A Meta-analysis of Intensive and Standard Antihypertensive Safety in Elderly Hypertensive Patients

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Abstract: Objective: To evaluate the effect of intensive and standard antihypertensive pressure on cardiovascular and cerebrovascular events, serious adverse events and all-cause deaths in elderly hypertensive patients. Methods: Pubmed, Embase, Cochrane, CNKI, Wanfang and CBM databases were searched. All of the included studies were the RCT trials. Relative risk (RR) and 95% confidence interval (95%CI) were used to evaluate differences in enhanced and standard antihypertensive outcomes. Statistical analysis was applied using the Stata 17.0 software. Results: Seven tests were retrieved to meet the conditions, Different antihypertensive effects showed overall statistical differences in the incidence of cardiovascular and cerebrovascular events, Significant decrease in the intensive antihypertensive group [P=0.000, RR95%CI:0.79(0.69-0.90)], Among them, the incidence of acute myocardial infarction (AMI) and acute coronary syndrome (ACS) was significantly reduced in the intensive antihypertensive group [P=0.000, RR95%CI:0.62(0.48-0.81)], The incidence of stroke events was significantly fewer in the intensive group [P=0.000, RR95%CI:0.62(0.48-0.81)]; There was no significant difference in the incidence of acute HF (AHF) between the two groups [P=0.242, RR95%CI:0.55(0.20-1.50)]. There was no significant statistical difference in the incidence of serious adverse events overall by different antihypertensive criteria [P=0.251,RR95%CI:1.12(0.92-1.36)], of which two groups were eGFR<30ml/min/1.73m2There was no significant statistical difference in the incidence [P=0.280,RR95%CI:1.46(0.74-2.89)], no significant statistical difference in the incidence of orthostatic hypotension [P=0.473,RR95%CI:1.47(0.51-4.23)], no significant statistical difference in the incidence of falls [P=0.607,RR95%CI:1.24(0.54-42.86)], and the incidence of syncope in the intensive antihypertensive group was higher than that in the standard antihypertensive group [P=0.009,RR95%CI:2.43(1.24-4.77)]. There was no significant statistical difference in the effect of different antihypertensive criteria on all-cause death [P=0.156,RR95%CI:0.92(0.81-1.03)]. Conclusion: Compared with the standard antihypertensive in elderly patients with hypertension, there is no significant statistical difference in the incidence of serious adverse events and all-cause mortality in the elderly, and the incidence of cardiovascular and cerebrovascular events in the elderly.

***Keywords*:** old age; intensive antihypertensive; safety; meta-analysis

1. Introduction

Hypertension is an important risk factor for cardiovascular disease and death in the elderly. Elderly hypertension has its unique characteristics, its best control target value has always been very controversial, many scholars advocate its appropriate relaxation, but in recent years, more and more research suggests that more active blood pressure control may make the elderly patients with hypertension benefit more, therefore some international hypertension guidelines lowered the blood pressure control of elderly patients with hypertension target[1-3] .

This study analyzed the safety of cardiovascular and cerebrovascular events, the rate of serious adverse events and all-cause death by intensive BP (systolic BP 110-130mmHg) and standard BP (systolic BP 130-150mmHg) in the elderly.

2. Data and methods

2.1 Literature inclusion criteria

① RCT trial; ② outcome measures: stroke, ASC, AHF, coronary revascularization, atrial fibrillation, serious adverse events (syncope, falls, postural hypotension, etc.) and all-cause death; ③ target population: hypertensive patients aged 60 years; ④ intervention protocol: randomized to intensive treatment group and standard treatment group.⑤ Follow-up time of 1 year.

2.2 Literature exclusion criteria

① review, case report, meeting minutes, etc.; ② patients with a history of ischemic or hemorrhagic stroke, patients with diabetes, hypertensive patients with ACS, AHF, coronary revascularization, and atrial fibrillation; several papers published by ③; ④ could not obtain data.

2.3 Search strategy

Pummed, Embase, Cochrane, CNKI, Wanfang, and CBM databases are searched electronically, and the search time is not completed until June 2023. Through medical keywords search, published literature including "old age", "enhanced blood pressure reduction" and other related words, and there is no limit on published language.

2.4 Screening, information extraction, and quality evaluation of the included literature

Literature retrieval, elimination, screening and information extraction were independently carried out by two researchers. After data extraction, cross-check was conducted. If there is any ambiguity, it should be settled by a third party through negotiation. The search type was mainly RCT test, a total of 2091 documents were selected, according to the title and keywords, the full text was read, and 7 studies were obtained[4-10]A total of 28,341 patients were included.

2.5 Statistical methods

Dichotomous variables were expressed as RR values and 95%CI, using a random effects model, with I2Values expressed heterogeneity between groups, and publication bias was estimated using funnel plots. Two-sided P <0.05 were considered as statistically significant, and statistical analysis was performed using the s t ata 17.0 version.

