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Comparison of direct medical cost between ramipril and candesartan in hospitalized acute decompensated heart failure at West Nusa Tenggara Regional Hospital

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Abstract

Introduction: Pharmacoeconomy is the field of study regarding costs analysis associated with the use of drugs in health care. The purpose of pharmacoeconomics is to compare a different drug used in the treatment with the same condition or can be the opposite, i.e. comparing different treatments in different circumstances. The purpose of this study is to determine and compare the average efficiency of direct medical costs between ramipril and candesartan combination drug in hospitalized heart failure patients with a payer perspective at the West Nusa Tenggara Regional General Hospital, Mataram, Indonesia.

Method: This study is part of an economic evaluation of direct medical cost analysis research in hospitalized heart failure patients with a payer perspective. Study design using a retrospective approach involving 45 patients with heart failure who met the study inclusion criteria and exclusion criteria. Independent t-test was used to compare the direct medical cost between ramipril and candesartan.

Results: The average gross total cost of using ramipril combination was Rp. 4,197,011 while the average total cost of using candesartan combination was Rp. 3,099,088. These results indicate there are savings in the average total cost of treatment for heart failure using candesartan that is Rp. 1,097,923. Candesartan combination provides the lowest value and is a more efficient choice compared to ramipril combination. Meanwhile, after t-test comparison reveal no significant different average direct medical costs in patients using the ramipril combination compared with the candesartan combination ($p>0.05$).

Conclusion: The results of this study indicate that there is no significant difference between the average direct medical costs in patients using ramipril compared with candesartan combination.

Keywords: heart failure, ramipril, candesartan, cost analysis, direct medical costs.

Introduction

The heart is the most important organ in circulation. The heart works to pump blood throughout the body to meet the body's metabolic needs at all times, both at rest and work. Most sufferers live after having a heart attack but then suffer heart failure.[1,2] Heart failure is a clinical syndrome caused by structural and/or functional abnormalities. Heart failure is a growing problem

throughout the world, with more than 20 million people affected by heart failure.[3-5] In developed countries the prevalence of heart failure in the adult age group reaches 2% of the population.[6] The prevalence of heart failure increases with age and affects 6-10% of people over 65 years.[7-9]

The World Health Organization (WHO) notes that 17.9 million people worldwide die from cardiovascular disorders with a percentage of 31% of deaths worldwide. More than 75% of cardiovascular sufferers occur in low and middle-income countries, and 80% of cardiovascular deaths are caused by heart attacks and strokes.[10] In Indonesia, as many as 13,395 people with heart failure undergoing hospitalization, while as many as 16,431 people were undergoing outpatient treatment in all hospitals around Indonesia. In 2018 the results of Basic Health Research showed that the incidence of heart failure increased by 1.5% in Indonesia. While in the West Nusa Tenggara region the prevalence is 0.8%.[11]

The additional cost-effectiveness ratio to expand the coverage of all heart failure patients is $ 9,700 per life-year gained obtained in the base case. An analysis of the worst case of heart failure assuming simultaneous conservative results in an additional cost-effective ratio of $ 110,000 per life-year gained. In a probabilistic sensitivity analysis, 99.74% of the possible additional ratios of cost-effective heart failure that were <$ 50,000 per life-year gained.[12,13] The cost of treatment is a very important issue for developing countries like Indonesia. One that affects the amount of the cost of handling heart failure is the type of drug used. Therefore in the treatment of heart failure a rational and comprehensive treatment is needed to achieve optimal medical service.[14-16]

Pharmacoeconomics is the field of study regarding costs analysis associated with the use of drugs in health care. The purpose of pharmacoeconomics is to compare a different drug used in the treatment with the same condition or can be the opposite, ie comparing different treatments in different conditions.[17] The results of the pharmacoeconomics can be used as a reference or assist policymakers in determining choices for available treatment alternatives so that health services become more efficient and economical. The study aims to determine and compare the average efficiency of direct medical costs between ramipril and candesartan combination drug in hospitalized heart failure patients with a payer perspective at the West Nusa Tenggara Regional General Hospital, Mataram, Indonesia.

