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Heritability and genetic correlations of obesity indices with ambulatory and office beat-to-beat blood pressure in the Oman Family Study

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States and Chinese National Surveys on Students' Constitution and Health (2005–2010) [4] examining trends in SBP/DBP among children and adolescents reported that BP increased over time but that this increase was reduced 12.0–40.5% after adjustment for BMI, indicating that the increase in BP was partially because of the rise in BMI. Meanwhile, a number of twin and family studies also showed familial aggregation of BMI and BP, which may be driven by shared genetic and/or environmental factors [7–9]. These twin and family studies estimated the genetic and environmental overlap between obesity and BP, but only used conventional office BP measurements and BMI as indicator of general obesity. Compared with office BP, ambulatory BP measurements have a number of advantages, such as providing a larger number of BP measurements, profiling BP behavior and capturing variations over 24-h. Most importantly, it is generally recognized to be more strongly associated with target organ damage and also a stronger predictor of cardiovascular morbidity and mortality [10]. Although BMI is the most commonly used surrogate marker of obesity, it lacks the capability of discriminating between body fat and lean mass [11]. A meta-analysis of 32 different studies on 31 968 individuals indicated that the BMI definition of obesity failed to identify nearly 50% of the population with excess percentage of body fat (%BF) [12]. The latter measure of %BF is recognized as a better predictor of cardiovascular risk factors than BMI [13]. In addition, more studies showed the importance of central or abdominal obesity measured by waist circumference and by fat distribution measured by waist-to-height ratio (WHtR) in predicting cardiovascular risk [14].

To more precisely and comprehensively estimate the genetic and environmental correlations between obesity and BP, we analyzed a number of obesity indices in relation to both ambulatory and office beat-to-beat BP measures using data from the Oman Family Study (OFS). The OFS is a population-based family study from an isolated population that is environmentally and genetically homogeneous and is expected to have better power to examine the genetic contributions to BP and obesity indices and their overlap than studies conducted in outbred, heterogeneous populations [15].

METHODS

Study population

Five large, extended and highly consanguineous families totaling 1231 individuals with 304, 142, 225, 279 and 281 volunteers, each living in a separate village within a perimeter of 20 km around the City of Nizwa. Interviewed people represented approximately 10–15% of the total number of individuals in these five pedigrees. They were 16–80 years old and all voluntarily took part in the study, appeared healthy, and had no clinical complaints as determined by a questionnaire. First cousin marriages represent more than 50% of all marriages (more information can be found in Supplementary Table 1, <http://links.lww.com/HJH/B305>). Polygamy is widely practiced with some men marrying up to four wives [16]. Because of intermarriages between the five pedigrees, SOLAR considered all volunteers in the cohort as one family whenever calculating heritability [17]. Relative

pairs of those five families were described in the supplemental table, <http://links.lww.com/HJH/B305>. The study was approved by the Medical Research and Ethics Committee of Sultan Qaboos University. A written and signed or thumb-printed rubber-stamped informed consent was obtained from each participant or a parent and/or legal guardian if participants were under the age of 18 years.

Ambulatory and office beat-to-beat blood pressure measurement

Ambulatory BP measurements were recorded for a 24-h period on the first home visit, using the auscultatory mode of the validated Schiller BR 102 ambulatory BP monitor (Schiller AG, Baar, Switzerland) [18]. With the participant seated, the appropriate size cuff was fixed to the nondominant arm and three BP readings taken, whereas at the same time, three additional BP readings were taken with a calibrated mercury sphygmomanometer on the dominant arm to confirm accuracy of the ambulatory BP measurements. Recordings were accepted and ambulatory BP recordings started when the average of both measurement methods did not differ by more than 5 mmHg. To reduce movement artefacts during ambulatory BP recordings, participants were discouraged from strenuous physical activity. The BP monitor was programmed to record BP every 30 min from 07:30 to 21:30 and every 60 min from 21:30 to 09:30, for a total of 26 h. The first 2 h of monitoring were considered as an adaptation period and were not included in the calculation of BP means. Recordings were accepted when the rate of invalid measurements because of, for example, artefacts was less than 25% and when the recording lasted for at least 20 consecutive hours. Quality control of data output from the 24-h monitor for SBP and DBP was performed by one technician, trained at identifying artefacts and outliers. The daytime and sleep periods were determined for each participant according to their actual waking and sleeping time as recorded in their diaries and confirmed by changes in BP. The average BP levels during the total 24-h and during daytime and sleep periods were calculated [19].

