Lebanon Mass Loss and Altered Muscular Aerobic Capacity after Bariatric Surgery

Na Zhou\textsuperscript{a} Corentin Scoubeau\textsuperscript{a,b} Kevin Forton\textsuperscript{a,c} Patricia Loi\textsuperscript{d} Jean Closset\textsuperscript{d}
Gael Deboeck\textsuperscript{e} Jean-Jacques Moraine\textsuperscript{a} Malgorzata Klass\textsuperscript{b,f} Vitalie Faoro\textsuperscript{a}

\textsuperscript{a}Cardio-Pulmonary Exercise Laboratory, Faculty of Motor Sciences, Université Libre de Bruxelles, Brussels, Belgium; \textsuperscript{b}Laboratory for Biometry and Exercise Nutrition, Faculty of Motor Sciences, Université Libre de Bruxelles, Brussels, Belgium; \textsuperscript{c}Department of Cardiology, Erasmus Hospital, Brussels, Belgium; \textsuperscript{d}Department of Gastric Surgery, Erasmus Hospital, Brussels, Belgium; \textsuperscript{e}Laboratory of Rehabilitation, Faculty of Motor Sciences, Université Libre de Bruxelles, Brussels, Belgium; \textsuperscript{f}Laboratory of Applied Biology, Faculty of Motor Sciences, Université Libre de Bruxelles, Brussels, Belgium

Keywords
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Abstract

\textbf{Introduction:} Patients undergoing weight loss surgery do not improve their aerobic capacity or peak oxygen uptake (VO\textsubscript{2}\textsuperscript{peak}) after bariatric surgery and some still complain about asthenia and/or breathlessness. We investigated the hypothesis that a post-surgery muscular limitation could impact the ventilatory response to exercise by evaluating the post-surgery changes in muscle mass, strength, and muscular aerobic capacity, measured by the first ventilatory threshold (VT).

\textbf{Methods:} Thirteen patients with obesity were referred to our university exercise laboratory before and 6 months after bariatric surgery and were matched by sex, age, and height to healthy subjects with normal weight. All subjects underwent a clinical examination, blood sampling, and body composition assessment by dual-energy X-ray absorptiometry, respiratory and limb muscle strength assessments, and cardiopulmonary exercise testing on a cyclo-ergometer.

\textbf{Results:} Bariatric surgery resulted in a loss of 34\% fat mass, 43\% visceral adipose tissue, and 12\% lean mass (LM) ($p < 0.001$). Absolute handgrip, quadriceps, or respiratory muscle strength remained unaffected, while quadriceps/handgrip strength relative to LM increased ($p < 0.05$). Absolute VO\textsubscript{2}\textsuperscript{peak} or VO\textsubscript{2}\textsuperscript{peak}/LM did not improve and the first VT was decreased after surgery (1.4 ± 0.3 vs. 1.1 ± 0.4 L min\textsuperscript{−1}, $p < 0.05$) and correlated to the exercising LM (LM legs) ($R = 0.84$, $p < 0.001$).

\textbf{Conclusions:} Although bariatric surgery has numerous beneficial effects, absolute VO\textsubscript{2}\textsuperscript{peak} does not improve and the weight loss-induced LM reduction is associated to an altered muscular aerobic capacity, as reflected by an early VT triggering early exercise hyperventilation.
Fat mass loss after bariatric surgery also leads to an increased peak oxygen uptake (\(VO_2\text{peak}\)) relative to body weight (expressed in \(\text{mL kg}^{-1} \text{min}^{-1}\)), which presents a great advantage for body weight-bearing efforts [6]. However, no study reported an increase in absolute \(VO_2\text{peak}\) (L/min), reflecting the intrinsic aerobic capacity [6]. Previous studies performed 6 months after surgery reported either a significant absolute \(VO_2\text{peak}\) drop [3, 7–10] or a tendency to decrease [11]. Thus, even when surgery is successful, absolute \(VO_2\text{peak}\) is not improved and some patients still complain about asthenia or and breathlessness [6]. The underlying mechanisms of those physical deconditioning symptomatology remain unclear. It has previously been suggested but not conclusively demonstrated that the muscle mass loss accompanying post-surgery weight loss may interfere with aerobic exercise performance after bariatric surgery [6, 12]. Indeed, the large-scale weight loss after bariatric surgery results not only in a substantial loss of fat mass (FM) but is also associated with significant lean mass (LM) loss, with muscle proteins serving as a source of amino acids for the functioning of other cells. Previous studies underlined the deleterious effects of excessive LM loss during weight loss programs on metabolism, thermoregulation, and functional capacity [13]. However, the link between post-bariatric surgery LM loss and the respiratory and cardiovascular response to maximal and submaximal aerobic exercise have been understudied until now. We, therefore, hypothesized that combining accurate body composition assessment (including leg LM), limbs, and respiratory muscle strength measurements, together with a cyclo-ergometer cardio-pulmonary exercise test (CPET), would allow us to describe the physiological influence of a muscle mass limitation on respiratory, cardiovascular, or metabolic response to exercise before and after bariatric surgery. We also believed that comparison with a control group of healthy subjects with normal weight matched for age, sex, and height would highlight the impact of overweight before bariatric surgery and enable to assess whether differences persist 6 months after weight loss surgery.

