

LA RIDUZIONE DELLA FORZA MUSCOLARE PUO' AVERE VALORE PREDITTIVO PER IMA E STROKE: LO STUDIO PURE

Deborah Brauser - May 14, 2015

HAMILTON, ON — Lack of muscle strength may point to an increased risk of a variety of detrimental outcomes (including CV- and non-CV-related death) in adults across the globe, suggest new findings from the Prospective Urban-Rural Epidemiology (PURE) study¹¹.

The current analysis of almost 140,000 adults from 17 countries showed highly significant inverse associations between grip strength and all-cause, CV, and non-CV mortality, as well as MI and stroke. In addition, grip strength was a significantly stronger predictor of all-cause mortality than was systolic blood pressure.

"We were surprised by the strength of the relationships found. Even when we took into account people's socioeconomic status, other health conditions, and level of education, we still found that the association between muscle strength and these various outcomes held," lead author Dr Darryl P Leong (McMaster University, Hamilton, ON), told heartwire from Medscape.

He added that grip strength could easily be measured in the office as a "risk-stratifying test"—especially in patients who have comorbidities. "Perhaps this test could identify patients who are particularly vulnerable to contracting illness of various sorts," said Leong.

The results were published online May 13, 2015 in the *Lancet*.

Tackling a Wider Patient Population

Leong noted that although past studies have shown an association between hand-grip strength and risk for death and CV disease, they have been mostly limited to high-income countries and/or with mostly white patient populations. "We felt these were important questions to ask in different people, because it's an inexpensive test and likely to be more useful in underresourced settings."

Between January 2003 and December 2009, the population-based PURE study enrolled 142,861 participants between the ages of 35 and 70 years from the following countries: Canada, Sweden, and United Arab Emirates (high income); Argentina, Brazil, Chile, Malaysia, Poland, South Africa, Turkey, China, Colombia, and Iran (middle income); and Bangladesh, India, Pakistan, and Zimbabwe (low income). The US was not included.

Demographic information was collected at baseline, as well as BP levels, body-mass index (BMI), and answers to the International Physical Activity Questionnaire (IPAQ) and food frequency questionnaires. The current analysis examined a cohort of 139,691 PURE participants who also had grip-strength measurements from a Jamar dynamometer.

At baseline, low grip strength was significantly linked to having CAD, heart failure, stroke, hypertension, or chronic obstructive pulmonary disease (COPD). A total of 2.4% of the cohort died within a median follow-up of 4 years. Of these, cause of death was known for 79%.

Significant associations were found at follow-up between weak grip strength and all-cause mortality (hazard ratio [HR] for every 5-kg decrease 1.16, $P < 0.0001$); CV and non-CV mortality (HR 1.17 for both), and stroke (HR 1.09; all $P < 0.0001$); as well as MI (HR 1.07, $P = 0.002$). There was no significant association with incident diabetes.

These associations were similar across all countries included in the study. However, only the high-income countries also had a significant association between grip strength and cancer ($P < 0.0001$).

Links between weak grip strength and all-cause and CV-related mortality remained significant for both sexes and across all ages.

Post hoc analysis showed that grip strength was a better predictor of death (HR 1.37, 95% CI 1.28–1.47) than systolic blood pressure (HR 1.15, 95% CI 1.10–1.21; both $P < 0.0001$), but the latter was a better predictor of incident CV-related disease (HR 1.39 vs 1.21, respectively; both $P < 0.0001$).

Both measures had an HR of 1.45 for predicting CV-related death ($P < 0.0001$) and were significantly better predictors of this outcome, all-cause death, and incident CV-related disease vs measurements of physical-activity levels.

"In people of diverse economic and sociocultural backgrounds, grip strength is a strong predictor of cardiovascular mortality and a moderately strong predictor of incident cardiovascular disease," write the investigators.

Leong noted that exercise of any type should be recommended to all patients as part of a daily routine. "But our study strengthens the case that strength-building exercises and resistance training should be part of this and not just cardiorespiratory exercise."

Marker of Underlying Aging Process?

DrAvanAihie Sayer (University of Southampton, UK) and Thomas BL Kirkwood (Newcastle University, UK) write in an accompanying editorial that although grip strength has been shown before to be "a simple but powerful predictor of future disability, morbidity, and mortality," important questions have remained, especially if it's generalizable among a widely differing group of people^[2].

