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Gender differences in eating habits, comorbidities and laboratory parameters of obese patients before a surgical intervention for weight reduction

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Graz, am 28.08.2013 Lisa Maria Brandner

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Abstract

Background: Worldwide about 1 billion of people is overweight and more than 300 million are obese (according to definition BMI >30kg/m²). In Austria prevalence of obesity is also increasing, as well as sequelae such as diabetes mellitus type 2, cardiovascular and orthopedic problems with a percentage of 13% for men and women. However, it seems that more women suffer from psychological strain related to obesity and data show women undergo bariatric surgery more often than men. There are also first leads that gender-specific differences may affect the success of surgery.

Aims: The aim of this study was to investigate gender-specific differences concerning eating habits, glucose, lipid- and vitamin-metabolism, as well as comorbidities at the time of the initial presentation at the obesity-outpatient-clinic of the division of endocrinology and metabolism of the Medical University Graz.

Methods: In this retrospective monocentric study 214 patients (77% n=164 females and 23% n=50 males, both with similar age and BMI) were evaluated. All patients were compared with descriptive statistics using data from routine assessment with questionnaires and laboratory tests.

Results: Women have a healthier body fat proportion, displaying a pear-shape (WHR=0,92±0,066). In contrast, men are prone to have the apple-shape (WHR=1,02±0,055). Eating habits differ as to 63% of females do comfort eating, while 37% of men eat nocturnally and 19% irregularly. A majority of both genders has feelings of guilt after eating (♀70%; ♂65%) and consumes snacks (♀68%; ♂60%). More than 90% of men and women display a positive family history for metabolic disease. 20% of males had DM type 2, 56% arterial hypertension and 58% liver parenchymal damage, whereas 21% of females suffered from depression. Lipids and liver parameters were significantly higher in men than women. Numbers for choice of treatment were nearly the same for both genders, nonetheless, in total more women consulted the clinic.

Conclusion: This study confirmed that gender-specific differences in obese people exist, which should be considered in the care and treatment of those patients. Further research has to be done in order to implement evidence based approaches.

Keywords: obesity, gender, eating habits, comorbidities, diabetes mellitus type 2, cardiovascular disease

Zusammenfassung

Hintergrund: Weltweit leidet ungefähr 1 Milliarde Menschen an Übergewicht und mehr als 300 Millionen sind fettleibig (gemäß der Definition BMI>30kg/m²). Auch in Österreich steigen Prävalenz und Folgeerkrankungen wie Diabetes mellitus Typ 2, kardiovaskuläre und orthopädische Probleme mit 13% für Männer und Frauen. Jedoch scheint es, dass Frauen mehr unter der psychischen Belastung leiden als Männer und sich laut Studien öfter für chirurgische Eingriffe zur Gewichtsreduktion entscheiden. Es gibt erste Hinweise, dass gender-spezifische Unterschiede den Erfolg bariatrischer Chirurgie beeinflussen.

Ziele: Das Ziel dieser Studie war die Untersuchung gender-spezifischer Unterschiede betreffend Glukose-, Lipid- und Vitamin-Metabolismus, Essverhalten als auch Begleiterkrankungen zum Zeitpunkt der initialen Präsentation an der Adipositas-Ambulanz der Abteilung für Endokrinologie und Stoffwechsel der Medizinischen Universität Graz.

Methoden: In dieser retrospektiven monozentrischen Studie wurden 214 Patienten (77% n=164 Frauen, 23% n=50 Männer, mit ähnlichem Alter und BMI) evaluiert. Von allen Patienten wurden Daten mit Fragebogen und Labor-Tests mittels deskriptiver Statistik verglichen.

Ergebnisse: Frauen weisen eine gesündere Körperfettverteilung als Männer auf (Birnen-Form mit WHR=0,92±0,066). Im Gegensatz dazu haben Männer eher die Apfel-Form (WHR=1,02±0,055). Frauen tendieren mehr zum Frustessen (63%), wobei 37% der Männer nächtliches Essen aufzeigen und 19% unregelmäßig essen. Die Mehrheit beider Geschlechter hat ein schlechtes Gewissen nach dem Essen (♀70%; ♂65%) und konsumiert Zwischenmahlzeiten (♀68%; ♂60%). Mehr als 90% aller Männer und Frauen weisen eine positive Familienanamnese auf. 20% der Männer haben bereits DM Typ 2, 56% arterielle Hypertonie, 58% Leberparenchymschaden, während 21% der Frauen an Depression leiden. Bei Männern waren Blutfette und Leberparameter höher. Die Wahl der Behandlungsart war ähnlich zwischen den Geschlechtern. Insgesamt waren mehr Frauen vorstellig.

Schlussfolgerung: Diese Studie bestätigte, dass gender-spezifische Unterschiede von Adipositas-Patienten bestehen, welche in der Betreuung und Behandlung berücksichtigt werden sollten. Mehr Forschung ist notwendig, um evidenzbasierte Empfehlungen zu implementieren.

Schlüsselworte: Adipositas, Gender, Essverhalten, Begleiterkrankungen, Diabetes mellitus Typ 2, Kardiovaskuläre Erkrankung

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Introduction

Per definition obesity is a body mass index of more than 30kg per m². In the last years, obesity and overweight have already reached epidemic dimensions. According to WHO statistics more than 200 million adult men and almost 300 million adult women worldwide were obese in 2008. This means that numbers of obese humans have doubled since 1980. In addition, childhood obesity is also increasing rapidly.(1) Correspondingly, obesity prevalence in Austria for men is 13% and for women as well.(2) The incidence for obesity is increasing similar for both genders.(3) Obesity is associated with a number of secondary diseases, which include metabolic diseases like diabetes type 2, cardiovascular diseases such as arteriosclerosis and arterial hypertension, orthopaedic complications, and even some kind of malignant diseases.(4) This leads to an increase of morbidity and a build-up of economic burden, as treatment of sequelae and unfitness for work cost more and more.
Obesity would be preventable – and is curable in most cases. However, often lifestyle modification and pharmacological treatment are not sufficient and patients decide to have a surgical procedure in order to lose weight, as for example a sleeve gastrectomy or a gastric bypass.
It seems that women suffer more from the psychological strain of obesity than men and accordingly more women chose a surgical method at an earlier time point. There are first leads that gender-specific differences affect the success of surgery. This will be dealt with in this diploma thesis.

Obesity

Definition

Obesity can be defined in several different ways.
Firstly, according to the World Health Organization, obesity is *defined as abnormal or excessive fat accumulation that may impair health. (...) A BMI greater than or equal to 30 kg/m² is obesity.*(1)
Secondly, the definition of Dr. Gerd Herold would be a rate of fat in relation to body weight of more than 30% for women and more than 20% for men.(5) However, both definitions overlap, so patients diagnosed will be approximately the same.

A third definition given by the book “Netters Allgemeinmedizin” is that obesity is a pathological accumulation of body fat relative to the norm.(4)

Epidemiology

Obesity incidence and prevalence are increasing steadily worldwide.(3) According to the “Gesundheitsstatistik 2011 of Statistik Austria”, a survey performed in 2006 and 2007 concerning health and related topics, numbers were as follows: Of the Austrian population 45% of men are overweight (BMI between 25 and 30kg/m²), 30% of women are overweight and 13% are obese (BMI of ≥30kg/m²) respectively.(2)

Pathogenesis

Weight is affected by several parameters. A gain in weight can be cause either by a surplus in intake (too much or too often), by wrong nutrition as for example a one-sided diet, or by a reduced digestion and slow metabolism. A loss in weight will be caused by the opposite. Furthermore, daily exercise has to be taken into account. Summarized, weight gain is caused by multiple factors, of which the chief components are *hypercaloric nutrition and low energy consumption with a genetic pre-disposition*.(6)

Furthermore, in certain cases an underlying disease and syndromes may be the cause of obesity. An example for a genetic cause is the Prader-Willi-Syndrome or the Laurence-Moon-Bardet-Biedl syndrome. The most common is athyreosis, which is an inborn absence of tissue of the thyroid gland, resulting in hypothyroidism.(7) Seldomly a lack of the appetite regulating hormone leptin results in severe obesity in early age and other defects in neurotransmitters may also be responsible.
However, sources must not always be innate, but could also be acquired. Examples are hypothyreosis, Cushing disease and all sorts of medication, such as antipsychotics, antiepileptic drugs, glucocorticoids, antihyperglycaemic drugs and also hormones can lead to weight gain.(8,9)
Another important factor that should not be underestimated is the social and psychological component of eating habits. Those are shaped by family, tradition, social status, occupational environment, spouses and partners. Moreover, feelings effect patterns as well, as for example stress and depression, premenstrual syndrome, nicotine withdrawal, winter depression and eating disorders in general.(6)

Regulation mechanisms of appetite, hunger and satiation

Appetite is the desire to eat. It is triggered by psychological factors both in positive as well as in negative ways, our senses in particular seeing, smelling and tasting and also by hunger.(5)

Hunger is influenced by glucose levels in blood; strain of the stomach and duodenum and also by hormones especially insulin and serotonin.(5)

Satiation is the product of neuronal, hormonal, psychological and metabolic components. Especially important are leptin, cholecystokinin and insulin.(5)

The responsible cerebral centre of satiation is the nucleus ventromedialis in the hypothalamus. The ventrolateral hypothalamus is responsible for appetite.(5)

A further aspect of how and how much and what is eaten is guided by sociocultural influences such as ideals of beauty, national-typical food and education.(5)

Dysfunction of eating habits

Since humans have existed, there have been eating disorders. Depending on time, culture and environment, different disorders are more prevalent than others. Some of the most frequent ones are anorexia, bulimia, hyperorexia and parorexia.

Table 1 - eating disorders

type of disorder	explanation
anorexia	reduced appetite and ingestion
(obese) bulimia	succession of binge eating and vomiting
hyperorexia	increased appetite for food; e.g. hyper metabolic diseases, diabetes, psychological
orthorexia nervosa	appeal to eat as healthy food as possible
parorexia	peculiar desire for nutrition; e.g. physiological during pregnancy

(5)

Diagnosis of overweight and obesity

A number of formulas can be used for calculating the ideal body weight of a person.

Broca-formula

The Broca formula has been used for many years.

$$\boxed{\textit{Body height [cm]-100cm=normal body weight [kg.}}$$

The ideal body weight of men would be the normal body weight -10% and for women -20% respectively. From the age of 65 years 2,5kg can be added.(10) However, this formula discriminates very short people, which would only be allowed little weight as well as very tall people, which are allowed too much weight. This formula works best for medium sized people. Moreover, body composition is not taken into account, as there is no differentiation between fat and muscle.

Body Mass Index

The body mass index is the most commonly used formula to calculate a person's ideal weight.

$$\boxed{\frac{body\ weight[kg]}{body\ size^2[m^2]} = BMI[kg/m^2]}$$

The result can then be classified according to categories.

Table 2 - http://www.hoptechno.com/bmiadults.htm 12.04.2013 22:13

WEIGHT lbs	100	105	110	115	120	125	130	135	140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	215
kgs	45.5	47.7	50.0	52.3	54.5	56.8	59.1	61.4	63.6	65.9	68.2	70.5	72.7	75.0	77.3	79.5	81.8	84.1	86.4	88.6	90.9	93.2	95.5	97.7
HEIGHT in/cm	Underweight					Healthy					Overweight					Obese					Extremely obese			
5'0" - 152.4	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
5'1" - 154.9	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	36	37	38	39	40
5'2" - 157.4	18	19	20	21	22	22	23	24	25	26	27	28	29	30	31	32	33	33	34	35	36	37	38	39
5'3" - 160.0	17	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	32	32	33	34	35	36	37	38
5'4" - 162.5	17	18	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	31	32	33	34	35	36	37
5'5" - 165.1	16	17	18	19	20	20	21	22	23	24	25	25	26	27	28	29	30	30	31	32	33	34	35	35
5'6" - 167.6	16	17	17	18	19	20	21	21	22	23	24	25	25	26	27	28	29	29	30	31	32	33	34	34
5'7" - 170.1	15	16	17	18	18	19	20	21	22	22	23	24	25	25	26	27	28	29	29	30	31	32	33	33
5'8" - 172.7	15	16	16	17	18	19	19	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	32	32
5'9" - 175.2	14	15	16	17	17	18	19	20	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	31
5'10" - 177.8	14	15	15	16	17	18	18	19	20	20	21	22	23	23	24	25	25	26	27	28	28	29	30	30
5'11" - 180.3	14	14	15	16	16	17	18	18	19	20	21	21	22	23	23	24	25	25	26	27	28	28	29	30
6'0" - 182.8	13	14	14	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27	28	29
6'1" - 185.4	13	13	14	15	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27	28
6'2" - 187.9	12	13	14	14	15	16	16	17	18	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27
6'3" - 190.5	12	13	13	14	15	15	16	16	17	18	18	19	20	20	21	21	22	23	23	24	25	25	26	26
6'4" - 193.0	12	12	13	14	14	15	15	16	17	17	18	18	19	20	20	21	22	22	23	23	24	25	25	26

Table 3 - adapted from http://apps.who.int/bmi/index.jsp?introPage=intro_3.html 14.04.2013 11:22

Classification	BMI [kg/m²]
Underweight	**<18,50**
Severe thinness	<16,00
Moderate thinness	16,00-16,99
Mild thinness	17,00-18,49
Normal range	**18,50-24,99**
Overweight	**≥25,00**
Pre-obese	25,00-29,99
Obese	**≥30,00**
Obese grade I	30,00-34,99
Obese grade II	35,00-39,99
Obese grade III = adipositas permagna	≥40,00

A major advantage of the BMI is that it can be corrected, if an extremity has been amputated. With the use of certain correction-constants the result can still be categorized correctly. The theoretical body weight, which can subsequently be used to calculate the BMI, is determined with the following correction constants:

Table 4 - adapted from http://www.diabetesstiftung.org/risiko-uebergewicht.html 14.04.201411:42

Extremity	correction coefficient
Hand	0,8
Forearm	2,2
Upper arm	8,5
Foot	1,8
Lower leg	5,3
Thigh	11,6
$\textbf{theoretical body weight} = \frac{\textbf{mass} * \textbf{100}}{(\textbf{100} - \sum\textbf{correction coefficients})}$	

A further advantage is the option of taking into account age, however only for children and adolescents between the ages 2 and 20.

The main drawback, as applies for the Broca-formula, is the fact that fat and muscle weight is not distinguished. In fact, it has been shown that different ethnic groups show different body composition and hence different risks for fat-associated-diseases. Therefore, it has been discussed to introduce altered categorizations for several ethnic groups, nonetheless, it has not yet been completed.(11,12)
Moreover, a highly important aspect is the fact that body fat proportions differ greatly in men and women. Generally, men present higher mass of muscles, whereas women have higher total body fat, located mostly in the breasts, hips and butt. This has evolutionary origins, as men were to hunt and gather food, for which they needed more muscles than women, who were to bear and nurture children, which more fat was needed for. Accordingly, this still lies in our genes.

