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Muscle wasting after coronary artery bypass graft surgery: impact on post-operative clinical status and effect of exercise-based rehabilitation

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ORIGINAL ARTICLE

Muscle wasting after coronary artery bypass graft surgery: impact on post-operative clinical status and effect of exercise-based rehabilitation

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ABSTRACT

Background: Coronary artery bypass graft (CABG) surgery is known to induce significant muscle wasting. It remains to be investigated whether muscle wasting after CABG surgery relates to a worse clinical status at entry of rehabilitation and exercise-based rehabilitation remediates such muscle wasting.
Design: Prospective observational study.
Methods: In 21 males, changes in lean tissue mass (LTM) after CABG surgery were assessed and during a 12-week endurance exercise-based rehabilitation intervention. Changes in blood parameters and cardiopulmonary exercise capacity were assessed, and relations with changes in LTM were analysed.
Results: LTM decreased by -1.9 ± 2.5 kg ($p < .05$) within 3 weeks after CABG surgery: greater LTM loss related to a lower ventilatory threshold at entry of rehabilitation ($r = 0.58$–0.61, $p < .05$). LTM was fully restored ($+2.1 \pm 2.4$ kg, $p < .05$) during rehabilitation.
Conclusion: In males, CABG-induced LTM reduction was associated with a worse aerobic exercise tolerance at entry of rehabilitation, but this LTM reduction was fully remediated by endurance exercise-based rehabilitation.

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Coronary bypass surgery; lean tissue mass; rehabilitation

Introduction

After coronary artery bypass graft (CABG) surgery significant muscle wasting is observed [1–3]. Although sarcopenia is related to elevated morbidity in heart failure patients [4], it remains unidentified whether patients with significant muscle wasting after CABG surgery are in need of modified intervention, and whether endurance exercise-based rehabilitation can fully remediate such muscle wasting. The aim of this study was, for the first time, to explore the impact of amount of muscle wasting after CABG surgery on clinical status at entry of rehabilitation and whether such muscle wasting is fully remediated by endurance exercise-based rehabilitation.

Methods

Population

This study was approved by the local medical ethical committee (Nr. B24320109465, Jessa Hospital, Hasselt, Belgium), adhered to the Helsinki declaration and all subjects signed an informed consent. Subjects with pulmonary, neurologic, oncologic and/or nephrologic disease, metal implants or previous CABG or valve surgery were excluded prior to study. Patients with previous percutaneous coronary intervention or myocardial infarction, but without heart failure, were allowed to participate in this study. The study sample size ($n = 30$) was based on previous studies assessing the impact of CABG surgery on lean tissue mass (LTM) [2,3] and impact of rehabilitation [5]. After inviting 119 eligible Caucasian candidates admitted to the hospital for elective CABG surgery, 30 subjects agreed to participate in this prospective observational cohort study (Supplementary Figure 1). Due to post-operative complications or failure to complete the rehabilitation programme, nine subjects were lost during follow-up.

Measurements

Before surgery, at entry of rehabilitation (18 ± 1 days after surgery), after 7 and 12 weeks of rehabilitation

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Supplemental data for this article can be accessed here.

Table 1. Impact of CABG surgery and rehabilitation on secondary outcomes.

