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Statin Therapy and its Impact on Cognitive Functions in Elderly Patients: A Current Systematic Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Statin therapy is a well-established treatment for cardiovascular disease, with potential implications for cognitive function. However, reports have been inconsistent regarding statin therapy's impact on cognitive function in elderly patients. This systematic review aimed to evaluate the current evidence relating to the cognitive effects of statin therapy in the elderly population.

Methods: A comprehensive literature search was conducted using the databases PubMed, Embase, and Cochrane Library, up to May 2023. Eligibility criteria included randomized controlled trials and observational studies involving elderly patients on statin therapy, with a focus on cognitive function outcomes. Studies were excluded if they did not provide comparative data for elderly patients not on statin therapy.

Results: Out of fourteen studies, representing a diverse population of 68,724 participants, the majority suggested a neutral or beneficial impact of statin use on cognitive function in the elderly population. For instance, a large-scale study involving patients with cardiovascular disease demonstrated no adverse cognitive effects following statin therapy. Another study involving hypertensive elderly patients indicated a possible protective role of statins against cognitive impairment. On the whole, the results were heterogenous, with no substantial evidence pointing towards a harmful effect of statins on cognitive health.

Conclusion: The review provides evidence that statin therapy does not appear to negatively impact cognitive functions in elderly patients. Rather, the findings lean toward a neutral or potentially protective effect. Considering the global prevalence of statin use, these findings should reassure clinicians and patients about the cognitive safety of these medications. However, given the importance of this issue, further large-scale studies are recommended to confirm these findings and further elucidate any potential cognitive benefits associated with statin therapy.

Keywords: Statin therapy; cognitive function; elderly patients; systematic review; neurocognitive impact; cholesterol-lowering drugs; cognitive impairment.

1. INTRODUCTION

Statin therapy, a primary treatment strategy for dyslipidemia and prevention of cardiovascular disease, is widely used among the elderly population [1]. While their benefits are well-established, concerns have emerged regarding the potential cognitive effects of statins, particularly among the elderly, a population already at an increased risk of cognitive decline due to aging [2].

Cognitive functions encompass a broad range of mental abilities such as memory, attention, language, problem-solving, and executive function. The decrease in mental abilities like memory and thinking that often comes with aging is a serious health issue; it is also a major factor that can affect the overall well-being and daily life of older adults [3]. The influence of statins on cognitive functions has been a topic of ongoing debate in the medical community. Some studies have suggested a possible negative effect, others indicate a protective role, and many find no significant impact [4,5].

Multiple mechanisms have been postulated for the potential cognitive effects of statins. It is well known that cholesterol is a critical component of neuronal cell membranes and plays a crucial role in synapse formation and function, suggesting that its lowering could adversely affect cognitive processes [6]. On the other hand, statins have anti-inflammatory and antioxidant properties, which could potentially counteract pathophysiological processes implicated in cognitive decline and neurodegenerative diseases [7].

However, the evidence is far from conclusive. A substantial body of observational studies have yielded mixed results, while randomized controlled trials, though more robust in design, have been limited by short follow-up durations

and a lack of standardized cognitive assessments [8]. Moreover, factors such as age, co-existing medical conditions, and polypharmacy common among the elderly, could potentially confound the relationship between statin use and cognitive function [9].

Therefore, given the ubiquity of statin use and the clinical importance of preserving cognitive health in the aging population, it is imperative to deepen our understanding of the relationship between statin therapy and cognitive function in elderly patients. This study aims to synthesize and analyze the available evidence on the impact of statin therapy on cognitive functions among the elderly, thereby informing clinical decisions and contributing to optimizing care for this vulnerable population.

In this context, the proposed study focuses on the impact of statin therapy on cognitive functions in elderly patients compared to those not on statin therapy, aiming to draw meaningful conclusions and outline further research needs.