Waist-hip-ratio

The waist-hip-ratio does not account for the ideal body weight, but then for the ideal body composition, as it compares the waist circumference with the hip circumference. Generally, people with fat depots particularly above the waist area, have a higher cardiovascular risk, as they possess more visceral fat, which is highly metabolic and have a negative impact on blood lipids. These are called “apple-shaped”.
In contrast, people with amounts of fat below the waist, so-called “pear-shaped”, are at a lower risk, due to low metabolic fat depots.

$$waist - hip - ratio = \frac{waist\ circumference\ [cm]}{hip\ circumference\ [cm]}$$

The ideal result for men is <1 and for women <0,85. Both, the BMI and the WHR are often used in combination to determine overweight and cardiovascular risks.

Graph 1 - http://health.nytimes.com/health/guides/specialtopic/weight-management/complications.html 14.04.2013 11:59

Therapy of obesity

Therapy of obesity bases on different pillars of weight reduction. Most effective is a total lifestyle modification consisting of a healthy diet, regular exercise and behavioural strategies in order to lose and afterwards maintain weight.(5)

Depending on the grade of obesity, success of taken actions and comorbidities pharmacologic therapy and also bariatric surgery can be added as supportive measures.(5)

Diet

First of all, a change from malnutrition to a balanced diet with a reduction in calories is incontrovertible. According to Hall KD et al. about 22kcal are needed to maintain a kilogram of body weight of a normal adult.(13) If weight loss of 0,5 kg per week is expected at the beginning, the daily metabolic rate should be decreased by 500 kcal, that is about 1200kcal/day. After several months, owing to weight loss and expenditure adaptions, the decrease in body weight takes place slower. What is more, a daily intake of less than 800kcal/day is not recommended, as in this case the body will switch to famine-mode and store received nutrients and consequently weight loss will be prevented. To give the patient an idea, a realistic weight loss after six months would be 5 per cent of the initial body weight.(13) As a result of different body composition, different energy expenditure and

metabolic rates, men generally lose weight faster than women and older people have a harder time than younger ones.(13)

There exist several different types of diets, which limit the daily intake of calories. They can be subsumed under four groups: balanced low-calorie diets/portion-controlled diets, low-fat diets, low carbohydrate diets, Mediterranean diet and fad diets.

Balanced low-calorie diets base upon a composition of nutrients, proteins, carbohydrates and essential fatty acids. Moreover, alcohol, beverages with high sugar amounts and sweets should be excluded.

Portion-controlled diets make use of formula diet drinks as the main component of meals. By those means calories are easy to count, nonetheless, variety is restricted.

Low-fat diets focus on a maximum caloric intake of 30% per day and healthy carbohydrates.

Low-carbohydrate diets work contrariwise and emphasise healthy fats and proteins.

The Mediterranean diet bases upon usual diets in Mediterranean areas, where people consume more monounsaturated fats, little alcohol, meat and dairy products and high amounts of vegetables, fruits, legumes and grains.

Several studies on different types of diets have shown that although some show greater effects concerning short term weight loss, they all draw level after one year and later. In addition to every type of diet a minimum of 2,5l water per day should be drunk, alcohol should be reduced to a minimum similarly as salt with a maximum of 5g/day. [1]

Exercise

Another important aspect is regular exercise. While studies have shown, that exercise alone does not lead to intended weight loss, and in addition to dietary changes merely brings about moderate weight loss, exercise nevertheless has beneficial effects on body composition, insulin sensitivity, blood pressure and maintenance of weight after weight reduction. Moreover, training compensates for loss of muscle mass due to diets. A further aspect of exercise is the increased energy consumption of calories, which recompenses the decreased basal metabolic rate owing to weight loss.(14)
Generally, all physical activity should concentrate on moderate endurance exercises, match

for physical ability of people and consist of 30 minute units five to seven times per week.(14)

Behavioural therapy

Behavioural therapy enhances and combines dietary and physical methods for weight loss.

Obesity is often caused by eating disorders, loss of sense of hunger and saturation, stress and frustration. All of these reasons can be dealt with by usage of behavioural strategies in order to relearn a natural sense of hunger and feeling of satiety, learning how to cope with stress and frustration other than eating, self-confidence and eating disorders such as binge eating. Behavioural therapy attempts to modify learned behaviours and preserve new-learnt healthy ones in order to lose and maintain weight.(5)

A major component is self-monitoring by recording intake with the help of a food diary and the amount of physical activity. Furthermore, stimuli and situations that lead to excessive amounts of food intake can be noted and dealt with in therapy, which is called "stimulus-control". Patients should identify such stimuli or situations with the intention of eliminating or modifying them in their favour.(15)

They should also focus on their food. This means that they are demanded *(...) to buy more fresh fruits and vegetables, to prepare easy-to-eat lower calorie foods and to place them prominently in the refrigerator or on the counter.*(15)

A further significant aspect is to slow down the eating rate by concentrating on the food, savouring it, drinking water in between so as to feel saturated earlier. Patients are advised to attend nutritional education tutorials so that they learn how to prepare a healthy meal. Also significant is the size of portions, which should be regular and defined.

Patients are asked to set goals for themselves, however, it is important for them to be realistic, in order to prevent frustration. Moreover, success can be rewarded with little tokens, money or vouchers.

According to studies, there is no significant difference between the success of individual or group therapies.(15) However, it is essential for obese people to receive social support. Their families' acceptance and support and especially of their spouses contributes significantly to their achievements.

As already mentioned before, behavioural therapy can boost physical activity by self-monitoring and regular meetings in group or individually with the therapist.

In most cases, behavioural therapy has a positive impact on weight loss and maintenance with the use of *regular patient education sessions, weight checks and peer support*.(15)

Pharmacological treatment

In practice drug therapy is not recommended as first attempt to treat obesity. Yet, it is indicated as supplementation to diet, exercise and behavioural methods. Pharmacological therapy is indicated as follows: *Anti-obesity drugs can be useful adjuncts to diet and exercise for obese adults with a BMI greater than 30kg/m², who have failed to achieve weight loss goals through diet and exercise alone. A trial of drug therapy is also warranted in patients with a BMI of 27 to 29,9kg/m²with comorbidities, or in those in whom gastrointestinal bypass surgery is being considered.*(16)

According to [George A. Bray, MD] pharmacological therapy is considered effective, if in the first month of therapy a minimum of 2 kg are lost, from three to six months a 5 per cent loss in relation to starting weight should be accomplished and after that, this weight should be maintained. As already mentioned above, indication for pharmacological obesity therapy is a BMI of more than 30kg/m² or of 27-29,9kg/m² with comorbidities, when those subjects have failed to accomplish weight loss solely with dietary measures, exercise and behavioural therapy. Concerning the diseases other than obesity, it is important when treating comorbidities such as diabetes, hypertension and cardiovascular diseases and likewise depression or epilepsy, drugs, which lead to weight loss, rather than to weight gain should be preferably used.

Orlistat – Xenical®

Orlistat is a fat digestion altering drug, which in combination with a moderate low-caloric diet can be used for long-term therapy of obesity. It inhibits gastrointestinal lipases and thus leads to reduced fat incorporation and increased excretion of fat. As a consequent side effect, it can lead to malabsorption of fat-soluble vitamins. Therefore users are recommended to take vitamin supplements daily. Moreover, patients, who take anticoagulants such as vitamin k antagonists should adapt their doses of coumarines. Furthermore, hypoglycaemias have been reported, so that obese patients with diabetes mellitus are advised to have frequent blood glucose controls. On the other hand, Orlistat

temporarily improves haemoglobin A1c parameters and similarly blood pressure and serum lipid values. In combination with a diet consisting of more than 30% fat, gastrointestinal problems have occurred more frequently. Therefore, patients are instructed to reduce their fat intakes, in order to avoid *(...) intestinal borborygmi and cramps, flatus, faecal incontinence, oily spotting and flatus with discharge*(17). Side effects also include headaches, hypoglycaemia, influenza, infections of the upper and lower airways, urinary tract infections, lassitude, menstrual pains and anxiety. Another complication can occur for people with chronic renal diseases plus dehydration, which can lead to hyperoxaluria and oxalate-nephropathy. Contraindications are hypersensitivity to any components of Xenical®, chronical malabsorption syndrome, cholestasis and during pregnancy and breastfeeding.

In conclusion, Orlistat can be an adjunct to the standard therapy of obesity, if precautions are taken in reference to contraindications and possible side effects.

Lorcaserin

Up to now Lorcaserin is only approved in the United States, not in Austria or other parts of Europe yet. However, it is in phase III of approval. In the same way as Fenfluramine (Ponderax®) and Dexfenfuramine (Isomeride®), it docks onto serotonin-receptors and thereby decreases appetite and leads to earlier satiety. Because of valvulopathy as a frequent side effect, Fenfluramine and Dexfenfuramine have lost licence in Austria. Lorcaserin on the other hand is selective for 5-HT_{2C}-receptors and no such consequences have been recorded. Nonetheless, there is still no long-term data available. Lorcaserin seems to be as effective as Orlistat and has other desirable effects such as improvements in blood pressure, heart rate and blood lipids, fasting glucose and insulin levels. Recorded side effects were nausea, vertigo and headaches. Upper respiratory infections, nasopharyngitis and back pain have also been noted. Furthermore, the risk of hypoglycaemia for diabetes patients is also increased, so that they should be monitored frequently. Lorcaserin is contraindicated during pregnancy, in combination with other serotonergic drugs because of possible serotonin syndrome and another contraindication is a creatinin clearance of less than 30ml/min.

In summary, Lorcaserin is so far only licenced in the United States, however, efficacy seems to be much the same as Orlistat.

Sympathomimetic drugs

The mechanism of sympathomimetic drugs is either the release of norepinephrine or inhibiting the reuptake of norepinephrine in the synaptic gap. This causes an early feeling of satiety. However, those substances are not approved in the market in Europe either. In the United States, they are approved for short-term therapy of obesity, which is limited to twelve weeks. Side effects are possible abuse, an increase in heart rate and blood pressure, insomnia, dry mouth, nervousness and constipation. Hence, sympathomimetic drugs are contraindicated for subjects suffering from hypertension, coronary heart disease, hyperthyroidism and drug abuse in their past.

Antidepressants

Antidepressants vary in consequence. Some do not affect weight, others lead to weight gain and few can avert weight gain. One of the few is bupropion, which is released under the name Zyban® in Austria. It is approved for application on people after smoking cessation, in order to prevent weight gain. It is contraindicated for eating disorders as bulimia and anorexia.

Antiepileptic drugs

Some antiepileptic drugs can also be connected with weight loss or the avoidance of weight gain. Two of them also approved in Austria are Topiramate (Topamax®) and Zonisamide (Zonegran®). Data suggests moderate weight loss related to their usage in antiepileptic therapy.

Combination drugs

The possibility of intervention in different pathways of the pathophysiology of obesity has led to combination of several drugs. Phentermine-Topiramate is suggested as an alternative for Orlistat and Lorcaserin, if people do not tolerate them. Nevertheless, this combination is not approved for the market in Austria.

Diabetes drugs

Metformin – Glucophage®

In Austria it is for instance approved as Glucophage®. It is a biguanid, which lowers basal and postprandial blood glucose levels. A desirable side effect can be reduced appetite. Moreover, it brings along positive changes of blood lipids, in particular a general decrease of cholesterol, LDL and triglycerides. The assumed mechanism bases on three different changes on molecular levels. Firstly, the production of glucose in the liver is reduced by inhibition of gluconeogenesis and glycogenolysis. Secondly, sensitivity to insulin is enhanced in the muscles, so that peripheral glucose absorption and utilisation are improved. Last but not least, intestinal glucose absorption is delayed and slowed down. In fact, metformin can be offered to obese patients, which are at risk for diabetes. By this, two birds can be killed with one stone. However, in Austria Metformin is only licenced for patients with diabetes.

Pramlintide

Peptide hormones are produced in the pancreas by beta cells. They are significant for gastric emptying and blood glucose levels. A synthetic analogue of a human peptide namely amylin has been called Pramlintide. Modest weight loss has been associated with it, by slowing down gastric emptying, reducing blood glucose concentrations after eating and furthermore, improving haemoglobin A1c values. One minor side effect is nausea. Nevertheless, it is another drug, not yet approved in the Austrian market, but in the United States.

Exenatide – Byetta®; Liraglutide – Victoza®

Exenatide is a further synthetically produced peptide, which works as a long-acting GLP-1-receptor agonist. Consequently, it results in similar effects as Pramlintide (slower gastric emptying and inhibited glucagon release). Furthermore, insulin secretion is stimulated glucose-dependently. Byetta® is approved for the treatment of type 2 diabetes mellitus in combination with oral anti-diabetics or basal insulin. Trials have shown, that weight loss is dose-dependent, however, with higher doses, side effects occur more frequently such as reduced appetite (which may be desirable), headaches, vertigo, abdominal pain, gastroesophageal reflux, meteorism and constipation.
Liraglutide is another GLP-1-receptor analalog, which is long-acting and leads to weight

loss. Nonetheless, as well as Byetta®, if taken in high doses, Victoza® can cause nausea, vomiting and diarrhoea.

On the whole, pharmacological therapy should be considered for obese subjects with more than 30kg/m² BMI or with 27-29,9kg/m² and at least one comorbidity, who have not been successful losing weight by modifying their diet, exercising and behavioural strategies. As first line medicine Orlistat should be an option and Lorcaserin as an alternative. Others still lead to side effects as major drawbacks or are yet only approved as main therapy for other diseases, as for example diabetes mellitus.

