Impact of the vertical sleeve gastrectomy on oxygen consumption kinetics among women post bariatric surgery

Claudia Miranda-Fuentes¹, Paulina Ibacache Saavedra^{1,2}, Pedro Delgado-Floody³, Marcelo Cano-Cappellacci⁴, Daniel Jerez-Mayorga¹, Edgardo Opazo Diaz⁴

¹Universidad Andres Bello, Escuela de Kinesiología, Facultad de Ciencias de la Rehabilitación. Chile, ²Facultad de Ciencias de la Salud. Universidad de Las Américas. Sede Viña del Mar. Chile, ³Departamento de Educación Física. Universidad de La Frontera. Temuco. Chile, ⁴Departamento de Kinesiología. Universidad de Chile. Chile,

> **Received:** 15.11.2018 **Accepted:** 18.02.2019

Summary

Introduction: Obesity is considered one of the main health problems of modern society, there are several treatments to reverse it, being bariatric surgery (BS) the most effective method in cases of severe obesity. Cardiorespiratory fitness (CRF) is an aspect of physical condition assessed through maximum oxygen consumption (VO_{2max}); the kinetics of VO_2 is a less studied aspect of CRF; it has been described that this variable allows estimation of the CRF without high physical efforts in comparison with other forms of evaluation; In spite of the above, there is no information regarding the impact that sleeve gastrectomy (SG) has on the CRF evaluated through this variable.

Objective: To determine the impact of SG on the VO₂ kinetics of women with obesity.

Material and method: Quasi-experimental study, 15 women with an age of $32,9 \pm 10,3$ years and an initial BMI of $35,2 \pm 3,9$ kg/m² participated. The sample is non-probabilistic through a group of volunteers evaluated at three times: before surgery (*pre*), 30 and 90 days post vertical gastrectomy (30*post* and 90*post* respectively). Body weight, body mass index (BMI), waist circumference (WC), VO_{2neak} and VO₂ kinetics were evaluated.

Results: After surgery, the variables body weight, CC and BMI reported a significant decrease (p < 0,001) compared to the pre-surgery moment. The relative VO_{2peak} (ml/kg/min) increases between 30*post* and 90*post* (p < 0,001); the absolute VO_{2peak} (L/min) decreased between the pre moments with 30*post* and *pre* with 90*post* (p < 0,05); the kinetics of VO₂ showed an increase in time at 30*post* (p < 0,05).

 Key words:
 an increase in time at 30post (p <0,05).</td>

 Obesity. Oxygen consumption.
 Conclusion: The VO₂ kinetics is increased in obese women undergoing SG at 30post surgery, which shows a deterioration of this capacity.

Impacto de la gastrectomía vertical sobre la cinética de consumo de oxígeno en mujeres post cirugía bariátrica

Resumen

Introducción: La obesidad es considerada uno de los principales problemas de salud de la sociedad moderna, existiendo variados tratamientos para revertirla, siendo la cirugía bariátrica (CB) el método más efectivo en los casos de obesidad severa. La capacidad cardiorrespiratoria (CCR) es un componente de la condición física valorada a través del consumo máximo de oxígeno (VO_{2max}); la cinética del VO_2 es un aspecto poco estudiado de la CCR; se ha descrito que esta variable permite estimar la CCR sin elevados esfuerzos físicos en comparación con otras formas de evaluación; a pesar de lo anterior, no existe información respecto del impacto que tiene la gastrectomía vertical (GV) sobre la CCR evaluada a través de esta variable. **Objetivo:** Determinar el impacto de la GV en la cinética del VO₂ de mujeres con obesidad.

Material y método: Estudio de tipo cuasi experimental, participaron 15 mujeres con edad de 32,9±10,3 años y un IMC inicial de 35,2±3,9 kg/m². La muestra es de tipo no probabilística a través de grupo de voluntarios evaluados en tres momentos: previo a la cirugía (*pre*), 30 y 90 días post gastrectomía vertical (30*post* y 90*post* respectivamente). Se evaluó peso corporal, índice de masa corporal (IMC), circunferencia cintura (CC), VO_{verte} y cinética del VO_v.

indice de masa corporal (IMC), circunferencia cintura (CC), VO_{2peak} y cinética del VO₂. **Resultados:** Post cirugía las variables peso corporal, CC e IMC reportan disminución significativa (p<0,001) respecto del momento pre cirugía. El VO_{2peak} relativo (ml/kg/min) aumentó entre 30*post* y 90*post* (p<0,001); el VO_{2peak} absoluto (L/min) disminuyó entre los momentos pre con 30*post* y *pre* con 90*post* (p<0,05); la cinética del VO₂ presentó un incremento del tiempo a los 30*post* (p<0,05).

