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Identifying metabolic syndrome without blood tests in young adults—The Terneuzen Birth Cohort

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Background: Within the context of the obesity epidemic identifying young adults at risk for type 2 diabetes and cardiovascular disease is important. A practical approach is based on the identification of metabolic syndrome (MetS). Our objective was to develop a simple and efficient stepwise strategy to identify MetS in young adults. **Methods:** Subjects were part of a birth cohort ($n = 2599$) in Terneuzen, The Netherlands, born in 1977–86. In 2004–05: 642 of these young adults participated in a physical examination and blood tests. Tree regression was used to determine the optimal decision strategy to identify MetS. **Results:** Overall prevalence of MetS, defined according to the NCEP ATPIII, was 7.5%. The tree regression yielded an optimal stepwise strategy that eliminated the need for blood tests for the diagnosis of MetS in 50–90% of the cases, depending on the accepted level of error. A large group (52% of the total) with BMI <35 had a normal waist circumference (WC) and normal blood pressure (BP). None of them had MetS. Subjects with BMI ≥35 all had MetS. If BMI <30, 38% had an increased WC or increased BP with a risk of MetS of only 6%. So for them the omission of blood tests could also be considered. **Conclusion:** In most young adults MetS can be identified or excluded without blood tests by a simple and stepwise strategy, based on the measurement of BMI, WC and BP. This makes it possible to develop simple prevention strategies for young adults at risk for type 2 diabetes and cardiovascular disease.

Keywords: metabolic syndrome, tree regression, young adults

Introduction

The dramatic increase in the prevalence of obesity[1–4] results in an increase in adverse levels of insulin and lipids, high blood pressure (BP) and type 2 diabetes, also in young adults.[5] Consequently, vascular damage will also occur in younger age-groups.[6,7] It is even anticipated that in the future more people will die from the complications of overnutrition than from starvation.[5–7]

For the development of prevention strategies early detection of persons who are at high risk for these complications of overweight and obesity is a prerequisite.

Metabolic syndrome (MetS), is a cluster of risk factors for type 2 diabetes and cardiovascular disease.[8–12] It is not sure that MetS as a cluster is better than its components in the prediction of cardiovascular disease. Besides, every component of MetS, in itself, merits specific attention and should be dealt with. However, it is also clear that the combined occurrence of these risk factors is associated with a high risk of the development of diabetes and cardiovascular disease, and—moreover—happens more often than could be expected on the basis of chance.[13,14] This makes identification of MetS a practical approach and a useful tool to identify people who are at high risk.

According to most definitions, MetS is based on concentrations of triglycerides, cholesterol, HDL-cholesterol and glucose. The blood tests that are necessary for the identification of MetS are an invasive and costly procedure. The objective of this study was to develop an efficient and simple stepwise strategy to identify MetS in young adults, based on data from the population-based Terneuzen Prevention Study (table 1).

Methods

Design and study population

The Terneuzen Birth Cohort consists of all 2599 children who were born between 1977 and 1986 in the city of Terneuzen. In 2004–05, a total of 2022 persons from the original cohort could be traced, and were invited to participate in a follow-up study. The follow-up study included measurements of weight, height, BP and waist circumference (WC). Data on baseline characteristics were obtained from questionnaires. Information about cigarette smoking was also gathered because smoking is an important short- and long-term risk factor, that might cause dislipidemie, high triglycerides and low HDL cholesterol.

The participants were also asked to undergo a vena puncture, following a fast of at least 12 h. The study protocol was approved by the Medical Ethics Committee of the VU University Medical Centre Amsterdam, and written informed consent was obtained from all participants.

Of the 2022 subjects who were invited, 920 (45%) responded, 163 of whom did not participate for logistic reasons. Of the remaining 757 participants, 642 had a vena puncture, and the analyses presented here apply to these cases. No differences from the original cohort were found with regard to mean age, the age of the mother at birth, birth weight or parity. However, there was a significant gender

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difference: the percentage men in the original cohort was higher than in our study population.

Physical examination and blood tests

The physical examinations were performed by two assistants who received standardized training at the Municipal Health Service in Terneuzen (GGD Zeeland). Weight was measured, with the subject in underwear, to the nearest 0.1 kg on an electronic self-zeroing scale. Standing height was measured to the nearest 0.1 cm with the aid of a stadiometer. WC was measured mid-way between the lower side of the lowest rib and the upper side of the pelvis, on bare skin, after a normal expiration, and with muscles relaxed. BP was measured twice (with a 5 min rest interval) on the left upper arm with the Omron 5-1, which is a fully automatic BP monitor. The mean values were used as outcomes.

