SUPPLEMENTAL MATERIAL

Methods

Echocardiography

All echocardiograms were performed with a preprogrammed acquisition protocol using dedicated Philips iE33 Ultrasound systems with Vision 2011. All views were obtained recording at least 3 full cardiac cycles for each view for patients if sinus rhythm and 5 or more for subjects in atrial fibrillation. From the paraesternal long-axis view, standard linear dimensions of the left ventricle (LV) and the left atrium (LA) were measured according to the recommendations of the American Society of Echocardiography (ASE)[1]. LV volumes were calculated by Simpson's method as the average from apical 4- and 2-chamber views and indexed by dividing by height$^{2.7}$, and LV ejection fraction was derived from LV volumes. LV deformation was assessed as LV longitudinal strain. LV end-diastolic endocardial borders were traced in both apical 4- and 2-chamber and then the software tracks and average peak systolic longitudinal strain is computed using TomTec Cardiac Performance Analysis package. LA volume was calculated as the average of apical 4- and 2-chamber views using the disks' method and indexed by dividing by height$^{2.7}$. LV diastolic function was assessed by measuring early transmitral velocity (E-wave), the peak lateral mitral annular relaxation velocities (E') and the ratio between them.

Right ventricular (RV) area was calculated from the apical 4-chamber view focused in the RV at end-diastole and end-systole and RV fractional area change was derived accordingly with the ASE guidelines.[2] In addition RV systolic function was assessed using the tricuspid annular peak systolic velocity measured from the lateral tricuspid annulus. Maximal peak tricuspid regurgitation velocity was measured and peak RV-to-right atrial systolic gradient was calculated as 4×(peak tricuspid regurgitation velocity).

Statistical Analysis

Although the limit of measurement for the assay used in this study is 3 ng/L, we used a limit of quantification of 5 ng/L in the primary analysis as concordance of hs-TnT values using this assay compared to the newer 4th generation assay by Roche is worse for values <5 ng/L in a clinical study performed in different labs with various platforms for this hsTnT assay.[3,4] In the ARIC study, in which all the assays were performed in one lab on the same platform, we have previously shown that levels between 3 and 5 ng/L are associated with significant increase in CV risk.[5] We therefore performed a sensitivity analysis repeating all our analyses using a threshold of 3 ng/L as the upper limit for the first category and lower limit for the second category of hs-TnT level. In this analysis, hs-TnT was modeled as an ordinal categorical variable using 5 categories employing sex-specific cutoffs: the first category was defined by undetectable values based on limit of measurement provided by the manufacturer (3 ng/L), the fifth category was defined by the sex-specific 90th percentile (≥14 ng/L for males and ≥8 ng/L for females), and the remainder of participants were divided into tertiles (for males: 3 - 5, 6- 8, and 9 - 13 ng/L; for females: 3 - 4, 5, and 6 - 7 ng/L). Distribution of participants along hs-TnT categories based on these thresholds is shown in Supplemental Table 2.

Supplemental Tables

Supplemental Table 1. Univariate and multivariable models for the relationship between OSA and hs-TnT stratified by sex.

	Men			Women		
	N	**OR [95%CI]**	**P value**	**N**	**OR [95%CI]**	**P value**
Unadjusted	752	1.20 [1.04 1.37]	0.011	893	1.48 [1.25 1.74]	<0.001
Model 1	750	0.98 [0.84 1.14]	0.80	892	1.34 [1.11 1.63]	0.003
Model 2	748	0.97 [0.83 1.12]	0.66	891	1.30 [1.07 1.58]	0.009
Model 3	746	0.99 [0.85 1.16]	0.94	885	1.25 [1.02 1.52]	0.03

Analysis based on ordinal logistic regression. Regression models: Model 1: adjusted by age and BMI; Model 2: additionally adjusted by HTN, DM, systolic blood pressure and smoking status; Model 3: additionally adjusted by alcohol intake, pulmonary function tests (FEV1 and FVC), chronic lung disease, estimated glomerular filtrated rate (eGFR) and blood levels of insulin, total cholesterol, LDL, HDL and triglycerides. Reported regression coefficients are those associated

with OSA severity defined by categories based on clinical definition. P for interaction between sex and OSA in the adjusted analysis: 0.04.

