Antihypertension Medication (Calcium-Channel Blockers and Angiotensin Converting Enzyme Inhibitors) on Blood Pressure Among Older People with Hypertension: A Meta-Analysis Study

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Abstract *- Many medications are used to treat high blood pressure. Calcium Channel Blockers (CCB) and Angiotensin Converting Enzyme Inhibitors (ACEI) are the most commonly prescribed for patients with hypertension. Both have proven to be effective in lowering blood pressure, but they can vary from one person to another, depending on patient characteristics. This study aims to investigate the effect of antihypertension medication CCB and ACEI on systolic blood pressure among older people with hypertension. Three databases were used in a comprehensive search conducted from February to March 2025 to find relevant research published in English from 2000 to 2025. The standard mean difference with a 95% confidence interval was used to determine the effect of antihypertension medication. Three randomized controlled trial studies with 6113 respondents over 50 years old with hypertension, which were divided into 3036 participants using CCB and 3077 using ACEI. The result showed that in older people with hypertension, CCB may provide a slightly greater reduction in systolic blood pressure compared to ACEI, but the difference is not statistically significant. The use of both drugs can be recommended for older people who have hypertension, independent of their comorbid conditions.*

Keywords: *Angiotensin Converting Enzyme Inhibitors, Blood Pressure, Calcium-Channel Blockers, Hypertension*

I. INTRODUCTION

Hypertension continues to affect millions of people and is one of the leading causes of cardiovascular problems, increasing morbidity and mortality worldwide (Yamal et al., 2023). As people become older, blood vessels become less flexible, often leading to higher blood pressure and put extra strain on the heart, and can quietly damage organs over time in which they become (Topuz & Topuz, 2024). Many older people may not feel any symptoms, but persistent high blood pressure puts extra strain on the heart, which contributes to left ventricular hypertrophy and eventually leads to heart failure (Rosenberg et al., 2020). It also silently harms the blood vessels, making them prone to blockages that can trigger heart attacks, strokes, or circulation problems. Managing high blood pressure is also about protecting the heart, preserving quality of life, and preventing serious health complications, especially in older people (Benetos et al., 2019).

Among the many medications that are used to treat high blood pressure, CCB like amlodipine and ACEI like lisinopril are some of the most commonly prescribed (Benetos et al., 2019). These medications work in different ways with the same purpose. CCB helps to relax blood vessels by limiting the flow of calcium into the Smooth Muscle Cells (SMC), while ACEI inhibitors help the body reduce intracellular calcium levels in SMC, promoting vasodilation and reducing blood pressure. It avoids extra fluid and reduces high blood pressure (Bhutto et al., 2024). Both have proven to be effective in lowering blood pressure, but they can vary from one person to another, depending on patient characteristics. There is limited evidence comparing the effects of the two classifications of the drugs, and more research is needed to understand the effectiveness of the medicines on blood pressure.

II. MATERIALS AND METHODS

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, which were used to write up this review, as shown in Figure 1. The PICO format was used, where population (P): Older people with hypertension, Intervention (I): CCB, Comparison (C): ACEI, and Outcome (O): Systolic Blood Pressure. A thorough search was conducted from February to March of 2024 using 3 databases, including Cochrane, Embase, and PubMed. Keywords or terms used for search were acute hypertension, arterial hypertension, blood pressure, cardiovascular hypertension, controlled hypertension, endocrine hypertension, high blood pressure, high renin hypertension, hypertensive disease, hypertensive effect, hypertensive reaction, hypertensive response, neurogenic hypertension, preexistent hypertension, salt high blood pressure, salt hypertension, secondary hypertension, and systemic hypertension (related to Hypertension) were used. Calcium blocker, calcium blocking agent, calcium channel antagonist, calcium channel blocker, calcium channel blockers, calcium entry blocker, calcium entry blocking agent, calcium inhibitor, and calcium channel blocking agent (related to Calcium Chanel blocker) were used. ACE inhibitor, angiotensin converting enzyme inhibiting agent, angiotensin converting enzyme inhibitor, angiotensin converting enzyme inhibitors, angiotensin i converting enzyme inhibitor, angiotensin-converting enzyme inhibitors, converting enzyme inhibitor, dipeptidyl carboxypeptidase i inhibitor, kininase ii inhibitor, peptidyl dipeptidase inhibitor, peptidyldipeptide hydrolase inhibitor, and dipeptidyl carboxypeptidase inhibitor (related to Angiotensin Converting Enzym Inhibitor) were used. Blood pressure systolic, blood systolic pressure, systolic pressure, and systolic blood pressure (related to Systolic Blood Pressure) were used. Randomized controlled trial, randomized control trial, randomized clinical trial, and RCT (related to Randomized Control Trial) were used.