Surgery

Surgical intervention in order to lose weight is commonly referred to as "bariatric surgery", *"from the Greek words "baros" meaning "weight" and "iatrikos" meaning "medicine".*(18)

The National Institutes of Health (NIH) Consensus Development Panel in 1991 agreed on indications for bariatric surgery as follows:

- Surgery should not be first line therapy of obesity, but only for patients, who have failed to lose weight by conservative treatment.
- Patients with a BMI of 40kg/m² or higher may be candidates for bariatric surgery.
- Patients have to be well-informed and motivated to participate in the treatment, changing of eating habits and long-term follow-ups.
- The operative risk should be acceptable.
- Bariatric surgery may also be considered for patients with a BMI of 35 to 40kg/m², if they are suffering from serious comorbidities as for instance sleep apnoea, cardiomyopathy, severe diabetes mellitus or physical problems caused by obesity such as joint diseases or social difficulties as for example employment- or family function-problems.(19)

Obesity-surgery can be split into three different types. Firstly, a restrictive method, that means size-reduction of the gastric reservoir in order to shrink caloric intake, is an option. This can be achieved either by implanting an intragastric balloon, gastric banding, gastroplasty or gastrectomy to form a tubular stomach. A second option is a malabsorptive technique, where the absorption of nutrients is inhibited. Examples for it are a jejunoileal bypass or a duodenal switch operation. Consequently, the third possibility is a combination

of the latter. Gastric bypass and biliopancreatic diversion with or without duodenal switch have restrictive as well as malabsorptive components.(5,18)

Sleeve gastrectomy (=SG)

A sleeve gastrectomy is, as the name already mentions, an incomplete gastrectomy, where, by removing most of the greater curvature, a tubular stomach is formed. The capacity of the stomach is thereby limited greatly and additionally, many ghrelin-producing cells have been removed with the resected part of the stomach. Ghrelin is an appetite-regulating hormone, which leads to a further weight reducing aspect. As this technique is quite simple, without the necessity of anastomoses, it counts to the safer methods. A possible side effect is reflux, which occurs in nearly 50% of patients.(18,20)

Vertical banded gastroplasty (=VBG)

Another restrictive method is the vertical banded gastroplasty. The stomach is divided into two parts by staples near the oesophagus, creating a small pouch at the small curvature, and a band around the greater curvature, leading to a restriction of emptying of the stomach. Moreover, satiety is sensed quickly. Nonetheless, patients can still eat soft or liquid high caloric food. Therefore, this surgical intervention may be ineffective. Furthermore, high rates of complications such as *staple line disruption, stomal stenosis, band erosion, band disruption, pouch dilatation, vomiting and gastroesophageal reflux disease*(18) have led to necessary revisions. Consequently, this type of operation is rarely done nowadays.(18)

Laparoscopic gastric banding (LAGB)

This procedure is, as already mentioned before, strictly restrictive. By laparoscopically implanting a tight band, which can later be readjusted by injecting saline into the infusion port, around the stomach entrance, the stomach is divided into a small pouch at the entrance, where food can only pass slowly and in very small portions. Contraindications for this procedure are *portal hypertension, connective tissue disorders with severe oesophageal dysmotility or chronic steroid use*(18). Even though this technique has a quite high rate of 40 per cent revisional surgery, it is the one with the lowest mortality rate of all bariatric surgeries.(21,22) *Major complications included pouch dilatation, band erosion*

and band infection. Minor complications included incisional hernias, port-tubing disconnections and port infections(23).

Intragastric balloon

By endoscopically implanting an indulgent balloon into the stomach, the patient persistently feels saturated. The balloon restricts the size of the stomach furthermore, which also contributes to less intake of food. Because of the relatively non-invasive technique, it seems to be a safe method, however, it is not widely spread.(18)

Roux-en-Y-gastric bypass

The gastric bypass is one of the most commonly performed bariatric surgeries. It has been practiced since 1960 and nowadays considered the gold standard. The procedure can be done open or laparoscopic. The main component is the restrictive effect, which stems from the bypass of the major part of the stomach and the duodenum. A small pouch of the proximal stomach is formed and anastomosed to the jejunum. Moreover, the bypassing of the duodenum and parts of the jejunum leads to a malabsorptive outcome.(18) As it is a great interference in the physiology of the digestive system, many complications can be the consequence. One potentially lethal complication is the distension of the gastric remnant. This can lead to peritonitis owing to leakage of gastric matter, which contains *acid, bile, pancreatic enzymes and bacteria*(23) and can cause severe damage in the abdomen. Another complication is stomal stenosis, which occurs more often in laparoscopic executions.(24) Marginal ulcers can lead to bleeding and perforation. Nevertheless, this complication can easily be treated with anti-acidic medication, cessation of smoking and stopping of NSAIDs. Moreover, infection with helicobacter pylori has been associated with higher rates of ulcers. Therefore, it is important to treat patients in order to avoid marginal ulcers. Cholelithiasis can be a further complication after gastric bypass surgery. The indication for surgical therapy has to be decided individually. Ventral incisional hernia occur more often after the open technique. On the other hand, laparoscopic procedures more often lead to internal hernias. Short bowel syndrome is also a possible complication, which can even involve intestinal transplantation. Early or late dumping syndrome is another complication, which nonetheless can lead to more weight loss, as patients are obliged to change their eating habits from simple sugars to complex carbohydrates, high fibre and protein contents. Gastric bypass can lead to metabolic and

nutritional derangements, due to a change in absorption of essential vitamins, minerals and micronutrients. Therefore, patients have to take compensatory medication and modify their eating habits. In few cases, it can lead to hyperoxaluria and nephrolithiasis. Renal failure is a feared complication, resulting from deposition of calcium oxalate in the kidneys. Postoperative hypoglycaemia is an easily dealt with problem. Patients once more have to change their diet. Owing to transformation of digestion, bowel habits will also change. Stools can be more frequent and steatorrhea can occur after extreme fat intake. Seldom, patients fail to lose weight or regain excessive amounts of weight after some time. Reasons can be a gastrogastric fistula, which can make another operation necessary, or dilatation of the pouch or the anastomosis. This again is caused by frequent excessive eating.(23)

Biliopancreatic diversion with or without duodenal switch

The biliopancreatic diversion consists of a partial gastrectomy and gastroileostomy with a long segment of Roux limb and a short common channel (the part of the small bowel that receives both food and biliopancreatic secretions) resulting in fat and starch malabsorption(18). Side effects are protein malnutrition, anaemia, diarrhoea, stomal ulceration, metabolic bone disease and deficiencies of fat-soluble vitamins.(25–27) The biliopancreatic diversion can be combined with a duodenal switch, which contains a sleeve gastrectomy and the pylorus is preserved. Nonetheless, this procedure poses the same risks as without duodenal switch, with high rates of morbidity and surgical mortality.(18)

Jejunoileal bypass (=JIB)

The jejunoileal bypass is no longer performed, due to high risks and frequent revision surgery (50% morbidity, 10% mortality).(18,27,28) The jejunum was divided close to the ligament of Treitz and connected to the ileum close to the ileocecal valve. Consequently, a long part of the small intestine is bypassed, which leads to malabsorption. The most severe complication is liver function deterioration and even the long-term complication of cirrhosis. Moreover, the surgically induced short bowel syndrome often led to electrolyte imbalances and renal failure. Therefore, patients, who have undergone jejunoileal bypass, should be closely monitored for long-term problems.(23)

Duodenal switch (=DS)

The duodenal switch is performed by a gastric sleeve resection and anastomosing the biliopancreatic limb to the distal ileum as well as the duodenum. This forms a common channel of 100cm and an enteric limb of 150cm. One component is the restriction, the other one is the malabsorptive result. Side effects are the same as for biliopancreatic diversion with duodenal switch. This led to rare performing of this technique.(18,23)

The choice, which procedure to perform on the individual patient, has to be made by weighing effectiveness, side effects and possible complications and patient behaviour against another. The success of bariatric surgery also depends on the behaviour of the patient after the operation. This will be described in the next passage.

Postsurgical care

Patients will have to effectively modify their diet and eating behaviour. Most important are behavioural measures as slow eating and increased chewing of food and avoiding eating and drinking together. Patients should wait at least 30 minutes after eating, before they drink something. Moreover, they should deliberately buy healthy food, with more protein amounts and reduced fat and calorie intake. Consequently, they should avoid large amounts of sugar and liquid foods, such as ice cream. Most important of all, patients should recognize satiety early and stop eating, because after most bariatric interventions, the size of their stomach will be restricted.
After most surgical methods, patients will have to take vitamin supplements and other micronutrients in order to counteract malnutrition, as absorption of those will be limited. Of course, they will have to see their doctor regularly to identify side-effects, short-term and long-term complications early enough to treat them or have revision surgery. Controls are appointed after 3, 6, 9 and 12 months, then yearly. (29) Patients should be alert and observe their bodily changes accurately. Any signs of side effects and complications have to be mentioned to a doctor immediately in order to be investigated and if required treated. During those check-ups the patient's blood count, iron, ferritin, vitamin B12, folic acid, liver- and kidney-function, electrolytes including calcium, total protein, albumin, fasting glucose, haemoglobin A1c, vitamin D and parathyroid hormone will be monitored, so as to supervise the correct dose of supplementation and identify deficits. Furthermore, an osteodensitometry will be performed to control bone density, which could be impaired by malabsorption.(29)

Many studies indicate a significant improvement of several obesity-related diseases. Some of them are diabetes, arterial hypertension, hypercholesterolemia, dyslipidaemia, sleep apnoea and gastroesophageal reflux disease. It is essential to monitor the impact of bariatric surgery on those related diseases and in the case of improvement modify correlating medication.
An important factor concerning women is that they are advised not to get pregnant for at least one year after surgery. However, birth control by oral contraception may be impaired on the grounds of the undergone changes in the digestive system. Therefore, women should use other contraception.(30)

Complications of obesity

Obesity can lead to a variety of complications, short-term as well as long-term.

Cardiovascular disease

One of the major complications is cardiovascular. Obesity is associated with an increased risk for coronary heart disease and strokes. Some studies have found correlation between obesity and CHD, others came to the conclusion that CHD results from other risk factors than obesity. The Nurses' Health Study found that mortality is increased by increasing BMI levels in 115195 women.(31) Another study performed on an Asian population showed that the risk of death was increasing with very high and very low BMI. The major reason for death was cardiovascular disease.(32) Concerning other risk factors, a study with more than 1000 men and women at the age of 70 compared subjects that were obese but did not have metabolic syndrome with subjects with a normal BMI but also no metabolic syndrome. Results demonstrated that obese patients displayed impaired vasoreactivity, increased mass of the left ventricle with reduced function and also limited coagulation and fibrinolysis.(33) Moreover, the Framingham Heart Study analysed male subjects on bases of their follow-up data of 30 years, concluding that men, who were non-smokers but obese, had higher mortality rates than non-smoking men with normal weight.(34) A prospective study performed on more than one million adults displayed lowest mortality rates for men and women of normal BMI. Higher BMI led to higher mortality rates due to cardiovascular disease, especially for men. Comparison of whites and blacks showed higher risks for whites.(35)
On the other hand, some studies have come to different conclusions. The Munster Heart Study revealed that risk factors as age, total serum cholesterol, low density lipoprotein

cholesterol, systolic and diastolic blood pressure and markers of inflammation and thrombosis accounted for the high deaths of coronary heart disease.(36) However, one could say, that those risk factors are products of obesity, so indirectly obesity again led to coronary heart disease.

Type 2 diabetes mellitus

About 80% of type 2 diabetes cases are the result of obesity. Then again diabetes is a major risk factor for coronary heart disease, which has a higher prevalence in the obese population. Consequently, one risk factor affects the other to become a vicious cycle. Moreover, trials have shown that after great weight loss by bariatric surgery, type 2 diabetes has come to remission, in some cases even long-term.(37)

Metabolic syndrome

Metabolic syndrome, also called syndrome X or insulin resistance syndrome, consists of high amounts of visceral fat distribution, dyslipoproteinaemia (high triglyceride and low high-density lipoprotein levels), hyperuricaemia, essential hypertension and an impairment of glucose tolerance or type 2 diabetes mellitus. Metabolic syndrome negatively effects the development of coronary heart disease or stroke by increasing the risk three times.(5,38)

Tumours

Certain types of tumours are associated with obesity. The pathophysiology is still unclear. It is believed that inflammation markers bring about the development of tumours. Nonetheless, numbers display a correlation of obesity with tumours, especially affecting the colon, rectum, endometrium, mamma and prostate.(5)

Hyperlipidaemia

As the Munster Heart Study has demonstrated, obesity accounts for changes in blood lipids. Most important changes are an increase in total cholesterol, low-density lipoprotein, very-low-density lipoprotein, triglycerides and what is more a decrease in high-density lipoprotein.(36) As a result, this contributes once again to an increased risk for coronary heart disease and atherosclerosis.

Arterial hypertension, left ventricular hypertrophy and heart failure

Obesity is also a risk factor for hypertension, as shown in the Nurses' Health Study, where an increase in BMI correlated with the occurrence of hypertension.(31) According to a

study on obesity and heart problems, systemic hypertension is frequently present in obese subjects. Because of the increase in blood volume correlating to weight gain, the heart is obliged to increase its pumping function, which often leads to left ventricular hypertrophy and even heart failure. The end-diastolic volume increases and the heart has to pump against increased filling pressure.(39,40)
The Framingham Heart Study investigated nearly 6000 subjects without a history of heart failure. They found a high risk of heart failure among obese subjects. In comparison with subjects of normal weight the risk was nearly twice higher. After adjustment for established risk factors, the increase in risk was five and seven per cent for men and women respectively for every single addition of BMI.(41) On the other hand, it seems to be protective to have a higher BMI for patients with a history of heart failure. Some studies have come to the conclusion, that overweight patients display rehospitalisation and death at lower rates.(42,43)

Hormone disorder

It has been found that obese men had an increase in aromatase of fat cells. This leads to higher oestrogen levels and lower testosterone. Consequently, this may cause impotency. On the other hand hormones in obese women change differently. Since androgens are increasing, they may suffer from hirsutism, hair loss, seborrhoea, acne, secondary amenorrhea, infertility and polycystic ovary syndrome.(5)

Other complications

Furthermore, obesity is a risk factor for thrombosis and thromboembolic complications, especially postsurgical, sleep apnoea, cholecystolithiasis, EPH gestosis and arthrosis, particularly of the hips and the knees.
Moreover, obesity leads to non-alcoholic fatty liver and striae and intertrigo. Striae develop on the grounds of quick weight gain and the strain on the connective tissue. Intertrigo is the result of skin rubbing on skin, because of enormous body fat amounts.
Another major complication is the psychological aspect of overweight. Often obese suffer from reactive depression and undergo a lot of social problems concerning their family, friends and work.(5)

In conclusion, obesity results in several diseases and is a risk factor for many. It is estimated that life expectancy is reduced by up to 20 years for obese people. Only less than 20% of obese subjects willing to lose weight achieve and maintain weight

reduction. Often bariatric surgery is the last chance for extremely obese people to lose weight.(5)

The SOS-Study, concentrating on morbidity and mortality of obese, found that by surgical intervention mortality was lowered by more than 30%. (44,45)

For a reduction of 10kg body mass mortality is lowered by >20%, diabetes-associated mortality is lowered by 30% and obesity-associated carcinomas are reduced by >40%.(5)

Benefits of weight loss

By considering the high risk of comorbidities and complications of obesity and statistics on the lowering of mortality and morbidity rates by weight reduction, it seems evident that weight reduction bears numerous benefits for obese patients.

Studies have shown that reducing body weight is an effective non-pharmacological treatment for hypertension, simultaneously treating a risk factor for coronary heart disease.(46,47)

Another study demonstrated that lifestyle changes as weight loss and regular exercise were even more effective than therapy with metformin in reducing type 2 diabetes.(48) In a small study of 60 recently diagnosed type 2 diabetes patients bariatric surgery with weight loss had a beneficial effect on diabetes, in some cases even going in remission.(49)

Furthermore, weight loss influences insulin resistance in a positive way, as a study on 45 obese women has shown.(50)

An improved lipid profile is also associated with weight loss.

