Lactate Kinetics Analysis Related to Low-Intensity Resistance Exercise: Randomized Control Trial

Abstract

Background: Virtual reality exercise (VRE) has been proven to overcome fatigue in hospital setting. However, no study analyzes how lactate, as fatigue biomarker, is affected by VRE. This study aims to analyze lactate kinetics as an exercise response after conventional multimodal exercise and virtual reality exercise (VRE) in hospitalized geriatric.

Methods: Sixty subjects were randomized into control and VRE group. VRE is given as adjuvant therapy to conventional multimodal exercise. Peripheral blood lactate was taken immediately before and after low-intensity resistance exercise at baseline and one week after. The comparison of lactate changes between groups was analyzed using the Mann-Whitney test.

Results: There is no difference in post-exercise lactate at day 1 and 7 between the two groups. Lactate concentrations reduce after low-intensity resistance exercise in subjects with high resting lactate -0,4 (-0,45 – 0,5) but remain escalated in the normal group 0,1 (-1 - 3,9) at day 1, $p < 0,001$.

Conclusion: There is no significant effect of VRE as an adjuvant therapy on post-exercise lactate. The next study needs to consider elevated baseline lactate to reduce bias. Also, the intensity of resistance exercise needs to be improved to high intensity through individual exercise test.

Keywords: Exercise, Geriatric, Lactate, Virtual Reality

Introduction

Advanced technology development of Virtual Reality (VR) has brought it from community utilization into the hospital setting.[1] VR has been used in a broad spectrum of diseases and health conditions as part of prevention, promotive, curative, and rehabilitation strategies.[2,3,4] Adaptation of VR in specific populations, such as children and the elderly, makes it more popular as an advanced technology alternative in clinical settings.[3,5] VR allows patients and medical team explore beyond hospital walls, thus enriching the medical management.

Fatigue is a clinical symptom that commonly found in the elderly. It brings geriatric syndromes and lead to disability.[6] Fatigue has been proven to be effectively managed by VR. VR effects on fatigue were dramatic and satisfaction. Fatigue was significantly decreased in VR group while almost no changes were observed in control group.[7,8] Few of the studies even proved that fatigue improves within 2 days after VR.[9]

VR activity had to be adjusted to the targeted disease or health condition. Actually, the pathophysiology of fatigue involves two main organs: brain and muscle.[10] Some biomarkers are also involved in fatigue, the most important are serotonin and lactate.[10,11] Previous study might be addressed VR intervention in one of organs and biomarkers involved in fatigue. VR that targeting brain and serotonin was designed as distraction intervention during unpleasant protocol such as chemotherapy or hemodialysis.[7,8] The distraction hopefully could divert subject's focus and enhance copying mechanism. VR that targeting muscle and lactate was designed as virtual reality exercise (VRE).[9] As principle of exercise, VRE must induced physical activity. VRE must improve muscle performance, qualitative and quantitative.

Unfortunately, all of previous VR studies measure fatigue using scale or questionnaires, could not directly prove the involvement of those organs and biomarkers.[1] This study aims to analyze lactate kinetics as an exercise response after conventional multimodal exercise and VRE in hospitalized geriatric.

METHODS

Subject

Sixty geriatric patients were recruited during their hospitalization at RSUPN Dr. Cipto Mangunkusumo (RSCM). As per description, subjects categorized as geriatric patients are not only because their age is more than 59 years old, but also because they have multiple comorbidities and geriatric syndromes. Subject was included if they able to communicate and their manual muscle test results are minimal 3. They were excluded if they had VR-sickness, severe psychosocial problem, and severe caregiver burden. They considered drop out if they were discharged, worsen clinical condition and death before finishing the research protocol.

Study design

Subjects were randomized into control and intervention group. Both groups get conventional multimodal exercise, the intervention group gets additional VRE as adjuvant therapy. Due to the nature of the exercise, the research was single blind. This study was registered in Health Research Ethical Committee, Faculty of Medicine, Universitas Indonesia, RSCM. Number of ethical approval letter is ND-47/UN2.F1/ETIK/PPM.00.02/2025.