Supplemental Table 2: Distribution of hs-TnT categories in the overall population and by category of OSA severity using a limit of detection of 5 ng/L for hs-TnT level. P values are based in p for trends using non-parametric test. F and M indicate the hs-TnT category thresholds for males and females respectively.

	Overall	**Men: OSA Severity**				**P for**	**Women: OSA Severity**				**P for**
	N=1645	**None (n=312)**	**Mild (n=267)**	**Moderate (n=108)**	**Severe (n=65)**	**trend**	**None (n=592)**	**Mild (n=208)**	**Moderate (n=58)**	**Severe (n=35)**	**trend**
Hs-TnT (µg/L)						**0.007**					**<0.001**
Undetectable (< 3 ng/L)	575 (35)	61 (20)	41 (15)	20 (19)	9 (14)		320 (54)	91 (44)	21 (36)	12 (34)	
M: 3 – 5 ng/L F: 3 – 4 ng/L	370 (23)	86 (28)	75 (28)	28 (26)	11 (17)		112 (19)	42 (20)	11 (19)	5 (14)	
M: 6 – 8 ng/L F: 5 ng/L	277 (17)	84 (27)	63 (24)	24 (22)	20 (31)		55 (9)	21 (10)	7 (12)	3 (9)	

M: 9 – 13 ng/L F: 6 – 7 ng/L	235 (14)	56 (18)	56 (21)	25 (23)	9 (14)		52 (9)	21 (10)	9 (15)	7 (20)
M: ≥ 14 ng/L F≥ 8 ng/L	188 (11)	25 (8)	32 (12)	11 (10)	16 (25)		53 (9)	33 (16)	10 (17)	8 (23)

Supplemental Table 3: Univariate and multivariable models for the relationship between OSA clinical categories and hs-TnT stratified by sex based on categories performed using 3 ng/L as threshold for detection. Analysis is based on ordinal logistic regression. Regression models: Model 1: adjusted by age and BMI; Model 2: additionally adjusted by history of HTN or DM, systolic blood pressure, and smoking status; Model 3: additionally adjusted by alcohol intake, pulmonary function tests (FEV_1 and FVC), chronic lung disease, estimated glomerular filtrated rate (eGFR) and blood levels of insulin, total cholesterol, LDL, HDL and triglycerides. Reported regression coefficients are those associated with OSA severity defined by categories based on clinical definition. P for interaction between sex and OSA category <0.001

	Men (n=468)			**Women (n=551)**		
	N	**OR [95%CI]**	**P value**	**N**	**OR [95%CI]**	**P value**
Unadjusted	752	1.20 [1.05 1.38]	0.007	893	1.45 [1.24 1.69]	<0.0001
Model 1	750	0.99 [0.86 1.15]	0.94	892	1.32 [1.11 1.58]	0.002
Model 2	748	0.98 [0.85 1.14]	0.80	891	1.27 [1.06 1.52]	0.008
Model 3	746	1.01 [0.86 1.17]	0.93	885	1.23 [1.02 1.47]	0.03

Supplemental Table 4: Univariate and multivariable models for the relationship between OSA clinical categories and hs-TnT stratified by sex in subjects undergoing polysolmnography and hs-TnT assessment within one year of each other. Analysis is based on ordinal logistic regression. Regression models: Model 1: adjusted by age and BMI; Model 2: additionally adjusted by history of HTN or DM, systolic blood pressure, and smoking status; Model 3: additionally adjusted by alcohol intake, pulmonary function tests (FEV_1 and FVC), chronic lung disease, estimated glomerular filtrated rate (eGFR) and blood levels of insulin, total cholesterol, LDL, HDL and triglycerides. Reported regression coefficients are those associated with OSA severity defined by categories based on clinical definition.