Palabras clave: Obesidad. Consumo de oxígeno. Cirugía bariátrica.

Conclusión: La cinética del VO_2 se ve incrementada en mujeres obesas intervenidas con GV a los 30 días post cirugía, lo que evidencia un deterioro de la capacidad cardiorrespiratoria.

Correspondence: Claudia Miranda Fuentes E-mail: cmiranda@unab.cl

Introduction

According to the World Health Organisation (WHO), obesity is defined as the abnormal or excessive accumulation of fat that can deteriorate health, and is considered to be one of the main problems faced by modern society¹. In Chile, according to the National Health Survey (NHS) 2016-2017, the prevalence of obesity was 31.2% (28.6% among men and 33.7% among women), the main cause considered to be lifestyle in terms of unhealthy eating habits, a lack of physical activity and sedentary behaviour, in addition to genetic, physiological, psychological, social, economic and educational factors². Treatments to combat obesity currently focus on reversing poor eating habits, increasing levels of physical activity, providing psychological support and administering pharmaceutical drugs³. In severe cases of obesity, or when the previously mentioned interventions have not had the desired effect, treatment moves on to Bariatric Surgery (BS)⁴, considered the most effective treatment in reducing weight in the long term, and proving highly effective for weight loss, leading to a considerable reduction in the associated co-morbilities⁴. Vertical Sleeve Gastrectomy (VSG) is the most used BS in the world, comprising 45.9%⁵ of all surgeries of this kind, and in Chile, it constitutes 70.8% of all BS⁶.

Physical condition is a combination of physical attributes related to the capacity to perform a task, and may or may not be related to health⁷. Cardio-Respiratory Capacity (CRC) is a component of this condition, used as a health and life-expectancy indicator, demonstrated through maximum oxygen consumption (VO_{2max})⁸. Assessing this variable requires the maximum CRC of the subject, a situation that may be high risk in some cases9. In obese patients, the assessment of this variable is generally sub-maximum, and the term VO_{2peak} is used to denominate the amount of oxygen consumed at the moment the test is stopped, expressed in absolute values (L/min) or values related to body weight (ml/kg/min).

One of the aspects that is rarely addressed regarding VO₂, is its kinetic at the start of the constant load exercise, represented by the tau measurement (τ), which consists in the time response of the VO₂, quantifying stabilisation after a constant load exercise lasting 6-10 minutes, representing the overall function of cardiovascular, pulmonary and muscular-skeletal system activity₁₀. Three phases can be discerned for the reaction of the increase of VO₂ in these conditions¹¹, with the τ value corresponding to the time in seconds in which 63% of the maximum VO₂ plateau is obtained with sub-maximum load in phase II, which has been proven to be sensitive to changes in CRC in subjects with cardio-respiratory pathologies12 and type II diabetes *mellitus*¹³, with the reduction of τ linked to an improvement in this capacity.

There is currently limited literature available describing the behaviour of τ in obese adult patients treated with VSG¹⁴. For this reason, the aim of this study was to describe the impact of VSG on the VO₂ kinetics of obese women.

Material and method

This study is quasi-experimental, with the participation of 15 women aged 32.9 ± 10.3 years of age; weight, height and starting BMI of 90.2 ± 10.49 kg; 1.6 ± 0.1 m and 35.2 ± 3.9 kg/m² respectively. The sample is

non-probabilistic, with a group of volunteers, who were assessed at three different points in time: before surgery (pre), as well as 30 and 90 days after surgical intervention (30 post and 90 post respectively). The inclusion criteria correspond to: $BMI \ge 30 \text{ kg/m}^2$, having fulfilled the surgical and anaesthetic criteria in order to undergo BS, and that the mentioned intervention is BS. Excluded patients were all those with previous BS, those with medical co-morbidities such as: chronic respiratory disease, heart disease, chronic liver disease or kidney failure, patients that used beta blockers, smokers, post-menopausal women, and patients that presented muscular-skeletal pathology that prevented them from performing the tests. Research and its protocols were aligned with the guidelines indicated in the 2013 Helsinki Declaration, approved by the Ethics Committee for Research on Humans at the University of Chile Medicine Faculty, Project No. 149-2014; all participants signed a previously informed consent form when their details were taken.

