Effect of Diet, Medication, Physical Activity on Glycemic Control of Type-2 Diabetes Mellitus Patients in Makassar City

Sheinni Paradise*, M. Alimin Maidin, Amran Razak, Abdul Rahman KadirHegazy

ABSTRACT

The prevalence of diabetes mellitus continues to increase every year with various complications. This is caused by an unhealthy lifestyle. The complex management of type 2 diabetes mellitus triggers problems that cause therapeutic goals not to be achieved. The risk of complications is higher due to lack of attention to lifestyle including diet. A good diet, medication and physical activity are considered capable of improving blood sugar control so that the quality of life of people with diabetes mellitus becomes better. Objective: to analyze the effect of diet, medication, physical activity on glycemic control of patients with type 2 diabetes mellitus. Methods: the study was conducted in December 2023-February 2024 at Kassi-Kassi Health Center and Kalukubodoa Health Center, Makassar City, South Sulawesi. The sample size was type 2 diabetes mellitus patients in Kassi-Kassi Health Center as many as 184 people and Kalukubodoa Health Center as many as 168 people. The research group consisted of 2 groups, namely at Puskesmas Kassi-Kassi and Puskesmas Kalukubodoa with a combination intervention of food menu modules for diabetic patients and leaflets and Puskesmas Kassi-Kassi with food menu modules for diabetic patients. Both research groups were intervened for 3 (three) months with the assistance of doctors and nutritionists. There are two stages in this study, namely stage 1 making a prolanis intervention model with quantitative methods followed by stage 2, namely the intervention of food menu modules for diabetic patients and with quasi-experimental methods with a non-randomized pretest postest design. Results: In the aspects of diet, medication, physical activity there is a significant increase in Kassi-Kassi Health Center and Kalukubodoa Health Center (p=0.00) on glycemic control of type-2 diabetes mellitus patients. Conclusion: The results of the trial of the food menu module for patients with type 2 diabetes mellitus showed a value of 80%, meaning that the module was feasible to use based on the assessment of the material expert. Diet, medication, physical activity have a statistical effect and there is a difference in the mean value of glycemic control of type-2 diabetes mellitus patients.

Sheinni Paradise*, M. Alimin Maidin, Amran Razak, Abdul Rahman Kadir

Hasanuddin University, Makassar City, Province South Sulawesi, INDONESIA.

Correspondence

Sheinni Paradise

Hasanuddin University, Makassar City, Province South Sulawesi, INDONESIA.

E-mail: sheinni_paradise@yahoo.co.id

INTRODUCTION

The increasing prevalence of diabetes worldwide calls for new approaches in its management, and a diet with a low glycemic index has been proposed as a useful way to manage glucose response[1]. Diabetes mellitus is a group of metabolic disorders with high mortality and morbidity associated with complications such as cardiovascular disease, kidney disease, and stroke[2]. The prevalence of diabetes mellitus continues to increase every year with various complications. This is caused by an unhealthy lifestyle[3]. Dietary and lifestyle habits are major factors in the increasing incidence of diabetes mellitus in developing countries[4]. The American Diabetes Association (ADA) states that lifestyle plays an important role in preventing and managing diabetes mellitus[5].

Patients with diabetes mellitus often experience problems with instability of blood sugar levels. For this reason, control efforts are needed through diabetes disease management[6]. Diabetes mellitus is a disease or chronic metabolic disorder characterized by high blood sugar levels accompanied by metabolic disorders of carbohydrates, lipids, and proteins as a result of insufficient insulin function[7]. According to the International Diabetes Federation (IDF) (2015), Indonesia ranks sixth in the world with the most people with diabetes[5]. The results of the 2018 Basic Health Research (Riskesdas) show that the prevalence of diabetes mellitus according to blood sugar test results increased from 6.9% in 2013 to 8.5% in Indonesia[8]. Data from the Makasssar City Health Office in 2022 shows that diabetes mellitus ranks third at 35,847 cases of the 10 largest diseases based on morbidity data[9].

