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From the Editor

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In this issue two papers deal with the metabolic syndrome. Helvaci et al looked at Medical treatment of metabolic syndrome. A series of consecutive patients at and above the age of 20 years were studied. The study included 1068 cases (628 females). Interestingly, 69.4% of cases had excess weight. Prevalence of excess weight increased from 28.7% of the third to 87.0% of the seventh decades. Parallel to the excess weight, prevalence of hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, impaired glucose tolerance, and white coat hypertension (WCH) increased until the seventh decade and decreased afterwards, significantly ($p<0.05$ nearly in all steps). Whereas prevalence of hypertension (HT), diabetes mellitus (DM), and coronary heart disease (CHD) always increased by decades ($p<0.05$ nearly in all steps) indicating their irreversible properties. The author concluded that the prevalence of excess weight increases after the age of 30 years, significantly. Parallel to its severity, it is associated with greater prevalence of HT, DM, and CHD. Acarbose should be initiated for patients with obesity after the age of 30 years due to nearly irreversible nature of obesity. Acarbose should be preferred against metformin due to the high prevalence of excessive anorexia induced metformin intolerance in the society.

In the second paper the authors looked at the association of Metabolic syndrome and umbilical hernia They did consecutive patients with an umbilical hernia and/or a surgical operation history for umbilical hernia were studied. There were 46 patients with umbilical hernia with a mean age of 62.0 years, and 73.9% of them were females. The hernia patients were heavier than the controls (85.1 versus 73.1 kg, $p= 0.001$). Although the prevalence of diabetes mellitus and coronary artery disease were also higher in the hernia group, the differences were nonsignificant probably due to the small size of the study group. The authors concluded that there are significant relationships between umbilical hernia and terminal consequences of metabolic syndrome including obesity and HT, probably on the bases of prolonged inflammatory and atherosclerotic effects beside pressure effect of excessive fat tissue on abdominal 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. Similarly, the inverse relationship between obesity and WCH may be explained by progression of WCH into HT in obese individuals.

Raja A et al attempt to compare sample adequacy obtained using two of the least invasive techniques; blind-TBNA and EBUS -TBNA that are routinely used for obtaining tissue samples for diagnosing mediastinal and hilar masses at King Hussain Medical Center (KHMC). A total of 73 patients underwent diagnostic interventional bronchoscopy for mediastinal and hilar mass in the period between January 2015 and March 2017. The results showed that EBUS-TBNA technique shows to have a higher diagnostic yield (79%) compared blind- TBNA technique (65%) although statically P value =0.2 show no significant difference between the two techniques. Still EBUS-TBNA has an advantage over the blind-TBNA especially for small and deep station lymph node or masses because It's real-time visualization during sampling, and helps to avoid any vascular injuries, also decreases the need for another attempt of sampling. The authors recommend using the both interventional bronchoscopy technique as standard procedure rather than the VAM or VAT, where it will help to minimize the number of open surgeries, complications and longtime hospital staying.

Interventional bronchoscopy in King Hussain medical center (KHMC) Jordan; methods evaluation and comparison

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ABSTRACT

Objectives: In this study our aim is to compare sample adequacy obtained using two of the least invasive techniques; blind-TBNA and EBUS-TBNA that are routinely used for obtaining tissue samples for diagnosing mediastinal and hilar masses at King Hussain Medical Center (KHMC).

Method: 73 patients underwent diagnostic interventional bronchoscopy for mediastinal and hilar mass in the period between January 2015 and March 2017; the p value was calculated using the two-sample proportion test to identify difference in the Population Proportions.

Results and Conclusion: EBUS-TBNA technique is shown to have a higher diagnostic yield (79%) compared to blind-TBNA technique (65%) although statically P value shows no significant difference between the two techniques. Still EBUS-TBNA has an advantage over the blind-TBNA especially for small and deep station lymph node or masses because its real-time visualization during sampling, helps to avoid any vascular injuries, and also decreases the need for another attempt of sampling.

Despite our short experience in this field, we have excellent results; both methods of interventional bronchoscopy techniques that are carried at KHMC are efficient and effective. Accordingly, we recommend using both interventional bronchoscopy techniques as standard procedure, where it will help to minimize the number of open surgeries, complications and longtime hospital staying.

Key words: EBUS-TBNA, hilar lymph node, Interventional bronchoscopy, mediastinal lymph node, ROSE test, TBNA

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Introduction

Interventional bronchoscopy has an excellent value as a diagnostic procedure in the pulmonary field. Many methods can be used to obtain diagnostic samples from mediastinal and hilar masses including conventional bronchoscopy transbronchial needle aspiration (blind-TBNA) technique, endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) and the more invasive video assisted mediastinoscopy (VAM) or video assisted thoracotomy (VAT). The major factors in choosing either of these techniques depends on mass accessibility and location.

In this study our aim is to compare sample adequacy obtained using two of the least invasive techniques; blind-TBNA and EBUS-TBNA that are routinely used for obtaining tissue samples for diagnosing mediastinal and hilar masses at King Hussain Medical Center (KHMC).

Materials and Method

All patients who underwent diagnostic bronchoscopy using blind-TBNA or EBUS-TBNA for hilar or/and mediastinal mass in the period between January 2015 and March 2017 were selected. The total number of patients identified was 73.

The p value was calculated using the two-sample proportion test to identify difference in the Population Proportions.

