



Metabesity and urological cancers

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Cite this article as: Atan A. Metabesity and urological cancers. Turk J Urol 2017; 43(4): 410-3

ABSTRACT

Metabolic syndrome is one of today's most important health problems. Due to increased prevalence of metabolic syndrome in society, studies done on this topic have increased in number. Although metabolic syndrome was previously considered to be important only for cardiovascular health, it has been learned that with new data, human health is compromised more thoroughly by metabolic syndrome and is also a danger to malignancy. As a result, a new definition in the form of metabesity has been introduced. In this review, available information on metabesity and urological cancers is presented.

Keywords: Metabolic syndrome; metabesity; prostate cancer; renal cancer.

Because of becoming widespread of sedentary life style and changes in dietary habits, the incidence of obesity and weight gain has increased.^[1,2] Metabolic syndrome which occurs to be connected to/with weight gain and obesity has become one of the most important health problems. In the Western World the incidence of metabolic syndrome in adult population was detected as 35-41%.^[3,4]

Nowadays, a standard definition of metabolic syndrome has not been made yet. Various societies have suggested different definitions. The first institutionalized definition was made by the World Health Organization (WHO) in the year 1998. Subsequently European Group for the Study of Insulin Resistance (EGIR) (1999), National Cholesterol Education Program-Adult Treatment Panel- III (NCEP-ATP-3) (2001), International Diabetes Foundation (IDF) (2005), American Heart Association / National Heart, Lung, and Blood Institute (AHA/NHLBI) (2005) defined metabolic syndrome. Lastly, joint interim definition made by IDF and AHA/NHLBI was published in 2009.^[5] The most current diagnostic criteria of metabolic syndrome are shown in Table 1.^[6]

Basic criteria used in these definitions include waist circumference, diabetes mellitus, dyslipidemia (decreased HDL, and increased TG), and hypertension. In addition to metabolic syndrome, the concept of diabetesity has come to an end. Diabetesity is a combination of diabetes and obesity. Dyslipidemia and hypertension may or may not be included in this entity.^[7] Recently, Dr. Alexander Fleming who is an endocrinologist and strategist added a different dimension to the definition of metabolic syndrome in a panel speech in the year 2013 and introduced the concept of metabesity (Figure 1). According to Dr. Fleming, metabesity describes all relevant conditions (diabetes mellitus, obesity, metabolic syndrome, cardiovascular disease, dyslipidemia, cancer promoting factors and accelerated aging) which impose a serious burden on healthcare, and economic state.^[8] The difference between concepts of metabesity and diabetesity is that metabesity describes conditions within a larger spectrum which deteriorate human health.

Although metabolic syndrome is generally perceived as an important health problem regarding cardiovascular health, with the con-

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Submitted:
20.09.2017

Accepted:
28.09.2017

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Available online at
www.turkishjournalofurology.com

cept of metabesity more comprehensive definition has been targeted. Regardless of the name, the most common urological problem associated with this clinical picture was erectile dysfunction. However, various studies performed have detected an association between metabolic syndrome and infertility, stone disease, overactive bladder, female urinary incontinence, benign prostatic hyperplasia, prostate cancer and renal cancer.^[9-11] In the light of the data obtained, the association between metabolic syndrome, and development of malignity has attracted attention of many researchers. In a recent review article this issue has been analyzed in detail.^[12] In the presence of metabolic syndrome, though very precise data concerning the mechanisms which lead to development of cancer have not been available^[13,14] some information about the role of obesity on the cancerogenesis have been obtained (Figure 2).^[15] In this review, the relationship between metabesity, and urologic malignancies will be presented in the light of international literature.

1. Renal cancer

Clear-cut data are not available about which metabolic syndrome component(s) is/are effective on the development of renal cancer associated with metabesity. In various studies the impact of obesity has been indicated.^[15-22] Some authors also reported effectiveness of diabetes mellitus and hypertension in their studies.^[17,22-25] Development of renal cancer due to these conditions has been associated with inflammation, insulin, and

insulin-like growth factor-1, renal hypoxia, hyperfiltration, and lipid peroxidation.^[11,26]

However in a study performed by Haggstrom et al.^[27] all components of metabolic syndrome have been correlation with the development of renal cancer. Increased body mass index, hypertension, hyperglycemia and hypertriglyceridemia especially in men and increased body mass index especially in women have been found to be important adverse factors.