	Preoperative		Entry of rehabilitation		7 weeks of rehabilitation		12 weeks of rehabilitation	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
Subject characteristics								
Age	64.3 ± 9	65 (10)	—	—	—	—	—	—
Sex (n = male)	21	—	—	—	—	—	—	—
Body mass index (kg/m^2)	**28.1 ± 4.1***	**27.47 (4.84)***	27.42 ± 4.3	26.61 (3.19)	27.47 ± 4.5	26.59 (3.81)	27.42 ± 4.7	26.97 (5.06)
Rehabilitation intervention								
Days (n)	—	—	—	—	22.5 ± 4.5#	22 (3)	38.2 ± 5	38 (4)
Duration session (min)	—	—	—	—	40.5 ± 1.6#	40 (0.0)	43.7 ± 2.3	45 (0.0)
Intensity (% of W peak)	—	—	**33.6 ± 8.5#**	33.3 (9.36)	52.4 ± 10.4	48.6 (10.75)	59.3 ± 12.5	60 (11.68)
Exercise capacity								
Cycling power output (W)	—	—	**118 ± 27#**	**120 (38)#**	144 ± 33	150 (44)	155 ± 46	157 (40)
Oxygen uptake (mL/min)	—	—	**1522 ± 284#**	**1507 (407)#**	1869 ± 371	1795 (302)	1941 ± 458	1916 (530)
First ventilatory threshold (mL/min)	—	—	**962 ± 48#**	**860 (300)#**	1184 ± 53	1175 (450)	1257 ± 69	1100 (500)
Second ventilatory threshold (mL/min)	—	—	**1233 ± 59#**	**1162 (360)#**	1472 ± 71	1408 (504)	1494 ± 87	1438 (759)
Heart rate (beats/min)	—	—	**109 ± 14#**	**109 (20)#**	125 ± 15	124 (47)	127 ± 18	129 (24)
Respiratory gas exchange ratio (RER)	—	—	1.16 ± 0.11	1.18 (0.15)	1.15 ± 0.09	1.16 (0.13)	1.16 ± 0.11	1.20 (0.14)
Test duration (s)	—	—	370 ± 119	363 (128)	405 ± 78	405 (126)	408 ± 97	420 (110)
Blood parameters								
Total cholesterol (mg/dL)	**155 ± 39***	**145 (63)***	132 ± 28	127 (36)	135 ± 22	131 (26)	138 ± 19	138 (32)
LDL cholesterol (mg/dL)	**84 ± 27***	**80 (21)***	72 ± 23	67 (24)	72 ± 18	72 (17)	71 ± 13	70 (23)
HDL cholesterol (mg/dL)	**40 ± 12***	**36 (10)***	**36 ± 9#**	**35 (9)#**	41 ± 10	41 (6)	44 ± 9	44 (7)
Triglyceride (mg/dL)	**158 ± 95***	**125 (153)***	117 ± 54	94 (72)	103 ± 39	103 (39)	116 ± 84	92 (46)
Glucose (mmol/L)	6.1 ± 2.3	5.7 (1.44)	6.2 ± 1.4	5.7 (1.28)	6.3 ± 1.8	5.8 (0.93)	6.2 ± 1.9	5.7 (1.17)
C-peptide (ng/mL)	2 ± 1	2.03 (1.2)	1.9 ± 0.8	1.91 (1.12)	1.7 ± 0.7	1.73 (0.68)	1.8 ± 0.7	1.77 (0.54)
Insulin (mU/L)	11.1 ± 6.3	10.6 (7.5)	11.8 ± 8.7	10.2 (9.4)	12.7 ± 7.5	12.3 (6.9)	11.5 ± 7.4	9.8 (4.5)
HOMA-IR index	3.2 ± 2.4	2.6 (2.37)	3.7 ± 4.2	3.1 (2.43)	4.1 ± 4.6	3.3 (2.49)	3.7 ± 4.6	2.7 (1.87)
C-Reactive protein (mg/dL)	0.51 ± 0.8	0.15 (0.26)	1.02 ± 1.9	0.50 (0.65)	0.54 ± 0.9	0.20 (0.41)	0.22 ± 0.2	0.15 (0.07)
Glycated haemoglobin (mmol/mol)	6.02 ± 0.7	5.8 (0.4)	5.69 ± 0.6	5.5 (0.4)	5.93 ± 0.7	5.8 (0.33)	6.12 ± 0.7	5.9 (0.4)
Cortisol (total; µg/dL)	18.9 ± 4.9	17.7 (5.3)	17.4 ± 5.4	16.7 (8.60)	18.2 ± 4.1	18.2 (5.5)	18.4 ± 3.7	18.5 (6.3)
Testosterone (total; ng/mL)	3.9 ± 1.7	3.9 (2.5)	3.7 ± 1.8	3.1 (1.4)	3.9 ± 1.4	3.8 (1.1)	4 ± 1.1	3.9 (1.1)
Sex hormone-binding globulin (nmol/L)	45 ± 17	44.92 (22)	43 ± 16	39 (22)	43 ± 18	39 (13)	42 ± 16	39.1 (18)
Insulin-like growth factor-1 (µg/L)	143 ± 40	143 (32)	151 ± 51	150 (103)	149 ± 39	149 (61)	138 ± 49	138 (77)
Growth hormone (µg/L)	**0.18 ± 0.1***	**0.18 (0.08)***	0.84 ± 0.88	0.70 (0.47)	0.48 ± 0.51	0.42 (0.35)	0.52 ± 0.57	0.26 (0.34)
Free androgen index (%)	32 ± 14	32 (16.5)	32 ± 17	27.5 (13.8)	33 ± 7	33.1 (5.5)	36 ± 9	35.8 (2.3)
Cortisol-to-testosterone ratio	5.5 ± 2.8	4.93 (2.31)	5.8 ± 2.7	5.96 (3.88)	5.2 ± 2.1	4.92 (2.0)	4.9 ± 1.6	4.95 (3.09)

Data are presented as mean ± SD. First ventilatory threshold was determined by V-slope method, second ventilatory threshold was determined by VE/VCO$_2$ slope method. HDL: high-density lipoprotein; HOMA-IR: homeostatic model assessment for insulin resistance; IQR: inter quartile range; LDL: low-density lipoprotein.

