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Cohort Study

Peak oxygen uptake and metabolic equivalents explained by six-minute walk test: A prospective observational study in predicting heart failure patient readmission

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ABSTRACT

Background: Current statistics indicate that the overall cost of heart disease exceeds IDR 6.67 trillion per year. This growing concern has led researches on heart failure patient readmission in developing countries, and opened discussions on tactics to suppress hospital readmission rates. This study assesses the potential of VO2max and METs obtained from the 6-min walk test in predicting heart failure patient readmission.

Methods: This seven-month prospective cohort study recruited patients with heart failure which then underwent the 6-min walk test before discharged. Walking distance, estimated VO2 max, and METs were calculated and recorded. Patients were then followed-up for 3 months to track readmissions under the same diagnosis during the research period. The correlation between VO2max and METs with patient readmission was assessed.

Results: A total of 93 samples were included in this study. The results demonstrated that VO2max and METs correlate with incidence of heart failure readmission $\leq$30 days post discharge, with VO2max showing a moderate ability to predict patient readmissions with a cut-off of 14.5 mL/kgBW/minute ($C = 0.750$, $p < 0.001$), while METs showed a weak ability to predict readmissions with a cut-off of 3.8 ($C = 0.743$, $p < 0.001$).

Conclusions: VO2 max and METs values acquired from 6MWT examination correlates with heart failure patient readmission $\leq$30 days. This knowledge can be used to prevent increased readmission rates, therefore hoping that it will be able to reduce the burden of treatment costs on heart failure patients.

1. Introduction

Heart failure is a clinical syndrome characterized by specific symptoms such as shortness of breath, ankle swelling, and fatigue, which are accompanied by signs of increased jugular venous pressure and rales heard over the lung bases as a result of structural and/or functional heart abnormalities [1]. In Southeast Asia alone, 9 million people were reported to suffer from heart failure with a prevalence of 6.7% in Malaysia and 4.5% in Singapore [2]. Taking into account the rapid development of current medical strategies, technological advances and improved medical services, the mortality rate of acute heart failure has shown to be decreasing. However, in disease progression, patients with heart failure are highly vulnerable to hospital readmission. Hospital readmissions or re-hospitalization of patients with heart failure are extremely common, that it has become a growing worldwide concern [3].

Although the amount of hospital costs incurred for heart failure is not clearly stated in Indonesia, current statistics indicate that the overall cost of heart disease incurred by the Health Insurance Administration exceeds IDR 6.67 trillion per year [4]. 856 patients with heart failure were observed in three studies: Diuretic Optimum Strategy Evaluation in Acute Heart Failure (DOSE AHF), Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS HF), Renal Optimization Strategies Evaluation in Acute Heart Failure (ROSE-AHF). The study recorded that 273 patients, almost 32% of patients, needed re-hospitalization and 11 patients died within 31–60 days without being readmitted [5].

With shifts in populations and the epidemiological transition of this

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disease, heart failure hospital readmission has then become a major public health problem, burdening low-middle income countries the most, including Indonesia. Yet, systematic proof of its present burden as stated before is quite scarce in quantity. As a consequence, several current conclusions with respect to the present burden of this disease's situation are based on extrapolations from studies carried out in high income countries, which may not be applicable in countries with minimal resources [6].

This growing concern has led researches on heart failure patient readmission in developing, low-middle income countries, and opened discussions on tactics to suppress hospital readmission rates. Assessment of functional capacity before patient discharge can help identify a patients' risk for readmission. Assessing functional capacity is a key step in the field of cardiac rehabilitation, which contributes to reducing cardiovascular events and re-hospitalization of patients with heart failure [7].

Functional capacity is an individual's ability to carry out daily activities that include physical, psychological, social, and spiritual activities. The functional capacity of a heart failure patient is affected by the amount of maximum oxygen demand. Heart failure patients experience a decrease in cardiac output which results in reduced oxygen supply in the body. The lower a person's functional capacity, the more the amount of maximum oxygen a person is required to uptake in order to easily carry out daily activities [8].

