Myocardial sestamibi uptake in healthy subjects is related to age, gender and habitus

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Summary

The object of this study was to evaluate the effect of gender, age and anthropometric data on regional isotope uptake in myocardial perfusion scintigraphy using ^{99m}Tc-MIBI-SPECT (myocardial sestamibi single-photon emission technique). Seventy-one healthy, non-smoking subjects, 42 men and 29 women between 40 and 80 years of age, with less than 5% likelihood of having coronary artery disease were studied. All subjects underwent a maximal exercise and rest MIBI-SPECT using a 2-day protocol and a 180° anterior circular rotation. No correction for scatter or attenuation was made. Normalized regional activity was different in men and women in the anterior and inferior regions, with higher values anteriorly in men and inferiorly in women. Regional activity also differed with age in both women and men with higher relative activity in the anterior regions in the oldest age groups. Higher activities were seen in the basal parts of the left ventricle at rest compared with stress in both men and women. Regional isotope uptake was significantly affected by habitus expressed as body mass index (BMI) and thoracic circumference. Different protocols for stress and rest seem to be needed for men and women in different age groups, and for stress and rest when performing semiquantitative MIBI-SPECT and comparing data with a normal file of healthy subjects. Furthermore, such anthropometric data as BMI and/or thoracic circumference should be considered in order to minimize the risk for false-positive or false-negative scintigraphic results.

Keywords: age, anthropometric data, gender, MIBI-SPECT, reference limits.

Introduction

The introduction of semiquantitative measurements of regional isotope uptake and comparative studies using polar maps from healthy reference groups have increased the diagnostic accuracy and objectivity of myocardial perfusion scintigraphy using single-photon emission technique (SPECT) (Depasquale *et al.*, 1988). Existing databases suggest different regional myocardial isotope uptake depending on gender (Eisner *et al.*, 1988; Garcia *et al.*, 1992; Van Train *et al.*, 1993). However, the existing normal reference files comprising healthy subjects do not include, for example, anthropometric data that could have an affect on photon attenuation.

Attenuation is caused by intervening organs and tissues between the heart and the gamma-camera and may be problematic, especially when examining obese persons or women with large breasts.

To improve the diagnostic accuracy of myocardial SPECT, different methods for attenuation correction, such as simultaneous emission and transmission tomography, have been proposed (Bailey *et al.*, 1987; Tan *et al.*, 1993). Despite these correction methods, there remain potential pitfalls and unexpected complications (King *et al.*, 1996).

The aim of this paper was to study to the extent to which anthropometric data, age and gender affects the regional myocardial radioisotope uptake recorded by ^{99m}Tc-MIBI-SPECT (myocardial sestamibi single-photon emission technique) in healthy men and women between 40 and 80 years of age.

Methods

Subjects

Eighty non-smoking subjects between 40 and 80 years of age with no history of cardiovascular disease were recruited from blood donor units and a local pensioners' association. All subjects underwent a maximal exercise stress test on the bicycle and an echocardiographic examination. Nine subjects were excluded owing to hypertension (2), atrial fibrilation (2) left ventricular hypertrophy on echocardiographic examination (1) or signs of silent ischaemic heart disease during an exercise ECG (4). Thus, the remaining 71 subjects, 42 men and 29 women, were normotensive, had normal resting and exercise ECGs and normal fasting blood levels of lipids and glucose. Based on these criteria, the risk for ischaemic heart disease (IHD) in a selected population under 70 years of age is less than 5% (Diamond & Forrester, 1979).

Anthropometric data

The height, weight, body mass index (BMI) and body size area (BSA) of the subjects and the circumference of the thorax at the cardiac level were measured.

Echocardiography

Echocardiographic measurements at rest were acquired from standard projections (parasternal and apical positions) with the subjects in the left lateral decubitus position using an Acuson XP 128 with a 2·5 or 3·5 MHz transducer (Acuson, Mountain View, CA, USA). Measurements were taken from 2-D and M-mode recordings and with pulsed and colour flow Doppler.