The first Population underwent conventional bronchoscope with blind TBNA for immense size lymph node from stations 2,4,7. The insertion site of TBNA needle was determined using anatomical landmarks and CT scan images. The needle used in sampling was eXcelon needle, sizes 19G or 20G [1].

The second Population technique was by using FUJIFILM convex probe (CP) EBUS, 7.5 MHz, diameter size6.9 mm. It was used for direct and real-time visualization of lymph node at stations 2,4,7,10. The obtained images were linked to an ultrasound scanner (FUJIFILM) with Doppler-flow imaging to localize any vascularity lesions, and hence avoid any vascular injuries during needle insertion. Sample collection was performed using a 22 gauge Echotip Ultra needle.

In both techniques, the jabbing technique was performed for sampling lymph nodes in average of 4 samples/lymph node, and for each sample 4-5 passes were done [2].

To check the presence of lymphocytes or malignant cells, we used the Rapid On-Site Evaluation test (ROSE) (DEF QUICK) [3], [4], but the final diagnosis was based on cytopathology report.

All our patients had moderate sedation using midazolam and fentanyl. This method is preferred for its advantage over deep sedation; it is cheaper, does not need anesthesia service or artificial airways and it is a very effective mode of anesthesia [5]. Both techniques were uneventful with no early or late complications.

Discussion and Results

Discussion: The differential diagnosis of lymphadenopathy is very wide and varies from benign to malignant causes, but every case needs tissue biopsy for definitive diagnosis. Obtaining such biopsy from these sites by classical methods; video assistedmediastinoscopy (VAM) or video assisted thoracotomy (VAT), is invasive, needs patient hospitalization and carries some risk of serious complications and is more expensive. On the other hand, new interventional bronchoscopy methods; EBUS-TBNA and blind-TBNA proved to be more effective and safer techniques mainly because they are less invasive. In addition, they have improved diagnostic yield in the investigation of pulmonary masses, nodules and lymphadenopathy (EBUS diagnostic yield 94%) [6].

According to The American College of Chest Physicians (ACCP) recommendations for attaining EBUS competence, a lab should fulfill the 50 supervised procedures, followed by 20 procedures per year to maintain competence. and we did; the procedure was performed by a well-trained team with enough experience based on the ACCP guidelines.

The big easy accessible lymph node was selected for blind-TBNA. For EBUS-TBNA, a smaller size, deep stations and adjacent to vascular structures lymph nodes were selected.

For the 73 patients, there were 54 male patients and 19 female patients, giving a male to female ratio of 2.8:1. The average age for all was 60 years.

According to the CT scan reports, lymph node size, nodal station, and relation to vascularity, 20 (27%) cases were selected for TBNA technique, and 53 (73%) cases were selected for EBUS technique. (Table 1).

The ROSE test was performed on the spot to adequacy of the samples (presence of lymphocytes or malignant cells). However, the final cytopathology report was used for assessing adequacy and final diagnosis.

Of the 73 samples, 18 samples (24.6% of all samples) were inadequate, despite that ROSE test had confirmed the presence of lymphocyte or malignant cells but there was not enough tissue material available for a definitive diagnosis and proper staining by pathologist, so they were excluded from the study. From the remaining 55 samples, 13 samples were obtained by TBNA technique and 42 samples were obtained by EBUS technique (see Table 2). EBUS-TBNA technique had a diagnostic accuracy of 79% of all EBUS samples, while the blind-TBNA technique had a diagnostic accuracy of 65% of all Blind-TBNA samples. The better accuracy is mostly attributed to real time visualization during sampling, though most of them were deep nodal station and small size (Table 3).

The final cytopathological diagnoses showed 29 (53%) cases with malignant diseases and 26 (47%) cases with benign diseases (Table 4).

Table 1: Number of EBUS and TBNA cases (%)

Gender	BLIND-TBNA (%)	EBUS (%)
M	*17 (31%).4*	*37 (82.2%)*
F	*3 (15.7%)*	*16 (84.2%)*
TOTAL	*20(27%)*	*53(73%)*

Table 2: Number of adequate/ inadequate samples

	Adequate	*Inadequate*	*Total*
EBUS	42	11	53
TBNA	13	7	20
total number	55	18	73

Table 3: Adequacy of EBU vs TBNA

	Adequate
EBUS	42/53
TBNA	13/20
% Adequacy of EBUS samples	79%
% Adequacy of blind-TBNA samples	65%

Table 4: Malignant vs Benign

Number of adequate	55
MALIGNANT (%)	29(53%)
Benign (%)	26(47%)

Table 5: Final diagnosis and percentage

MALIGNANT (29 cases)			Benign (26 cases)		
NSCLC	17	58.6%	SARCOIDOSIS	10	38%
SCLC	3	10.3%	REACTIVE	3	12%
LYMPHOMA	4	13.8%	NORMAL	13	50%
METS	1	3.4%			
AMYLOIDOSIS	1	3.4%			
Poor differentiation	3	10.3%			

Among the malignant cases, 17 cases were NSCLC, 3 cases were SCLC, and 4 cases were lymphomas, one metastatic case and one case of amyloidosis; in addition, three cases were reported as poorly differentiated carcinoma. On the other hand, benign cases included 10 cases of sarcoidosis, 3 reactive lymph nodes and 13 cases showed no significant changes (Table 5).