A simple, cost-effective, yet accurate method to measure a patient's functional capacity is by conducting a 6-min walk test (6MWT), a method suitable for even health facilities with the most limited resources [9]. The 6-min walk test (6MWT) is proved to adequately reflect the level of functional capacity in completing daily activities [10]. The 6MWT is the most frequently used cardiac training test not only used to assess a person's functional capacity, but also used to assess a patient's therapeutic response, and is even useful in predicting morbidity and mortality [9].

Data shows that values such as peak oxygen uptake (VO2max) and metabolic equivalents (METs) obtained from the 6-min walk test (6MWT) have high prognostic value in predicting cardiac morbidity and mortality in patients with congestive heart failure [7]. This makes VO2max and METs become both highly essential parameters which may be potentially used as patient re-hospitalization risk predictors. VO2max is a good indicator for measuring a person's cardiorespiratory endurance, which is the maximum amount of oxygen that can be consumed during intense physical activity until fatigue finally occurs [11]. The higher the value, the better the cardiorespiratory endurance [12], this affects one's physical fitness. Therefore, the higher VO2max, the better a person's fitness will be, which will help the individual to perform daily activities optimally. As for metabolic equivalents (METs), it is a physiological concept that is currently widely used as a procedure to determine the amount of energy during physical activity, which also determines an individual's fitness state [13].

This study aims to analyze peak oxygen uptake (VO2max) and metabolic equivalents (METs) obtained from the 6-min walk test as predictors for heart failure patient readmission in Makassar, Indonesia.

2. Methods

This prospective cohort study was conducted at Wahidin Sudirohusodo Hospital's Cardiac Center over a period of seven months, from June 2019 to December 2019, after obtaining clearance from the Institutional Ethical Committee. We analyzed the patient's VO2max and METs results which we obtained after the patients went through the 6-min walk test as the independent variables and its effect on patient readmission as the dependent variable. Sample collection was conducted with a purposive sampling method. Minimum sample size was determined using the Kelsey's Formula. Inclusion criteria were patients diagnosed with Samples that were included were all hospitalized heart failure patients with an ejection fraction below 40%, aged above 18 years-old, were hemodynamically stable, had no cognitive nor anatomical deficits which may affect walking abilities, and lastly were willing to be included in this study, followed up, and have given consent to all procedures and examinations. Exclusion criteria were decompensated heart failure patients, patients who have undergone interventional procedures with the aim of correcting structural cardiac disorders such as cardiac resynchronization therapy (CRT), coronary artery bypass graft (CABG), and heart valve replacement, as well as patients were not willing to be included in this study or followed up. Patients' data including clinical history, laboratory work-up, and echocardiography results were obtained from patient medical records and hospital computer systems.

All patients then underwent the 6-min walk test 1 day before discharged. The patient's walking distance, estimated VO2 max, and METs were calculated and recorded. Calculations for both VO2 max and METs are stated as follows ([14,15]):

$$\mathbf{VO_2max} = \mathbf{0.03} \times \mathbf{walkingdistance(meter)} + \mathbf{3.98}$$

$$\mathbf{MET_S} = \frac{\mathbf{VO2max}}{\mathbf{3.5}}$$

Demographic characteristics and VO2max were presented in mean ± standard deviation. Walking distance was presented in meters and were divided into three categories; below 200 m, 200–300 m and above 300 m. METs values were classified into three categories as well; below 5, 5–7 and above 7.

Patients were then followed-up for 3 months by telephone and were routinely checked on the hospital's inpatient registration computer system. Readmission or re-hospitalization under the same diagnosis within 30 days, 60 days and 90 days following prior hospitalization was recorded.

Statistical analysis was carried out using SPSS and SAP programs. The correlation between VO2max and METs with patient readmission was assessed using One Way Anova. Cut-off values for VO2max and METs including its sensitivity and specificity were determined using receiver operating characteristic (ROC) curve.

This work has been reported in line with the STROCSS criteria [16] and was approved by the Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University and Dr. Wahidin Sudirohusodo Hospital and is registered on a publicly accessible database, Research Registry (UIN: researchregistry7572) https://www.researchregistry.com/browse-the-registry#home/registrationdetails/61e90afde629477ddc6bc5cb/.

