REVIEW ARTICLE

Metabolic syndrome and the kidney

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The clustering of cardiovascular risk factors was noted early in 1920s, but in the 1980s a link specifically between the cardiovascular risk cluster and insulin resistance had been postulated. Such clustering of cardiovascular metabolic risk factors was designated "metabolic syndrome". Recently it was found that metabolic syndrome impacts not only on cardiovascular, but also on renal function. Today the metabolic syndrome is recognized as a novel risk factor of chronic kidney disease. The links between obesity, metabolic syndrome and chronic kidney disease are not fully explained by the known association between obesity and diabetes or hypertension, respectively. Even in the absence of these conditions obesity is associated with increased glomerular filtration rate and renal blood flow, glomerulomegaly, depletion of podocytes and in extreme cases with focal segmental glomerulosclerosis. For the pathogenesis of kidney disease in patients with the metabolic syndrome it is relevant that insulin resistance is linked to increased tubular reabsorption of sodium. Amongst others recent evidence points to adverse effects of aldosterone on podocytes resulting from hypothetical stimulants of aldosterone synthesis by visceral adipocytes. In view of the current growing obesity pandemic the connection between obesity, metabolic syndrome and chronic kidney disease has become a public health issue. (NEFROL. DIAL. POL. 2009, 13, 192-197)

Key words:
• chronic kidney disease
• metabolic syndrome
• obesity
• insulin resistance
• aldosterone

Zespół metaboliczny a nerki

Udział metabolicznych czynników ryzyka w patogenezie chorób układu sercowo-naczyniowego sugerowano już w latach 20-tych XX wieku, ale dopiero w latach 80-tych XX wieku powiązano te czynniki ze zjawiskiem insulinooporności i nazwano je zespołem metabolicznym. Ostatnio potwierdzono, że zespół metaboliczny wpływa na czynność nerek i może być jednoznacznie uznany za nowy czynnik ryzyka przewlekłej choroby nerek. Związki pomiędzy zespołem metabolicznym, otyłością i przewlekłą chorobą nerek nie wynikają jedynie z częstszego współwystępowania cukrzycy typu 2 lub nadciśnienia tętniczego u osób otyłych. Otyłość wiąże się ponadto ze zwiększonym przesączaniem kłębuszkowym i zwiększeniem przepływu krwi przez nerki, zwiększeniem wymiarów kłębuszka nerkowego, a w następstwie tego u niektórych chorych z rozwojem ogniskowego szkliwienia kłębuszków nerkowych. W patogenezie przewlekłej choroby nerek na tle zespołu metabolicznego uczestniczy również zwiększona reabsorpcja sodu w kanalikach nerkowych spowodowana insulinoopornością. Ostatnio stwierdzono bezpośredni, niekorzystny wpływ aldosteronu na strukturę i funkcję podocytów. Hiperaldosteronizm u chorych z zespołem metabolicznym może być spowodowany między innymi uwalnianiem przez tkankę tłuszczową czynników nasilających syntezę tego hormonu. Uwzględniając aktualną pandemię otyłości, związki pomiędzy otyłością, zespołem metabolicznym i przewlekłą chorobą nerek stają się istotnym problemem zdrowia publicznego i sytuacja ta wymaga wdrożenia szeroko zakrojonych metod zarówno profilaktycznych jak i leczniczych. (NEPHROL. DIAL. POL. 2009, 13, 192-197)

Słowa kluczowe:
• przewlekła choroba nerek
• zespół metaboliczny
• otyłość
• insulinooporność
• aldosteron

Conflict of interests: none declared

History of the metabolic syndrome and insulin resistance

Clustering of metabolic and cardiovascular risk factors had been observed in the 1920ies by Hitzenberger [26], but it was the Banting lecture in 1988 where G. Reaven linked specifically insulin resistance to a number of cardiovascular risk factors, a constellation which he called "syndrome X" [50]. This proposal was later extended and led to the concept of the "metabolic syndrome". Currently the most widely used criteria of the metabolic syndrome were established by the National Cholesterol Education Program (Adult Treatment Panel III) (table 1) [60].