Methods

Study Population

Thirteen patients with obesity (6 men/7 women, 49 ± 14 years old, 168 ± 7 cm, 112 ± 17 kg, body mass index [BMI]: 39.5 ± 3.5 kg m\(^{-2}\)) recruited from the local University Hospital, Department of Gastric Surgery performed identical experimental protocol on two occasions: before and 6 months after bariatric surgery. Each patient with obesity included in the present study was individually paired to a healthy subject with normal weight matched by race, sex, age, and height recruited in his social environment. The characteristics of all 26 participants are shown in Table 1.

All participants gave their informed written consent to the study, approved by the local Ethical Committee (reference: P2016/448). Patients suffering from heavy musculoskeletal, cardiovascular, or pulmonary disease or under beta blockers were excluded. However, 5 patients with obesity suffered from mild arterial hypertension, 5 from sleep-apnea, 3 from impaired glucose tolerance, and 7 dyslipidemia. All patients with obesity underwent bariatric surgery without complications: sleeve gastrectomy \((n = 12)\) or laparoscopic Roux-en-Y gastric bypass \((n = 1)\). After bariatric surgery, all patients benefited from a nutritional follow-up with appointments every 2 months with the same dietician. All patients were counseled about the principles of healthy eating, with 3 small meals per day, at least 5 daily servings of fresh fruits and vegetables and vitamin supplements. Protein intake recommendations were individualized regarding sex, age, and weight. A minimal protein intake of 60 g/day and up to 1.5 g/kg ideal weight per day was targeted.

The patients were advised to increase their daily physical activities and to walk as much as possible. However, no controlled or structured exercise training was imposed or proposed.

Healthy subjects with normal weight declared themselves as healthy and free from any proven pathology. All participants had a normal electrocardiogram (ECG) at rest.

Experimental Protocol

All subjects were invited to the laboratory to perform the following test sequence: clinical examination and fasting blood sampling, body composition assessment, respiratory and skeletal muscle strength assessment followed by a CPET. Patients with obesity repeated the protocol 6 months after bariatric surgery.

Clinical Assessment

Clinical assessment included a medical history, clinical examination with measurements of resting blood pressure (sphygmomanometry), ECG, pulsed oximetry (Nelcor Puritan Bennett Inc., Pleasanton, CA, USA), and fasting blood sampling. Fasting blood tests were analyzed for metabolic syndrome assessment by the same hospital laboratory with measurements of fasting glycemia, triglyceride, and high-density lipoprotein cholesterol. The hemoglobin level was also evaluated, being a determinant of \(O_2\) transport and a potential limiting factor of the \(VO_2\text{peak}\).

The Global Physical Activity Questionnaire (GPAQ) was used to assess self-estimated moderate and vigorous intensity activities amount and self-estimated sedentary behavior [14]. The questionnaires were completed by the investigator during an interview with each of the participants.

Anthropometry

All the measurements were performed in the morning after an overnight fast. Stature was measured to the nearest 0.5 cm with a wall-mounted stadiometer. Weight was measured to the nearest 0.1 kg on a standing weighting scale (BC-418; TANITA, Tokyo, Japan) wearing no shoes and light clothing. BMI was expressed in kg/m\(^2\) where kg is the person’s weight in kilograms and m\(^2\) is the height in meters squared. The percentage of excess of BMI loss after surgery was calculated based on an ideal BMI of 25 kg/m\(^2\). Waist circumference was assessed with a standard flexible nonelas
 metric tape over the midpoint between the last rib and the iliac crest with the patient standing and exhaling. Total and regional FM and LM were acquired using dual energy X-ray absorptiometry (Lunar Prodigy; GE Healthcare, Madison, WI, USA) and analyzed using enCORE software (version 15.0). The regions of interest (ROI) for regional body composition (left and right arm, left and right leg, trunk) were first defined automatically by the software. Then the arm and leg ROI were manually corrected by the investigator to make them cut proximally across the coracoid process and the line along the lower ramus and the opening of the acetabulum, respectively [15]. Visceral adipose tissue analysis was performed using fully automated software (CoreScan; GE Healthcare). The software segments the abdominal fat measured by dual energy X-ray absorptiometry into subcutaneous fat and visceral fat within the android region of the abdomen. VAT is then estimated by subtracting subcutaneous fat from the total android fat. The method has previously been validated against computed tomography in patients with a wide range of BMI [16, 17].

