

News and Views

Waist-Calf Circumference Ratio: A Better Predictor of Mortality Risk in Older Adults?

Older adults, especially the very elderly, with higher waist-calf circumference ratio (WCR) are at a higher risk of all-cause and cause-specific mortality, according to a new study published in the journal *BMC Public Health*.¹ The study further suggests WCR as a better predictor of mortality compared to body mass index (BMI).

In this study, the associations between mortality (due to any cause as well as a specific cause such as respiratory disease, heart disease, cancer) and anthropometric measures namely WCR, waist circumference (WC), calf circumference (CC) and BMI, in older adults aged 65 years and above (mean age 84.7 years) was analyzed. Scientists from the Department of Geriatrics and Cardiology at Jiujiang First People's Hospital in Jiujiang, China collaborated on this research. For this, they reviewed data of 4,627 participants from the 2014 Chinese Longitudinal Healthy Longevity Survey carried out in 22 provinces of China and followed them up in 2018. More than half (52%) of the study subjects were female.

A total of 1,671 (36.1%) deaths occurred during a median follow-up of 3.5 years; of these, ~23% (n = 332) deaths were due to cardiovascular disease (CVD), 5.3% (n = 88) due to cancer, 10.4% (n = 174) due to respiratory diseases, while 61.5% (n = 1,027) were from other causes. Patients with higher WCR, calculated as the ratio of WC and CC, were older and less educated; women were more likely to have higher WCR. They were nonsmokers, did not drink alcohol, did not exercise regularly and ate fewer vegetables in their diet.

The risk of all-cause mortality was found to be higher in participants in the highest quartile (third and fourth) of WCR with hazard ratio (HR) of 1.22 and 1.42 versus those in second quartile. The risk of CVD-related mortality and death due to other causes was also increased in the fourth quartile of WCR with HR of 1.88 and 1.37, respectively. Subjects in the lowest quartile of CC (vs, second quartile) were at a greater risk of all-cause,

CVD (HR 1.69) and other-cause mortality (HR 1.46), whereas those in the highest quartile had a decreased risk of all-cause and other-cause mortality such as cancer (HR 0.71).

The risk of death due to cancer was more than doubled among participants in the first and fourth quartiles of WC with HRs of 2.19 and 2.69, respectively. However, the association of WC with all-cause mortality was not significant. The risk of death due to any cause (HR 1.15) and mortality related to respiratory diseases (HR 1.56) was increased among those in the lowest quartile of BMI.

The association of calf circumference with all-cause and CVD mortality was particularly strong among the very elderly participants aged 80 years and older compared to the younger subjects.

This study shows that patients with higher WCR and lower CC were at a greater risk of all-cause, CVD, and other-cause mortality. WC was associated with only cancer-related mortality and no significant association was found between WC and all-cause mortality, while lower BMI was associated with an increased risk of all-cause and respiratory disease mortality. These findings therefore suggest that WCR, which incorporates both central obesity and muscle mass, may be more useful as a predictor of all-cause and cause-specific mortality especially in the very elderly vis-a-vis BMI, WC or CC alone.

Reference

1. Dai M, et al. Association of waist-calf circumference ratio, waist circumference, calf circumference, and body mass index with all-cause and cause-specific mortality in older adults: a cohort study. *BMC Public Health*. 2023;23(1):1777.

High Mortality Risk among Smokers with Suspected Bronchiectasis

Persons who have been smokers for a long time with suspected bronchiectasis are at a higher risk of dying within a decade irrespective of their lung function, suggests a new research published in the *Annals of Internal Medicine*.¹

Alejandro A Diaz, from the Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital in Boston, USA and colleagues conducted this prospective observational study to determine the association between suspected bronchiectasis and mortality in former and current smokers with a smoking history of 10 or more pack-years. A total of 7,662 adults, aged 45 to 80 years (mean age 60 years), from the COPD Gene (Genetic Epidemiology of Chronic Obstructive

Pulmonary Disease) study were selected for this study; 52% of them were female. On spirometry, 3,277 had normal spirometry results, 986 showed preserved ratio impaired spirometry (PRISm), while 3,399 showed obstructive pattern on spirometry. The primary end point of the study was a diagnosis of suspected bronchiectasis, which was defined as an airway-to-artery ratio (AAR) >1 of >1% on CT scan + 2 of the following symptoms: cough, phlegm, dyspnea and/or history of ≥ 2 exacerbations; 17.6% of the study group were found to have suspected bronchiectasis, while 37.7% had none of these criteria and acted as controls. Nearly 30% (n = 2,095) of the participants died over a median follow-up of 11 years.