Conventional Multimodal Exercise

Exercise protocol that is given during hospitalization had been standardized and approved as RSCM clinical practice guideline. Exercise prescription was given after the subjects going through functional assessment conducted by physiatrists. The prescription described the frequency, intensity, interval, and type of exercise that is adjusted to subject's clinical condition. Each subject could have more than one type of exercise, but the most common combination consists of breathing, resistance, and aerobic exercises.

Virtual Reality Exercise

VRAGMENT software was administered as VRE to the intervention group. VRAGMENT is an abbreviation of Virtual Reality for Cognitive and Dementia. It was innovated in 2022 by

Universitas Indonesia through the collaboration of Indonesian Medical Education and Research Institute (IMERI), Physical Medicine & Rehabilitation (PM&R) Department and Industrial Engineering Department. VRAGMENT runs on the Oculus Meta Quest 2®. In VRAGMENT, subjects should make phone call, groceries and making payment. Those activities in virtual environment initiated real movement of neck, trunk, arms, and legs.

Lactate Kinetic Measurement

Capillary blood lactate sample was examined using StatStrip® from Nova Biomedical. Measurement range of StatStrip® is 0,3 – 20,0 mmol/L. Lactate examination conducts at baseline and one week after the exercise program. Blood samples were collected immediately pre and post-standardized low-intensity resistance training.

Statistical Analysis

The data collected were analyzed using SPSS statistics (version 24.0). Demography and clinical data were presented in mean (standard deviation), or median (minimum – maximum), or proportion in percentage. The difference of lactate kinetics between group was analyzed using Mann-Whitney test.

RESULTS

Subject's characteristics between groups were homogenous. Mean age of subjects was 68 years, and most of them were male. Main diagnosis proportion was almost same between both groups, as described in table 1. The five most common diagnoses in both groups were Neoplasm, Hepatitis, Pneumonia, Cholangitis, and Gastroenteritis.

Table 1. Subject's Characteristic

	Control (n = 29)	VRE (n=32)	p
Age, $\overline{x}$(SD)	68,31 (5,90)	68,06 (5,53)	0,866
Gender			0,723
Male, n (%)	15 (51,7)	18 (56,3)	
Main Diagnosis, n (%)			0,581
Hepatitis	7 (24,1)	2 (22,2)	
Pneumonia	4 (13,8)	5 (15,6)	
Cellulites	2 (6,9)	2 (6,3)	
Neoplasm	8 (27,6)	11 (34,4)	
SLE	0	1 (3,1)	
Cholangitis	4 (13,8)	5 (15,6)	
Gastroenteritis	3 (10,3)	2 (6,3)	
Fracture	0	2 (6,3)	
Nephrolithiasis	0	1 (3,1)	
Heart Failure	1 (3,4)	1 (3,1)	

VRE = Virtual Reality Exergame

There is no difference in post-exercise lactate in day 1 and 7 between groups, as describe in Table 2.

Table 2. Post-Exercise Lactate Between Study Groups

Post-Exercise Lactate	Control	VRE	p
Day 1	1,6 (0,6 -3,3)	1,5 (0,6 – 4,2)	0,882
Day 7	1,4 (0,4 – 3,6)	1,6 (0,6 -5,5)	0,123
Δ Day 1 to 7	0,0 (-1,5 – 1,9)	0,0 (-1,5 – 2,7)	0,923

Δ Day 1 to 7 = Post-Exercise lactate Day 1 - Post-Exercise lactate Day

The pattern pre and post exercise lactate at day 1 and 7 was described in figure 1S. Higher post-exercise lactate than pre-exercise was found only in VRE group at Day 7.