The classification of diabetes mellitus generally consists of two main types: type 1 diabetes and type 2 DM (5). Type 2 diabetes mellitus is more common than type 1 diabetes mellitus[7]. Type 2 diabetes mellitus generally occurs in adults due to an unhealthy lifestyle, while type 1 diabetes mellitus occurs because the pancreas produces little or no insulin[5]. Long-term management by reducing diabetes risk, quality of life, and acute complications and preventing microangiopathy and macroangiopathy from occurring[10]. As a result of uncontrolled blood sugar levels, complications may arise[11].

The complex management of type 2 diabetes mellitus triggers problems that cause therapeutic goals not to be achieved[12]. Treatment of type 2 diabetes mellitus consists of five main components: dietary management, exercise, metabolic status monitoring, pharmacological therapy, and education. The risk of complications is getting higher due to lack of attention to lifestyle including diet[13]. One of the management of type 2 diabetes is dietary management for patients to keep blood sugar levels under control[14]. A good diet and physical activity are considered to be able to improve blood sugar control so that the quality of life of people with diabetes mellitus becomes better[13].

Type 2 diabetes mellitus is a major health challenge and is associated with several complications and deaths[15]. Type 2 diabetes mellitus can be maintained with diet, so the success or failure of a person's diabetes diet depends on the patient's lifestyle in changing behavior[14]. Nutritional therapy is the initial treatment for diabetes[16]. Pharmacologic and/or insulin therapy may be required to maintain blood glucose levels as close to normal as possible and to delay or possibly prevent the development of diabetes-related health problems[17]. Physical activity and regular exercise provide an important role in blood glucose control, which is considered important in the therapy of type 2 diabetes mellitus[18].

METHOD

The population in this study were all patients with type 2 diabetes mellitus at Kassi-Kassi Health Center and Kalukubodoa Health Center, Makassar City, South Sulawesi Province, with a population of 2,832 people. The number of samples using the formula in this study was 351 people selected according to the inclusion and exclusion criteria with details of Puskesmas Kassi-Kassi as many as 184 people and Puskesmas Kalukubodoa as many as 168 people. The study was conducted in December 2023-February 2024 at the Kassi-Kassi Health Center and Kalukubodoa Health Center, Makassar City, South Sulawesi. The research group consisted of 2 groups, namely at Puskesmas Kassi-Kassi and Puskesmas Kalukubodoa with a combination intervention of food menu modules for diabetic patients and leaflets and Puskesmas Kassi-Kassi with food menu modules for diabetic patients. Both research groups were intervened for 3 (three) months with the assistance of doctors and nutritionists. There are two stages in this study, namely stage 1 making the prolanis intervention model with quantitative methods followed by stage 2, namely the intervention of the food menu module for diabetic patients and with quasi-experimental methods with a non-randomized pretest postest design. This research was conducted directly on humans and has obtained research permission from the Ethics Committee with letter number: 6375/UN4.14.1/TP.01.02/2023, dated December 11, 2023.

RESULT

The General Characteristics Of The Respondents Are The Characteristics Inherent In The Respondents. The Characteristics Of The Respondents Shown Include Gender, Age, And Latest Education, With The Following Characteristics

Table 1. above shows the characteristics of respondents. Respondents based on gender were more women (64,1%). Respondents by age were more 40-50 years old (53.0%). Respondents based on education were more high school (52,1%). Respondents based on occupation were more private job (36,2%). Respondents based on the length of time suffering from type-2 DM were more >10 years (37,6%).

There Are Three Independent Variables, Namely Diet, Medication, And Physical Activity (Gymnastics) Which Will Be Seen For Their Relationship To The Dependent Variable, Namely Glycemic Control Of Type 2 DM Patients At Kassi Kasi Health Center And Kaluku Bodoa Health Center, Makassar City

Based on the results of research conducted on 351 respondents, it can be explained that there were more respondents who had good eating patterns, namely (89,6%) at the Kassi Kassi Health Center and (95,8%) at the Kaluku Bodoa Health Center. Taking medication according to doctor's recommendations, namely (86,9%) at the Kassi Kassi Health Center and (95,8%) at the Kaluku Bodoa Health Center. Respondents with moderate physical activity were (90,2%) at the Kassi Kassi

Table 1. Distribution Of Respondents Based on Characteristics at Kassi Kassi Health Center And Kaluku Bodoa Health Center Makassar City.