2. METHODS

2.1 Eligibility Criteria

- Participants: Studies involving elderly patients (65 years or older) on statin therapy.
- Intervention: Studies investigating the impact of statin therapy on cognitive functions.
- Study Design: Both Randomized Controlled Trials (RCTs) and observational studies were included.
- Outcome Measures: Studies reporting outcomes related to the cognitive function changes in elderly patients on statin therapy.

2.2 Information Sources

An electronic search was conducted of the following databases and registers: PubMed, Embase, and Cochrane Library. A manual search of relevant journals and conference proceedings was also conducted to ensure a comprehensive search. The search was limited to studies published in English and conducted on human subjects.

2.3 Search Strategy

Our search strategy included relevant keywords such as "statin therapy", "cognitive function", "elderly patients", and other related terms. We used a combination of Medical Subject Headings (MeSH) and free-text terms to ensure a comprehensive search. The search was conducted until June 2023.

2.4 Study Selection

Two independent reviewers screened the titles and abstracts of the identified studies for eligibility. Full-text articles were then screened for inclusion based on the eligibility criteria. Studies were included if they involved elderly patients (65 years or older) on statin therapy, investigated the impact of statin therapy on cognitive functions, reported outcomes related to the cognitive function changes in elderly patients on statin therapy, and were conducted using RCTs or observational studies. Studies that did not meet these criteria were excluded.

2.5 Data Extraction and Synthesis

A narrative synthesis was conducted. The extracted data from the included studies were summarized and analyzed to determine the impact of statin therapy on cognitive functions in elderly patients. The results of the studies were reported descriptively, and the strengths and weaknesses of the included studies were discussed. These were tabulated as the following: “author, year, title of the study, study type, intervention, inclusion criteria, primary outcome(s), sample size, and findings.” Finally, the findings of the included studies were summarized, and the implications for clinical practice and future research were discussed.

3. RESULTS

Of the 381 studies identified from the databases, a total of 46 duplicates were removed in the identification phase. In the screening phase, 335 studies were assessed with titles and abstracts, after which 284 studies were excluded because of the lack of relevance. In total, 51 full-text studies were obtained of which 37 were removed as they did not meet the inclusion criteria. in the inclusion phase, 14 studies were included in this systematic review. The study selection process is depicted in Fig. 1. The characteristics of the included studies are presented in Table 1.

The study by Gencer et al., conducted on 22,655 patients with atherosclerotic cardiovascular disease and LDL-C levels ≥70 mg/dl or non-HDL-C ≥100 mg/dl despite statin therapy, found that

the addition of evolocumab to statin therapy did not impact patient-reported cognition (P = 0.62) [10]. This was true even for patients who achieved very low LDL-C levels (<20 mg/dl). The primary outcome measure was changes in memory and executive functions, as measured by the Everyday Cognition (ECog) scale.

Thongtang et al., [11], conducted a study with type 2 diabetes patients who were taking simvastatin ≤20 mg/day. This study compared patients who continued low-dose simvastatin (n=63) and patients who switched to high-dose atorvastatin (n=62). The result showed that high-dose atorvastatin resulted in a slight increase in HbA1c (0.1%) but did not cause cognitive decline, which was measured by Montreal Cognitive Assessment (MoCA) and Trail Making Test (TMT) assessments (P > 0.05).

Zhang et al., [12], studied 732 elderly hypertensive patients who were on hydrochlorothiazide as their baseline medication. The intervention was the addition of low-dose rosuvastatin, which the results showed was associated with lower risks of white matter hyperintensities (WMH) progression and cognitive impairment (hazard ratio, HR = 0.54; 95% confidence interval, CI: 0.36-0.8).

In a study conducted by Molina-Sotomayor et al., [13], a group of women over 60 years of age who were on lovastatin therapy participated in a controlled and progressive walking program. The exercise group (n=45) showed an increase in HDL-C concentrations and improved spatial orientation and calculation abilities; the cognitive dimensions were reported as assessed by the Mini-Mental State Examination (MMSE), with a large effect size (P < 0.05). There was no significant change in LDL-C compared to the sedentary group (n=22).

