doi: 10.1111/cob.12002

Risk factors associated with the metabolic syndrome in abdominal obesity

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Received 2 April 2012; revised 6 August 2012; accepted 12 August 2012

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Summary

Obesity is associated with the metabolic syndrome. However, not all obese individuals have cardiovascular risk factors (CVRF). It is not clear how many abdominally obese individuals are free of CVRF and what distinguishes them from the group of obese individuals with CVRF. In this study, we aimed to assess the associated factors and prevalence of abdominal obesity without CVRF. In our cross-sectional analysis, we included $n = 4244$ subjects from the Study of Health in Pomerania (SHIP), a population-based study and $n = 6671$ subjects from the Diabetes Cardiovascular Risk-Evaluation: Targets and Essential Data for Commitment of Treatment (DETECT) study, a representative primary care study in Germany. We defined abdominal obesity by waist-to-height ratio (WHtR) of 0.5 or greater. We assessed how many subjects with abdominal obesity had CVRF based on the definition of the metabolic syndrome. We analysed which conditions were associated with the absence of CVRF in abdominal obesity. In SHIP and DETECT, 2652 (62.5%) and 5126 (76.8%) subjects had a WHtR $\geq$ 0.5. Among those with a WHtR $\geq$ 0.5, 9.0% and 13.8% were free of CVRF and 49.9% and 52.7% had at least two CVRF in SHIP and DETECT, respectively. In both studies, after backward elimination, age, male sex, body mass index and high liver enzymes and unemployment were consistently inversely associated with the absence of CVRF. Among abdominally obese subjects, the prevalence of metabolically healthy subjects is low. Conditions consistently associated with the absence of CVRF in abdominal obesity are younger age, female sex, low BMI, and normal liver enzymes, the latter likely reflecting the absence of steatohepatitis.

Keywords: Dyslipidemia, hypertension, metabolic syndrome, waist-to-height ratio.

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BMI, body mass index; CV, cardiovascular; CVRF, cardiovascular risk factors; DETECT, Diabetes Cardiovascular Risk-Evaluation: Targets and Essential Data for Commitment of Treatment; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; hsCRP, high sensitive C-reactive protein; SHIP, Study of Health in Pomerania; WC, waist circumference; WHO, World Health Organization; WHtR, waist-to-height ratio.

Introduction

Identification of obese individuals with a favourable metabolic profile is important. It allows targeting those who will benefit most from medical or lifestyle interventions. Low waist circumference (WC) (1), a low degree of inflammation (2) and normal liver enzymes (3) are conditions associated with 'metabolically healthy obesity'. Generally, the body mass index (BMI) has been used to identify obese individuals (4). Three percent to 40% of all obese individuals have been reported to have a metabolically healthy phenotype (5).

However, the association of favourable metabolic profiles in obesity have not been studied using definitions of abdominal obesity. Previous studies have shown the potential of alternative measures of abdominal obesity to outperform the BMI in predicting cardiovascular (CV) risk (6–8).

The waist-to-height ratio (WHtR) performed better than WC and other measures of abdominal obesity in predicting CV risk even though it has been debated whether this difference is clinically relevant (6,8,9).The most commonly used measure of abdominal obesity to date is the WC. However, intuitively the WHtR seems more adequate than the WC as it accounts for differences in body height that might bias WC measurements. We have also shown that the WC underestimates the amount of body fat and associated CV risk factors (CVRF) accumulation in short subjects and overestimates it in tall subjects and that this is not the case with the WHtR (10). Therefore, we decided to use the WHtR for the definition of abdominal obesity.

In this study, we aimed to assess the prevalence of the metabolically healthy phenotype, as defined as the absence of metabolic syndrome risk factors in abdominal obesity. We additionally aimed to identify factors associated with the metabolically healthy phenotype of abdominal obesity. To test for generalizability, we included two independent cohorts. We cross-sectionally analysed two cohorts from Germany: the Study of Health in Pomerania (SHIP), a cohort, representative for the general population,; and the Diabetes Cardiovascular Risk-Evaluation: Targets and Essential Data for Commitment of Treatment (DETECT) study, a primary care cohort.

