Obesity Diagnosis and Treatment

Research Article Open Access

The Ability to Oxidize Lipids at Exercise in Surgically Weight-Reduced Obese Patients is Restored but Shifted to a Lower Exercise Intensity [Version 1, Awaiting Peer Review]

Jean-Frédéric Brun[1]*, Marlène Richou[1], Valentin Lasteyrie[1], François Bughin[1], Mathieu Sardinoux[1], David Nocca[2], Christine Fédou[3] and Jacques Mercier[1]

[1]UMR CNRS 9214-Inserm U1046, «Physiopathologie & Médecine Expérimentale du Cœur et des Muscles – PHYMEDEXP», Unité d'Explorations Métaboliques (CERAMM), Université de Montpellier, Département de Physiologie Clinique, Hôpital Lapeyronie CHU Montpellier, France
[2]Service de Chirurgie Digestive, France
[3]Service d'Endocrinologie, France

***Corresponding author:** Jean-Frédéric Brun, Unité d'Explorations Métaboliques (CERAMM), Université de Montpellier, Département de Physiologie Clinique, Hôpital Lapeyronie CHU Montpellier, France, Email: j-brun@chu-montpellier.fr

Original Submission

Received: January 13, 2017
Accepted: February 05, 2017
Published: February 15, 2017

Open Peer Review Status: Awaiting Peer Review

How to cite this article: Jean-Frédéric Brun, Marlène Richou, Valentin Lasteyrie, François Bughin, Mathieu Sardinoux, David Nocca, Christine Fédou, Jacques Mercier. The Ability to Oxidize Lipids at Exercise in Surgically Weight-Reduced Obese Patients is Restored but Shifted to a Lower Exercise Intensity [Version 1, Awaiting Peer Review]. Obes Diagn Treat. (2017) 1: 2.1

Abstract

We evaluated the influence of bariatric surgery on the balance of energy substrates during exercise, compared to matched obese and nonobese subjects. Exercise calorimetry was used for determining the LIPOXmax (exercise level at which lipid oxidation reaches a maximum) in 28 obese patients after bariatric surgery (17 by sleeve gastrectomy, 7 by Roux-en-Y gastric by-pass and 4 by gastric ring), compared to two groups of obese, 33 matched with the preoperative BMI and 87 matched for the actual BMI, and 322 nonobese subjects, matched for age and gender. The LIPOXmax occurs at a lower exercise intensity in obese patients treated by bariatric surgery (23 ± 0.33 %Pmax) compared to each of the other groups (p<0.001). The maximal lipid oxidation rate was higher in the WL group compared to OC (p<0.001) and was similar to the WLC maximal lipox rate. However it remained lower than in the control group (p=0.005). In conclusion, patients who have lost an average of 42 kg after bariatric surgery have an improved ability to oxidize fat at exercise but their peak of lipid oxidation is shifted to lower exercise intensities.

Keywords

Weight Loss; Bariatric Surgery; Exercise; Lipid Oxidation; LIPOXmax

Introduction

Exercise is an important tool in the management of obesity [1], although its effects on weight loss, considered alone, are generally described as rather moderate [2]. It is well established that it improves the efficiency of weight reducing procedures and prevents weight regain [1].

Progresses in bariatric surgery over the last decades have given it an increasing importance in the treatment of obesity, due to its potent and long lasting effects of weight loss that results in a decrease in obesity related morbidities [3].

It is attractive to develop combined strategies in which exercise will be employed to improve the effects of bariatric surgery and provide to patient the possibility to become less sedentary on the long term, as has been successfully done in other chronic diseases.

However, in the case of obesity after bariatric surgery, the question arises of which kind of exercise should be proposed. Recent studies propose in metabolic diseases (obesity, diabetes mellitus) to target exercise training at the intensity level where lipid oxidation is maximal (LIPOXmax) [4-7]. Interestingly, a preliminary report indicates that this variety of exercise training improves the weight-reducing effect of sleeve gastrectomy [8].