	Men (n=468)			**Women (n=551)**		
	N	**OR [95%CI]**	**P value**	**N**	**OR [95%CI]**	**P value**
Unadjusted	468	1.20 [1.01 1.43]	0.039	551	1.46 [1.18 1.81]	0.001
Model 1	467	0.99 [0.82 1.20]	0.95	551	1.26 [0.97 1.62]	0.07
Model 2	465	0.96 [0.80 1.17]	0.71	550	1.20 [0.93 1.56]	0.16
Model 3	464	1.01 [0.83 1.24]	0.89	544	1.19 [0.91 1.56]	0.20

Supplemental Table 5: Univariate and multivariable models for the relationship between OSA clinical categories and hs-CRP for the overall population. Interaction between OSA and sex was not significant (p=0.84). Analysis is based on linear regression. Regression models: Model 1: adjusted by age and BMI; Model 2: additionally adjusted by history of HTN or DM, systolic blood pressure, and smoking status; Model 3: additionally adjusted by alcohol intake, pulmonary function tests (FEV_1 and FVC), chronic lung disease, estimated glomerular filtrated rate (eGFR) and blood levels of insulin, total cholesterol, LDL, HDL and triglycerides. Reported regression coefficients are those associated with OSA severity defined by categories based on clinical definition

	N	**Hs-CRP**	
		Beta Coefficient [95%CI]	**P value**
Unadjusted	1644	0.13 [0.07 0.19]	<0.001
Model 1	1641	-0.04 [-0.10 0.02]	0.19
Model 2	1637	-0.04 [-0.10 0.02]	0.17
Model 3	1630	-0.01 [-0.06 0.05]	0.86

Supplemental Table 6: Echocardiographic characteristics by OSA categories for each sex. P value is based in multivariable linear regression adjusted by age, BMI, prevalent hypertension and diabetes, systolic blood pressure, smoking status, and by the use of statins, beta-blockers, RAS inhibitors, or mineralocorticoids receptor antagonists at both times points (polysomnography and echocardiography), and by self-reported use of CPAP at the time of the echocardiography.

	Men (n=369): OSA Severity				**Adjusted P value**	**Women (534): OSA Severity**				**Adjusted P value**
	None (n=165)	**Mild (n=128)**	**Moderate (n=51)**	**Severe (n=25)**		**None (n=376)**	**Mild (n=107)**	**Moderate (n=32)**	**Severe (n=19)**	
LV Morphology										
LVEDVI ($ml/m^{2.7}$)	48.3 (10.2)	50.0 (10.4)	52.0 (9.4)	47.5 (9.6)	0.6	39.5 (7.6)	40.4 (8.6)	41.5 (8.5)	42.8 (8.6)	0.5
IVS (cm)	1.05 (0.14)	1.06 (0.17)	1.09 (0.14)	1.14 (0.20)	0.3	0.96 (0.13)	1.03 (0.15)	1.08 (0.14)	1.14 (0.15)	0.001
LVMI ($g/m^{2.7}$)	35.3 (8.7)	36.5 (9.1)	41.4 (10.7)	41.4 (12.8)	0.1	34.8 (8.4)	38.6 (8.4)	45.5 (11.4)	51.8 (13.1)	0.001
LV Systolic and Diastolic Function										
LV EF (%)	65 (5)	65 (6)	64 (5)	66 (5)	0.7	66 (5)	68 (5)	66 (6)	66 (5)	0.3
LAVI	11.6	13.0	12.3 (3.6)	12.2	0.6	11.6	12.4	13.0 (3.5)	15.5	0.5