3. Results

The number of samples that met the criteria of this study were 93 samples. Of the total number of samples, a majority were male patients (n = 57; 61.3%). In terms of age, it was found that the mean age of the samples included was 56.1 years, with the youngest aged 27 years-old and the oldest being 82 years-old. The average body weight in this study was 57.4 kg with the lowest body weight being 34 kg and the highest being 75 kg. While the average body height was 159 m with the lowest being 145 m and the highest being 179 m.

Each patient underwent 6MWT examination and their walking distance, VO2max and METs were calculated. Measurement results showed, the average 6 min walking distance (6MWD) is 228.3 m, making most patients having a walking distance within the 200–300 m range (n = 42; 45.2%) (Table 1). The average METs value obtained was 3.9, making most patients having a METs below 5 (n = 64; 68.8%). For patient readmission, the highest number of patients with readmissions was in the ≤30 day category (n = 33; 35.5%). The reasons for readmission in each category can be seen in Table 1. The average value for VO2max was 13.75 ± 6068. Estimated VO2max and ejection fraction values can be seen in Table 2.

VO2max and METs for each readmission group were then analyzed

Table 1
Demographic characteristics, 6MWT parameters and patient readmission observations (categorical variables).

Variable		n	Percentage (%)
Gender	Male	57	61,3%
	Female	36	38,7%
6MWD (m)	<200	33	35,5%
	200–300	42	45,2%
	>300	18	19,4%
METs	<5	64	68,8%
	5–7	26	28,0%
	>7	3	3,2%
Readmission ≤30 days	Yes	33	35,5%
	No	60	64,5%
Readmission 31–60 days	Yes	32	34,4%
	No	61	65,6%
Readmission >60 days	Yes	25	26,9%
	No	68	73,1%
Reasons for Readmission	**Fluid Overload**		
	Readmission ≤30 days	28	30,1%
	Readmission 31–60 days	3	3,2%
	Readmission >60 days	1	1,1%
	Poor Compliance With Therapy		
	Readmission ≤30 days	17	18,3%
	Readmission 31–60 days	6	6,5%
	Readmission >60 days	10	10,8%
	Infection/due to other comorbidities		
	Readmission ≤30 days	8	8,6%
	Readmission 31–60 days	8	8,6%
	Readmission >60 days	9	9,7%

Table 2
Demographic characteristics and 6MWT parameters (numerical variables).

	Minimum	Maximum	Mean	Std. Deviation
Age	27	81	56,11	10,135
Body Weight	34	78	57,41	9056
Body Height	145	178	159,48	6087
Ejection Fraction	15,60	39,92	28,44	8324
VO2max	2,94	35,15	13,75	6068

using the one way ANOVA method. Before conducting this analysis, it was made sure that all data were eligible for this test. Only data for readmissions ≤30 days were normally distributed. While the homogeneity of the three readmission groups met the requirements, but only one readmission group met the requirements for the Post Hoc test which was the ≤30 day readmission group. The results found that out of the three parameters, only one group, readmission within ≤30 days group, showed a significant impact on readmission incidence, while the groups did not show a significant correlation with the readmission incidence. For VO2max and METs, a significant p value of <0.001 was found. (Table 3). This implies that an increase in VO2max and METs values correlates with a decrease in the number of readmission incidents within ≤30 days.

Cut-off values for VO2max and METs were then assessed and

Table 3
Comparison between 6MWT parameters with hospital readmission.

Variable	Readmission	Homogenity Sig.>0.05	ANOVA Sig.<0.05	Post Hoc
6MWD	≤30 days	0.749	<0.001	<0.001
VO2max	31–60 days	0.433	0.22[a]	NS[a]
	>60 days	0.543	0.63[a]	NS[a]
	≤30 days	0.542	<0.001	0.001
	31–60 days	0.771	0.24[a]	NS[a]
	>60 days	0.366	0.547[a]	NS[a]
METs	≤30 days	0.629	<0.001	0.001
	31–60 days	0.869	0.22[a]	NS[a]
	>60 days	0.668	0.39[a]	NS[a]

[a] NS = not significant.

