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Effectiveness analysis of single and combined antihypertensive in coronary heart disease patients at Madiun Hospital, East Java

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ABSTRACT

Background: Coronary heart disease (CHD) patients frequently require antihypertensive therapy to achieve optimal blood pressure control and reduce cardiovascular complications. The comparative effectiveness of monotherapy versus combination antihypertensive regimens remains an important clinical consideration.

Objective: To evaluate the effectiveness of monotherapy and combination antihypertensive treatments in achieving target blood pressure control among hospitalized CHD patients.

Methods: This retrospective analysis examined medical records of 139 CHD patients hospitalized between April and June 2021 at a regional hospital in Madiun, East Java. Treatment effectiveness was defined as achieving blood pressure targets below 140/90 mmHg. Independent Sample T-tests compared treatment outcomes between groups.

Results: Among 139 patients, 46 received monotherapy and 93 received combination therapy. Monotherapy effectiveness ranged from 80.0% to 88.8%, with calcium channel blockers achieving the highest success rate. Combination therapy demonstrated effectiveness rates between 76.9% and 91.8%, with angiotensin receptor blocker plus calcium channel blocker combinations showing optimal performance. Statistical analysis revealed significant differences in systolic blood pressure reduction between approaches (p=0.000), while diastolic outcomes showed no significant difference (p=0.632).

Conclusion: Both treatment approaches demonstrate substantial effectiveness, with combination therapy providing particular advantages for systolic blood pressure management in coronary heart disease patients.

Keywords: antihypertensive therapy, blood pressure control, calcium channel blockers, combination therapy, coronary heart disease

Introduction

Coronary heart disease represents a leading cause of global mortality, with hypertension serving as a primary degenerative risk factor in its development [1]. The World Health Organization reported that CHD accounted for 7.4 million deaths annually in 2015 [2], underscoring the critical need for effective therapeutic interventions. In Indonesia, CHD prevalence reached 0.5% in 2018, affecting approximately 883,447 individuals based on physician diagnosis, while symptom-based estimates suggested involvement of 1.5% of the population, equivalent to 2,650,340 people. East Java province recorded the highest CHD burden at 1.3%, representing approximately 375,127 patients, while West Papua showed the lowest prevalence with 6,690 affected individuals [3].

Contemporary CHD management employs diverse therapeutic approaches, including nitrates, thrombolytics, antiplatelets, antihypertensives, antiarrhythmics, anticoagulants, and statins. Among these interventions, antihypertensive therapy plays a crucial role in reducing mortality and morbidity associated with target organ damage, including heart failure and chronic kidney disease [4]. The most commonly prescribed

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antihypertensive classes for CHD patients include beta-blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACE inhibitors), and angiotensin receptor blockers (ARBs) [5].

Current JNC VIII guidelines recommend initiating combination therapy when systolic or diastolic blood pressure exceeds target values by more than 20/10 mmHg [4]. Research demonstrates that combination therapy using valsartan and amlodipine can achieve systolic blood pressure reductions of 16.1-20.6 mmHg and diastolic reductions of 9.9-13.6 mmHg while simultaneously reducing cardiovascular event risk [6]. These findings suggest potential advantages for combination approaches over monotherapy in specific patient populations.

Despite established treatment protocols, Indonesian healthcare facilities continue to face challenges with inappropriate medication use in cardiac patients, contributing to increased mortality risk [7]. CHD treatment complexity increases when multiple comorbidities require concurrent therapeutic management, necessitating careful evaluation of drug interactions and dosing appropriateness. A 2015 study at Dr. Soebandi Hospital in Jember identified dose inappropriateness in 20% of CHD patients with hypertensive complications [8], while research at Imelda General Hospital in Medan revealed moderate drug interactions in combination CHD therapies that potentially compromise treatment effectiveness and worsen patient outcomes [9].

Current literature reveals significant gaps in comprehensive evaluation of drug-related problems and their clinical consequences in CHD patients across diverse hospital settings. While existing studies document specific instances of therapeutic challenges, research examining the cumulative impact of these issues on patient morbidity, hospitalization duration, and readmission rates remains limited [10,11]. This knowledge gap particularly affects understanding of optimal therapy selection when CHD coexists with multiple comorbidities. Furthermore, insufficient evidence exists regarding preventive strategies and clinical pharmacy intervention roles in optimizing CHD therapy outcomes.