If our null hypothesis is that there is no difference between the blind TBNA technique and the EBUS-TBNA technique and after simple analysis to see the difference in Population Proportions we found our P-value is 0.2, which means we fail to reject our null hypothesis and there is not sufficient evidence to conclude that one technique is preferred over the other statistically.

Conclusions

EBUS-TBNA technique shows to have a higher diagnostic yield (79%) compared to blind-TBNA technique (65%) although statistically P value shows no significant difference between the two techniques. Still EBUS-TBNA has an advantage over the blind-TBNA especially for small and deep station lymph node or masses because tts real-time visualization during sampling, helps to avoid any vascular injuries, and also decreases the need for another attempt of sampling.

Despite our short experience in this field, we have excellent results, both methods of interventional bronchoscopy techniques that are carried out at KHMC are efficient and effective. Accordingly, we recommend using for interventional bronchoscopy both techniques as standard procedure, where it will help to minimize the number of open surgeries, complications and longtime hospital stay.

This study can be improved by increasing number of cases studied. The future step will be comparing EBUS-TBNA with Video Assisted Mediastinoscopy (VAM) or Video Assisted Thoracotomy (VAT).

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Medical treatment of metabolic syndrome in the fourth decade

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ABSTRACT

Background: **Obesity may be found among one of the irreversible consequences of metabolic syndrome.**

Method: **Consecutive patients at and above the age of 20 years were studied.**

Results: **The study included 1,068 cases (628 emales). Interestingly, 69.4% of cases had excess weight. Prevalence of excess weight increased from 28.7% of the third to 87.0% of the seventh decades, gradually ($p<0.05$ nearly in all steps). Prevalence of excess weight showed its most significant increase between the third to fourth decades (28.7% versus 63.6%, $p<0.001$). Parallel to the excess weight, prevalence of hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, impaired glucose tolerance, and white coat hypertension (WCH) increased until the seventh decade and decreased afterwards, significantly ($p<0.05$ nearly in all steps), whereas prevalence of hypertension (HT), diabetes mellitus (DM), and coronary heart disease (CHD) always increased by decades ($p<0.05$ nearly in all steps) indicating their irreversible properties. On the other hand, nearly half of the study cases (48.4%) had WCH or HT, and the mean ages showed significant increases from the sustained normotension towards WCH and HT cases (38.8, 48.2, and 55.3 years, respectively, $p<0.001$ for both).**

Conclusion: **Prevalence of excess weight increases after the age of 30 years, significantly. Parallel to its severity, it is associated with greater prevalence of HT, DM, and CHD. Acarbose should be initiated for patients with obesity after the age of 30 years due to nearly irreversible nature of obesity. Acarbose should be preferred to metformin due to the high prevalence of excessive anorexia induced metformin intolerance in society.**

Key words: **Umbilical hernia, metabolic syndrome, obesity, hypertriglyceridemia, hyperbetalipoproteinemia**

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Introduction

Due to the prolonged survival of human beings, systemic atherosclerosis may be one of the major health problems in this century, and its association with some metabolic parameters and smoking and alcohol are collected in the box of metabolic syndrome (1, 2). The syndrome is characterized by a chronic low-grade inflammatory process on vascular endothelium all over the body (3). The inflammatory process is exaggerated by some factors including aging, physical inactivity, excess weight, smoking, alcohol, chronic infection and inflammations, and cancers (4, 5). The inflammatory process can be slowed down with lifestyle changes, diet, and exercise (6). The syndrome includes some pioneer parameters such as physical inactivity, animal-rich diet, overweight, white coat hypertension (WCH), impaired fasting glucose, impaired glucose tolerance (IGT), hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, smoking, and alcohol for the development of irreversible consequences such as obesity, hypertension (HT), type 2 diabetes mellitus (DM), chronic obstructive pulmonary disease, chronic liver disease, chronic renal disease, peripheric artery disease, coronary heart disease (CHD), and stroke (7-10). The syndrome has become so common all over the world, for instance nearly one third of people in the United States were affected in 2017 (11). The syndrome induced accelerated atherosclerosis may be the leading cause of early aging and premature death for both genders. Physical inactivity induced excess weight may be the major underlying cause of the metabolic syndrome. Excess weight is characterized by increased mass of adipose tissue anywhere in the body. The chronic inflammation induced endothelial dysfunction may be the action way of excess weight for the increased atherogenicity (12, 13). There are several reports about beneficial effects of acarbose and metformin on excess weight (14-16). We tried to understand when we should start medical treatment of excess weight in the present study.