For the office beat-to-beat BP measurement, after reporting to the field research center at 0700 h and removing the BP monitor, participants were made to rest in supine position for 10 min on a comfortable bed, in a quiet office with a temperature between 24 and 26 °C. Measurements were acquired for the subsequent 10 min using the Task Force Monitor (CNS Systems, Graz, Austria). The beat-to-beat BP was recorded using the vascular unloading technique whereby finger cuff readings were recorded, automatically counterchecked and corrected every minute, by the oscillometric BP measurements recorded from the contralateral upper arm.

Participants taking antihypertensive medications ($n = 189$) were not asked to stop medication, but the measured BP results were corrected (+15 mmHg for SBP and +10 mmHg for DBP) prior to analysis as recommended by previous studies [20,21].

Measurement of obesity indices

Height and weight were measured using standard methods. Waist circumference was measured by a soft tape at the

largest circumference between the lowest rib and iliac crest. %BF was assessed using electrical impedance (Tanita, Tokyo, Japan) [22], which showed good consistency compared with dual-energy X-ray absorptiometry as the recognized gold standard for measuring %BF (difference controlled within 5%). BMI was calculated as weight/height², where the units of weight and height are kilogram (kg) and meter (m), respectively. WHtR was calculated as waist circumference/height, where the units of waist circumference and height are both centimeters (cm).

Statistical analysis

Descriptive statistics were used to present the baseline characteristics of the study sample and Student's *t*-tests were used to test for sex differences in the means. Prior to analysis, distributions of all variables were checked. To obtain better approximations of normal distributions, measurements of BMI and all BP variables were transformed by natural logarithm. No outliers (more than four standard deviations from the mean) were observed. SOLAR (v7.2.5) software [23] was used to perform univariate and bivariate quantitative genetic analyses. SOLAR uses a variance-component method to analyze family-based quantitative data by decomposing the phenotypic variance into genetic and environmental components using the observed covariance in the trait among family members (Equation 1).

$$\sigma_p^2 = 2\Phi\sigma_G^2 + I\sigma_E^2, \quad (1)$$

where Φ is a $n \times n$ matrix of kinship coefficients, σ_p^2 is the phenotypic variance, σ_G^2 is the variance because of the additive genetic effects, σ_E^2 is the variance because of the environmental effects and I is the identity matrix of order n . Each genetic and environmental variance component is accompanied by a structuring matrix that predicts the covariance among individuals associated to that component. The structuring matrix for σ_G^2 is twice the kinship coefficient (2Φ) and for unmeasured, nongenetic factors (i.e. σ_E^2), it is the identity matrix I . SOLAR estimates the narrow sense heritability (h^2) by the proportion of the phenotypic variance that can be attributed to additive genetic effects, that is, $h^2 = \sigma_G^2 / \sigma_p^2$. The significance of h^2 was determined by using a likelihood ratio test where the log-likelihood of the estimated model is compared with that of the nested model where σ_G^2 is fixed to zero using a chi-square test with 1 degree of freedom [24].

Bivariate quantitative genetic analyses were conducted to estimate the genetic and environmental correlations of obesity indices with BP using SOLAR. The model is an extension of that shown in Equation 1, where the phenotypic covariance between two individuals for two traits is given by a 2×2 covariance matrix and can be calculated as in Equation 2:

$$r_p = \left(\sqrt{b_{BP}^2} \times r_G \times \sqrt{b_{Obesity}^2} \right) + \left(\sqrt{e_{BP}^2} \times r_E \times \sqrt{e_{Obesity}^2} \right), \quad (2)$$

where r_G is the additive genetic correlation and r_E the environmental correlation between obesity indices and BP,

and e^2 is the environmental contribution to the overall phenotypic variance of the particular BP or obesity indices. With r_G , the extent of common genetic effects on the two traits being analyzed is measured (i.e. pleiotropy). To test for the significance of shared genetic effects ($|r_G| > 0$), r_G was first estimated and subsequently fixed to zero in a nested sub-model allowing for a comparison of the two models using a likelihood ratio test. Similarly, to test for complete overlap of genetic effects ($|r_G| = 1$), r_G was fixed to one and compared with the more general model in which it was freely estimated. If $r_G = 0$, it means that the two traits being analyzed are influenced by independent genetic factors. If $|r_G| = 1$, the genetic factors are completely shared [24,25].

