

## News and Views

### Muscle Fat: A Novel Risk Factor for Cognitive Impairment

Older adults with high amounts of fat in the skeletal muscles are at risk of greater and faster cognitive decline, according to a new study published June 7, 2023 in the *Journal of the American Geriatrics Society*.<sup>1</sup>

Rosano et al measured the intermuscular adipose tissue of the thigh muscle using CT scans in 1,634 adults, aged 69 to 79 years at year 1 and year 6. They also evaluated the participants for cognitive function using the minimal state exam (3MS) at years 1, 3, 5, 8 and 10. Almost half (48%) of the selected study subjects were female and 35% were Black.

The researchers found that the intermuscular adipose tissue of the thigh muscle increased by 4.85 cm<sup>2</sup> (Year 1-6) and the cognitive function declined by 3.20 points (Year 6-10) on the 3MS test. Increase in thigh fat content of 4.85 cm<sup>2</sup> was associated with decrease of an additional 3.60 points on 3MS.

In this study, a 5-year increase in the fat content of thigh muscle was significantly associated with cognitive impairment suggesting skeletal muscle adiposity as a novel risk factor for cognitive decline. This association between muscle fat and cognitive decline was independent of muscle strength, body composition including the traditional risk factors for dementia. Hence, older adults must be advised to lead a healthy lifestyle with a healthy and well-balanced diet and daily exercise.

#### Reference

1. Rosano C, et al. Increase in skeletal muscular adiposity and cognitive decline in a biracial cohort of older men and women. *J Am Geriatr Soc*. 2023 Jun 7.

### Upper-Extremity Impairments in Type 1 Diabetes

Patients with type 1 diabetes have a high prevalence of upper-extremity impairments such as frozen shoulder, carpal tunnel syndrome, trigger finger and Dupuytren contracture, according to a recent study published in the June 2023 issue of the journal *Diabetes Care*.<sup>1</sup>

This cross-sectional study aimed to determine the prevalence of four upper-extremity impairments namely frozen shoulder, carpal tunnel syndrome, trigger finger and Dupuytren contracture among 2,245 Danish patients with type 1 diabetes. The matched

control group included 841 individuals from the general population. Socioeconomic and clinical data was sourced from national registers. The symptoms and diagnosis of upper-extremity impairments were self-reported via questionnaires.

Results showed that patients with type 1 diabetes were 3 times more likely to have frozen shoulder and carpal tunnel syndrome with odds ratio (OR) of 3.5. The prevalence of Dupuytren contracture was 4 times higher with OR of 4.3, while the prevalence of trigger finger was 5 times higher with OR of 5.0. Type 1 diabetes patients had a higher probability of coexisting impairments compared to the control group. The study also explored various factors associated with upper-extremity impairments. The association was greater among those with long-standing diabetes. A correlation between older age, higher body mass index (BMI), female sex, higher glycated hemoglobin (HbA1c), macro- and microvascular complications and higher risk of occurrence of upper-extremity impairments was also observed.

Although the study only demonstrates an association, nevertheless these findings do show a high prevalence of upper-extremity impairments among patients with type 1 diabetes. Hence, they should be regularly screened for upper-extremity impairments for timely interventions since they have significant adverse effects on working ability and consequently work performance and productivity. Additionally, it may contribute to low health-related quality of life.

#### Reference

1. Wagner S, et al. Upper-extremity impairments in type 1 diabetes: results from a controlled nationwide study. *Diabetes Care*. 2023;46(6):1204-8.

### “Arexvy” the First RSV Vaccine Approved by EU Against Common Respiratory Virus

The European Commission has approved the first RSV (Respiratory Syncytial Virus) vaccine “Arexvy” for persons aged 60 and older manufactured by GlaxoSmithKline. The approval comes shortly after the United States approved the medicine, last month.

The vaccine results from decades of research into how to protect susceptible people from the prevalent sickness.