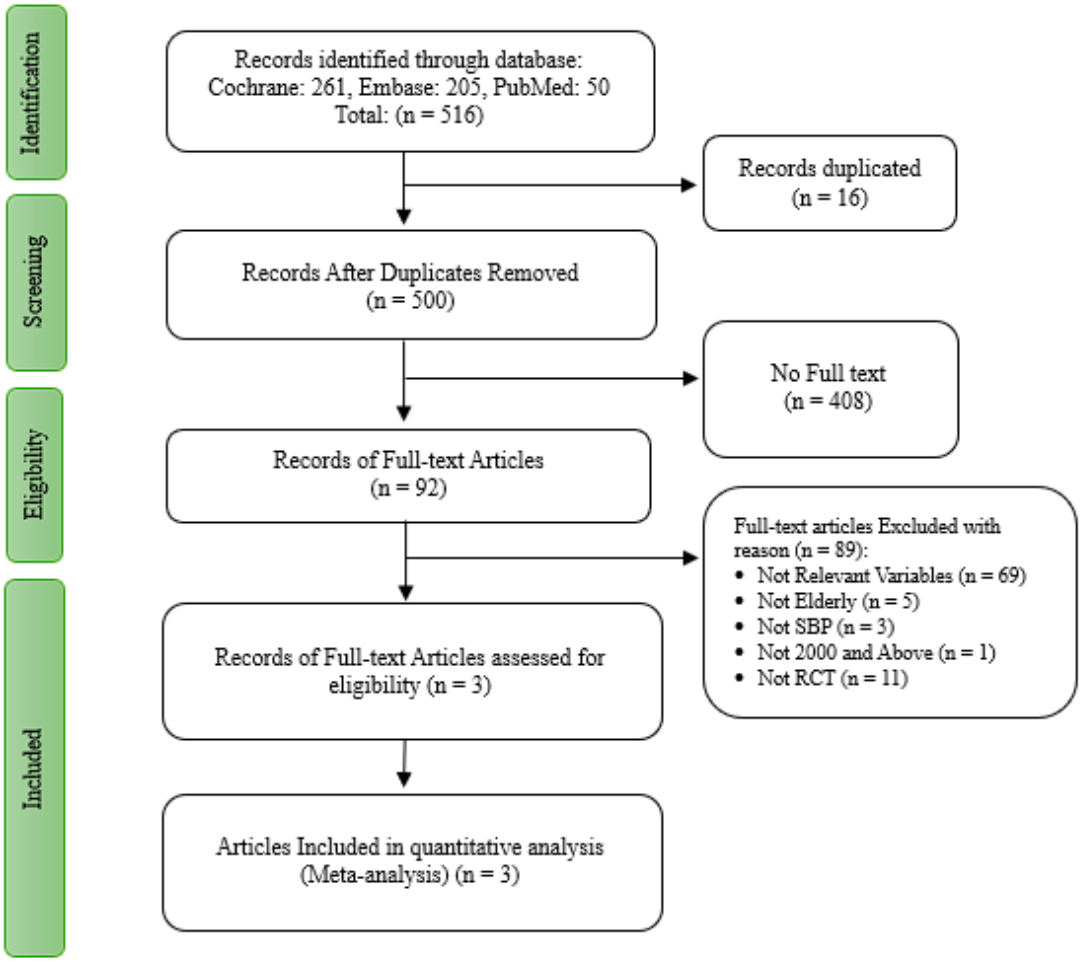


Figure 1. Studies Selection Process

Studies from 2000 to 2025 of the randomized controlled trial (RCT) design were included in this study. After identifying pertinent research using the PICO method, these studies were further scrutinized to eliminate duplicates. Screening of titles and abstracts was conducted to obtain studies that evaluated the effect of antihypertension medication CCB and ACEI on systolic blood pressure among older people with hypertension. After that, several studies that fulfilled the inclusion and exclusion criteria were selected. English-language articles, older people with hypertension, antihypertension CCB and ACEI, SBP outcomes, and the RCT study design with intervention and control groups were all required for inclusion, whereas animal studies, systematic reviews, and meta-analyses were excluded in this study. The search procedure was closed after all reviewers had looked through the full-text publications' reference lists and found no more research that satisfied the study's inclusion requirements.