Procedures

Upon arriving at the laboratory, each subject had been previously required to fast for 4 hours and not to perform intense physical activity within the 24 hour period before assessment. The CC was assessed with a ROSSCRAFT[®] adult tape measure graduated in centimetres, to establish the middle point between the iliac crest and the lowest part of the ribs. Weight and height were measured with a DETECTO 439 (Detecto, Webb City, United States) graduated weighing scale/height measure. BMI was measured to estimate the degree of obesity (kg/m²).

To measure the cardio-respiratory variables, Metalyzer 3b equipment, Cortex (CORTEX Biophysik, Leipzig, Germany) and a Monark 915E cycle-ergometer (Monark Exercise AB, Vansbro, Sweden) were used. To obtain VO₂ and VO_{2neak} kinetic data, the protocol consisted in the measurement of 2 minutes resting base cardio-respiratory parameters on the cycle-ergometer, then whilst pedalling at a speed of 60 rpm at a constant load of 0.5 watts per kilogram of body weight (W/kg) for 6 minutes to obtain the tau data. After this, to obtain the VO_{2nexk} values, the load was increased at steps of 20 or 25 W (depending on the level of physical activity) every two minutes until exhaustion or to the point of reaching a respiratory quotient (RER) \geq 1.1, perceived exertion \geq 7 on the modified Borg Scale, or until the subject presented muscle fatigue that prevented the pedal speed from remaining at 60 rpm¹⁵. Following this, pedalling without load was performed for 3 minutes to cool down. Tau values were established following the protocol described by Poole¹⁶, in which the value was obtained from the 6 first minutes on the cycleergometer exercise test. The VO₂ by ventilation values were transformed to obtain values with the 1Hz frequency, to be modelled mathematically in accordance with the equation that defines the VO₂ response, at a constant load and at moderate intensities, described below (Figure 1):

Figure 1. Formula to calculate the oxygen consumption kinetics.

 $\dot{V}O_2(t) = \dot{V}O_2$ basal + amplitud $\left(1 - e^{-\frac{t-TD}{\tau}}\right)$

Where VO₂(t) is the VO₂ at any time t, base VO₂ is the VO₂ before starting the exercise, range is the "stable state" towards which the VO₂ is projected, TD is the time delay that precedes the increase in muscular VO₂ and τ is the time constant that describes the rate at which VO2 increases to a stable state¹⁶.

Statistical analysis

The statistical analysis was performed using IBM® SPSS® Statistics software, version 24.0 (Chicago, USA). The continuous variables were expressed as average and standard deviation prior to an analysis of data normality using the Shapiro-Wilk test. Quantitative variable comparisons were established using the ANOVA test of a factor of repeated measures and post-hoc analysis of Bonferroni. The p<0.05 values were considered to be statistically significant.

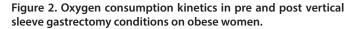
Results

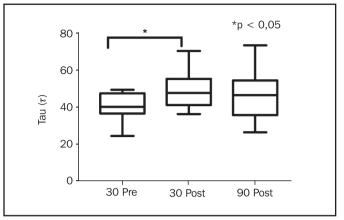
The women presented type II obesity in the assessment prior to surgical intervention (BMI 35.2 \pm 3.9 kg/m²), shifting to a condition of pre-obesity (28.5 \pm 3.4 kg/m²) three months later¹⁷; significant reductions were reported 30 and 90 days post surgery, in body weight, CC and BMI variables, as well as between *30 post* and 90 post (p<0.001) (Table 1).

In relation to relative VO_{2peak} (ml/kg/min), this displayed significant changes between the pre and 90 post periods (p<0.001), and in turn, the absolute VO_{2peak} value (L/min) reduced between the pre and 30 post moments (p<0.001) and 90 post (p<0.002) (Table 1). In turn, the VO₂ kinetic presented significant differences between the pre and 30 post periods (p<0.05) (Figure 2).