Methods and procedures

Design

SHIP is a longitudinal population-based cohort study in West Pomerania, a region in the Northeast of Germany. The net sample comprised 6267 eligible subjects. All subjects received a maximum of three written invitations. In cases of non-response, letters were followed by phone calls or home visits if contact by phone was not possible. Eventually, a total of 4308 subjects participated in the baseline examination (response proportion 69%) (11).

DETECT is a nationally representative epidemiological study of 55 518 unselected consecutive patients (59% women; 18 years or older) in 3188 primary care offices in Germany, including a prospective sub-study in a random subset of 7519 patients, characterized additionally by an extensive standardized laboratory program (12).

Subjects

Both studies conformed to the principles of the Declaration of Helsinki and were approved by the local ethics committees. All participants gave written informed consent. SHIP only included subjects of Caucasian origin. In DETECT, we did not record ethnicity, but, being representative of the German population, the participants were mainly of Caucasian ethnicity. Complete information on anthropometric and clinical parameters was available for $n = 4244$ (female: 2159) in the SHIP study and for $n = 6671$ (female: 3949) in the DETECT trial. The data from this sample sized were analysed.

Instruments and measures

Information in SHIP and DETECT was collected by study nurses and by the treating physicians, respectively. Blood was sampled and medical information was collected as described previously (8). Subjects were either fasting or non-fasting in DETECT and non-fasting in SHIP. In both studies, blood samples were shipped to the central laboratory within 24 h at room temperature and all parameters were measured in the central laboratory. Reagents and secondary standard were used as recommended by the manufacturer.

Anthropometric characteristics and blood pressure were measured according to written, standardized instructions in accordance with World Health Organization standards in both studies (WHO 1987). WC was measured to the nearest 0.1 cm midway between the lower rib margin and the iliac crest in the horizontal plane, using an inelastic tape measure.

Physical activity was defined as individuals' self-reported physical activity of 2 h or more per week.

We defined the following CVRF based on the metabolic syndrome by ATP III guidelines and modified them for non-fasting blood values as described previously (13):

1. Glucose disturbance: non-fasting glucose >8.0 mmol L^{-1} (144 mg dL^{-1}) of haemoglobin (HbA1c) >6.5% or antidiabetic therapy;

2. Low high-density lipoprotein (HDL) cholesterol: HDL cholesterol: <1.03 mmol L^{-1} (<40 mg dL^{-1}; men); <1.29 mmol L^{-1} (<50 mg dL^{-1}; women);

Table 1 Baseline characteristics in SHIP

	Total*	WHtR < 0.5		WHtR ≥ 0.5	
	n (%)	0 CVRF *n* (%)	≥2 CVRF *n* (%)	0 CVRF *n* (%)	≥2 CVRF *n* (%)
Number of subjects	4244	781	182	240	1311
Age; years; mean (SD)	49.7 (16.4)	35.6 (11.4)	48.8 (17.2)	46.4 (14.7)	57.7 (13.6)
Age group 18–44	1711 (40.3)	619 (79.3)	78 (42.9)	112 (46.7)	261 (19.9)
Age group 45–65	1643 (38.7)	152 (19.5)	65 (35.7)	99 (41.3)	611 (46.6)
Age group 66+	890 (21.0)	10 (1.3)	39 (21.4)	29 (12.1)	439 (33.5)
Male gender	2085 (49.1)	194 (24.8)	82 (45.1)	108 (45.0)	838 (63.9)
Body mass index; kg m^{-2}; mean (SD)	27.3 (4.8)	22.6 (2.3)	24.1 (2.3)	28.6 (3.5)	30.5 (4.2)
WHtR; mean (SD)	0.53 (0.08)	0.43 (0.03)	0.47 (0.03)	0.55 (0.04)	0.59 (0.06)
Waist circumference; cm; mean (SD)	89.3 (13.9)	73.6 (7.0)	79.8 (6.1)	91.9 (7.6)	99.9 (10.4)
More than 10 years of education	2529 (60.0)	689 (88.6)	114 (62.6)	151 (65.1)	575 (44.2)
Married	2761 (65.3)	414 (53.0)	102 (56.0)	153 (63.8)	933 (71.2)
Employed	2045 (48.8)	555 (72.9)	85 (47.2)	144 (62.3)	446 (34.4)
Current smoker	1277 (30.2)	307 (39.3)	63 (34.6)	79 (33.5)	325 (24.9)
Low physical activity	3177 (75.2)	523 (67.0)	131 (72.0)	181 (76.7)	1050 (80.4)

*Data based on subjects with complete assessment of weight, height, plasma glucose, HbA1c, HDL cholesterol, triglyceride and systolic blood pressure.
CVRF, cardiovascular risk factors; SD, standard deviation; WHtR, waist-to-height ratio.