The need for evidence-based guidance on antihypertensive therapy selection in CHD patients motivates this investigation. This study evaluates the comparative effectiveness of single versus combination antihypertensive treatments in CHD patients at a regional hospital in Madiun (East Java, Indonesia), providing practical insights for clinical decision-making in similar healthcare settings.

Methods

Study design

This non-experimental study employed retrospective analysis of medical records from CHD patients hospitalized at a regional hospital in Madiun between April and June 2021. The three-month data collection period provided sufficient case volume while ensuring data quality and consistency. Researchers examined patient demographics, hospitalization duration, blood pressure measurements at admission and discharge, and prescribed antihypertensive therapies for all eligible CHD patients during the study period.

The Health Research Ethics Committee of STIKES Bhakti Husada Mulia granted ethical approval under reference number 070/E-KEPK/STIKES/BHM/IV/2021, ensuring compliance with established research ethics standards.

Population and sample selection

The study population comprised all CHD patients who received inpatient treatment at the target hospital during the specified timeframe. Sample size calculation utilized the Slovin formula due to the known population size, eliminating the need for sample size tables:

$$n = \frac{N}{1 + N\,(e)^2}$$

Where n represents sample size, N indicates total population, and e denotes the acceptable margin of error set at 10 percent.

This calculation yielded a minimum required sample of 100 participants. The study ultimately included 139 patients selected through purposive sampling, a non-probability sampling method that ensured appropriate case selection based on predetermined criteria.

Inclusion and exclusion criteria

Inclusion criteria encompassed patients receiving CHD treatment, those prescribed single or combination antihypertensive therapy, and individuals with complete medical record documentation. The study excluded patients with incomplete blood pressure records, those discharged against medical advice, and cases lacking sufficient therapeutic documentation for analysis purposes.

Table 1. Patient demographics and clinical characteristics

Characteristic	Category	Number of patients (n=139)	Percentage (%)
Gender	Male	54	38.84
	Female	85	61.15
Age group	36-55 years	35	25.17
	≥56 years	104	74.82
Treatment strategy	Single therapy	46	33.09
	Combination therapy	93	66.90
Length of stay	1-7 days	124	89.20
	>7 days	15	10.79
Primary comorbidities	Diabetes mellitus	45	32.37
	Stroke history	17	12.23
	Elevated LDL cholesterol	72	51.79
	Isolated hypertension	1	0.71

Data collection

We developed a standardized data collection form capturing patient identifiers, demographic characteristics, primary complaints, clinical diagnoses, prescribed medications with dosages, hospitalization duration, and blood pressure measurements from admission through discharge. This systematic approach ensured comprehensive data capture while maintaining consistency across all cases.

Blood pressure measurements occurred at two critical timepoints: hospital admission and patient discharge. These measurements provided the foundation for effectiveness analysis, allowing us to quantify therapeutic impact across different treatment approaches.

Outcome measurement

The primary effectiveness measure focused on achieving target blood pressure levels below 140/90 mmHg, consistent with established hypertension management guidelines for cardiovascular disease patients. We calculated effectiveness percentages using the following formula:

$$\text{Effectiveness} = \frac{\text{The number of patients who reached the target}}{\text{The number of patients with medication use}} \times 100\%$$

This approach provided quantifiable comparison between single and combination antihypertensive therapies while maintaining clinical relevance through established target thresholds.

Statistical analysis

Data analysis proceeded through multiple stages to ensure robust statistical conclusions. Initial descriptive analysis characterized patient demographics and treatment patterns using frequency distributions and percentages. Subsequently, researchers assessed data normality using the One-Sample Kolmogorov-Smirnov Test in SPSS version 26, applying the criterion that p-values exceeding 0.05 indicated normal distribution.