RESULTS

A total of 1231 participants with a median age of 28 years (interquartile range: 21–45) were included in the analyses. Slightly more women participated in the study (54.9%). Men were taller and heavier, but no significant sex differences were found for age. In general, men had significantly higher BP. There were no significant sex differences for BMI and waist circumference, but men had lower %BF and WHtR than women (Table 1).

Results of the univariate analyses showed that heritability estimates (h^2) ranged from 30.2 to 38.2% for daytime BP, 16.8–21.4% for sleeping BP 32.1–40.4% for 24-h BP and 22–24.4% for office beat-to-beat BP. Heritability estimates were similar for ambulatory daytime and 24-h BP, but higher than ambulatory sleep and office beat-to-beat BP. Heritability estimates of BMI, %BF, waist circumference and WHtR were 67.8, 52.2, 37.3 and 37.9%, respectively. Heritability estimates of all the traits were highly significantly different from 0 (Table 2).

The results of the bivariate quantitative genetic analyses showed consistently significant and positive phenotypic correlations between different obesity measurements and ambulatory daytime BP (r_p : 0.14–0.20), sleeping BP (r_p : 0.20–0.27), 24-h BP (r_p : 0.18–0.23) and office beat-to-beat BP (r_p : 0.14–0.32) (Table 3). The genetic correlations between BP and obesity indices were always larger than the environmental correlations, no matter whether BP was assessed during the daytime (r_G : 0.23–0.35 vs. r_E : 0.01–0.12), at night (r_G : 0.34–0.49 vs. r_E : 0.07–0.20), during 24-h (r_G : 0.26–0.39 vs. r_E : 0.05–0.16) or as beat-to-beat measurement at the office (r_G : 0.16–0.50 vs. r_E : 0.12–0.31), except for BMI and office beat-to-beat DBP (r_G : 0.20 vs. r_E : 0.22).

The genetic correlations of the different obesity indices (BMI, %BF, waist circumference and WHtR) with ambulatory BP seemed to be higher in sleeping BP (r_G : 0.34–0.49) compared with daytime BP (r_G : 0.23–0.35) and 24-h BP (r_G : 0.26–0.39). Table 3 shows that all these r_G s were significantly greater than 0 except for the one between WHtR and daytime SBP ($r_G = 0.23$, $P = 0.051$). However, as expected, the genetic factors were not completely shared as all r_G s were significantly less than 1. No large differences were found between the genetic correlations of SBP (r_G : 0.23–0.50) and DBP (r_G : 0.16–0.49) with the different obesity measures.

TABLE 1. Descriptive statistics of the Oman Family Study stratified by sex

Characteristics	Men		Women		P value
	N	Statistic ^a	N	Statistic ^a	
Anthropometric measurements					
Age (years)	554	26.5 (20.0–42.0)	677	30.0 (22.0–45.0)	NS
Height (cm)	554	165.7 (7.3)	677	152.2 (5.5)	<0.01
Weight (kg)	554	67.0 (58.0–77.0)	677	56.0 (49.5–67.0)	<0.01
BP measures					
Daytime SBP (mmHg)	534	127.0 (121.0–135.0)	644	119.0 (111.0–128.0)	<0.01
Daytime DBP (mmHg)	534	82.0 (76.8–89.0)	644	80.0 (74.0–88.0)	<0.01
Sleep SBP (mmHg)	513	109.0 (102.0–118.5)	625	104.0 (95.0–114.5)	<0.01
Sleep DBP (mmHg)	513	68.0 (61.0–75.0)	625	66.0 (59.0–73.0)	<0.05
Total 24-h SBP (mmHg)	523	124.0 (117.0–131.0)	632	116.0 (108.0–125.0)	<0.01
Total 24-h DBP (mmHg)	523	79.0 (74.0–86.0)	632	77.0 (71.3–84.0)	<0.01
Office beat-to-beat SBP (mmHg)	507	116.4 (108.2–124.9)	616	105.1 (98.2–113.0)	<0.01
Office beat-to-beat DBP (mmHg)	507	74.0 (68.0–82.1)	616	66.6 (60.4–73.0)	<0.01
Obesity index					
BMI (kg/m ²)	554	24.6 (20.9–28.2)	677	24.7 (21.2–28.6)	NS
Body fat (%)	537	17.9 (8.4)	657	28.2 (9.8)	<0.01
Waist circumference (cm)	537	81.0 (14.3)	657	81.2 (14.5)	NS
Waist-to-height ratio	537	0.49 (0.09)	657	0.53 (0.10)	<0.01