3. High triglycerides: triglycerides >2.3 mmol L^{-1} (204 mg dL^{-1}) or lipid therapy;
4. Hypertension: blood pressure: >130/85 mmHg or antihypertensive therapy.

Statistical analyses

We defined subjects with a WHtR of 0.5 or larger as abdominally obese. This was a cut-off that was shown to best discriminate individuals with and without CVRF in a meta-analysis (14). A second action level of 0.6 was suggested in the literature (9). We assessed the prevalence of 0–4 CVRF among WHtR groups. We assessed the prevalences of 0, 1 and 2 or more CVRF by abdominal obese and lean state in the whole group and separated by sex and age groups.

We then calculated logistic regression analyses with the following variables as predictors of the absence of CVRF in abdominal obesity (WHtR ≥ 0.5, 0 CVRF) and the presence of at least two CVRF in abdominally lean state (WHtR < 0.5, ≥2 RF): smoking, physical activity, alcohol consumption, alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), estimated glomerulary filtration rate (eGFR), high sensitive C-reactive protein (hsCRP), marital status (married vs. single, divorced or widowed), educational level (<10 years vs. ≥10 years school), employment status (employed vs. unemployed, homemaker or retired). These variables were selected on suspected potential association with CVRF. ALAT and ASAT were selected as markers of steatosis hepatitis. All models were calculated both unadjusted and after adjustment for age, sex and BMI. In a further step, we included all significant predictors in a multivariable model using backward elimination, also including age, sex and BMI.

A two-sided *P* value of <0.05 was considered statistically significant. All statistical analyses were performed using STATA 10.1 (Stata Corporation, College Station, TX, USA).

Results

Tables 1 and 2 display the baseline characteristics of abdominally lean and obese subjects with and without CVRF in SHIP and DETECT, respectively. In both cohorts, abdominally obese subjects without CVRF were younger and had a lower BMI and WHtR than obese subjects with CVRF.

The prevalence of abdominal obesity action level 1 and 2 was 62.5% and 19.9% in SHIP and 76.8% and 31.2% in DETECT, respectively. The prevalences of RF according to WHtR are shown in Table 3. In SHIP, 9.0% and 3.4% of subjects with a WHtR of 0.5 or larger and 0.6 or larger, respectively, were free of CVRF. In DETECT, 13.8% and 6.9% of subjects with a WHtR of 0.5 or larger and 0.6 or larger, respectively, were free of CVRF. The prevalences of at least two CVRF among participants with a WHTR of 0.5 or larger were as follows: hypertension 83.4% (SHIP) and 74.1% (DETECT), low HDHL cholesterol 30.8% (SHIP) and 37.9% (DETECT), high triglycerides 34.4% (SHIP) and 36.9% (DETECT), and glucose disturbance 16.4% (SHIP) and 20.1% (DETECT).