RSV often causes mild, cold-like symptoms, but it can be dangerous for young children, the elderly, those with weakened immune systems and people with underlying medical issues. In extreme situations, it can result in pneumonia and bronchiolitis, an inflammation of the tiny airways deep inside the lungs. Analysts have predicted that the market for this newly launched vaccine might be worth more than \$10 billion in the following 10 years. Pfizer and Moderna are two more manufacturers expected to release similar products shortly.

Arexvy's clearance was recommended by the drug watchdog for the European Union in April, following a trial with 25,000 participants across 17 nations. The European Medicines Agency reported that the vaccination provided 83% protection against RSV-related illnesses in persons 60 or older, with typically few adverse effects. The vaccine uses a synthetic protein and an adjuvant material to encourage antibodies and T cells that aid in warding off RSV infection.

By the end of the year, Moderna hopes to have received approval for and access to their RSV vaccine. Previously, the European Union approved an RSV preventative medicine in 2022 developed by the French pharmaceutical company Sanofi and the British pharmaceutical company AstraZeneca.

(Source: <https://medicalxpress.com/news/2023-06-eu-vaccine-common-respiratory-virus.html>)

### Rise Against Liver Diseases: A Step Forward in NASH Awareness

Indians are mostly affected by many lifestyle-related diseases, such as nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).

NAFLD affects people who drink little to no alcohol due to the buildup of extra fat in the liver cells. A person has a simple fat buildup called nonalcoholic fatty liver (NAFL) when there is no inflammation or cell damage present, while a person has NASH when there is inflammation or cell damage in addition to the simple fat buildup, which may lead to difficulties in the future. Even while NASH can have major health consequences, those who have it frequently experience few or no symptoms, leading to progressive inflammation and swelling and the production of scar tissue over time.

The National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS) was established by the Global Liver Institute to stop liver fibrosis (NAFLD) and to take proactive preventative actions against this threat.

A National Level Centre of Excellence has been established to create standards for diagnosis, raise public awareness, educate health care workers, and create a framework for monitoring and assessment. A liver biopsy is necessary in severe instances, but basic blood tests and radiologic examinations can screen for NAFLD.

The NPCDCS has started a media campaign to raise awareness of noncommunicable diseases (NCDs) across the country using a variety of offline and online media platforms. Recently, patient monitoring and adherence to preventive and treatment measures have been made easier for patients by introducing patient support groups and patient awareness initiatives like LivAlert.

(Source: <https://health.economictimes.indiatimes.com/news/industry/step-up-for-nash-livalert-to-confront-the-silent-threat-of-liver-diseases/100830633>)

### “Kangaroo Mother Care” Increase the Child's Chances of Survival: Study

The findings of a review of research conducted in India and published in the *BMJ Global Health Journal* reported that a form of care involving skin-to-skin contact between a mother and her prematurely delivered infant might dramatically increase the child's chances of survival.

The study discovered that the intervention appeared to be much more beneficial in lowering mortality and infection when it started within 24 hours of delivery and continued for at least 8 hours daily.

The World Health Organization (WHO) advises “kangaroo mother care” (KMC) as the recommended level of care after a low birth weight infant's condition has stabilized clinically. However, still, it needs to be clarified what the best strategy is.

The study evaluated 31 trials, including 15,559 newborns. It revealed that KMC appears to lower mortality risk by 32% either during labor and delivery in a hospital or by 28 days following delivery while also lowering the risk of severe infection by 15%. The mortality benefits were larger when the daily KMC length was at least 8 hours, as opposed to KMC of a lower duration.

The review's authors stated that there was generally little to no risk of bias in the included studies and that there was moderate to strong confidence in the strength of the evidence supporting the primary outcomes.

(Source: <https://www.tribuneindia.com/news/health/close-contact-between-mother-and-premature-baby-may-boost-infants-survival-study-514705>)

### Residual Dyspnea Predictive of Poor Response to Single-inhaler Triple Therapy in Asthma

Asthma patients, who remain symptomatic despite treatment with inhaled corticosteroids/long-acting  $\beta_2$  agonists may be prescribed single-inhaler triple therapy (SITT) as short-term treatment. To investigate factors that would predict a beneficial response with SITT in patients with asthma, researchers from Japan enrolled 45 patients in a retrospective study.<sup>1</sup> These patients had been prescribed the SITT from March 2019 to March 2021. Predictors of responsiveness to 4 weeks of therapy were assessed. The demographic information along with data about residual respiratory symptoms, type 2 biomarkers and pulmonary function prior to the use of SITT was obtained from the medical records of the patients.