The daytime and sleep periods were determined for each participant according to their actual waking and sleeping time as recorded in their diaries. One hundred and eighty-nine participants took antihypertensive medications and measured BP results were corrected (+15 mmHg for SBP and +10 mmHg for DBP) prior to analysis as recommended by previous studies. NS, non-significant.

^aData expressed as mean (SD) for normally distributed variable or median (interquartile range) in case of skewed distribution.

No significant environmental correlations were observed between the different obesity indices and ambulatory BP, except for sleep SBP with BMI, waist circumference or WHtR and 24-h SBP with waist circumference or WHtR. However, the environmental correlations between office beat-to-beat BP and obesity indices were all significantly different from 0 (r_E : 0.12–0.31; $P < 0.05$) and usually larger than those between ambulatory BP and obesity indices (r_E : 0.01–0.20).

DISCUSSION

The aim of our study was to estimate the heritability of ambulatory and office beat-to-beat BP and various indices of obesity and to explore to what extent they shared genetic and/or environmental factors. Our study echoed previous findings on the heritability estimates and the positive phenotypic, genetic and environmental correlations between

office BP and BMI. Here we confirmed substantial genetic correlations between ambulatory BP and other indices of general obesity (%BF), abdominal obesity (waist circumference) and fat distribution (WHtR). Shared genetic factors contributed more to the phenotypic correlations than environmental factors. The genetic correlations seemed to vary under different conditions as they were higher during sleep than for daytime SBP and DBP.

Our study found moderate heritability for ambulatory and office beat-to-beat SBP and DBP, which varied for different measurement conditions. It was higher for daytime compared with sleep BP and the heritabilities of office beat-to-beat BP were lower compared with those for ambulatory daytime and 24-h BP measurements. These results were in line with the univariate BP heritability estimates we published previously [19] and similar to other family studies of ambulatory BP conducted in different populations (SBP: ranging from 0.25 to 0.39; DBP: ranging from 0.20 to 0.41) [26–29]. For example, Fava *et al.* [26] reported that in 118 Swedish families with 260 siblings (without antihypertensive treatment), heritabilities were significant for ambulatory night-time SBP (37%), DBP (32%), ambulatory daytime SBP (33%), 24-h SBP (30%) and DBP (29%) ($P < 0.05$ for all). Another family study conducted in 1009 individuals from 271 nuclear Swiss families also reported significant heritability for ambulatory daytime SBP (39%), night-time SBP (25%), 24-h SBP (37%) and ambulatory daytime DBP (28%), night-time DBP (20%), 24-h DBP (26%), respectively [29]. In a study of African families consisting of 314 individuals (147 men and 167 women) and with at least two hypertensive siblings, the heritability estimates for ambulatory SBP and DBP were 0.37 and 0.24, respectively for daytime and 0.34 and 0.37 for night-time measurements ($P < 0.05$ for all estimates) [27]. A study of 520 white European nuclear families including 2020 individuals reported heritabilities of 0.33 for mean 24-h SBP and 0.41 for mean 24-h DBP [28].