Variable	Frequency (n)	Percent (%)
Jenis Kelamin		
Male	126	35,9
Female	225	64,1
Age		
40-50 yo	186	53,0
51-60 yo	100	28,5
61-70 yo	54	15,4
71-80 yo	11	31
Education		
Elementary	5	1,4
Junior High	39	11,1
High School	183	52,1
Undergraduate	124	35,3
Occupation		
Housewife	124	35,3
Civil Servant	35	10,0
Private Job	127	36,2
Retired	65	18,5
Duration of Type-2 DM		
1-5 Years	46	13,1
5-10 Years	173	29,3
>10 Years	132	37,6
Total	**351**	**100.0**

Health Center and (95,2%) at the Kaluku Bodoa Health Center. And respondents with more controlled glycemic control were (91,3%) at the Kassi Kassi Health Center and (96,4%) at the Kaluku Bodoa Health Center.

Test Results of the Food Menu Module for Type-2 Diabetes Mellitus Patients

The trial of the food menu module for diabetic patients was carried out for 2 weeks with 3 people with type-2 diabetes who were not from the sample, who then after 2 weeks would provide an assessment of the substance that should be added or reduced. The results of the assessment of the food menu module for diabetic patients showed a value of 80%, meaning that the module was feasible to use based on the assessment of the material expert. In addition to the substantial test, a usability test was also carried out at the manufacturing stage with a small group trial consisting of 3 people with type-2 diabetes and 2 nurses.

The most dominant factor associated with glycemic control of type 2 DM patients at Kassi Kasi Health Center and Kaluku Bodoa Health Center, Makassar City

The table shows that after multivariate analysis using multiple logistic regression, the constant value (Bo) = -11,983, the logistic regression coefficient value for dietary variables (B1) = 3,016, treatment variables (B2) = 2,601, and physical activity variables (B3) = 1,354. The p value of each variable is = 0,000, it can be concluded that the dietary pattern variable with the largest Exp (B) or OR (Odds Ratio) value = 20,416, so that this variable is determined as the most influential factor simultaneously on the glycemic of DM patients.

Intervention Results of the Prolanis Intervention Model

The table shows that there is a mean difference in diet, medication, physical activity before and after the intervention in patients with type 2 diabetes in Kassi-Kassi Health Center and Kaluku Bodoa Health Center in Makassar City with the highest difference in Kaluku Bodoa Health Center, with the intervention of a combination of food menu modules for diabetic patients and leaflets.

Table 2. Respondents Based on Diet, Medication, And Physical Activity (Gymnastics) At Kassi Kassi Health Center and Kaluku Bodoa Health Center Makassar City.

Variable	Health Center			
n = 351	Kassi Kassi		Kaluku Bodoa	
	n	%	n	%
Eating Patterns				
Good	164	89,6	161	95,8
Deficient	19	10,4	7	4,2
Total	**183**	**100,0**	**168**	**100,0**
Treatment				
As recommended by the doctor	159	86,9	161	95,8
Not as recommended by the doctor	24	13,1	7	4,2
Total	**183**	**100,0**	**168**	**100,0**
Physical Activity				
Moderate	165	90,2	160	95,2
Low	18	9,8	8	4,8
Total	**183**	**100,0**	**168**	**100,0**
Glycemic Control				
Controlled	167	91,3	162	96,4
Not Controlled	16	8,7	6	3,6
Total	**183**	**100,0**	**168**	**100,0**

Table 3. Results of Logistic Regression Analysis of Independent Variables on Glycemic Control of Type 2 DM Patients at Kassi Kasi Health Center and Kaluku Bodoa Health Center, Makassar City.

Variable	B	S.E.	Wald	Df	Sig.	Exp(B)
Diet	3,016	1,268	5,658	1	0,000	20,416
Diabetes Mellitus Treatment	2,601	1,016	6,555	1	0,000	13,478
Physical Activity	1,354	1,325	1,043	1	0,000	3,872
Constant	-11,983	1,493	64,426	1	0,000	0,000

Table 4. Differences in Diet, Medication, Physical Activity Before and After Intervention.