Materials and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. We studied consecutive check up patients at and above the age of 20 years. Their medical histories including smoking habit, DM, dyslipidemia, and already used medications were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and an electrocardiography was performed. Current regular smokers at least for six pack-months and cases with a history of five pack-years were accepted as smokers, and cigar or pipe smokers were excluded. Patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and 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 physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared, and underweight is defined as a BMI of lower than 18.5 kg/m2, normal weight between 18.5-24.9 kg/m2, overweight between 25.0-29.9 kg/m2, and obesity as a BMI of 30.0 kg/m2 or greater (17). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 110 and 125 mg/dL, and diagnosis of cases with a two-hour plasma glucose level 200 mg/dL or higher is DM and between 140-199 mg/dL is IGT. Additionally, dyslipidemia is diagnosed when LDL-C is 160 mg/dL or higher and/or triglyceride is 200 mg/dL or higher and/or HDL-C is lower than 40 mg/dL (17). A stress electrocardiography was performed in suspected cases, and a coronary angiography was obtained just for the stress electrocardiography positive cases. So CHD was diagnosed either angiographically or with a history of coronary artery stenting and/or coronary artery bypass graft surgery. Office blood pressure (OBP) was checked after a five-minute rest in seated position with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous two hours. 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 HT, after 10 minutes of education about proper blood pressure (BP) measurement techniques (18). The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length, and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of five minutes in the seated position before measurement. An additional 24-hour ambulatory blood pressure monitoring (ABP) was obtained just in cases with a higher OBP and/or HBP measurements. It was performed with oscillometrical equipment (SpaceLabs 90207, Redmond, Washington, USA) set to take a reading every 10 minutes throughout the 24 hours. Normal daily activities were allowed, and subjects were told to keep the arm relaxed during measurements. Eventually, HT is defined as a BP of 135/85 mmHg or greater on mean daytime (between 10 a.m. to 8 p.m.) ABP (18). WCH is defined as an OBP of 140/90 mmHg or greater, but mean daytime ABP of lower than 135/85 mmHg and sustained normotension (NT) as an OBP of lower than 140/90 mmHg together with an average HBP of lower than 135/85 mmHg (18). Eventually, prevalence of smoking, excess weight including overweight and obesity, hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IGT, DM, WCH, HT, and CHD were detected in decades and 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 1,068 cases (628 females and 440 males). Due to just 20 cases found in the ninth decade, they were not included for the statistical comparison. Prevalence of smoking showed a significant progression during the passage from the third to the fourth decades (11.0% versus 32.4%, $p<0.001$), and then it remained as nearly stable in the following decades ($p>0.05$ for all). There were only 19 (1.7%) cases with underweight and 307 (28.7%) cases with normal weight, so 69.4% (742) of cases at and above the age of 20 years had excess weight. The prevalence of excess weight increased from 28.7% of the third to 87.0% of the seventh decades, gradually ($p<0.05$ nearly in all steps), and then decreased to 78.5% of the eight decade ($p<0.05$). Interestingly, the prevalence of excess weight

Table 1: Characteristic features of the study cases

Variables	Third decade	p-value	Fourth decade	p-value	Fifth decade	p-value	Sixth decade	p-value	Seventh decade	p-value	Eighth decade
Number	181		157		246		249		108		107
Smoking	11.0%	*<0.001*	*32.4%*	Ns*	28.8%	Ns	31.7%	Ns	23.1%	Ns	23.3%
Excess weight	28.7%	*<0.001*	*63.6%*	*<0.001*	*78.4%*	Ns	*83.1%*	Ns	*87.0%*	*<0.05*	*78.5%*
Hyperbetalipoproteinemia	1.6%	*<0.001*	*12.7%*	Ns	*15.8%*	Ns	*19.6%*	Ns	*23.1%*	*<0.05*	*14.0%*
Hypertriglyceridemia	5.5%	*<0.001*	*15.2%*	*<0.05*	*20.3%*	*<0.05*	*25.7%*	Ns	*24.0%*	*<0.01*	*11.2%*
Dyslipidemia	6.6%	*<0.001*	*26.7%*	Ns	*31.7%*	*<0.05*	*38.9%*	Ns	*39.8%*	*<0.001*	*20.5%*
IGT†	0.5%	Ns	1.2%	*<0.001*	*10.1%*	*<0.001*	*19.6%*	Ns	*21.2%*	Ns	*15.8%*
DM‡	0.5%	Ns	1.9%	*<0.001*	*11.7%*	*<0.001*	*21.6%*	Ns	*25.0%*	Ns	*26.1%*
WCH§	23.2%	Ns	24.2%	*<0.01*	*33.3%*	*<0.001*	*44.5%*	Ns	*40.7%*	*<0.01*	*25.2%*
HT¶	0.0%	*<0.01*	*5.0%*	*<0.001*	*10.4%*	*<0.001*	*20.4%*	*<0.01*	*31.4%*	Ns	*38.3%*
*CHD***	0.0%	Ns	0.0%	*<0.05*	*3.6%*	*<0.001*	*12.8%*	*<0.01*	*22.2%*	Ns	*24.2%*

*Nonsignificant (p>0.05) †Impaired glucose tolerance ‡Diabetes mellitus
§White coat hypertension ¶Hypertension **Coronary heart disease

Table 2: Comparison of the study cases according to their blood pressure features

Variables	Sustained NT*	*p*-value	WCH†	*p*-value	HT‡
Prevalence	***51.5% (551)***		***32.6% (349)***		***15.7% (168)***
Mean age (year)	***38.8 ± 12.3 (15-83)***	***<0.001***	***48.2 ± 11.3 (15-79)***	***<0.001***	***55.3 ± 10.3 (33-85)***
Female ratio	57.1% (315)	Ns§	63.3% (221)	Ns	65.4% (110)

*Normotension †White coat hypertension ‡Hypertension §Nonsignificant (p>0.05)

showed its most significant increase during the passage from the third to the fourth decades (28.7% versus 63.6%, p<0.001). Parallel to the increasing prevalence of excess weight, prevalence of hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IGT, and WCH increased until the seventh decade of life and decreased afterwards, significantly (p<0.05 nearly in all steps) whereas prevalence of HT, DM, and CHD always increased by decades without any decrease, significantly (p<0.05 nearly in all steps), indicating their irreversible properties (Table 1). On the other hand, the prevalence of WCH and HT were 32.6% and 15.7% among the study cases. In another definition, nearly half of the study cases (48.4%) had WCH or HT, probably parallel to the higher prevalence of excess weight in them (69.4%). Although the female ratios were similar in the sustained NT, WCH, and HT cases (57.1%, 63.3%, and 65.4%, respectively, p>0.05 for both), the mean ages showed significant increases from the sustained NT towards WCH and HT cases (38.8, 48.2, and 55.3 years, respectively, p<0.001 for both) (Table 2).