Myocardial perfusion scintigraphy

Myocardial perfusion was studied during upright maximal exercise on a cycle ergometer (Siemens Ergomed 840L, Erlangen, Germany) and at rest. At peak exercise, 700-MBq ^{99m}Tc-MIBI (DuPont, MA, USA) was injected through an intravenous port and exercise was continued for another minute. A 12-lead ECG was recorded before, during and up to 6 min after terminating the exercise. Blood pressure and heart rate were followed during and after the exercise test. SPECT acquisition was carried out 30 min after injection of the isotope with the patient in the supine position. To minimize gall bladder activity, all subjects were given a light, fatty meal between the ^{99m}Tc-MIBI injection and imaging. A scintigraphic study at rest was made 24 h after the exercise MIBI-SPECT. MIBI (500 MBq) was injected followed by a SPECT registration 45 min later.

Data acquisition and processing

Scintigraphic data were acquired with a single-head gamma-camera (XT/C, General Electric, Milwaukee, WI, USA) linked to a General Electric Star 3200 computer. A general-purpose collimator was used, and a 20% energy window was centred over the 140-keV photo peak. Projection data were collected at 32 angles over a semicircular 180-degree orbit (45 degrees right anterior oblique to 45 degrees left posterior oblique) and stored in 64×64 matrices. The acquisition time was 30 s per projection for both stress and resting studies. Short-axis slices of the left ventricle were reconstructed from the transaxial sections and polar maps, excluding the most apical and basal parts of the left ventricle, displaying the regional MIBI distribution at rest and stress that were created. The polar maps were then divided into eight segments (Fig. 1), and normalized activity, expressed as the percentage of maximal activity in each segment, was measured under stress and resting conditions. No corrections for attenuation or scatter were made.

Statistical methods

Multiple repeated analysis of variance followed by Duncan's new multiple-range test, multiple regression analysis or, when applicable, the paired *t*-test were used. *P*-values $<0{\cdot}05$ were considered to be significant. Values are reported as means ± SD.

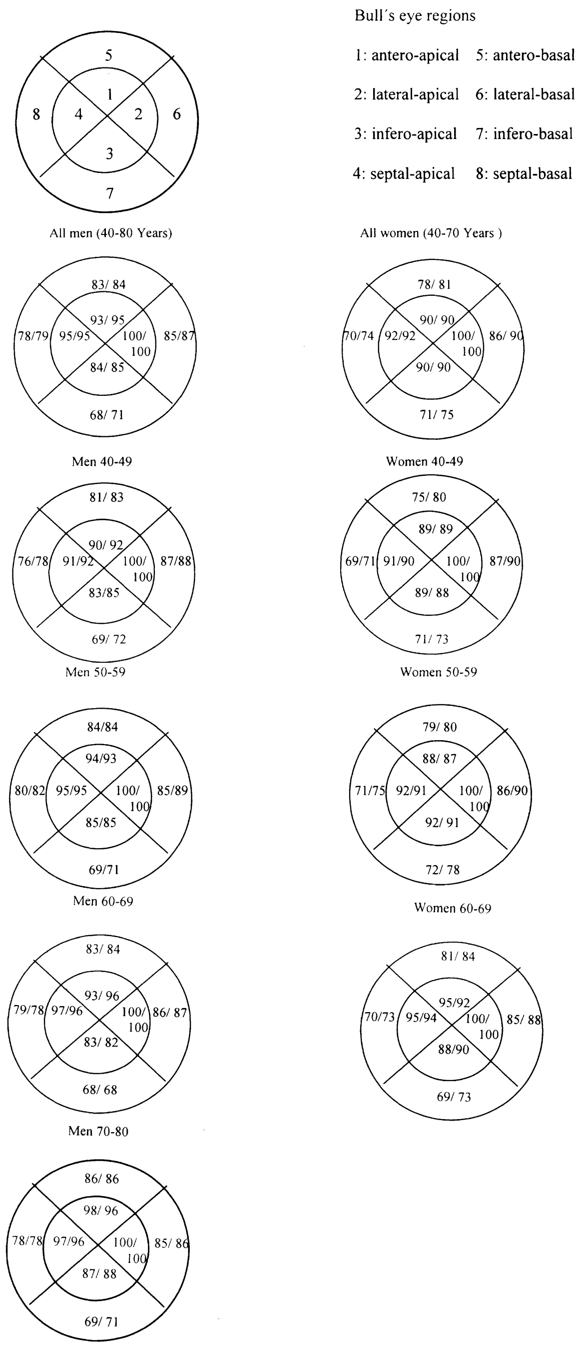

Figure 1 Regional left ventricular isotope uptake expressed as the percentage of maximal uptake during stress/rest.