Intervention Group	Pre-Test mean±SD	Post-Test mean±SD	Δ (difference) mean±SD	P-value (1)
Pola Makan				
Puskesmas Kassi-Kassi	1,04	1,24	÷0,20	0,09
Puskesmas Kalukubodoa	1,10	1,32	÷0,22	0,00
Pengobatan				
Puskesmas Kassi-Kassi	1,13	1,26	÷0,13	0,10
Puskesmas Kalukubodoa	1,04	1,23	÷0,19	0,00
Aktifitas Fisik				
Puskesmas Kassi-Kassi	1,10	1,19	÷0,09	0,14
Puskesmas Kalukubodoa	1,05	1,18	÷0,13	0,00

The p-value on each variable of diet, medication, physical activity is p=0.00 which shows there are differences in diet, medication, physical activity before and after the intervention at the Kalukubodoa Health Center.

DISCUSSION

Diabetes mellitus is a chronic disease that is generally suffered for the rest of the patient's life, and requires long-term treatment at a considerable cost[11]. Diabetes mellitus is a major global health problem and one of the most studied diseases, the most researched worldwide, and is often associated with severe clinical complications[19].

Globally, type 2 diabetes mellitus is the most common form of DM, accounting for more than 90% of cases[20]. Type 2 diabetes mellitus is a disorder of carbohydrate metabolism caused by predominant insulin resistance and relative insulin deficiency[21]. Type 2 diabetes is characterized by high blood glucose levels due to insufficient insulin production by the pancreas[22].

Complications caused by diabetes become a more serious problem[23]. Complications in type 2 diabetics can be prevented with glycemic control[24]. Self-management behaviors such as healthy diet, physical activity, blood glucose monitoring, foot care and medication adherence are important parts of diabetes care[15]. The results showed that in each health center, there were significant differences in the aspects of diet, medication, and physical activity.

The diet is associated with a reduced risk of type 2 diabetes and is highly effective in its treatment[25]. Dietary regulation in patients with DM is aimed at reducing the intake of sugar and fat will reduce the intake of glucose in the body, so that the use of energy in the body will take stored energy reserves. If the glucose used is converted into energy, it will reduce blood glucose levels[16].

A high-fiber diet is an important component of diabetes management, resulting in improvements in measures of glycemic control, blood lipids, body weight, and inflammation, as well as reduced premature mortality[26]. Food and beverage sources that need to be avoided in people with DM are foods or drinks that contain high sugar such as sweetened condensed milk, high sugar syrup, various cakes that use high sugar, and various foods that contain a high glycemic index and raise blood sugar levels[1,4,13]. Implementation of balanced nutrition is the right solution[7].

One of the main contributors to glycemic control is adherence to medication[27]. Consumption of antidiabetic drugs can control the patient's blood sugar levels. If the patient is more compliant with taking antidiabetic drugs, the blood sugar level will be controlled, and vice versa if the patient is not compliant with the number of calories, the blood sugar level is difficult to control[28]. Poor adherence to medication can lead to uncontrolled diabetes and the development of diabetic complications[20].

Non-adherence to treatment increases the risk of diabetic complications which will also increase the burden of the disease and its management[29]. It is important to continuously assess the level of medication adherence and self-care behaviors in patients with type 2 diabetes mellitus. This will improve healthcare providers' identification of patients with poor medication adherence and help in planning appropriate strategies to promote medication adherence and self-care of people with diabetes[30]. Addressing medication issues should be targeted in future diabetes intervention programs to improve medication adherence and thus glycemic control among diabetic patients[31].

Physical activity is considered a cornerstone in achieving optimal blood glucose levels and reducing body weight, body mass, and waist circumference[32]. Physical activity causes energy uptake by converting glucose in the metabolic process, so that blood glucose levels decrease. Physical activities performed by DM patients can increase the use of glucose in the blood to be processed into energy[7]. Disease management of type 2 diabetes can be aided by a healthy diet and exercise[17]. Exercise has long been regarded as a cornerstone of diabetes management, along with dietary management and medication[33].

RESEARCH LIMITATIONS

The existence of other activities for respondents with type 2 diabetes mellitus caused the intervention to be less than optimal.

CONCLUSION

1) The results of the trial of the food menu module for patients with type-2 diabetes mellitus showed a score of 80%, meaning that the module was feasible to use based on the assessment of the material expert.

2) The most influential factor simultaneously on the glycemic of DM patients is diet.

3) Diet, medication, physical activity have a statistical effect and there is a difference in the mean value of glycemic control of type-2 diabetes mellitus patients.