This composite is a predictor of cardiovascular risk [54]. The purpose of this index was the consideration that in order to fight cardiovascular (CV) disease in obese individuals, evaluating and treating every obese subject would be a daunting task; therefore the panel decided to focus on overwe-

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ight and obese subject with evidence of medical complications [60].

The scientific basis of this construct is questionable and has been criticized [30]: it has been argued that insulin resistance as a unifying concept is uncertain, that the criteria are somewhat arbitrary and that the CV risk associated with this syndrome is no greater than the sum of the parts. Moreover, treatment of the syndrome comprises simply the treatment of its components. These shortcomings of the concept of a "metabolic syndrome" are easily explained: power is lost by dichotomization of continuous variables, correlated factors are used which no longer serve as independent predictors and age and smoking as powerful predictors are not included [2]. Nevertheless, the concept of the metabolic syndrome can be justified as a tool to promote public awareness and for the use as a counseling too, but undoubtedly the price that has to be paid is that it is not an ideal predictor of CV disease and that it is a poor instrument to resolve scientific issues [21]. What has been a matter of particular concern is the recent observation that both prevalence and incidence of obesity and metabolic syndrome in young individuals are increasing, raising concern of a potential decline in life expectancy in the future [45,38]. This concern is heightened by the observation that insulin resistance, estimated by the HOMA index, is found in 52.1% of obese adolescents [37].

Metabolic syndrome and kidney malfunction

It has been known for some time that a high body mass index (BMI) during childhood is significantly related to the risk of CV disease at adult age. In the Carnegie (Boyd-Orr) survey in the prewar Britain (1937-1939) 2399 individuals were reexamined recently. The adjusted risk of ischemic heart disease in adult life in individuals whose BMI at age 2-14 years was above the 75th centile was twice higher (p=0.04) than in those whose BMI was between the 25th and 49th centiles [23].

So it comes not as a surprise that BMI at young age is not only a cardiovascular risk factor but also an important determinant of chronic kidney disease (CKD). In a Swedish nationwide case-control study in individuals with a BMI $\geq$ 25 kg/m^2 at age 20 years compared to individuals with BMI < 25 kg/m^2 the risk of advanced CKD (serum creatinine concentration > 3.4 mg/dl for men or >2.8 mg/dl for women) was higher by a factor of 3.1 (2.1-4.8) [16].

The relation between BMI and CKD stage 5 in US adults was established by Hsu et al. [28]: in a large cohort of > 320 000 adult subjects who were followed for 15 to 35 years in the Kaiser Permanente program of Northern California, a higher BMI was a strong independent risk factor for CKD stage 5 even after adjustment for other major risk factors that are associated with CKD stage 5 such as smoking, hypertension and diabetes (table 2). This relationship was independent of hypertension and diabetes and was more pronounced in individuals younger than 40 years (for BMI > 40 kg/m^2 in individuals age < 40 years the relative risk was 11.6 vs only 4.8 in individuals age $\geq$ 40 years). It is likely that at higher age the competing cardiovascular risk artificially reduces the chance to progress to CKD stage 5, thus causing underestimation of the impact of obesity on renal function. Similarly, Iseki et al. found in a population of more than 100 000 subjects in Okinawa who had been followed for 17 years that in men a high BMI was associated with an increased risk for CKD stage 5. The risk was independent of the presence of hypertension or proteinuria. It is also of interest that in Asian individuals the risk of CKD stage 5 starts to rise at a BMI 21-22 kg/m^2 [29] as compared to

Table I
Definition of metabolic syndrome NCEP ATP III.
Definicja zespołu metabolicznego wg kryteriów NCEP III.

	RISK FACTOR / CZYNNIK RYZYKA	DEFINING LEVEL / WARTOŚĆ DEFINIUJĄCA
1.	Abdominal obesity (waist circumference) / Otyłość trzewna (obwód talii)	
	males / mężczyźni	> 102 cm
	females / kobiety	> 88 cm
2.	Triglycerides / Triglicerydy	≥ 150 mg/dl
3.	HDL-C / Cholesterol HDL	
	males / mężczyźni	< 40 mg/dl
	females / kobiety	< 50 mg/dl
4.	Blood pressure / Ciśnienie tętnicze	≥ 130/85 mmHg
5.	Fasting glucose / Glikemia na czczo	≥ 110 mg/dl

The diagnosis of MS require at least 3 of 5 risk factors.
Rozpoznanie zespołu metabolicznego wymaga występowania co najmniej 3 z 5 czynników ryzyka.
Based on: Third Raport of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report Circulation 2002, 106, 3143.
Na podstawie: Third Raport of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report Circulation 2002, 106, 3143.