Fasting venous blood samples were drawn in the clinical chemistry laboratory of the Community Hospital in Terneuzen. After centrifugation (10 min $1500 \times g$), plasma was analysed with a routine clinical chemical analyser, Synchron LX20PRO (Beckman Coulter Inc, USA). The parameters that were measured were glucose, cholesterol, HDL cholesterol and triglycerides. External quality control was performed.[15–17]

Table 1 Adult treatment panel III definition of MetS: at least three out of five criteria[11]

Criteria	Cut-off points	
1. Central obesity	WC (cm)	
	Men	>102
	Women	>88
2. Elevated triglycerides	Triglycerides (mmol/l)	≥1.7
3. Reduced HDL cholesterol	HDL cholesterol (mmol/l)	
	Men	<1.0
	Women	<1.3
4. Raised BP	Systolic (mmHg)	≥130
	Diastolic (mmHg)	≥85
5. Elevated fasting plasma glucose	Fasting plasma glucose (mmol/l)	≥5.6

Statistical analysis

The characteristics of the participants were summarized by means, standard deviations and percentages, subdivided into three body mass index (BMI = weight/height^2) categories. Age and gender-specific international BMI criteria for overweight and obesity were applied for the 17-years-olds, and adult cut-off points for all older participants.[18]

Differences in baseline characteristics and the prevalence of (components of) MetS between weight groups were assessed with *t*-tests, ANOVA and χ^2 tests.

Linear regression analysis was performed to study the relationships between variables, and the correlation between smoking and the components of MetS were tested with χ^2 tests, ANOVA and logistic regression analyses. Analyses were performed with SPSS statistical software, version 14.0 for Windows (SPSS Inc. Chicago, IL).

Tree regression analyses were performed with the S-PLUS 7 `tree` function. Given a set of predictors, this method searches for the cut-off point on any of the predictor that will optimally discriminate MetS from non-MetS. Subsequently, the sample is split into two parts, and the process is repeated for each part. The process is repeated again until no further useful splits can be made. The result is a binary tree.[19,20] BMI, WC, BP and the biochemical measurements were used as predictors. The binary tree was pruned and adapted in such a way that easily measured variables (BMI, WC, BP) were located at the top of the tree.

Results

The mean age of the 642 participants was 23.1 years (23.2 for men and 23.0 for women), 68.5% were of normal weight, 21.2% were overweight (not obese) and 5.6% were obese.

No differences in baseline characteristics were found between these three groups. The percentages of MetS components were substantially higher in overweight and obese subjects (table 2). Significant linear associations were found between BMI and all MetS components ($P < 0.001$). The overall prevalence of MetS in this group of young adults was 7.5%. In those with normal weight, overweight (not obese) and obesity, the percentage was, respectively, 1.7, 16.2 and 50.0%. The percentage of smokers was, respectively, 29.7, 30.5 and 44.8% (table 2).

Table 2 Subject characteristics and (components of) MetS related to BMI groups ($n = 642$)

	Normal weight BMI < 25	Overweight 25 ≤ BMI < 30	Obesity BMI ≥ 30	Total
Count (%)	470 (68.5)	136 (21.2)	36 (5.6)	642 (100)
Subject characteristics				
Age (years) mean (SD)†	22.8 (2.9)	23.7 (2.7)	24.4 (2.9)	23.1 (2.9)
Gender, men (%) (*n*)†	42.6 (200)	40.4 (55)	30.6 (11)	41.4 (266)
BMI: mean (SD)‡	21.6 (2.0)	26.9 (1.3)	33.2 (3.0)	23.4 (3.7)
Smoking cigarettes(%) (*n*)**,†	29.7	30.5	44.8	30.6
Level of education (%) (*n*)†*	441	129	34	604
Low (%) (*n*)†	18.1 (80)	24.8 (32)	23.5 (8)	19.9 (120)
Medium (%) (*n*)†	60.1 (265)	54.3 (70)	58.8 (20)	58.8 (355)
High (%) (*n*)†	21.8 (96)	20.9 (27)	17.6 (6)	21.4 (129)
(Components of) MetS (%)				
Central obesity‡	1.1	30.9	86.1	12.1
High BP§	39.4	48.5	63.9	42.7
Low HDL cholesterol‡	24.9	36.0	58.3	29.1
High triglycerides‡	5.1	14.0	19.4	7.8
High fasting plasma glucose§§	9.8	14.7	25.0	11.7
MetS‡	1.7	16.2	50.0	7.5