"Poor muscle strength has been proposed to directly affect mortality through its association with increased disability. However, the findings from PURE suggest that associations with cardiovascular disease and its risk factors might be an additional pathway," they write.

Although the editorialists praise "the international breadth and methodological rigor" of the current analysis, they cite that its depth was lacking in some areas, including "the limitations of observational epidemiology" and that some of the associations deserve further investigation. They also note that the link between grip strength and cancer may have come about by chance.

Still, "loss of grip strength . . . might be a particularly good marker of underlying aging processes, perhaps because of the rarity of muscle-specific diseases contributing to change in muscle function," they write, adding that "linkage of epidemiological findings to new approaches in muscle biology could yield informative insights into the nature of human aging."

UN INTERESSANTE CASO CLINICO DI INTERAZIONE TRA FARMACI IN UNA DONNA ANZIANA

An 83-year-old woman with type 2 diabetes mellitus is brought in for evaluation for altered mental status. She has been feeling poorly for the past 2 weeks, and has been undergoing treatment for presumed *Helicobacter pylori* gastritis and a urinary tract infection. Her current medications are bismuth subsalicylate, glyburide, sitagliptin, omeprazole, amoxicillin, trimethoprim/sulfamethoxazole (TMP/SMX), and lisinopril.

Laboratory test results include the following:

- Sodium: 132 mEq/mL
- Potassium: 5 mEq/mL
- Chloride: 100 mEq/mL
- Glucose: 30 mg/dL

What is the most probable cause of her hypoglycemia?

- Amoxicillin-glyburide interaction
- Amoxicillin-sitagliptin interaction
- Omeprazole-glyburide interaction
- TMP/SMX-glyburide interaction

Antibiotic Drug Effects and Interactions

This is a case of trimethoprim-induced hypoglycemia. The patient in this case also has a slightly elevated serum potassium level, which may also be from the TMP/SMX.

The first question is: Why is this woman on glyburide? Glyburide has a longer half-life and carries a higher risk for sustained hypoglycemia than other sulfonylureas. While the information provided in this case does not allow a determination of renal function, glipizide is preferred in patients with

poor renal function. Many clinicians avoid use of sulfonylureas in the elderly because of the hypoglycemia risk

A recent study^[1] assessed the prevalence of emergency room visits due to hypoglycemia among older persons with diabetes who were coadministered TMP/SMX and sulfonylureas. The study population included approximately 35,000 Medicare beneficiaries who were taking glyburide or glipizide in 2008. Prescription of TMP/SMX was common, occurring in almost 17% of patients taking glyburide or glipizide in 2008-2010, varying from 4.0% to 35.9% across regions. Sulfonylurea users prescribed co-trimoxazole had a significantly higher risk for emergency room visits for hypoglycemia (odds ratio, 3.89; 95% confidence interval, 2.29-6.60 for glipizide; and odds ratio, 3.78; 95% confidence interval, 1.81-7.90 for glyburide with co-trimoxazole). When patients taking TMP/SMX were compared with those who were taking amoxicillin, the researchers found an almost fourfold increased risk for hypoglycemia with use of TMP/SMX.

Why does this happen? Sulfamethoxazole can inhibit the CYP2C9 subunit of P450 system that is important for metabolism of many drugs, including glyburide.^[2]

Antibiotics that inhibit CYP2C9 include:

- Clarithromycin;
- Erythromycin;
- Fluconazole;
- Itraconazole
- Ketoconazole;
- Metronidazole; and
- Sulfamethoxazole.

Clarithromycin is at the top of the list, and its use significantly increases the risk for drug interactions. Erythromycin, while also a potent CYP2CP inhibitor, is not commonly used anymore. The azole antifungals, metronidazole, and sulfamethoxazole also are potent inhibitors of CYP2C9. These drugs can also cause drug-drug interactions with statins.

The take-home message: Be aware of the sulfonylurea drug interactions that can occur. Hypoglycemia as a drug interaction side effect occurs more commonly in the elderly, and our population is aging.

FARMACI PER LA DEMENZA ASSOCIATI A SEVERA PERDITA DI PESO

Fran Lowry

August 17, 2015

Cholinesterase inhibitors (donepezil [multiple brands], galantamine [*Razadyne*, Janssen Pharmaceuticals, Inc], rivastigmine [*Exelon*, Novartis Pharmaceuticals Corporation]) are commonly used to treat patients with dementia, although their efficacy in improving cognitive function is slight.