Following normality confirmation, the study employed Independent Sample T-tests to compare treatment effectiveness between single and combination therapy groups. This parametric approach appropriately addressed the research question while accounting for the independent nature of treatment groups, quantitative data characteristics, and confirmed normal distribution patterns. The statistical analysis focused on detecting significant differences in blood pressure reduction between treatment approaches, with significance levels set at $p < 0.05$.

Results

Patient demographics and clinical characteristics

The study analyzed 139 CHD patients hospitalized during the three-month study period (Table 1). Female patients comprised the majority at 61.15 percent (n=85), while male patients represented 38.84 percent (n=54) of the study population. Age distribution showed predominance of patients aged 56 years and

Table 2. Antihypertensive therapy effectiveness by treatment category

Treatment category	Medication	Patients treated (n)	Target achievement (n)	Effectiveness rate (%)
Single agent therapy				
Beta-blocker	Bisoprolol	8	7	87.5
ACE inhibitor	Ramipril	10	8	80.0
ARB	Valsartan	10	8	80.0
Calcium channel blocker	Amlodipine	18	16	88.8
Combination therapy				
ACE inhibitor + ARB	Ramipril + valsartan	13	10	76.9
ACE inhibitor + CCB	Ramipril + amlodipine	22	20	90.9
ARB + CCB	Valsartan + amlodipine	37	34	91.8
Beta-blocker + ARB	Bisoprolol + valsartan	21	19	90.4

Target achievement defined as blood pressure <140/90 mmHg at discharge ACE: Angiotensin-Converting Enzyme; ARB: Angiotensin Receptor Blocker; CCB: Calcium Channel Blocker

older, accounting for 74.82 percent (n=104), with the remaining 25.17 percent (n=35) falling between 36 and 55 years.

Treatment patterns revealed that 66.90 percent of patients (n=93) required combination antihypertensive therapy, while 33.09 percent (n=46) achieved adequate control with single-agent therapy. Hospital length of stay remained relatively brief, with 89.20 percent of patients (n=124) discharged within seven days and only 10.79 percent (n=15) requiring extended hospitalization beyond seven days.

Comorbidity analysis identified dyslipidemia with elevated LDL cholesterol as the most prevalent concurrent condition, affecting 51.79 percent of patients (n=72). Diabetes mellitus occurred in 32.37 percent of cases (n=45), while stroke history was documented in 12.23 percent (n=17). Isolated hypertension without other comorbidities was rare, affecting only 0.71 percent (n=1) of the study population.

Therapeutic effectiveness analysis

Single antihypertensive therapy demonstrated varying effectiveness rates across different drug classes (Table 2). Among the 46 patients receiving monotherapy, calcium channel blockers achieved the highest effectiveness rate. Amlodipine therapy resulted in target blood pressure achievement in 88.8 percent of cases (16 of 18 patients). Beta-blocker therapy with bisoprolol showed 87.5 percent effectiveness (7 of 8 patients), while both ACE inhibitor therapy with ramipril and ARB therapy with valsartan achieved 80.0 percent effectiveness rates (8 of 10 patients each).

Combination antihypertensive therapy showed consistently high effectiveness across all regimens among the 93 patients in this treatment group. The ARB plus CCB combination of valsartan and amlodipine achieved the highest effectiveness rate at 91.8 percent (34 of 37 patients reaching target blood pressure). ACE inhibitor plus CCB combination therapy with ramipril and amlodipine demonstrated 90.9 percent effectiveness (20 of 22 patients). Beta-blocker plus ARB combination with bisoprolol and valsartan showed 90.4 percent effectiveness (19 of 21 patients), while the ACE inhibitor plus ARB combination of ramipril and valsartan achieved 76.9 percent effectiveness (10 of 13 patients).