*Significant difference between preoperative parameters compared with entry of rehabilitation (start rehabilitation) ($p < .05$).

#Significant difference between entry and end of rehabilitation ($p < .05$).

Bold values represent the significant difference ($p < .05$).

body composition was assessed by whole-body dual X-ray absorptiometry (Lunar DPXL, Wisconsin) [1]. In addition, cardiopulmonary exercise capacity was assessed by ergospirometry (Jaeger CPX Masterscreen, see Table 1 for parameters) on bike with a 1-min incremental work stage protocol until exhaustion (RER >1.10) [1]. Fasting (07.00–09.00 AM) whole-blood, plasma and serum samples were assessed at entry and after 7 and 12 weeks of rehabilitation by state-of-the-art methods in a clinical laboratory (see Table 1 for parameters) [1]. Primary outcome measure in this study was LTM. Secondary outcome measures physical fitness and blood parameters.

Rehabilitation

The rehabilitation intervention (see Table 1 for exercise modalities) involved endurance exercise training for three times/week at an intensity between the first and second ventilatory threshold (heart rate monitored), for a period of 12 weeks. Every session patients executed 15 min of walking, 20 min of cycling and 10 min of arm cranking.

Statistical analysis

Statistical analyses were executed by SPSS v.24.0 (SPSS Inc., Chicago). Data are presented as mean ± SD and median (interquartile range). Changes in parameters were analysed by Wilcoxon signed ranks tests (data were not normally distributed according to Shapiro–Wilk test), in which Bonferroni corrections for multiple comparisons were applied. Relationships between parameters were analysed by univariate Spearman correlations corrected for age, weight and height. Statistical significance was set at $p < .05$ (two-tailed).

Results

Impact of CABG surgery and rehabilitation on secondary outcomes

After CABG surgery significant decrease were observed in BMI, blood total, LDL and HDL cholesterol, and triglyceride concentrations, and increments in blood growth hormone concentrations ($p < .05$). During rehabilitation significant increments in exercise tolerance and blood HDL cholesterol concentrations were observed ($p < .05$, Table 1). Whole-body fat mass decreased after CABG surgery (-1.3 ± 0.4 kg, $p < .05$) and further during rehabilitation (-2.2 ± 1.0 kg, $p < .05$) (Figure 1).

Table 2. Relations between change in LTM after CABG surgery and clinical status at entry of rehabilitation.

	Correlation coefficient (*r*) total change in LTM (kg)	Correlation coefficient (*r*) relative change in LTM (%)
Exercise capacity		
Cycling power output (W_{max})	0.19	0.21
Cycling power output (% predicted)	0.31	0.32
Oxygen uptake (mL/min)	0.28	0.29
Oxygen uptake (% predicted)	0.34	0.35
First ventilatory threshold (mL/min)	**0.59***	**0.61***
Second ventilatory threshold (mL/min)	0.43	0.44
Blood parameters		
Total cholesterol (mg/dL)	−0.22	−0.26
LDL cholesterol (mg/dL)	−0.27	−0.30
HDL cholesterol (mg/dL)	0.17	0.16
Triglyceride (mg/dL)	−0.13	−0.15
Glucose (mmol/L)	0.07	0.10
C-peptide (ng/mL)	−0.38	−0.40
Insulin (mU/L)	−0.34	−0.34
HOMA-IR index	−0.27	−0.27
C-Reactive protein (mg/dL)	0.42	0.42
Glycated haemoglobin (mmol/mol)	−0.25	−0.22
Cortisol (total; µg/dL)	−0.30	−0.31
Testosterone (total; ng/mL)	−0.17	−0.18
Sex hormone-binding globulin (nmol/L)	−0.01	−0.02
Insulin-like growth factor-1 (µg/L)	−0.16	−0.18
Growth hormone (µg/L)	−0.14	−0.14
Free androgen index (%)	−0.30	−0.26
Cortisol-to-testosterone ratio	0.01	0.02

Correlations were corrected for age, body height and weight. HDL: high-density lipoprotein; HOMA-IR: homeostatic model assessment for insulin resistance; LDL: low-density lipoprotein; LTM: lean tissue mass.
*Significant correlation ($p < .05$).

