Umbilical hernia should alert physicians about terminal endpoints of the metabolic syndrome in adults

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ABSTRACT

Background: There may be some significant associations between the umbilical hernia and terminal endpoints of the metabolic syndrome in adults.

Method: Consecutive patients with an umbilical hernia and/or a surgical repair history of the umbilical hernia were included into the study.

Results: There are 46 patients with the umbilical hernia with a mean age of 62.0 years, and 73.9% of them were female. Body mass index of the hernia group was higher, significantly (33.6 versus 29.1 kg/m2, p= 0.000). Although the prevalence of hypertension (HT) was higher in the hernia group (50.0% versus 27.3%, p<0.01), mean triglycerides and low density lipoproteins were lower in them (p<0.05 for all). Although the prevalence of diabetes mellitus (DM) and coronary heart disease (CHD) were also higher in the hernia patients, the differences were nonsignificant, probably due to the small sample size of the hernia group.

Conclusion: There may be some significant associations between the umbilical hernia and terminal endpoints of the metabolic syndrome, probably on the bases of prolonged inflammatory, atherosclerotic, and pressure effects of excessive fat tissue on abdominal wall muscles. The inverse relationships between obesity and hypertriglyceridemia and hyperbetalipoproteinemia may be explained by the hepatic fat accumulation, inflammation, and fibrosis induced relatively lost hepatic functions in obese individuals. So the umbilical hernia should alert the physicians about terminal endpoints of the metabolic syndrome including obesity, HT, DM, CHD, cirrhosis, peripheric artery disease, chronic obstructive pulmonary disease, chronic renal disease, mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, and cancers in adults.

Key words: Umbilical hernia, metabolic syndrome, obesity, atherosclerosis, end-organ insufficiency

Introduction

Chronic endothelial damage may be the major underlying cause of aging and death by causing end-organ insufficiencies in human beings (1, 2). Much higher blood pressure (BP) of the afferent vasculature may be the major underlying cause by inducing recurrent injuries on vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the process. Therefore the term of venosclerosis is not as famous as atherosclerosis in the literature. Due to the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic natures, those eventually reduce blood supply to the terminal organs, and increase systolic and decrease diastolic BP further. Some of the well-known accelerating factors of the inflammatory process are physical inactivity, sedentary lifestyle, excess weight, animal-rich diet, smoking, alcohol, chronic inflammations, and prolonged infections for the development of terminal consequences including obesity, hypertension (HT), type 2 diabetes mellitus (DM), cirrhosis, peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, dementia, end-organ insufficiencies, cancers, early aging, and premature death (3, 4). Although early withdrawal of the accelerating factors can delay terminal consequences, after development of HT, DM, cirrhosis, COPD, CRD, CHD, PAD, mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, cancers, and aging, endothelial changes can not be reversed completely due to their fibrotic natures (5, 6). The accelerating factors and terminal endpoints are researched under the titles of metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome in the literature, extensively (7, 8). On the other hand, there may be some significant associations between the umbilical hernia and terminal endpoints of the metabolic syndrome in adults.