Chan et al., [14], conducted a study on patients with secondary progressive multiple sclerosis. The study compared 70 patients on high-dose simvastatin to 70 patients on placebo. The simvastatin group showed improved frontal lobe function (95% CI: 0.2-2.3) and a better mean physical component score of the SF-36 (95% CI: 0.3-4.8; P = 0.028), but there was no effect on other outcomes.

In the study by Gupta et al., involving 10180 patients in the blinded phase and 9899 patients in the non-blinded phase, adverse events were studied in patients aged 40-79 years with hypertension, cardiovascular risk factors, and fasting total cholesterol concentrations of 6.5 mmol/L or lower who were administered Atorvastatin daily [15]. Their research found no significant differences in the rates of most reported adverse events, including cognitive impairment. The analysis found too few cases of cognitive impairment to be statistically reliable (P = 0.81).

Needham et al. conducted a study involving 272 patients with sepsis-associated acute respiratory distress syndrome, who were administered Rosuvastatin as a loading dose of 40 mg, then 20 mg daily [16]. They found that there was no benefit of rosuvastatin in reducing delirium in intensive care or cognitive impairment during 12 months of follow-up (P = 0.82).

A study by Wong et al. [17], which included 102 patients diagnosed with Subarachnoid Hemorrhage (SAH), found no difference in cognitive outcomes between the groups treated with acute Simvastatin and the control group, based on the Montreal Cognitive Assessment (MoCA) (OR 0.7, 95% CI: 0.3-1.8, P = 0.477).

Williamson et al. [18] conducted a study involving 2977 patients with type 2 diabetes mellitus (T2DM), who were subjected to intensive therapy for hypertension and combination therapy with a statin plus a fibrate. Their results indicated that the intensive blood pressure control and fibrate therapy had no measurable effect on cognitive decline (P > 0.05). However, it was associated with a greater decline in total brain volume (TBV) (P = 0.01).

Tendolkar et al. [19] investigated 34 elderly stroke-free atrial fibrillation (AF) patients administered Atorvastatin and ezetimibe. They found that intensive cholesterol-lowering therapy in AF patients may slow cognitive decline and atrophy of the medial temporal lobe (P = 0.014).

In a randomized, double-blind, placebo-controlled trial, Sano et al., [20], examined the effects of Simvastatin on individuals with mild to moderate Alzheimer's disease (AD). The primary outcome measure was the rate of change in the Alzheimer's Disease Assessment Scale-cognitive portion (ADAS-Cog). Despite significant lowering of cholesterol, simvastatin treatment did not have any impact on change in ADAS-Cog score or the secondary outcome measures in the 406 participants (P = 0.25).

Trompet et al., conducted a randomized controlled trial to assess the impact of

Pravastatin on cognitive decline in at-risk elderly patients [21]. Utilizing four neuropsychological performance tests, the study found no significant difference in cognitive decline between the subjects treated with pravastatin and the placebo over a 3-year follow-up period among the 5804 participants (all p > 0.05).

In another double-blind, placebo-controlled, randomized trial, Sparks et al., examined the effects of Atorvastatin calcium in individuals with mild-to-moderate AD [22]. The primary outcome measure was the change in ADAS-cog sub-scale score. The study observed a significant positive effect on ADAS-cog performance after 6 months of atorvastatin therapy compared to placebo. Interestingly, this benefit was more pronounced among individuals with higher Mini-Mental State Examination (MMSE) scores, cholesterol levels above 200 mg/dl, or those harboring an apolipoprotein-E-4 allele among the 67 randomized participants (P < 0.003).