Discussion

Obesity may be found among one of the irreversible consequences of the metabolic syndrome since after development of obesity, nonpharmaceutical approaches provide limited success to heal obesity (16, 19). Excess weight may lead to a chronic low-grade inflammation on vascular endothelium all over the body, and risk of death from all causes including cardiovascular diseases and cancers increase parallel to severity of excess weight in all age groups (20). The chronic low-grade inflammation on vascular endothelium may even cause genetic changes in the cells, and the systemic atherosclerotic process may decrease clearance of malignant cells by the immune system, effectively (21). Similarly, effects of excess weight on BP were shown previously that the prevalence of sustained NT was significantly higher in the underweight (80.3%) than the normal weight (64.0%) and overweight cases (31.5%, p<0.05 for both) (22), and 52.8% of cases with HT had obesity against 14.5% of cases with sustained NT (p<0.001) (23). So the major component of the metabolic syndrome may appear as excess weight, which is probably the main cause of insulin resistance, dyslipidemia, IGT, and WCH via a chronic low-grade inflammatory process on vascular endothelium (6). Stopping of weight gain with regular activity or diet, even in the absence of a prominent weight loss, probably results with resolution of many parameters of the syndrome (16, 24). But according to our opinion, limitation of excess weight as an excessive fat tissue in and around the abdomen under the heading of abdominal obesity is meaningless, instead it should be defined as overweight or obesity via BMI since adipocytes function as an endocrine organ by producing a variety of cytokines and hormones anywhere in the body (6). The resulting hyperactivity of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with the chronic low-grade inflammation on vascular endothelium terminating with insulin resistance and an elevated BP. Similarly, Adult Treatment Panel III reported that although some people classified as overweight have a larger muscular mass, most of them actually had excessive fat tissue, too (17).

WCH is associated with many parameters of the metabolic syndrome (25), and more than 85% of cases with the syndrome have elevated BP levels (6). We observed very high prevalence of WCH even in early decades of life in the present study, for example 23.2% in the third and 24.2% in the fourth decades. The high prevalence of WCH in society were also shown by some other reports (26-28). When we compared the sustained NT, WCH, and HT groups in another study, prevalence of nearly all of the health problems including IGT, obesity, DM, and CHD had significant progressions from the sustained NT towards the WCH and HT groups, and the WCH group was found as a progression step in between (23). But as an interesting finding, the prevalence of dyslipidemia was the highest in the WCH group, and it was 41.6% among them whereas they were 19.6% in the sustained NT (p<0.001) and 35.5% in the HT groups (p<0.05) (23). Similar results showing the higher prevalence of dyslipidemia among the WCH cases were observed in another study, too (29). The relatively lower prevalence of dyslipidemia in the HT cases may be explained by the already increased adipose tissue per taken fat in them, since prevalence of obesity was significantly higher in the HT against the WCH groups (52.8% versus 44.1%, p<0.01) (23). So the detected higher prevalence of WCH even in early decades, despite the lower prevalence of excess weight in these age groups, may show a trend of weight gain and its terminal consequences. Probably all of the above associations are closely related with the metabolic syndrome since WCH and dyslipidemia may be the two initial signs of the syndrome. On the other hand, WCH is a different entity from borderline or mild HT due to the completely normal HBP and ABP measurements in the WCH cases.

Acarbose, a pseudotetrasaccharide, is a natural microbial product derived from culture broths of Actinoplanes strain SE 50. It is an alpha-glucosidase inhibitor. It binds reversibly, competitively, and in a dose-dependent manner to oligosaccharide binding site of alpha-glucosidase enzymes in the brush border of the small intestinal mucosa. It inhibits glycoamylase, sucrase, maltase, dextranase, and pancreatic alpha-amylase. It has little affinity for isomaltase but it does not have any effect on beta-glucosidases such as lactase. As a result, it delays the intestinal hydrolysis of oligo- and disaccharides by alpha-glucosidases mainly in the upper half of the small intestine. Consequently,