TABLE 2. Heritability estimates of blood pressure and obesity measurements

Traits	N	h^2	SE	P-value
BP measures				
Daytime SBP	1178	0.302	0.048	4.27×10^{-23}
Daytime DBP	1178	0.382	0.052	2.15×10^{-30}
Sleep SBP	1138	0.214	0.049	4.32×10^{-10}
Sleep DBP	1138	0.168	0.047	8.0×10^{-6}
Total 24-h SBP	1155	0.321	0.051	8.27×10^{-23}
Total 24-h DBP	1155	0.404	0.054	3.59×10^{-30}
Office beat-to-beat SBP	1123	0.244	0.053	5.1×10^{-10}
Office beat-to-beat DBP	1123	0.220	0.052	1.19×10^{-8}
Obesity index				
BMI	1231	0.678	0.050	7.70×10^{-57}
Body fat	1214	0.522	0.056	2.35×10^{-35}
Waist circumference	1204	0.373	0.053	7.30×10^{-21}
Waist-to-height ratio	1204	0.379	0.053	3.23×10^{-22}

Models were adjusted for age, sex, age², age × sex and age² × sex. BP, blood pressure.

TABLE 3. Bivariate quantitative genetic analysis results of obesity indices with ambulatory daytime, sleep, 24-h and office beat-to-beat SBP and DBP showing the genetic, environmental and phenotypic correlations

	N	Genetic correlation, r_G (SE)	Environmental correlation, r_E (SE)	Phenotypic correlation, r_P	Proportions of r_P (A/E)	Genetic correlation, r_G (SE)	Environmental correlation, r_E (SE)	Phenotypic correlation, r_P	Proportions of r_P (A/E)
					Ambulatory daytime SBP				
BMI	1231	0.31 ^a (0.09)	0.04 (0.07)	0.17 ^c	0.88/0.12	0.34 ^a (0.08)	0.05 (0.08)	0.20 ^c	0.89/0.11
Body fat	1222	0.31 ^a (0.11)	0.01 (0.06)	0.14 ^c	0.96/0.04	0.35 ^a (0.09)	0.06 (0.06)	0.19 ^c	0.84/0.16
Waist circumference	1223	0.25 ^a (0.11)	0.11 (0.05)	0.16 ^c	0.55/0.45	0.34 ^a (0.10)	0.08 (0.06)	0.18 ^c	0.74/0.26
Waist-to-height ratio	1223	0.23 (0.11)	0.12 (0.05)	0.16 ^c	0.51/0.49	0.32 ^a (0.10)	0.09 (0.06)	0.18 ^c	0.70/0.30
					Ambulatory sleep SBP				
BMI	1231	0.43 ^a (0.10)	0.18 ^b (0.07)	0.27 ^c	0.64/0.36	0.49 ^a (0.10)	0.07 (0.07)	0.22 ^c	0.82/0.18
Body fat	1222	0.43 ^a (0.12)	0.12 (0.06)	0.23 ^c	0.69/0.31	0.49 ^a (0.11)	0.07 (0.05)	0.21 ^c	0.80/0.20
Waist circumference	1219	0.36 ^a (0.12)	0.19 ^b (0.05)	0.24 ^c	0.47/0.53	0.44 ^a (0.12)	0.11 (0.05)	0.20 ^c	0.63/0.37
Waist-to-height ratio	1219	0.34 ^a (0.12)	0.20 ^b (0.05)	0.24 ^c	0.44/0.56	0.42 ^a (0.12)	0.10 (0.05)	0.20 ^c	0.64/0.36
					Ambulatory 24-h SBP				
BMI	1231	0.33 ^a (0.09)	0.10 (0.07)	0.21 ^c	0.77/0.23	0.38 ^a (0.08)	0.05 (0.08)	0.23 ^c	0.90/0.10
Body fat	1222	0.35 ^a (0.10)	0.06 (0.06)	0.18 ^c	0.82/0.18	0.38 ^a (0.09)	0.08 (0.07)	0.23 ^c	0.82/0.18
Waist circumference	1220	0.29 ^a (0.11)	0.14 ^b (0.06)	0.20 ^c	0.55/0.45	0.39 ^a (0.10)	0.09 (0.06)	0.22 ^c	0.76/0.24
Waist-to-height ratio	1220	0.26 ^a (0.11)	0.16 ^b (0.06)	0.20 ^c	0.49/0.51	0.36 ^a (0.10)	0.11 (0.06)	0.21 ^c	0.70/0.30
					Office beat-to-beat SBP				
BMI	1231	0.42 ^a (0.10)	0.31 ^b (0.06)	0.32 ^c	0.53/0.47	0.20 ^a (0.12)	0.22 ^b (0.07)	0.19 ^c	0.39/0.61
Body fat	1224	0.50 ^a (0.12)	0.17 ^b (0.05)	0.27 ^c	0.57/0.43	0.34 ^a (0.14)	0.12 ^b (0.05)	0.18 ^c	0.54/0.46
Waist circumference	1219	0.32 ^a (0.14)	0.24 ^b (0.05)	0.26 ^c	0.34/0.66	0.21 ^a (0.15)	0.15 ^b (0.05)	0.16 ^c	0.33/0.67
Waist-to-height ratio	1219	0.29 ^a (0.14)	0.23 ^b (0.05)	0.24 ^c	0.34/0.66	0.16 ^a (0.15)	0.14 ^b (0.05)	0.14 ^c	0.29/0.71