Method

This study is part of a hospital economic evaluation of direct medical cost analysis in acute decompensated heart failure hospitalization. Study design using a retrospective approach with a payer's perspective.[18] The inclusion criteria in this study were patients with main diagnoses of acute decompensated heart failure who were hospitalized in West Nusa Tenggara Regional Hospital who were seeking treatment in the period 2018.

The type of data in this study is secondary data from hospital information system (SIRS), where the data obtained was the primary diagnosed heart failure patient data that met the patient criteria in the study which included age, sex, concomitant diseases and use of combination of

ramipril (furosemide 40 mg, spironolactone 25 mg, bisoprolol 5 mg, ramipril 5 mg) or using a combination of candesartan (furosemide 40 mg, spironolactone 25 mg, bisoprolol 5 mg, candesartan 16 mg) West Nusa Tenggara Regional Hospital 2018. The criteria used in assessing costs is the comparison between heart failure patients using the combination of ramipril compared to candesartan combination. A total of 240 patients diagnosed with heart failure who received treatment at West Nusa Tenggara Regional Hospital in2018, 45 samples were obtained that met the inclusion criteria, 33 patients were using the Ramipril combination and 12 patients using the candesartan combination.

Statistical analysis in this study using SPSS version 21.0 (IBM Corporation, Armonk, NY, USA). Independent t-tes was used to compare direct medical cost between ramipril and candesartan combination. All value considered significant if $p<0.05$.

Result

Characteristics of the study

Table 1. Clinical characteristics

Characteristics	Drugs combination		Total (n=45)		Percentage (%)	
	Ramipril	Candesartan	Ramipril n=33	Candesartan n= 12	Ramipril	Candesartan
Sex	Male Female	Male Perempuan	17 16	8 4	51.51% 48.48%	66.66% 33.33%
Age	18-65 years ≥ 65 years	36-65 tahun ≥ 65 tahun	27 6	7 5	81.81% 18.18%	58.33% 41.66%
Comorbidities	With comorbidities Without comorbidities	With comorbidities Without comorbidities	3 30	0 12	90.9% 9.1%	100% 0%
Status	Alive Death	Alive Death	14 19	4 8	42.42% 57.57%	33.33% 66.66%

Based on the results of this study indicate that inpatient heart failure patients in RSUDP NTB who received therapy with the combination of ramipril were 17 people (51.52%) were male and 16 people (48.48%) were female. While those who received candesartan therapy were 8 people (66.67%) who were male and 4 people (33.33%) were female. These results indicate that more heart failure patients are male than female. Meanwhile, in age characteristics shows, 18-65 years of age most diagnosed with heart failure by 81.82% and age ≥ 65 years by 18.18%. While the characteristics of age at Candesartan are age 35-65 years as much as 58.34% and age ≥ 65 years as much as 41.66%. Based on characteristics of concomitant diseases in the ramipril combination group of 90.9% had concomitant diseases and as many as 9.1% who did not have concomitant diseases. Whereas in the candesartan combination group all patients had concomitant disease (100%). In both groups it was seen that the majority of heart failure patients in the were mostly

accompanied by concomitant diseases. Life status characteristics shows in the ramipril group patients mostly died (57.58%) compared to the number of living patients by 42.42%. Whereas in the candesartan group it was known that heart failure patients who died by 66.67% and patients living by 33.33% (**Table 1**).

Direct Medical Cost

The description of medical expenses at the hospital can be used as input in determining the planning and control of hospital services. Costs that will be calculated in this study are direct medical costs including ramipril and candesartan drugs, other drugs, medical equipment costs, doctor's fees, nurse fees, laboratory fees and accommodation costs.