Three-fourth (75%) of the enrolled patients were found to respond to the short-term treatment with SITT. Patients who did not respond to the inhaler therapy had significantly lower forced vital capacity (FVC) (%predicted) values and experienced dyspnea more often than responders. The type 2 biomarkers (sputum and blood eosinophils, exhaled nitric oxide levels and serum periostin) were comparable between the two groups.

Factors found to be predictors of poor or no response to SITT were residual dyspnea, low FVC (%predicted) and FVC (%predicted) <80% with OR of 0.14, 1.05 and 0.11, respectively. On multivariate analysis, residual dyspnea prior to being prescribed the inhaler therapy was associated with poor response to SITT (OR 0.14). Patients with residual dyspnea also had significantly lower forced expiratory flow 25-75 (FEF<sub>25-75</sub>) (%predicted) values compared to patients who did not have residual dyspnea before the use of SITT.

At least 75% of the patients responded to short-term treatment with the SITT in this study; this effect was independent of the demographics or type 2 phenotype. Residual dyspnea, indicative of small airways dysfunction, therefore may be predictive of poor response to inhaler therapy in these patients, as shown in this study.

#### Reference

1. Ito K, et al. Residual dyspnea may predict small airways dysfunction and poor responsiveness to single-inhaler triple therapy in asthmatic patients. *Am J Respir Crit Care Med.* 2023;207:A1299.

### Early versus Interval Postpartum IUD Placement

Early placement of intrauterine device (IUD) at 2 to 4 weeks after childbirth was not inferior to later placement

at 6 to 8 weeks postpartum with comparable complete expulsion rates between the two groups, according to a study published in *JAMA*.<sup>1</sup>

The randomized noninferiority trial was conducted with the objective to determine IUD expulsion rates inserted in the early postpartum versus IUDs placed at the standard interval after childbirth. For this, 404 women, with mean age of 29.9 years, who had delivered between March 2018 to July 2021 were selected for the study. IUD was inserted 2 to 4 weeks after delivery in 203 women, while 210 received it after 6 to 8 weeks of childbirth. A total of 294 women who underwent IUD placement were available for follow-up at 6 months.

Complete expulsion, which was the primary study outcome, occurred in 2% (3/149) in the early placement group compared to none (0/145) in the interval placement group with between-group difference of 2.0. The partial expulsion rate, a secondary outcome, was 9.4% in the early placement group versus 7.6% in the interval placement group with a between-group difference of 1.8. At 6 months, the use of IUDs, which was also a secondary outcome of the study, was comparable between the two groups; 69.5% (early group) versus 67.2% (interval group).

Based on these findings, the study concluded that early IUD placement was noninferior to later postpartum IUD placement for complete expulsion, but not for partial expulsion. "Understanding the risk of expulsion at these time points may help patients and clinicians make informed choices about the timing of IUD placement", conclude the authors.

#### Reference

1. Averbach S, et al. Early vs interval postpartum intrauterine device placement: a randomized clinical trial. *JAMA.* 2023;329(11):910-7.

### Stem Cell-based Therapy can Repair Damage to the Heart and Enhance Function

According to a study published in the *Nature Partner Journal, Regenerative Medicine*, stem cells transplanted into an injured heart have the ability to repair damaged tissue and improve heart function. Ischemic heart disease, caused by diminished blood flow to the heart, is the most common cause of death worldwide.

The study developed a new protocol for producing heart muscle precursor cells using pluripotent or immature stem cells. They injected these precursor cells into the area of the heart damaged by myocardial infarction and found that they could grow into new heart muscle cells.

Previous studies have shown that transplanting beating heart cells into the damaged area of the heart leads to ventricular arrhythmia. Hence, the researchers transplanted nonbeating heart cells into the damaged heart in the study. After the transplantation, the cells expanded and acquired a rhythm similar to the rest of the heart.