Persons with underweight (BMI < 18.50; $n = 30$) are included in the normal weight category: no statistical differences concerning subject characteristics and MetS (components) were found between underweight and normal weight persons, †no statistical significance, *missing data for $n = 38$, **missing data for $n = 57$
‡$P < 0.001$, §$P = 0.005$, §§$P = 0.011$

When comparing the baseline characteristics of the total study population with those of subjects with MetS, it appeared that MetS more often occurred between 23 and 28 years of age than between 18 and 22 years of age [OR 1.27, 95%CI (1.09–1.45)]. The prevalence of MetS appeared to be higher in smokers than in non-smokers (9.2 versus 5.6%) but this difference was not statistically significant. Logistic regression showed a significant relation between smoking and triglycerides and HDL cholesterol, independent of BMI and gender.

The frequencies of all components of MetS were higher in subjects with MetS than in subjects with no MetS, especially reduced HDL cholesterol (70.8%) central obesity (77.1%) and elevated BP (87.5%) (table 3).

Several binary regression trees were calculated. Figure 1 presents the final model, in which several branches have been combined into one branch to reduce complexity. The tree analysis showed that the most efficient categorization of BMI was very close to the usual discretization of BMI in obesity versus no obesity, but differed from the usual categories of BMI in normal weight, overweight and obesity (table 2). If BMI <30, refining the BMI categories was of no additional value in estimating the risk of MetS. However, if the BMI ≥30 estimates improved by dividing this category in two categories.

Table 3 Subject characteristics and components of MetS in subjects with MetS compared with subjects with no MetS (%)

	MetS (*n* = 48)	No MetS (*n* = 594)	All participants (*n* = 642)
Subject characteristics			
Age (years) mean (SD)†	24.0 (2.8)	23.0 (2.9)	23.1 (2.9)
Gender (men %)[a]	35.4	41.9	41.4
BMI category (%)‡			
Normal weight (%)	16.7	77.8	73.2
Overweight (%)	45.8	19.2	21.2
Obesity (%)	37.5	3.0	5.6
Smoking, (%)[a]	39.6	26.9	27.9
Level of education (%)†			
Low	34.1	18.8	19.9
Medium	47.7	59.6	58.3
High	18.2	21.6	21.4
Components of MetS (%)			
Central obesity‡	77.1	6.9	12.1
High triglycerides‡	45.8	4.7	7.8
Low HDL cholesterol‡	70.8	25.8	29.1
High BP‡	87.5	39.1	42.7
High fasting plasma glucose‡	43.8	9.1	11.7