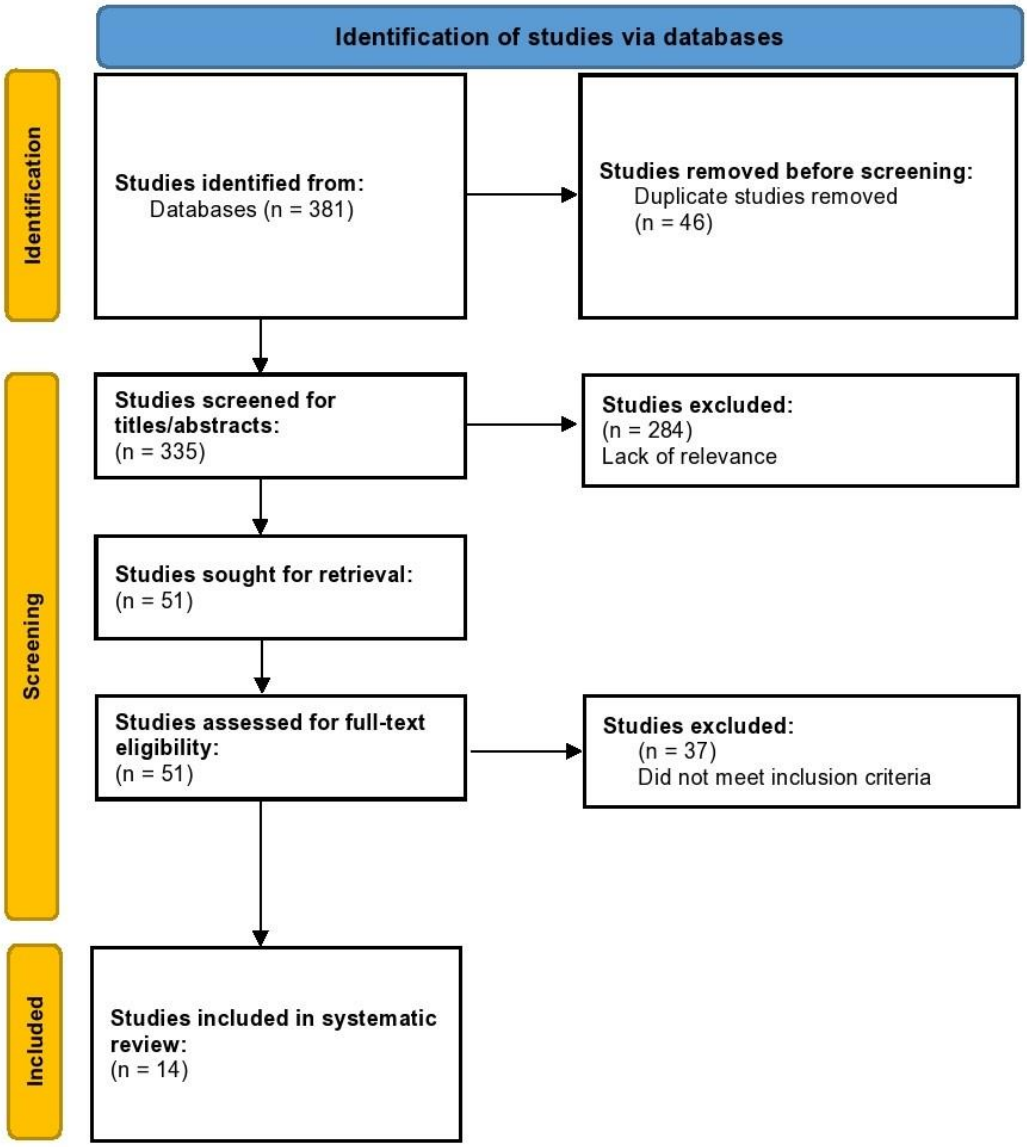

Fig. 1. Prisma flowchart depicting the study selection process

Table 1. Characteristics of the included studies (N=14)

