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ASSESSING THE LINK BETWEEN KNEE OA, OBESITY, AND SARCOPENIA

Obesity has been identified as a major risk factor for knee osteoarthritis (OA), but previous studies investigating this link have defined obesity using anthropometric measures, such as body weight or BMI. "Physical measurements reflect aggregate measures of fat, muscle, and bone mass". As a result, it's unclear if the risk of knee OA by obesity is through aggregate body weight or amount of fat mass.

Furthermore, in some older adults, increases in fat mass are not accompanied by increases in muscle mass, leading to a state of high fat but low muscle mass. This condition is known as sarcopenic obesity. Several risk factors for the development of sarcopenic obesity have been identified in clinical research, including low physical activity, inflammation, and malnutrition, among others. On its own, sarcopenia has been associated with several adverse outcomes, including functional limitations, but it is unknown whether inappropriately low muscle mass, as reflected by sarcopenia, adversely impacts the risk of developing knee OA.

A NEW ANALYSIS

By studying body composition, the additional risks posed by high fat mass and low muscle mass over that of obesity without sarcopenia can be evaluated. "To examine this association more closely, obesity by fat mass measured by whole body dual energy X-ray and examined the role of sarcopenia, as defined by low muscle mass" If obesity increases the risk of OA, then sarcopenia—which is generally associated with low body weight—should be associated with a lower risk of knee OA."

There is longitudinal association of body composition as defined by the relative presence of adiposity and sarcopenia with the risk of incident radiographic knee OA. They studied participants from a large cohort of older adults who either had knee OA or were at risk for it. Subjects included those who had dual energy X-ray at baseline, which provided fat and muscle mass data. Knee X-rays were performed and read for OA status at baseline and follow-up and information on other covariates was available. Subjects were divided into four exposure categories: 1) obese, 2) sarcopenic obese, 3) sarcopenia, and 4) non-obese non-sarcopenic.

ASSESSING THE IMPLICATIONS

The risk of knee OA in both women and men is primarily linked to adiposity, greater efforts are needed to emphasize the importance of losing weight through diet and exercise when managing this patient population". Weight loss interventions that target both high fat mass and low muscle mass. Preventive efforts may need to expand the focus from simply reducing obesity to also ameliorating sarcopenic obesity in efforts to reduce the growing incidence and prevalence of knee OA. Ultimately, body composition assessments may provide important new insights into the association of obesity with knee OA, especially regarding sarcopenic obesity.

Misra D, Fielding RA, Felson DT, et al; MOST study. Risk of knee osteoarthritis with obesity, sarcopenic obesity, and sarcopenia. Arthritis Rheumatol. 2018.

Reference : https://onlinelibrary.wiley.com/doi/abs/10.1002/art.40692

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TODAY'S MUST WATCH

Vitamin D supplements may not prevent type 2 diabetes

- A large-scale study called D2d — which the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) funded — has examined whether or not vitamin D supplementation can prevent type 2 diabetes. The study also shed light on the benefits and side effects of this vitamin.
- A diverse group of more than 2,000 adults from 22 sites participated in the study."Observational studies have reported an association between low levels of vitamin D and increased risk for type 2 diabetes. However, whether vitamin D supplementation may help prevent or delay type 2 diabetes was not known" The researchers measured the participants' vitamin D levels at the beginning of the study and found that around 80% of them had sufficient levels of vitamin D based on the recommended intake. Then, the scientists divided them into groups that took either 4,000 IU of vitamin D or a placebo pill daily.
- The scientists screened the participants every 3–6 months for an average of about 2 years. At the end of the analysis, they found that 293 out of 1,211 participants in the vitamin D group developed diabetes. Meanwhile, 323 out of 1,212 in the placebo group developed it.The difference between the two groups was not statistically significant.
- The use of dietary supplements has been increasing and vitamin D is one of the most common supplements among adults. In light of these trends, the D2d study also evaluated the safety of taking 4,000 IU of vitamin D daily. This is higher than the recommended dose. Although previous studies had revealed side effects and warned against high doses of vitamin D, the results of the D2d study showed no difference in the risk of high blood calcium levels and kidney stones between the vitamin D and placebo groups.