Table 2 Baseline characteristics in DETECT

	Total*	WHtR < 0.5		WHtR ≥ 0.5	
	n (%)	0 CVRF *n* (%)	≥2 CVRF *n* (%)	0 CVRF *n* (%)	≥2 CVRF *n* (%)
Number of subjects	6671	810	232	706	2702
Age; years; mean (SD)	57.6 (14.3)	44.5 (11.4)	58.5 (15.7)	51.5 (12.7)	62.9 (11.9)
Age group 18–44	1411 (21.2)	443 (54.7)	51 (22.0)	228 (32.3)	231 (8.6)
Age group 45–65	3031 (45.4)	328 (40.5)	94 (40.5)	357 (50.6)	1222 (45.2)
Age group 66+	2229 (33.4)	39 (4.8)	87 (37.5)	121 (17.1)	1249 (46.2)
Male gender	2722 (40.8)	134 (16.5)	66 (28.5)	279 (39.5)	1382 (51.2)
Body mass index; kg m^{-2}; mean (SD)	27.2 (4.9)	22.0 (2.2)	23.4 (2.8)	26.5 (3.6)	29.5 (4.8)
WHtR; mean (SD)	0.56 (0.09)	0.45 (0.03)	0.46 (0.03)	0.56 (0.05)	0.61 (0.07)
Waist circumference; cm; mean (SD)	94.9 (14.9)	75.2 (6.8)	78.0 (6.6)	94.9 (9.4)	103.2 (12.1)
More than 10 years of education	3615 (55.7)	679 (85.5)	129 (57.9)	463 (67.1)	1117 (42.8)
Married	4588 (69.7)	531 (66.0)	136 (59.7)	508 (73.4)	1883 (70.8)
Employed	2629 (39.9)	598 (74.8)	79 (34.2)	428 (61.3)	667 (25.0)
Current smoker	1337 (20.7)	218 (27.7)	60 (26.7)	171 (25.2)	437 (16.7)
Low physical activity	1942 (31.5)	227 (28.6)	72 (34.1)	225 (33.3)	777 (32.0)

*Data based on subjects with complete assessment of weight, height, plasma glucose, HbA1c, HDL cholesterol, triglyceride and systolic blood pressure.
CVRF, cardiovascular risk factors; SD, standard deviation; WHtR, waist -to-height ratio.

Table 3 Prevalence of cardiovascular risk factors by WHtR

	WHtR < 0.5	WHtR ≥ 0.5	WHtR ≥ 0.6
SHIP (*n* = 4244)			
n (%)	1592 (37.5)	2652 (62.5)	864 (19.9)
No risk factor	49.1	9.0	3.4
Two or more risk factors	11.4	49.4	62.8
One risk factor	39.5	41.5	33.8
Two risk factors	8.5	29.4	31.1
Three risk factors	2.4	15.5	22.9
Four risk factors	0.5	4.6	8.8
DETECT (*n* = 6671)			
n (%)	1545 (23.2)	5126 (76.8)	2084 (31.2)
No risk factor	52.4	13.8	6.9
Two or more risk factors	15.0	52.7	65.0
One risk factor	32.6	33.5	28.1
Two risk factors	11.2	28.9	31.5
Three risk factors	3.3	17.5	23.2
Four risk factors	0.5	6.3	10.3

DETECT, Diabetes Cardiovascular Risk-Evaluation: Targets and Essential Data for Commitment of Treatment; SHIP, Study of Health in Pomerania; WHtR, waist -to-height ratio.

Among abdominally obese subjects aged 18–44, 45–65 and 66 years or more, 6.6%, 6.0% and 3.3%, respectively, were free of CVRF in SHIP and 16.2%, 11.8% and 5.4%, respectively, were free of CVRF in DETECT.

Tables 4 and 5 display the results of logistic regression for factors associated with the absence of RF in abdominal obesity (WHtR ≥ 0.5). In SHIP, after backward elimination, male sex, age, BMI and ALAT were inversely related and being employed was positively related with absence of CVRF in abdominal obesity.

In DETECT, after backward elimination, male sex, age, BMI, current smoking, GFR and ALAT were inversely related and alcohol consumption, being employed and ASAT were positively related with absence of RF in abdominal obesity.

Discussion

In this cross-sectional analysis of two large studies, we analysed the associations of abdominal obesity with the prevalence of cardiometabolic risk factors and conditions associated with the absence of CVRF in abdominal obesity.

Several studies have addressed the question of metabolically healthy obesity (1–3). We are the first to assess the prevalence of metabolically healthy obesity using a measure of abdominal obesity. We think this is of high importance since measures of abdominal obesity are better prognostic indicators of CV risk than BMI (6–8,10).