Along with adjusted blood fats, decline in weight has a positive influence on C-reactive protein concentrations. A study on 61 obese postmenopausal women displays that concentrations of C - reactive protein in blood plasma are notably increased and decrease correlates with reduction in body fat.(51)

Moreover, in premenopausal women, elevated levels of tumour necrosis factor-alpha, interleukin-6, P-selectin, intercellular adhesion molecule-1 and vascular adhesion molecule-1 were found. After one year and a minimum of 10% weight loss, cytokine and adhesion concentrations were found to be reduced, as well as an *improvement of vascular responses to L-arginine* was noted. This stands for an improvement of the endothelial function in response to weight reduction.(52)

To summarize the mentioned trials, it can be said that a reduction of body fat and weight has several beneficial effects on risk factors for diseases, especially coronary heart disease.

Therefore, weight reduction can be recognized as an important part of therapy and prevention of coronary heart disease.(53)

As already mentioned in the introduction, international data suggests gender-medical differences concerning obesity management and treatment. Significance of gender specific issues in general is increasing steadily. The focus on gender medicine is warranted with raising obesity prevalence and incidence. However, studies concentrating on obesity-related gender issues and especially focusing on bariatric surgery are rare. Therefore, I have turned my attention to this topic, intending to evaluate gender specific differences in obese patients, who consult the obesity outpatient clinic. Further knowledge regarding gender specific differences is mandatory in order to improve the effectiveness of care and treatment of obese patients.

Study

Aims

The objective of this study was to assess gender specific differences in glucose, lipid- and vitamin-metabolism, eating behaviour as well as comorbidities such as diabetes, hypertension, hyperlipidaemia, hypothyroidism, renal failure and osteoporosis of male and female subjects. Data collection was performed from the time point of initial presentation at the obesity-outpatient-clinic of the division of endocrinology and metabolism of the Medical University Graz since its establishment in November 2009.

Method

Firstly, after ethical approval data was collected from all possible subjects consulting the obesity-outpatient-clinic of the Medical University Graz from November 2009 to August 2012. Data was inserted into a Microsoft excel data file and subject data with excluding criteria was eliminated. Statistical calculations were performed and statistical significance assessed with a student's t-test.
Furthermore, diagrams were drafted for comparison of the gained results, which are interpreted and discussed in this diploma thesis.

Design

The study is a retrospective monocentric comparative study. Since the initiation of the a structured obesity-outpatient-clinic of the division of endocrinology and metabolism more

than 200 subjects have been examined, informed on therapy possibilities, treated, questioned and followed after surgical intervention.

Subjects

Patients came to initial presentation at the obesity-outpatient-clinic between November 2009 and August 2012.
Including criteria were an age of minimum 18 years, body mass index of ≥30kg/m² and patients were considering bariatric surgery as the next step towards weight loss.
Exclusion criteria were an already performed bariatric intervention, a body mass index of <30kg/m² and incomplete or missing data.
After the collection of presented patients in the mentioned time period and elimination of those, who did not match inclusion criteria or had to be excluded, a total collection of 214 subjects was found.

Procedure and statistics

Data was collected and accumulated in an anonymised file with subjects being numbered from 001 to 214. A subject list with corresponding numbers was kept separately.
At their initial presentation patients were weighed, measured, asked to complete a questionnaire on their eating habits, family history, past history and a blood sample collected to determine several parameters.
An example of the questionnaire is added in the appendix.
Parameters conducted from the questionnaire were: if there had been a straining situation or event when weight gain commenced, if the patient had tried any weight reducing methods before, how many portions and how big are they per day, does the patient eat snacks or in-between meals, does the patient eat at night, does he or she have eating attacks, das he or she feel guilty afterwards, does he or she eat because of frustration or for comfort, is there any feeling of satiety and hunger. Events counted as “straining situations” were for example a case of death of a family member or close friend, divorce or relationship trouble, cessation of smoking, stress, problems at work or mobbing, depression, psychosis or other cases of disease. Additionally, the need to take medication, which leads to weight gain, was also included.
Moreover, already diagnosed diseases as for instance diabetes mellitus, arterial hypertension, liver parenchymal damage and depression were asked for. Further questions concerned family history of metabolic syndrome, obesity, hypertension, diabetes mellitus

or coronary heart disease. Patients were also asked whether they drink alcohol and/or smoke.

Statistical calculations performed were mostly percentage of prevalence, mean and standard deviation, minimum and maximum and in order to assess the significance a student's t-test was performed for blood parameters' results.

Blood parameters were: blood count (erythrocytes, leukocytes, thrombocytes, haemoglobin, haematocrit), creatinin, uric acid, aspartate-transaminase (AST), alanine-transaminase (ALT), gamma-glutamyl-transferase (GGT), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), total cholesterol, ferritin, iron, vitamin B12, folic acid, thyrotropin (TSH=thyroid stimulating hormone), free thyroxin (T_4), free triiodothyronin (T_3), C-peptide, insulin, fasting glucose, haemoglobin A1c (HbA1c), vitamin D, phosphate, potassium, calcium, alkaline phosphatase, prolactin b, testosterone and crosslaps. Moreover, insulin resistance was calculated by means of the homeostasis model assessment (HOMA).

Other parameters noted or measured were gender, age, weight, size, calculated body mass index, waist- and hip circumference and the calculated waist-hip-ratio and which type of proceeding was planned (conservative, sleeve gastrectomy or gastric bypass).

This data was analysed with the help of descriptive statistics, with the main emphasis on gender comparison.

Ethical aspects

It is not likely that subjects of this study will have to bear any physical or psychological strain or damage from this study, as it is retrospective. However, they will probably not derive an advantage from it either, but future treatment strategies will take in account gender specific aspects.

Names and other data underlie medical confidentiality. Moreover, to prevent breaches of privacy, data was anonymised.

Approval for this study was given by the ethics committee of the medical university of Graz.

Results

Demographic data *(age [years], weight [kg], BMI [kg/m²], waist circumference [cm], hip circumference [cm], waist-hip-ratio)*

The cohort consisted of 214 obese patients, of which 164 (76,6%) were female and 50 (23,4%) were male. The female mean age was 41,4±13,5 years and the male 41,8±14. Mean weight of females was 117,7±20kg and of males 140,5±32kg. Body mass index was 42,8±6,6kg/m² for women and 43,9±8,3kg/m² for men. Women had a waist circumference of 128,1±13cm and a hip circumference of 139,1±13cm and men 137,9±12cm and 135,2±16cm respectively. Women had a medium waist-hip-ratio of 0,92±0,066 and men 1,02±0,055.

Diagram 1 - boxplot: characteristics female cohort

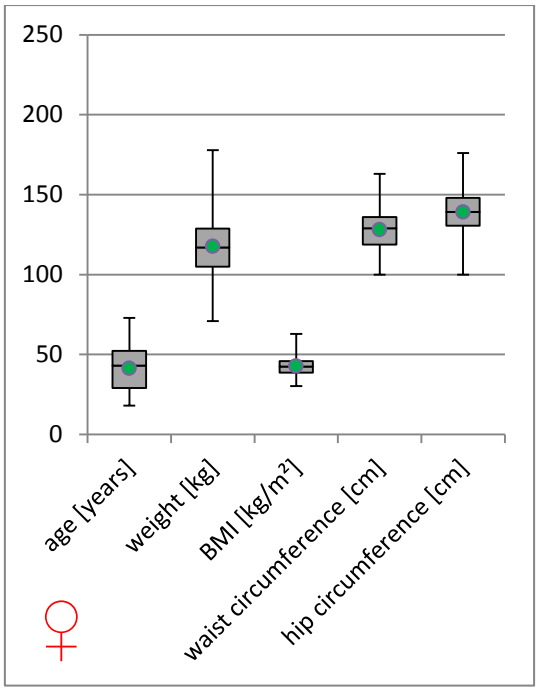
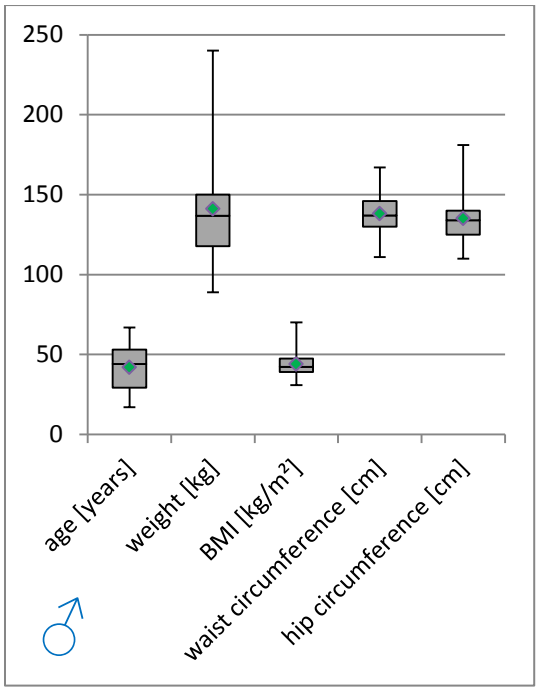


Diagram 2 - boxplot: characteristics male cohort

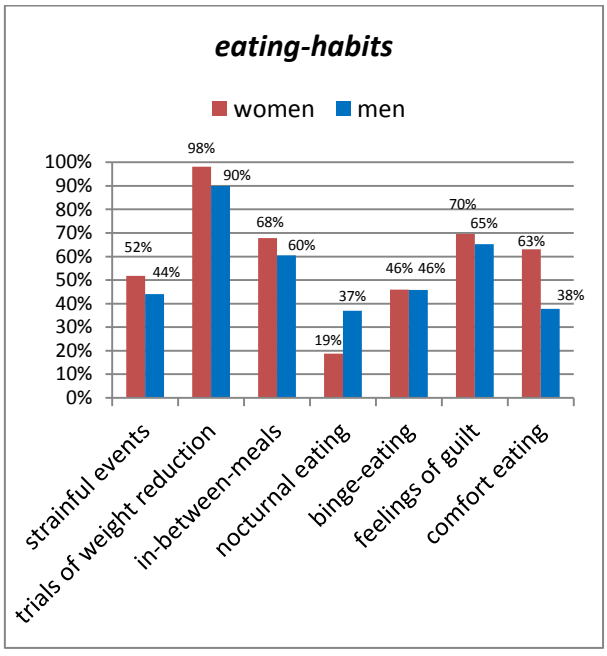


As can be seen in Diagram 1 and Diagram 2, the male and female distribution of age and BMI are very similar, which allows suitable comparison of the two cohorts.

Eating habits ***(straining situation at beginning of weight gain [yes/no], unsuccessful weight reduction trials [yes/no], in-between-meals/snacks [yes/no], nocturnal eating [yes/no], binge eating/eating attacks [yes/no], comfort eating [yes/no], portions [normal/small/large/irregular/numerous], feeling of hunger [normal/no/little/persistent/vast], feeling of saturation [yes-good/no/little/late/little&late])***

Patients were asked, whether they could identify themselves with either or more of the mentioned eating habits or if anything had happened that had led to weight gain. Furthermore, their answers concerning food portions were divided into normal, small or large of size, irregular eating and numerous, which is to say more than 3 meals daily. Hunger was assessed as normal feeling of hunger, none, little, intense and persistent feeling of hunger. Saturation was split into good feeling of saturation after eating, none, late onset, little saturation, and little and late onset. Results of eating habits can be seen in diagram 3. Strainful events at the time when weight gain started applied for 52% of women and 44% of men. 98% of women and 90% of men had already tried to lose weight. 68% of women eat snacks and have in-between-meals, 19% eat late in the evening or at night, 46% do eat uncontrollably, 63% comfort themselves by eating and 70% have feelings of guilt afterwards. Numbers for men are 60%; 37%; 46%, 38% and 65% respectively

Diagram 3 - bar chart: eating habits



Portion sizes were split up into normal, little and large, whatever patients found a suitable match for the majority of their meals. Moreover, irregular eating and constant numerous eating could be stated in addition. Results can be seen in diagram 4 below.

Diagram 4 - bar chart: portions

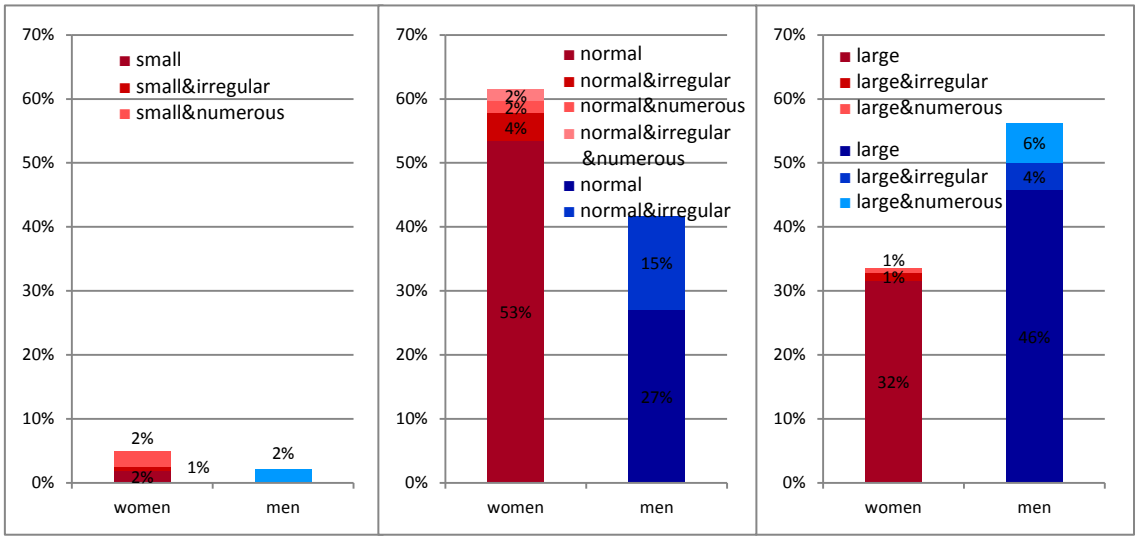


Diagram 5 and 6 demonstrate feelings of satiety and hunger. 65% of women say, they have a good feeling of satiety after eating and 71% of men. Furthermore, of the women 6% stated they had no feeling of satiety, 25% little, 3% late and 1% little and late. Results for men were 2%, 21%, 4% and 2% respectively. The feeling of hunger felt normal for 62% of women, 3% felt no hunger at all, 22% little, 10% said the feeling was persistent even after eating and 3% felt vast hunger. Men's results were 66% of normal feeling of hunger, 8% no hunger, 17% little and 9% persistent.