VO2max in this study showed that the level of sensitivity and specificity was moderate in predicting the incidence of readmissions ≤30 days (Fig. 1) with an AUC value of 0.750 ($p < 0.001$) (Table 4) while METs showed weak sensitivity and specificity in predicting the incidence of readmissions ≤30 days (Fig. 2) with an AUC value of 0.599 ($p < 0.001$) (Table 4). The cut-off value for VO2max is 14.5 mm/kgBW/minute, while for METs is 3.8.

4. Discussion

This study focused on discovering the potential use of peak oxygen uptake (VO2max) and metabolic equivalents (METs) obtained from the 6-min walk test as predictors for heart failure patient readmission in a tertiary healthcare setting in Indonesia. The results demonstrated that VO2max and METs correlate with incidence of heart failure readmission ≤30 days post discharge. It is implied that an increase in VO2max and METs values correlates with a decrease in the number of readmission incidents.

Regarding VO2max, the results showed that VO2max had a moderate yet significant predictive ability to predict patient readmissions ≤30 days ($C = 0.750$, $p < 0.001$). This implies that VO2max is a parameter that has moderate sensitivity and specificity in predicting the incidence of readmissions ≤30 days, making it a parameter that has sufficiently optimal abilities in predicting the incidence of readmission in patients with heart failure. VO2max is showed to be a better predictor of heart failure patient readmission, especially during a longer follow-up period [17]. In other studies, VO2max is said to be able to predict the cause for re-hospitalization or even death in heart failure patients ($p < 0.001$) using a 95% confidence interval [18]. Other variables that affect VO2max are mentioned in other studies for instance, body height is declared to correlate to VO2max ($r2 = 0.381$) [19]. Body weight is also said to affect VO2max. A study found that the lower the patient's body weight is, the better VO2max value obtained. Body weight is then concluded to affect VO2max by 4.356% [20].

Aside from these findings, it was also found that METs had a weak yet significant ability to predict readmissions ≤30 days ($C = 0.743$, $p < 0.001$). This implies that METs is a parameter that has weak sensitivity and specificity in predicting the incidence of readmission ≤30 days. The cut-off value for METs in predicting readmissions ≤30 days was 3.8. Other studies discussed the correlation between the METs value and the

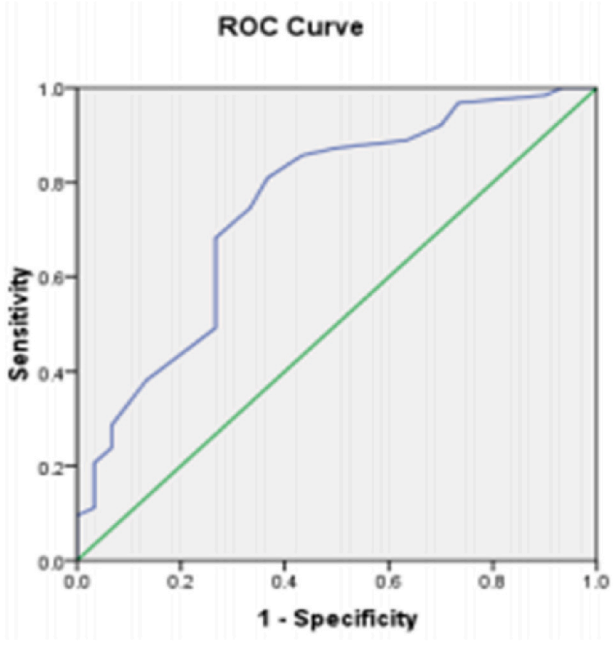

Fig. 1. ROC Curve for VO2max on Patient Readmission Incidence ≤30 days.

Table 4
VO2max and METs as a parameter of readmission incidence within ≤30 days.