**Muscle Strength Measurements**

Isometric quadriceps strength was measured during knee extension using a digital force gauge (Sauter FK 1K, Balingen, Germany) in a sitting position, knee angle at 90°. Relative quadriceps strength was expressed as the ratio of absolute quadriceps strength divided by the lower limb LM. During handgrip muscle strength evaluation, subjects were asked to squeeze a dynamometer as hard as possible (Idass Fitness, Cornwall, UK) in a standardized standing position, with a 90° shoulder flexion and complete elbow extension. Relative handgrip strength was expressed as the ratio of absolute handgrip strength divided by the upper limb LM.

A respiratory pressure meter (Micro RPM; CareFusion, Wokingham, UK) was used to assess the respiratory muscle strength. This unit measured the maximum inspiratory pressure (MIP) and expiratory pressure (MEP). The device was connected to a PC running PUMA (MicroRPM) allowing real-time display of respiratory pressure. Measurements were performed according to ATS/ERS statements for respiratory muscle testing at rest, in the seated position with a nasal clip [18]. MIP was determined as the maximal pressure recorded during an inspiration maneuver starting from residual lung volume. MEP was determined as the maximal pressure recorded during an expiration maneuver starting from total lung capacity. Muscle strength measurements were repeated at least five times, with minimum three reproducible maneuvers (variation equal or less than 10%) and the highest value was considered for analyses.

**CPET**

Aerobic capacity was assessed using a classical incremental CPET on an electrically braked cyclo-ergometer (Ergoselect II

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Table 1. Participant’s anthropometric, body composition, metabolic, physical activity characteristics

|                      | Pre-surgery | Post-surgery | Controls |
|----------------------|-------------|--------------|----------|
| Men/women ratio      | 6/7         | 6/7          | 6/7      |
| Age, years           | 49±14       | 49±14        | 48±13    |
| Height, m            | 1.68±0.07   | 1.68±0.07    | 1.73±0.07|
| Weight, kg           | 112±17      | 87±16**      | 70±11**  |
| BMI, kg m⁻²          | 39.5±3.5    | 30.7±3.4**   | 23.3±3.1*** |
| Total body FM, kg    | 53±9        | 36±10**      | 19±6**   |
| Percentage body fat, %| 49±4        | 41±5**       | 31±7***  |
| VAT, g               | 2,685±1,329 | 1,490±750*** | 660±743** |
| Trunk FM, kg         | 29±4        | 19±4**       | 9±3**    |
| Arms FM, kg          | 5±1         | 4±1**        | 2±0**    |
| Legs FM, kg          | 18±6        | 12±5**       | 8±2**    |
| Total body LM, kg    | 56±10       | 49±8**       | 46±7     |
| Trunk LM, kg         | 25±4        | 23±4**       | 21±3**   |
| Arms LM, kg          | 6±1         | 5±1**        | 5±2**    |
| Legs LM, kg          | 21±4        | 18±3**       | 18±4**   |
| Hemoglobin, mg dL⁻¹  | 13.4±1.7    | 13.8±1.1     | 14.5±0.9 |
| Waist circumference, cm| 127±9      | 106±10**     | 85±10**  |
| Mean BPrest, mm Hg   | 99±13       | 84±13**      | 90±13    |
| Fasting glycemia, mg dL⁻¹| 107±30     | 85±13**      | 93±10    |
| Triglyceride, mg dL⁻¹| 136±59     | 94±45        | 93±52    |
| HDL-C, mg dL⁻¹       | 47±13       | 56±11        | 65±19*** |
| GPAQ sedentary time, min day⁻¹| 56±2158 | 576±180 | 496±196 |
| GPAQ moderate physical activity time, min wk⁻¹| 438±536 | 627±584| 507±433 |
| GPAQ vigorous physical activity time, min wk⁻¹| 0±0      | 9±23         | 106±107** |