Tabel 2. Medication cost between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average medication cost (IDR)
Ramipril	VIP	5	71,773	14,355
	1	2	44,213	22,106
	2	7	77,017	11,002
	3	19	242,055	12,739
Candesartan	VIP	3	74,948	24,983
	1	1	26,964	26,964
	2	2	24,771	12,385
	3	6	123,401	20,566

Based on **table 2**, the average cost of drugs for heart failure patients using a combination of ramipril and candesartan combination has a different amount of costs. The difference in costs in each class is influenced by differences in length of stay, the number of drugs used and comorbidities besides heart failure and the types of drugs consumed so that it affects the costs that must be paid by the payer. The payer in this case is the Indonesian National Health Insurance Administering Agency (BPJS).

Table 3. Others medication cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average medication cost (IDR)
Ramipril	VIP	5	1,918,688	383.738
	1	2	5,497,997	2,748,998
	2	7	766,951	110,993
	3	19	19,897,806	1,047,252
Candesartan	VIP	3	1,849,651	616,550
	1	1	318,754	318,754
	2	2	148,499	74,249
	3	6	1,991,553	331,925

Based on **table 3**, the average cost of other drugs for heart failure patients using the combination of ramipril and candesartan combination has a different amount of costs. Costs for drugs other than heart failure include medications used to treat comorbidities in addition to heart failure. Common comorbidities in heart failure patients are hypertension, diabetes mellitus, and myocardial infarction. Non-cardiovascular drugs used include ranitidine, lansoprazole, metformin, simvastatin, clopidogrel, and ceftriaxone.

Tabel 4. Medical equipment cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average equipment cost (IDR)
Ramipril	VIP	5	573,594	114,719
	1	2	643,676	321,838
	2	7	620,930	88,704
	3	19	26,330,366	1,385,808
Candesartan	VIP	3	845,265	281,755
	1	1	219,409	219,409
	2	2	54,062	27,031
	3	6	1,140,748	190,124

Based on table 4, the average cost of medical devices for heart failure patients using a combination of ramipril and candesartan has a different amount of costs. The difference in the cost

of medical equipment in each class is influenced by differences in length of stay and the number of equipment used, so that it affects the cost that must be paid by the payer.

Tabel 5. Average doctor visit and hospitalization cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average fee cost (IDR)
Doctor visit fee				
Ramipril	VIP	5	2,625,000	525,000
	1	2	1,020,000	510,000
	2	7	1,000,000	142,857
	3	19	3,620,000	190,526
Candesartan	VIP	3	3,875,000	1,291,667
	1	1	180,000	180,000
	2	2	220,000	110,000
	3	6	1,200,000	200,000
Hospitalization cost				
Ramipril	VIP	5	5,695,350	1,139,070
	1	2	5,898,600	2,949,300
	2	7	3,579,200	511,314
	3	19	17,974,973	946,051
Candesartan	VIP	3	3,647,133	1,215,711
	1	1	394,600	394,600
	2	2	741,223	370,616
	3	6	5,030,075	838,345

Based on table 5, the average cost of doctors fee and hospitalization cost using a combination of ramipril and candesartan combination has a different amount of costs. The difference in costs in each class is influenced by differences in length of stay, number of drugs, medical equipment and service (oxygen installation, blood sampling, adult infusion set), and comorbidities in addition to heart failure and types of drugs used, so that influenced the costs to be paid by the National Health Insurance (BPJS).