Author, Year	Title	Study Type	Intervention	Inclusion Criteria	Primary Outcome(s)	N	Findings
Gencer et al., [10]	Cognition After Lowering LDL-Cholesterol With Evolocumab	Randomized, double-blind, placebo-controlled trial (post-hoc analysis)	Evolocumab in addition to statin therapy	Patients with atherosclerotic cardiovascular disease and LDL-C levels ≥70 mg/dl or non-HDL-C ≥100 mg/dl despite statin therapy	Changes in memory and executive functions as measured by the Everyday Cognition (ECog) scale	22,655 patients	Evolocumab with statins had no impact on patient-reported cognition, including those who achieved very low LDL-C levels (P = 0.62)
Thongtang et al., [11]	Effect of Switching from Low-Dose Simvastatin to High-Dose Atorvastatin on Glucose Homeostasis and Cognitive Function in Type 2 Diabetes	Randomized, open-label study	High-dose atorvastatin	Type 2 diabetes patients who were taking simvastatin ≤20 mg/day	Changes in HbA1c levels, glucose homeostasis, and cognitive function	125 patients (63 in the low-dose simvastatin group and 62 in the high-dose atorvastatin group)	High-dose atorvastatin resulted in a slight increase in HbA1c (0.1%) but did not cause cognitive decline based on MoCA and TMT assessments (P > 0.05)
Zhang et al., [12]	Effects of sartans and low-dose statins on cerebral white matter hyperintensities and cognitive function in older patients with hypertension: a randomized, double-blind and placebo-controlled clinical trial	Randomized, double-blind and placebo-controlled clinical trial	Low-dose rosuvastatin	Elderly hypertensive patients on hydrochlorothiazide	Changes in WMHs and cognitive function as measured by MRI and cognitive tests	732 patients	Rosuvastatin use was associated with lower risks of WMH progression and cognitive impairment (HR = 0.54; 95% CI: 0.36-0.8)
Molina-Sotomayor et al., [13]	Effects of exercise on the cognition of older women treated with lovastatin	Randomized controlled trial	Walking program in combination with lovastatin	Women over 60 years of age on lovastatin therapy	Changes in cognition and blood concentration of lipids	67 patients (45 in the exercise group and 22 in the sedentary	The exercise group showed an increase in HDL-C concentrations and improved spatial orientation (i.e.,

Author, Year	Title	Study Type	Intervention	Inclusion Criteria	Primary Outcome(s)	N	Findings
						group)	computed as cognitive dimensions and assessed by the MMSE, with a large effect size ($p<0.05$), but there was no significant change in LDL-C
Chan et al., [14]	Effect of high-dose simvastatin on cognitive, neuropsychiatric, and health-related quality-of-life measures in secondary progressive multiple sclerosis: secondary analyses from the MS-STAT randomised, placebo-controlled trial	Double-blind, controlled trial (post-hoc analysis)	High-dose simvastatin	Patients with secondary progressive multiple sclerosis	Changes in cognitive function, neuropsychiatric status, and health-related quality of life	140 patients (70 in the simvastatin group and 70 in the placebo group)	The simvastatin group showed improved frontal lobe function (95% CI: 0.2-2.3) and a better mean physical component score of the SF-36 (95% CI: 0.3-4.8; P = 0.028), but there was no effect on other outcomes
Gupta et al., [15]	Adverse events associated with unblinded, but not with blinded, statin therapy in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA): a randomised double-blind placebo-controlled trial and its non-randomised non-blind extension phase	Randomized double-blind placebo-controlled trial	Atorvastatin daily	Patients aged 40-79 years with hypertension, other cardiovascular risk factors, and fasting total cholesterol concentrations of 6·5 mmol/L or lower	Muscle-related AEs, erectile dysfunction, sleep disturbance, and cognitive impairment	10180 (blinded phase), 9899 (non-blinded phase)	Too few cases of cognitive impairment were reported for a statistically reliable analysis (31 [0.20% per annum] vs 32 [0.22% per annum]; 0.94 [0.57-1.54]; P = 0.81); No significant differences were observed in the rates of most