Models were adjusted for age, sex, age², age × sex and age² × sex. r_E , environmental correlation; r_G , genetic correlation; r_P , phenotypic correlation; SE, standard error. A/E is the percentage of the phenotypic correlation that is caused by genes (A) or environment (E), based on the following equation:

$$r_P = \left(\sqrt{h_{BP}^2} \times r_G \times \sqrt{h_{Obesity}^2} \right) + \left(\sqrt{e_{BP}^2} \times r_E \times \sqrt{e_{Obesity}^2} \right).$$

^aGenetic correlations significantly different from 0 ($P < 0.05$).

^bEnvironmental correlations significantly different from 0 ($P < 0.05$).

^cPhenotypic correlations significantly different from 0 ($P < 0.05$).

Some of this variation in BP heritability estimates may be because of different genes contributing to BP regulation under different measurement conditions, such as daytime vs. night-time or office vs. real life, which was also shown in previous twin studies [30,31]. For daytime vs. night-time we confirmed this in our own data by performing bivariate analyses of ambulatory BP during daytime and sleep. The genetic correlation between daytime and sleep was 0.83 for SBP and 0.69 for DBP. Both correlations were significantly different from 1 ($P < 0.001$) indicating partly different genes influencing BP during these measurement conditions. These results are further supported by findings from mouse model studies showing rhythmic gene expression in normal heart and aorta under light–dark conditions with two major peaks: one in the light and one in the dark [32,33].

Earlier heritability estimates of obesity indices varied among different populations (BMI: ranging from 0.16 to 0.85; %BF: ranging from 0.35 to 0.43; waist circumference: ranging from 0.37 to 0.81) [34–36]. Taking abdominal obesity as an example, Davey *et al.* [37] reported that the heritability was over 90% for abdominal obesity in an Indian population, whereas a family study in an Old Order Amish community showed a heritability of 37% for waist circumference and 13% for waist-to-hip ratio, respectively [38]. Compared with above studies, our study reported moderate (37.3–67.8%) heritability estimates for the obesity indices.

Our study found consistently significant and positive phenotypic correlations between BP and obesity indices. This pattern was consistent with results from large-scale epidemiological studies [39]. Virginija *et al.* [39] reported that significant associations (adjusted odds ratio ranged from 2.6 to 7.4) were found between overweight, obesity,

or high waist circumference with high BP after adjusting for age and sex among Lithuanian adolescents. Some animal studies have suggested that the association between obesity and BP was mediated by leptin [40], but human studies do not support this [41]. In our own data, %BF showed the largest correlation with leptin ($r = 0.764$; $P < 0.01$), followed by the other three obesity indices (r ranging from 0.472 to 0.621; all P values < 0.01). Compared with the four obesity indices, we found much lower correlations (r ranging from -0.035 to 0.144) of leptin with the different BP measurements in our study. The pattern of correlations between leptin and BP measures closely mimicked the results for %BF, but were much more modest and often nonsignificant (Supplementary Table 2, <http://links.lww.com/HJH/B305>). Obesity is the well-recognized risk factor for hypertension and genetic factors may play an important role in this association. Howe *et al.* [42] reported that a genetic risk score composed of 32 BMI loci identified in genome-wide association studies (GWAS) was strongly associated with SBP both at age 6 and 17 years and in a meta-analysis [43] on 57 464 hypertensive cases and 41 256 controls, it was found that the first GWAS-identified obesity gene (*FTO*, also known as FTO alpha-ketoglutarate-dependent dioxygenase and located on chromosome 16. It was the first gene identified in a genome-wide association study of BMI as an index of general obesity [44]) was significantly associated with hypertension.