Data Extraction and Quality Assessment

Data extraction was performed independently to obtain information on eligible studies, such as age, study design, medication used (variables of the study), dose and

duration of treatment, sample size, risk factors included (comorbidities), outcome, and validity test through JBI and kappa scores. Quality assessment was performed independently, and differences of opinion were resolved through consensus among the reviewers. The internal validity of the studies was evaluated using the Joanna Briggs Institute (JBI) Appraisal Tools, which consists of 13 items with four possible answers: "yes, no, unclear, and NA." The data obtained was then tested using Fleiss Kappa analysis to determine the level of agreement between the raters, in this case using four raters.

The Cochrane Handbook for Systematic Review of Interventions' criteria and the RoB 2 tool were used to evaluate each study's risk of bias from reviewers independently, and any discrepancies were settled by discussion. The potential of each bias source was assessed as high, low, or unclear, providing a report with a justification for the assessment in the form of a risk of bias summary and risk of bias graph (Figure 2).

The funnel plot was used to determine the publication bias in this study. Figure 3 shows that the included studies are within the bias line, which means that the heterogeneity of the studies is low and the risk of publication bias is low. The lower the publication bias, the more valid the results found in the study.

Data Synthesis and Statistical Analysis

Review Manager (RevMan 5.4) software was used for statistical analysis. The heterogeneity of the study analysis data results was tested using the Chi-square test. When $I^2 < 50\%$, there was no statistically significant heterogeneity among the results of the studies, and the fixed-effect model was used for analysis. However, when $I^2 > 50\%$, statistical heterogeneity and a random-effect model were used for analysis. The outcomes were expressed as a change from the baseline to the follow-up. The results obtained were presented by the standardized mean difference (SMD), a confidence interval (CI) of 95%, and a significance level of 0.05.

III. RESULTS AND DISCUSSION

Description of Selected Studies

A total of 516 studies were collected from five databases (Cochrane: 261, Embase: 205, PubMed: 50). Meanwhile, 16 studies were removed based on duplication, and 408 studies were removed due to not providing full text. After the full text screening, 3 studies were included for analysis, and 89 studies were excluded for the following reasons namely, non-relevant variables (n: 69), non-older people population (n: 5), non-systolic blood pressure outcome (n: 3), published under 2000 (n: 1), and lack of RCT study design (n: 11).

Characteristics and Quality of the Studies

A total of 3 studies with RCT design were included from 2000 to 2025. The studies included 6113 respondents over 50 years old with hypertension, which was divided into 3036 participants using CCB and 3077 using ACEI. Additionally, as indicated in Table 1, the study's quality was evaluated using the JBI score and Fleiss Kappa analysis result, which had a score of 8 out of 13, with K: 1 and P: <0.0001.

Table 1. Characteristics of studies

No	Author	Age	Study Design	Hypertension Medication		Sample Size	Risk Factors Included	Outcome	JBI Score / Fleiss Kappa
				Med	Dose				Kappa/Sig
1	Rahman et al., 2006	CCB: 70.8 ± 7.6 ACEI: 70.6 ± 7.9	Post hoc subgroup analysis of a multicenter randomized, double-blind, controlled trial.	CCB: Amlodipine ACEI: Lisinopril	1:1 (6 Years)	CCB: 1516 ACEI: 1533	Myocardial infarction (MI), Stroke, Left Ventricular Hypertrophy, Type 2 Diabetes, Atherosclerotic CVD, HDL cholesterol level of < 0.91 mmol/L	Systolic BP	JBI: 8/13 K: 1 P: <0.001
2	Rahman et al., 2012	CCB: 70.8 ± 7.6 ACEI: 70.6 ± 7.9	Long-term post-trial follow-up of a randomized clinical trial.	CCB: Amlodipine ACEI: Lisinopril	1:1 (average 8.8 Years)	CCB: 1479 ACEI: 1501	CHD	Systolic BP	JBI: 8/13 K: 1 P <0.001
3	Yilmaz et al., 2010	CCB: 53.8 ± 17.6 ACEI: 49.2 ± 13.4	Randomized, parallel-group comparative study.	CCB: Amlodipine ACEI: Lisinopril	1:1 (1 Year)	CCB: 41 ACEI: 43	ESRD,	Systolic BP	JBI: 8/13 K: 1 P <0.001

A publication bias test was conducted using the Cochrane Handbook for Systematic Review of Interventions' Risk of Bias criteria and the RoB 2 tool (Figure 2). The results indicated that of the seven bias statement items, the majority exhibited values greater than 50%. The risk of bias was summarized where the three studies provided information on how the randomization was generated, and they were indicated as low risk of bias. Two studies provided details about how allocation was concealed, and one study had an unclear risk of bias. Due to the nature of the intervention, all the studies were blinded to the intervention and the outcome of the assessment, which had a low risk of performance and detection bias.