Table II
Adjusted relative risk for chronic kidney disease stage 5 according to body mass index.
Skorygowane ryzyko względne rozwoju przewlekłej choroby nerek w stadium 5 w zależności od wskaźnika masy ciała.

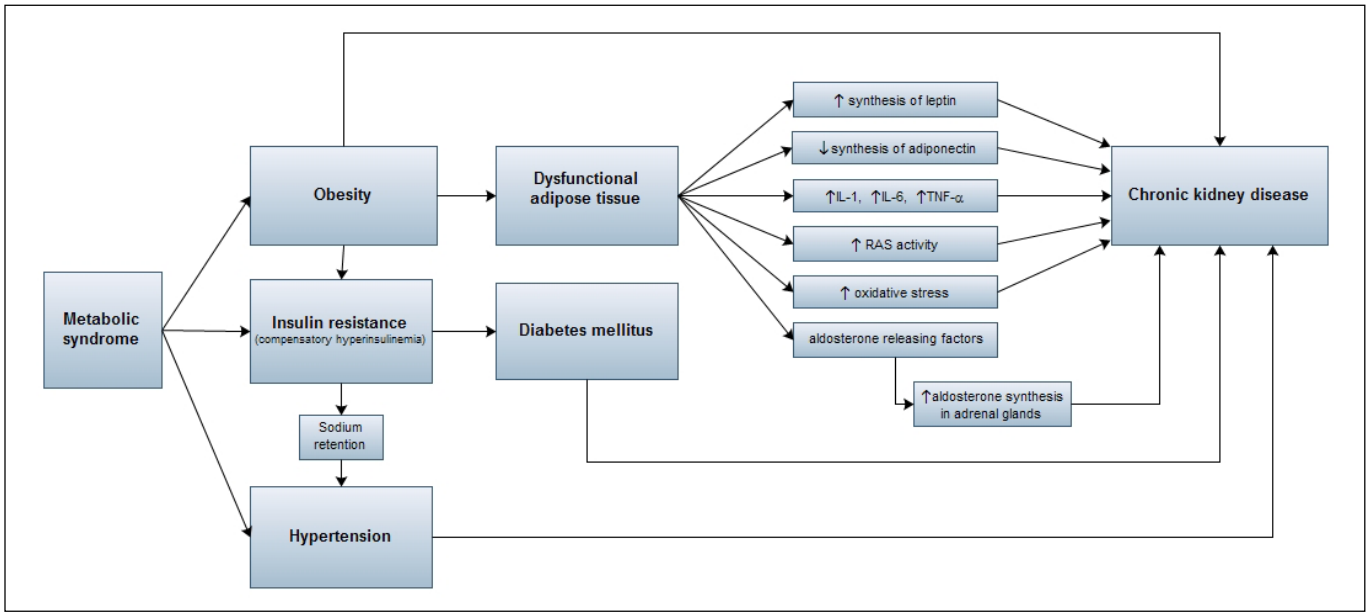
BMI category /Zakres BMI [kg/m^2]	Number of subjects /Liczba badanych	Adjusted RR (95% CI) of CKD stage 5 /Skorygowane RR (95% CI) rozwoju CKD w stadium 5
18.5-24.9	186730	1.00
25.0-29.9	93357	1.87 (1.64-2.14)
30.0-34.9	21856	3.57 (3.05-4.18)
35.0-39.9	5540	6.12 (4.97-7.54)
≥40.0	2417	7.07 (5.37-9.31)

BMI - body mass index, RR - relative risk, CKD - chronic kidney disease, CI- confidence interval
Based on: Hsu CY, McCulloch CE, Iribarren C et al.: Body mass index and risk for end-stage renal disease. Ann Intern Med. 2006, 144, 21.
BMI - wskaźnik masy ciała, RR - ryzyko względne, CKD - przewlekła choroba nerek, CI - przedział ufności
Na podstawie: Hsu CY, McCulloch CE, Iribarren C et al.: Body mass index and risk for end-stage renal disease. Ann Intern Med. 2006, 144, 21.