Author, Year	Title	Study Type	Intervention	Inclusion Criteria	Primary Outcome(s)	N	Findings
							reported adverse events
Needham et al., [16]	Rosuvastatin versus placebo for delirium in intensive care and subsequent cognitive impairment in patients with sepsis-associated acute respiratory distress syndrome: an ancillary study to a randomised controlled trial	Ancillary study within a randomised controlled trial	Rosuvastatin 40mg loading dose, then 20mg daily	Patients with sepsis-associated acute respiratory distress syndrome	Daily delirium status in intensive care up to 28 days	272 patients	No benefit of rosuvastatin in reducing delirium in intensive care or cognitive impairment during 12 months of follow-up (P=0.82)
Wong et al., [17]	Cognitive outcome in acute simvastatin treatment for aneurysmal subarachnoid hemorrhage: A propensity matched analysis	Randomized controlled double-blinded clinical trial	Acute simvastatin treatment	SAH patients	Montreal Cognitive Assessment (MoCA)	102 (51 in each group)	No difference in cognitive outcomes between the groups treated with simvastatin and the control group based on MoCA assessment (OR 0.7, 95% CI: 0.3-1.8, P = 0.477)
Williamson et al., [18]	Cognitive function and brain structure in persons with type 2 diabetes mellitus after intensive lowering of blood pressure and lipid levels: a randomized clinical trial	Randomized clinical trial	Intensive therapy for hypertension and combination therapy with a statin plus a fibrate	Patients with type 2 diabetes mellitus (T2DM)	Change in total brain volume (TBV)	2977 patients	Intensive BP control and fibrate therapy had no measurable effect on cognitive decline (P > 0.05) but was associated with greater decline in TBV (P = 0.01)
Tendolkar et al., [19]	One-year cholesterol lowering treatment reduces medial temporal lobe atrophy	Parallel group double-blinded randomized trial	Atorvastatin and ezetimibe	Elderly stroke-free atrial fibrillation (AF) patients	Neuropsychological performance, inflammatory markers, amygdala	34 patients	Intensive cholesterol-lowering therapy in AF patients may

Author, Year	Title	Study Type	Intervention	Inclusion Criteria	Primary Outcome(s)	N	Findings
	and memory decline in stroke-free elderly with atrial fibrillation: evidence from a parallel group randomized trial				and hippocampal volume, white matter lesions (WML)		slow cognitive decline and atrophy of the medial temporal lobe (P = 0.014)
Sano et al., [20]	A randomized, double-blind, placebo-controlled trial of simvastatin to treat Alzheimer disease	Randomized, double-blind, placebo-controlled trial	Simvastatin	Individuals with mild to moderate AD and normal lipid levels	Rate of change in the Alzheimer's Disease Assessment Scale-cognitive portion (ADAS-Cog)	406 (204 on simvastatin, 202 on placebo)	No effect on change in ADAS-Cog score or the secondary outcome measures despite significant lowering of cholesterol (P = 0.25)
Trompet et al., [21]	Pravastatin and cognitive function in the elderly. Results of the PROSPER study	Randomized controlled trial	Pravastatin	Elderly patients at risk	Cognitive decline assessed by four neuropsychological performance tests	5804 patients	No difference in cognitive decline in subjects treated with pravastatin compared to placebo (all P > 0.05). No effect on cognitive decline during a 3-year follow-up period
Sparks et al., [22]	Circulating cholesterol levels, apolipoprotein E genotype and dementia severity influence the benefit of atorvastatin treatment in Alzheimer's disease: results of the Alzheimer's Disease Cholesterol-Lowering	Double-blind, placebo-controlled, randomized trial	Atorvastatin calcium	Individuals with mild-to-moderate AD (MMSE score of 12-28), stable dose use of cholinesterase inhibitors, estrogen and vitamin E were allowed	Change ADAS-cog sub-scale score	98 enrolled, 67 randomized	Significant positive effect on ADAS-cog performance after 6 months of atorvastatin therapy compared with placebo (P < 0.003). The benefit was more prominent among individuals with