Now, a study of more than 6000 patients aged 65 years and older from the Veterans Affairs health system shows their use is associated with significant, potentially serious, weight loss.

The finding should alert clinicians to be wary about using these drugs in older adults, says MeeraSheffrin, MD, from the University of California, San Francisco, School of Medicine and the San Francisco Veterans Affairs Medical Center.

"I'd like clinicians to consider this as a real risk and think about potentially dangerous weight loss when they prescribe these medications," DrSheffrin told *Medscape Medical News*.

"This is very relevant to patient care because unintentional weight loss in older adults is associated with many adverse outcomes, including increased rates of institutionalization and mortality, a decline in functional status, and poorer quality of life," she said.

The study was published online August 3 in *Journal of the American Geriatrics Society*.

Questionable Benefit

DrSheffrin added that although cholinesterase inhibitors do have modest benefits for some patients with dementia, most patients do not derive any benefit at all from these drugs.

"Often they get a trial of this medication to see if it might help, and never stop. I don't think clinicians adequately consider or discuss with family members the possible harms. They just look for something to help treat these patients with dementia, and there are not a lot of good treatments. They may explain about the gastrointestinal side effects, such as the nausea, vomiting, and diarrhea that can occur with the cholinesterase inhibitors. But these tend to go away after a month or so. However, **this serious weight loss is one side effect that may not go away,**" DrSheffrin said.

Clinicians should consider not only whether a patient may be helped by a cholinesterase inhibitor but also whether that patient may be harmed.

"These are probably not good drugs to give to someone who is already starting to show some weight loss or muscle wasting," she said.

From her clinical experience, DrSheffrin noticed that serious weight loss may be a side effect of the cholinesterase inhibitors. However, to her knowledge, there have been no studies attempting to evaluate their effects on weight in real-world populations.

"In randomized, controlled trials, you get mostly healthy patients. We decided to do this study in a VA health system using just ordinary clinic patients across the nation. We had a lot of patients, and you can pick up side effects that may not be as common, and you can also get patients who are not the really healthy, robust patients included in clinical trials to see if the weight loss was a real side effect," she said.

In this retrospective cohort study, DrSheffrin and her group used national Veterans Affairs data from 2007 to 2010 to compare weight loss in individuals with dementia who were newly prescribed cholinesterase inhibitors with weight loss of patients who were newly prescribed long-term regimens of other medications. The primary outcome was time to 10-pound weight loss during a 12-month period.

"A 10-pound weight loss was chosen as the primary outcome because it represents a degree of weight loss that a clinician would notice and that might prompt further action in considering causes and examination of weight loss," DrSheffrin noted.

Of 6504 individuals that met their study's inclusion criteria, 1188 were started on cholinesterase inhibitors. These were matched with 2189 individuals who were started on other medications.

The patients who were prescribed cholinesterase inhibitors were generally older, took fewer medications at baseline, and had a lower baseline weight.

The most commonly prescribed cholinesterase inhibitor was donepezil (58%, 694 patients), followed by galantamine (41%, 482 patients) and rivastigmine (1%, 12 patients).

Of patients who started other long-term medication regimens, the most common prescriptions were for amlodipine, simvastatin, omeprazole, hydrochlorothiazide, and docusate.

The researchers found that at 12 months, 78% of dementia patients were still receiving the cholinesterase inhibitors, compared with 66% of patients who were receiving other medications.

Patients receiving cholinesterase inhibitors had a higher risk for weight loss than matched control patients (hazard ratio [HR], 1.23; 95% confidence interval [CI], 1.07 - 1.41).

About 29.3% of patients receiving cholinesterase inhibitors experienced weight loss of 10 pounds or more, compared with 22.8% of nonusers.

"Dementia patients do lose weight over time. It's part of the natural course of the disease. But 29% of the cholinesterase group lost weight. This corresponds to a number needed to harm of 21, so if you treated 21 patients with dementia with these drugs over a year, one of them would have this serious weight loss, not just 1 or 2 pounds, but 10 pounds.

"I may not care so much if my patient loses 1 or 2 pounds if their memory is better, but if their memory is a little bit better and they've lost 10 pounds, then I start to worry," DrSheffrin said.