Table III
Central fat distribution (waist to hip ratio) corrected for BMI is related to:
Otyłość brzuszna (współczynnik talia/biodro) skorygowana względem BMI jest związana z:

greater risk of microalbuminuria / większym ryzykiem mikroalbuminurii	**RR** 1.7 (1.19-2.35)
greater risk of diminished e**GFR** / większym ryzykiem zmniejszania e**GFR**	
lean / osoby z prawidłową masą ciała	**RR** 1.9 (1.19-3.12)
overweight / osoby z nadwagą	**RR** 2.0 (1.19-3.19)
obese / chorzy otyli	**RR** 2.7 (1.46-4.85)

RR - relative risk
Data from: Pinto-Sietsma SJ, Navis G, Janssen WM, et al.: A central body fat distribution is related to renal function impairment, even in lean subjects. Am J Kidney Dis 2003, 41, 733.
RR - ryzyko względne
Na podstawie: Pinto-Sietsma SJ, Navis G, Janssen WM, et al.: A central body fat distribution is related to renal function impairment, even in lean subjects. Am J Kidney Dis 2003, 41, 733.



Rycina 1
Mechanisms linking metabolic syndrome and chronic renal disease. IL-1 - interleukin 1; IL-6 - interleukin-6; TNFα - tumor necrosis factor alpha.
Mechanizmyłączące zespół metabolizny z przewlekłą chorobą nerek. IL-1 - interleukina 1; IL-6 - interleukina 6; TNFα - czynnik martwicy nowotworu.

25 kg/m^2 in Caucasoids [28]. Similarly in a recent retrospective cohort study with 20 years of follow-up in 74986 adults of the general population in Norway (HUNT study I) an increased risk of CKD was observed if the BMI was ≥ 30 kg/m^2 [40].

In the past it was argued that the effect of obesity in CKD is an indirect effect caused by the association of obesity with diabetes and hypertension. The study of Hsu et al. [28] documented such a relation in the absence of diabetes and hypertension suggesting direct effects of obesity via alternative mechanisms. Obesity causes glomerular enlargement and glomerular hyperfiltration, increased mesangial matrix and mesangial cell proliferation, podocyte hypertrophy, focal segmental or global glomerulosclerosis and interstitial fibrosis. These glomerular abnormalities are accompanied by proteinuria and lead to progressive loss of renal function [56]. Adverse conditions *in utero* with faulty fetal programming may cause development of fewer nephrons, thus predisposing to chronic kidney disease and hypertension in adult life; in parallel such individuals have also a propensity to develop obesity, metabolic syndrome and a high cardiovascular risk profile, although undoubtedly lifestyle also plays a major role. Specifically visceral obesity and the associated insulin resistance lead to a spectrum of renal abnormalities: inappropriate activation of the renin-angiotensin system (RAS) and oxidative stress in the kidney, causing an impaired pressure/natiuresis relationship, salt sensitivity of blood pressure, excessive aldosterone action on the mineralocorticoid receptor, activation of the symphatetic nervous system, endothelial cell dysfunction, vasoconstriction and in the kidney glomerular hypertension, mesangial cell proliferation and mesangial matrix production with mesangial expansion.