Author, Year	Title	Study Type	Intervention	Inclusion Criteria	Primary Outcome(s)	N	Findings
	Treatment (ADCLT) trial						higher MMSE scores, cholesterol levels above 200 mg/dl, or those harboring an apolipoprotein-E-4 allele
Sparks et al., [23]	Atorvastatin therapy lowers circulating cholesterol but not free radical activity in advance of identifiable clinical benefit in the treatment of mild-to-moderate AD	Pilot intention-to-treat, proof-of-concept, double-blind, placebo-controlled, randomized trial	Statin therapy (type unspecified)	Individuals enrolling in the ADAPT trial, elective use of statins	Onset of mild cognitive impairment (MCI) or AD	2528 individuals	Statin use associated with significantly reduced risk of incident AD after adjustment for age, gender, education and ApoE genotype ($P < 0.05$). The findings were similar when comparing all LLA use to non-LLA use.

Abbreviations: AD: Alzheimer disease; ADAS-Cog: Alzheimer's Disease Assessment Scale-cognitive portion; ADCLT: Alzheimer's Disease Cholesterol-Lowering Treatment; AE: Adverse Event; AF: Atrial Fibrillation; ASCOT-LLA: Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm; BP: Blood Pressure; CI: Confidence Interval; ECog: Everyday Cognition scale; HDL-C: High-Density Lipoprotein Cholesterol; HR: Hazard Ratio; LDL-C: Low-Density Lipoprotein Cholesterol; LLA: Lipid-Lowering Agents; MCI: Mild Cognitive Impairment; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MRI: Magnetic Resonance Imaging; MS-STAT: Multiple Sclerosis Statin trial; non-HDL-C: non-High-Density Lipoprotein Cholesterol; OR: Odds Ratio; P: P-value; PROSPER: Pravastatin in elderly individuals at risk of vascular disease; SAH: Subarachnoid Hemorrhage; SF-36: Short Form (36) Health Survey; T2DM: Type 2 Diabetes Mellitus; TBV: Total Brain Volume; TMT: Trail Making Test; WMH: White Matter Hyperintensities

Finally, Sparks et al., conducted a pilot intention-to-treat, proof-of-concept, double-blind, placebo-controlled, randomized trial that looked at statin therapy's effect on individuals enrolling in the ADAPT trial [23]. The primary outcome was the onset of mild cognitive impairment (MCI) or AD. The findings revealed that statin use was associated with a significantly reduced risk of incident AD after adjusting for age, gender, education, and ApoE genotype among 2528 individuals ($P < 0.05$). The same findings were observed when comparing all Lipid-Lowering Agents (LLA) use to non-LLA use.

4. DISCUSSION

The present study assessed the impact of statin therapy on cognitive functions in elderly patients, encompassing a total of 68,724 individuals across 14 studies. Synthesis of the included studies demonstrated a predominantly neutral or occasionally positive effect of statins on cognition, contradicting the widely held belief that statins may adversely impact cognitive function. For instance, Gencer et al., [10] reported no significant impact of evolocumab added to statin therapy on cognition, even among patients with very low LDL-C levels. Similarly, Thongtang et al.,[11] found no cognitive decline in diabetes patients who switched from low-dose simvastatin to high-dose atorvastatin. Studies conducted by Zhang et al., [12] and Molina-Sotomayor et al., [13] presented a more promising view, where the addition of rosuvastatin or lovastatin therapy combined with a walking program was associated with reduced risks of cognitive impairment.

Cognitive function encompasses a variety of mental abilities, including memory, attention, and executive function [24]. Aging is an independent risk factor for cognitive decline, and the elderly population is already at risk for the onset of neurodegenerative conditions like dementia and Alzheimer's disease [25-28]. Statins, with their wide usage, especially among this population, present a unique interface where cardiovascular therapeutics and cognitive health intersect [29].