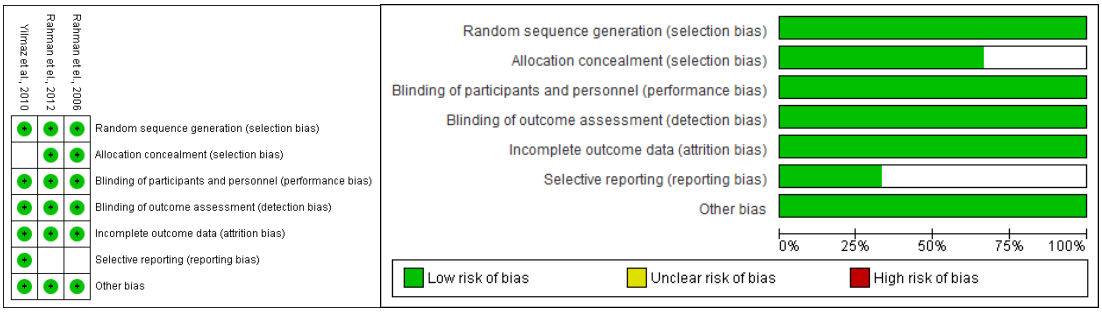


Figure 2. Risk of Bias Summary and Graph

The same thing is also shown in attrition bias; the data shows that all three studies show complete outcome data. This indicates a low bias. In contrast to reporting bias, there were two studies reported as unclear in the selective reporting of data. Finally, all the studies were at low risk of other bias. All studies reported have an explanation for collecting data, inclusion and exclusion criteria, and the number of samples used in the study.

The funnel plot was utilized to ascertain the presence of publication bias in this study (Figure 3). The included studies are situated within the bias line, indicating that the heterogeneity of the studies is minimal and the risk of publication bias is low. The presence of publication bias can compromise the validity of study results.

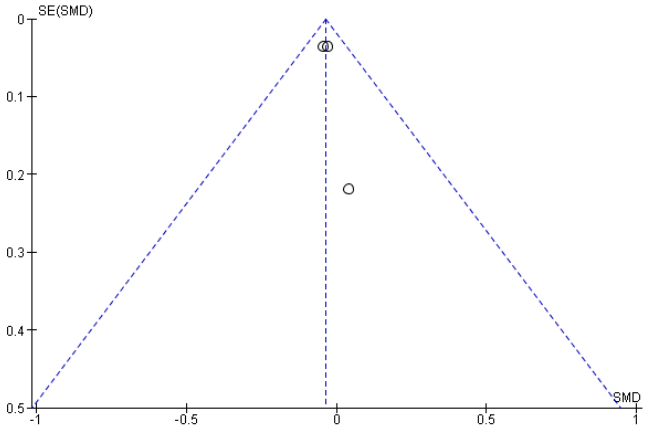


Figure 3. Funnel Plot

SBP Differences Between CCB and ACEI Intervention Among Older People with Hypertension

To determine the significance of the difference in mean SBP in the older people with hypertension using CCB and ACEI drugs, a Standard Mean Difference (SMD) effect measure with Fixed Analysis model and 95% Confidence Interval (CI) was conducted as shown in Figure 4.

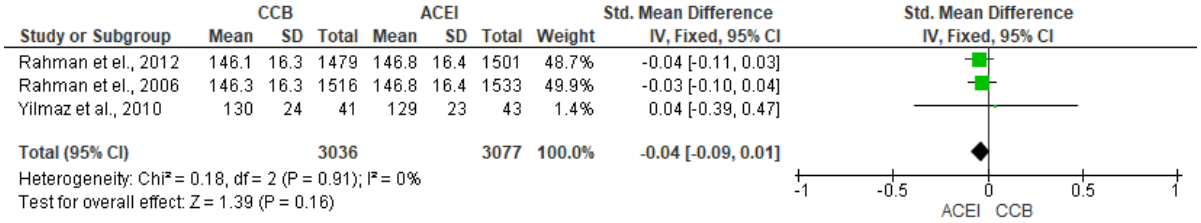


Figure 4. Mean SBP in the older people with CCB and ACEI groups

Figure 4 shows that there is no significant difference in the mean SBP between the older people in the CCB group and the ACEI group. The data, which consists of the CCB group with n: 3077 and the ACEI with n: 3036, shows that there is a total for the overall effect with P: 0.16. Further, the result shows that there is a Standard Mean Difference (SMD) of -0.04, with 95% CI: -0.09 to 0.01. It indicates that the mean SBP blood pressure in older people who use CCB is lower than the older people who use ACEI. The result also found that I^2: 0% indicates that the population used is homogeneous, and Fixed Analysis can be used as the analysis model.