Diagram 5 - pie chart: satiety

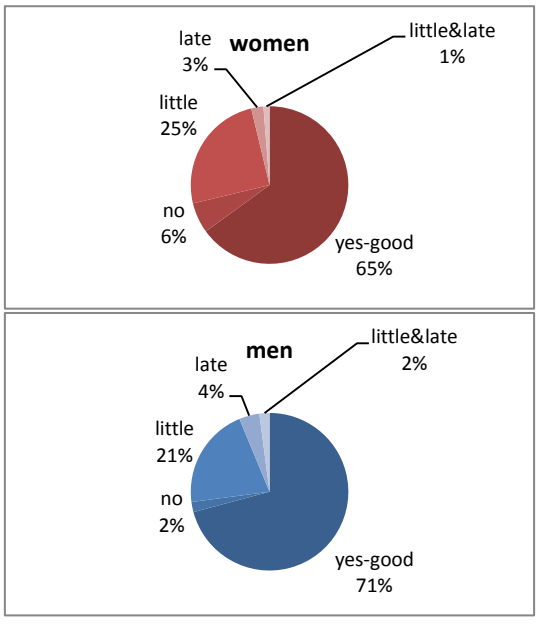
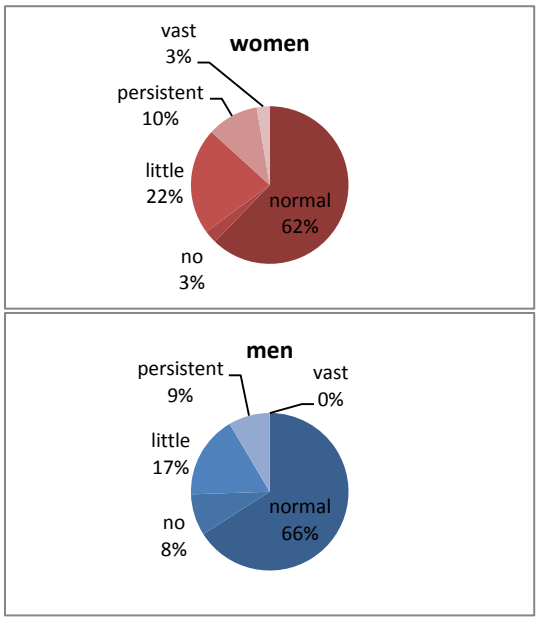


Diagram 6 - pie chart: hunger



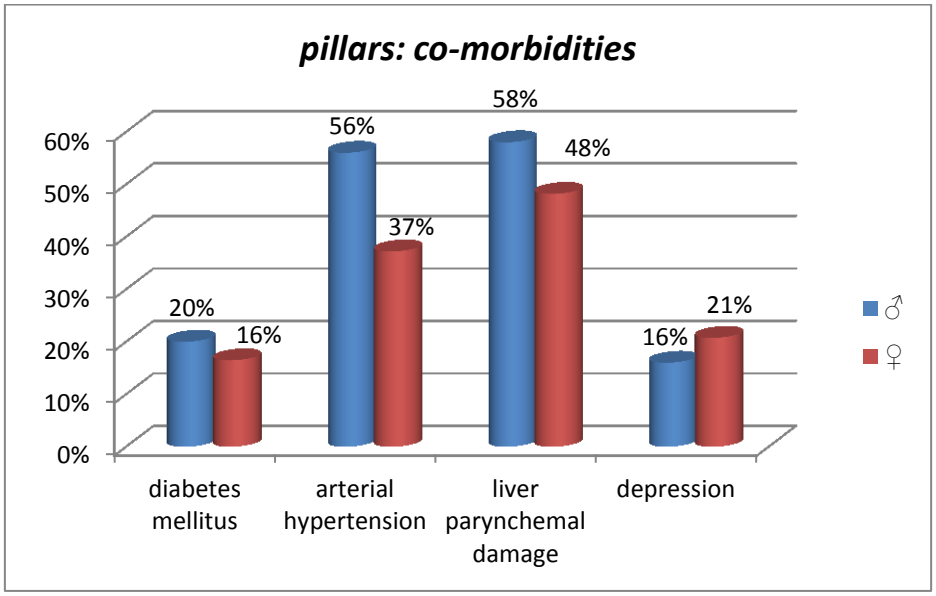
Positive family history *(metabolic syndrome: insulin resistance, arterial hypertension, dyslipidaemia, abdominal obesity; diabetes mellitus or either of them [yes/no])*

The patients were asked if any close relative, such as parents, siblings or grandparents had suffered from obesity-related diseases, obesity itself, metabolic syndrome or any component alone or diabetes mellitus of any type. This was valid for 93% of females and 94% of males.

Pre-existing diseases *(diabetes mellitus [yes/no], arterial hypertension [yes/no], liver parenchymal damage [yes/no], depression [yes/no])*

Furthermore, it was explored whether, at the time of consultation, patients had already been diagnosed with the before mentioned diseases. Results show that 20% of men suffer from diabetes mellitus, 56% from arterial hypertension, 58% from liver parenchymal damage and 16% from depression. Respective numbers for women are 16%; 37%; 48% and 21%.

Diagram 7 - pillar chart: co-morbidities

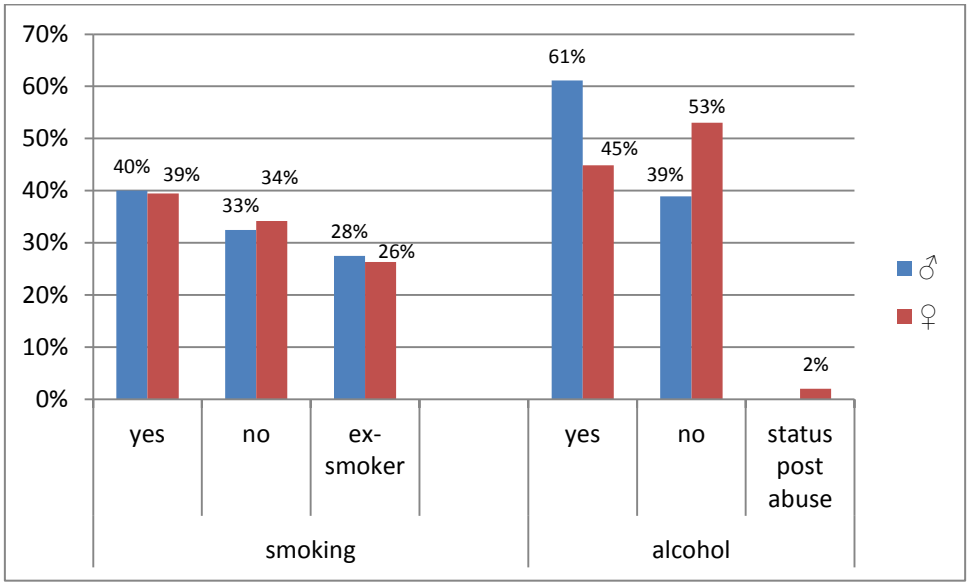


Smoking and alcohol *(smoking [yes/no/ex-smoker], alcohol [yes/no/status after abuse])*

Another aspect was smoking and alcohol habits of patients. 40% of men smoke regularly, 33% do not smoke at all and 28% have ceased smoking. 39% of women are smokers, 34%

do not smoke and 26% do not smoke any more. 61% of men stated that they drank alcohol on a regular basis, in contrast to 45%. 39% of men and 53% of women do not drink any alcohol and 2% (n=1) does not drink alcohol because of former alcohol abuse.

Diagram 8 - bar chart: smoking and alcohol



Blood parameters

To visualize the gained data, box-and-whisker diagrams were produced for all the stated results.

Carbohydrate metabolism (HOMA, C-peptide, insulin, fasting glucose, HbA1c)

Diagram 9 – boxplot: *female* HOMA, C-peptide

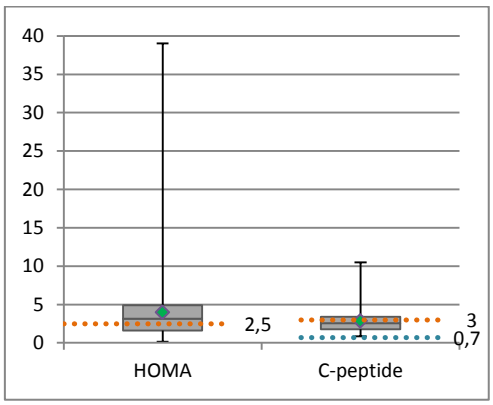


Diagram 10 – boxplot: *male* HOMA, C-peptide

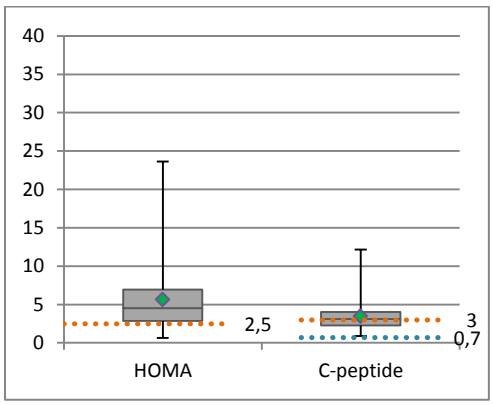


Diagram 11 - boxplot: *female* insulin, glucose, HbA1C

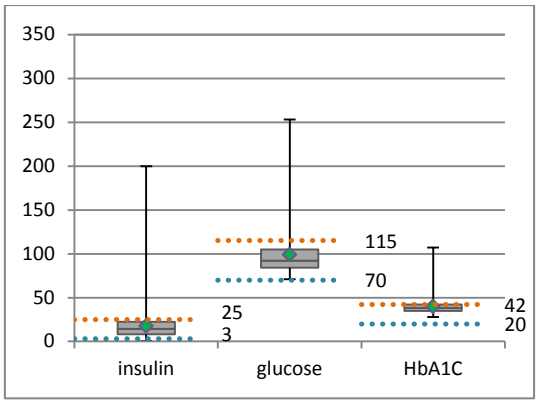
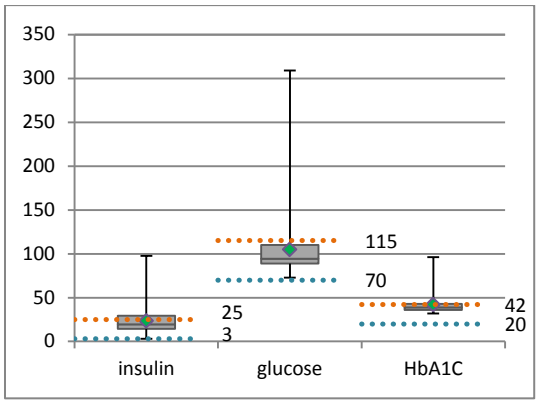


Diagram 12 - boxplot: *male* insulin, glucose, HbA1C



Calculated mean HOMA-IR for women was 3,96±4,25 and for men 5,64±4,85 (p=0,03). The measured mean amounts of C-peptide, insulin, fasting glucose and HbA1c were 2,82±1,46ng/ml; 17,66±18,52mU/l; 98,80±25,85mg/dl and 39,90±9,68mmol/mol for women respectively and 3,46±1,89ng/ml; 23,41±16,52mU/l; 104,62±36,04mg/dl and 41,84±12,17mmol/mol for men respectively (p<0,05; p<0,05; p=0,30; p=0,32 respectively).

Blood lipids (triglycerides, total cholesterol, LDL, HDL)

Diagram 13 - boxplot: *female* blood lipids

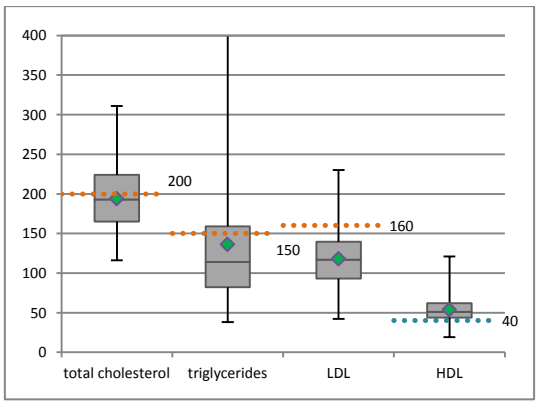
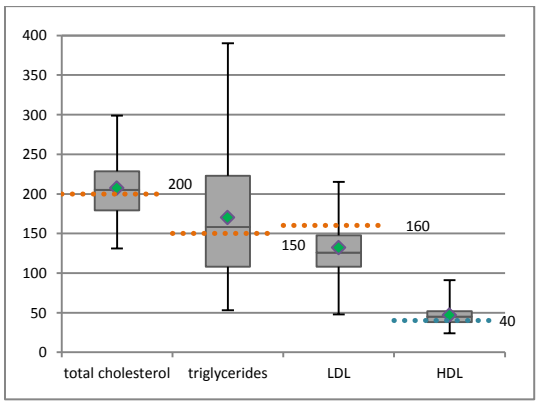


Diagram 14 - boxplot: *male* blood lipids



Women displayed a mean total cholesterol of 194,1±36,7mg/dl, triglycerides of 136,3±100,4mg/dl, LDL of 118,1±30,8mg/dl and HDL of 53,7±15,8mg/dl. Corresponding results for men were 207,3±40,4mg/dl, 170,1±80,6mg/dl, 132,2±35,7mg/dl and 47±12,9mg/dl (p=0,04; p<0,02; p<0,02; p=0,003 respectively).

