Endothelial function after adjustable gastric banding, vasomotion and glucose tolerance

Published: 08-07-2011
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We will investigate endothelial function before and after bariatric surgery.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON36611

Source
ToetsingOnline

Brief title
Endothelial function after adjustable gastric banding

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Vascular hypertensive disorders

Synonym
glucose tolerance, Microvascular dysfunction

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: banding, endothelium, microcirculation, Vasomotion

Outcome measures

Primary outcome

-Change in the vasomotion signal

-Change in endothelial response to acetylcholine

-Change in glucose-tolerance, as measured by OGTT

Secondary outcome

none

Study description

Background summary

The global epidemic of obesity is bringing in its wake a catastrophic increase in the prevalence of metabolic diseases. As a result, obesity-related diseases, such as diabetes, hypertension, dyslipidaemia have surpassed tobacco use as a cause of death1, 2. Obesity is a major cause of insulin resistance, which has been implicated in the rising prevalence of the metabolic syndrome, a cluster of risk factors which confers an increased risk for type 2 diabetes and cardiovascular disease (CVD)3. The mechanisms underlying this clustering are incompletely understood. Obesity-associated microvascular dysfunction (especially the impaired vasodilator response) explains part of this clustering and predisposes obese subjects to CVD4, 5. Microvascular dysfunction, by affecting both flow resistance and perfusion, is important not only in the development of obesity-related target-organ damage in the heart and kidney, but also in the development of cardiovascular risk factors such as hypertension and insulin resistance 6-9.

Prevention of cardiovascular risk can be achieved by addressing all risk-factors independently, as is most often done, however targeting obesity will possibly yield better effects 10.
The most effective treatment for obesity is bariatric surgery 11. Bariatric surgery comprises all gastrointestinal surgery aimed at a reduction of (excess) weight. There are several types of bariatric surgery, such as Laparoscopic Adjustable Gastric Banding (LAGB), a gastric sleeve operation, Roux-en-Y

Gastric Bypass (RYGB) along with other techniques.

After bariatric surgery, insulin sensitivity is known to ameliorate, as well as blood pressure, cardiac function, endothelial function and overall cardiovascular risk 10, 12, 13. Endothelial function in the brachial artery - studied by flow mediated dilation- has been found to improve three months after bariatric surgery 14. Endothelial function has also been found to improve four months after bariatric surgery in the dorsal hand vein15, as well as in the whole forearm (using strain-gauge plethysmography) 16. These studies assessed large vessels or indirect measures of the microcirculation. However, the microcirculation seems to be the most interesting site to study, since all aforementioned risk factors are believed to be linked through microvascular dysfunction 4.
The microcirculation is the main site for pressure dissipation, and thus an important contributor to the peripheral resistance 17. Also, because the microcirculation constitutes a ubiquitous vascular network in the body, it has a large total area available for the distribution of nutrients, waste products, and hormones such as insulin 18. Insulin promotes its own delivery through an increased microvascular recruitment with higher insulin levels 19. This effect is blunted in obese subjects 19.

One non-invase method of determining microvascular function is to use LaserDoppler flowmetry (LDF). LDF utilises a laser beam which penetrates the skin. A fraction of the light is backscattered by moving blood cells and undergoes a frequency shift according to the Doppler principle, generating a received signal proportional to local tissue perfusion 6, 20-23. In this LDF signal, repeating oscillations, so called vasomotion, can be distinguished. This rhythmic dilatation and contraction of arterioles is thought to be an important regulator of microvascular blood flow and thus even tissue perfusion.
Within the LDF signal, six frequency domains can be distinguished, a cardiac, respiratory, myogenic, neurogenic, endothelial-NO dependent and an endothelial-NO independent domain. The latter 4 domains are thought to contribute to arteriolar vasoreactivity. With insulin resistance, the insulin-mediated increase in the myogenic domain is impaired in rats 24. Vasomotion analysis in obese humans has shown an impaired neurogenic and endothelial domain compared to normal weight subjects(22).

A second use of LDF to investigate microvascular function is in combination with iontophoresis. Iontophoresis is a non-invasive method of drug application which allows the local transfer of charged substances across the skin using a small electric current. Acetylcholine - endothelium dependent vasodilation - (1%, Miochol) will be delivered using an anodal current 7 x (0.1 mA for 20 sec.), with 60 sec. interval between each dose. Sodium nitroprusside - ednothelium independent vasodilation - (0.01%, Nipride) will be delivered using a cathodal current; 9 x (0.2 mA for 20 sec.), with 90 sec. intervals.

We will study microvascular function using these non-invasive non-burdening methods in patients before, and after bariatric surgery at 2-4-8 weeks, to see whether endothelial function improves with weight loss, and at which time-point.

Study objective

We will investigate endothelial function before and after bariatric surgery.

Study design

An observational study with invasive measurements in subjects scheduled for bariatric surgery

Study burden and risks

participants will visit our facility 5 times, for a screening/first visit before BS procedure, and a second visit before the surgery, and for three visits after bariatric surgery procedure. A visit involves a 5 point OGTT, laserDoppler analysis (no risks involved), and iontophoresis of acetylcholine (ACh) and sodiumnitroprusside (SNP) (no risk involved). Participants will have no direct health benefit from participation. They will receive a fee of ¤80 for participating, as well as remuneration of their travelling expenses.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. age 18-55 years
2. BMI > 35
3. Eligible for adjustable gastric banding

Exclusion criteria

1. cardiovascular disease (stroke, coronary artery disease, peripheral vascular disease, heart failure)
2. pulmonary disease
3. diabetes mellitus (FPG > 7.8 mmol/l)
4. renal failure
5. smoking
6. alcohol use > 4 U/day
7. use of medication (antihypertensive drugs, lipid lowering drugs, corticosteroids, NSAIDs, ciclosporin A, rifampicin)
8. pregnancy
9. insufficient knowledge of the Dutch language.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	26
Type:	Actual

Ethics review

Approved WMO Date:	08-07-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL32569.029.10

Study results

Summary results

Trial never started