the absorption of monosaccharides after a meal is delayed and transport through the mucosal surfaces into the circulation is interrupted. On the other hand, it does not have any direct effect on absorption of glucose. Although the acute effect is seen within a few minutes, its effects can last up to 5 hours. Acarbose should be taken with the first bite of a meal. The suppression of alpha-glucosidases is persistent with long-term use and the effect with continued use can be maintained over years. Up to now, treatment failure has not been reported with acarbose. Initial therapy with an alpha-glucosidase inhibitor often results with carbohydrates appearing in the colon, where bacterial fermentation occurs, accounting for the frequency and severity of gastrointestinal adverse effects such as flatulence, loose stool, and abdominal discomfort (30). If started with a low dosage and titrated slowly, acarbose-induced gastrointestinal side effects are occasional and generally tolerable (31). Long-term treatment with acarbose increases colonic bacterial mass, that of lactobacteria in particular. The finally impaired carbohydrate absorption, increased bacterial carbohydrate fermentation, and fecal acidification mimic effects of lactulose in patients with liver cirrhosis and portosystemic encephalopathy. So acarbose has a favourable therapeutic profile for the long-term treatment of patients with type 2 DM and liver cirrhosis. Similarly, observed changes in bacterial flora and decreased stool pH and beta-hydroxybutyrate may be associated with anti-proliferative effects on epithelial cells of the colon that may potentially decrease the risk of carcinogenesis. Acarbose is poorly absorbed and systemic bioavailability is low. After oral administration, less than 2% of the unchanged drug enters into the circulation, with most of the remaining in the lumen of the gastrointestinal tract. Thus there is no need for dosage adjustment in slight renal insufficiency. After a high carbohydrate meal, acarbose lowers the postprandial rise in blood glucose by 20% and secondarily FPG by 15% (14). Similarly, it lowers fasting and postprandial insulin levels. The initial improvement in blood glucose with acarbose tends to be modest, but efficacy steadily improves with long-term use, and is maintained over several years without evidence of decreased effect or treatment failure. The beneficial effects of acarbose on serum lipids were also described with a dose-dependent manner (14), since dietary carbohydrates are key precursors of lipogenesis, and insulin plays a central role for postprandial lipid metabolism. Carbohydrate-induced postprandial triglyceride synthesis is reduced for several hours by acarbose, so acarbose lowers plasma triglyceride levels (14). The same beneficial effect was also seen in non-diabetic patients with hypertriglyceridemia, and acarbose reduced LDL-C significantly, but HDL-C remained as unchanged in hyperinsulinemic and overweight patients with IGT (32). Significantly elevated levels of ursocholic acids in the stool appear to be the additive consequence of a decreased rate of absorption and increased intestinal motility secondary to the changes of intestinal bacteria. Acarbose may lower serum LDL-C via an increased fecal bifido bacteria, fecal biliary acids, and LDL-C uptake by the liver. Acarbose together with insulin therapy was identified to be associated with greater improvement in oxidative stress and inflammation in patients with type 2 DM compared with using insulin alone (33). Similarly, acarbose may improve release of glucagon-like peptide-1, inhibit platelet activation, increase epithelial nitrous oxide synthase activity and nitrous oxide concentrations, promote weight loss, decrease BP, and eventually prevent endothelial dysfunction (14). As a result, acarbose prevents CHD and other cardiovascular complications in patients with excess weight even in the absence of IGT and DM (34, 35). According to our clinical experiences, although some authors reported that the patient population suitable for acarbose is limited (36), acarbose should be considered as a first-line antidiabetic agent, particularly for patients with excess weight, and it is an effective pharmacological option for the prediabetic patients with excess weight. Based on more than 20 years of clinical use of acarbose, several studies have reported neither any significant toxicity nor any effect on patients' eating habits (15).

Metformin, a biguanide, is not metabolized and 90% of absorbed drug is eliminated as unchanged in the urine. Plasma protein binding is negligible, so the drug is dialyzable. According to the literature, antihyperglycemic effect of metformin is largely caused by inhibition of hepatic gluconeogenesis, increased insulin-mediated glucose disposal, and inhibition of fatty acid oxidation (37). Reduction of intestinal glucose absorption has been postulated as another mechanism of action (38). Interestingly, 25.9% of patients stopped metformin therapy due to an excessively lost appetite in a previous study (16). Additionally, 14.1% of patients with overweight or obesity in the metformin group rose either to normal weight or overweight group with a prominent weight loss in the same study (16). According to our opinion, the major effect of metformin is a powerful inhibition of appetite. Similar results indicating the beneficial effects of metformin on the BMI, BP, FPG, and serum lipids were reported by some other authors (39, 40). Probably a major component of the metabolic syndrome may be an excess weight which can be prevented by suppression of appetite via metformin. So treatment of excess weight with metformin will probably prevent not only the IGT or DM but most of the other consequences of excess weight, too. Due to the low risk of significant side effects of metformin, even we have never seen in our clinic before, it can be initiated for the majority of cases with excess weight, but clinicians must be careful above the age of 70 years due to risks of comorbid disorders including chronic renal failure, a tendency to develop sepsis, and debility induced weight loss in elders. On the other hand, although 25.9% of patients stopped the metformin therapy due to excessive anorexia in the above study (16), only 10.6% of patients stopped the acarbose therapy due to excessive flatulence or loose stool in the other study (19). So acarbose intolerance is significantly lower than metformin intolerance in the society ($p<0.001$) (19). Eventually, acarbose can be used in a larger patient population than metformin, therefore we did not put an upper limit of age to start acarbose for patients in the above study (19), but we were not able to start metformin above the age of 70 years to avoid debility induced weight loss and metformin-induced lactic acidosis in elders in the other study (16).

As a conclusion, prevalence of excess weight increases after the age of 30 years, significantly. Parallel to its severity, it is associated with greater prevalence of HT, DM, and CHD. Acarbose should be initiated for patients with obesity after the age of 30 years due to the nearly irreversible nature of obesity. Acarbose should be preferred against metformin due to the high prevalence of excessive anorexia induced metformin intolerance in the society.