Liver parameters (AST, ALT, GGT, AP)

Diagram 15 - boxplot: *female* liver parameters

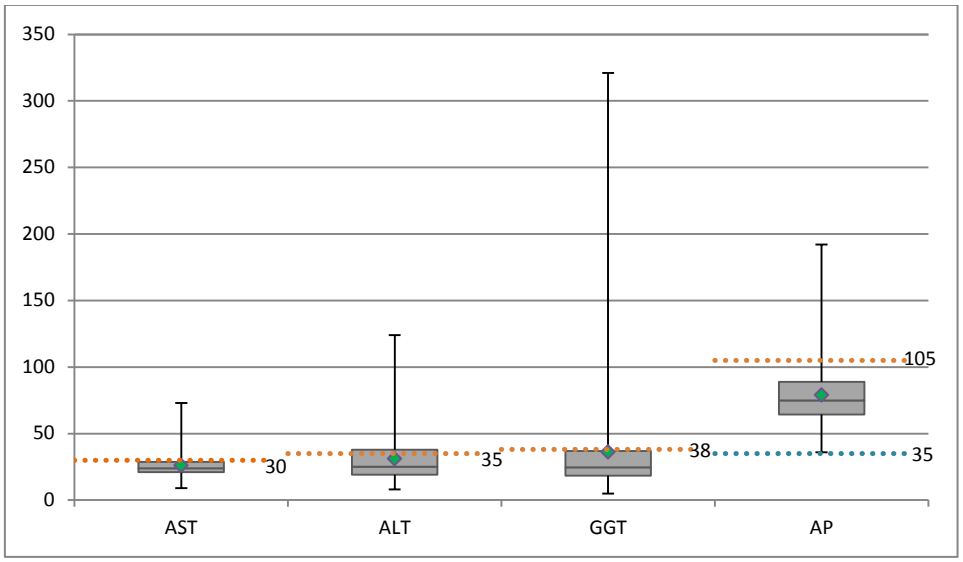
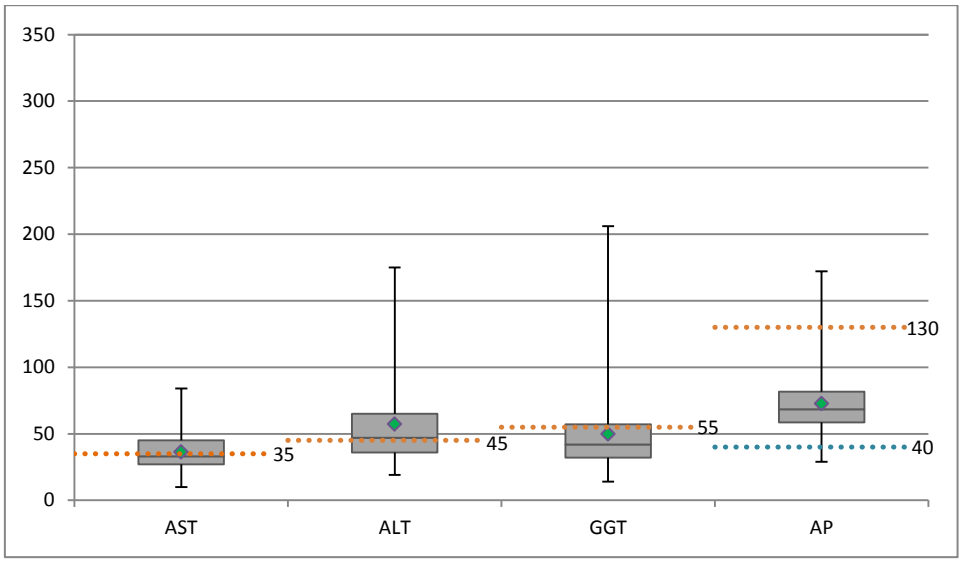


Diagram 16 - boxplot: *male* liver parameters



The mean of females' liver parameters were in the before mentioned order 26,0±9,5U/l; 31,1±19,2U/l; 36,0±39,9U/l; 78,9±22,6U/l. Values for males were 36,3±13,6U/l; 57,1±30,6U/l; 49,8±32,1U/l; 71,7±28,6U/l (p=0,000007; p=0,0000006; p=0,015; p=0,18; p<0,02; p=0,003 respectively).

Kidney parameters (creatinin, uric acid)

Diagram 17 - boxplot: *female* kidney parameters

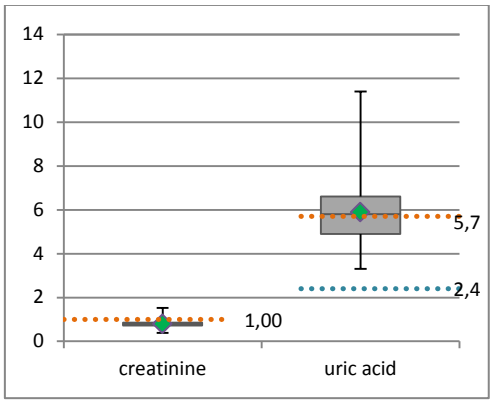
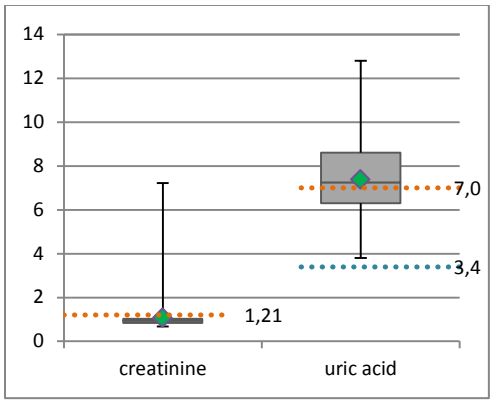


Diagram 18 - boxplot: *male* kidney parameters



Mean of women's creatinin was 0,80±0,15mg/dl and uric acid 5,88±1,33mg/dl. Men's were 1,07±0,89mg/dl creatinin and 7,37±1,65mg/dl uric acid. Creatinin was significantly lower as expected in women ($p<0,04$) stemming from the lower muscle mass; uric acid was significantly lower in women than men ($p<0,0000002$) respectively.

Iron metabolism (ferritin, available iron)

Diagram 19 - boxplot: *female* iron metabolism

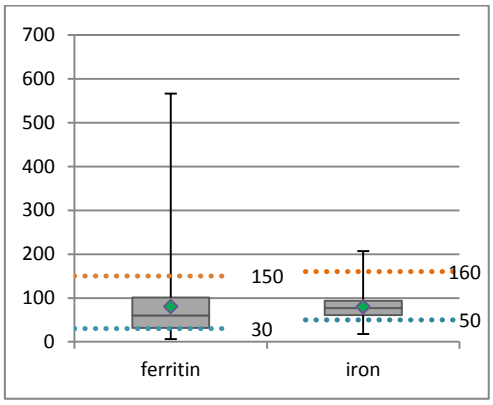
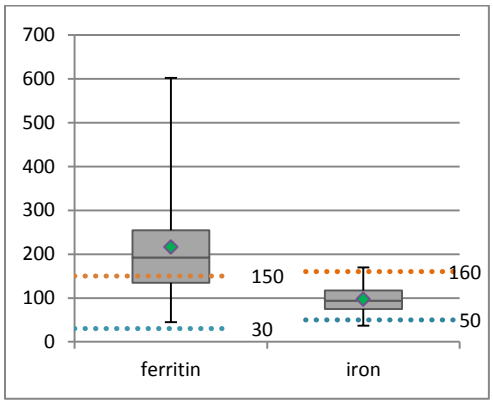


Diagram 20 - boxplot: *male* iron metabolism



Mean ferritin of females was 80,4±75,5µg/l and available iron 79,8±28,5µg/dl. For males it was 216,0±132,1 µg/l ($p<0,00000002$) and 96,8±30,5 ($p<0,002$) respectively.

Vitamin B (folic acid, vitamin B12)

Diagram 21 - boxplot: *female* folic acid

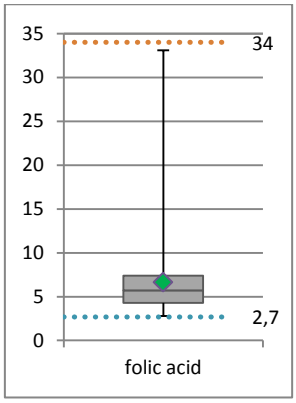


Diagram 22 - boxplot: *male* folic acid

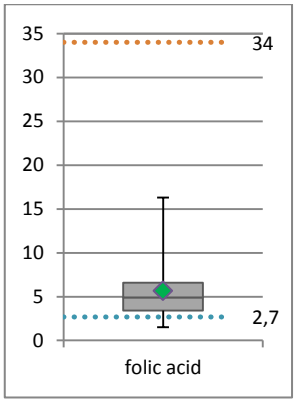


Diagram 23 - boxplot: *female* vitamin B12

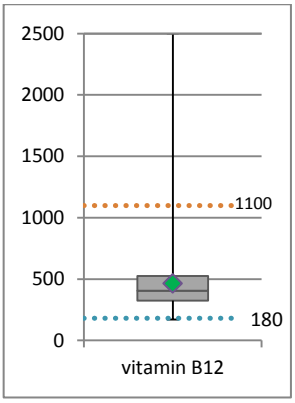
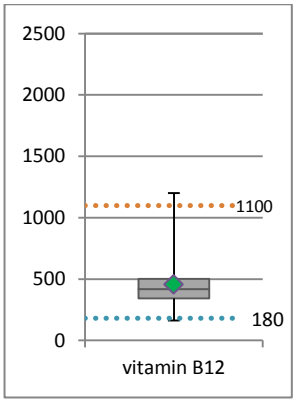


Diagram 24 - boxplot: *male* vitamin B12



Mean results for folic acid and vitamin B12 were 6,7±4,0 µg/l and 465,1±251,7pg/ml for women and for men 5,7±3,3 µg/l (p=0,11) and 455,5±183,0pg/ml (p=0,79) respectively.

Thyroid gland (TSH, free T3, free T4)

Diagram 25 - boxplot: *female* thyroid parameters

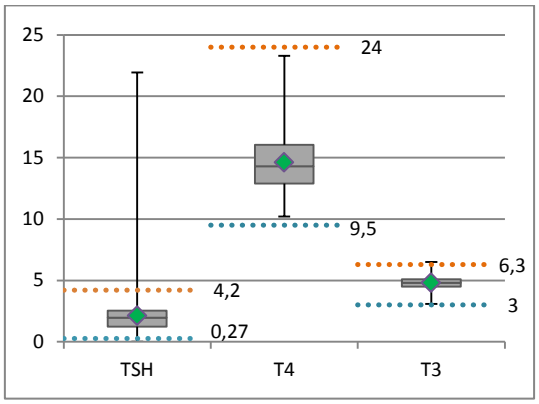
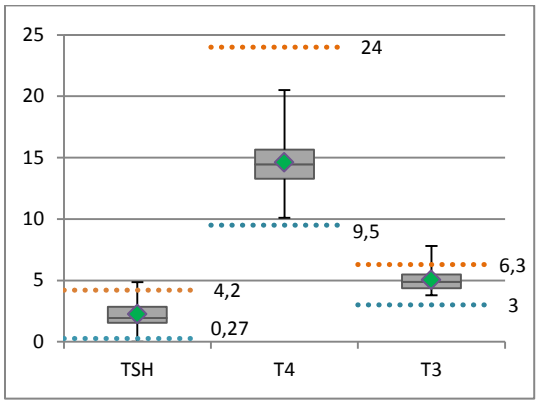


Diagram 26 - boxplot: *male* thyroid parameters



Mean values in the corresponding order are TSH 2,1±1,9µU/ml; free T4 14,6 ±2,6pmol/l and free T3 4,8±0,6 pmol/l of women and respectively for men 2,3±1,0 µU/ml; 14,6±2,3 pmol/l and 5,0±0,8 pmol/l (p=0,52; p=0,08; p=0,97).

Bone metabolism (vitamin D, phosphate, calcium, β-crosslaps)

Diagram 27 - boxplot: *female* bone metabolism

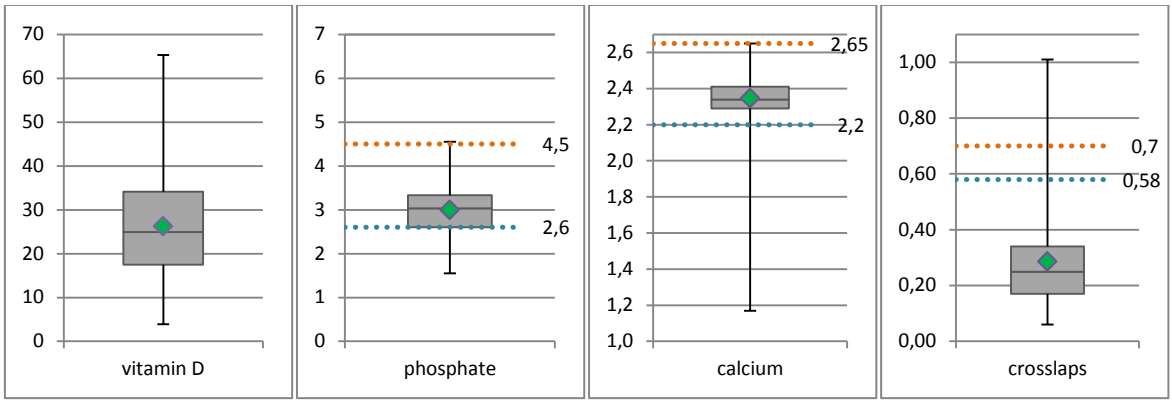
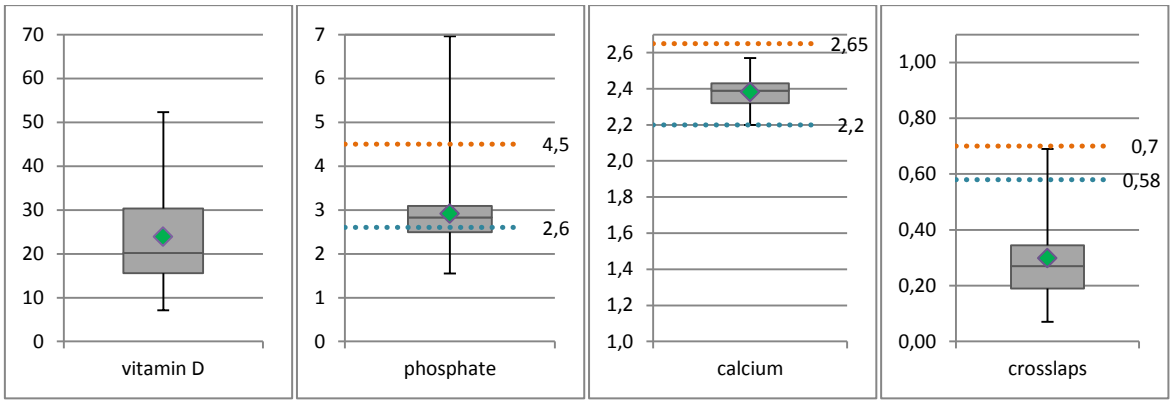


Diagram 28 - boxplot: *male* bone metabolism



The female mean of vitamin D was 26,23±11,63ng/l, for phosphate 2,99±0,52mg/dl, for calcium 2,35±0,14mg/dl and for crosslaps 0,29±0,17ng/ml. The male mean of vitamin D was 23,91±11,53ng/l, for phosphate 2,92±0,81mg/dl, for calcium 2,38±0,08mg/dl and for crosslaps 0,30±0,16ng/ml (p=0,23; p=0,56; p<0,03; p=0,67).