VAT, visceral adipose tissue; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol. * p < 0.05, ** p < 0.01, *** p < 0.001: pre-surgery versus controls. * p < 0.05, ** p < 0.01, *** p < 0.001: post-surgery versus controls. $p<0.05, $$$ p<0.001: pre-surgery versus post-surgery.
Exercise Capacity Post-Bariatric Surgery

Six months after bariatric surgery, all these parameters were significantly decreased (Table 1) with a mean total body weight loss of 22% (−25 ± 8 kg), which represents a change in BMI of −8.8 ± 2.8 kg/m² and an excess of BMI loss of −23 ± 7%. The FM loss induced by bariatric surgery (−34 ± 11%) was associated to a decrease in LM (−12 ± 3%). Regional post-surgery changes in FM and LM are shown in Figure 1. For FM, the greatest change was observed for VAT (−43 ± 16%), while LM was homogeneous reduced in all body regions after surgery and was no more significantly different from healthy subjects with normal weight. Six months after surgery, VAT, total FM, and relative FM (%) remained significantly higher in patients as compared to healthy subjects with normal weight.

Metabolic Characteristics
Bariatric surgery improved metabolic parameters (mean blood pressure, high-density lipoprotein cholesterol, triglyceride, fasting glycemia) which were no more different from healthy subjects with normal weight. Hb levels remained unaffected by surgery (Table 1).

Daily Physical Activity Level
The results of the GPAQ questionnaire are exposed in Table 1. After bariatric surgery, self-estimated sedentary, and vigorous physical activity time remained unchanged and moderate activity time was slightly improved. No difference in daily sedentary time and weekly moderate activity time were observable when comparing post-surgery patients with obesity versus healthy subjects with normal weight but vigorous physical activity time remained lower in patients.
Limbs and Respiratory Muscle Strength

After bariatric surgery, the relative handgrip and quadriceps force was improved and no more different from healthy controls (Table 2). Neither obesity nor bariatric surgery affected inspiratory or expiratory muscle strength (Table 2).

Aerobic Capacity

CPET results are displayed in Table 3. Bariatric surgery increased maximal workload, RER, VE/VO₂, VO₂ relative to body weight, and HR/VO₂ slope (beat/L) but absolute VO₂ at the VT was reduced. The latest is illustrated in Figure 2 as well as the different ways of expressing VO₂Peak before and after bariatric surgery. No change in VO₂ relative to body weight, relative to LM or relative to LM legs at the VT was observed (Table 3; Fig. 2).

After bariatric surgery, the maximal VO₂ (absolute, relative to body weight or relative to LM) and the VT level were lower than in control subjects. Absolute VT measured during cycling CPET was positively correlated to the LM of the legs, 6 months after bariatric surgery and in control subjects, but not in the pre-surgery condition (Fig. 3).
Discussion

The present results confirm the positive effects of bariatric surgery on metabolic prognostic factors and the muscle strength/LM ratio. However, 6 months after bariatric surgery, absolute VO₂peak did not improve, and the VT was reduced. This appeared in a context of a 12% decrease in lean body mass. The presently observed positive correlation between the cycling LM and the VT measured during a cyclo-ergometer CPET after bariatric surgery gives credit to the tested hypothesis of a post-surgery muscular aerobic capacity limitation impacting the ventilatory response to exercise, characterized by early anaerobic metabolism and early hyperventilation stimulations.

While patients with obesity are known to have impaired skeletal muscle aerobic function, previous studies reported that bariatric surgery may have beneficial qualitative muscular effects on oxidative capacity but associated to a quantitative muscular alteration [20, 21]. Indeed, during the heavy weight loss phase, proteolysis provides a source of amino acids needed for metabolic cell functions causing muscle mass reduction [13]. The present study reported a 12% LM loss 6 months after surgery with the legs LM after weight loss positively correlated to the VO₂ at the VT (Fig. 3b). This suggests that even if weight loss
may have beneficial effects on aerobic muscle function, a lower muscle mass after surgery overrides the positive qualitative effects and is associated to an overall lower muscular aerobic capacity, as reflected by lower VT. This is of importance as VT represents the energy requirement level above which anaerobic metabolism is activated and is associated with a consequent hyperventilation response [22, 23]. Interestingly, a low VT associated to a high maximal RER is typically observed in muscular deconditioning conditions with early triggering of the anaerobic metabolism activation and early hyperventilation response [24]. As the VE-breathlessness relationship during exercise has been shown to remain unaffected after bariatric surgery, one can suspect that this early exercise induced hyperventilation may cause respiratory discomfort at lower submaximal exercise intensities [25].