Material and methods

The study was performed in the Medical Faculty of the Mustafa Kemal University between March 2007 and January 2010. Consecutive patients with an umbilical hernia and/or a surgical repair history of the umbilical hernia were collected in the first, and age and sex-matched controls were collected into the second groups. Their medical histories including smoking habit, and already used medications were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglycerides, low density lipoproteins (LDL), and an electrocardiography was performed. Current daily smokers at least for the last six months and cases with a history of five pack-years were accepted as smokers. Insulin using diabetics and patients with devastating illnesses including malignancies, chronic renal failure, decompensated cirrhosis, uncontrolled hyper- or hypothyroidism, and congestive heart failure were excluded to avoid their possible effects on weight. Body mass index (BMI) of each case was calculated by the measurements of the Same Clinician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (9). Office blood pressure (OBP) was checked after a five-minute of rest in seated position with the mercury sphygmomanometer on three visits, and no smoking was permitted during the previous two-hour. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked hypertension after a 10-minute education about proper BP measurement techniques (10). A 24-hour ambulatory blood pressure monitoring was not required due to its equal effectiveness with HBP measurements (11). Eventually, HT is defined as a BP of 135/85 mmHg or greater on HBP measurements (10). White coat hypertension (WCH) is defined as an OBP of 140/90 mmHg or greater but mean HBP of lower than 135/85 mmHg, and masked HT as an OBP of lower than 140/90 mmHg but mean HBP of 135/85 mmHg or greater (10). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already taking antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 100 and 125 mg/dL, and diagnosis of cases with a two-hour plasma glucose level of 200 mg/dL or higher is DM (9). A stress electrocardiography was performed in suspected cases, and a coronary angiography was obtained only for the stress electrocardiography positive cases. Eventually, mean weight, height, BMI, triglycerides, and LDL values and prevalences of smoking, WCH, HT, DM, and CHD were detected in each group, and results were compared in between. Mann-Whitney U Test, Independent-Samples T Test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 46 patients in the umbilical hernia and 84 cases in the control groups. Mean age of the umbilical hernia patients was 62.0 years, and 73.9% of them were female. Prevalence of smoking was lower in the umbilical hernia group, nonsignificantly (13.0% versus 19.0%, $p>0.05$). Although the mean heights of the two groups were similar (157.4 versus 158.7 cm, $p>0.05$), the umbilical hernia patients were heavier than the control cases, significantly (85.1 versus 73.1 kg, $p= 0.001$). As a result, the BMI was also higher in the umbilical hernia patients, significantly (33.6 versus 29.1 kg/m2, $p= 0.000$). Interestingly, although the significantly higher mean weight and BMI of the patients with the umbilical hernia, the mean triglycerides and LDL values and prevalence of WCH were significantly lower in them ($p<0.05$ for all). On the other hand, prevalence of HT was significantly higher in the umbilical hernia group (50.0% versus 27.3%, $p<0.01$). Although the prevalences of DM and CHD were also higher in the umbilical hernia group, the differences were nonsignificant, probably due to the small size of the umbilical hernia group (Table 1).

Table 1: Characteristic features of the study cases

Variables	Cases with umbilical hernia	*p*-value	Control cases
Number	46		84
Female ratio	73.9%	Ns*	73.8%
Mean age (year)	62.0 ± 13.2 (29-82)	Ns	62.2 ± 13.0 (29-83)
Prevalence of smoking	13.0%	Ns	19.0%
Mean weight (kg)	85.1 ± 20.8 (54-172)	0.001	73.1 ± 13.1 (44-104)
Mean height (cm)	157.4 ± 11.2 (134-191)	Ns	158.7 ± 10.0 (138-181)
Mean BMI† (kg/m2)	33.6 ± 5.7 (21.0-47.1)	0.000	29.1 ± 5.4 (17.2-42.9)
Mean triglycerides (mg/dL)	119.6 ± 69.2 (49-361)	0.041	145.9 ± 76.9 (56-394)
Mean LDL‡(mg/dL)	120.2 ± 35.5 (49-193)	0.042	138.0 ± 42.1 (10-239)
Prevalence of WCH§	23.9%	<0.05	41.6%
Prevalence of HT‖	50.0%	<0.01	27.3%
Prevalence of DM¶	30.4%	Ns	28.5%
Prevalence of CHD**	17.3%	Ns	13.0%

*Nonsignificant (p>0.05) †Body mass index ‡Low density lipoproteins §White coat hypertension ‖Hypertension ¶Diabetes mellitus **Coronary heart disease

Discussion

Umbilical hernias are common anomalies of the abdominal wall in both genders. The majority of physicians agree that most of the umbilical hernias in adults have an acquired origin, and only 10% of adults with umbilical hernias have congenital causes (12). The umbilical hernias are more common in females both in children and adults (13, 14). They are more common under the age of four and over the age of 50 years (13). They are particularly common in premature babies (up to 84%), overweight children, and middle-aged multiparous women. According to the literature, their prevalence is around 2% in adults. As also observed in the present study, the umbilical hernias are commonly associated with terminal endpoints of the metabolic syndrome including obesity, HT, DM, cirrhosis, CHD, PAD, COPD, CRD, mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, and cancers (15). There are not great differences between the various ethnic groups, supporting the possible acquired etiologies such as the metabolic syndrome in adults (13). Umbilical hernias occur when a part of the intestine protrudes through a weak spot in the abdominal wall muscles at the site of umbilicus. Babies are prone to this malformation due to the process of fetal development during which abdominal organs develop outside the abdominal cavity, and then, they return into the abdominal cavity through an opening which will become the umbilicus. Importantly, the umbilical hernias must be distinguished from paraumbilical hernias, defects in one side of the midline at the umbilical region in adults, and from omphaloceles in newborns. Most umbilical hernias close on their own by the age of one year, although up to 10% may take longer to heal in infants. To prevent complications, the umbilical hernias, those that do not disappear by the age of four years or those that appear during adulthood may need surgical operations for repair. The umbilical hernias may become incarcerated or strangulated, but the risk is low, since the underlying defect of the abdominal wall is larger than found in the inguinal ones. The risk of incarceration is half of the inguinal hernias, but three times higher than the femoral ones in an American series (16). Incarceration is predominantly seen in females, and up to 90% of incarcerated hernias of umbilicus occur in women with a mortality rate up to 25% (16). There is also a greater risk of incarceration in the cirrhotic patients receiving medical treatment for ascites, carrying an implant of a peritoneo-venous shunt, or getting an evacuating paracentesis (17). The higher prevalence of umbilical hernias in patients with cirrhosis may also support the pressure effect of intra-abdominal fluid on abdominal wall muscles (18). Obesity, pregnancy, ascites, and peritoneal dialysis induced abdominal wall distensions may cause pulling of the abdominal wall muscles and deterioration of connective tissue over the umbilicus. The frequent association of the umbilical hernias with other abdominal wall defects may also support the possible etiologic role of the biophysical changes (13). In the previous study of 291 cases with umbilical hernias, 42% of them were associated with another hernia, and 5% of them were associated with more than two hernias (13). Abnormal dispositions of the umbilical fascia may be one of the factors contributing to herniations (19). Tendinous fibers coming from the muscles of both sides of the abdominal wall decussate obliquely at the linea alba, acquiring different levels of complexity (20). Simpler