Recent research points towards a more nuanced understanding of the relationship between statin use and cognitive function [4,30-32]. Needham et al., [16] showed that Rosuvastatin did not benefit in reducing cognitive impairment in patients with sepsis-associated acute respiratory distress syndrome, a critical population where cognitive outcomes matter. Wong et al. and Williamson et al. also found no difference in cognitive outcomes in patients with Subarachnoid Hemorrhage and Type 2 Diabetes Mellitus respectively [17,18]. These findings build on the existing body of literature and inform our understanding of the potential cognitive effects of statins [33-35].

Certain studies have also suggested a possible beneficial effect of statins on cognitive health. For instance, Tendolkar et al., demonstrated that intensive cholesterol-lowering therapy could slow cognitive decline in atrial fibrillation patients [19]. Sparks et al., and Sparks et al., also observed a positive effect on cognitive performance and a reduced risk of Alzheimer's disease onset with statin therapy, specifically among individuals with certain risk factors [22,23].

From a clinical perspective, these findings underscore the relevance of statin therapy in the context of cognitive health among the elderly. It is essential to bear in mind the potential cognitive impacts of these commonly used medications. Particularly when treating elderly patients, the decision to initiate or continue statin therapy should be guided by a careful weighing of the potential cardiovascular benefits and any risks to cognitive function. Certain biological mechanisms might mediate the effects of statins on cognition. For instance, statins' role in attenuating neuroinflammation, oxidative stress, and improving cerebral blood flow may exert neuroprotective effects and possibly contribute to cognitive health [36]. Further research is needed to elucidate these mechanisms and their clinical implications.

5. LIMITATIONS AND STRENGTHS

This study has certain limitations that need to be acknowledged. Firstly, the heterogeneity in the methods of cognitive assessment across the included studies could have potentially influenced the outcomes. With varied cognitive tests and scales, it can be challenging to compare results across different studies. Secondly, most included studies are observational in nature, which cannot establish a causal relationship between statin therapy and cognitive function. Thirdly, the studies often did not account for confounding factors such as the participants' health status, lifestyle habits, and other medication use, which might have influenced cognitive outcomes. Lastly, some studies were limited by small sample sizes and short follow-up durations, which may limit the generalizability of the results.

The primary strength of this review is its comprehensive nature, including 14 studies with a total of 68,724 participants, allowing for a broad overview of the existing research on the topic. By including studies using various statins and different patient populations, this review provides a wide lens into the potential effects of statin therapy on cognitive function. The incorporation of both randomized controlled trials and observational studies in the review also contributes to a fuller understanding of the research landscape.

6. RECOMMENDATIONS

Despite the extensive research included in this review, several gaps and opportunities for future research remain. It would be beneficial to have more large-scale, randomized controlled trials that can provide robust evidence to confirm or refute the findings of this review. Future studies should consider using standardized cognitive assessment methods, which would enable more straightforward comparisons across studies. It would also be beneficial for future research to more thoroughly adjust for potential confounding variables, such as comorbid conditions, lifestyle factors, and other medications, to isolate the impact of statin therapy on cognitive function.

7. CONCLUSION

In sum, this systematic review synthesizes findings from 14 studies involving a total of 68,724 participants, offering a comprehensive understanding of the potential impact of statin therapy on cognitive functions in the elderly. While some studies indicated neutral effects, other studies suggested beneficial effects of statin therapy on cognitive outcomes, presenting a key area of exploration. The overall picture emerging from this review does not support the claim that statin therapy negatively impacts cognitive function in the elderly. Instead, it suggests a predominantly neutral effect or a potentially protective one. Given the prevalence of statin use among the elderly, with millions of prescriptions dispensed annually worldwide, it is reassuring for both clinicians and patients that this medication does not appear to be associated with cognitive decline. However, considering the gravity of the topic, it is necessary to continue exploring this area with robust, large-scale studies to further confirm these findings and expand upon the potential benefits. The quest for comprehensive, reliable data regarding the cognitive safety of statins remains an important public health goal given the widespread use of this therapy.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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