"There are some patients who might benefit from these drugs, and certain doctors and neurologists use them more often," she added. "They may see different patients than we see, but my sense is the same. These drugs don't do very much, people prescribe them thinking they won't hurt, but they don't really help very much, and they might, indeed, do harm."

Cause for Concern

Commenting on the findings for *Medscape Medical News*, Donovan T. Maust, MD, University of Michigan Health System, Ann Arbor, said: "**Unintended weight loss is common for many patients with dementia, so this work by DrSheffrin and her colleagues addressing this very widely used family of medications is cause for concern.**"

"The potential for a 10-pound weight loss in light of the very modest benefits of cholinesterase inhibitors should give pause to providers and families," DrMaust said.

Steve Koh, MD, MPH, a geriatric psychiatrist from the University of California, San Diego, and chair of the American Psychiatric Association's Scientific Program Committee, said: "The study by Sheffrin et al is an important addition to our ability to best care for our aging population with neurocognitive disorders like Alzheimer's disease."

The gastrointestinal side effects of cholinesterase inhibitors have been known for some time, DrKoh said.

"This study shows us that the medications can lead to unwanted weight loss, which can then lead to increased morbidity for our patients.As a geriatric psychiatrist, this strengthens my opinion that consistent and routine assessment of weight for our patients is important and that any medication's potential benefit and risk need to be both considered. Further, it should, yet again, inform us that medications for mental health or cognitive issues can have other effects in the body, and as physicians, we need to be ever vigilant for our patients."

DrSheffrin, DrMaust, and DrKoh report no relevant financial relationships.

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5 SCELTE SAGGE DA FARE IN GERIATRIA

L'iniziativa "Choosing Wisely", lanciata nel 2012 da *American Board of Internal Medicine* (ABIM) ha l'obiettivo di ridurre l'uso eccessivo di test e procedure a favore di scelte intelligenti ed efficaci di cura. Da allora, almeno 30 società professionali hanno aderito all'iniziativa e pubblicato gli elenchi delle pratiche comuni che dovrebbero essere messe in discussione sia da operatori sanitari sia da pazienti.

A Febbraio 2014, l'*American Geriatrics Society* ha esteso la sua prima lista e indicato 10 pratiche da mettere in discussione.

Vediamo qui le prime 5.

1. No, all'alimentazione tramite tubi percutanei nei pazienti con demenza avanzata: scegliete l'alimentazione assistita per os
2. No, agli antipsicotici di prima scelta per la terapia dei disturbi di comportamento e sintomi psicologici di demenza
3. No, a un obiettivo terapeutico di Hbglicosilata $A_{1c} < 7.5\%$ nella maggior parte dei pazienti con più di 65 anni. Il controllo moderato è meglio
4. No, all'uso di benzodiazepine o altri sedativi ipnotici negli anziani come prima scelta per la gestione dell'insonnia, agitazione o delirio
5. No, alla terapia antibiotica in presenza di batteri nelle urine in assenza di specifici sintomi urinari.

Gemma C Morabito, Dirigente medico UOC Medicina d'Urgenza e Pronto Soccorso, AO Sant'Andrea, Roma.

1) Choosing Wisely: An initiative of the ABIM Foundation. www.choosingwisely.org;

2) http://www.choosingwisely.org/wp-content/uploads/2014/02/AGS-10things-List_feb2014.pdf

GOTTA E RISCHIO DI DEMENZA

A Nationwide Population-Based Cohort Study

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Arthritis Res Ther. 2015;17(139)

Abstract and Introduction

Abstract

Introduction: Uric acid was proposed to have anti-oxidant property and possible neuroprotective effects. We examined the association between gout and dementia with population database.

Methods: The study utilized the claims data from the nationwide representative sample of Taiwan National Health Insurance Research Database (NHIRD). We ascertained patients with gout and dementia covering vascular and non-vascular (including Alzheimer's) subtypes using International Classification of Diseases Ninth Revision, Clinical Modification (ICD9-CM) codes. A control group matched on sex, age, and index date of gout patients was randomly sampled with a ratio of 1:4 from the same database for comparison.