Discussion

The aim of this study was to describe the impact of BS on VO₂ kinetic. First off, it is relevant to highlight that in this study, a detailed body composition assessment was not taken into account, whereby the researchers consider it pertinent to express the changes in the CRC values obtained in their absolute form (VO_{2peak} absolute (L/min) as opposed to normalising them by body weight; as such it is brought to





light that just 30 days post surgical intervention are enough to present significant deterioration of this capacity; the results obtained are similar to those put forward by Browning *et al.* who analysed the parameters of this variable in obese subjects intervened with BS, affirming an average reduction of 2.6 L/min to 2.4 L/min at 3 months post intervention18. The aforementioned can be explained by the loss of lean mass and not fat mass¹⁹; on the other hand, significant body weight loss has been verified, associated specifically to predominantly fat mass in the first months following this kind of surgery²⁰.

With regards to the results of the VO_2 kinetic obtained in this research, it is important to highlight that this variable describes the dynamic response of this gas to sudden changes in the external work rate, proving to be dependent upon the intensity of the exercise when this exceeds the gas exchange threshold^{21,22}. The results obtained of the VO_2 kinetic reveal that 30 days after BS, a significant increase can be seen in the stabilisation response time of this variable to the work load imposed by the activity, which indicates a slower fundamental component in the VO_2 kinetic, determining a greater oxygen deficit during the transition of resting to exercise. The results obtained can be compared to those put forward by Neunhaeuserer et al. who also refer to an increase in this variable among obese subjects who have undergone VSG BS²³.

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Table 1. Ellect of the vertical si	iceve gastrectority on the	physical capacities of obese women.

Variables	Evaluations			Bonferroni (Post hoc)			
	pre	30post	90post	p value	pre vs. 30post	pre vs. 90post	30post vs. 90post
Weight (kg)	91.5 ± 11.0	82.2 ± 11.2	74.2 ± 9.9	<0.001	9.3 (<0.001) **	17.3 (<0.001) **	8.0 (<0.001) **
BMI (kg/m²)	35.2 ± 3.9	31.6 ± 3.9	28.5 ± 3.5	<0.001	3.6 (<0.001) **	6.6 (<0.001) **	3.0 (<0.001) **
CC (cm)	109.5 ± 6.7	102.5 ± 7.1	94.9 ± 7.9	<0.001	7.1 (<0.001) **	14.5 (<0.001) **	7.4 (<0.001) **
VO _{2peak} (L/min)	1.9 ± 0.2	1.6 ± 0.3	1.6 ± 0.2	<0.001	0.2 (<0.001) **	0.2 (<0.005) *	-0.05 (0.402)
VO _{2peak} (ml/kg/min)	21.0 ± 3.6	19.6 ± 2.6	22.5 ± 2.8	<0.001	1.3 (0.077)	-1.4 (0.099)	-2.8 (<0.001) **
Tau (τ)	39.8 ± 6.8	48.8 ± 9.5	46.1 ± 12.4	<0.001	-9.0 (<0.005) *	-6.3 (0.124)	2.7 (1.00)

The data is presented as averages and standard deviation, p value, ANOVA Test and Bonferroni Test. Tau (τ): Oxygen consumption kinetics; BMI: Body Mass Index. *p < 0.05 ** < 0.001.

This results highlights that this kind of intervention negatively influences tolerance to exercise, suggesting that an increase in this variable (τ) slows down oxidative muscular metabolism activation²⁴, which is a possible cause of a lower energy expenditure per activity faced with a reduction of body weight post BS. On the other hand, Simoneau and Kelley highlighted that in subjects with health conditions associated to poor nutrition through overeating, there is a reduced activity of oxidative enzymes and a disproportionate increase of the activity of glycolytic enzymes, which could explain the τ results obtained in this research²⁵. In the same sphere, literature has revealed τ values close to ~10 seconds in healthy individuals with a high level of physical training²⁶ and between 20 to 60 seconds in healthy adults²⁷; the publications displayed have described that the increase of oxygen capture at the start of exercise demonstrates the circulatory adjustments to the metabolic modifications induced by this activity, where the oxygen contribution is not a limiting factor of performance during sub-maximum exercise. which reflects efficient muscular bioenergy and an effective tissue-level oxygen diffusion²⁸, conditions that are not present in subjects with obesity¹⁵. On the other hand, literature has also revealed τ behaviour in obese adults (without surgical intervention), with data discovered close to 58.7 \pm 35.8 seconds²³; subjects with pulmonary vascular disease 74 \pm 16 seconds²⁹ and with type II diabetes *mellitus* 55.7 \pm 20.6 seconds³⁰; attributing the increase of this variable to the intensity of physical exercise employed and the capacity of the cardio-respiratory system to respond to the greater demand of this activity. Other antecedents have reported that obese subjects present muscular-skeletal changes both structurally (associated mainly to the higher proportion of type IIb muscle fibres³¹) and to the amount of muscle compared to normalweight subjects³², which entails the consequent incapacity to increase the oxidation of fats during β -adrenergic stimulation in exercise, with the subsequent increase of intramuscular fat storage³³. In turn, with regards to the functioning of the respiratory system, information has been found stating that these subject present a lower flow value upon performing physical exercise, which must be compensated for by increasing the respiratory frequency, accelerating the start of the ventilatory threshold, speeding up the appearance of the slow VO₂ component, infringing upon tolerance of effort and adaptation to physical effort³⁴.