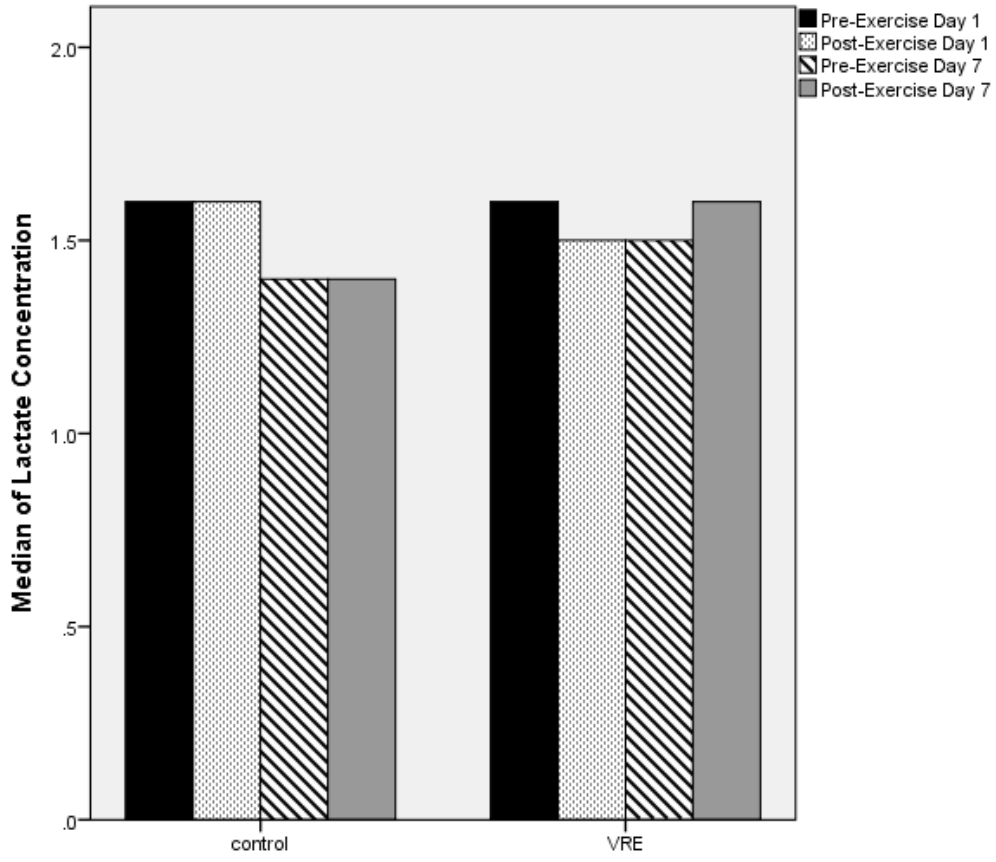

Figure 1. Pre and Post-exercise lactate between control and VRE group in day 1 and day 7.

An analytical study of the effect of pre-exercise elevated lactate is presented in Table 2. There was a significant difference of post-exercise lactate between subjects with normal and elevated pre-exercise lactate at day 1.

Table 3. Post-exercise lactate based on baseline resting lactate concentration at Day 1

Post- Exercise Lactate	Resting Lactate Concentration at Day 1		p
	Normal	Elevated	
Day 1	1,3 (0,6 – 4,2)	2,3 (0,6 – 3,6)	0,001*
Day 7	1,3 (0,4 – 3,9)	1,7 (0,6 – 5,5)	0,124
Δ Day 1 to 7	0,0 (-1,5 – 1,4)	0,1 (-1,5 – 2,7)	0,205

Δ Day 1 to 7 = Post-Exercise lactate Day 1 - Post-Exercise lactate Day 7. * shows statistically significant, p<0,05.

As described in Figure 2, if we look deeper in those subjects with elevated resting lactate at Day 1, both the control and the VRE groups showed a consistent decrease in post-exercise

lactate levels in Day 7 compare to Day 1. The decreased in VRE group seemed to be lower than the control group.