Tabel 6. Average laboratory cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average cost (IDR)
Laboratory cost				
Kombinasi	VIP	5	4.707.050	941.410
Ramipril	1	2	1,645,000	822,500
	2	7	2,389,783	341,397
	3	19	8,306,340	422,965
Kombinasi	VIP	3	1.749.000	583.000
Candesartan	1	1	205,000	205,000
	2	2	389,000	194,500
	3	6	1,690,000	281,666
Accommodation cost				
Ramipril	VIP	5	6.500.000	1.300.000
	1	2	2,550,000	1,275,000
	2	7	1,875,000	267,857
	3	19	6,300,000	331,578
Candesartan	VIP	3	8.150.000	2.716.667
	1	1	300,000	300,000
	2	2	450,000	225,000
	3	6	1,450,000	241,666

Based on table 6, there is a difference in the cost of the laboratory and accommodation between ramipril and candesartan combination. Laboratory examination costs are preoperative and postoperative preparations, for patients who will undergo surgery required an individual examination based on the patient's condition. Differences in patient conditions cause different types, amounts and laboratory costs that must be incurred during treatment. Meanwhile, difference in accommodation cost due to class difference that affects the costs borne by patients. The cost for each class is different because the facilities of each room class are different. The cost of the VIP class is greater because the number of beds in the room has complete facilities compared to other treatment classes.

Table 7. Average emergency and intensive cardiac care unit cost comparison between ramipril and candesartan combination

Medication	Item total cost (IDR)	Average cost (IDR)
Emergency department cost		
Kombinasi Ramipril	2,900,000	241,667
Kombinasi Candesartan	1,000,000	142,857
Intensive cardiac care unit cost		
Kombinasi Ramipril	3,500,000	700,000
Kombinasi Candesartan	0	0

Based on table 7, the average cost of emergency room much higher in the ramipril combination Rp. 241,667 compared to the candesartan combination of Rp. 142,857. This is because the actual number of patients who get the ramipril combination more than patients who get the candesartan combination. Meanwhile, the average cost of the intensive cardiac care unit on the ramipril combination is Rp. 700,000, while for candesartan combinations Rp. 0. This happens due to samples in studies that received candesartan combination therapy none were treated in the intensive ward.

Direct medical cost analysis

Table 8. Direct medical cost comparison between ramipril and candesartan

Medication	Inpatient class	Number of patient	Total direct medical cost (IDR)	Average direct medical cost (IDR)	p
Ramipril	VIP	5	22.591.455	4.518.291	
	1	2	19,049,486	9,524,743	
	2	7	11,908,881	1,701,269	
	3	19	84,951,540	4,471,134	**0.570**
Total			**138,501,362**	**4,197,011**	
Candesartan	VIP	3	20,290,997	6,763,666	
	1	1	1,744,727	1,744,727	

	2	2	2,027,555	1,013,778	
	3	6	13,125,777	2,187,630	
Total			**37,189,056**	**3,099,088**	
Mean difference of direct medical cost			**IDR 1,097,923**		

Based on table 8, the average direct medical costs of patients using the Ramipril combination amounted to IDR 4,197,011 while the average direct medical costs of patients using the candesartan combination amounted to IDR 3,099,088. The difference between the average direct medical costs between a combination of ramipril and candesartan is Rp. 1,097,088. These results can illustrate that candesartan drugs are more cost-effective than ramipril drugs. Candesartan can provide lower economic value in the treatment of heart failure compared with ramipril. Meanwhile, after t-test comparison we found p=0.570 (p<0.05) which means there is no significant difference between the average direct medical costs in patients using the ramipril combination compared with the candesartan combination. However, mathematically the cost of candesartan is more efficient compared to ramipril. Graph comparison between all cost parameter can be seen in figure 1.