We found that the presence of abdominal obesity defined by a WHtR ≥ 0.5 was higher in DETECT, representing a nationally representative primary care population with 77%, than in SHIP, representing the general population of Northeast Germany with 63%. Among abdominally obese subjects, a similar proportion of participants in both cohorts had at least two RF and 14% and 9% were free of cardiometabolic risk factors in DETECT and SHIP, respectively. We additionally found that female sex, younger age,

Table 4 Predictors of the absence of CVRF vs. two or more CVRF in abdominally obese subjects in SHIP. Unadjusted and adjusted univariate analyses and multivariate analyses with backward selection

	Two or more CVRF *n* = 1311 *n* (%)	No CVRF *n* = 240 *n* (%)	RR†	95% CI	*P* value	RR‡	95% CI	*P* value	RR§	95% CI	*P* value
Standard risk factors											
Male gender	838 (63.9)	108 (45.0)	0.52	0.41,0.66	<0.001	0.40	0.33,0.50	<0.001	0.61	0.39,0.95	0.027
Age; mean (SD)	57.7 (13.6)	46.4 (14.7)	0.96	0.95,0.96	<0.001	0.95	0.95,0.96	<0.001	0.95	0.94,0.97	<0.001
Body mass index; mean (SD)	30.5 (4.2)	28.6 (3.5)	0.89	0.86,0.93	<0.001	0.86	0.83,0.89	<0.001	0.92	0.88,0.97	0.002
WHtR; mean (SD)¶	0.59 (0.06)	0.55 (0.04)	0.22	0.17,0.30	<0.001	0.43	0.30,0.62	<0.001			
Current smoker	325 (24.9)	79 (33.5)	1.42	1.11,1.81	0.005	0.85	0.66,1.08	0.175			
Low physical activity	1050 (80.4)	181 (76.7)	0.83	0.63,1.09	0.188	0.91	0.71,1.17	0.451			
Alcohol consumption; mean (SD)	2.55 (4.61)	1.83 (3.43)	0.96	0.92,1.00	0.031	0.97	0.94,1.01	0.093			
Married	933 (71.2)	153 (63.8)	0.78	0.61,0.99	0.041	1.02	0.81,1.27	0.889			
Years of education >10	575 (44.2)	151 (65.1)	2.07	1.61,2.66	<0.001	1.11	0.85,1.44	0.434			
Employed	446 (34.4)	144 (62.3)	2.63	2.06,3.37	<0.001	1.34	1.03,1.75	0.029	1.66	1.02,2.70	0.040
Endocrine and inflammatory markers											
hsCRP in mg L^{-1}; mean (SD)	6.61 (9.98)	5.92 (5.80)	0.99	0.96,1.02	0.495	1.00	0.98,1.02	0.842			
Liver and kidney function											
ASAT in U L^{-1}; mean (SD)	24.7 (14.7)	20.7 (6.5)	0.96	0.94,0.97	<0.001	0.97	0.96,0.99	0.001			
ALAT in U L^{-1}; mean (SD)	35.6 (24.7)	27.3 (15.2)	0.98	0.97,0.99	<0.001	0.98	0.97,0.99	<0.001	0.98	0.97,1.00	0.041
eGFR*; mean (SD)	76.1 (15.6)	82.3 (14.0)	1.02	1.01,1.03	<0.001	1.00	1.00,1.01	0.336			

Abdominally obese: WHtR ≥ 0.5; CVRF, cardiovascular risk factors.

*GFR, $creatinine^{-1.154} * age^{-0.203}$ for male and $creatinine^{-1.154} * age^{-0.203} * 0.742$ for female.

†Unadjusted.

‡Adjusted for age, gender and body mass index.

§Multivariate analyses with backward selection.

¶Increase for 0.1 units.

ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; CI, confidence interval; eGFR, estimated glomerulary filtration rate; hsCRP, high sensitive C-reactive protein; RR, risk ratio; SD, standard deviation; WHtR, waist -to-height ratio.

lower BMI, lower ALAT and being employed were consistently associated with the absence of CVRF in abdominal obesity in both studies.

It is not surprising that abdominal obesity was more common in DETECT than in SHIP since an accumulation of subjects with more health risks including obesity can be expected in a primary care population relative to a cohort from the general population.