Results

Anthropometric data and the exercise capacity for healthy subjects are shown in Tables 1 (men) and 2 (women). There were no correlations between age or any of the anthropometric parameters.

Normalized regional myocardial isotope uptake for men and women and for different age groups are presented in Fig. 1 and in Tables 3a and b. The highest relative isotope uptake during stress and rest was seen in the apical-lateral part of the left ventricle (region 2) in both men and women and in all age groups.

Gender differences (Fig. 1)

The men had higher uptakes in the anterior regions during stress and rest (region 1, $P = 0{\cdot}026$ and $P<0{\cdot}001$ and region 5 $P<0{\cdot}001$ for both stress and rest) and in the basal–septal region (region 8, $P<0{\cdot}001$ for stress and rest). Women had higher uptakes in the inferior regions (region 3 during stress and rest, $P = 0{\cdot}002$ and 0·02, respectively, and in region 7 at rest, $P = 0{\cdot}02$).

Age differences (Fig. 1, Tables 3a and 3b)

Among men the oldest subjects had higher uptakes than the youngest ones during stress in the antero-apical region (region 1, $P<0{\cdot}001$) and in the apical–septal region (region 4, $P = 0{\cdot}004$). A near significant difference in the same region was also seen between men aged 40–49 years and 60–69 years, with a higher relative uptake in the older group ($P = 0{\cdot}06$). At rest, differences were seen in the antero-apical region (region 1) with higher uptakes in the oldest group than in men aged 40–69 years, $P = 0{\cdot}009$.

In women, differences during stress were seen in the anterior regions (1 and 5) where the oldest subjects had higher relative uptakes than the younger women ($P = 0{\cdot}002$). At rest, the same regions differed with higher uptakes in the oldest age group with P-values of 0·027 and 0·040.

Stress vs. rest (Fig. 2)

Higher relative isotope uptakes were seen in both men and women in the basal parts of the left ventricle at rest than under stress.

In men, higher relative uptakes were seen at rest in the basal-lateral and basal-inferior regions (regions 6 and 7, $P<0{\cdot}001$). A near significant difference

Table 1 Anthropometric data in healthy men. Values are expressed as means ± SD

	Age groups (years)			
	40–49 (*n* = 10)	50–59 (*n* = 10)	60–69 (*n* = 10)	70–80 (*n* = 12)
Age (years)	44·8 ± 2·8	54·0 ± 2·4	63·7 ± 2·5	74·9 ± 2·4
Weight (kg)	82·7 ± 10·1	82·4 ± 7·6	77·5 ± 10·3	78·4 ± 10·9
Height (m)	1·79 ± 0·1	1·82 ± 0·1	1·77 ± 0·1	1·75 ± 0·06
BMI (kg m^{-2})†	24·9 ± 2	25·9 ± 3·3	25·0 ± 3·0	25·8 ± 3·5
BSA (m^2)‡	2·01 ± 0·12	2·03 ± 0·09	1·94 ± 0·16	1·93 ± 0·13
Thoracic circumference (cm)§	99·8 ± 6·5	100·6 ± 6·4	99·4 ± 7·0	103·1 ± 6·9
Exercise capacity (watts)¶	255 ± 51·9	246 ± 34·1	202 ± 31·6	172 ± 19·2
Exercise capacity (W kg^{-1})††	3·14 ± 0·81	3·03 ± 0·58	2·64 ± 0·52	2·23 ± 0·37

†Body mass index.
‡Body size area.
§Thoracic circumference at cardiac level.
¶Maximal exercise capacity.
††Maximal exercise capacity corrected for body-weight.