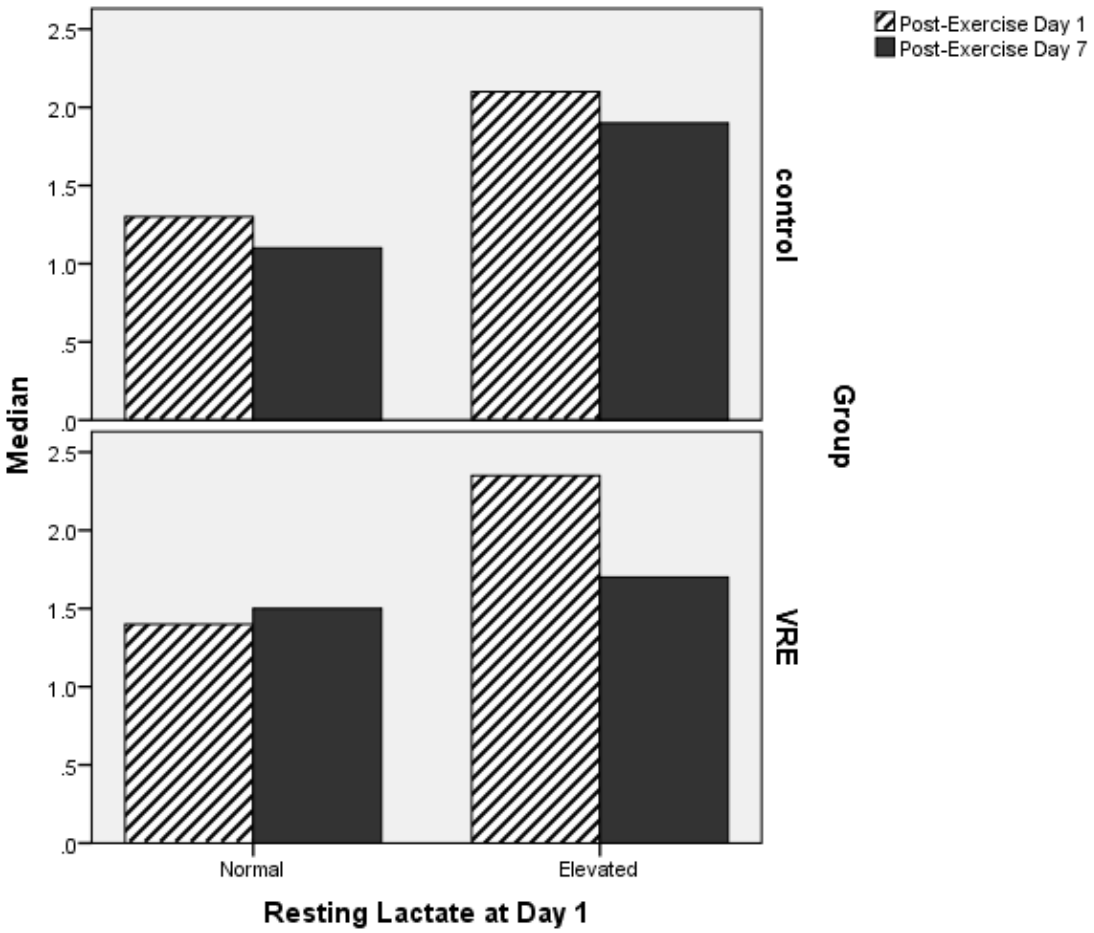

Figure 2. Post-exercise lactate between control and VRE group in day 1 and day 7.

DISCUSSION

This study did not demonstrate the significance of the VRE effects on lactate kinetics (Table 2.). However, this study could describe the lactate kinetics of conventional training and VRE, particularly in the subgroup with elevated resting lactate levels on day 1 (Table 3. and Figure 2.). The decrease in post-exercise lactate on day 7 compared to day 1 indicates that the subjects were becoming more trained, and muscle performance was improving.

Previous study had proven that routine exercise with fixed load, after a certain period, does not statistically influence resting blood lactate concentrations; however, it might decrease the post-exercise lactate concentrations.[12] In that study, the Standardized Mean Difference (SMD) was 0,73 mmol/L decreased from baseline. That is obviously different from this study, which remained unchanged. The difference is most likely caused by the relatively short observation interval in this study, which is 1 week, while in the previous study it was 12 weeks.