Interestingly, however, abdominally obese subjects were not healthier in SHIP and the prevalence of the metabolically healthy phenotype was even slightly higher among primary care patients. The reasons for this are unclear. Differences in reporting or measurement biases in the two studies seem unlikely. In both studies, blood pressure was measured according to standardized instructions and the other factors were measured in a central laboratory in all subjects. The higher prevalence of cardiometabolic risk factors in SHIP than in DETECT was mainly due to a higher prevalence of hypertension. Potentially, regional differences play a role. A comparison of the SHIP population from Pomerania with the KORA cohort, a population from southern Germany that was tested with a similar protocol revealed a higher prevalence of high blood pressure in Pomerania (15). Unsurprisingly, male sex and higher age were consistently associated with presence the unhealthy phenotype. These are factors known to be associated with poorer CV health conditions. BMI was a further predictor of RF. Abdominally obese subjects with the unhealthy phenotype had a higher BMI.

Additional consistent associations with ALAT show that liver disease is also involved, potentially indicating non-alcoholic fatty liver disease. This is consistent with the findings by Messier *et al*. (3). Non-alcoholic steatohepatitis is the most common cause of elevated liver enzymes. It is associated with the metabolic syndrome and type 2 diabetes even though the causal direction is not clarified yet (16). Recent research suggests that non-alcoholic steatohepatitis is a major determinant of CV risk. Treatment targeted to liver pathology such as polyunsaturated fatty acids, statins or ursodeoxycholic acids, among others have been discussed to be used for the reduction of CV risk (17). The association of ALAT with CVRF supports this hypothesis. We can not explain why high ASAT was associated with absence of CVRF. This association was not consistent across cohorts. Therefore, it is most likely a chance effect of one cohort.

Table 5 Predictors of the absence of CVRF vs. two or more CVRF in abdominally obese subjects in DETECT. Unadjusted and adjusted univariate analyses and multivariate analyses with backward selection

	Two or more CVRF $n = 2702$ n (%)	No CVRF $n = 706$ n (%)	RR‡	95% CI	*P* value	RR§	95% CI	*P* value	RR§	95% CI	*P* value
Standard risk factors											
Male gender	1382 (51.2)	279 (39.5)	0.69	0.60, 0.79	<0.001	0.71	0.63, 0.81	<0.001	0.80	0.68, 0.93	0.004
Age; mean (SD)	62.9 (11.9)	51.5 (12.7)	0.95	0.95, 0.96	<0.001	0.95	0.95, 0.96	<0.001	0.96	0.95, 0.97	<0.001
Body mass index; mean (SD)	29.5 (4.8)	26.5 (3.6)	0.87	0.85, 0.88	<0.001	0.88	0.86, 0.89	<0.001	0.89	0.88, 0.91	<0.001
WHtR; mean (SD)¶	0.61 (0.07)	0.56 (0.05)	0.32	0.28, 0.37	<0.001	0.60	0.52, 0.71	<0.001			
Current smoker	437 (16.7)	171 (25.2)	1.49	1.28, 1.73	<0.001	0.89	0.77, 1.03	0.109	0.83	0.71, 0.97	0.019
Low physical activity	777 (32.0)	225 (33.3)	1.05	0.91, 1.21	0.525	0.92	0.81, 1.04	0.171			
Alcohol consumption; mean (SD)	169.3 (358.2)	181.3 (402.5)	1.00	0.999, 1.001	0.460	1.00	0.999, 1.001	0.057	1.002	1.001, 1.003	0.011
Married	1883 (70.8)	508 (73.4)	1.11	0.95, 1.29	0.186	1.14	0.99, 1.30	0.062			
Years of education >10	1117 (42.8)	463 (67.1)	2.22	1.92, 2.56	<0.001	1.17	1.01, 1.36	0.040			
Employed	667 (25.0)	428 (61.3)	3.29	2.88, 3.76	<0.001	1.62	1.39, 1.89	<0.001	1.60	1.35, 1.89	<0.001
Endocrine and inflammatory markers											
hsCRP in mg L^{-1}; mean (SD)	5.30 (7.31)	4.41 (7.64)	0.98	0.97, 1.00	0.026	1.00	0.99, 1.01	0.455			
Liver and kidney function											
ASAT in U L^{-1}; mean (SD)	34.0 (15.9)	31.6 (11.8)	0.99	0.98, 0.99	<0.001	0.99	0.99, 1.00	0.014	1.01	1.01, 1.02	<0.001
ALAT in U L^{-1}; mean (SD)	34.3 (22.0)	28.2 (14.3)	0.98	0.98, 0.99	<0.001	0.99	0.98, 0.99	<0.001	0.98	0.97, 0.99	<0.001
eGFR*; mean (SD)	57.0 (12.3)	58.1 (9.7)	1.01	1.00, 1.01	0.012	0.99	0.99, 1.00	0.003	0.99	0.98, 1.00	0.005