2. Prostate cancer

Diverse results have been cited in the international literature about the development of prostate cancer in the presence of metabolic syndrome. Some authors reported that metabolic syndrome did not promote the development of prostate cancer.^[28,29] In an Australian study, it was found that increases in waist circumference, and triglyceride levels decreased the risk of development of prostate cancer.^[13] In a more recent study, decrease in the development of prostate cancer in the presence of overweightness or obesity and diabetes mellitus has been indicated.^[30]

Although general opinion asserts that metabolic syndrome has an impact on the development of prostate cancer, any consensus does not exists concerning which component(s) of metabolic syndrome play(s) a role in the development of prostate cancer. Some authors have reported that none of the components of metabolic syndrome are directly associated with the development of prostate cancer. However, they have also indicated that with an increase in the number of metabolic syndrome components, risk of development of prostate cancer and its aggressiveness also increase.^[31]

Also in a most current meta-analysis, it has been detected that metabolic syndrome is a probable risk factor for the develop-

Table 1. Diagnostic criteria of metabolic syndrome^[6]

Body weight	Waist circumference specific to the ethnicity and population in question
Lipid panel	
Triglyceride level	≤150 mg/dL
HDL level	Male, <40 mg/dL; women, <50 mg/dL or use of HDL-lowering drug
Hypertension	≤135/85 mmHg or receiving antihypertensive medical treatment
Glycemia	≤100 mg/dL

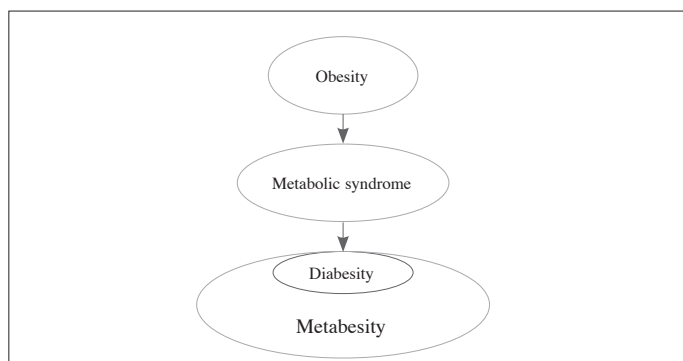


Figure 1. Relationship between obesity and metabesity

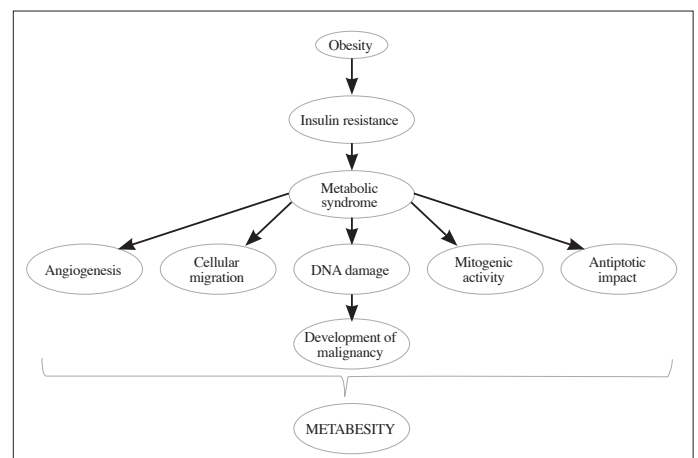


Figure 2. Association between obesity, and malignancy^[15]

ment of prostate cancer, besides it is an important factor predicting worse prognosis. In this group of patients, metabolic syndrome is associated with worse pathologic outcomes after radical prostatectomy as Gleason score ≥ 8 , extracapsular invasion, seminal vesicle involvement, positive surgical margin, and biochemical.^[32] In this study, it is determined that only one component of metabolic syndrome, namely hypertension, plays a role in the development of prostate cancer.^[32] In another study, evidence suggesting the role of higher TG levels (another metabolic syndrome component) in the development of prostate cancer was obtained.^[33] Besides, some studies have demonstrated the association between overweightness/ obesity and prostate cancer.^[34,35]

The factors which are thought to be effective between components of metabolic syndrome and biology of prostate cancer include sex hormones, endocrine disruptors, inflammation, lipids and proteins modified by prooxidative microenvironment. Insulin and insulin-like hormones as growth factors play important roles.^[36,37] Increases in the levels of estradiol, and sex hormone-binding globulin and sex hormone-binding globulin, and decreased free testosterone levels have been indicated to be effective on this process.^[38,39] Endocrine disruptors are substances which disrupts synthesis, secretions, effects, elimination of naturally existing hormones in human beings, and their binding to receptors including drugs, pesticides, plastic additives, organic contaminants. Most of them are xenoestrogens or antiandrogens.^[40] Changes in cytokines and leptin levels due to increased inflammation in metabolic syndrome have been shown to play a role in prostate cancer development.^[41]

In conclusion, metabesity which is introduced as a novel concept into our use will occupy an important place in our clinical practice. Therefore components of metabolic syndrome should be considered in the practice of urological oncology.

Peer-review: This manuscript was prepared by the invitation of the Editorial Board and its scientific evaluation was carried out by the Editorial Board.

Conflict of Interest: No conflict of interest was declared by the author.

Financial Disclosure: The author declared that this study has received no financial support.

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