Analysis plan for central obesity and risk for aortic aneurysm and aortic dissection

1 Background

Measures of central obesity, namely waist circumference (WC) and waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), have been adopted as more accurate predictors of cardiovascular disease .Yet, to our knowledge, very little is known about the role of central obesity in relation to the risk of aortic aneurysm (AA) and aortic dissection (AD).

2 Objective

The aim of this study is to examine the relationship between central obesity and the risk of AA and AD in Norwegian population and to test if

1. There is an association between increased WC and AA/AD

2. There is an association between increased WHR and AA/AD

3. There is an association between increased WHtR and AA/AD

3 Notation

WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio, AA: aortic aneurysm Disorder, AD: aortic dissection

4 Study population

Population are from The CONOR (Cohort of Norway) study, which includes 10 different cohorts and is an established collaboration of population-based surveys in Norway. Altogether 309,742 individuals were invited to the 10 surveys. The overall participation rate was 58% (n =181,872).

4.1 Exclusion criteria

The following subjects will be excluded from the analysis:

1. Subject with missing data on central obesity (i.e.,WC,WHR and WHtR)
2. Subjects with recorded AA/AD before cohort enrolment

5 Data management

5.1 Datasets and data sources

In the analyzes we will utlize the following datasets:

1. Cohort of Norway
2. Statistics Norway
3. Norwegian Patient Register
4. Cause of Death Register

5.2 Definition of AA/AD

1. Code I71.1-71.9 from the International Classification of Diseases (ICD) Tenth Revision will be used to identify cases of AA, and code I71.0 will be used to identify cases of AD from Norwegian Patient Register.
2. Information on the cause of death due to AA/AD will be obtained from ICD codes for the underlying cause of death in the Cause of Death registry.

5.3 Variables to analyze

Below are the variables to be considered in the analyses listed:

1. Sex
2. Age
3. ICD codes from Norwegian Patient Register and the Cause of Death registry
4. Education level
5. Smoking status
6. Occupation
7. Marital status
8. Self-reated health status
9. Physical activity
10. Alcohol consumption
11. Coffee consumption
12. Depression
13. Other physical disorders
14. Use of medication and supplements
15. Date for emigration
16. Date of death
17. Date of diagnosis of AA/AD

18. Height, waist and hip circumference

5.4 Derived variables

The following set of variables are calculated given the variables above:

1. WC: waist circumference

2. WHR: waist-to-hip ratio

3. WHtR: waist-to-height ratio

4. CENS: 1 or 0 of the subject has been censored or not

5. EVENT: 1 or 0 if the subject has been diagnosed with AA/AD

6. Time: days from inclusion to either incident AA/AD or censoring due to death from other causes, emigration or end of follow-up.

7. Education: low education corresponds to schooling < 10 years, middle education to 10–12 and high education to >12 years of schooling.

8. PA: Physical activity is categorized into inactive, moderately active, highly active.

6 Plans for statistical analyzes

6.1 Statistical analyzes

6.1.1 Design

The study will be considered as a prospective cohort design. Participants will be followed-up from baseline (1994-2003) to 2019.

6.1.2 Statistical models

Cox proportional regression models will be used to calculate the hazard ratios of AA/AD for categories of WC, WHR and WHtR, respectively.

To explore dose-dependent associations, we will also present the hazard ratios for all values of each exposure using spline-based curves.

Subjects with missing values on any of the covariates included in any of the fitted models will be excluded from all the analyses. For all models the calendar time at follow up will be used as time scale.

Response: AA

AA_f1.....: Age + Sex

AA_f2.....: AA_f1+ education +smoking status + occupation + marital status + PA + alcohol consumption + coffee consumption + self-reated health.

AA_f3.....: AA_f2 + depression + Other physical disorders

AA_f4.....: AA_f3 + depression + Use of medication and supplements

Response: AD

AD_f1.....: Age + Sex

AD_f2.....: AD_f1+ education +smoking status + occupation + marital status + PA + alcohol consumption + coffee consumption + self-reated health.

AD_f3.....: AD_f2 + depression + Other physical disorders

AD_f4.....: AD_f3 + depression + Use of medication and supplements

6.1.2 Table

The following tables will be produced:

Table 1. Characteristics of the study population

Age, years (mean±SD)	
Female, n (%)	
Waist circumference, cm (mean±SD)	
Waist-to-hip ratio (mean±SD)	
Waist-to-height ratio (mean±SD)	
Heavy coffee consumption, n (%)	
Current smoker, n (%)	
Heavy drinkers, n (%)	
University, n (%)	

Physically inactive, n (%)	
Unmarried, n (%)	

Values, mean ± standard deviation or number (percent).

Table 2. Hazard ratios for aortic aneurysm by waist circumference,waist-hip ratio and waist-to-height ratio

	Events	Incidence rate	Crude HR	95% CI	Adjusted HR	95%CI
Waist circumference (cm)						
≤88 /102 women/men						
>88 /102 women/men						
Waist-hip ratio						
<0.85 /0.90 women/men						
≥0.85 /0.90 women/men						
Waist-to-height ratio						
<0.492/0.536 women/men						
≥0.492/0.536 women/men						

HR: hazard ratios, CI: confidence intervals

Table 3. Hazard ratios for aortic dissection by waist circumference, waist-hip ratio and waist-to-height ratio

	Events	Incidence rate	Crude HR	95% CI	Adjusted HR	95%CI
Waist circumference (cm)						
≤88 /102 women/men						
>88 /102 women/men						
Waist-hip ratio						
<0.85 /0.90 women/men						

≥0.85 /0.90 women/men						
Waist-to-height ratio						
<0.492/0.536 women/men						
≥0.492/0.536 women/men						

HR: hazard ratios, CI: confidence intervals