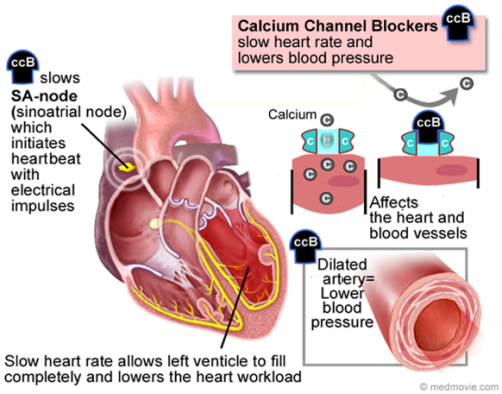
Discussion

This study compared the mean SBP between the CCB group and the ACEI group among older people with hypertension. The comparison was carried out to address the issues related to which group of hypertension medications is more effective in lowering blood pressure for people with hypertension, especially in older people. The issue was raised in relation to the utilization of various classes of antihypertensive medications among the older population. Both classes of medications are frequently prescribed for patients with hypertension.

The result shows that there is no significant difference in mean SBP between a group of older people with hypertension using CCB and a group of older people with hypertension using ACEI. The finding indicates that in terms of effectiveness, both classes of drugs can be used by older people suffering from hypertension and commonly prescribed as first-line treatments. Both drug classes are effective in lowering blood pressure in older patients, but their mechanisms of action, patient responses, and suitability can differ based on individual clinical profiles. CCB medications are particularly effective in reducing systolic blood pressure, which tends to be more elevated in older people due to arterial stiffness. CCBs such as amlodipine and nifedipine work by relaxing the smooth muscles of blood vessels, leading to vasodilation and reduced vascular resistance (Huang et al., 2019; Singh et al., 2023; and Yin et al., 2022). On the other hand, ACEI lowers blood pressure by inhibiting the conversion of angiotensin I to angiotensin II. This also leads to vasodilation, reduced blood volume, and ultimately decreased blood pressure (Ahmad et al., 2023; Nather et al., 2019; and Zheng et al., 2022).

Although there is no significant difference in the mean value of SBP, the standard mean difference data shows that the mean SBP blood pressure in the older people who use CCB is lower than the older people who use ACEI with SMD: -0.04. It shows that CCB is more effective in lowering SBP by as much as 0.04 than ACEI in older people with hypertension. The impact of CCB on systolic blood pressure in the older population is more about managing arterial stiffness. CCB acts primarily as a vasodilator of the peripheral vasculature. This is accomplished via preferential binding to and blocking of L-type calcium channels located in the tunica media of the peripheral vasculature (Jones et al., 2024). The subsequent decrease in the influx of calcium prevents the contraction of smooth muscle cells, thereby causing vasodilation (Figure 2). This causes decreased vessel tone, total peripheral resistance, and afterload, which therefore lowers blood pressure, hence their use in treating hypertension (Ottolini et al., 2019; and Touyz et al., 2018).

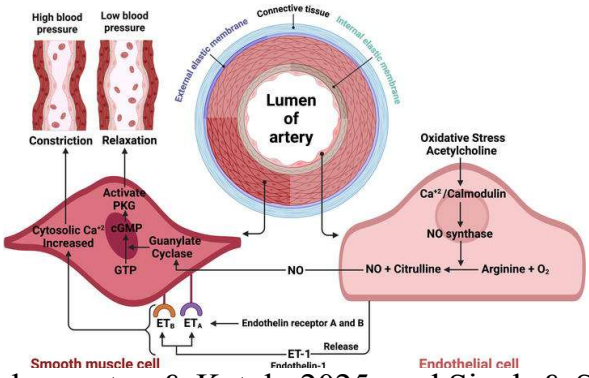
CCB works by directly inhibiting the entry of calcium ions into the smooth muscle cells lining blood vessels and cardiomyocytes. This blockade reduces intracellular calcium, which is essential for muscle contraction, leading to relaxation and dilation of blood vessels (vasodilation). The result is a decrease in vascular resistance, which lowers blood pressure and reduces the workload on the heart (Godfraind, 2017; and Tülümen & Borggrefe, 2020).