It has been shown that in obese individuals sodium intake causes a greater increase of glomerular filtration rate (GFR), possibly via extracellular volume expansion or via secretion of cardiotonic steroids [33, 55]. In animal experiments, abnormal tubular feedback with increased sodium reabsorption in the loop of Henle causes preglomerular vasodilatation and raised glomerular presssure. A contributory factor may be glomerular enlargement, resulting in a high filtration surface. Glomerular enlargement has been documented in obese individuals [56, 11] and insulin resistance with decreased adiponectin concentrations is a known feature of obesity [13, 57]. In adolescents with metabolic syndrome Tomaszewski et al. documented hyperfiltration by Cockcroft-Gault creatinine clearance [62]. Increasing numbers of components of the metabolic syndrome were associated with increasing values of creatinine clearance. A causal relationship between obesity and abnormal renal hemodynamics is suggested by the observation that after weight reduction GFR and RPF (renal plasma flow) decreased significantly as did albuminuria [9]. The filtration fraction, a surrogate marker for glomerular hypertension, is strictly related to the BMI; interestingly this is seen not only in obese individuals, but throughout the range of BMI values from 16 to 30 kg/m^2, i.e. even in normal weight individuals [7].

In this context, it is of interest that even in men as young as 18 years unadjusted values of the estimated creatinine clearance are progressively higher in individuals with progressively higher BMI [62]. Interestingly in kidney donors, the postdonation glomerular reserve, i.e. the increase of GFR after dopamine infusion, is progressively lower for individuals with higher BMI and with higher age [53].

Obesity per se can be the cause of progressive renal malfunction in the absence of primary kidney disease. Weisinger [63] described the occurrence of idiopathic focal segmental glomerulosclerosis with nephrotic proteinuria and renal failure in morbidly obese individuals with no primary renal disease; this observation has been widely confirmed [31]. The incidence of this specific form of focal segmental glomerulosclerosis (obesity related glomerulopathy - ORG) has recently increased progressively [63]. In a large biopsy study in the US (including 6818 kidney biopsies from 1986 to 2000) a tenfold increase of the incidence of ORG was found during the past 15 years [31]. Moreover in the general population a relation was found between body weight gain and increase in albuminuria (the PREVEND study evaluating 6894 subjects during a 4.2 years follow-up) [4]. In individuals undergoing uninephrectomy, proteinuria and progressive loss of renal function were noted only if the individuals had a BMI > 25 kg/m^2 [48].

In individuals with known primary renal disease, the loss of renal function is faster in the obese [49] and this has been particularly well documented in patients with IgA-glomerulonephritis [5]. Similar observations were also made in kidney graft recipients [14,39]. A causal role is also suggested by a recent metaanalysis. It included 13 studies and assessed obese patients with CKD and glomerular hyperfiltration to study the relation between intentional weight loss and renal parameters: during 7.4 months of follow-up a decrease of BMI by 3.67 kg/m^2 was associated with a decrease of proteinuria (by 1.31 g/24h) as well as a decrease of systolic blood pressure [43]. Moreover in the population-based study cited above, a decrease of albuminuria was related to a decrease of body weight [4]. The connection between proteinuria and progression of kidney disease seems to be causal, at least in part, as suggested by animal experiments and clinical observations [1].

In individuals with the metabolic syndrome, the risk of coronary heart disease increases not only with the number of meta-

bolic syndrome components; rather at any given number of metabolic syndrome components, the risk of CV disease is further increased when urinary albumin excretion is high [32]. Epidemiological observational studies show that the prevalence of microalbuminuria and the prevalence of CKD (eGFR 60 ml/min/kg/m^2) increase with the number of components of the metabolic syndrome [32]. Similarly, in a 9 year study on non-diabetic individuals the incidence of CKD was significantly higher in patients with the metabolic syndrome: the relative risk was 1.43 (1.18-1.73) in individuals with compared to individuals without metabolic syndrome [35]. Of particular concern is the observation that in a Finnish study on type 1 diabetics (FinnDiane study) the metabolic syndrome was found in about 40% of participants overall. The prevalence of the MS increased progressively for increasing stages of diabetic nephropathy, i.e. patients with normoalbuminuria (28%), microalbuminuriua (44%), macroalbuminuria (62%) and chronic kidney disease stage 5 (68%) [61]. Against this background, the observation of Fox et al. is of interest: the risk to develop CKD (eGFR < 60ml/min/1,73m^2) increases progressively for individuals with normal glucose tolerance (4%), individuals with impaired fasting glucose/impaired glucose tolerance (6% and 8% respectively), newly diagnosed diabetes (15%) and known diabetes (20%) [17].