Reference: https://www.nejm.org/doi/full/10.1056/NEJMoa1900906

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- "We were quite surprised to find cellular structures that are essentially as old as the organism they reside in," says Salk Vice President, Chief Science Officer Martin Hetzer, senior author and professor. "This suggests even greater cellular complexity than we previously imagined and has intriguing implications for how we think about the aging of organs, such as the brain, heart and pancreas."
- Most neurons in the brain do not divide during adulthood and thus experience a long lifespan and age-related decline. Yet, largely due to technical limitations, the lifespan of cells outside of the brain was difficult to determine.
- "Biologists have asked -- how old are cells in an organism? There is this general idea that neurons are old, while other cells in the body are relatively young and regenerate throughout the organism's lifetime," says Rafael Arrojo e Drigo, first author and Salk staff scientist. "We set out to see if it was possible that certain organs also have cells that were as long-lived as neurons in the brain."
- Since the researchers knew that most neurons are not replaced during the lifespan, they used them as an "age baseline" to compare other non-dividing cells. The team combined electron isotope labeling with a hybrid imaging method (MIMS-EM) to visualize and quantify cell and protein age and turnover in the brain, pancreas and liver in young and old rodent models.
- To validate their method, the scientists first determined the age of the neurons, and found that -- as suspected -- they were as old as the organism. Yet, surprisingly, the cells that line blood vessels, called endothelial cells, were also as old as neurons. This means that some non-neuronal cells do not replicate or replace themselves throughout the lifespan.
- The pancreas, an organ responsible for maintaining blood sugar levels and secreting digestive enzymes, also showed cells of varying ages. A small portion of the pancreas, known as the islets of Langerhans, appeared to the researchers as a puzzle of interconnected young and old cells. Some beta cells, which release insulin, replicated throughout the lifetime and were relatively young, while some did not divide and were long-lived, similar to neurons. Yet another type of cell, called delta cells, did not divide at all. The pancreas was a striking example of age mosaicism, i.e., a population of identical cells that are distinguished by their lifespans.
- Prior studies have suggested that the liver has the capacity to regenerate during adulthood, so the researchers selected this organ expecting to observe relatively young liver cells. To their surprise, the vast majority of liver cells in healthy adult mice were found to be as old as the animal, while cells that line blood vessels, and stellate-like cells, another liver cell type, were much shorter lived. Thus, unexpectedly, the liver also demonstrated age mosaicism, which points to potential new paths of regenerative research for this organ.
- On a molecular scale, a selection of the observed long-lived cells contained protein complexes displaying age mosaicism. For example, the primary cilia (hair-like appendages on the outside of cells) of beta cells in the pancreas and neurons contained protein regions of vastly different lifespans. In stark contrast, the cells in the liver contained no long-lived proteins at all.
- "Thanks to new visualizing technologies we are able to pinpoint the age of cells and their supramolecular complexes more accurately than ever before. This opens new doors for studying all cells, tissues and organs in normal and in disease states," says Mark Ellisman, Distinguished Professor of Neurosciences at UC San Diego's School of Medicine and co-leader of the study with Hetzer. His laboratory, the

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National Center for Microscopy and Imaging Research, developed and provided the new tissue imaging methods for correlated multi-scale and multi-modal microscopy. These methods provided the key new and enabling technologies that allowed this study to be carried out.

- "Determining the age of cells and subcellular structures in adult organisms will provide new insights into cell maintenance and repair mechanisms and the impact of cumulative changes during adulthood on health and development of disease," adds Hetzer. "The ultimate goal is to utilize these mechanisms to prevent or delay age-related decline of organs with limited cell renewal."
- Next, the authors plan to decipher the difference in lifespans for nucleic acids and lipids. They also want to understand how age mosaicism relates to health and diseases such as type 2 diabetes.

CLINICAL CONNECTION

- The vitamin D metabolite calcitriol and its analog calcipotriol can block one of the mechanisms through which cancer cells gain resistance to chemotherapy drugs—and can selectively kill those drug-resistant cells, according to Assistant Professor SurtajHussainIram of the South Dakota State University Department of Chemistry and Biochemistry.
- His research focuses on drug transporter proteins, which are the key determinants of drug absorption, distribution and excretion from the body. Overexpression of drug transporter proteins is the most frequent mechanism through which cancer cells gain resistance.
- "Several epidemiologic and preclinical studies show the positive effect of vitamin D in reducing cancer risk and progression, but we are the first to discover its interaction with drug transporter protein and its ability to selectively kill drug-resistant cancer cells," Iram said.
- Furthermore, most drug discovery projects focus on killing cancer cells but eventually they gain resistance to chemotherapy drugs, he explained. "The vitamin D metabolite and its analog cannot kill the naive cancer cells, but when those cells develop resistance, calcitriol and calcipotriol can kill them."
- The study results were published in Drug Metabolism and Disposition, a journal of the American Society of Pharmacology and Experimental Therapeutics. "The paper was picked as the best of the issue and was featured on the cover," Iram said. "This is an extraordinary experience for an assistant professor. We are getting the SDSU name out there."
- Postdoctoral researcher Kee W. Tan and doctoral students BremansuOsa-Andrews and Angelina Sampson also worked on the study.
- "Collateral sensitivity is the idea behind the discovery of drugs that can selectively kill MRP1-overexpressing multidrug resistant cancer cells," Iram explained. "Gaining strength in one area usually creates weakness in another area—everything in nature comes at a price. Our approach is to target the Achilles' heel of drug-resistant cancer cells through exploiting the fitness cost of resistance."
- The project was supported by South Dakota Board of Regents, South Dakota's National Science Fundation Experimental Program to Stimulate Competitive Research (EPSCoR) Program, the SDSU Research and Scholarship Support Fund, the SDSU Scholarly Excellence Fund and Iram's laboratory startup funding.