After adjusting for variables such as age, sex, BMI, smoking status, subjects identified as suspected bronchiectasis were found to be at higher risk of mortality at 10 years compared to the controls. The difference in probability of 10-year mortality was 0.15 among adults with suspected bronchiectasis + normal spirometry, 0.07 in those with suspected bronchiectasis + PRISm spirometry and 0.06 in those with suspected bronchiectasis + obstructive spirometry versus those without suspected bronchiectasis. In a subgroup analysis of patients with suspected bronchiectasis based only on CT criteria, the 10-year mortality risk was no longer significant among those with normal spirometry with a lower difference in 10-year mortality probability (0.04) compared with the no suspected bronchiectasis group.

Among those with obstructive spirometry and suspected bronchiectasis, the 10-year mortality probability was comparable between those with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 1 to 2 COPD and GOLD stage 3 to 4 COPD at 0.29 versus 0.28, respectively.

To conclude, adults with suspected bronchiectasis along with obstructive spirometry are more likely to die within the next decade as shown in this study. Surprisingly, smokers with suspected bronchiectasis but normal lung function were also found to be at higher risk of mortality. Results of this study suggest that incidental detection of features suggestive of bronchiectasis on a chest CT scan coupled with respiratory symptoms, in a person, who is a current or former smoker, warrants thorough evaluation for bronchiectasis.

Reference

1. Diaz AA, et al. Suspected bronchiectasis and mortality in adults with a history of smoking who have normal and impaired lung function: a cohort study. *Ann Intern Med.* 2023;176(10):1340-8.

NT-proBNP: A Marker of CV Risk in Persons with Prediabetes?

Prediabetes is characterized by blood glucose levels, which are higher than normal, but below the cut-off for a diagnosis of diabetes. It is therefore often not taken seriously and ignored. Prediabetes is now recognized as a part of the continuum of dysglycemia as described in a Position Statement of the American Association of Clinical Endocrinologists (AACE), which defined four stages of dysglycemia-based chronic disease: insulin resistance (Stage 1), prediabetes (Stage 2), type 2 diabetes (Stage 3) and vascular complications (Stage 4).¹ People with prediabetes will progress to overt type 2 diabetes in due course of time. There is a lot of evidence to show that prediabetes is not as benign as it was considered to be. People with prediabetes also have CVD risk factors. Hence, compared to normoglycemic individuals, persons with prediabetes are at a significantly higher risk of atherosclerotic cardiovascular disease (ASCVD) and are more likely to suffer an adverse cardiovascular (CV) event.

Can measuring N-terminal pro-B-type natriuretic peptide (NT-proBNP) predict new onset of CVD in persons with prediabetes? To explore this hypothesis, researchers from Cleveland Clinic enrolled 3,235 subjects with prediabetes, who were being evaluated for CV risk.² The participants were followed for occurrence of MACE at 3 years and death due to any cause at 5 years.

Results showed that plasma NT-proBNP was associated with 6 times increased risk of incident MACE at 3 years with HR of 6.04 and 8 times increased 5-year mortality risk (HR 8.64). This association was seen to persist even after adjusting for variables such as CV risk factors, CVD, left ventricular ejection fraction (LVEF) and use of medications (diuretics) with adjusted HR (aHR) of 2.65 for 3-year MACE (major adverse cardiovascular events) and 3.45 for 5-year mortality. "NT-proBNP significantly improved the clinical prognostic value (C-statistic, NRI, IDI) for both 3-year MACE and 5-year death when added to models", noted the authors.

Early intervention to prevent progression to type 2 diabetes is important to prevent the associated macro- and microvascular complications of type 2 diabetes. These findings validate NT-proBNP as a useful aid in predicting the risk of incident MACE and long-term mortality in persons with prediabetes. Identification of at-risk individuals expedites initiation of aggressive preventive measures – lifestyle-based or pharmacotherapy – to prevent acute CV events before they are diagnosed with type 2 diabetes.