However, in the case of obese subjects that have lost an important quantity of fat after bariatric surgery, there is no information available about the exercise intensity level at which this maximal lipid oxidation occurs.

Thus, the purpose of this study was to determine LIPOXmax in obese patients that had lost weight after bariatric surgery, prior to define strategies in which exercise training will be employed associated to surgery.

Research Design and Methods

Subjects

Four groups of patients were studied. One group consisted of 28 previously grade 3 obese patients (BMI > 40 Kg/m²) who underwent bariatric surgery to induce weight loss (WL group) after a multidisciplinary evaluation. The operative procedure consisted in 17 laparoscopic sleeve gastrectomy with conservation of the antrum as described by Nocca and al [9], 7 laparoscopic Roux-en-Y gastric bypass as described by Gagner and al [10], and 4 laparoscopic gastric banding by Pars Flacida approach (Swedish Adjustable Gastric Banding) as described by Forsell and all [11].

The average BMI in this group before surgery was 45.5 ± 1.3 Kg/m²; after a follow-up of 12.9 ± 3.6 months, an average weight loss of 41.7 ± 0.8 Kg was obtained, with a significant decrease of BMI from 45.5 ± 1.3 to 32.7 ± 1.2 Kg/m².

Two other groups of obese patients were matched for age, gender, and respectively for post weight loss BMI (weight loss control group (WLC), BMI: 32.35 ± 0.01 Kg/m²) and for initial BMI (obese control group (OC), BMI: 45.23 ± 0.14 Kg/m²). See table 1.

Table 1

		Weight Loss group n=28	Obese control group n=33	Weight Loss control group n=87	Control group n=322
		Post-operative patients	Matched for pre-operative BMI	Matched for post-operative BMI	
Age (years)		38.6 ± 2.34	42.9 ± 0.41	39.9 ± 0.14	36.4 ± 1.23§
BMI (Kg/m²) 38.9 ± 2.3		45.5 ± 1.3 (pre-operative)	45.23 ± 0.14	32.35 ± 0.01	22.38 ± 2.04
COP	Watts	50.9 ±0.74	51.2 ± 1.23	62.2 ± 0.46	41 ±3.4
	%Pmax	27% ± 0.42	36% ± 1.08	34.5% ± 0.2	37% ± 1.7
LIPOX-max	Watts	42.9 ± 0.54	52.2 ± 0.8	55.8 ± 0.35	53 ± 2.6
	%Pmax	23% ± 0.33	34% ± 0.4***	30.4% ± 0.13**	33% ± 1.2***
Maximal lipid oxidation rate (mg.Kg^{-1}.min^{-1})		2.34 ± 0.21	1.26 ±0.13***	2.38 ±0.13	3.43 ± 0.21**

An additional control group (C group) was composed by 322 non obese patients (BMI: 22.38 ± 2.04 Kg/m²).

All subjects in control groups (WLC, OC and C groups) were stable for weight, sedentary and not performing regular exercise.

The experimental design consisted of comparing the balance of energy substrates during exercise by indirect exercise calorimetry to evaluate influence of bariatric surgery in obese patients.

Exercise Testing

All subjects were asked to come and perform test in the morning after an overnight fast (12 hours).

As generally used to individualize the increment of exercise intensity during cardiopulmonary exercise testing, the theoretical maximal aerobic power (P_{max}), corresponding to the power reached when theoretical VO_{2max} is reached, was calculated from Wassermann's equations modified for overweight subjects.

The test consisted of five six minute steady-state workloads at 20, 30, 40, 50, and 60% of P_{max}. Consequently, they underwent a test with the same relative incremental workload and were compared at the same percentage of their P_{max}.

The subjects performed the test on an electromagnetically braked cycle ergometer (Ergoline Bosch 500). Heart rate and electrocardiographic parameters were monitored continuously throughout the test by standard 12-lead procedures. Metabolic and ventilatory responses were assessed using a digital computer based breath to breath exercise analyzing system (Jaeger MS-CPX). Thus, we could measure VO_2, VCO_2 (in ml/min) and calculate the non-protein respiratory quotient ($RER=VCO_2/VO_2$).