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Umbilical hernia may also be a sequel of metabolic syndrome

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ABSTRACT

Background: **We tried to understand whether or not there is a relationship between umbilical hernia and metabolic syndrome.**

Methods: **Consecutive patients with an umbilical hernia and/or a surgical operation history for umbilical hernia were studied.**

Results: **There were 46 patients with umbilical hernia with a mean age of 62.0 years, and 73.9% of them were females. The hernia patients were heavier than the controls (85.1 versus 73.1 kg, p= 0.001). Body mass index of them was also higher (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 values of triglyceride and low density lipoproteins and prevalence of white coat hypertension (WCH) were lower in them (p<0.05 for all). Although the prevalence of diabetes mellitus and coronary artery disease were also higher in the hernia group, the differences were non-significant probably due to the small size of the study group.**

Conclusion: **There are significant relationships between umbilical hernia and terminal consequences of metabolic syndrome including obesity and HT, probably on the bases of prolonged inflammatory and atherosclerotic effects beside pressure effect of excessive fat tissue on abdominal 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. Similarly, the inverse relationship between obesity and WCH may be explained by progression of WCH into HT in obese individuals. So obesity may actually be a precirrhotic condition for the human body.**

Key words: **Umbilical hernia, metabolic syndrome, obesity, h ypertriglyceridemia, hyperbetalipoproteinemia**

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Introduction

Due to the prolonged survival of human beings, systemic atherosclerosis may be the major health problem in this century, and its association with physical inactivity, excess weight, smoking, and alcohol is collected under the title of metabolic syndrome (1, 2). The syndrome is characterized by a low-grade chronic inflammatory process on vascular endothelium all over the body (3). The inflammatory process is accelerated by some factors including sedentary lifestyle, excess weight, smoking, alcohol, chronic infection and inflammation, and cancers (4, 5). The syndrome can be slowed down with appropriate non-pharmaceutical approaches including lifestyle changes, diet, exercise, cessation of smoking, and withdrawal of alcohol (6). The syndrome contains reversible indicators including overweight, white coat hypertension (WCH), impaired fasting glucose, impaired glucose tolerance (IGT), hyperlipoproteinemias, alcohol, and smoking for the development of irreversible consequences including obesity, hypertension (HT), type 2 diabetes mellitus (DM), chronic obstructive pulmonary disease, cirrhosis, chronic renal disease, peripheric artery disease, coronary artery disease (CAD), and stroke (7). In another perspective, the metabolic syndrome may be the most important disease of the human lifespan, decreasing its quality and duration, at the moment. The syndrome has become increasingly common all over the world, for instance 50 million people in the United States are affected (8). The syndrome induced accelerated atherosclerotic process all over the body may be the leading cause of early aging and premature death for both genders. For example, CAD is the leading cause of death in developed countries. On the other hand, umbilical hernias are also common pathologies in society both in adults and children. We tried to understand whether or not there are some statistically significant relationships between umbilical hernia and reversible parameters and irreversible consequences of the metabolic syndrome in the present study.

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 operation history for umbilical hernia were collected in the first, and age and sex-matched controls were collected into the second group. Their medical histories including smoking habit, HT, DM, CAD, and already used medications were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride, 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 rest in seated position with the mercury sphygmomanometer on three visits, and no smoking was permitted during the previous two hours. 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 10 minutes of education about proper blood pressure (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). 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, triglyceride, and LDL values and prevalences of smoking, WCH, HT, DM, and CAD 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 hernia cases was 62.0 years, and 73.9% (34) of them were female. Although the mean heights of the two groups were similar (157.4 versus 158.7 cm, $p>0.05$), the umbilical hernia patients were significantly heavier than the control cases (85.1 versus 73.1 kg, $p= 0.001$). Eventually, the BMI was also higher in the hernia patients (33.6 versus 29.1 kg/m2, $p= 0.000$). Interestingly, although the significantly higher mean weight and BMI of the hernia patients, the mean triglyceride 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 hernia group (50.0% versus 27.3%, $p<0.01$). Although the prevalences of DM and CAD were also higher in the hernia group, the differences were statistically non-significant, probably due to the small size of the study group (Table 1 - next page).

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 triglyceride (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 CAD***	*17.3%*	Ns	13.0%

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

Discussion

Umbilical hernias are common anomalies of the abdominal wall both in adults and children. The majority of scientists agree that most of the umbilical hernias in adults have an acquired origin, and only 10% of adults with umbilical hernias have the pathology, congenitally (12). In different series, umbilical hernias are more common in women both in infancy and adulthood, particularly in middle-aged multiparous women (12-14). Umbilical hernia is more common under the age of four and over the age of 50 years (13). It is particularly common in premature babies (up to 84%) and overweight children. According to the literature, its prevalence is around 2% in adults, and more common in patients with obesity, cirrhosis, congestive heart failure, chronic renal failure, and cancers (15). There are no major differences between the various ethnic groups in adults, supporting the possible acquired etiologies (13). Umbilical hernias occur when a part of the intestine protrudes through a weak spot in the abdominal muscles at the site of umbilicus. Babies are prone to this malformation because of 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, umbilical hernia must be distinguished from paraumbilical hernia, a defect in one side of the midline at the umbilical region in adults and from omphalocele in newborns. Most umbilical hernias close on their own by the age of one year, although up to 10% may take longer to heal. To prevent complications, umbilical hernias that do not disappear by the age of four years or those that appear during adulthood may need surgical repair. As occurs in other defects of the abdominal wall, 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. So 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 a female complication 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 cirrhotics receiving medical treatment for ascites, carrying an implant of a peritoneo-venous shunt, or getting an evacuating paracentesis (17). Because of the significant associations of the umbilical hernias with decompensated cirrhosis, congestive heart failure, chronic renal failure, and cancers in the literature (14, 15), we excluded such terminal cases due to their possible effects on weight in the study. Interestingly, all of the above pathologies are found among terminal consequences of the metabolic syndrome. On the other hand, the higher prevalence of umbilical hernia in cases with decompensated cirrhosis may also support the pressure effect of in-

intra-abdominal fluid on abdominal muscles (18). Similar to the literature, we detected the female ratio as 73.9% in the umbilical hernia group, and the mean weight and BMI of them were significantly higher than the controls (85.1 versus 73.1 kg, p= 0.001 and 33.6 versus 29.1 kg/m2, p= 0.000, respectively).