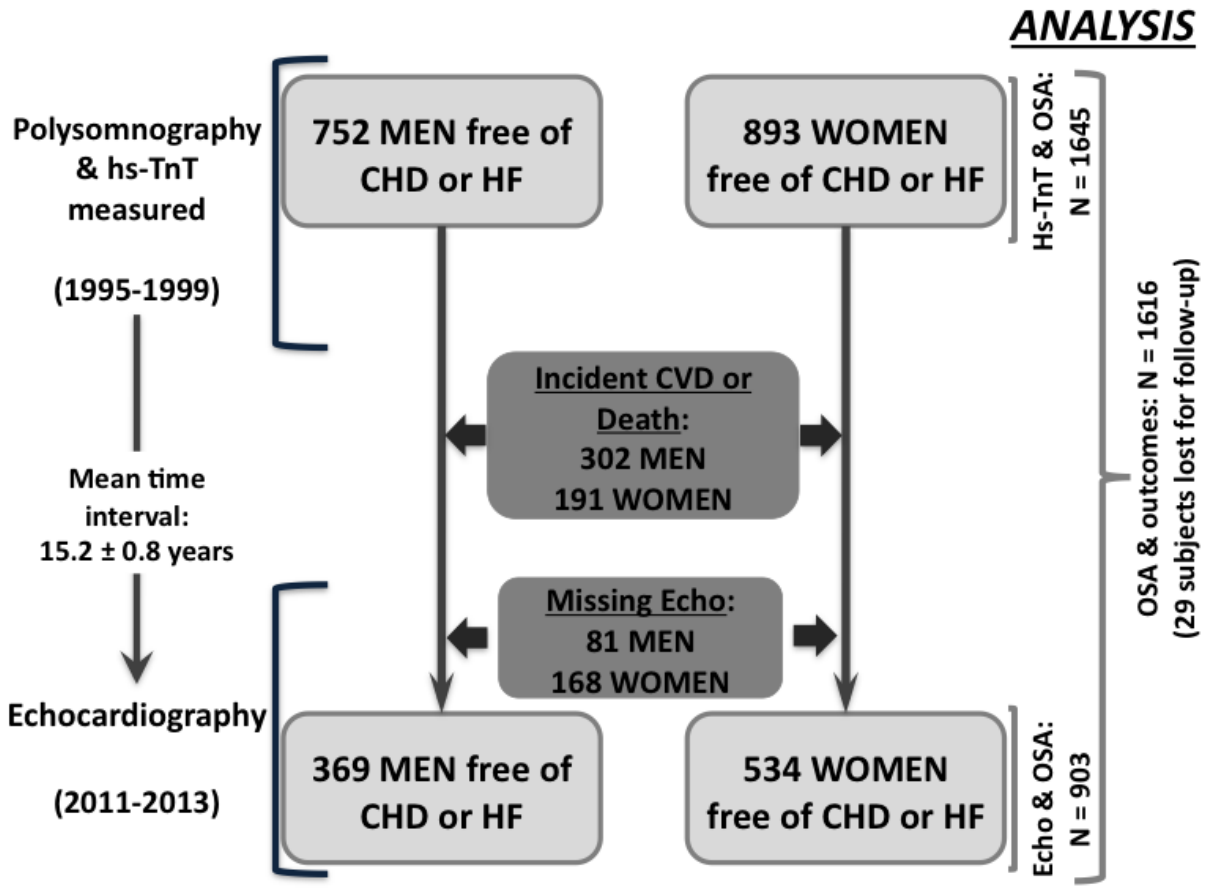
	($ml/m^{2.7}$)	(4.1)	(4.9)		(3.8)		(3.5)	(3.7)		(4.8)	
	E/E'	8.7 (2.9)	9.7 (3.3)	10.3 (4.4)	10.1 (4.1)	0.06	10.2 (3.5)	10.5 (3.5)	11.0 (3.8)	11.8 (4.1)	0.4
RV Morphology and Function											
	RVEDA (cm^2)	22.3 (5.4)	22.0 (4.7)	23.7 (4.5)	22.6 (4.8)	0.9	16.9 (3.7)	17.9 (3.7)	18.5 (4.3)	19.1 (4.5)	0.5
	RVFAC (%)	51 (7)	50 (8)	51 (8)	50 (7)	0.1	54 (8)	53 (8)	52 (6)	52 (6)	0.9
	TR velocity (m/sec)	2.33 (0.24)	2.35 (0.25)	2.38 (0.22)	2.42 (0.20)	0.4	2.36 (0.25)	2.39 (0.27)	2.32 (0.28)	2.40 (0.24)	0.8

LVEDVI: LV end diastolic volume index, IVS: interventricular septum, RWT: relative wall thickness, LVMI: LV mass index, LV EF: LV ejection fraction, LV LS: LV longitudinal strain, LAVI: left atrium volume index, E wave: early transmitral flow velocity, E/E': ratio early transmitral flow velocity to early diastolic velocity of mitral annulus, RVEDA: RV end diastolic area, RVFAC: RV fraction area change, TA S': tricuspid annular peak systolic velocity

Supplemental Figure Legends

Supplemental Figure 1. Population flowchart

Supplemental Figure:



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