



Defense Health Agency

Defense and Veterans Brain Injury Center “Clinical Updates in Brain Injury Science Today [CUBIST]” Podcast

“Association Between Statin Use and Risk of Dementia After a Concussion”

TRT: 10m 29s

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Defense and Veterans Brain Injury Center “Clinical Updates in Brain Injury Science Today [CUBIST]” Podcast

Episode 206: Statin use in dementia patients

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Betsy Myhre: The views, opinions, and findings contained in this podcast are those of the host and subject matter experts. They should not be construed as official Department of Defense positions, policies, or decisions unless designated by other official documentation.

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Myhre: Hi! Welcome to Clinical Updates in Brain Injury Science Today, or CUBIST, a podcast for health care providers about current research on traumatic brain injury, also known as TBI.

This program is produced by the Defense and Veterans Brain Injury Center, otherwise known as DVBIC. I’m your host today, Betsy Myhre. I’m a nurse practitioner in the Clinical Practice and Clinical Recommendations division here at DVBIC.

In today’s episode, I’ll be talking with Dr. Donald Marion. Dr. Marion is a neurosurgeon at DVBIC. Don and I will discuss a study entitled: Association between Statin Use and Risk of Dementia after a Concussion, by Redelmeier and all and published in JAMA Neurology, May 20, 2019.

Myhre: Hi, Don.

Don Marion: Hi, Betsy, how are you today?

Myhre: Great. What were the key findings of this study?

Marion: This was a very large dual-cohort study was conducted using a provincial health insurance database in Ontario, Canada, of subjects enrolled from 1993 to 2016 to test whether statin therapy is associated with an increased or decreased risk of dementia after a concussion. The study identified 28,815 patients diagnosed as having a concussion (median age, 76 years; 61.3% female), of whom 7,058 (24.5%) received a statin. A total of 4,727 patients subsequently developed dementia over a mean follow-up of 3.9 years. Patients who received a statin had a 13% reduced risk of dementia compared with patients who did not receive a statin (relative risk, 0.87; 95% CI, 0.81-0.93; $P < .001$). The decreased risk of dementia associated with statin use applied to diverse patient groups, remained independent of other

cardiovascular medication use, intensified over time, was distinct from the risk of subsequent depression, and was not observed in patients after an ankle sprain.

Myhre: Don, why did the researchers look at statins?

Marion: Statins are the nickname for a class of medications that are hydroxymethylglutaryl coenzyme A reductase inhibitors, and are typically prescribed to treat hyperlipidemia (high serum cholesterol levels). Laboratory investigations have found that statins can effectively treat edema, oxidative stress, amyloid deposition, and inflammation, all problems that have been associated with TBI, and with dementia. By decreasing serum cholesterol levels it also is postulated that statins help limit plaque formation in the lumen of arteries, particularly the carotid arteries, thereby preserving or improving cerebral blood flow. Importantly, however, prior clinical trials of statins for the treatment of established dementia do not find benefit.

Myhre: Have there been other clinical trials of statins for the treatment of concussion?

Marion: Yes, Betsy, that's a good question. There have been at least four other clinical trials, as well as a Cochrane Review published by McGuinness in 2016. Small sample sizes, selective enrollment, and brief follow-ups have severely limited those studies, and none found a significant benefit from treatment with statins.

Myhre: There are a number of different statin medications on the market-which one was used in this study?

Marion: Atorvastatin, cerivastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin and simvastatin were all used but of the 7,058 patients prescribed statins, nearly 50% were treated with atorvastatin (Lipitor), and 35% received either rosuvastatin (Crestor) or simvastatin (Zocor). There was no indication in the paper about reasons for the use of a specific statin.

Myhre: Why did some people receive statin medications and others did not? Specifically, is it possible that those who benefitted from statin therapy were also more socioeconomically advantaged and could afford better health care?

Marion: That's a great question Betsy. During the study universal Canadian health insurance covered outpatient medical care for all individuals, with no out-of-pocket costs to patients. In addition, the Ontario Drug Benefit Program covered prescription medications for all patients 65 and older. Thus, no one who wanted to receive care was excluded because they couldn't afford it.

Myhre: How was the study done?

Marion: Sure, patients who were 66 and older, diagnosed as having had a concussion in the past by ICD-9 code 850, were identified in the Ontario Health Insurance Plan. Those who were admitted to the hospital within two days of a concussion, or who died within 90 days, were excluded. The primary analysis compared patients who had received a statin prescription within 90 days after a concussion with patients who had not. For 83% of those prescribed a statin it was a continuation of pre-concussion treatment. Computerized linkage to health care records and a demographic registry provided information about age, sex, and other baseline characteristics. However, there was no information about smoking status, daily exercise, genetic factors, family history or other risk factors for dementia. The primary outcome measure was dementia according to ICD-9 codes 290, 331 and 797 as recorded in the Ontario Health Insurance Plan database. All survivors had a minimum follow up of three years. To specifically test the effect of concussion on the risk for dementia, the study was replicated with the cohorts having an ankle sprain rather than a concussion.

Myhre: What were the limitations on this study?

Marion: There was no information about confounding risk factors for dementia, such as smoking, family history, and daily exercise. There also was no analysis of the impact of dosing or duration of statin treatment. Follow-up duration was five years or less yet it can take decades for dementia to develop.

Myhre: Don, in my experience, a lot of patients with dementia have falls. And so that would increase the risk of having a concussion. And so how did the researchers ensure that the patients didn't already have dementia?

Marion: Great question, Betsy. As matter of fact, I've neglected to mention that that was another exclusion criteria, specifically patients with a history of dementia or delirium, and the five years prior to the study were excluded. So that was removed as a confounding variable.

Myhre: Great, thanks. What are the key take-aways from this study?

Marion: In a very large captive cohort (n=28,815) of older patients with a history of concussion, treatment with statins was associated with a 13% reduction in the risk for dementia compared with those not treated with statins. Although the incidence of some of the other known risk factors for dementia were not available, the design of this study and very large number of patients are compelling regarding the potential benefit of statin therapy.

Myhre: Thank you Don for your insights. That's all we have time for today. We hope you enjoyed this quick literature update.

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"CUBIST" is produced and edited by Vincent White and was hosted today by me, Betsy Myhre. It is a product of the Defense and Veteran's Brain Injury Center, led by Division Chief CAPT Scott Pyne, Medical Corps, U.S. Navy.

Thank you for listening to this episode. Next time, we will discuss TBI research getting attention in the mainstream press.

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