Our study also identified significant genetic contributions to the phenotypic correlation of different obesity indices with ambulatory and office beat-to-beat BP. This pattern was generally in line with twin and family studies of conventionally measured BP and BMI [7–9]. For example,

Schieken, *et al.* [7] found a significant phenotypic correlation between SBP and BMI in a twin study of children ($r=0.29$) and showed that the percentage of variance of SBP explained by genetic factors common between SBP and BMI was 8%. Similar findings were reported in an adult study of Chinese twins, which showed that the genetic and unique environmental correlations were 0.38 and 0.17, respectively, between BMI and SBP and 0.48 and 0.12 between BMI and DBP. The genetic factors influencing both BMI and BP accounted for 6 and 7% of the total variance in SBP and DBP, respectively [8]. In a large family study of 2912 individuals from 767 adult nuclear families, the phenotypic correlation between SBP and BMI was 0.36 and the genetic correlation was 0.30 [9]. Our study did not find significant environmental correlations between ambulatory BP and obesity indices, except for sleep SBP with BMI, waist circumference and WHtR and for 24-h BP with waist circumference and WHtR. Thus, shared genetic factors had a larger contribution to the phenotypic correlations between ambulatory BP and obesity than environmental factors. However, it was found that all environmental correlations of obesity indices with office beat-to-beat BP were significantly different from 0 and were higher than with ambulatory BP. In addition, in the current study, genetic correlations with obesity indices seemed to be lower for daytime BP than for sleeping BP but no differences were found between SBP and DBP. This might possibly be because of partly different genes regulating daytime and night-time BP [30,45].

A strength of this family study is that it was conducted in a homogeneous Arab population, in which the individuals had a very similar genetic background (tradition of encouraging consanguineous marriage) and shared environmental effects (living in a relatively isolated region). Consequently, it was expected to have somewhat better power to examine the genetic contributions to BP and obesity indices than studies conducted in outbred, heterogeneous populations [15]. Another strength is that BP values were measured using 24-h ambulatory monitoring, which is believed to better predict target organ damage than conventional BP methods [46]; and various indices, including %BF as a more accurate measure of general obesity than BMI, waist circumference representing abdominal obesity and WHtR representing fat distribution, were used to capture different aspects of obesity. Furthermore, the effects of hypertension medication were corrected to optimally preserve genetic variability as recommended by previous studies [20,21] to ensure data quality. However, there are also some limitations of this study. Firstly, although our study contained data on more than 1200 participants, the sample size may still not be large enough to clearly discriminate between genetic and/or environmental correlations among different obesity indices and/or BP conditions. Secondly, waist-to-hip ratio (WHR) would also be a good index to represent central obesity, but unfortunately hip circumference was only measured in part of the sample. Instead, we decided to use WHtR, on which we had complete data and showed a strong phenotypic correlation ($r_p=0.62$, $P<0.01$) with WHR for the part of the sample of which WHR was available. Furthermore, previous studies also reported that

WHtR and WHR had comparable correlations with SBP ($r: 0.41$ vs. 0.36) or DBP ($r: 0.35$ vs. 0.31) [47].

In conclusion, our study quantified the considerable genetic overlap between a variety of obesity indices and both ambulatory and office beat-to-beat BP and highlights the relevance and potential of identification of pleiotropic genes. More advanced analyses, for example, GWAS could and should be undertaken to discover the specific genes both influencing obesity indices and BP, and thus help unravel the shared genetic background of these two clinically relevant traits.

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Conflicts of interest

There are no conflicts of interest.

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