Table 2 Anthropometric data in healthy women. Values are expressed as means ± SD

Age groups	40–49 (*n* = 11)	50–59 (*n* = 8)	60–70 (*n* = 10)
Age (years)	44·4 ± 2·7	55·3 ± 2·6	64·5 ± 2·9
Weight (kg)	64·5 ± 8·1	64·8 ± 8·3	66·2 ± 7·4
Height (m)	1·66 ± 0·1	1·65 ± 0·1	1·66 ± 0·02
BMI (kg m^{-2})†	23·5 ± 3·6	23·7 ± 2·6	24·0 ± 2·6
BSA (m^2)‡	1·71 ± 0·10	1·71 ± 0·13	1·73 ± 0·09
Thoracic circumf. (cm)§	91·8 ± 7·6	95·7 ± 11·2	95·2 ± 8·6
Exercise capacity (watts)¶	182 ± 32·5	168 ± 28·7	147 ± 33·7
Exercise capacity (W kg^{-1})††	2·87 ± 0·54	2·63 ± 0·54	2·22 ± 0·49

†Body mass index.
‡Body size area.
§Thoracic circumference at cardiac level.
¶Maximal exercise capacity.
††Maximal exercise capacity corrected for body-weight.

($P = 0·05$) was seen in the basal-septal region (region 8).

In women, higher relative uptakes were seen at rest in the apical-septal region (region 4) with a *P*-value of 0·04 and in the basal regions of the left ventricle (regions 5–7) with $P<0·001$.

Regional isotope uptake in relation to anthropometric data (Table 4)

When entered in a multiple regression equation, age, gender, BMI and thoracic circumference all contributed independently to the prediction of isotope uptake. Thus, during stress age made a significant contribution in regions 1, 4 and 5 ($P<0·001$), gender in regions 1 ($P = 0·02$), 3 ($P<0·001$), 5 ($P = 0·03$), 7 ($P = 0·01$) and 8 ($P = 0·005$), BMI in regions 4 ($P<0·001$), 5 ($P = 0·013$), 7 ($P = 0·01$) and 8 ($P<0·001$) and thoracic circumference in region 1 ($P = 0·04$). At rest, age made a significant contribution in regions 1 ($P<0·001$), 4 ($P = 0·01$), 5 ($P = 0·004$) and 6 ($P = 0·007$), gender in regions 1, 3 ($P<0·001$), 5 ($P = 0·04$), 7 ($P = 0·02$) and 8 ($P = 0·006$), BMI in regions 1 ($P = 0·003$), 3, 4 and

Table 3a Normalized activity distribution in the eight myocardial regions during stress and rest in men as mean values and SDs

	Region	Mean ± SD	Range
All men	1	93 ± 5/95 ± 5	80–100/85–100
	2	100 ± 2/100 ± 2	94–100/94–100
	3	84 ± 4/85 ± 5	72–96/74–95
	4	95 ± 4/95 ± 4	82–100/82–100
	5	83 ± 5/84 ± 5	71–100/71–95
	6	85 ± 4/87 ± 4	76–93/76–96
	7	68 ± 3/71 ± 5	59–85/63–74
	8	78 ± 6/79 ± 5	67–99/66–91
40–49	1	90 ± 5/92 ± 5	80–97/85–98
	2	100 ± 2/100 ± 3	96–100/94–100
	3	84 ± 5/85 ± 5	76–91/77–94
	4	91 ± 5/92 ± 5	82–98/82–99
	5	81 ± 7/83 ± 7	71–94/71–93
	6	87 ± 4/89 ± 5	77–93/82–96
	7	69 ± 3/72 ± 5	65–73/66–79
	8	76 ± 5/78 ± 8	67–82/66–88
50–59	1	94 ± 4/93 ± 3	86–100/89–100
	2	100 ± 2/100 ± 2	97–100/94–100
	3	85 ± 5/85 ± 5	77–92/79–92
	4	95 ± 4/95 ± 3	89–100/91–100
	5	84 ± 4/84 ± 4	76–88/78–92
	6	85 ± 4/89 ± 3	81–90/84–92
	7	69 ± 3/71 ± 3	63–72/68–75
	8	80 ± 7/82 ± 5	68–86/72–91
60–69	1	93 ± 5/96 ± 3	83–98/92–99
	2	100 ± 3/100 ± 2	97–100/96–100
	3	83 ± 6/82 ± 5	72–90/74–89
	4	97 ± 7/96 ± 7	86–100/88–100
	5	83 ± 5/84 ± 4	73–89/78–88
	6	86 ± 3/87 ± 4	84–93/84–92
	7	68 ± 6/68 ± 5	60–77/63–79
	8	79 ± 7/78 ± 7	73–91/70–84
70–80	1	98 ± 3/96 ± 3	90–100/91–100
	2	100 ± 3/100 ± 2	94–100/96–100
	3	87 ± 6/88 ± 4	77–96/83–95
	4	97 ± 3/97 ± 3	90–100/91–100
	5	86 ± 8/86 ± 7	73–100/71–95
	6	85 ± 5/86 ± 5	76–93/76–92
	7	69 ± 7/71 ± 5	59–85/65–84
	8	78 ± 9/78 ± 7	68–99/66–90