Cardiovascular Response to Exercise

In the present study, weight loss surgery stimulated the chronotropic response as reflected by the increase of the HR versus absolute $\dot{V}O_2$ slope. Neunhaeuserer et al. [3] suggested that since cardiovascular and pulmonary function are not supposed to be negatively affected by bariatric surgery, an increased chronotropic response rather reflects a cardiac compensatory effect of a decreased muscular aerobic capacity.

Maximal $\dot{V}O_2$ pulse, the product of maximal stroke volume ($SV_{\text{max}}$) and peak arteriovenous oxygen content difference ($Ca-v\dot{O}_2$peak), was previously found to be unchanged or declined after surgery, in relation to an altered muscular oxygen extraction ($Ca-v\dot{O}_2$peak) [6]. Maximal $\dot{V}O_2$ pulse corrected for the exercising muscle mass (LM legs) better reflects $SV_{\text{max}}$ when comparing situations of quantitative mass changes (cfr post-surgery reduction of LM). This indirect index of $SV_{\text{max}}$ remained unaffected after surgery in the present study, suggesting little or no influence of weight loss on $SV_{\text{max}}$. Therefore, according to Fick’s Principle, it might be speculated that identical absolute $VO_2$peak after surgery was related to an unchanged $SV_{\text{max}}$ and a compensatory chronotropic stimulation in response to a lower $Ca-v\dot{O}_2$ induced by lower limb muscle mass loss.

Respiratory Response to Exercise

Previous studies reported that VAT and subcutaneous trunk fat loss after bariatric surgery improves overall pulmonary function with reduced work of breathing an enhanced ventilatory response to exercise resulting in improved gas exchange [26, 27]. In the present study, subjects suffering from obesity showed no ventilatory efficiency or chemosensibility alteration with no ventilatory limitation or exercise induced hypoxemia. However, post-bariatric surgery increase in maximal VE/VO$_2$ might reflect a muscular deconditioning state with high hyperventilatory response to exercise.

Muscle Strength

The present results show no difference in MIP and MEP between the pre- and post-surgery conditions and compared to healthy subjects with normal weight. Previous studies showed conflicting results with either unchanged [28], increased [29], or reduced [30] respiratory muscle strength 6 months after bariatric surgery. Type II errors, male/female equilibrium, initial BMI, FM distribution, and loss may account for discrepancies between studies.

The increase in relative (but not absolute) limb muscle strength after the bariatric surgery, among others mechanisms, could be related to an improvement in both muscle activation (triggered by the increased moderate physical activity time) and/or alleviation of central obesity (VAT loss), known to affect muscular metabolism pathways and inflammation [31].

Limitations

The number of patients evaluated before and after bariatric surgery was small and thus type II also type I errors could have occurred in spite of a paired sample design or a careful matching. Moreover, physical activity levels were assessed using a physical activity questionnaire which presents a lower reliability as compared to objective methods [32]. While GPAQ validity may be criticized, a recent systematic review by Keating et al. [32] showed a good to very good reliability for quantifying time spent in moderate and vigorous activities. To improve GPAQ validity, we used the interviewer-administered version of the questionnaire since it presents a higher correlation with accelerometer measurements for moderate-to-vigorous physical activity than the self-administered version [33]. It should also be emphasized that both nutritional status and physical activity levels highly influence the post-bariatric surgery LM loss and may therefore have influenced the present results. The adherence to the protein intake recommendations may interfere with LM loss but was not measured in the present study.

Conclusion

Bariatric surgery reduced total FM and VAT with considerable positive metabolic benefits associated with a preserved cardiovascular response to exercise resulting in
unchanged aerobic capacity. However, bariatric surgery results in a substantial LM loss which is associated with a decreased VT. Indeed, LM is correlated to the VT suggesting that a lower LM alters the muscular aerobic capacity after bariatric surgery. Consequently, a slightly increased chronotropic response to exercise and an early triggering of exercise hyperventilation response are observed. The present results support the idea that a muscular aerobic capacity limitation should be taken into consideration during bariatric surgery follow-up in particular when LM loss, low VT, or exercise breathlessness complaints are observed.

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Statement of Ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all individual participants included in the study, approved by the local Ethical Committee (reference: P2016/448).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Concept and design: N.Z., V.F., P.L., J.C., and J.-J.M. Data acquisition and Investigation: N.Z., C.S., K.F., and M.K. Data analysis and interpretation: N.Z., C.S., V.F., K.F., M.K., and G.D. Writing – original draft: N.Z. and V.F. Review and editing: N.Z., M.K., K.F., G.D., J.-J.M., J.C., and P.L. Coordinator – overall and concrete affairs: N.Z.

Data Availability Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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255
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