3. Results

3.1 Characteristics of the included literature

Seven RCT articles were finally selected[4-10], Independent information extraction by 2 fellows, and the extracted information are detailed in Table 1.

3.2 Methodological quality assessment

Literature meeting the inclusion criteria were evaluated for the risk of bias. For evaluation using the risk of bias assessment tool-Cochrane manual, the evaluation items include: 1. sequence generation 2. allocation concealment 3. Blind 4. Incomplete outcome data 5. selective outcome report 6. Other sources of bias. Assessment outcome identification: A (low risk of bias), B (unknown risk of bias), C (high risk of bias). The quality evaluation was also conducted independently by two researchers, and in case of ambiguity, it was discussed by a third party.

3.3 Outcome Analysis

(1) The effect of intensive antihypertensive and standard antihypertensive patients on the cardiovascular and cerebrovascular morbidity was significantly different, and the incidence of cardiovascular and cerebrovascular events in the intensive antihypertensive group was significantly reduced [P=0.000,RR95%CI:0.79(0.69-0.90)].among:a. The incidence of AMI and ACS was significantly reduced in the intensive antihypertensive group [P=0.000,RR95%CI:0.62(0.48-0.81)]; b. The incidence of stroke events was significantly reduced in the intensive antihypertensive group [P=0.000,RR95% CI:0.62(0.48-0.81)]; c. There was no significant statistical difference in AHF occurrence [P=0.242,RR95%CI:0.55(0.20-1.50)].

(2) Incidence of serious adverse events in the intensive and standard antihypertensive groups (including eGFR<30ml/min/1.73m2, Syncope, fall, postural hypotension, etc.), with no significant statistical difference [P=0.251,RR95% CI:1.12(0.92-1.36)].among:a.eGFR＜30ml/min/1.73m2Incidence,with no significant statistical difference [P=0.280,RR95 %CI:1.46(0.74-2.89)]; b. The incidence of syncope was statistically different, and the incidence of syncope was higher in the intensified antihypertensive group than in the standard antihypertensive group [P=0.009,RR95%CI:2.43(1.24-4.77)];c. Incidence of orthostatic hypotension with no significant statistical difference [P=0.473,RR95%CI:1.47(0.51-4.23)]; d. Prevalence of falls, without significant statistical difference [P=0.607,RR95%CI:1.24(0.54-42.86)].

(3) The incidence of all-cause death in the elderly and standard antihypertensive groups, with no significant statistical difference [P=0.156,RR95%CI:0.92(0.81-1.03)].

Table 1. Basic characteristics of inclusion in literature

Study, year	Country	Mean age (years)	Male than (%)	Follow-up (year)	Sample size (person)		Cognitive Impairment (human)		Baseline MMSE (sub-part)		Outcome MMSE (points)		Cardiovascular and cerebrovascular event (human)		Serious Adverse Event (person)		All-cause death (person)		Quality of literature
					I	S	I	S	I	S	I	S	I	S	I	S	I	S	
STEP,2021[12]	China	66	45%	4	4243	4268	46	42	28.90	28.92	28.96	29.08	147	196	21	21	42	39	A
SPRLNT MIND,2015[13]	America	68	63%	4	4678	4683	149	176	NA	NA	NA	NA	62	176	1793	1736	155	210	A
Sysr-Eur,1998[14]	Europe	70	35%	5			48	39	29	29	24.00	23.00	340	39	NA	NA	NA	NA	A
PODCAST,2017[15]	Britain	74	77%	2	41	42	2	0	NA	NA	NA	NA	1	3	18	22	4	3	A
ACCORD BP,2010[16]	United States, Canada	62	53%	5.8	2362	2371	NA	NA	27.25	27.25	27.00	26.95	36	62	136	88	150	144	A
INF INITY,2019[18]	Britain	80	46%	3	99	100	NA	NA	NA	NA	NA	NA	1	2	36	38	2	4	A
SPS3,2013[20]	Of North America, Latin America, and Spain	63	63%	3	1501	1519	192	184	NA	NA	NA	NA	125	152	23	15	106	101	A