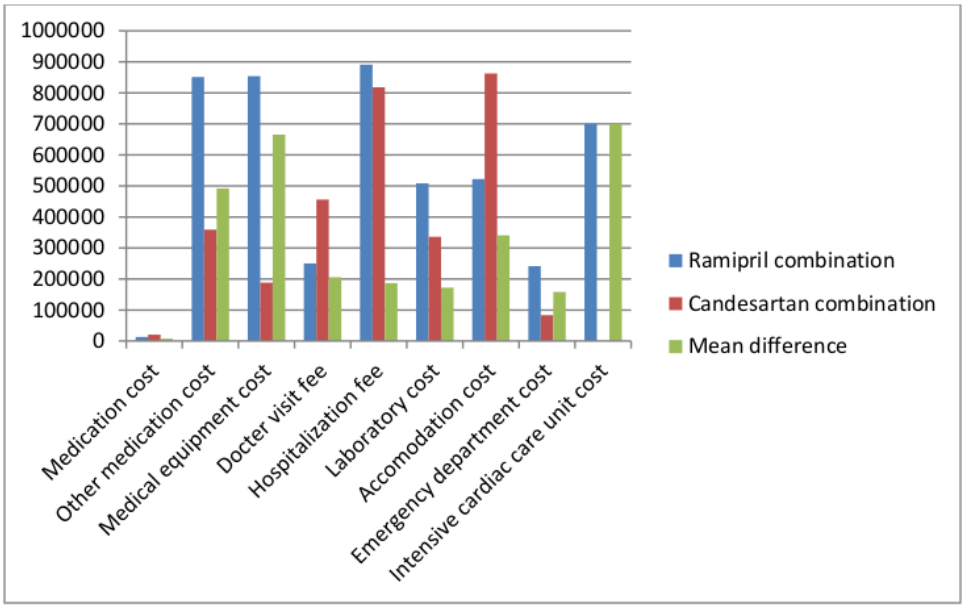

Figure 1. Comparison graph between all study parameter between ramipril and candesartan combination.

Discussion

According to Choi et al. the incidence of heart failure is more common in men than women, this is related to lifestyle and other risk factor such as smoking and alcohol consumption.[19] Study

by Mosterd et al. age is one of the factors that influence the incidence of heart failure, older age contribute as a factor for developing heart failure by 10% if it is not matched by a healthy lifestyle.[7] Lawson et al. study >85% of patients with heart failure have comorbidities or comorbidities.[20] The World Health Organization (WHO) notes that 17.9 million people worldwide die from cardiovascular disorders with a percentage of 31% of deaths worldwide.[10]

The cost of each patient varies due to the length of time the patient has been inpatient and treatment. The results obtained are similar to Rahmawati et al. research which states that the use of candesartan drugs is more efficient than the use of other medications for treatment in patients with heart failure.[21]

Another study conducted by Schadlich et al. Regarding coss effectiveness of ramipril in patients with heart failure in myocardial infarction in Germany, there is a variation in the value of ramipril that is 2500 to 8300 deutschmarks (DM) per life-year gained and ramipril shows a favourable cost incremental cost-effectiveness ratio in heart failure treatment compared to placebo.[22]

Another study conducted in Indonesia by Baroroh et al. Regarding the cost-effectiveness of candesartan compared to the combination of candesartan amlodipine in patients with hypertension in the setting of an outpatient clinic, it shows that candesartan alone has a better cost-effectiveness of IDR 580,993 in one month of treatment.[23]

Conclusion

We concluded there was no significant difference between the average direct medical costs in patients using the ramipril combination compared with the candesartan combination. Economically the candesartan combination drug saves more costs (IDR 3,099,088) compared to the ramipril combination (IDR 4,197,011) with an average difference in cost of Rp. 1,097,923.

Conflict of interest

The authors declare there is no conflict of interest regarding publication of current study.

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The current study doesn't receive any specific grant from government or any private sectors.

Ethical statement

This study was conducted after obtaining ethical clearance from director of West Nusa Tenggara Regional Hospital, with ethical clearance reference number number 070/2037/RSUDP NTB.

