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Commentary: Statins for secondary prevention after coronary artery bypass grafting: Pleiotropic effects and dementia risk

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In this issue, Pan and colleagues¹ present a study using population-based data from the SWEDEHEART registry to report on the impact of statins on major adverse events after coronary artery bypass grafting (CABG). Their results demonstrate decisively that the use of statins is associated with a decreased risk of all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, the need for new revascularization or angiography, and, interestingly, dementia. These effects were observed in both men and women, and in those younger than and older than 75 years of age, and were not dependent on whether patients were taking high-, intermediate- or low-dose statins.

The effect of statins is fundamentally based on their ability to inhibit the enzyme 3-hydroxy-3-methyl-glutaryl-coenzyme A, reducing endogenous plasma cholesterol synthesis in the liver.² What we commonly forget is that these drugs have many other pleiotropic effects; statins not only directly affect lipid metabolism but also complex intracellular signaling pathways. It is well-known they increase endothelial nitric oxide synthetase production, reduce multiple inflammatory processes, stabilize atherosclerotic plaques, and restore platelet activity and anticoagulation processes.^{2,3} Because of these effects, it is not surprising that, when tolerated, these

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Statins are essential secondary prevention after CABG, but new research suggests we should investigate potential pleiotropic effects and their impact on the risk of dementia.

medications will exert a very significant effect on major adverse cardiovascular events and survival for patients' cardiovascular disease, including those who have undergone CABG. In this case as in so many others, understanding the pharmacologic mechanisms using the tools of basic and translational science help inform our interpretations of clinical and registry database studies, and vice versa.

Perhaps one of the most novel findings of the paper by Pang and colleagues¹ was the finding of a negative association between statin use and dementia. This finding is interesting but must be interpreted with caution in the setting of this study and its methodology. Published studies have correlated cardiovascular health and neurocognitive impairment (dementia), and therefore it is reasonable to observe that drugs used for secondary prevention of cardiovascular events could also impact neurovascular health. However, at least one meta-analysis has failed to find significant evidence that statins reduce the risk of dementia.⁴ This is an area that is in need of additional research, including basic science studies to more clearly elucidate the potential pleiotropic mechanisms of statins, and prospective clinical trials and retrospective registry studies to more clearly describe any associations with dementia and other neurocognitive impairments.

In this instance, the results of a large study of the SWEDEHEART registry evaluating the secondary preventive

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effects of statins found an interesting association between statin use and a decreased risk of dementia, but the most relevant clinical information to be derived from this study is the tremendous benefits of statins for the secondary prevention after CABG and the need for surgeons, cardiologists, and primary care providers to ensure patients can be maintained on these essential medications to reap the long-term benefits.

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Commentary: Inattention to detail is the hallmark of mediocrity

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Coronary artery bypass graft (CABG) surgery has undergone several innovative phases over the last number of decades. These include, for example, off-pump surgery, total arterial bypass grafting and minimally invasive approaches, sophisticated surgical techniques for the anastomoses, improved myocardial protection techniques, as well as improvements in the technology of extracorporeal circulation. These advances have improved the results in terms of mortality and morbidity perceptibly.^{1,2}

However, postoperative management is just as important as the surgical techniques, especially for the long-term outcome. Several papers have been published showing the importance of postoperative pharmacologic strategies for improved long-term survival, which recommend β -blockers, renin-angiotensin-aldosterone system inhibitors, platelet inhibitors, and statins.¹⁻³ While strict postoperative medication plans are used for the majority of patients with coronary artery disease after interventional treatments, this is rarely the case after CABG.

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Results after coronary artery bypass graft surgery are affected by the surgical procedure and the secondary prevention; therefore, postoperative medication (especially statins) is fundamental.

The present study⁴ is extremely important to highlight once again the imperative necessity of postoperative medication in the long term. This very unique study, in which data are generated from 5 mandatory national registries and merged for the study (ie, Swedish Cardiac Surgery Registry, National Patient Register, National Cause of Death Register, Swedish Population Register, and Swedish Prescribed Drug Register), uses the unique identification number allocated to all Swedish residents.

In fact, the study found that ongoing statin treatment was associated with a reduced risk for all of the investigated outcome variables. Patients often fear stroke and dementia as much as death; therefore, many other factors other than mortality are of importance. Previous studies have shown that younger, but not older, patients undergoing CABG have an increased risk of dementia in comparison with an aged- and sex-matched control population.⁵ The present

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