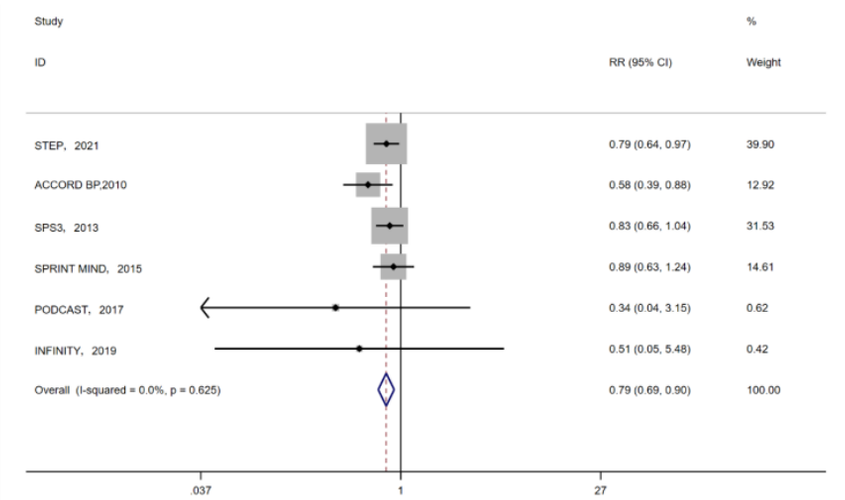

Figure 1. Incidence of Cardiovascular and Cerebrovascular Events

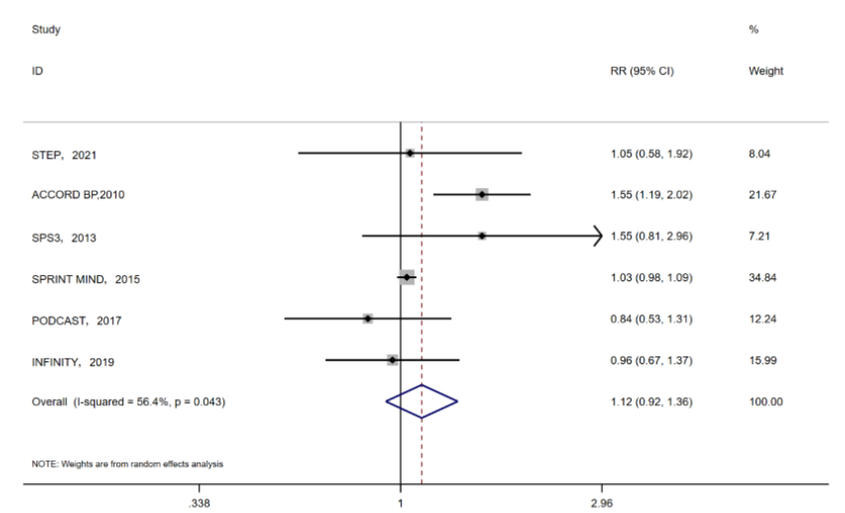

Figure 2. Incidence of Serious Adverse Events

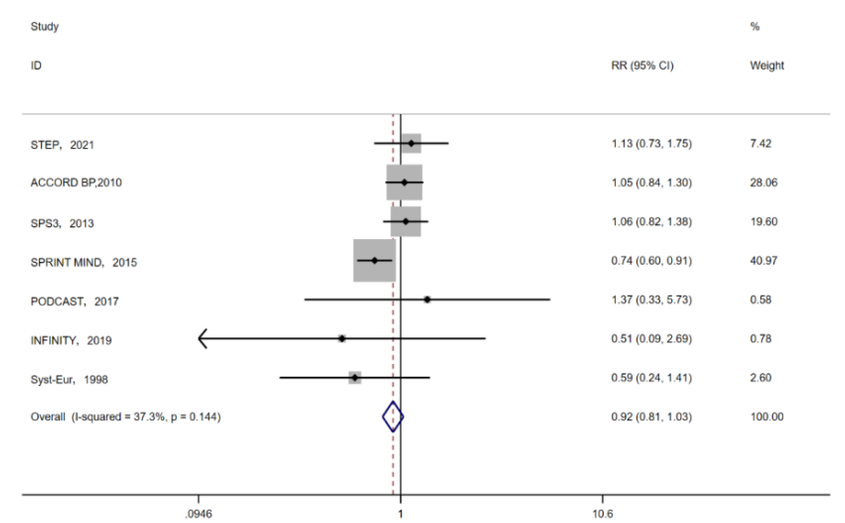

Figure 3. All-Cause Mortality Rate

4. Discussion

First of all, the 7 studies included in this meta-analysis were high-quality literature, which analyzed the common safety indicators of intensive antihypertensive pressure in the elderly. The number of people included was large and the data was reliable. There was no statistical difference in the baseline data of different antihypertensive groups, so the analysis results were statistically significant. Secondly, it is worth noting that the study of the safety of intensive and standard antihypertensive comparison in elderly patients with hypertension is based on the analysis of the results of the included trials, and it does not represent the safety results of specific antihypertensive drugs.

5. Conclusion

The incidence of cardiovascular and cerebrovascular events in the elderly was significantly reduced, among which the incidence of AMI, ACS and stroke decreased significantly, while there was no significant difference in the incidence of AHF. In the eGFR<30ml/min/1.73m2, There was no significant statistical difference in the incidence of orthostatic hypotension and falls, and the incidence of syncope in the intensive antihypertensive group was higher than that in the standard antihypertensive group. There was no significant statistical difference in all-cause death by the different antihypertensive criteria.

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