5 ($P<0{\cdot}001$), 7 ($P = 0{\cdot}03$) and 8 ($P<0{\cdot}001$) and thoracic circumference in region 1 ($P<0{\cdot}001$) and 5 ($P = 0{\cdot}04$).

Discussion

Our results show that the regional myocardial isotope uptake using ^{99m}Tc-MIBI in healthy subjects between

Table 3b Normalized activity distribution in the eight myocardial regions during stress and rest in women as mean values and SDs

	Region	Mean ± SD	Range
All women	1	90 ± 4/90 ± 4	80–100/82–100
	2	100 ± 2/100 ± 2	95–100/96–100
	3	90 ± 6/90 ± 6	77–97/77–100
	4	92 ± 5/92 ± 5	88–100/80–100
	5	78 ± 4/81 ± 4	73–90/72–95
	6	86 ± 4/90 ± 5	79–94/80–98
	7	71 ± 4/75 ± 5	67–80/67–86
	8	70 ± 6/74 ± 6	60–79/60–84
40–49	1	89 ± 4/89 ± 2	80–94/84–92
	2	100 ± 2/100 ± 3	96–100/97–100
	3	89 ± 5/88 ± 6	77–94/77–94
	4	91 ± 6/90 ± 6	80–98/80–99
	5	75 ± 3/80 ± 4	73–80/74–84
	6	87 ± 4/90 ± 4	83–93/83–94
	7	71 ± 3/73 ± 5	67–77/67–82
	8	69 ± 6/71 ± 6	60–78/60–80
50–59	1	88 ± 3/87 ± 3	82–92/82–91
	2	100 ± 1/100 ± 2	97–100/96–100
	3	92 ± 5/91 ± 6	83–96/82–97
	4	92 ± 3/91 ± 2	87–95/88–94
	5	79 ± 1/80 ± 4	77–80/72–83
	6	86 ± 3/90 ± 3	82–90/84–95
	7	72 ± 2/78 ± 4	70–74/72–86
	8	71 ± 5/75 ± 3	66–79/71–81
60–70	1	95 ± 4/92 ± 4	91–100/89–100
	2	100 ± 3/100 ± 3	95–100/96–100
	3	88 ± 7/90 ± 5	80–97/82–100
	4	95 ± 5/94 ± 7	84–100/85–100
	5	81 ± 5/84 ± 5	76–90/80–95
	6	85 ± 5/88 ± 7	79–94/80–98
	7	69 ± 4/73 ± 6	67–80/69–86

40 and 80 years of age differs between men and women. This is in accord with previous studies (DePasquale *et al.*, 1988; Eisner *et al.*, 1988). Apart from gender-dependent differences, there were also differences related to habitus, such as BMI and thoracic circumference, and age. Furthermore, there are differences in regional isotope uptake between stress and resting conditions, implying a need for different stress and rest protocols when comparing ^{99m}Tc-MIBI data for patients with those for healthy subjects in a normal database. Higher relative MIBI uptakes were seen in both men and women at rest than under stress in the peripheral but not in the central parts of the left ventricle. The reason for this phenomenon is not clear. In myocardial scintigraphy