decussations may be found in cases with umbilical hernias in which the sac protrudes at the midline. Obesity, pregnancy, ascites, and peritoneal dialysis induced excess pressure on abdominal wall muscles may facilitate rupture of the fibers which decussate in a simple fashion at the linea alba on the umbilicus. In contrast, patients with more complex (triple) decussations may present with paraumbilical hernias in the above conditions. On the other hand, recanalized umbilical veins and deterioration of connective tissue secondary to the accelerated atherosclerotic process of the metabolic syndrome may also facilitate the herniations in cirrhosis.

Obesity may be the major endpoint of the metabolic syndrome, since after development of obesity, nonpharmaceutical approaches provide limited benefit either to heal obesity or to prevent its complications. Overweight and obesity probably lead to a chronic and low-grade inflammation on vascular endothelium, and risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess weight in all age groups (21). The low-grade chronic inflammation may also cause genetic changes on the epithelial cells, and the systemic atherosclerotic process may decrease clearance of malignant cells by the immune system, effectively (22). Overweight and obesity are associated with many coagulation and fibrinolytic abnormalities suggesting that they cause a prothrombotic and proinflammatory state (23). The chronic inflammatory process is characterized by lipid-induced injury, invasion of macrophages, proliferation of smooth muscle cells, endothelial dysfunction, and increased atherogenicity (24, 25). For example, elevated C-reactive protein (CRP) levels in serum carry predictive power for the development of major cardiovascular events (26, 27). Overweight and obesity are considered as strong factors for controlling of CRP concentration in serum, since adipose tissue produces biologically active leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines (28, 29). On the other hand, individuals with excess weight will have an increased circulating blood volume as well as an increased cardiac output, thought to be the result of increased oxygen demand of the excessive fat tissue. The prolonged increase in circulating blood volume may lead to myocardial hypertrophy and decreased compliance, in addition to the common comorbidity of atherosclerosis and HT. In addition to systemic atherosclerosis and HT, FPG and serum cholesterol increased and high density lipoproteins decreased with increased BMI (30). Similarly, the prevalences of CHD and stroke, particularly ischemic stroke, increased with elevated BMI values in another study (31). Eventually, the risk of death from all causes including cardiovascular diseases and cancers increased throughout the range of moderate and severe excess weight for both genders in all age groups (21). The female predominance of the umbilical hernias in adults may also be explained by pregnancies and the higher prevalence of obesity in females. But hormonal status of females and some other factors should take additional roles in the process to be able to explain the high prevalence of umbilical hernias even in the period of infancy in females. Similarly, varicous dilatations in the lower extremities are much more common in females, and most of them develop during labour, probably due to vasodilatory effects of estrogen. This vasodilatation may also disturb the abdominal wall muscles in women in the process of umbilical hernias.