a: Not statistically significant
†$P < 0.05$; ‡$P < 0.001$

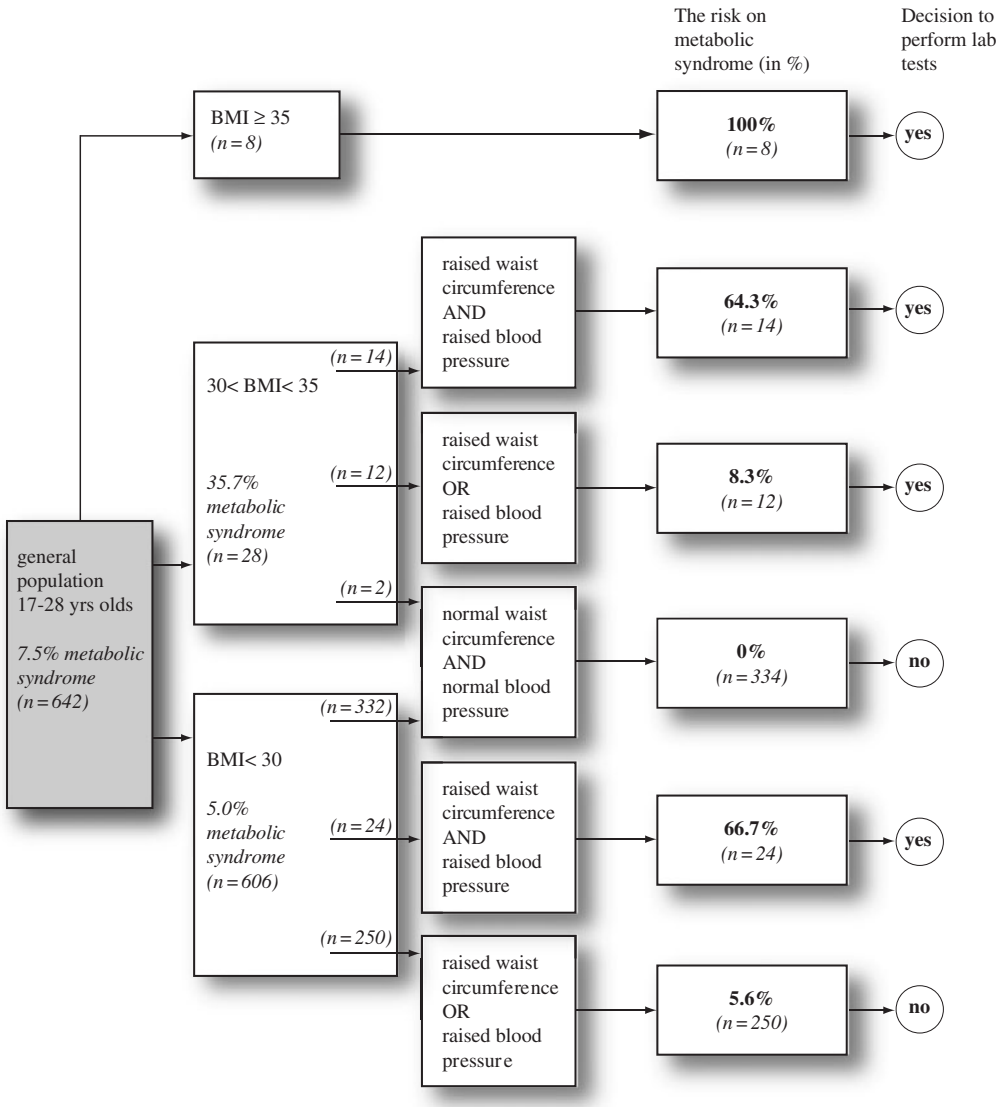

Figure 1 Decision tree for estimating the risk on MetS in percent (*n* = number of subjects)

Figure 1 shows the following:

- In participants with BMI ≥35, the risk of MetS is 100%.
- In participants with BMI ≥30 and BMI <35, the overall risk is 35.7%. The risk greatly depends on WC and BP. When both are elevated the risk is 64.3%, when only one is elevated the risk is 8.3%, but when neither are elevated the risk is zero.
- With a BMI <30, the overall risk is 5.0%. If both WC and BP were elevated the risk is 66.7%, if only one of these is elevated it is 5.6%, but if neither are elevated the risk is zero.

Note that: (i) Eight out of 642 participants were definitely classified as having MetS, (ii) 334 out of 642 participants were definitely classified as not having MetS and (iii) 250 out of 642 participants could be classified as not having MetS with an error rate of 5.6%. If we are prepared to accept this error, then 583 out of 642 (90%) can be classified with a tiny error without the need for a blood sample.

Discussion

The results of this observational study shows that with this simple stepwise strategy most young adults with MetS can be identified or excluded by use of BMI, WC and BP without any need for blood tests.

Tree regression analysis showed that MetS is present in all young adults with a BMI ≥35. For these young adults no additional blood tests or measurements are needed to identify those who are at high risk of developing type 2 diabetes and/or cardiovascular disease.

If BMI <35, BP and WC should be measured. If both are normal, there is no risk of MetS and blood tests are of no additional value in assessing MetS.

If BMI <35, and both WC and BP are elevated, the risk of MetS is high and additional blood tests should be performed. If only WC or only BP is elevated, the risk of MetS is comparable with the risk in the general population of young adults. In such cases the decision to perform additional diagnostic blood tests might depend on other factors, such as the absolute WC or BP, and smoking habits.