They also observed that after transplanting nonbeating heart cells, the incidence of arrhythmias was cut by half.

(Source: <https://www.daijiworld.com/news/newsDisplay?newsID=1088393>)

### Sixty Percent of Diabetes Cases Found in India are Reversible: ICMR Chief

According to recent data from a 12-year study investigating the incidence of metabolic NCDs, including diabetes, India has nearly doubled the number of people with diabetes than previously expected.

The Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study, a cross-sectional population-based survey of individuals aged 20 and older drawn from urban and rural areas of 31 states and union territories, discovered a diabetes prevalence in the population of 11.4% or 101 million people. This is 1.68 times higher than the previously estimated 60 million diabetes cases in India.

The new study published in *The Lancet* showed that the prevalence of prediabetes, hypertension, general obesity and dyslipidemia in India is around 15.3%, 35.5%, 39.5% and 81.2%, respectively.

Dr Rajiv Bahl, Chief of the ICMR, stated that prediabetes is entirely reversible and that 60% of diabetes cases can be reversed by following a healthy diet and regular exercise regimen.

A total of 1,13,043 individuals were included in the study, of which 79,506 were from rural areas, and 33,537 were from urban areas. The study also showed that Punjab was the leader in obesity, hypertension and dyslipidemia, all risk factors for major NCDs.

(Source: <https://www.tribuneindia.com/news/health/60-pc-diabetes-reversible-icmr-chief-on-finding-101-mn-diabetics-in-india-515676>)

### NPPA Fixed the Retail Prices of 23 Drugs, Including Diabetes and Blood Pressure Drugs

Recently, the National Pharmaceutical Pricing Authority (NPPA) fixed the retail prices of 23 formulations, including the medications used to treat diabetes and high blood pressure. The national drug pricing

regulator has set the prices of the drugs based on the decision made during the 113th Authority meeting held on May 26, 2023. The prices of these drugs were fixed as per the Drugs (Price Control) Order, 2013.

The NPPA has fixed the price of 1 tablet of diabetes drugs, namely gliclazide ER and metformin hydrochloride tablets, at Rs. 10.03. Similarly, the retail price of 1 tablet of antihypertensive medications such as telmisartan, chlorthalidone and cilnidipine tablets has been fixed at Rs. 13.17.

The retail price of 1 tablet of the pain reliever medications trypsin, bromelain, rutoside trihydrate and diclofenac sodium has been fixed at Rs. 20.51. The NPPA has also revised the ceiling price of 15 scheduled formulations under the Drugs (Prices Control) Order 2013 (NLEM 2022).

They have also fixed the ceiling price for two scheduled formulations.

(Source: [https://www.business-standard.com/industry/news/nppa-fixes-retail-prices-of-23-drug-including-diabetes-blood-pressure-123060900710\\_1.html](https://www.business-standard.com/industry/news/nppa-fixes-retail-prices-of-23-drug-including-diabetes-blood-pressure-123060900710_1.html))

### Incidence of New-onset Type 2 Diabetes in Lean NAFLD

NAFLD typically occurs in persons with obesity. But now NAFLD is increasingly being observed in those with normal BMI and has been termed "lean NAFLD". Although the disease is less severe in the lean, it progresses through a similar spectrum of diseases and shares similar comorbid metabolic disorders like type 2 diabetes, dyslipidemia and metabolic syndrome as in NAFLD in persons with obesity.<sup>1</sup>

To determine the incidence of new-onset type 2 diabetes among people with lean NAFLD, a meta-analysis of studies was carried out.<sup>2</sup> Published studies on lean NAFLD up to December 2022 were screened after a thorough search of PubMed, Scopus, Cochrane and Web of Science databases and 16 observational studies were selected for the final meta-analysis.

Out of the 3,04,975 adult patients included, 7.7% had lean NAFLD. Over a follow-up period of 5.05 years, there were nearly 1,300 cases of incident diabetes.