Conclusion

It is suggested that the VO_2 kinetic increases in obese women intervened with BS 30 days post surgery, therefore, the time needed to stabilise the cardio-respiratory response to work load imposed is slower. The latter is highly useful in clinical terms for the treatment of subjects with this health condition, as it is relevant when it comes to planning physical exercises guidelines for this particular demographic.

Conflict of Interest

The authors claim to have no conflict of interest whatsoever.

Bibliography

- 1. World Health Organization. Obesity and overweigth 2017 [cited 2018 May 31]. Disponible en: http://www.who.int/es/news-room/fact-sheets/detail/obesity-and-overweight.
- Ministerior de Salud, Gobierno de Chile. Encuesta Nacional de Salud 2016-2017 Primeros resultados 2017 [cited 2018 January 29]. Disponible en: http://web.minsal. cl/wp-content/uploads/2017/11/ENS-2016-17_PRIMEROS-RESULTADOS.pdf.
- Yarborough CM, 3rd, Brethauer S, Burton WN, Fabius RJ, Hymel P, Kothari S, et al. Obesity in the Workplace: Impact, Outcomes, and Recommendations. J Occup Environ Med. 2018;60(1):97-107.
- le Roux CW, Heneghan HM. Bariatric Surgery for Obesity. Med Clin North Am. 2018; 102(1):165-82.
- Plamper A, Deitel M, Rheinwalt KP. Letter to the Editor: Bariatric Surgery and Endoluminal Procedures: IFSO Worldwide Survey 2014. *Obesity Surgery*. 2018;28(1):249-50.
- Angrisani L, Santonicola A, Iovino P, Formisano G, Buchwald H, Scopinaro N. Bariatric Surgery Worldwide 2013. Obesity surgery. 2015;25(10):1822-32.
- Castillo-Garzon MJ, Ruiz JR, Ortega FB, Gutierrez A. Anti-aging therapy through fitness enhancement. *Clin Interv Aging*. 2006;1 (3):213-20.
- Lee DC, Sui X, Ortega FB, Kim YS, Church TS, Winett RA, et al. Comparisons of leisuretime physical activity and cardiorespiratory fitness as predictors of all-cause mortality in men and women. Brit J Sport Med. 2011;45(6):504-10.
- Mezzani A, Agostoni P, Cohen-Solal A, Corra U, Jegier A, Kouidi E, et al. Standards for the use of cardiopulmonary exercise testing for the functional evaluation of cardiac patients: a report from the Exercise Physiology Section of the European Association for Cardiovascular Prevention and Rehabilitation. European journal of cardiovascular prevention and rehabilitation: official journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology. 2009;16(3):249-67.
- Grassi B. Oxygen uptake kinetics: old and recent lessons from experiments on isolated muscle in situ. *Eur J Appl Physiol.* 2003;90(3-4):242-9.
- Grassi B, Poole DC, Richardson RS, Knight DR, Erickson BK, Wagner PD. Muscle O2 uptake kinetics in humans: implications for metabolic control. JAppl Physiol. 1996;80(3):988-98.
- Borghi-Silva A, Beltrame T, Reis MS, Sampaio LMM, Catai AM, Arena R, et al. Relationship between oxygen consumption kinetics and BODE Index in COPD patients. Int J Chronic Obstr. 2012;7:711-8.
- Brandenburg SL, Reusch JEB, Bauer TA, Jeffers BW, Hiatt WR, Regensteiner JG. Effects of exercise training on oxygen uptake kinetic responses in women with type 2 diabetes. *Diabetes Care*. 1999;22(10):1640-6.
- Neunhaeuserer D, Gasperetti A, Savalla F, Gobbo S, Bullo V, Bergamin M, et al. Functional Evaluation in Obese Patients Before and After Sleeve Gastrectomy. Obesity surgery. 2017;27(12):3230-9.
- 15. Littleton SW. Impact of obesity on respiratory function. Respirology. 2012;17(1):43-9.
- 16. Poole DC, Jones AM. Oxygen uptake kinetics. Compr Physiol. 2012;2(2):933-96.
- World Health Organization. Obesity and overweigth 10 facts about obesity 2017 [cited 2019. Disponible en: https://www.who.int/es/news-room/fact-sheets/detail/ obesity-and-overweight.
- Browning MG, Franco RL, Herrick JE, Arrowood JA, Evans RK. Assessment of Cardiopulmonary Responses to Treadmill Walking Following Gastric Bypass Surgery. *Obesity* Surgery. 2017;27(1):96-101.
- Muñoz R, Hernández J, Palacio A, Maiz C, Pérez G. El ejercicio físico disminuye la pérdida de masa magra en pacientes obesos sometidos a cirugía bariátrica. *Rev Chil Cir.* 2016;68:411-6.
- Chaston TB, Dixon JB, O'Brien PE. Changes in fat-free mass during significant weight loss: a systematic review. *Int J Obes (Lond)*. 2007;31(5):743-50.
- McNarry MA, Kingsley MI, Lewis MJ. Influence of exercise intensity on pulmonary oxygen uptake kinetics in young and late middle-aged adults. *Am J Physiol Regul Integr Comp Physiol*. 2012;303(8):R791-8.
- Miranda C, Ibacache P, Opazo E, Rojas J, Cano M. Uso de la cinética del consumo de oxígeno para la evaluación de la capacidad cardiorrespiratoria en pacientes con obesidad. *Rev Med Chile.* 2018;146:15-21.
- Neunhaeuserer D, Gasperetti A, Savalla F, Gobbo S, Bullo V, Bergamin M, et al. Functional Evaluation in Obese Patients Before and After Sleeve Gastrectomy. Obes Surg. 2017;27(12):3230-9.