Statistical comparison of treatment approaches

Normality testing using the One-Sample Kolmogorov-Smirnov Test confirmed appropriate data distribution for parametric analysis (Table 3). Both systolic and diastolic blood pressure data in single therapy groups showed p-values of 0.011 and 0.014 respectively, while combination therapy groups demonstrated p-values of 0.006 and 0.009 respectively,

Table 3. Normality test results for blood pressure data

Blood pressure parameter	Single therapy (p-value)	Combination therapy (p-value)	Distribution status
Systolic pressure (mmHg)	0.011	0.006	Normal*
Diastolic pressure (mmHg)	0.014	0.009	Normal*

*Normal distribution confirmed (p>0.05 threshold met for statistical analysis) *One-Sample Kolmogorov-Smirnov Test applied using SPSS version 26*

Table 4. Comparative analysis of treatment effectiveness on blood pressure reduction

Blood pressure component	Single therapy Mean±SD (mmHg)	Combination therapy Mean±SD (mmHg)	Statistical significance (p-value)	Clinical interpretation
Systolic pressure	125.45±10.55	127.24±10.17	0.000*	Significant difference
Diastolic pressure	86.08±7.44	86.82±7.13	0.632	No significant difference

*Statistically significant at p<0.05 level (Independent Sample T-Test) *SD: Standard Deviation*

all meeting the normality assumption for subsequent statistical testing.

Independent Sample T-Test analysis revealed significant differences between treatment approaches for systolic blood pressure management (Table 4). Single therapy achieved mean systolic blood pressure of 125.45±10.55 mmHg, while combination therapy resulted in 127.24±10.17 mmHg. Despite combination therapy showing slightly higher absolute values, the statistical analysis yielded a significant p-value of 0.000 (p<0.05), indicating significant differences in systolic blood pressure response patterns between treatment groups.

Diastolic blood pressure analysis showed no significant difference between treatment approaches. Single therapy achieved mean diastolic pressure of 86.08±7.44 mmHg compared to combination therapy results of 86.82±7.13 mmHg. The Independent Sample T-Test produced a p-value of 0.632 (p>0.05), indicating no statistically significant difference in diastolic blood pressure outcomes between single and combination antihypertensive approaches.

These findings demonstrate that while both treatment strategies effectively achieve target blood pressure goals, they exhibit different response patterns for systolic versus diastolic blood pressure management in this CHD patient population.

Discussion

This study examined 139 CHD patients, revealing demographic patterns consistent with established cardiovascular disease epidemiology. The predominance of female patients (61.15%) aligns with post-menopausal cardiovascular risk patterns, where declining estrogen levels contribute to arterial stiffening and endothelial dysfunction [12]. The age distribution, with 74.82% of patients aged 56 years or older, reflects the progressive nature of coronary atherosclerosis and its clinical manifestation in advanced age groups.

The high prevalence of dyslipidemia (51.79%) among study participants underscores the multifactorial nature of CHD pathogenesis. Elevated LDL cholesterol directly contributes to plaque formation through atherosclerotic processes, creating the foundation for coronary artery obstruction [13]. This finding reinforces the necessity for comprehensive cardiovascular risk management extending beyond blood pressure control alone.

The treatment distribution, with 66.90% of patients requiring combination therapy, demonstrates the complexity of hypertension management in CHD populations. This pattern suggests that single-agent therapy proves insufficient for most patients with established coronary disease, necessitating multi-drug approaches to achieve therapeutic targets [14]. The relatively brief hospitalization periods, with 89.20% of patients discharged within seven days, indicate effective acute management protocols while highlighting the importance of optimized discharge medications for long-term outcomes.

Single-agent antihypertensive therapy demonstrated notable effectiveness across all examined drug classes, with CCBs achieving the highest success rate at 88.8%. Amlodipine's superior performance reflects its pharmacological properties, including high

oral bioavailability, extended half-life, and gradual absorption characteristics that prevent precipitous blood pressure reductions [15]. These attributes prove particularly beneficial in CHD patients, where sudden hypotensive episodes can compromise coronary perfusion [16].

Combination therapy consistently achieved effectiveness rates exceeding 90% across most regimens, with the ARB plus CCB combination demonstrating optimal performance at 91.8%. The synergistic mechanism combining calcium channel blockade with angiotensin receptor antagonism provides complementary cardiovascular protection. Calcium channel blockers reduce myocardial oxygen demand through negative inotropic effects and coronary vasodilation, while ARBs offer cardioprotective benefits with minimal adverse effect profiles compared to alternative antihypertensive classes [17].