Obesity, pregnancy, ascites, or peritoneal dialysis induced abdominal wall distension may cause pulling of the abdominal muscles and deterioration of connective tissue over the umbilicus. Similarly, the frequent association of umbilical hernia with other abdominal wall defects may also support the possible etiologic role of biophysical changes (13). In a 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). For instance, abnormal dispositions of the umbilical fascia may be one of the factors contributing to herniation (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 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 malnutrition may also facilitate the herniation in cirrhotic patients.

Obesity is probably found among one of the irreversible endpoints of the metabolic syndrome, since after development of obesity, non-pharmaceutical approaches provide limited success 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 weight excess 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, elevations of serum C-reactive protein (CRP) 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, and it is involved in the regulation of cytokines, so individuals with overweight and obesity have elevated levels of CRP (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 extra 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 the atherosclerosis and HT, prevalences of high FPG, high serum cholesterol, and low high density lipoproteins (HDL) were all raised with increases in BMI (30). Similarly, the prevalences of CAD and stroke, particularly ischemic stroke, increased with an elevated BMI 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 infancy. For example, varicous dilatations of the lower extremities are much more common in females, and most of them develop during labour, probably due to the vasodilative effects of estrogen. This vasodilatation may also disturb muscular structure of the abdominal wall in women in the process of umbilical hernias, as in recanalized umbilical veins in cirrhosis.

There are also some hepatic consequences of excess weight. 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 an 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 10 to 25% of affected patients (32). Excessive fat accumulation in hepatocytes is called hepatosteatosis. It progresses to NAFLD, steatohepatitis, fibrosis, cirrhosis, hepatocellular carcinoma, and 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 has become the most common cause of chronic liver disease even in children and adolescents (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 atherosclerotic process (35). NAFLD shares many features of the metabolic syndrome as a highly atherogenic condition, and may cause hepatic inflammation and cellular injury especially 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 carotid artery intimal medial thickness 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 syndrome (37). Interestingly, although the

presence of significant progression according to the BMI and body weight ($p<0.000$ for all) from the normal weight towards the overweight and obesity groups, and although the presence of a highly significant difference according to mean alanine aminotransferase (ALT) values between the normal weight and overweight groups (39.7 versus 53.5 U/L, $p<0.001$), the difference between the overweight and obesity groups was non-significant according to the mean ALT values in serum (53.5 versus 53.5 U/L, $p>0.05$) (38). As a similar trend, prevalence of dyslipidemia was significantly lower in the normal weight than the overweight groups (25.0% versus 45.2%, $p<0.001$), but there was a non-significant difference between the overweight and obesity groups, too (45.2% versus 37.5%, $p>0.05$) (38). These findings may also be explained by the hepatic fat accumulation, inflammation, and fibrosis induced relatively lost hepatic functions in obese individuals. So obesity may actually be a precirrhotic condition in the body.

In another study (39), when the authors compared the sustained normotension (NT), WCH, and HT groups, prevalence of nearly all of the pathologies including obesity, IGT, DM, and CAD showed significant progressions from the sustained NT towards the WCH and HT groups, and the WCH group was found as a progression step in between. Except for the prevalence of overweight, prevalence of all of the other pathologies were significantly higher in the WCH than the sustained NT cases (39). The similar progressions were observed nearly in all of the pathologic conditions between the WCH and HT groups, too, but interestingly there was only one parameter, dyslipidemia, that showed higher prevalence in the WCH against the HT groups (39). The prevalence of dyslipidemia was the highest in the WCH group and it was 41.6% versus 19.6% ($p<0.001$) in the sustained NT and 35.5% in the HT groups ($p<0.05$) (39). Against a previous study indicating serum triglyceride and cholesterol levels did not differ significantly between the NT, WCH, and sustained HT cases in men in the literature (40), the similar results indicating higher prevalences of dyslipidemia in WCH cases were also observed in another study, previously (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, CAD, stroke problems in 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 HT against the WCH groups ($p<0.01$) (39). So WCH and hyperlipoproteinemias may show accelerating trend of gaining weight. By this way, the detected higher prevalence of WCH even in the second (33.3%) and in the third decades (46.6%) (11), despite the lower prevalence of obesity in these age groups, may show the trend of gaining weight, and the WCH and hyperlipoproteinemias may be pioneer signs of obesity and many associated disorders in future.

As a conclusion, there are significant relationships between umbilical hernia and terminal consequences of the metabolic syndrome including obesity and HT, probably on the bases of prolonged inflammatory and atherosclerotic effects, beside the pressure effect of the excessive fat tissue on abdominal 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. Similarly, the inverse relationship between obesity and WCH may be explained by the progression of WCH into HT in obese individuals. So obesity may actually be a precirrhotic condition for the human body.

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