Calculation of Substrate Utilization, COP and LIPOXmax

Lipid oxidation (Lipox) and carbohydrate utilization (Glucox) rates were calculated by indirect calorimetry from gas exchange measurements according to the non-protein respiratory quotient technique as previously reported [4].

VO_2 and VCO_2 were determined as the mean of measurements during the fifth and sixth minutes of each step, where CO_2 production from bicarbonates to compensate for lactate acidosis becomes negligible [12].

This technique provided carbohydrate and lipid oxidation rates at different exercise intensities.

Additionally, after smoothing the curves, we calculated the two parameters quantifying the balance between carbohydrates and lipids induced by increasing exercise intensity: the maximal lipid oxidation point (LIPOXmax) and the Crossover Point (COP).

The LIPOXmax is the exercise intensity at which lipid oxidation reaches its maximal level before decreasing while carbohydrate utilization further increases. It is calculated as previously reported after smoothing of the curve plotting lipid oxidation as a function of power [4]. The maximal lipid oxidation rate at the LIPOXmax was expressed in $mg.kg^{-1}.min^{-1}$.

The crossover point (COP) is the exercise intensity at which the part of carbohydrate utilization used to provide energy becomes predominant over lipid oxidation. Beyond this point, the subject is referred to as "glucodependent". It was calculated as the exercise intensity where 70% of the substrates used to provide energy are carbohydrates and 30% are lipids, according to Brooks and Mercier. [13].

The LIPOXmax and the COP were expressed either in absolute power values (watts) or in percentage of the theoretical P_{max} ($\%P_{max}$).

Validity and reproducibility of this test were assessed in a previous publication. Coefficients of variation (CV) were calculated for RER, LIPOXmax and COP at four different intensities. CV of RER were between 2.8 and 4.75%. CV of LIPOXmax and COP was respectively 11.41%P_{max} and 11.63%P_{max}. VO_2, CO_2, RER, CHO and lipid oxidation rates were also compared during the incremental test and during single steady-state workloads of the same intensity performed at random order. These parameters were not significantly different.

Statistical Analysis

Overall comparisons between mean values were performed by Kruskall-Wallis one way ANOVA on ranks, followed by pairwise multiple comparisons using Dunn's method. Significant differences were accepted at p<0.05. All values are mean ± S.E.M. Statistical analyses were performed with SigmaStat 1.0 (Jandel Scientific GmbH, Germany).

Results

Indirect Exercise Calorimetry

Calorimetry

There were no significant differences between obese groups in COP neither expressed in absolute power values nor in $\%P_{max}$. However, it seems to be a trend for a shift to lower exercise intensity for WeightLoss group (27 ± 0.42 $\%P_{max}$) compared to post-operative matched group (WLC group: 34.5 ± 0.02 $\%P_{max}$) (p=0.08). The COP in non-obese controls subjects (C group) occurs at a higher exercise intensity level (37 ± 0.01 $\%P_{max}$; p=0.029).

LIPOXmax and Maximal Lipid Oxidation Level

The LIPOXmax occurs at a significant lower exercise intensity (23 ± 0.33 $\%P_{max}$) in the WL group compared to all others groups (WLC group: 30.4 ± 0.13 $\%P_{max}$, p=0.002; OC group: 34 ± 0.42 $\%P_{max}$, p=0.001 and C group: 33 ± 1.2 $\%P_{max}$, p<0.001). Results are presented in figure 1.