Impact of CABG surgery and rehabilitation on LTM

Lean tissue mass decreased by -1.9 ± 2.5 kg after CABG surgery ($p < .05$) (Figure 1), followed by significant increments and full restoration ($+2.1 \pm 2.4$ kg, $p < .05$) during rehabilitation (Figure 1).

Relations between LTM reductions after CABG surgery and clinical status at entry of rehabilitation

Significant correlations ($p < .05$) were found between decrease in LTM after CABG surgery and first ventilatory threshold during exercise testing at entry of rehabilitation ($r = 0.59$–0.61, $p < .05$) (Table 2, Supplementary Figure 2).

Discussion

The major findings of this study were that in males (1) greater LTM reduction after CABG was related to a lower first ventilatory threshold during exercise testing at entry of rehabilitation, and (2) Such LTM reduction was fully restored during endurance exercise-based rehabilitation.

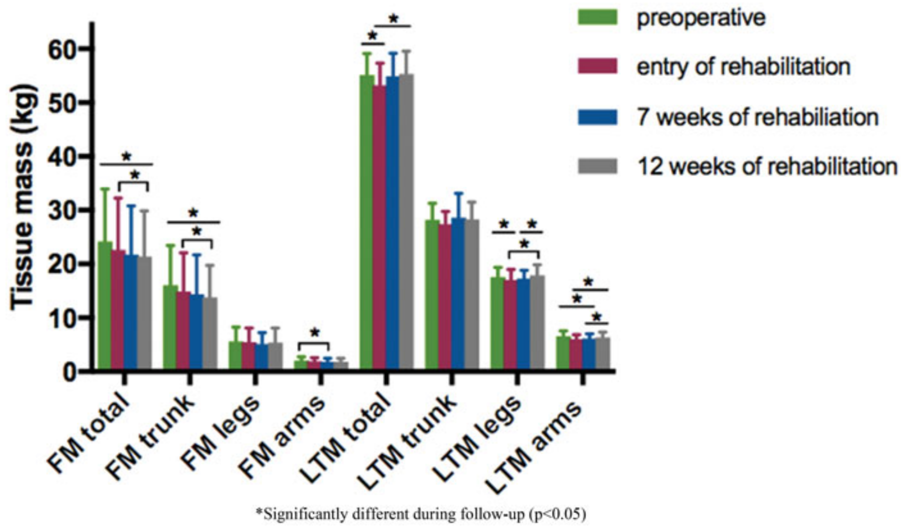

Figure 1. Change in fat mass (FM) and lean tissue mass (LTM) after CABG surgery and during rehabilitation. *Significantly different during follow-up ($p < .05$).

In line with a previous study showing that muscle wasting after CABG surgery was associated with decreased vitality [3], we further noticed that greater LTM reduction after CABG surgery related to a lower first ventilatory threshold during exercise testing ($r = 0.58–0.61$, $p < .05$) at entry of rehabilitation. Moreover, a possible aetiology of muscle mass change could not be explained by measured parameters in this study. Our data may thus indicate that patients with greater LTM reduction after CABG surgery may experience greater physical limitations to exercise, despite equal peak oxygen uptake. Regardless that there was no relation between training modalities and changes in LTM during rehabilitation, these patients may require adaptations in training modalities, such as initiating exercise intervention at a lower exercise intensity, or at least monitoring of perceived exertion. It remains to be addressed whether these patients are in need of additional strength training exercises as well, because the impact of such modification in exercise intervention on ventilatory threshold, specifically in CABG patients, remains uncertain [6].

Endurance exercise-based rehabilitation for 12 weeks led to a full restoration of LTM after CABG surgery. This positive effect was already noticed after seven weeks of intervention. In previous studies, increments in LTM have been observed in patients after CABG surgery when following exercise intervention [5], but our data also indicate, for the first time, that the amount of LTM gain is sufficient to fully compensate for the post-operative LTM loss. It thus follows that endurance exercise training only may be sufficient to remediate LTM loss after CABG surgery.

This study was limited by the examination of males only and the smaller sample size.

Disclosure statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author contribution

DH and PD conceived and designed the study. DH and KV acquired the data. DH and HB analysed and interpreted the data. DH, HB, KV, MH, JLR, IF, BOE and PD drafted the manuscript. DH, HB, KV, MH, JLR, IF, BOE and PD critically revised the manuscript for important intellectual content. DH, BOE and PD supervised the study. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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