Hormones (basal prolactin, testosterone)

Diagram 29 - boxplot: *female* prolactin b, testosterone

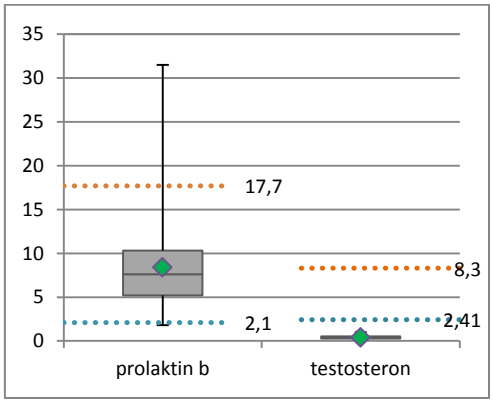
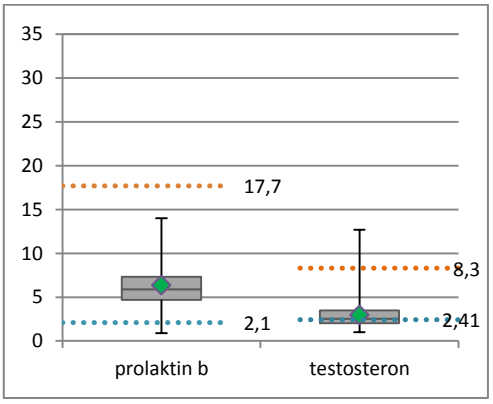


Diagram 30 - boxplot: *male* prolactin b, testosterone

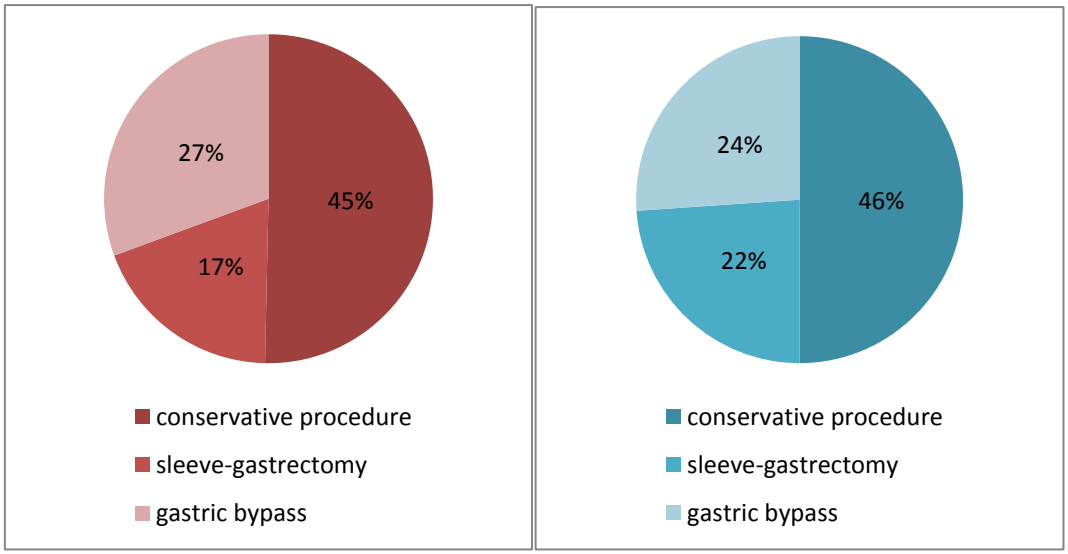


Mean prolactin b was 8,4±4,4ng/ml for women and 6,4±2,4ng/ml for men (p=0,0002). Mean testosterone was lower as expected with 0,40±0,20ng/ml for women and 2,94±1,89ng/ml for men (p<0,0000000003).

Choice of treatment *(conservative procedure [yes/no], sleeve-gastrectomy [yes/no], gastric bypass [yes/no])*

The decision about weight-loss method for treatment of morbid obesity was similar (conservative procedure 45% female, 46% male, sleeve-gastrectomy 17% and 22% respectively and gastric bypass 27% and 24% respectively). Even though there is no obvious difference between the two genders, it has to be taken into account that in total more women have consulted the outpatient clinic, which is to say that in absolute numbers, more women decide to have bariatric surgery.

Diagram 31 - pie chart: choice of treatment



Discussion

Cohort Characteristics

Mean weight of females was with 117,7±20kg significantly lower than the mean weight of men with 140,5±32kg, however, the body mass index was nearly the same with 42,8±6,6kg/m² and 43,9±8,3kg/m² respectively. On the other hand body fat distribution differed between women with a waist circumference of 128,1±13cm and a hip circumference of 139,1±13cm and men with 137,9±12cm and 135,2±16cm respectively. Consequently, women had a medium waist-hip-ratio of 0,92±0,066 and men 1,02±0,055. This confirms what is already known, that women commonly manifest pear-shape and men mostly apple-shape, which can be concluded to a higher visceral fat amount in men than in women. On the other hand, it has to be recognized that body fat percentage and its relationship to the BMI differs midst different ethnic groups.(11,12)

Eating habits

It is obvious that the most significant differences between the genders are nocturnal eating, which is done twice as often as by men than women (♂37% and ♀19%) and comfort eating, which, in contrast, nearly twice as many women admit doing (♀63% and ♂38%). Even if the contrast is not as obvious regarding strainful events and former trials of weight reduction, numbers are to some degree higher for females (♀52% contrary to ♂44% and ♀98% contrary to ♂90%), which may be interpreted as greater suffering of women and a higher tendency of coping-incapacity. In combination with the elevated percentage of comfort eating, this leads to the conclusion, that women habitually cope with problems and compensate their feelings with the help of food. The same is also true for snack-eating and in-between-meals (♀68%, ♂60%), and feelings of guilt (♀70%, ♂65%), which again may be interpreted as coping mechanisms. But the numbers relating to feelings of guilt have to be dealt with carefully, as the data comes from only 69 women and 23 men, who had answered this question. Consequently, it is only a small fraction of the total cohort. The high percentage of already performed trials of weight reduction shows that women yet again struggle with their overweight and try to manage weight loss. This concludes in a vicious cycle.

It can be said that portion sizes, number of portions and irregularity of meals of women and men differ greatly, as is obvious in Diagram 4.
Most women claim to eat normal portioned meals, compared to men, who eat mostly large

portions. Small portions are rare. It is also obvious that a great percentage of men have the problem of eating normal portions, however not regularly, but very irregularly.

As can be seen, there are no exceptional differences in relation to feelings of satiety and hunger between males and females. Distribution of women is much the same as of men.

Family history, co-morbidities, smoking and alcohol

Clearly, the fact that 93% of females and 94% of males display a positive family history as such, accounts for a genetic pre-disposition of obesity and related diseases. Moreover, this can also be seen as a predisposition of other factors contributing to obesity and related diseases for the reason that those patients have grown up seeing their parents and grand-parents obese, eating too much, not exercising enough, eating too fast and irregular or too much. All of these habits were also learned and absorbed.

Results show that men suffer more from physical maladies (DM type 2 20%, art. Hypertension 56%, LPD 58%), which is quite different to women, who more often suffer from psychological disorders (21%). This also explains the fact that in total more women have come to consult the obesity outpatient-clinic. They experience physical and psychological impairment owing to obesity and therefore want to lose weight and improve their situation. Contrasting to women, men do not seem to recognize obesity as a psychological impairment and might also contribute their diseases not to obesity but to age or their gender and therefore do not acknowledge the fact that they can be supported in refining their health and body shape.

Another aspect was smoking and alcohol habits of patients. Results have to be interpreted carefully, as only few of the consultants felt comfortable answering this question. 40 men and 114 women answered the smoking and only 18 men and 49 women answered the alcohol question.
Statistics regarding smoking habits of men and women has a lot in common. Nonetheless, drinking habits are very unlike. Men seem to more often drink alcohol than women (♂61%, ♀45%) and women seem to more often not drink alcohol at all (♀53%, ♂39%).

Blood parameters

The diagrams exemplify that although the mean HOMA-scores both of men and women were pathological, men's were higher than women's. The outcome is statistically significant with a p=0,03. While the highest outlier was in the female cohort, female values

did not vary as much and the middle 50% of the values lie within the range of 1,60 and 4,89, whereas the male middle 50% already start at a pathological value of 2,84 and range to 6,95.
The homeostasis model assessment is a tool for labeling insulin sensitivity and subsequently insulin resistance, as several studies have shown. Furthermore, it works especially well for patients with high visceral fat deposits.(54) Matthews et al. also showed that HOMA correlated well with results of euglycaemic clamp tests.(55) As it is a more convenient test, easier, cheaper and more time-sparing to perform than oral glucose tolerance testing, it was used as an indicator for insulin resistance and beginning metabolic syndrome of the patients, considering that only a fifth of men and a sixth of women had already been diagnosed with diabetes.
This leads to the assumption that obese men more often already suffer from insulin resistance, even though not yet from diabetes.
Moreover, a study performed on non-obese – concerning BMI – subjects demonstrated that HOMA could also be used as a follow-up indicator for type 2 diabetes patients.(56) According to The San Antonio Heart Study, there is also an association between HOMA and the incidence of cardiovascular disease.(57) This coincides with the gained results, that men feature significantly higher numbers of arterial hypertension and subsequently atherosclerotic diseases, leading to cardiovascular incidents.

C-peptide (significant with $p<0,05$)is being split off during the transformation of proinsulin to insulin and emitted into blood.(58) It has been affirmed to correlate positively with insulin secretion rates and therefore patients with diabetes mellitus type 2 and peripheral insulin resistance hold higher c-peptide concentrations.(59) Still, clearance of c-peptide is predominantly performed by the kidney, which makes it the limiting factor.(60) Inukai et al concluded from a study performed in 2009 on type 2 diabetes patients that high c-peptide levels are coupled with a high BMI, high serum triglycerides and hypertension. Low c-peptide levels concentrations, which are associated with more frequent hyperglycemic situations result in the advancement of diabetic microangiopathies.(61) Moreover, a study performed on diabetic men found a correlation between high c-peptide rates after stimulation with glucagon and incidences of coronary heart disease.(62) Our study showed no significant difference between the genders. Therefore, it can be assumed, that c-peptide values are independent of gender.

Male and female values of insulin, fasting glucose and hemoglobin A1c do not bear any significant differences. Hence, the same assumption can be made about those values as for c-peptide: there is no relevant gender specific difference concerning insulin production, blood glucose levels and long-term values, even though results for insulin are statistically significant with $p<0,05$.

Results for blood lipids were all statistically significant. Those of men have a lot in common with those of women; however triglycerides are generally higher in men than in women and evince a greater variance. Moreover, LDL is slightly higher, opposed to HDL, which is slightly lower. These Dyslipidemia can have a primary origin as metabolic disorders or – most commonly – secondary causes, which include: *type 2 diabetes mellitus, excessive alcohol consumption, cholestatic liver diseases, nephrotic syndrome, chronic renal failure, hypothyroidism, cigarette smoking, obesity and drugs*.(63) Hypertriglyceridemia is very common in type 2 diabetes patients, as a higher glucose and fatty acid availability is the cause.(64) Furthermore, disproportionate alcohol consumption also leads to an increase in triglycerides and the effect is even stronger for diabetics.(65) Looking at those facts, higher triglycerides in men seem to stem from circumstance that more men of the cohort are diabetics (20%), suffer from liver parenchymal damage (58%) and more men drink alcohol than women (61% men in contrast to nearly 45% women). As all subjects are obese and their body mass index seems very homogen, another reason for dyslipidemia could be the lengthier waist circumference of men. Consequently, they possess more visceral fat, which is associated with a higher morbidity.

Looking at liver parameters such as AST ($p=0,000007$), ALT ($p=0,0000006$), GGT ($p=0,015$) and AP (statistically not significant), I would like to point out that mean values of all liver parameters were considerably higher in men than in women, except alkaline phosphatase, which was slightly lower.
Studies have shown that a great fraction of morbidly obese patients, as well as moderately obese, show histological abnormalities of the liver and frequent liver dysfunction.(66,67) Hence, obesity is considered an independent risk factor for liver parenchymal damage and men are even at higher risk.(68,69) Studies concerning bariatric surgery are controversial. Even though liver parameters improve with the weight loss after gastroplasty and gastric bypass (70), jejunoileal bypass frequently leads to steatohepatitis.(71) Other factors considered risk factors are type 2 diabetes, alcohol, drugs and poor nutrition.(66) The findings of higher liver parameters in men support the cited studies that men more

commonly display liver damage. Furthermore 58% of men, in contrast to 48% of women, have beforehand been diagnosed with liver parenchymal damage, adopting this statement even further.
It is unclear, why women have higher alkaline phosphatase. A possibility could be the connection to higher osteoporosis prevalence in women, as AP levels change with rates of bone metabolism.

There seems to be no significant difference between creatinin scores, except for a very high outlier in men. Thus, there appears to be no connection with obesity.
For uric acid parameters, it is important to mention that different reference values apply for gender – the male ones lie higher than the female. Both distributions are very similar ($p<0,04$ and $p<0,0000002$). Reasons for this could be that uric acid positively correlates with body mass index, waist-hip-ratio – that is body fat distribution in favor of visceral fat, alcohol consumption and postprandial insulin levels and negatively with age, as studies have shown.(72,73) Furthermore, uric acid clearance correlates with insulin resistance and are under suspicion to be another component of the metabolic syndrome.(74,75) A further aspect of high uric acid is the possibility of predicting incidents of cardiovascular disease, because studies have shown that high levels are another independent risk factor for cardiovascular mortality.(76,77)
Reasons for hyperuricaemia can be primary as an impaired clearance in the kidneys or hyper production of uric acid of genetic origins as well as secondary. Secondary forms again impair clearance for example kidney diseases, lactacidosis, ketoacidosis and drugs; or they lead to overproduction because of e.g. leukemia, polycythemia, hemolytic anemia and tumorlysis-syndrome.(5) Even if according to reference values male and female results are quite similar, men show higher absolute values of uric acid, which again may stem from higher prevalence of diabetes and lower waist-hip-ratios, signifying higher amounts of visceral fat.

Although mean ferritin and iron values of women are generally lower than those of men, the medium 50% are still within reference values. Even so, men's ferritin levels are largely elevated ($p<0,00000002$ and $p<0,002$).
Yanoff et al published in 2007 that obesity and hyperemia were associated. Serum iron was lower; however ferritin was higher in obese subjects.(78) Zafon et al found the same results and contributed them to three possible origins. Either decreased iron intake, or impaired intestinal uptake or inflammation, which leads to insufficient bioavailability.(79)

Another study confirmed these results and McClung concluded that by obesity caused inflammation resulted in iron deficiency.(80)
Other studies found a connection between elevated serum ferritin and metabolic syndrome and type 2 diabetes mellitus among Chinese population and Korean postmenopausal women.(81,82) Others also linked raised ferritin with metabolic syndrome and diabetes mellitus, but also with insulin resistance in Americans.(83,84) A further accompanying disease was found to be nonalcoholic fatty liver disease.(85) Another important aspect is that obesity is often related with iron deficiency before and also after bariatric surgery.(86–88) Moreover, there seems to be a positive correlation of body fat distribution and serum ferritin.(89)
Taking all those studies and facts into account, it appears reasonable that men have higher serum ferritin levels in comparison to women, as they have worse body fat distribution, higher prevalence of metabolic syndrome associated diseases and less loss through menstrual bleeding. Furthermore, women seem to have lower iron and ferritin levels owing to the fact that they have monthly hemorrhage and probably insufficient intake due to different eating habits.