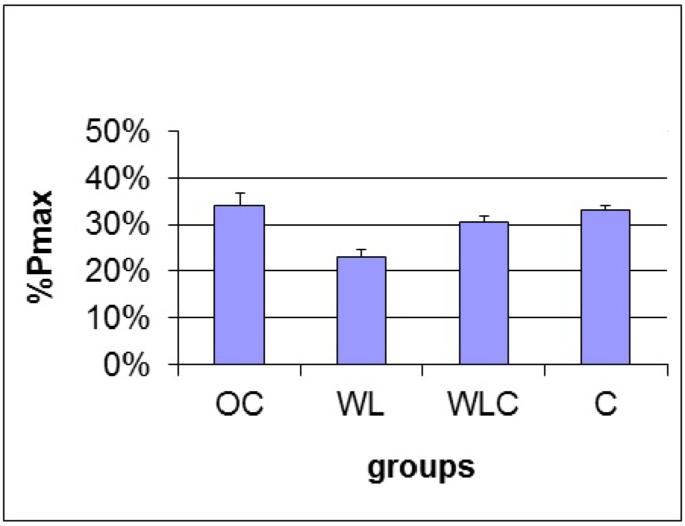

Figure 1: LIPOXmax ($\%P_{max}$).

Concerning the maximal lipid oxidation rates at LIPOXmax, a significant difference was observed with a higher maximal lipox rate for WL group compared to OC group, matched for pre-operative BMI (2.34 ± 0.13 $mg.Kg^{-1}.min^{-1}$ vs. 1.26 ± 0.13 $mg.Kg^{-1}.min^{-1}$; p<0.001) . this rate was similar to the WLC maximal lipox rate (2.34 ± 0.13 $mg.Kg^{-1}.min^{-1}$ vs. 2.39 ± 0.13 $mg.Kg^{-1}.min^{-1}$; ns) but remain lower than control group (2.34 ± 0.13 $mg.Kg^{-1}.min^{-1}$ vs. 3.43 ± 0.21 $mg.Kg^{-1}.min^{-1}$; p=0.005) (Figure 1).

These increase maximal lipox rate in WL group was observed despite the LIPOXmax shift to lower exercise intensity. (Figure 2).

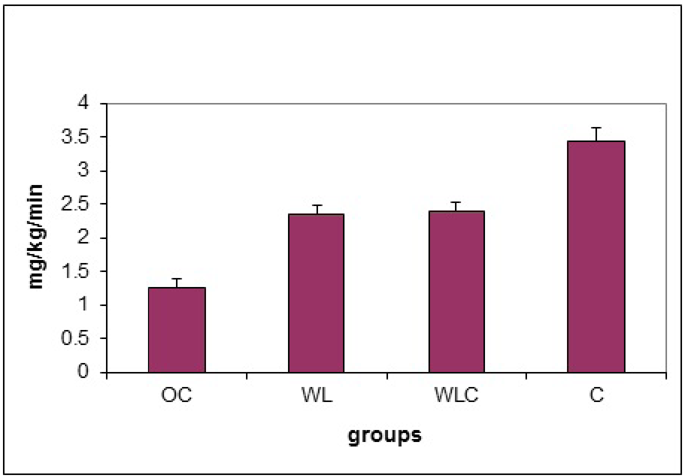

Figure 2: Maximum lipid oxidation rate.

This shift to lower $\%P_{max}$ was not due to an artificial "weight-loss effect" resulting in decreased theoretical P_{max}, indeed theoretical P_{max} calculated from Wassermann's equations were similar in WL group before and after weight loss. Besides, there were no significant difference between theoretical P_{max} calculated either from Wassermann's equation or Astrand's nomogram.

Discussion

The main results of this study, as shown in figure 2, are that obese patients that have lost an average 41 Kg after bariatric surgery exhibit a higher maximal lipid oxidation rate than obese patients matched for their pre-operatory BMI. This maximal lipid oxidation rate is at the same level as obese patients matched for their post-operatory BMI. These results suggest that the maximal lipid oxidation rate has been restored after the important weight loss induced by bariatric surgery. By contrast, the exercise intensity at which this LIPOXmax occurs is shifted to a lower value compared to those two groups of obese subjects.