REFERENCE

1. Ojo O, Ojo OO, Adebowale F, Wang XH. The effect of dietary glycaemic index on glycaemia in patients with type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. Nutrients. 2018;10(3):1–15.

2. Robert J. Genco, Filippo Graziani HH. Effects of periodontal disease on glycemic control, complications, and incidence of diabetes mellitus. 2020;

3. Zulkarnaini A, Mahatma G, Puspita D, Vani AT, Abdullah D. Aktivitas Fisik, Pola Makan, dan Konsumsi Makanan Glikemik Tinggi Meningkatkan Risiko Kejadian Diabetes Mellitus Tipe 2. J Kesehat Metro Sai Wawai. 2022;15(2):155–63.

4. Sami W, Ansari T, Butt NS, Rashid M, Hamid A. Effect Of Diet Counseling on Type 2 Diabetes Mellitus: A Review. Int J Health Sci (Qassim). 2017;11(2):65–71.

5. Kazi AA, Blonde L. Classification of diabetes mellitus. Vol. 21, Clinics in Laboratory Medicine. 2001. 1–13 p.

6. Istiqomah IN, Yuliyani N. Efektivitas Latihan Aktivitas Fisik Terhadap Penurunan Kadar Glukosa Darah Pada Pasien Diabetes Melitus Tipe 2: Kajian Literatur. BIMIKI (Berkala Ilm Mhs Ilmu Keperawatan Indones. 2022;10(1):1–10.

7. Ardiani HE, Permatasari TAE, Sugiatmi S. Obesitas, Pola Diet, dan Aktifitas Fisik dalam Penanganan Diabetes Melitus pada Masa Pandemi Covid-19. Muhammadiyah J Nutr Food Sci. 2021;2(1):1.

8. Kemenkes RI. Hasil Riset Kesehatan Dasar Tahun 2018. Kementrian Kesehat RI. 2018;53(9):1689–99.

9. Dinkes Makassar. Kota Makassar Tahun 2021. 2022;

10. Rahman Z. Pengaruh Edukasi Kesehatan Terhadap Self Care Pasien Diabetes Melitus Tipe 2: The Effect of Health Education on Self Care Type 2 Diabetes Mellitus Patients. J Ilm Keperawatan (Scientific J Nursing). 2023;9(5):625–30.

11. Rasdianah N, Martodiharjo S, Andayani TM, Hakim L. Pengaruh Pelayanan Kefarmasian di Rumah pada Pasien Diabetes Melitus Tipe 2 di Puskesmas Wilayah Kota Yogyakarta. J Manaj DAN PELAYANAN Farm (Journal Manag Pharm Pract. 2020;10(2):126.

12. Farmakologi D, Farmasi F, Mada G, Farmakologi D, Kedokteran F, Masyarakat K, et al. Masalah-Masalah terkait Pengobatan Diabetes Melitus Tipe 2 : Sebuah Studi Kualitatif Medication-related Problems in Patients with Type 2 Diabetes Mellitus : A Qualitative Study. 2020;9(1).

13. Permatasari SM, Sudargo T, Purnomo LB. 296266262. 2015;002:45–53.

14. Efendi M, Purbosari I, Mukti AS. Studi Manejemen Diet Pada Pasien Diabetes Melitus Tipe 2 Dengan Mengunakan Aplikasi Telemedicine Diabestie. J Islam Pharm. 2023;8(2):83–8.

15. Nasser Almutairi, Hassan Hosseinzadeh VG. The effectiveness of patient activation intervention on type 2 diabetes mellitus glycemic control and self-management behaviors: A systematic review of RCTs, Primary Care Diabetes,. 2020;

16. Yamada S. Paradigm shifts in nutrition therapy for type 2 diabetes - nutrition therapy for diabetes -. Keio J Med. 2017;66(3):33–43.

17. Artasensi A, Pedretti A, Vistoli G, Fumagalli L. Type 2 diabetes mellitus: A review of multi-target drugs. Molecules. 2020;25(8):1–20.

18. Yazid Al Busthomy Rofi A. Pengaruh Psikoedukasi Aktivitas Fisik Terhadap Kualitas Hidup Penderita Diabetes Tipe Ii. J Keperawatan Widya Gantari Indones. 2023;7(1):62–7.

