained after controlling for waist–hip ratio, diabetes and coronary calcium score percentile.
‡As defined by the BQ.
BQ, Berlin Questionnaire; OSA, obstructive sleep apnoea.

an acute fashion, which is only less commonly observed in the general population. Hence, it will be important to determine other cardiovascular pathophysiological changes that may be associated with OSA in the WTC first responders. However, studies are now showing that climate change can affect air quality leading to elevated levels of particulates in the environment.[42 43] It is reasonable to consider if such events can increase OSA and also lead to LVDD. Further studies are needed to define the relationship between OSA and LVDD in diverse populations under diverse exposure conditions. As this study demonstrates, while controlling for pertinent variables, there is a strong relationship between OSA and LVDD.

Author affiliations
[1]Department of Medicine (Cardiology), Icahn School of Medicine at Mount Sinai, New York, New York, USA
[2]Department of Medicine, The Medical City, Pasig City, Philippines
[3]Department of Environmental Medicine and Public Health, Icahn Shcool of Medicine at Mount Sinai, New York, New York, USA
[4]Department of Medicine, The George Institute of Global Health, University of New South Wales, Sydney, New South Wales, Australia
[5]Department of Medicine, The George Institute of Global Health, Imperial College of London, London, UK

Disclaimer The funding agency had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study was approved by the Icahn School of Medicine at Mount Sinai Program for the Protection of Human Subjects, and written informed consent was obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

ORCID iD
Rupa Lakshmi Iyengar-Kapuganti http://orcid.org/0000-0001-5013-3694

REFERENCES

1 Drager LF, Togeiro SM, Polotsky VY, et al. Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome. *J Am Coll Cardiol* 2013;62:569–76.

2 Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998;97:1837–47.

3 Krumholz HM, Larson M, Levy D. Prognosis of left ventricular geometric patterns in the Framingham heart study. *J Am Coll Cardiol* 1995;25:879–84.

4 Dong J-Y, Zhang Y-H, Qin L-Q. Obstructive sleep apnea and cardiovascular risk: meta-analysis of prospective cohort studies. *Atherosclerosis* 2013;229:489–95.

5 Gaines J, Vgontzas AN, Fernandez-Mendoza J, et al. Obstructive sleep apnea and the metabolic syndrome: the road to clinically-meaningful phenotyping, improved prognosis, and personalized treatment. *Sleep Med Rev* 2018;42:211–9.

6 Baguet J-P, Barone-Rochette G, Tamisier R, et al. Mechanisms of cardiac dysfunction in obstructive sleep apnea. *Nat Rev Cardiol* 2012;9:679–88.

7 Khayat R, Pleister A. Consequences of obstructive sleep apnea: cardiovascular risk of obstructive sleep apnea and whether continuous positive airway pressure reduces that risk. *Sleep Med Clin* 2016;11:273–86.

8 Bauters F, Rietzschel ER, Hertegonne KBC, et al. The link between obstructive sleep apnea and cardiovascular disease. *Curr Atheroscler Rep* 2016;18:1.

9 Dredla BK, Castillo PR. Cardiovascular consequences of obstructive sleep apnea. *Curr Cardiol Rep* 2019;21:137.

10 Young T, Palta M, Dempsey J, et al. Burden of sleep apnea: rationale, design, and major findings of the Wisconsin sleep cohort study. *WMJ* 2009;108:246–9.

11 Lanier GM, Vaishnava P, Kosmas CE, et al. An update on diastolic dysfunction. *Cardiol Rev* 2012;20:230–6.

12 Thomas L, Marwick TH, Popescu BA, et al. Left atrial structure and function, and left ventricular diastolic dysfunction: JACC state-of-the-art review. *J Am Coll Cardiol* 2019;73:1961–77.

13 Chen Y-L, Su M-C, Liu W-H, et al. Influence and predicting variables of obstructive sleep apnea on cardiac function and remodeling in patients without congestive heart failure. *J Clin Sleep Med* 2014;10:57–64.

14 Prejbisz A, Florczak E, Pręgowska-Chwała B, et al. Relationship between obstructive sleep apnea and markers of cardiovascular alterations in never-treated hypertensive patients. *Hypertens Res* 2014;37:573–9 https://www.nature.com/articles/hr201443#supplementary-information

15 Usui Y, Takata Y, Inoue Y, et al. Coexistence of obstructive sleep apnoea and metabolic syndrome is independently associated with left ventricular hypertrophy and diastolic dysfunction. *Sleep Breath* 2012;16:677–84.

16 Tavil Y, Kanbay A, Şen N, et al. The relationship between aortic stiffness and cardiac function in patients with obstructive sleep apnea, independently from systemic hypertension. *J Am Soc Echocardiogr* 2007;20:366–72.