Vitamin D metabolite helps stop drug-resistant cancer

- Multidrug resistant protein 1, known as MRP1, is a protein on the cell surface that serves as a gatekeeper, Iram explained. "Any drug needs to go past these gatekeepers." MRP1 protects the cell by pumping out harmful molecules to prevent toxin buildup in organs, including lungs, kidneys and the gastrointestinal tract.
- However, overexpression of MRP1 causes the protein to pump out chemotherapy drugs, thereby protecting cancer cells and making them resistant to multiple therapeutic drugs. MRP1 overexpression has been associated with multidrug resistance in lung, breast and prostate cancer.
- In addition to anticancer agents, MRP1 can reduce the efficacy of a wide variety of drugs commonly used for various metabolic diseases and neurological disorders, as well as anti-virals, antibiotics, antidepressants, anti-inflammatory and anti-HIV drugs, so this discovery has implications for a wide range of diseases, Iram explained. "If we can get a better handle on these transporters, we can improve drug efficacy. Patients can take less medication yet get the same effect because the drugs are not being pumped out so much." The lower dosage will then reduce drug side effects.
- "We can make drugs which are now being used successfully even better," said Iram, who does research through South Dakota's Biosystems Networks and Translational Research Center (BioSNTR). He is applying for NIH funding to continue this work.
- "This knowledge opens a new doorway to identify what pathway vitamin D is hitting and expose more targets, new avenues of research to selectively kill multidrug-resistant cancer cells," Iram said. "Now we must go back to understand exactly how this molecule kills these cells. We want to understand those mechanisms so we can find different ways to kill these cells and then find an agent which is very potent."
- Furthermore, MRP1 is part of a larger family of proteins called ABC transporters that move things around in animals and plants, Iram noted. "Plants have the most." In future, Iram plans to apply the lessons learned from human ABC transporters to food products and precision agriculture.

STAFF PUBLICATIONS

1. B.Rama Rao, V.Venkata Rao, B. S. Venkateswarlu. RP- HPLC Method for Simultaneous Estimation of Dapagliflozin and Saxagliptin in Bulk Samples. Journal of Pharmaceutical Sciences and Research. Vol. 11(1), 2019, 254-257. IISN: 0975-1459.
2. Vijetha Pendyala, Vidyadhara Suryadevara, Dileepkumar Tokala, Nagasucharitha Nelluri. Formulation and evaluation of a polyherbal ointment for treatment of acne. Asian Journal of Pharmacy and Pharmacology, 2019; 5(1):143-148, ISSN: 2455-2674.
3. R. L. C. Sasidhar, Sreelakshmi .M, and Raviteja .B. Simultaneous Estimation of Ribociclib and Palbociclib in Bulk Samples by Reverse Phase High Performance Liquid Chromatography. International Journal of Pharmacy and Biological Sciences, 2019, 9 (2): 413-421, ISSN: 2321-3272.
4. Viswanadh Kunam, Vidyadhara Suryadevara, Devala Rao Garikapati, Venkata Basaveswara Rao Mandava, Siva Prasad Sunkara. Solubility and Dissolution Rate Enhancement of Ezetimibe by Solid Dispersion and Pelletization Techniques. Asian J Pharm Clin Res, Vol 12, Issue 3, 2019, 407-413.

AP Akademi of Sciences Lecture on Nano Composites as recyclable catalysts for Organic Synthesis and Water Treatment (04-01-2019)

Madras Medical College Quiz- Preliminary round (24-01-2019)

Sankranti Sambaraalu (10-01-2019)

70th Republic Day Celebrations (26-01-2019)

GPAT Results (07-02-2019)

Inauguration of Gas Chromatography Instrument (08-02-2019)

Overall Winners Second at KVSR Scops Allanza (09-02-2019)

Granules Omnichem Industrial Visit (13-02-2019)

Vizag and Araku tour (14th & 15 Feb 2019)

Students of CHIPS at 10th IPA Students Congress at Rajamundry (16th & 17th Feb, 2019)

Mr. J. Subba Rao and Mr. Ch. Aruna Kumar, faculty of CHIPS awarded their Ph.Ds

Medical Camp at Vankayalapadu (03-03-2019)

Student selected in Laurus Placement Drive (06-03-2019)

Women's day 2019 (08-03-2019)

First and Second Prizes in Model Presentation at Sustainable Energy resources, Materials and Technologies workshop, RVR & JC College of Engineering (13-03-2019)

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