Substrate utilization during exercise in grade 3 obese patients after weight loss, and compared with that in weight matched patients has been already examined in previous studies. [14-15]. Actually, most of these studies used only one-step steady-state workload and not, as we did here, multiple step steady-state workloads. Such an experimental design is unable to describe the bell-shaped curve of lipid oxidation. This could explain some discrepancies among the reported results. It seems obvious that exercise tests using several steps and allowing COP and LIPOXmax determination can provide a more precise picture of the balance of substrates during exercise. Dealing with a bell-shaped curve, and given the wide inter-individual variability of this balance of substrates in a population, it is impossible to know whether a single steady-state workload is actually situated below or above the LIPOXmax. This makes the comparison of single workloads difficult to interpret. In this study, a picture of the bell-shaped curve is given in every subject, allowing a comparison among all the groups.

This study is cross-sectional and should be confirmed by a prospective one which is in progress in our unit, but it is very likely to suggest that bariatric surgery-induced weight loss improves the ability to oxidize lipids an sets it at a level of subjects exhibiting this lower BMI, but that a marked left-shifting occurs, so that the power intensity at which lipid oxidation is maximal, the LIPOXmax, is lowered.

Such a shift may be a mechanism of resistance to weight reduction that could be counteracted by adequate training. Presumably, if theoretical levels of exercise targeting are proposed without taking into account this specific situation, training would act rather at the level where carbohydrates are the major fuel used for oxidation. We have previously demonstrated that training above the LIPOXmax mostly improves the ability to oxidize CHO at exercise rather than the oxidation of lipids [16-17]. In others terms, training based on common guidelines will mostly improve carbohydrate rather than lipid oxidation.

Although training regardless its metabolic meaning has been shown to be beneficial in the management of obesity [18] our working hypothesis is that a precise targeting at the LIPOXmax will make it more efficient. Such a procedure has been shown to be effective for reducing fat mass while maintaining lean mass, and improve further ability to oxidize fat during exercise [5, 19]. Most of its weight-lowering effect seems to be explained by an impact on eating behavior [6].

The lipid oxidation rate measured with this procedure of exercise calorimetry at the level of LIPOXmax has been shown to be the same as the lipid oxidation rate maintained over 45 min. of steady state exercise targeted at LIPOXmax [20].

Thus, it is attractive to propose in such obese patients to target training at the individual LIPOXmax they exhibit after weight reduction. The efficiency of this procedure as well as its advantage over less specific training guideline require to be specifically studied.

On the whole, this study shows that previously grade 3 obese patients, that have lost 41 kg on the average, are able to oxidize lipids at exercise, and thus are likely to obtain benefit from exercise training. However, their ability to oxidize lipids is shifted at a lower exercise intensity so that it seems logic to propose a specific targeting of exercise training to these patients. Further studies are in progress to answer to this question.

References

1. Dombrowski SU, Knittle K, Avenell A, Araújo-Soares V, Sniehotta FF. Long term maintenance of weight loss with non-surgical interventions in obese adults: systematic review and meta-analyses of randomised controlled trials. BMJ. 2014; 348: g2646.
2. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M,

Baillargeon JP, et al. Effects of Lifestyle Interventions That Include a Physical Activity Component in Class II and III Obese Individuals: A Systematic Review and Meta-Analysis. PLoS ONE. 2015; 10: e0119017.

3. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, et al. Bariatric Surgery: A Systematic Review and Meta-analysis. JAMA. 2004; 292: 1724–1737.

4. Pérez-Martin A, Dumortier M, Raynaud E, Brun JF, Fédou C, et al. Balance of substrate oxidation during submaximal exercise in lean and obese people. Diabetes & Metabolism. 2008; 27: 466.

5. Besnier F, Lenclume V, Gérardin P, Fianu A, Martinez J, et al. Individualized Exercise Training at Maximal Fat Oxidation Combined with Fruit and Vegetable-Rich Diet in Overweight or Obese Women: The LIPOXmax-Réunion Randomized Controlled Trial. PLoS One. 2015; 10: e0139246.