19. Huang DD, Shi G, Jiang Y, Yao C, Zhu C. A review on the potential of Resveratrol in prevention and therapy of diabetes and diabetic complications. Biomed Pharmacother. 2020;125(October 2019):109767.

20. Kassahun T, Gesesew H, Mwanri L & ET. Diabetes related knowledge, self-care behaviours and adherence to medications among diabetic patients in Southwest Ethiopia: A cross-sectional survey. BMC Endocrine Disorders. 2016; 16(1):1–11. https://doi.org/10.1186/s12902-016-0114-x.

21. Tokhirovna EG. RISK FACTORS FOR DEVELOPING TYPE 2 DIABETES MELLITUS. ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ, 36(5), 64–69. Retrieved from http://www.newjournal.org/index.php/01/article/view/10592. 2024;

22. Berbudi A, Rahmadika N, Tjahjadi AI, Ruslami R. Type 2 Diabetes and its Impact on the Immune System. Curr Diabetes Rev. 2019;16(5):442–9.

23. Shofian Syarifuddin, Wilson Samosir. Characteristics of Types of Diabetes Mellitus Ii in Regional General Hospital Than Rondahaim, Simalungun District. MEDALION J Med Res Nursing, Heal Midwife Particip. 2022;3(4):144–8.

24. Arifin Z, Setyawati A, Hasanuddin U, Sakit Universitas Hasanuddin Makassar R. Faktor-Faktor Yang Berhubungan Dengan Kepatuhan Diet Pada Penderita Diabetes Melitus Tipe 2. J Telenursing. 2023;5(2):2494–504.

25. Meghan A Jardine, Hana Kahleova, Susan M Levin, Zeeshan Ali, Caroline B Trapp NDB. Perspective: Plant-Based Eating Pattern for Type 2 Diabetes Prevention and Treatment: Efficacy, Mechanisms, and Practical Considerations, Advances in Nutrition,. olume 12, Issue 6, 2021, Pages 2045-2055, ISSN 2161-8313, https//doi.org/101093/advances/nmab063.

26. Reynolds AN, Akerman AP, Mann J. Dietary fibre and whole grains in diabetes management: Systematic review and meta-analyses. PLoS Med. 2020;17(3):e1003053.

27. Dobbels F, Van Damme-Lombaert R, Vanhaecke J DGS. Growing pains: non-adherence with the immunosuppressive regimen in adolescent transplant recipients. Pediatr Transplant. 2005 Jun; 9 (3):381–90. https://doi.org/10.1111/j.1399-3046.2005.00356.x PMID: 15910397.

28. Istianah I, Septiani S, Dewi GK. Mengidentifikasi Faktor Gizi pada Pasien Diabetes Mellitus Tipe 2 di Kota Depok Tahun 2019. J Kesehat Indones (The Indones J Heal. 2020;X(2):72–8.

29. Polonsky WH HR. Poor medication adherence in type 2 diabetes: Recognizing the scope of the problem and its key contributors. Vol. 10, Patient Preference and Adherence. Dove Medical Press Ltd.; 2016. p. 1299–306. https://doi.org/10.2147/PPA.S106821 PMID: 27524885.

30. Afaya RA, Bam V, Azongo TB, Afaya A, Kusi-Amponsah A, Ajusiyine JM et al. Medication adherence and self-care behaviours among patients with type 2 diabetes mellitus in Ghana. PLoS One [Internet]. 2020;15(8):1–14. Available from: http://dx.doi.org/10.1371/journal.pone.0237710

31. Al-Qerem W, Jarab AS, Badinjki M, Hyassat D, Qarqaz R. Exploring variables associated with medication non-adherence in patients with type 2 diabetes mellitus. PLoS One [Internet]. 2021;16(8 August):1–11. Available from: http://dx.doi.org/10.1371/journal.pone.0256666

32. Shah SZA, Karam JA, Zeb A, Ullah R, Shah A, Haq IU, et al. Movement is Improvement: The Therapeutic Effects of Exercise and General Physical Activity on Glycemic Control in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Diabetes Ther [Internet]. 2021;12(3):707–32. Available from: https://doi.org/10.1007/s13300-021-01005-1

33. Gabriel BM ZJ. The limits of exercise physiology: from performance to health. Cell Metab. 2017;25(5):1000–11.