- 24. Grassi B. Oxygen uptake kinetics: Why are they so slow? And what do they tell us? J Physiol Pharmacol. 2006;57 Suppl 10:53-65.
- Simoneau JA, Kelley DE. Altered glycolytic and oxidative capacities of skeletal muscle contribute to insulin resistance in NIDDM. J Appl Physiol (1985). 1997;83(1):166-71.
- Koppo K, Bouckaert J, Jones AM. Effects of training status and exercise intensity on phase II VO₂ kinetics. *Med Sci Sports Exerc.* 2004;36(2):225-32.
- 27. Whipp BJ, Rossiter HB, Ward SA. Exertional oxygen uptake kinetics: a stamen of stamina? *Biochemical Society transactions*. 2002;30(2):237-47.
- Ba A, Bregeon F, Delliaux S, Cisse F, Samb A, Jammes Y. Cardiopulmonary response to exercise in COPD and overweight patients: relationship between unloaded cycling and maximal oxygen uptake profiles. *Biomed Res Int.* 2015;378469.
- Sietsema KE. Oxygen uptake kinetics in response to exercise in patients with pulmonary vascular disease. Am Rev Respir Dis. 1992;145(5):1052-7.

- Regensteiner JG, Bauer TA, Reusch JE, Brandenburg SL, Sippel JM, Vogelsong AM, et al. Abnormal oxygen uptake kinetic responses in women with type II diabetes mellitus. J Appl Physiol (1985). 1998;85(1):310-7.
- Pattanakuhar S, Pongchaidecha A, Chattipakorn N, Chattipakorn SC. The effect of exercise on skeletal muscle fibre type distribution in obesity: From cellular levels to clinical application. Obes Res Clin Pract. 2017;11(5s1):112-32.
- Ciolac EG, Greve JA. Exercise-induced improvements in cardiorespiratory fitness and heart rate response to exercise are impaired in overweight/obese postmenopausal women. *Clinics*. 2011;66(4):583-9.
- Blaak EE. Basic disturbances in skeletal muscle fatty acid metabolism in obesity and type 2 diabetes *mellitus*. *Proc Nutr Soc*. 2004;63(2):323-30.
- 34. Arena R, Cahalin LP. Evaluation of cardiorespiratory fitness and respiratory muscle function in the obese population. *Prog Cardiovasc Dis.* 2014;56(4):457-64.