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39	www.theplantbasedeater.com Internet Source	<1%
40	Eristina, T M Andayani, R A Oetari. "Direct medical cost and utility analysis of diabetics	<1%

outpatient at Karanganyar public hospital", IOP Conference Series: Materials Science and Engineering, 2017
Publication

41 Mark A. Hlatky, Paul A. Heidenreich. "The Year in Epidemiology, Health Services Research, and Outcomes Research", Journal of the American College of Cardiology, 2011 <1%
Publication

42 Mi-Hyang Jung, Hack-Lyoung Kim, Jae Hyuk Choi, Sunki Lee et al. "Heart failure awareness in the Korean general population: Results from the nationwide survey", PLOS ONE, 2019 <1%
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43 Submitted to University of Technology, Sydney <1%
Student Paper

44 Torbjørn Omland. "Advances in congestive heart failure management in the intensive care unit: B-type natriuretic peptides in evaluation of acute heart failure", Critical Care Medicine, 2008 <1%
Publication

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Gmail **Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>**

revision required (Bali Med J 1871)

6 messages

Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> Sat, May 23, 2020 at 8:41 AM
To: nuqi.gra@gmail.com

Dear Authors,
Thank you for submitting your article entitled: **"Comparison of direct medical cost between ramipril and candesartan in hospitalized acute decompensated heart failure at West Nusa Tenggara Regional Hospital"**

Based on our author guidelines, Your article fulfilled the minimal required structure,
https://www.balimedicaljournal.org/index.php/bmj/pages/view/authorguidlines
In order to have a better-structured article, we suggest you edit based on a checklist and the collection in our archive (https://www.balimedicaljournal.org/index.php/bmj/issue/archive).

According to the new International regulation, please fulfill the requirements below:
1. Please include Ethical clearance number/statement at the end of the manuscript if the bacteria were collected from clinical isolates (**confirmed**).
2. Please state your conflict of interest in the paper. (**unconfirmed**)
3. Please state the funding (if any) in your paper. (**unconfirmed**)
4. Please state each author's contribution. (**unconfirmed**)
5. Based on our proofreading application, we detected184 critical grammatical errors.

According to our initial review, your article needs Minor Revision. Please revise your article and send it back to us in **7 days**

Please find the attached revision note for your manuscript and do not forget to full fill the icjme author list and contributor list

Thank you for trusting us with your hard work and we are looking forward to your response.

Warm regards,

Executive Editor BaliMedJ

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3 attachments

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Contribution Details (3).docx
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nurul qiyaam <nuqi.gra@gmail.com> Mon, May 25, 2020 at 2.32 PM
To: Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Dear Editoria Team of Bali Med J

Thank you for your advice revision, soon I will sent the revision along with ICJME author list and contributor list

Best regards
Nurul Qiyaam
[Quoted text hidden]

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nurul qiyaam <nuqi.gra@gmail.com> Mon, Jun 8, 2020 at 11:02 AM
To: Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Dear Editoria Team of Bali Med J
I have sent the revision trough out the system, I also attached the revised manuscript along with the ICJME author list and contributor list in the attached ment below

Warm and regards

Nurul Qiyaam
[Quoted text hidden]

3 attachments

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Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> Tue, Jun 9, 2020 at 10:33 AM
To: nurul qiyaam <nuqi.gra@gmail.com>

Dear Author

We had received your full revision

Soon we will come back for final decision

Best and regards
Managing Editor Bali Med J
[Quoted text hidden]

Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> Wed, Jun 24, 2020 at 2:12 PM
To: nurul qiyaam <nuqi.gra@gmail.com>

Dear author: please find the attached acceptance letter and invoice billing for your manuscript

Letter of Acceptance
24 June 2020

Dear: Nurul Qiyaam*, Baiq Leny Nopitasari, Cyntiya Rahmawati, Baiq Nurbaety, Emasiska Ajeng Pratiwi
Pharmachy Department, Faculty of Medicine, Universitas Muhammadiyah Mataram, Indonesia
*Corresponding email author: nuqi.gra@gmail.com
I am very excited to accept your paper entitled:
"Comparison of direct medical cost between ramipril and candesartan in hospitalized acute decompensated heart failure at West Nusa Tenggara Regional Hospital."
Your paper will be published in the issue of Vol. 9 Number 2, 2020.
http://dx.doi.org/10.15562/bmj.v9i2.1871
(Online Link: http://balimedicaljournal.org/index.php/bmj/article/view/1871).
And it usually takes 2 to 4 months for your journal to show up at Google Scholar, but if you need it fast, you may add it up manually using your google scholar account. The CrossRef and DOI number usually activate in 3 until 6 months.
Bali Medical Journal is indexed in Web of Sciences (Thomson Reuters) and many other indexing organization: http://balimedicaljournal.org/index.php/bmj/pages/view/indexing