There are several consequences of the metabolic syndrome on the liver. Nonalcoholic fatty liver disease (NAFLD) is a term used to define a spectrum of disorders characterized by macrovesicular steatosis which occurs in the absence of consumption of alcohol in amount considered to be harmful to the liver. Since the chance of NAFLD is directly proportional to BMI, and there is a high prevalence of excess weight in society, NAFLD is also becoming an important health problem all over the world. According to the literature, sustained liver injury will lead to progressive fibrosis and cirrhosis in up to 25% of affected patients (32). Excessive fat accumulation in hepatocytes is called as hepatosteatosis. It progresses to NAFLD, steatohepatitis, fibrosis, cirrhosis, hepatocellular carcinoma, and eventually hepatic failure. There are two histologic patterns of NAFLD including fatty liver alone and nonalcoholic steatohepatitis (NASH). NASH represents a shift from simple steatosis to an inflammatory component. Excess weight may be the main factor in exacerbating hepatic inflammation and fibrogenesis in NASH. NAFLD affects up to one third of the world population, and it is the most common cause of chronic liver disease even in children and adolescents at the moment (33, 34). The recent rise in the prevalence of excess weight likely explains the NAFLD epidemic, worldwide (35). NAFLD is combined with a low-grade chronic inflammatory state, which results with hypercoagulability, endothelial dysfunction, and an accelerated atherosclerosis (35). NAFLD shares many features of the metabolic syndrome as a highly atherogenic condition, and it may cause hepatic inflammation and cellular injury, particularly at the endothelial level. Beside terminating with cirrhosis, NAFLD is associated with a significantly greater overall mortality as well as with an increased prevalence of cardiovascular diseases (34). Authors reported independent associations between NAFLD and impaired flow-mediated vasodilation and increased intima-media thickness of the carotid artery as the reliable markers of subclinical atherosclerosis (34), so NAFLD may also be a predictor of cardiovascular disease (36). NAFLD may actually be considered as the hepatic component of metabolic syndrome since hepatic fat accumulation is highly correlated with the components of the metabolic syndrome (37). Similar to the present study, although the prevalence of dyslipidemia was significantly lower in the normal weight than the overweight groups (25.0% versus 45.2%, $p<0.001$), there was a nonsignificant difference between the overweight and obesity groups (45.2% versus 37.5%, $p>0.05$) (38). These findings may be explained by the hepatic fat accumulation, inflammation, and fibrosis induced relatively lost hepatic functions in obese individuals.

WCH may be a progression step between the sustained normotension (NT) and overt HT in the metabolic syndrome. When the authors compared the sustained NT, WCH, and overt HT groups, prevalence of nearly all of the pathologies including obesity, impaired glucose tolerance, DM, and CHD showed significant progressions from the sustained NT towards the WCH and overt HT groups (39). Nearly all of the pathologies were significantly higher in the WCH than the sustained NT groups (39). The similar progressions were observed nearly in all of the pathologic conditions between the WCH and overt HT groups, too, but interestingly the prevalence of dyslipidemia was the highest in the WCH group, and it was 41.6% versus 19.6% of the sustained NT ($p<0.001$) and 35.5% of the overt HT groups

($p<0.05$) (39). Against a previous study indicating serum triglycerides and cholesterol levels did not differ significantly between the NT, WCH, and sustained HT cases in men (40), the similar results indicating higher prevalence of dyslipidemia in the WCH cases were also observed in another study (41). So the higher prevalence of dyslipidemia in the WCH group may explain the adverse effects of WCH on health, since the dyslipidemia comes with obesity, HT, DM, CHD, stroke like problems in the future. Again the lower prevalence of dyslipidemia in the HT group may be explained by the hepatic fat accumulation, inflammation, and fibrosis induced relatively lost hepatic functions in obese individuals, since the prevalence of obesity was significantly higher in the overt HT than the WCH groups ($p<0.01$) (39). So WCH and hyperlipoproteinemias may show accelerating trend of getting weight. By this way, the detected higher prevalences of WCH even in the second (33.3%) and in the third decades (46.6%), despite the lower prevalences of obesity in these age groups, may show the trend of getting weight (11), and the WCH and hyperlipoproteinemias may be the alarming signs of obesity and several consequences of it in the future.

As a conclusion, there may be some significant associations between the umbilical hernia and terminal endpoints of the metabolic syndrome, probably on the bases of prolonged inflammatory, atherosclerotic, and pressure effects of excessive fat tissue on abdominal wall muscles. The inverse relationships between obesity and hypertriglyceridemia and hyperbetalipoproteinemia may be explained by the hepatic fat accumulation, inflammation, and fibrosis induced relatively lost hepatic functions in obese individuals. So the umbilical hernia should alert the physicians about terminal endpoints of the metabolic syndrome including obesity, HT, DM, CHD, cirrhosis, PAD, COPD, CRD, mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, and cancers in adults.

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