Variable	AUC (C)	p	95% C·I.		Cut-Off Value
			Lower Bound	Upper Bound	
VO2max	0.750	<0.001	0.640	0.859	14.5
METs	0.599	<0.001	0.436	0.761	3.8

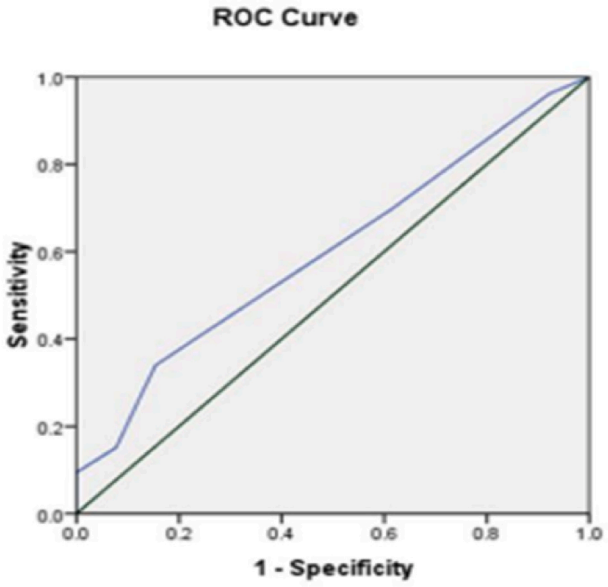

Fig. 2. Roc curve for METs on patient readmission incidence ≤30 Days.

readmission of heart failure patients, and found it to be about 30% [21]. A study which included 179 heart failure patients aged 33 to 88 years-old has used METs to predict patient readmission and obtained a METs value below 3.3 up to 5.3 to be fairly suitable [22]. The results of this study are in line with this said research, by obtaining a cut-off value of 3.8 for METs in predicting readmissions in ≤30 days. METs values obtained for women aged 25–54 years in Bogor, Indonesia, using the GPAQ tool mostly tends to over-estimate with an average METs value of 4.271 ± 2.874 [23]. Myers et al. demonstrated that each 1 metabolic equivalent (METs) increase in functional capacity reduced 12% risk of death in cardiovascular patients [24].

There are a number of researches that contradict our findings such as one prospective cohort study conducted in USA which concluded improved functional or exercise capacity was not associated with improvements in cardiac function at rest or with stress [25], therefore it is difficult to say that either VO2max or METs even hold a significant value in predicting patient outcomes.

This research has its limitations which necessarily inform interpretation of the results found in this study. This study is a single-center, observational study with a relatively small sample size and short-term follow-up period, therefore it is unsure whether these results do indeed reflect the same in conditions elsewhere. But our findings has been found potentially applicable and very useful for low-resource settings.

5. Conclusion

VO_2 max and METs values acquired from 6MWT examination correlates with heart failure patient readmission ≤30 days. The results showing that for patients with heart failure, the lower the VO2max, with a cut-off of 14.5 mL/kgBW/minute, the higher the risk of readmissions within 30 days. Also, the lower the METs value with a cut-off of 3.8, the higher the risk of readmissions within 30 days. Knowing the cut-off of VO2max and METs can be used as a reference to create a comprehensive treatment flow for heart failure patients to prevent increased readmission rates, therefore hoping that it will be able to reduce the burden of treatment costs on heart failure patients. Further research is then much needed before adapted into clinical practice.

Ethical approval and consent to participate

The study was approved by the Institutional Ethics Committee of Biomedical Research in Humans of Faculty of Medicine, Hasanuddin University and Dr. Wahidin Sudirohusodo Hospital, Makassar. Informed consent was obtained from all individual participants included in the study.

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Author statement

Muzakkir Amir – Data collection and interpretation, editing of the manuscript, literature review.
Peter Kabo - Data collection and interpretation, editing of the manuscript.
Idar Mappangara – Data collection, literature review.
Zaenab Djafar - Data collection, literature review.
Andi Alfian Zainuddin - Editing of the manuscript, literature review.
Melda Warliani - Editing of the manuscript, literature review.
Asni Mustafa – Drafting of the manuscript, Editing of the manuscript.

Consent

Informed consent was obtained from all individual participants included in the study.

Registration of research studies

This study has been registered on Research Registry with registration number researchregistry7572 (https://www.researchregistry.com/browse-the-registry#home/registrationdetails/61e90afde629477ddc6bc5cb/).

Guarantor

Muzakkir Amir.
Peter Kabo.
Idar Mappangara.
Zaenab Djafar.
Andi Alfian Zainuddin.
Melda Warliani.
Asni Mustafa.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

All of the authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103652.

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