Results: From 2002 to 2008, 28,769 gout patients who were older than 50 years old were identified, and 114,742 control patients was matched into the study. During follow-up, 7,119 patients developed dementia (1,214 with gout, and 5,905 without gout). After adjusting for age, sex, and relevant comorbidities, a Cox regression analysis showed that gout patients had a lower risk of developing non-vascular dementia (hazard ratio (HR): 0.77; 95% confidence interval (CI): 0.72 - 0.83; $p < 0.001$) and vascular dementia (HR: 0.76; 95% CI: 0.65 - 0.88; $p < 0.001$).

Conclusions: Patients with gout have a lower risk of developing dementia. This phenomenon exists for both non-vascular and vascular types of dementia.

Per articolo in extenso vedi Medscape: [Gout and the Risk of Dementia](#)

ArthritisResearch&Therapy, 2015-05-28

IL DELIRIUM POSTOPERATORIO ESITA IN SCARSI OUTCOMES NEGLI ANZIANI

Settembre 9, 2015

BOSTON -- September 9, 2015 -- Delirium is a significant and independent contributing factor to poor postsurgical outcomes in older adults, according to a study published online by JAMA Surgery.

The findings suggest that the combination of major postoperative complications and delirium demonstrate a strong combined effect on adverse outcomes in older adults undergoing major surgery.

“Delirium, which is characterised by a sudden onset of confusion, is a concern for older adults having surgery or who are hospitalised,” said Sharon K. Inouye, Aging Brain Center at the Institute for Aging Research (IFAR) at Hebrew SeniorLife, and Harvard Medical School, Boston, Massachusetts. “Our study explores the association of postoperative complications and delirium, with adverse results following surgery.”

The prospective study included 566 patients aged 70 years and older without dementia or delirium at the time of elective major orthopaedic, vascular, or abdominal surgeries. Participants had a minimum hospital stay of 3 days. Major postoperative complications were defined as life altering or threatening, and based on the Accordion Severity (grade ≥ 2). Daily measures of delirium were determined using the Confusion Assessment Method and validated chart-review.

A major complication occurred in 8% of study subjects and 24% of participants developed delirium. Major postoperative complications alone contributed to prolonged length of hospital stay. Delirium alone was found to significantly increase all adverse outcomes following surgery, including prolonged hospital stay, institutional discharge, and 30-day readmission.

Furthermore, the group who experience both major complications following surgery and delirium had the highest rates of all adverse outcomes. While, delirium alone exerted the highest risk of adverse outcomes at the population level compared with other major surgical complications.

“Delirium is highly prevalent among older adults who undergo surgery or are hospitalised and should be considered a leading postoperative complication leading to adverse outcomes,” said Lauren Gleason, MD, Brigham and Women's Hospital, Boston, Massachusetts. “Clinicians should be aware of the negative impact of delirium and look for ways to mitigate its effect on older patients in their care through use of preventative strategies, proactive geriatric consultation, and co-management services.”

TERAPIA FARMACOLOGICA E MORTALITÀ NELLA FIBRILLAZIONE ATRIALE. UNO STUDIO DI COORTE CON PAZIENTI ULTRASETTANTACINQUENNI IN SVEZIA

Age Ageing. 2015;44(2):232-238.

La fibrillazione atriale (FA) è l'aritmia cardiaca più frequente ed è trattata con diverse classi di farmaci cardiovascolari. I farmaci cardiovascolari possono avere un diverso impatto sulla sopravvivenza nei pazienti anziani con fibrillazione atriale in un contesto di assistenza sanitaria di base. Una coorte di 3.020 uomini e 3.749 donne di età ≥ 75 e con diagnosi di FA è stata selezionata da 75 centri di assistenza primaria in Svezia. Nel complesso, la mortalità è stata del 18,2%. Il risultato principale di questo studio è stata l'aumentata sopravvivenza associata con la terapia anticoagulante vs nessun trattamento e vs antiplastrinici di 1,95 anni (95% intervallo di confidenza (IC) 1,43-2,48) e 0,78 anni (95% CI 0,38-1,18), rispettivamente. Un' aumentata sopravvivenza si è vista anche nei pazienti che assumevano tiazidici e calcio-antagonisti di 0,81 anni (95% CI 0,43-1,18) e 0,83 anni (95% CI 0,47-1,18), rispettivamente. Non c'erano differenze tra uomini e donne. I risultati di questo studio di coorte suggeriscono che **anticoagulanti, tiazidici e calcio-antagonisti possono portare ad una maggiore sopravvivenza nei pazienti anziani con fibrillazione atriale.**