References

1. Mechanick JL, et al. Dysglycemia-based chronic disease: an American Association of Clinical Endocrinologists position statement. *Endocr Pract.* 2018;24(11):995-1011.
2. Witkowski M, et al. NT-proBNP and cardiovascular event risk in individuals with prediabetes undergoing cardiovascular evaluation. *Diabetes Res Clin Pract.* 2023;205:110923.

Management of Cesarean Scar Ectopic Pregnancy

Hysteroscopic resection was superior to ultrasound-guided dilation and evacuation (D&E) for the management of cesarean scar ectopic pregnancy, suggests a new study published in the *American Journal of Obstetrics & Gynecology*.¹

This single-center trial was conducted at the University of Naples Federico II in Naples, Italy, between February 2020 and August 2022. For this they selected 54 women, mean age 34 years, with singleton cesarean scar ectopic pregnancies below 8 weeks and 6 days of gestation and myometrium thickness of ≥ 1 mm and who had chosen to terminate the pregnancy. All the women included had undergone previous, ranging from 1 to 3, cesarean births. The participants were randomized 1:1 to management with hysteroscopic resection (intervention group) or ultrasound-guided D&E (control group) 1 to 5 days after the last methotrexate dose. Both groups were administered injection methotrexate (50 mg/m²) prior to the procedure on day 1. A second dose was given on the third day. Seven (25.9%) women in the intervention group and 3 in the control group (11.1%) were administered a third dose of methotrexate due to persistent fetal heart activity. The objective of the study was to compare the efficacy of the two procedures for the treatment of cesarean scar ectopic pregnancy. The primary end point was the success rate of the procedures in either group, while the secondary end points comprised duration of hospitalization, need for additional procedures, complications, maternal ICU admission and death.

One hundred percent success rate, defined as “no further treatment required until the complete resolution of the cesarean scar ectopic pregnancy”, was noted in the women who underwent hysteroscopic resection, while in the control group, the success rate was 81.5% with a relative risk of 1.22. The resolution of the pregnancy was determined on the basis of decrease in β -hCG (beta-human chorionic gonadotropin) and finding of no residual gestational material in the endometrial cavity. Five women in the control group required additional procedures viz. laparotomic uterine segmental resection and hysteroscopic resection in one each and

hysterectomies in three cases. Hemorrhage occurred in nearly 15% women in the control group versus 3.7% in the intervention group. Length of hospitalization was shorter in the intervention group compared to the control group; 9.0 days versus 10.0 days, respectively with a mean difference of -1.00 days. None of the participants required intensive care and no maternal deaths occurred. This study demonstrates greater success rate of hysteroscopic resection for the management of cesarean scar ectopic pregnancy in comparison to ultrasound-guided D&E. Shorter length of hospital stay and lower hemorrhage rate were added advantages of hysteroscopy.

Reference

1. Di Spiezio Sardo A, et al. Hysteroscopic resection vs ultrasound-guided dilation and evacuation for treatment of cesarean scar ectopic pregnancy: a randomized clinical trial. *Am J Obstet Gynecol.* 2023;229(4):437.e1-437.e7.

Study Reveals: Leprosy can Affect the Brain and Spinal Cord

A recent systematic review and meta-analysis published in *The Royal Society of Tropical Medicine and Hygiene* revealed that leprosy can affect peripheral nerves, the brain and the spinal cord. The research paper was titled “The Spectrum of Central Nervous System Manifestations in Leprosy: A Systematic Review of Published Case Reports and Case Series.”

Professor RK Garg, Head of the Neurology Department at KGMU, commented that earlier, it was believed that *Mycobacterium leprae*, the bacteria that causes leprosy, primarily troubles the peripheral nerves and does not affect the brain and spinal cord. Hence, the systematic review aimed to explore the involvement of the central nervous system (CNS) in leprosy by analyzing various cohort studies, individual cases and case series. In total, 34 records were identified, consisting of 18 cohort studies and 16 reports describing 27 isolated cases. The study author explained that macroscopic changes in the spinal cord were observed, with *M. leprae* being detected in neurons of the medulla oblongata, the connection between the brainstem and the spinal cord. Additionally, spinal cord and brachial plexus abnormalities were detected in 78% of the patients.

Currently, multidrug therapy is the standard treatment for leprosy. Professor Garg clarified that there would be no immediate alteration in treatment protocols. However, he emphasized the need for doctors to exercise caution, considering that leprosy can affect the brain and spinal cord.

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