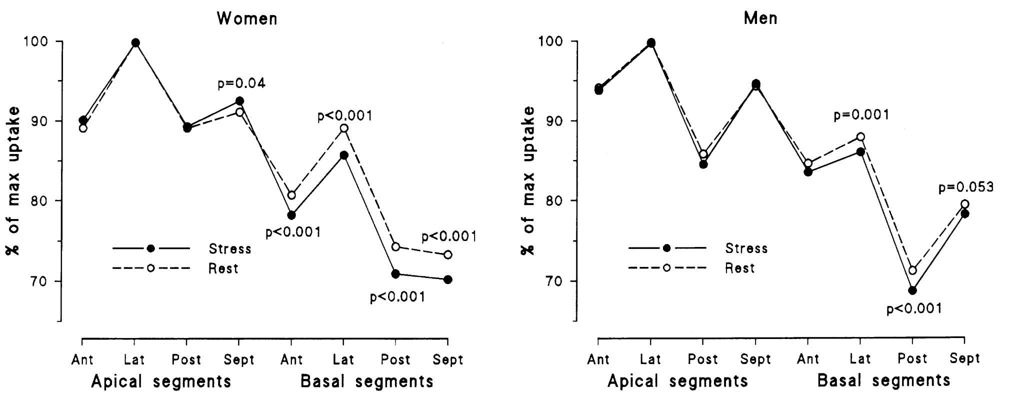

Figure 2 Regional left ventricular isotope uptake during stress and rest in women (left) and men (right). Values are presented as the percentage of maximal isotope uptake during stress and rest respectively.

using thallium-201, regional differences in isotope uptake between stress and rest have been recorded owing to a upward motion of the heart (cardiac creep) occurring early on after heavy exercise and during the early stress acquisition period after exercise (Depuey & Garcia, 1989). However, with ^{99m}Tc-MIBI, this phenomenon is unlikely as both stress and rest acquisitions are carried out 30 min or more after isotope injection.

Commercially available normal databases (C-equal, Cedars Sinai) have gender- and activity-specific files but do not adjust for anthropometric data such as BMI or thoracic circumference, which, in our study, affect attenuation and the resulting myocardial isotope uptake. This could reduce the diagnostic accuracy of MIBI-SPECT, especially when examining very thin or obese persons.

Toft *et al.* (1997) also found that the use of reference files in ^{99m}Tc-MIBI-SPECT requires a gender-matched and, for men, possibly also an age-matched reference population. However, no age differences were seen among women in their study. Also, contrary to our results, Toft *et al.* (1997) found similar normalized regional activities during rest and stress, suggesting that there is no need for different protocols for rest and stress. Furthermore, no correlations between BMI and regional isotope activity were found, neither in men nor in women, contrary to our results. Some of the differences between Toft's results and ours may be explained by the fact that, in our study, the left ventricle was divided into eight instead of four segments, resulting in a more detailed analysis of regional differences. Another difference is that Toft *et al.* used elliptical rotation during SPECT acquisition, whereas we used circular rotation.

Limitations of the study

We cannot draw any final clinical conclusions from our results. To test whether corrections for habitus, age or if different protocols for stress and rest affects the diagnostic value of MIBI-SPECT, using semi-quantitative evaluation, a study on patients with angiographically proven coronary heart disease ought to be performed.

Conclusion

The present data show that the regional myocardial distribution of ^{99m}Tc-MIBI in healthy subjects between 40 and 80 years of age varies in relation to age, gender and anthropometric data. Regional isotope uptake also differs between stress and rest in both men and women. Therefore, separate protocols seem to be needed for men and women, for different age groups and for stress and rest when performing semiquantitative MIBI-SPECT and comparing data with a normal file of healthy subjects. Furthermore, anthropometric data, such as BMI and/or thoracic circumference, ought to be considered in order to improve further the diagnostic accuracy of myocardial MIBI-SPECT.