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25. UDL-Edge (Malaysia)

Please do not hesitate to contact us if you need anything. It has been a pleasure for us to proofread and edit your work, and we are looking forward to your colleagues and your other papers in the near future

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2 attachments

38947_612 Letter of Acceptance 1871 Nurul Qiyaam.pdf
260K

INV2-MH39-EBSC-6RCR-BQ98.pdf
30K

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nurul qiyaam <nuqi.gra@gmail.com> Sat, Jun 27, 2020 at 12:20 AM
To: Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Dear Editorial Board Member of Bali Med J

Thank you for the acceptance letter, its an honor to be published in your journal

Please find the attached payment proof for my manuscript

Warm regards
Nurul Qiyaam

Pada tanggal Rab, 28 Sep 2022 pukul 22.47 Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> menulis:
>
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1871-bmj-payment.jpeg
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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	The study design has already indicated in the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	The abstract has presented informative and balanced summary of the study
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	The background of the study has been clearly explained.
Objectives	3	State specific objectives, including any prespecified hypotheses	The objective(s) of the study clearly stated in the introduction section
Methods			
Study design	4	Present key elements of study design early in the paper	Clearly presented in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	The setting, location, and relevant dates has been described
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	The inclusion and exclusion criteria not clearly described.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	The outcome of the study has been stated in the paper
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Clearly described in the paper
Bias	9	Describe any efforts to address potential sources of bias	Not described
Study size	10	Explain how the study size was arrived at	Not described in the paper
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Data analysis has been clearly described using descriptive, independent t-test or mann whitney test
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	The statistical method has been described
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	Not explained in the paper
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	Described well in the result section

		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Not described
		(c) Consider use of a flow diagram	Not described
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	The characteristics has been described in table 1
		(b) Indicate number of participants with missing data for each variable of interest	Not explicitly stated, but can be inferred
Outcome data	15*	Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Descriptive method with spearman test, and chi-square test.
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	All analysis performed has been well presented
Discussion			
Key results	18	Summarise key results with reference to study objectives	Well described
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	The limitation not stated at the discussion section
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	The interpretation of the results obtained has been carefully interpreted with comparison of results of similar studies
Generalisability	21	Discuss the generalisability (external validity) of the study results	Not clearly described
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Not described

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

In order to make current manuscript better we advice the following revision

1. Please not use all capital in Running title
2. Please divide the abstract into intro, method, result, and conclusion.
3. Kindly describe the aim of the study at the introduction section
4. Kindly describe the rationale of the study at the introduction section (why we have to evaluate cost effectiveness between Ramipril and candesartan since bot are very simlliar medication belong to ACE-I and ARB group)
5. Describe the inclusion and exclusion criteria at the method section.
6. Make sure to add limitation of the study at the end of discussion section.
7. Kindly double check your manuscript all the reference must be cited in the text or vice versa.
8. Any comparison regarding simmiliar study must be added at the discussion section, may be any comparison from Indonesia regarding cost effectiveness of cadesartan and ramipril
9. Make sure to add conflict of interest, funding, acknowledgement, and ethical aspect of the study. Since those kind of thing are very important in journal article.