Source: (Medmovie, 2025)

Figure 5. Calcium Channel Blocker

Although CCB medications are statistically more likely to lower blood pressure than ACEI medications, there is no significant difference between the two. Blood pressure regulation is a complex process that involves many different parts of the body that extend beyond the RAAS. Different cells are very important for keeping blood pressure steady and making sure your body gets the blood and oxygen it needs, no matter what's going on inside or outside your body (Touyz et al., 2018). Stimulation causes smooth muscle cells (SMCs) to contract, narrowing blood vessels and increasing BP. Their ability to contract and relax finely controls blood vessel diameter, regulating resistance and blood flow distribution. Contraction is triggered by rising intracellular calcium levels, promoting interactions between actin and myosin filaments, while relaxation occurs as calcium levels drop, allowing vessel dilation (Figure 5) (Ottolini et al., 2019; and Touyz et al., 2018).



Source: (Senbonmatzu & Katoh, 2025; and Singh & Singh, 2024)

Figure 6. The role of Smooth muscle cells in blood pressure.

Angiotensin II from the RAAS plays a critical role by increasing intracellular calcium levels in SMCs, promoting vasoconstriction, and elevating BP. Stimulation, such as neurotransmitter binding like acetylcholine, induces calcium influx from extracellular and internal sources. Elevated calcium levels activate calmodulin, which then activates myosin light chain kinase, triggering interactions between actin and myosin filaments that result in cell contraction (Figure 6) (Blumenthal & Stull, 1980; Fang et al., 2023; Holzapfel et al., 1983; and Stull et al., 2011). This interaction emphasizes the essential relationship between SMC function, RAAS activation, and overall BP regulation. ACEI plays the opposite role, inhibiting Angiotensin II in its activity to increase intracellular calcium levels, resulting in a decrease in blood pressure within the blood vessels. (Van-Lier et al., 2021).

The results of this study are supported by several previous research results. The difference in blood pressure in patients with hypertension after using CCB and ACEI drugs is not significant (Cushman, 2016; Remonti et al., 2016; and Sinnott et al., 2020). In those studies, both ACEIs and CCBs are generally well tolerated, but CCBs may have a slightly better tolerability profile. In line with the result, this study found that both classes of drugs can reduce blood pressure, but CCB reduces blood pressure more than ACEI. It is probable that CCB directly relaxes the smooth muscles in the arterial walls, leading to vasodilation and a more immediate and effective reduction in systolic pressure (Iepsen et al., 2024; and Sueta et al., 2017). CCBs have been demonstrated to reduce cardiovascular incidents in patients diagnosed with isolated systolic hypertension, as well as in elderly and high-risk patients. Accordingly, the use of

CCBs is recommended for the treatment of hypertension in elderly patients, isolated systolic hypertension, angina pectoris, and coronary vasospasm (Lee, 2023). While ACEI acts indirectly by affecting RAAS, which may be less active in older adults, making ACEIs less potent in this population (Alghatrif et al., 2021; Bueno & Frasca, 2023; and Sobhy et al., 2024).

IV. CONCLUSION

This study found that CCB may provide a slightly greater reduction in systolic blood pressure compared to ACEI, but the difference is not statistically significant among older people with hypertension. The use of both drugs can be recommended for older people who have hypertension, independent of their comorbid conditions. However, further studies are recommended to conduct subgroup analysis on comorbidities to further investigate the effects of the two classes of hypertension medications. In addition, future studies need to evaluate the antihypertensive effects of CCBs and ACEIs not only on systolic blood pressure, but also on other relevant clinical outcomes such as stroke incidence, heart failure, mortality, and patient quality of life. Subgroup analysis based on common comorbidities in the elderly, such as diabetes or chronic kidney disease, is also important to determine more specific responses in certain groups.

In addition to the effectiveness aspect, future studies need to comprehensively assess the side effect profile and long-term safety of these two classes of drugs in the elderly. Assessment of the effect of variations in dose and duration of therapy on effectiveness and safety, as well as exploration of other factors that may influence therapeutic response, are also needed. Thus, the results of future studies are expected to provide more robust and applicable recommendations for the management of hypertension in the elderly.

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