CHEST Online Supplement

C-reactive Protein and Risk of OSA in Four US Cohorts

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e-Table 1. Circulating levels of C-reactive protein at baseline and risk of developing moderate-to-severe OSA (AHI≥15) in MESA[1]

	Quintiles of CRP					Per doubling of CRP	P-trend
	Q1	Q2	Q3	Q4	Q5		
MESA							
Median (mg/L)	0.43	0.96	1.79	3.50	7.96		
Cases/N	104/382	142/387	110/382	130/386	125/382		
Model 1[2]	1.00 (ref)	1.52 (1.10, 2.09)	1.07 (0.76, 1.49)	1.56 (1.12, 2.19)	1.87 (1.32, 2.65)	1.12 (1.05, 1.20)	0.001
Model 2[3]	1.00 (ref)	1.30 (0.94, 1.81)	0.84 (0.59, 1.18)	1.05 (0.74, 1.50)	1.02 (0.69, 1.49)	0.98 (0.91, 1.06)	0.61

[1]The follow-up period was 2000-2012 for MESA

[2]Model 1: Adjusted for age, race/ethnicity, sex, menopausal status in women, smoking, sleep duration, diet quality, physical activity, diabetes and hypertension.

[3]Model 2: Model 1 + continuous BMI

e-Table 2. Associations of baseline CRP (per doubling) with OSA severity measured by AHI in MESA

	Cases	Model 1[1]		Model 2[2]
		OR (95% CI)		
AHI				
<5	688	Reference		Reference
5-14	620	1.21 (1.13, 1.31)		1.10 (1.01, 1.19)
15-29	347	1.20 (1.10, 1.32)		1.03 (0.93, 1.14)
≥30	264	1.28 (1.16, 1.42)		1.02 (0.91, 1.15)

[1]Model 1: Adjusted for cohort, age, race/ethnicity, sex, menopausal status in women, smoking, sleep duration, diet quality, physical activity, diabetes and hypertension.

[2]Model 2: Model 1 + continuous BMI

e-Table 3. Circulating levels of C-reactive protein at baseline and risk of developing OSA, excluding participants with high C-reactive protein levels >10 mg/L[1]

	Quintiles of CRP					Per doubling of CRP	P-trend
	Q1	Q2	Q3	Q4	Q5		
NHS (N=1,722)							
Median (mg/L)	0.59	1.39	2.33	4.02	6.74		
Cases/N	8/344	11/345	12/344	16/345	17/344		
Model 1[2]	1.00 (ref)	1.41 (0.55, 3.60)	1.49 (0.59, 3.72)	1.92 (0.80, 4.60)	2.10 (0.88, 5.04)	1.21 (0.99, 1.49)	0.06
Model 2[3]	1.00 (ref)	1.13 (0.44, 2.91)	1.06 (0.42, 2.72)	1.09 (0.44, 2.73)	1.12 (0.45, 2.82)	1.02 (0.82, 1.26)	0.86
NHSII (N=3,835)							
Median (mg/L)	0.37	0.61	0.97	1.62	3.17		
Cases/N	19/768	19/766	44/768	81/766	105/767		
Model 1[2]	1.00 (ref)	0.97 (0.51, 1.86)	2.26 (1.30, 3.93)	4.24 (2.53, 7.11)	5.31 (3.17, 8.90)	1.76 (1.57, 1.97)	<.0001
Model 2[3]	1.00 (ref)	0.85 (0.44, 1.62)	1.70 (0.97, 2.98)	2.53 (1.48, 4.32)	2.13 (1.21, 3.74)	1.33 (1.16, 1.52)	<.0001
HPFS (N=3,024)							
Median (mg/L)	0.26	0.55	0.92	1.60	3.46		
Cases/N	63/604	68/606	73/604	88/605	98/605		
Model 1[2]	1.00 (ref)	1.04 (0.72, 1.51)	1.14 (0.79, 1.65)	1.46 (1.02, 2.09)	1.55 (1.09, 2.22)	1.14 (1.05, 1.23)	0.001
Model 2[3]	1.00 (ref)	0.93 (0.64, 1.36)	0.97 (0.67, 1.41)	1.15 (0.80, 1.66)	1.11 (0.76, 1.62)	1.06 (0.97, 1.15)	0.21

MESA (N=1,786)

Median (mg/L)	0.41	0.91	1.60	2.99	5.82		
Cases/N	39/362	49/351	58/359	47/357	54/357		
Model 1[2]	1.00 (ref)	1.28 (0.81, 2.04)	1.55 (0.99, 2.45)	1.29 (0.80, 2.09)	1.95 (1.20, 3.16)	1.16 (1.04, 1.30)	0.007
Model 2[3]	1.00 (ref)	1.05 (0.66, 1.70)	1.22 (0.77, 1.95)	0.83 (0.50, 1.37)	1.02 (0.61, 1.73)	0.99 (0.88, 1.12)	0.87

Pooled analysis (N=10,367)

Median (mg/L)	0.35	0.70	1.23	2.31	5.52		
Cases/N	131/2,073	153/2,073	202/2,074	238/2,074	245/2,073		
Model 1[2]	1.00 (ref)	1.24 (0.97, 1.58)	1.66 (1.32, 2.11)	2.14 (1.70, 2.70)	2.46 (1.94, 3.12)	1.27 (1.20, 1.34)	<.0001
Model 2[3]	1.00 (ref)	1.10 (0.86, 1.42)	1.28 (1.00, 1.63)	1.44 (1.13, 1.83)	1.29 (1.00, 1.67)	1.07 (1.01, 1.14)	0.02

[1]The follow-up period was 2002-2012 for NHS, 1995-2013 for NHSII, 1996-2012 for HPFS and 2000-2012 for MESA

[2]Model 1: Adjusted for cohort (pooled analysis), age, race/ethnicity, sex (MESA and pooled analysis), menopausal status in women, smoking, sleep duration, diet quality, physical activity, diabetes and hypertension.

[3]Model 2: Model 1 + continuous BMI

e-Table 4. Subgroup associations between C-reactive protein (per doubling) and OSA risk by age, sex, menopausal status and BMI in individual cohorts

	NHS	NHSII	HPFS	MESA	P-heterogeneity by cohort
			OR (95% CI)		
Age					
<55 years	--	1.32 (1.17, 1.50)	1.05 (0.92, 1.21)	0.97 (0.80, 1.17)	0.008
≥55 years	1.00 (0.84, 1.18)	--	1.05 (0.95, 1.15)	0.99 (0.88, 1.12)	0.77
Sex					
Men	--	--	1.05 (0.98, 1.14)	0.96 (0.81, 1.13)	0.43
Women	1.00 (0.84, 1.18)	1.32 (1.17, 1.50)	--	0.99 (0.87, 1.13)	0.003
Menopausal status					
Premenopausal	--	1.32 (1.16, 1.50)	--	1.16 (0.76, 1.77)	0.57
Postmenopausal	1.00 (0.84, 1.18)	1.14 (0.65, 2.02)	--	0.96 (0.78, 1.16)	0.83
BMI					
<25 kg/m^2	1.28 (0.43, 3.84)	1.26 (0.92, 1.73)	1.20 (1.05, 1.38)	1.15 (0.91, 1.46)	0.97
≥25 kg/m^2	0.90 (0.71, 1.15)	1.10 (0.95, 1.28)	1.00 (0.91, 1.10)	0.94 (0.84, 1.05)	0.32

Adjusted for age, race/ethnicity, sex (MESA only), menopausal status in women, smoking, sleep duration, recent physical exams (NHS/NHSII and HPFS), diet quality, physical activity, diabetes, hypertension and BMI.

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