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Presentation type (s):	Lightening Talk

Comparison of combination treatment in hypertension

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Abstract

Currently, the American and European guidelines recommend initial combination treatment in high-risk hypertension patients. However, the real-world evidence of head-to-head comparison among the recommended regimens is still limited. We aim to compare the therapeutic effectiveness of combination regimens between patients initiating dual antihypertensive treatment. From Korean National Health Insurance sample cohort database, we identified eligible patients without previous history of cardiovascular disease who were started on and received prescription of dual anti-hypertensive treatment for more than 180 days between 2003 and 2012. The patients were matched for each comparison set by large scale propensity score matching. Primary end point was all-cause mortality. The results suggest that there is no significant difference of all-cause mortality among recommended dual combination treatment regimen.

Introduction

High blood pressure is the leading global burden causing death and disability. Since monotherapy is often insufficient or slow to reach blood pressure target quickly, combination therapy is recommended as the first-line treatment for selected patients with hypertension by the recent guidelines[1]. Only a few randomized clinical trials (RCT), however, have directly compared the effects of different regimens of combination[2–4]. In addition to limited number of evidences from head-to-head comparison, baseline high risk for cardiovascular outcome and previous history of anti-hypertensive medication of participants also make the findings from RCTs difficult to apply to clinical practice. To the best of our knowledge, real-world comparative effectiveness research comparing the various regimens of combination treatment in patients with essential hypertension has not been conducted until now.

Purpose

We aim to compare the therapeutic effectiveness of combination regimens between patients initiating dual antihypertensive treatment.

Methods

From Korean National Health Insurance sample cohort database, we identified eligible patients without previous history of cardiovascular disease who were started on and received prescription of dual anti-hypertensive treatment for more than 180 days between 2003 and 2012. The patients were matched for each comparison set by large scale propensity score matching to compare the efficacy of to ACEi/ARB (A) + Thiazide diuretics (D) vs A + Calcium channel blocker (C), C+D vs A+C, and C+D vs A+D combination treatment[5]. Primary end point was all-cause mortality. Secondary end points were: cardiovascular death, newly developed myocardial infarction, newly developed heart failure, newly developed stroke and all-composite end points above.

The protocol and analytic code are available at github

(https://github.com/OHDSI/StudyProtocolSandbox/tree/master/HypertensionCombination)

Results

Total of 14098 patients were identified to meet eligible criteria with follow-up duration of 5.31 ± 3.12 years. Among them, 4149, 1738 and 2381 patients were allocated to A + D vs A + C, C+D vs A+C, and C+D vs A+D groups,

respectively. There was no significance difference in the primary endpoint between groups (Table 1, Figure 1). All three recommended regimens had similar efficacy in secondary endpoints (all P>0.05).

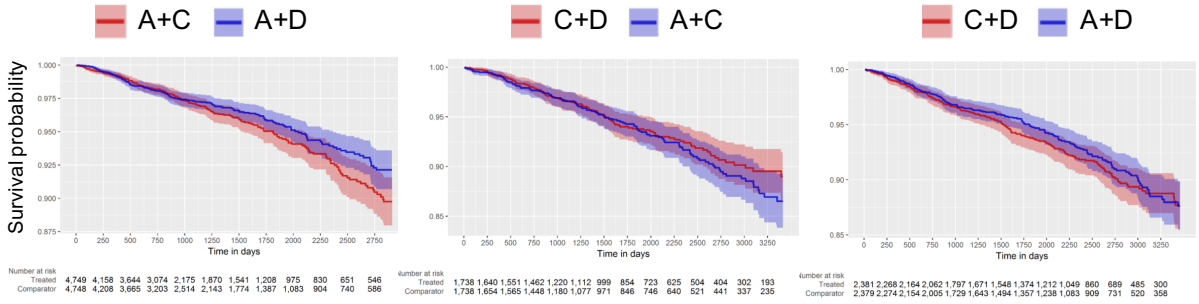

Figure 1. Survival curve after large-scale propensity score matching

Table 1. All-cause mortality between dual combination treatment group after large scale propensity score matching

Active drug group	Comparator group	Number of active group after matching	Number of comparator group after matching	Hazard ratio	95% CI	*P* value
A+C	A+D	4751	4751	1.11	0.84-1.49	0.465
C+D	A+C	1739	1739	1.03	0.71-1.33	0.465
C+D	A+D	2382	2382	1.09	0.85-1.41	0.478

Abbreviations: CI, confidential interval; A, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; B, β-blocker; C, calcium channel blocker; D, thiazide-diuretics; CV, cardiovascular

Conclusions

To our knowledge, this is the first real-world comparative effectiveness research comparing the recommended regimens of dual combination treatment in patient initiating antihypertensive medication. The results suggest that there is no significant difference of all-cause mortality among recommended dual combination treatment regimen

References

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