Analysis of data published in the journal *Diabetes Research and Clinical Practice* showed that participants with lean NAFLD were twice more likely to develop incident diabetes compared to those who did not have NAFLD with a hazard ratio (HR) of 2.72. The adjusted HR (aHR) of incident diabetes in subjects with overweight/obesity but without NAFLD was 1.32. While among the participants with overweight/obesity and

NAFLD, the aHR was 2.98. Patients with NAFLD were nearly 3.5 times more likely to develop type 2 diabetes, if they had advanced high NAFLD fibrosis scores with HR of 3.48.

This study shows that the risk of type 2 diabetes was higher in people with lean NAFLD compared to the lean without NAFLD. The risk of developing diabetes was equivalent between the lean and overweight/obese individuals with NAFLD suggesting that NAFLD, more than overweight/obesity, was a risk factor for type 2 diabetes in this patient group. Patients with increasing NAFLD fibrosis score were at greater risk.

### References

1. Ahadi M, et al. A review of non-alcoholic fatty liver disease in non-obese and lean individuals. *J Gastroenterol Hepatol.* 2021;36(6):1497-507.
2. Gao Y, et al. Lean nonalcoholic fatty liver disease and risk of incident type 2 diabetes mellitus: a literature review and meta-analysis. *Diabetes Res Clin Pract.* 2023;200:110699.

### Diabetes, Weight Loss Drug can Reduce Alcohol Dependence by Half

According to a study published in *eBioMedicine*, semaglutide can help reduce alcohol dependence by half. Semaglutide is the first medication to act on the glucagon-like peptide 1 (GLP-1) receptor that is available in tablet form. The findings of the study showed that the drug significantly reduced alcohol consumption and alcohol consumption in conjunction with relapses in the test subjects. Interestingly, semaglutide reduced alcohol intake equally in male and female test subjects. Relapses in alcohol consumption is a significant problem for the individual with alcohol dependence, as they tend to drink more than before the withdrawal after relapse.

In the study, the researchers examined the mechanism by which the medication reduced alcohol consumption. They found that the drug reduced alcohol-induced reward in the brain, which reduced alcohol consumption. They explained that semaglutide affected the brain's reward system in test subjects, especially the nucleus accumbens area of the brain, which is part of the limbic system.

(Source: <https://www.daijiworld.com/news/newsDisplay?newsID=1088981>)

### Even Moderate Alcohol Consumption can Increase the Risk of Over 60 Diseases

In a study published in *Nature Medicine*, moderate consumption of alcohol was associated with an increased risk of 60 diseases, including cataracts and

gastric ulcers. Each year more than 3 million deaths are reported due to the consumption of alcohol, with an increasing prevalence in many low and middle-income countries.

In the study, researchers from the University of Oxford, UK and Peking University, China, enrolled 5,12,000 adults from urban and rural areas in China and assessed the effect of alcohol consumption on 200 different diseases.

The study's findings showed that alcohol consumption increased the risk for 61 diseases among men. WHO has established 28 conditions out of these 61 diseases as alcohol-related disorders. These 28 diseases included stroke, gastrointestinal cancers, etc.

Further, genetic analysis to probe the link of alcohol consumption with various diseases showed that every 4 drinks per day were associated with a 14% increased risk of established alcohol-related disease, a 6% higher risk of conditions not previously known to be alcohol-related, and twofold increased risk of liver cirrhosis and gout. A higher intake of alcohol was also associated with an increased risk of stroke in a dose-response manner. However, no such association was observed between alcohol consumption and increased risk for ischemic heart disease.

(Source: <https://www.timesnownews.com/health/even-moderate-alcohol-intake-can-raise-risk-for-over-60-diseases-study-article-100913796#:~:text=Even%20if%20you%20consume%20alcohol,ulcers%2C%20warned%20a%20new%20study>)

### Impact of Hair Cortisol Levels in Newborns on Sleep

Neonates born with higher levels of cortisol in their hair take longer time to sleep at 7 months of age, suggests a study presented at the recently concluded annual meeting of the Associated Professional Sleep Societies, SLEEP 2023 and also published in the journal *Sleep*.<sup>1,2</sup>

Researchers from University of Colorado, University of Denver and University of Illinois obtained hair cortisol from 70 infants within 2 days of birth, more than half of whom were female (57.1%). The average gestational age at birth was 39.4 weeks. These infants were a part of the Care Project, a longitudinal study in Denver, Colorado. None of them had received exogenous glucocorticoids prenatally. Sleep was evaluated with the aid of the Brief Infant Sleep Questionnaire (BISQ), filled by the parents, when the infants were 7 months old. The aim of the study was to investigate if neonatal hair cortisol was associated with sleep health in infancy. Neonatal hair cortisol is an index of cortisol production by the fetus.