The overall prevalence of MetS in our study sample was 7.5%, which is comparable with the prevalence (5.2–10.3%) of MetS among young adults in Finland.[19] However, it was lower than that found in two other Dutch studies among young adults,[1,2] in which the age of the subjects was higher than in our study. This is consistent with the finding that the prevalence of the MetS depends on age.[2]

The frequencies of (components of) MetS were significantly higher in overweight or obese subjects. The components of MetS that were most frequently found were a high WC, high BP and a low HDL cholesterol. However, the stepwise method does not require the assessment of HDL cholesterol in the majority of cases.

The frequencies of obesity and a high WC in our study correspond with the frequencies reported in young adults in the Netherlands.[21,22] However, the percentage of young adults with an elevated BP in our study was higher than in other studies.[22,23] This could be the consequence of increased childhood obesity carrying over into adulthood. The prevalences of low HDL cholesterol and raised triglycerides are similar to those reported in other studies.[1,24,25]

Of the 2022 subjects who were invited to participate, 642 provided all data. Our sample might be selective, therefore. However, we found no statistically significant differences in any of the known variables of the original cohort, with the exception of gender. We do not expect that this gender difference will influence the findings because we found no gender differences in the main analysis.

The cut-off points for the different components of MetS according to the NCEP ATP III 2005 definition, are based on samples that are older than our study population. Since the levels of cardiovascular risk factors are associated with age, these cut-off points might underestimate the number of young adults who are at risk of developing type 2 diabetes and cardiovascular disease.

MetS increases the risk of cardiovascular morbidity and mortality 1.3–3 times and triples the risk of diabetes.[9,26–29]. The prognosis of type 2 diabetes with onset at an earlier age is even worse, causing a decline in quality of life and a shorter life-expectancy.[30] Since MetS was found in over 7% of our sample, there is an urgent need to identify young adults with MetS and to develop prevention and treatment programmes for this specific age-group. This is especially important because these youngsters seldom consult medical professionals.

Note that the tree model was based on just one single data set, and is restricted to people under 30 years of age. Because of the risk of data-fitting, we recommend that our results should be validated in other samples. As the prevalence of MetS increases with age, optimal trees for samples of other ages may be potentially quite different. However, the same methodology can be applied to suitable data from other age groups.

Despite the limitations in the study design, our results show great potential for the development of prevention strategies for young adults who are at high risk for type 2 diabetes and cardiovascular disease in the primary health care setting. Also in less frequent combinations, such as a BMI between 30 and 35 and a normal WC and BP (5.6% of the persons with this BMI), the omission of blood tests may have an important impact at population level. A blood test is not a very high risk test, and has a relatively limited burden at individual level. But, from a public health point of view, the burden is of much more concern. With regard to the rapid increase in the prevalence of overweight and obesity, the medical burden, the costs and time investments are enormous. Additional information on WC and BP, especially in those with a BMI <30 will result in the need for fewer blood tests.

The public health focus is on the management of excess weight, and not primarily on blood tests for lipid profiling. Lifestyle modification may be sufficient to prevent disease progression.

Serological tests for lipid profiling are often not needed to assess or exclude MetS. However, for high risk groups the decision to request blood tests will also depend on therapeutic considerations, certainly if lifestyle modification does not succeed or does not produce the required result (figure 1).

By following simple, stepwise methods in the diagnosis of MetS tremendous savings could be made in terms of laboratory and consultancy costs. Depending on the accepted level of error, between 50% and 90% of blood tests are superfluous for the diagnosis of MetS.

Because there is a need for identifying young adults who are at risk for type 2 diabetes and cardiovascular disease, cost-effective prevention and effective treatment programmes must be developed. Because of the prevalence and the risk of smoking, this is a very import lifestyle factor that should be dealt with in young people, especially in those with even more risk factors related to overweight. Youngsters who smoke and are diagnosed with MetS, should be offered an even more rigorous prevention programme that focuses on several lifestyle factors, directed at both smoking and weight reduction.

Our results can contribute to the development of more efficient, cheaper and less invasive ways to assess the presence of MetS in young adults.

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Conflicts of interest: None declared.

Key points

In the context of the obesity epidemic it is important to identify young people who are at risk for type 2 diabetes and cardiovascular disease.
By a simple and stepwise strategy, the presence of MetS in most young adults can be assessed without blood tests by measuring BMI, WC and BP. The results show great potential for the development of cost-effective prevention strategies for young adults who are at high risk for type 2 diabetes and cardiovascular disease.

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