The role of visceral fat

Results of studies in two last decades clearly showed that adipose tissue, especially visceral adipose tissue, is an active endocrine organ. Adipose tissue is a major source of several factors (hormones, cytokines, chemokines, growth factors and complement factors) commonly referred to as adipokines, that affect many physiological and pathophysiological processes. The list of these factors is long and includes among others: inflammatory cytokines (tumour necrosis factor α, interleukins-1ß, 6, 8) and hormones (leptin, adiponectin). In individuals with visceral obesity the secretion of the above mentioned inflammatory cytokines and leptin is elevated. In contrast the synthesis of adiponectin is decreased [10]. As recently reviewed all of these adipokines may be involved in the onset and the progression of CKD [10] (Figure 1).

Visceral obesity, identified by an elevated waist circumference, is a powerful predictor of the 6-year incidence of microalbuminuria as documented by the DESIR study [6]. In agreement with this finding, Pinto-Sietsma et al. found that with increasing waist to hip ratio (WHR) the relative risk of a diminished eGFR increased 2.7 fold for a WHR 0.45-0.81 compared to a WHR 0.96-1.39 [47]. Of particular concern is the observation that not only overweight and obese subjects, but even lean subjects (BMI < 25 kg/m^2) had a higher relative risk of diminished eGFR if they had an increased WHR (RR 1.9; 1.19-3.12) (Table 3) [47]. Therefore, a central pattern of fat distribution, not overweight or obesity per se, seems to be important for the development of renal impairment.

This has led to the recent concept of "normal weight obesity". In the International Health and Nutrition Examination Survey, Reinberg et al. (in press) demonstrated in the subgroup of 2127 individuals with BMI 18.5-24.5 kg/m^2 that an elevated waist circumference was associated with a significantly higher prevalence of cardiovascular risk factors.

Metabolic syndrome and hypertension

Besides the above mentioned abnormalities of adipokines (elevated plasma leptin concentration and reduced plasma adiponectin concentration) the hallmark of the metabolic syndrome is insulin resistance with compensatory hyperinsulinemia. The latter is associated with the following:

- sodium retention,
- inappropriate activation of the renin-angiotensin-aldosterone system,
- oxidative stress.

The model of the obese dog on high fat diet [25] showed that obesity causes a shift of the pressure/natriuresis relationship to the right: i.e. higher mean arterial pressure values are required to enable the kidney to eliminate dietary sodium in the urine. This is true also in man. In the study of Suzuki et al. salt sensitivity was tightly correlated to insulin sensitivity [59].

In general hypertensive individuals are more insulin resistant and have higher insulin levels [58, 52]. It is particularly the visceral, not the subcutaneous, fat area which is correlated to insulin sensitivity [3]. A causal role of visceral fat is also suggested by the observation that after bariatric surgery insulin resistance decreases in parallel with the reduction of the visceral fat area [8]. The blood pressure response to dietary salt was more pronounced in patients with the metabolic syndrome (and associated insulin resistance): reducing salt intake from 8.2 g/day to 2.3 g/day lowered systolic blood pressure by 8.7 ± 1.3 mmHg in subjects with 4-5 components of the metabolic syndrome, by 6.0 ± 1.1 mmHg in those with 3 components and failed to modify the blood pressure of subjects with 1 or no component of the metabolic syndrome [27].

There is an insulin resistance paradox. How should sodium reabsorption in the kidney and sympathetic activation in the central nervous system be caused by insulin if these patients are insulin resistant? The answer to this paradox is that insulin sensitivity is diminished only in muscle, adipose tissue, liver and some other tissues, whilst the response to insulin is normal in the kidney [51] and the nervous system. The antinatriuretic effect of insulin, which is independent of GFR, renal hemodynamics, renal innervation or glycemia, had been documented by Nizet et al. [44] in the isolated dog kidney; in human it was confirmed by DeFronzo et al. [12]. Investigators also showed that it is insulinemia, not hyperglycemia, which is responsible for renal sodium retention [42].