6. Guiraudou M, Romain AJ, Mawunu M, Bedjih K, Fédou C, et al. Effets chroniques de l'exercice ciblé au niveau d'oxydation maximale des lipides (LIPOXmax) sur le comportement alimentaire de sujets obèses sédentaires. Sci. Sports. 2016; 31: 13–18.

7. Bordenave S, Metz L, Flavier S, Lambert K, Ghanassia E, et al. Training-induced improvement in lipid oxidation in type 2 diabetes mellitus is related to alterations in muscle mitochondrial activity. Effect of endurance training in type 2 diabetes. Diabetes Metab. 2008; 34: 162-168.

8. Drapier E, Fédou C, Ghanassia E, Nocca D, Mercier J, et al. L'exercice en endurance à faible intensité renforce-t-il l'efficacité amaigrissante d'une gastrectomie en manchon ? Sci. Sports. 2016; 31: 162-165.

9. Nocca D, Krawczykowsky D, Bomans B, Noël P, Picot MC, et al. A Prospective Multicenter Study of 163 Sleeve Gastrectomies: Results at 1 and 2 Years. Obesity Surgery. 2008; 18: 560-565.

10. Gagner M, Garcia-Ruiz A, Arca MJ, Heniford TB. Laparoscopic isolated gastric bypass for morbid obesity. Surg Endosc. 1999; 13: S19.

11. Forsell P, Hellers G, Hell E. The Swedish Adjustable Gastric Banding (SAGB) for morbid obesity-Weight loss, complications, pouch volume, and stoma diameter in a four-year follow-up. Acta Chir. Austriaca. 1998; 30: 161-165.

12. MacRae HSH, Noakes TD, Dennis SC. Role of decreased carbohydrate oxidation on slower rises in ventilation with increasing exercise intensity after training. Eur. J. Appl. Physiol. 1995; 71: 523-529.

13. Brooks GA, Mercier J. Balance of carbohydrate and lipid utilization during exercise: the "crossover" concept. J Appl Physiol. 1994; 76: 2253–2261.

14. Guesbeck NR, Hickey MS, MacDonald KG, Pories WJ, Harper I, et al. Substrate utilization during exercise in formerly morbidly obese women. J Appl Physiol. 2001; 90: 1007–1012.

15. Ezell DM, Geiselman PJ, Anderson AM, Dowdy ML, Womble LG, et al. Substrate oxidation and availability during acute exercise in non-obese, obese, and post-obese sedentary females. Int J Obes Relat Metab Disord J Int Assoc Study Obes. 1999; 23: 1047–1056.

16. Manetta J, Brun JF, Perez-Martin A, Callis A, Prefaut C, et al. Fuel oxidation during exercise in middle-aged men: role of training and glucose disposal. Med Sci Sports Exerc. 2002; 34: 423–429.

17. Brandou F, Savy-Pacaux AM, Marie J, Bauloz M, Maret-Fleuret I, et al. Impact of high- and low-intensity targeted exercise training on the type of substrate utilization in obese boys submitted to a hypocaloric diet. Diabetes Metab. 2005; 31: 327-335.

18. Bensimhon DR, Kraus WE, Donahue MP. Obesity and physical activity: a review. Am. Heart J. 2006; 151: 598-603.

19. Brun JF, Jean E, Ghanassia E, Flavier S, Mercier J. Metabolic training: new paradigms of exercise training for metabolic diseases with exercise calorimetry targeting individuals. Ann. Réadapt. Médecine Phys. 2007; 50: 528-534.

20. Jean E, Flavier S, Mercier J, Brun JF. Exercise calorimetry with 6 min steps closely predicts the lipid oxidation flow rate of a 45 min steady state targeted training session at the level of maximal lipid oxidation (lipoxmax). Fundamental and Clinical Pharmacology. 2007; 21: 95: 470.