Table 4 Summary of stepwise multiple regression analysis for regional myocardial MIBI uptake

	Stress						Rest				
	β	SE	β	SE	*P*-value		β	SE	β	SE	*P*-value
Region 1											
Multiple $r = 0.62$, $r^2 = 0.38$, $P<0.001$						Multiple $r = 0.62$, $r^2 = 0.38$, $P<0.001$					
Age	0.60	0.11	0.27	0.05	< 0.001	Gender	−0.53	0.99	−4.88	0.91	< 0.001
Gender	−0.26	0.11	−2.84	1.22	0.02	Age	0.47	0.10	0.19	0.38	< 0.001
Circumf	−0.35	0.17	−0.24	0.12	0.04	Circumf	−0.56	0.15	−0.32	0.09	< 0.001
BMI	0.24	0.15	0.42	0.27	0.12	BMI	0.42	0.14	0.62	0.20	0.003
Region 3											
Multiple $r = 0.61$, $r^2 = 0.37$, $P<0.001$						Multiple $r = 0.49$, $r^2 = 0.24$, $P<0.001$					
Gender	0.59	0.11	7.04	1.32	< 0.001	BMI	0.40	0.11	0.79	0.22	< 0.001
Circumf	0.32	0.16	0.24	0.12	0.05	Gender	0.40	0.11	4.99	1.43	< 0.001
BMI	0.22	0.15	0.41	0.29	0.15	Age	0.14	0.11	0.08	0.06	0.22
Region 4											
Multiple $r = 0.60$, $r^2 = 0.36$, $P<0.001$						Multiple $r = 0.56$, $r^2 = 0.31$, $P<0.001$					
BMI	0.61	0.15	1.00	0.26	< 0.001	BMI	0.57	0.16	0.97	0.27	< 0.001
Age	0.38	0.11	0.18	0.05	< 0.001	Age	0.29	0.11	0.14	0.05	0.013
Circumf	−0.23	0.16	−0.15	0.11	0.15	Gender	−0.18	0.12	−1.98	1.25	0.12
						Circumf	−0.27	0.18	−0.18	0.12	0.14
Region 5											
Multiple $r = 0.60$, $r^2 = 0.36$, $P<0.001$						Multiple $r = 0.54$, $r^2 = 0.30$, $P<0.001$					
Age	0.36	0.10	0.20	0.06	< 0.001	BMI	0.56	0.16	1.10	0.32	0.001
BMI	0.26	0.10	0.53	0.21	0.013	Age	0.33	0.11	0.18	0.06	0.004
Gender	−0.24	0.11	−3.04	1.36	0.03	Circumf	−0.38	0.18	−0.30	0.14	0.04
						Gender	−0.24	0.12	−3.02	1.46	0.04
Region 6											
Multiple $r = 0.21$, $r^2 = 0.05$, $P = 0.21$						Multiple $r = 0.34$, $r^2 = 0.11$, $P<0.018$					
Circumf	0.19	0.13	0.10	0.07	0.14	Age	−0.32	0.12	−0.14	0.05	0.007
Age	−0.18	0.13	−0.07	0.05	0.17	BMI	0.14	0.12	0.23	0.19	0.22
Region 7											
Multiple $r = 0.37$, $r^2 = 0.14$, $P = 0.007$						Multiple $r = 0.34$, $r^2 = 0.12$, $P<0.015$					
Gender	0.31	0.12	2.85	1.09	0.01	Gender	0.29	0.12	3.80	1.55	0.02
BMI	0.30	0.12	0.44	0.17	0.01	BMI	0.27	0.11	0.56	0.25	0.03
Region 8											
Multiple $r = 0.63$, $r^2 = 0.39$, $P<0.001$						Multiple $r = 0.55$, $r^2 = 0.30$, $P<0.001$					
BMI	0.43	0.10	1.67	0.38	< 0.001	BMI	0.39	0.11	0.96	0.26	< 0.001
Gender	−0.30	0.10	−7.32	2.50	0.005	Gender	−0.30	0.11	−4.72	1.67	0.006

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