Vitamin B12 levels of both genders are very much the same, while results are not statistically significant. Even though both maximum outliers are too high, those can be neglected, as both means and also the medium 50 percent of both cohorts are within normal ranges. A study performed on Mexican non-pregnant women came to the result that obesity was a risk factor for reduced vitamin B12 plasma concentration status.(90) However, this cannot be confirmed by my gained results, considering all cohort subjects are obese and they lie within reference values.
On the other hand, although not statistically significant, folic acid levels are to some extent higher for women. This seems inconsistent with the previously mentioned study on Mexican women, which came to the result that obese women also had folate deficiency in nearly 15%.(90) Another study in Atlanta on nearly 3000 women came to the result that maternal obesity with a BMI greater than 29 is a risk factor for anencephaly and spina bifida, which I relate with folate deficiency in obese women.(91) Nonetheless, as I have already mentioned, my results are in contradiction to the stated studies.

There seems to be absolutely no noteworthy difference between male and female TSH, T4 and T3 serum levels, of which no parameter result is statistically significant. They resemble each other very well. Some studies stated that obese and morbidly obese had

elevated T3, T4 and some even TSH levels. These seemed to decrease during fasting and weight loss.(92,93) This could explain the normal thyroid status of this study's cohort, as they came to lose weight and had been trying already with conservative measures. Other studies confirmed augmented TSH, T3 and T4 likewise, however those were performed on children.(94,95)

According to several studies, vitamin D levels inversely correlate with BMI, total body fat, body weight, waist circumference and even HbA1C.(96–98) Moreover, bioavailability seems to be decreased in obese subjects.(99) Reasons may be the accumulation in body fat compartments and decreased sunlight exposure owing to the psychological strain because of low self-esteem due to their body shape.(97,99) It is obvious that female vitamin D levels in my cohort are significantly higher than the male. This may stem from the fact that women have better waist hip ratios, therefore lower body fat percentage, even though both genders have quite similar BMI. If separated into 25-hydroxy vitamin D (calcidiol) and 1,25-vitamin D (calcitriol), studies found that calcitriol increased in obese subjects, whereas calcidiol decreased.(100,101) However, in our study, only 25-hydroxy vitamin D levels were measured.

A study dealing with hypertension and obesity found that calcitriol stimulates the entry of calcium into human adipocytes, which then again stimulates lipogenesis and inhibits lipolysis and furthermore, leads to an accumulation of triglycerides. Consequently, the suppression of calcitriol could be a focus of treatment of obesity and hypertension.(102) Nonetheless, 1,25-vitamin D was not determined in this study. Therefore, no data-based statement can be made on this aspect. However, calcium values show no difference between the genders and lie within normal ranges.

A further study discovered that calcium positively correlated with BMI and waist-hip-ratio, whereas phosphate negatively correlated with those two parameters.(103) As already mentioned, this cannot be confirmed, as calcium levels are normal and statistically relevant ($p<0,03$). Moreover, phosphate status is also within the norm regarding both genders, apart from slightly higher levels in women, which may be due to vaguely higher vitamin D-concentrations. These results are supported by two studies, which also found alterations in calcium and phosphate levels in obese to be rare.(100,101)

Another parameter concerning osteoporosis we looked at was β-crosslaps. No significant differences were found. Furthermore, not only the mean but also the medium 50% of both

genders lie below pathological values. This correlates with the above described results that gender differences are quite minimal concerning osteo metabolism.

Female prolactin b levels are slightly higher than male levels. Nonetheless, the contrast is not substantial. Furthermore, prolactin b of both genders lies within the boundaries of normal range.
In contrast, female testosterone is very low, which can be explained by the fact that women physiologically have quite low amounts of it. Nevertheless, male amounts are typical, because they are higher, conversely to women. If it were lower, this could lead to promotion of body fat accumulation; however, this is not the case, so it cannot be linked to obesity.

Limitations

This study is limited by several factors contributing to the necessity to do further research on this topic.
Firstly, the completion of the questionnaire is quite subjective, as everybody can understand terms such as normal portion size or irregular eating very differently. Furthermore, in order to be able to compare data, answers have to be closed or possible answers have to be given as a choice. This again restricts the patients and can lead to bias. Another disadvantage of the form is the question concerning eating habits. It is asked how often, how much and in which situations patients eat, however, we do not know what they eat. They could either consume healthy, small-portioned snacks such as vegetables or a glass of milk, or in contrast they could stuff themselves with high caloric, unhealthy, fatty huge portions of fast food or sweets. This changes results drastically.
Moreover, positive family history of metabolic syndrome was asked. This has been interpreted by me as a genetic component. Nonetheless, it has to be taken into account that humans do not only inherit genes from their parents, but also traditions, habits, affinities and repelling things. This influences eating habits, practices of shopping, exercises, cooking customs, etc.; all of which can be contributed to body weight, health status and opinion.
A further aspect which has to be assessed critically is the smoking and alcohol status of the subjects. Primarily, only few have answered this question, which is not very representative. Secondly, it is not definite, that patients have answered this question truthfully. Some might be ashamed to do so and others might understate the truth.

Preexisting diseases have not been diagnosed by this respective study. If a patient had a medical record of preexisting diseases, it was adopted as such. We do not know which criteria have led to this diagnosis or who has done so. Consequently, some numbers may be biased, as it is known that certain diseases are more likely to be diagnosed for women or for men. One example is depression, which is less often diagnosed for men than for women.(104) In order to improve this aspect, all diagnoses counted would have to be according to international diagnosis criteria and performed by respective specialists. HOMA is a very respectable parameter to compare insulin resistance, as it is easily performed and a fast and less elaborate calculation in comparison to an oral glucose tolerance test. Even so, it only represents a static value. Nonetheless, oral tolerance testing would have been too much of an effort for each patient. Furthermore, it is quite displeasing for the patients; hence I believe that not all would have consented to this procedure. Hemoglobin A1C is also a good value to measure and compare long-term glucose levels. Nonetheless, proper results can be bought with frequent hypoglycemia in patients with diabetes mellitus due to certain therapies, which acutely is even more dangerous. Another limitation is that subjects' medications were not taken into account. The effect would be that constant medication disguises certain pathologies in blood parameters, as for example too high blood lipid levels or deficiency of hormones and vitamins. Even though blood samples were taken in the morning in uninebration, long-term effects of the medication will still influence results. On the other hand, considering the fact that patients are medicated and have healthier blood parameters, their risk factors will consequently decline and the outcome will be better.
Comparatively, folic acid status could also be better because of frequent consultations and medical examinations, because of the upcoming bariatric surgery.
Ferritin and iron status could not only be affected by gender itself, as for example monthly bleeding and consequent loss, but also by gender-specific eating habits, such as the fact that men eat more meat than women. Moreover, already treated deficiency with the use of medication could also falsify results.
Furthermore, liver damage does not always correlate with liver parameters, as the liver can compensate for a long time until blood parameters will show an effect. Therefore, a histologic biopsy would be the best comparable characteristic, yet it is an intervention with risks and discomfort for the patients.
Concerning the numbers of conservative treatment or bariatric surgery, it has to be taken into account that these decisions are not the recommended procedures by medics, but the

patients' personal wishes.
Last but not least, it has to be beard in mind that total numbers of male and female subjects differ, as for 164 women and 50 men the ratio ensues 1:3,28. As a result, female facts are more representative then male ones.

Conclusion

The gained results lead to the following conclusions.
Concerning body fat, women have a healthier body fat proportion, displaying a pear-shape (waist-hip-ratio=0,92±0,066). In contrast, men display the apple-shape (waist-hip-ratio=1,02±0,055), which accumulates more visceral fat and has a higher risk of cardiovascular diseases. This leads to the conclusion that men have a higher risk of cardiovascular mortality owing to obesity than women and therefore have to be medically checked more often concerning their overweight and other risk factors.
A very important aspect of the treatment of obesity is the modification of eating habits. Concluding from the gained results that women have more problems with comfort eating (63%), while men more often eat nocturnally (37%) and irregularly (19%), the behavioral approach should direct treatment at this aspect. As a majority of both genders has feelings of guilt after eating (♀70%; ♂65%) and consumes a lot of snacks and in-between-meals (♀68%; ♂60%), this should also be focused on.
There seems to be no gender difference between hunger and satiety of obese. Even though, about one fourth of men and women feel little satiety and about one third has problems concerning constant feeling of hunger. Those patients could also be treated with behavioral therapy and should eat slowly and deliberately in order to improve their recognition of hunger and satiety.
Due to the fact that more than 90% of both men (94%) and women (93%) display a positive family history of metabolic syndrome, obesity, and other cardiovascular morbidities, their relatives should also be advise to undergo treatment and behavioral therapy in order to help the patient improve his or her eating habits. This will be even more effective, if the spouse or other family members living in the same household do so, as habits convey vice-versa.
Comorbidities are quite different between genders. As already mentioned before, men more often suffer from physical diseases (diabetes mellitus 20%, arterial hypertension 56%, liver parenchymal damage 58%), whereas women more often suffer from

psychological ones, such as depression (20,73%) Therefore, diagnosis and treatment should focus on these diseases according to gender. However, those results could stem from gender-bias, that is to say that women are oftener diagnosed with depression than men, or from the fact that the male gender already has a higher genetical predisposition for cardiovascular diseases. Therefore, it is my believe, that diseases not typical for gender should not be overseen.

Results for HOMA were higher pathological for men than for women, but pathological for both genders ($p=0,03$) This correlates with the results on insulin and c-peptide ($p<0,05$ for both). I concluded from these results that although few of the patients had been diagnose with diabetes, a high percentage of them already have insulin resistance. This is a very important aspect for the treatment of obesity.

Furthermore, the results for blood lipids, which were all statistically significant (total cholesterol $p=0,04$; triglycerides $p<0,02$; LDL $p<0,02$; HDL $p=0,003$), showed that men have very high values of triglycerides, which is what medication should focus on for them. Nonetheless, obese subjects of both genders should be treated for dyslipidemia.

Liver parameters seemed to be normal for females, however AST and ALT were slightly pathological for men ($p=0,000007$ and $p=0,0000006$ respectively). Hence, liver controls should be more frequently performed on male obese.

Kidney parameters showed a tendency of high values of uric acid for both men and women, although male were higher, even though reference values are adapted for gender ($p<0,0000002$). As a consequence, gout could occur with a higher risk in obese men, which should be observed carefully.

Although I expected iron deficiency in obese subjects, the majority of values was within normal ranges. Men even had higher ferritin levels than normal (ferritin $p<0,00000002$; iron $p<0,002$). Nonetheless, iron metabolism should be monitored closely after bariatric surgery, as these can lead to deficiencies.

Results for folic acid and vitamin B12 were not statistically significant, in the same way as thyroid parameters. Concerning bone metabolism, the only statistically significant parameter was calcium ($p<0.03$), which was physiological for both genders. Moreover, hormones (basal prolactin $p=0,0002$ and testosterone $p<0,0000000003$) were also not altered pathologically.

Last but not least, numbers for choice of treatment, either conservative, sleeve-gastrectomy or gastric bypass were nearly the same for both genders (conservative procedure ♀45%; ♂46%; sleeve gastrectomy ♀17%; ♂22%, gastric bypass ♀27%; ♂ 24%). Nevertheless, it

has to be taken into account that in total more women decided to consult the obesity-outpatient clinic and to undergo bariatric surgery in order to lose weight, which I contribute to the psychological strain.

In conclusion, several aspects gained from this study should be considered in the care and treatment of obese patients. Nonetheless, further research has to be done in order to find even better approaches.

Register of Illustrations

Appendix

Erstvorstellung ADIPOSITAS Datum:

Name: Gewicht: ..... kg / Größe: ..... cm

Geb.-Dat.: BMI: ..... (kg/m^2)

Geschlecht: ☐ w. ☐ m. Bauchumfang: ..... cm (in der Mitte zwischen Rippenbogen und Beckenkante gemessen)

RR: ……/……. / Puls:……. Hüftumfang: ..... cm (auf Trochanterhöhe gemessen)

Gewichtsverlauf (siehe Einlageblatt):

Adipositas seit: Höchstgewicht: ..... kg

wann? .....

Situationen / Ereignisse zur Zeit der Gewichtszunahme: .....

.....

Gewichtsreduktionversuche (kontrolliert – Wo? Wann? Wieviel abgenommen?) :

☐ Diäten ..... ☐ Medikamente .....

☐ Programme ..... ☐ andere .....

Zielgewicht (lt. Pat.): ..... kg

Essverhalten:

Portionen (Größe / Frequenz): ☐ Zwischenmahlzeiten ☐ Nächtlich. Essen

Süsse / Fette Tendenzen (prämenstruell): ☐ nein ☐ ja

Ess-Attacken: ☐ nein ☐ ja → wann? ..... → wie oft? ..... / Woche

☐ sehr schnelles Essen ☐ Essen ohne Hungergefühl

☐ Essen bis zur unangenehmen Völle, Übelkeit ☐ Essen allein

☐ Schuldgefühl nach Essattacke Erbrechen danach: ☐ nein ☐ ja

Frustessen (Frust, Stress, Ärger, Zweifel, Belohnung) : ☐ Ja ☐ wenig ☐ nein

Sättigungsgefühl: ☐ ja ☐ wenig ☐ nein

Hungergefühl: ☐ anhaltend auch nach Essen ☐ wenig ☐ nein

Anorexia nervosa: ☐ nein ☐ ja

Raucher: ☐ nein ☐ nein seit ..... ☐ ja (..... Zigaretten/Tag)

Alkohol: ☐ nein ☐ nein seit ..... ☐ ja (.....g/Woche) (1/2l Wein = 2 Fl. Bier = 40g Alkohol)

Familienanamnese:

☐ Adipositas ..... ☐ Dyslipidämie .....

☐ Diabetes ..... ☐ KHK, MI .....

☐ Hypertonus ..... ☐ malig. Erkrankungen .....

☐ andere .....

Vorerkrankungen:

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Medikamente:

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Allergien:

☐ nein ☐ ja → .....

Gynäkologische Anamnese (falls zutreffend):

Bisherige SS: ☐ nein ☐ ja

→ ☐ normal ☐ Aborte ☐ Mißbildungen

Menses: ☐ regelm. ☐ unregelm.

Bewegung bisher (Was? Wie oft, St./Woche?)

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Diagnosen:

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Status praesens:

AZ , Pat. klar u. orientiert

Caput/Collum: Skleren , Konjunktiven , Pupillen , isokor.

SD , HNAP , LK

Cor: HT rein, rhythmisch, normocard

Pulmo: VA bds, gute Basenverschieblichkeit

Bauch:

Extremitäten: Pulse A.tib.post. u A.dors.ped. , Ödeme , Läsionen , Varizen

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