Abdominally obese: WHtR ≥ 0.5; CVRF, cardiovascular risk factors.

*GFR, $creatinine^{-1.154} * age^{-0.203}$ for male and $creatinine^{-1.154} * age^{-0.203} * 0.742$ for female.

‡Adjusted for age, gender and body mass index.

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¶Increase for 0.1 units.

ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; CI, confidence interval; eGFR, estimated glomerulary filtration rate; hsCRP, high sensitive C-reactive protein; RR, risk ratio; SD, standard deviation; WHtR, waist -to-height ratio.

It is of note and somewhat surprising that physical activity was consistently found to be not associated with the metabolically healthy phenotype in both studies. Apparently, physical activity has little influence on the metabolic phenotype once abdominal obesity is present. Interestingly, also CRP levels were not associated with presence or absence of RF. This is not in line with the findings of Karelis *et al*. (2): However, Karelis *et al*. (2) analysed a smaller cohort and defined risk factors in a different way using insulin resistance determined by hyperinsulinemic-euglycemic clamp. We cannot rule out that we would have found different results if we would have used this approach. However, our aim was to analyse commonly used CVRF that can be easily assessed in everyday clinical practice. Therefore, we based our work on commonly established factors of the metabolic syndrome.

Several limitations of our study need to be addressed. Our subjects were not fasting. Therefore, we could not measure insulin resistance. However, we included HbA1c as a measure of long-term glycaemia. Even though elevated ALAT is suggestive of steatohepatitis, we cannot rule out alternative causes of elevated liver enzymes.

The DETECT study was limited by the fact that ethnicity was not recorded. Most of the participants studied here were Caucasians. We do not know if the results can be generalized to other populations. Also, because of the cross-sectional approach, we do not know whether the factors associated with the healthy phenotype of obesity are causes, consequences or epiphenomena of the observed outcomes.

In summary, we have identified several factors consistently associated with the absence of CVRF in abdominal obesity: lower age, female sex, low ALAT, lower BMI. These are consistent with previous findings and extend these findings to abdominal obesity and a larger population.

Funding

DETECT is a cross-sectional and prospective longitudinal, nationwide clinical epidemiological study. DETECT is supported by an unrestricted educational grant of Pfizer GmbH, Karlsruhe, Germany.

Members of the DETECT study group include principal investigator: Professor Dr. H.-U. Wittchen; staff members: Dipl.-Psych. L. Pieper, Dipl.-Math. J. Klotsche, Dr. T. Eichler, Dr. H. Glaesmer, E. Katze; steering committee: Professor Dr. H. Lehnert (Lübeck), Professor Dr. G. K. Stalla (München), Professor Dr. A. M. Zeiher (Frankfurt); advisory board: Professor Dr. W. März (Mannheim/Graz), Professor Dr. S. Silber (München), Professor Dr. Dr. U. Koch (Hamburg), Priv.-Doz. Dr. D. Pittrow (München/Dresden), Professor Dr. M. Wehling (Mannheim), Dr. D. Leistner (Frankfurt), Priv.-Doz. Dr. H. J. Schneider (München), Dr. C. Sievers (München).

SHIP is part of the Community Medicine Research net (CMR) of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research, the Ministry of Cultural Affairs, as well as the Social Ministry of the Federal State of Mecklenburg-West Pomerania. The CMR encompasses several research projects, which share data from the population-based SHIP (http://ship.community-medicine.de). Statistical analyses were supported by the Competence Network Diabetes of the German Federal Ministry of Education and Research.

Disclosure

The authors have no conflict of interest to declare.

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