There is a paradox here. In normal subjects after each meal there is transient hyperinsulinemia – but despite this blood pressure does not change. In contrast in insulin resistant subjects, hyperinsulinemia causes increased sodium reabsorption, salt sensitive blood pressure and hypertension. It has been argued that in insulin resistant subjects the antinatiuretic effect of insulin is present in the kidney, whilst in the vascular periphery eNOS activity is diminished. As a result, less vasodilatory nitric oxide (NO) is produced and NO-mediated vasodilatation is reduced or abrogated which is necessary to counteract the sodium dependent blood pressure increase. This explanation is presumably not exhaustive and inappropriate activation of the RAS and aldosterone excess may be additional causes.

The links between metabolic syndrome, albuminuria and kidney dysfunction

An important recently identified pathomechanism in obesity is the non-classical stimulation of the mineralocorticoid receptor by elevated concentrations of aldosterone or even aldosterone concentrations within the normal range of aldosterone. The latter is caused by the sensitization of the mineralocorticoid receptor by inflammatory factors and changes in redox potential. In addition to the activation of the renin-angiotensin system in the kidney as well as in visceral adipocytes [20] aldosterone secretion is also increased independent of classical stimuli as first described by Erhart-Bornstein et al. [15] and confirmed by others [19]. This stimulation of the adrenal cortex occurs independent of ACTH, potassium and angiotensin II and is presumably mediated by an oxidized and polyunsaturated fatty acid (12,13epoxy-9keto-ctrans, octadecenoic acid; EKODE) [34] and/or by other aldosterone-releasing factors produced by visceral adipocytes [18]. The relevance of this to the metabolic syndrome has been suggested by recent animal experiments [41]. In the cultured adrenocortical cells aldosterone synthase gene expression and aldosterone synthesis was increased when the adrenal cells were incubated with medium derived from visceral fat cells of SHR/cp rats (a model of the metabolic syndrome), but not of SHR rats. The obese SHR/cp rat, as well as, SHR/N-cp rat (another model of metabolic syndrome) were proteinuric; furthermore the kidneys showed tubulointerstitial changes, glomerular enlargement, lower podocyte number and desmin staining of podocytes was reduced. This was accompanied by proteinuria. Proteinuria was reduced by the administration of tempol, a superoxide dismutase mimetic, suggesting a pathogenetic role of oxidative stress [41, 21]. Moreover in this experiment podocyte injury was reversible and abrogated by the aldosterone antagonist eplerenon.

Numerous observations suggest a role of elevated leptin in the genesis of renal disease of obesity, e.g. via sympathetic nerveous activation and hypertension, via generation of oxidative stress, via induction of TGF-ß and upregulation of TGF-ß receptors as well as by induction of proinflammatory responses [24].

The most exciting finding has been recently that low adiponectin in animal models caused albuminuria, the molecular mechanism of which has been characterized in very

great detail [57].

The impact of sleep-apnea

One of the most interesting new findings linking metabolic syndrome, obesity and renal function is the documentation that glomerular enlargement is more prevalent in morbidly obese patients with (51%) than without sleep apnea (28%) [56]. Sleep apnea activates the sympathetic nervous system, promotes systemic hypertension and activates the renin-angiotensin axis, thus causing glomerular hypertension [46].

Because of size limitations this review cannot be complete. The reader will find further information on glomerular hypertension, endothelial cell dysfunction, vasoconstriction and matrix proliferation as well as fibrous tissue expansion in the glomerulus and tubular interstitium in a recent review by Lastra [36].

Conclusions

It is clear from the above that obesity, specifically visceral obesity, has become a major cause of renal malfunction. In morbidly obese patients an obesity related primary kidney disease, i.e. focal segmental glomerulosclerosis, may be found. In obese patients with primary kidney disease the course of kidney disease is aggravated by more severe proteinuria and accelerated loss of renal function. The mechanism(s) through which visceral obesity causes hypertension (as a potent factor of renal damage) include insulin mediated increase of renal sodium reabsorption despite extrarenal insulin resistance. Apart from the known activation of the renin-angiotensin system (both in the kidney and in extrarenal tissue, specifically visceral fat cells) and the activation of the sympathetic nerve system, one novel factor susceptible to intervention is non-classical activation of the adrenal aldosterone synthesis.

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