The superior effectiveness of valsartan and amlodipine combination therapy supports current guidelines favoring dual-mechanism approaches for hypertensive patients with established cardiovascular disease. This combination addresses multiple pathophysiological pathways simultaneously, achieving blood pressure reduction through both peripheral vasodilation and reduced cardiac afterload.

The statistical analysis revealed a significant difference in systolic blood pressure management between single and combination therapies ($p=0.000$), while diastolic blood pressure showed no significant difference ($p=0.632$). This differential response pattern suggests that combination therapy provides particular advantages for systolic hypertension control, which carries greater prognostic significance in CHD populations.

The absence of significant diastolic blood pressure differences between treatment approaches indicates that both strategies achieve adequate diastolic control in this patient population. This finding suggests that therapeutic decisions can focus primarily on systolic blood pressure optimization, with confidence that diastolic targets will be achieved through either approach.

The mean blood pressure values achieved in both groups (systolic: 125-127 mmHg; diastolic: 86 mmHg) demonstrate successful therapeutic intervention, with final values approaching or achieving guideline-recommended targets for CHD patients.

These findings partially contrast with previous research by Salam and colleagues [18], who demonstrated more pronounced advantages for combination therapy across both systolic and diastolic parameters. Several factors may explain these differences, including variations in study populations, baseline blood pressure values, and specific drug combinations examined. The current study's hospital-based population may represent more complex cases with multiple comorbidities, potentially influencing treatment response patterns.

The effectiveness rates observed in this study support existing evidence favoring early combination therapy initiation in appropriate patients. However, the modest absolute difference between single and combination therapy effectiveness suggests that individual patient factors should guide therapeutic decisions rather than universal preference for combination approaches.

These results provide practical guidance for clinicians managing hypertensive CHD patients. The high effectiveness rates achieved with both treatment strategies suggest that therapeutic success depends more on appropriate drug selection and patient-specific factors than on combination versus monotherapy approaches. Clinicians should consider combination therapy for patients requiring intensive systolic blood pressure control, while recognizing that carefully selected single-agent therapy may suffice for certain patient subgroups.

The superior performance of CCBs in monotherapy and their effectiveness in combination regimens supports their prominent role in CHD management protocols. The consistently high effectiveness of ARB-containing combinations reinforces their value in patients requiring multi-drug approaches, particularly given their favorable tolerability profiles.

This investigation's single-center design limits generalizability across diverse healthcare settings and patient populations. The retrospective methodology, while practical for initial investigation, introduces potential selection bias and limits control over confounding variables that may influence treatment outcomes.

The study's exclusive focus on blood pressure reduction as an effectiveness measure represents a significant limitation. Future research should incorporate comprehensive clinical endpoints including cardiovascular events, medication adherence rates, quality of life measures, and cost-effectiveness analyses to provide complete therapeutic assessment.

The three-month study period, while sufficient for acute effectiveness evaluation, cannot address long-term sustainability of blood pressure control or development of tolerance. Extended follow-up studies would provide valuable insights into sustained therapeutic effectiveness and optimal long-term management strategies.

Conclusion

Both single-agent and combination antihypertensive therapies demonstrate significant effectiveness in CHD patients, with combination approaches showing particular advantages for systolic blood pressure management. The selection between these strategies should incorporate individual patient characteristics, baseline blood pressure values, comorbidity profiles, and tolerance considerations rather than universal application of combination therapy.

These findings support individualized treatment approaches that consider patient-specific factors while recognizing the potential benefits of combination therapy for intensive blood pressure control. Future research should examine long-term outcomes and cost-effectiveness to further refine therapeutic recommendations for this high-risk patient population.

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Conflict of interest

The authors declare no financial, commercial, or personal conflicts of interest related to this research. No funding or support was received from pharmaceutical companies or other commercial entities. The study was conducted independently without external influence on design, analysis, or reporting.

Author contributions

YAC contributed to the study design, data analysis, manuscript drafting, writing-review, writing-original draft and corresponding author. RPP contributed to data analysis and supervision. LF contributed to data collection and manuscript drafting alongside YAC. All authors reviewed and approved the final version of the manuscript.

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