After adjusting for gestational age at birth and family income-to-needs ratio, the researchers found that higher neonatal hair cortisol levels were indicative of poor sleep at 7 months in the form of longer sleep onset latency as assessed by the BISQ. However, no association was noted between neonatal hair cortisol levels and nighttime sleep duration, number of night awakenings and nighttime wake duration.

This study demonstrates that higher fetal cortisol levels during late pregnancy may adversely affect sleep in infants suggesting a prenatal influence on sleep during infancy. Cortisol is the stress hormone. It is produced by the activity of the hypothalamic-pituitary-adrenal (HPA) axis. The sleep cycle may be disrupted if the HPA axis is active resulting in high levels of cortisol. This manifests as fragmented sleep, insomnia and overall shorter sleep time. The authors write that “specifically, cortisol may inform the shift from multiphasic to monophasic sleep as well as the accumulation of sleep pressure throughout the day, impacting sleep onset latency.”

However, only sleep onset latency was affected and not overall sleep. Nevertheless, these findings merit further studies to investigate the impact of high neonatal cortisol on sleep during childhood.

### References

1. Benefield T, et al. Abstract 0121. Newborn hair cortisol and sleep health in infancy. *Sleep*. 2023;46(Suppl 1):A54-A55.
2. Newborns with higher hair cortisol levels take longer to fall asleep. May 30, 2023. <https://www.sleepmeeting.org/newborns-higher-hair-cortisol-levels-take-longer-fall-asleep/>. Accessed June 12, 2023.

### Early Hysterectomy and Risk of Heart Disease

The risk of heart disease is known to be higher among postmenopausal women. A new study from South Korea has shown that women who had a hysterectomy done before 50 years of age were at a higher risk for heart disease, stroke in particular. The study findings are published in *JAMA Network Open*.<sup>1</sup>

Jin-Sung Yuk from the Dept. of Obstetrics and Gynecology, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea and co-researchers conducted this retrospective study to examine if hysterectomy before age 50 years increased the risk of new onset cardiovascular disease (CVD). For this, they sourced data of 55,539 women who underwent a hysterectomy, with a median age of 45 years, from the National Health Insurance database from January 2011 to December 2014 and matched them with 55,539 women, who did not undergo a hysterectomy.

Over nearly 8 years (median) of follow-up, the hysterectomy group had a greater risk of CVD with the incidence of heart disease being 115 per 1,00,000 person-years compared with 96 per 1,00,000 person-years in the nonhysterectomy group. After adjustment for multiple variables, women who underwent hysterectomy were at a higher risk of developing heart disease compared to those who did not have the surgery with HR of 1.25. The risk of stroke was found to be significantly increased among women in the hysterectomy group with HR of 1.31. But the occurrence of myocardial infarction (HR 1.06) and coronary artery revascularization (HR 1.03) were similar between both groups. When women who also had an oophorectomy were excluded from the analysis, the risk of heart disease was still higher in women with hysterectomy (HR 1.24).

These findings suggest that hysterectomy in women younger than 50 years resulting in early menopause is associated with increased risk of heart disease, especially stroke. The authors write that “because the incidence of CVD was not high, a change in clinical practice may not be needed”. Nevertheless, women undergoing early hysterectomy should be educated about the risk of heart disease and recommended a healthy lifestyle to prevent a cardiovascular event.

### Reference

1. Yuk JS, et al. Association of early hysterectomy with risk of cardiovascular disease in Korean women. *JAMA Netw Open*. 2023;6(6):e2317145.