Another factor that may cause lactate not to change within 1 week, is an acute lactate response that does not align with the physiological pattern. Physiologically, the average concentration of blood lactate after resistance training increases compared to baseline, with a sequential average of 0.94(0.38) to 1.58(0.54) mmol/L.[13] In this study, the physiological responses were only observed in the intervention group during the evaluation period, as shown in Figure 1.

This may be caused by the symptom-limited resistance exercise methods that was applied to the subjects. In this method, exercise would be terminated when the subject was fatigue and cannot continue the exercise. In normal or trained subjects, this condition would occur when the lactate threshold (LT) is exceeded,[14] leading to fatigue. In this study, the subjects had various conditions that could affect fatigue. The main diagnoses of subjects were dominated

with infection and inflammatory diseases. Those might lead to premature exercise due to fatigue arising from various uncontrolled factors in this research.[10]

Another possible cause was the disruption of glycogenolysis metabolic function. Glycogenolysis is an anaerobic metabolism process in which glycogen is converted into ATP, occurring in the liver, muscles, and adipose tissue. Previous studies have shown that subjects with glycogenolysis disorders significantly experience an increase in lactate uptake after exercise for several minutes, leading to a decrease in blood lactate levels.[15] In contrast, the control group experiences an increase in lactate production, resulting in higher blood lactate levels. Glycogenolysis impairment can occur due to genetic diseases or increased insulin activity. Insulin stimulates the body to meet its needs through aerobic metabolism, while concurrently increasing Protein Phosphatase I (PPI), which ultimately reduces glycogenolysis. This aerobic metabolism will also increase lactate uptake as one of the fuels for aerobic metabolism.[16] Considering that hepatitis is one of the 5 most common diseases (Table 1.), glycogenolysis disorders in the majority of subjects in this study might had occurred.

This study presents protocol and analysis for single-blinded randomized control trial analyzing the effect of VRE in managing fatigue. Previous studies have proven that VRE was effective in managing fatigue,[1,17] but this study advances for some reasons. The VRE used VRAGMENT, which was designed in Bahasa and Indonesian culture. The groceries in the virtual market were local brands. Payment in the virtual market was also using Indonesian virtual money. Fatigue was measured with lactate, which responded immediately after resistance exercise. This could control the effect of others such as infection and inflammation, that might appear during hospitalization and affect lactate concentration (Table 1). Also, the control group of this study had standard inpatient exercises, not untreated group as previous study. Standard inpatient exercises had proven to manage fatigue.[18] The last

reason was geriatric as the target population. Geriatric already well known prone to fatigue since they had multiple comorbidities.

Lactate kinetics is a concept to simulate models of lactate production and removal from blood. Some factors may induce lactate kinetics, one of them is exercise. After exercise, blood lactate concentration remains improved as glycogenolysis happens, at the beginning of exercise and after aerobic threshold exceeded. Lactate removal as exercise respond could take place as lactate reuptake by muscle to be utilized as aerobic metabolism fuel.[19]

The descriptive data shows that one week of conservative multimodal exercises could reduce post-exercise lactate, Table 2. It may conclude that subjects got used to training and underwent less fatigue than at baseline, though the reduction was not statistically or clinically significant.[12]

On the other hand, the VRE group shows physiological lactate kinetics on day 7, Figure 1. This indicated that the resistance exercise intensity that was performed fulfilled the overload principle. The overload principle refers to the concept of gradually increasing the intensity, duration, or frequency of exercise. This is important to stimulate fitness improvement.[20] Unfortunately, the important finding above did not meet the criteria for statistical and clinical significance. However, the descriptive data suggest that VRE has potential in enhancing conservative exercise to meet the overload exercise principle.

Since lactate concentration in this study is still affected by elevated resting lactate (Table 3 and Figure 3), the next study needs to consider elevated baseline lactate to reduce bias. Also, the intensity of resistance exercise needs to be improved to high intensity through an individual exercise test.

Conflicts of Interest

The authors confirm no conflict of interest in this study

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