17 Arias MA, García-Río F, Alonso-Fernández A, et al. Obstructive sleep apnea syndrome affects left ventricular diastolic function. *Circulation* 2005;112:375–83.

18 Aslan K, Deniz A, Cayli M, et al. Early left ventricular functional alterations in patients with obstructive sleep apnea syndrome. *Cardiol J* 2013;20:519–25.

19 Bayram NA, Ciftci B, Bayram H, et al. Effects of continuous positive airway pressure therapy on right ventricular function assessment by tissue doppler imaging in patients with obstructive sleep apnea syndrome. *Echocardiography* 2008;25:1071–8.

20 Yu L, Li H, Liu X, et al. Left ventricular remodeling and dysfunction in obstructive sleep apnea : systematic review and meta-analysis. *Herz* 2020;45:726–38. Remodeling und Dysfunktion linksventrikulär bei obstruktiver Schlafapnoe : systematische Übersichtsarbeit und Metaanalyse.

21 D'Andrea A, Canora A, Sperlongano S, 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;20:76.

22 Gaasch WH, Little WC. Assessment of left ventricular diastolic function and recognition of diastolic heart failure. *Circulation* 2007;116:591–3.

23 AlJaroudi WA, Thomas JD, Rodriguez LL, et al. Prognostic value of diastolic dysfunction: state of the art review. *Cardiol Rev* 2014;22:79–90.

24 Wisnivesky JP, Teitelbaum SL, Todd AC, et al. Persistence of multiple illnesses in world Trade center rescue and recovery workers: a cohort study. *Lancet* 2011;378:888–97.

25 Webber MP, Lee R, Soo J, et al. Prevalence and incidence of high risk for obstructive sleep apnea in world trade Center-exposed rescue/recovery workers. *Sleep Breath* 2011;15:283–94.

26 Glaser MS, Shah N, Webber MP, *et al*. Obstructive sleep apnea and world Trade center exposure. *J Occup Environ Med* 2014;56:S30–4.

27 Liu X, Yip J, Zeig-Owens R, *et al*. The effect of World Trade center exposure on the timing of diagnoses of obstructive airway disease, chronic rhinosinusitis, and gastroesophageal reflux disease. *Front Public Health* 2017;5:2.

28 Prezant DJ, Weiden M, Banauch GI, *et al*. Cough and bronchial responsiveness in firefighters at the world Trade center site. *N Engl J Med* 2002;347:806–15.

29 McClelland RL, Chung H, Detrano R, *et al*. Distribution of coronary artery calcium by race, gender, and age: results from the multi-ethnic study of atherosclerosis (MESA). *Circulation* 2006;113:30–7.

30 Netzer NC, Stoohs RA, Netzer CM, *et al*. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999;131:485–91.

31 Thurtell MJ, Bruce BB, Rye DB, *et al*. The Berlin questionnaire screens for obstructive sleep apnea in idiopathic intracranial hypertension. *J Neuroophthalmol* 2011;31:316–9.

32 Nagueh SF, Smiseth OA, Appleton CP, *et al*. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the american society of echocardiography and the European association of cardiovascular imaging. *J Am Soc Echocardiogr* 2016;29:277–314.

33 Lang RM, Badano LP, Mor-Avi V, *et al*. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American society of echocardiography and the European association of cardiovascular imaging. *Eur Heart J Cardiovasc Imaging* 2015;16:233–71.

34 Niroumand M, Kuperstein R, Sasson Z, *et al*. Impact of obstructive sleep apnea on left ventricular mass and diastolic function. *Am J Respir Crit Care Med* 2001;163:1632–6.

35 Peppard PE, Young T, Barnet JH, *et al*. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol* 2013;177:1006–14.

36 Young T, Palta M, Dempsey J, *et al*. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med Overseas Ed* 1993;328:1230–5.

37 Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. *The Lancet* 2014;383:736–47.

38 Yeghiazarians Y, Jneid H, Tietjens JR, *et al*. Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American heart association. *Circulation* 2021;144:e56–67.

39 Bibbins-Domingo K, Grossman DC, *et al*, US Preventive Services Task Force. Screening for obstructive sleep apnea in adults: US preventive services Task force recommendation statement. *JAMA* 2017;317:407–14.

40 Jeong E-M, Dudley SC. Diastolic dysfunction: potential new diagnostics and therapies. *Circulation Journal* 2015;79:470–7.

41 Seidell JC. Waist circumference and waist/hip ratio in relation to all-cause mortality, cancer and sleep apnea. *Eur J Clin Nutr* 2010;64:35–41.

42 Silva RA, West JJ, Lamarque J-F, *et al*. Future global mortality from changes in air pollution attributable to climate change. *Nat Clim Chang* 2017;7:647–51.

43 Doherty RM, Heal MR, O'Connor FM. Climate change impacts on human health over Europe through its effect on air quality. *Environ Health* 2017;16:118.