Journal:

1. Thomas MC. Diuretics, ACE inhibitors and NSAIDs – the triple whammy. Med J Aust. 2000;172:184–185.
2. Guilbert TW, Morgan WJ, Zeiger RS, Mauger DT, Boehmer SJ, Szefler SJ, et al. Long-term inhaled corticosteroids in preschool children at high risk for asthma. N Engl J Med. 2006;354:1985–97.

Sitasi WEB:

1. Thomas ABC. Vancouver reference style [Internet]. Oaktown (ON): University of Oaktown, Department of Science; 2007 Nov 1 [updated 2008 Jan 11; cited 2008 Feb 19]. Available from: http://www.org-name.org

Chapter di dalam buku:

1. Bjork CE Jr, McLeod RD. Formatting citations. In: Laurent B 3rd, Cool JR, editors. A history of citations and references. 5th ed. Geneva (Switzerland): Tangelo Press; 2006. p. 93-7.

Buku utuh:

1. Thomas ABC, editor. Vancouver reference style: a history. New York: Z&E Publishers; 2007. 582 p.

Author response to reviewer comment:

In order to make current manuscript better we advice the following revision

1. Please not use all capital in Running title
   Response: has been revised in the manuscript
2. Please divide the abstract into intro, method, result, and conclusion.
   Response: has been revised in manuscript revision
3. Kindly describe the aim of the study at the introduction section
   Response: Has been added at the end of introduction section, please kindly check our revision manuscript (The study aims to determine and compare the average efficiency of direct medical costs between ramipril and candesartan combination drug in hospitalized heart failure patients with a payer perspective at the West Nusa Tenggara Regional General Hospital, Mataram, Indonesia)
4. Kindly describe the rationale of the study at the introduction section (why we have to evaluate cost effectiveness between Ramipril and candesartan since bot are very simillar medication belong to ACE-I and ARB group).
   Response: The average gross total cost of using ramipril combination was Rp. 4,197,011 while the average total cost of using candesartan combination was Rp. 3,099,088. These results indicate there are savings in the average total cost of treatment for heart failure using candesartan that is Rp. 1,097,923. (since there is gap discrepancies between the two medication, and both of medication are commonly prescribed in the setting of in patient and outpatient clinics, price gap might be further analyzed between the two medication
5. Describe the inclusion and exclusion criteria at the method section.
   Response: Our inclusion data was inpatient with acute decompensated heart failure with candesartan and ramipril and candesartan medication, and detailed about medication course during hospitalization
6. Make sure to add limitation of the study at the end of discussion section.
   Response: with all do respect, our study only want to compare the direct medical cost between ramipril and candesartan in our hospital, and we would not described any limitation at the end of discussion. We has been make a conclusion no significant difference between ramipril and candesartan medication in terms of in hospital direct cost. I hope the reviewer will understand our reasoning.
7. Kindly double check your manuscript all the reference must be cited in the text or vice versa.
   Response: thank you for your comment, we have bee double check our manuscript, so all the citation in text appear in the reference section
8. Any comparison regarding simmiliar study must be added at the discussion section, may be any comparison from Indonesia regarding cost effectiveness of cadesartan and ramipril
1. Reponse: Since our study comparing medical cost of ramipril and candesartan in Indonesia, of course we compare our study to another simmiliar study in Indonesia: Rahmawati C, Nurwahyuni A. Analysis of the Minimal Cost of Antihypertensive Medication between the Combination of Ramipril-Spironolactone with Valsartan in Congestive Heart Failure Patients at XY Hospital in Jakarta in 2014. Journal of Indonesian Health Economics. 2017:1(4):191-200. Please see discussion section for the revision (The cost of each patient varies due to the length of time the patient has been inpatient and treatment. The results obtained are similar to Rahmawati et al. research which states that the use of candesartan drugs is more efficient than the use of other medications for treatment in patients with heart failure)

9. Make sure to add conflict of interest, funding, acknowledgement, and ethical aspect of the study. Since those kind of thing are very important in journal article.
   Response: revised done, please see at the end of conclusion section.