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Relation of Body Mass Index (BMI) to Disease Free (DFS) and Distant Disease Free Survivals (DDFS) Among Turkish Women with Operable Breast Carcinoma

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Background: The correlation between body mass index (BMI) and patient and tumor characteristics related to prognosis has not been well explored and may help to elucidate the mechanisms involved in the carcinogenesis. Because of the equivocal, inconsistent and uncertain research results as well as racial and ethnic differences, we aimed to evaluate the prognostic significance of high BMI in Turkish women with operable breast carcinoma.
Methods: Two hundred and sixty-six patients who had operable invasive breast carcinoma diagnosed from 2000 through 2004 in a single institution were evaluated for their demographic features, BMI, histopathological/immunohistochemical examinations and treatments. Quetelet BMI [weight (kg)/height $(m)^2$] categories were selected according to the World Health Organization definition. Disease free survival (DSF) as well as distant disease free survival (DDSF) analyses were performed to identify independent prognostic factors.
Results: Post-menopausal patients were significantly in the higher quartile of BMI than pre-menopausal patients ($P = 0.003$). While post-menopausal obese patients had worse DSF and DDFS ($P = 0.001$), vascular invasion was the independent prognostic factor for both survival indices ($P = 0.031$).
Conclusions: Post-menopausal obese Turkish women are at increased risk of developing breast tumors with aggressive phenotype and obesity is a strong predictor of poor DSF and DDFS. Preventive strategies to reduce not only the prevalence of obesity and breast cancer but also the mortality must be recognized as the cost-effective public-health policy for Turkey.

Key words: body mass index – breast cancer – prognosis – survival

INTRODUCTION

Obesity, which can be defined as the malnutrition of the developed world, has an increasing prevalence in Europe and the USA. It is, however, not restricted to western populations, and its prevalence varies among regions, countries, races and ethnic groups (1). Turkey is a developing country between Europe and Asia with a population of 67.8 million. The female population is 33.5 million. The number of females age $\geq$30 is about 14.0 million (2). Epidemiological surveys in Turkey have revealed higher prevalence of obesity in females than males with a peak in the 50–59 year old group. In the 1990 cohort of The Heart Disease and Risk Factors in Turkish Adults (TEKHARF) study for those age 30 and over, the prevalence of obesity was 12% in males and 32% in females. A decade later, the TEKHARF 2001/2002 cohort (a large multicenter nationwide study) revealed a striking increase to 25% in Turkish males and 44% in Turkish females (3).

According to the most recent reports of the Turkish Cancer Registry, breast cancer is the most common female cancer, accounting for 24.1% of all cancers diagnosed among women and the incidence was 7.32 per 100 000 (2390 new cases) in 1999 (4). According to the GLOBOCAN 2002, the crude as well as age-standardized incidence and mortality rates of breast cancer in Turkey per 100 000 were 19.9, 22.0 and 8.8, 9.7 (6729 new cases and 2970 deaths) respectively (5). It is the second most common cause of cancer-related mortality among Turkish women (4).

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More specifically, Fidaner et al. also reported that breast cancer was the most frequent cancer in women, accounting for 26.7% of female cancers in western Turkey. In 1996–2000, the crude and age-standardized incidence rates, per 100 000 were 31.6 and 31.1 in Izmir (6).

The relationship between breast cancer and obesity is not straightforward. In most but not all case-control and prospective cohort studies, an inverse relationship has been found between weight and breast cancer among pre-menopausal women. However, some data suggest the increased risk of pre-menopausal breast cancer with adult weight gain and central obesity (1). Most large epidemiological studies have found that overweight or obese women are at increased risk of developing post-menopausal breast cancer (7). The relative risk (RR) of developing post-menopausal breast cancer was found to be 1.26 (95% CI: 1.09–1.46) in women with BMI of 28 kg/m^2 or above on analysis of pooled data from seven prospective cohort studies including 337 819 women and 4385 incident invasive breast cancer cases (8).

Previous studies have noted a modest negative association between obesity and survival of breast cancer (9–18). It is suggested that higher BMI is associated with a more advanced stage at diagnosis such as higher tumor size and/or more axillary node involvement, and patient-related delay in the diagnosis of breast cancer. Obese women are twice as likely to present to a health-care professional more than 3 months after first noticing the symptoms due to having big breasts (1,12,19). Alternatively, presence of confounding factors such as increased preponderance of obesity in the lower socio-economic population and lower level of education are associated with delay (20).

Radiotherapy, chemotherapy and hormonal treatment may be adversely affected by the presence of obesity causing poor survival (14,18, 21–24).

Despite the accumulating data, the correlation between BMI and patient and tumor characteristics related to prognosis has not been explored completely. However, some study results are equivocal, inconsistent and uncertain, and also the issue of racial and ethnic differences has not been well examined. Few studies included patients receiving systemic adjuvant therapy.

With the high female population and increasing prevalence of obesity in Turkey, we aimed to search for loco-regional and distant recurrences among obese women with operable breast cancer after adjuvant treatments.

PATIENTS AND METHODS

From 2000 through 2004, 266 Turkish women with Stage I–II and operable Stage IIIA, IIIC breast carcinoma (2002 AJCC TNM staging system) who received adjuvant systemic treatments and have also been followed up in the Department of Hematology/Oncology, Medical School Hospital at Dokuz Eylul University were evaluated. Body weight, height and BMI of all patients at the time of admission to the clinic have been recorded accurately as part of the treatment protocol. Demographic, histopathological and adjuvant treatment data were collected from the medical records reviewed. Each patient's menopausal status was determined at the time of diagnosis.

Expression of HER-2/neu was determined immunohistochemically. A score of 0 was given if there was no membrane staining or if staining was present in less than 10% of tumor cells, 1+ for faint, barely perceptible membrane staining in more than 10% of tumor cells with stain involving only part of the cell membrane, 2+ for weak or moderate complete membrane staining in more than 10% of tumor cells, and 3+ for strong complete membrane staining in more than 10% of tumor cells. The ER/PR status was also assessed by immunohistochemical assays. The nuclear staining in more than 10% of tumor cells is considered as positive for ER and the nuclear staining in more than 5% of tumor cells is considered positive for PR, but specimens with nuclear staining in $\geq$1% of tumor cells were considered positive for endocrine treatment in our study. Peritumor blood and lymphatic vessel invasions (BVI, LVI) were detected by the presence of tumor cells in the lumen. Blood vessels were identified by the erythrocytes in the lumen, an endothelial cell lining, and the presence of elastic tissue around large vessels. Only BVI of the doubtful cases were determined using Factor VIII-related antigen staining and elastica van Gieson staining.

Quetelet body mass index (BMI) (weight in kg/height in m^2) were selected according to the World Health Organization definition: underweight, <18.5 kg/m^2; normal range between 18.5 and 24.9 kg/m^2; grade 1 overweight between 25 and 29.9 kg/m^2; grade 2 overweight (obesity) between 30 and 39.9 kg/m^2; grade 3 overweight (morbid obesity) >40 kg/m^2. There was no patient in the underweight group. We combined the grade 2 overweight group with the grade 3 overweight group, resulting in three BMI categories: Group 1, normal (18.5–24.9); Group 2, overweight (25–29.9) and Group 3, obese/morbid obese ($\geq$30.0).

In our institution, patients who underwent appropriate primary surgery (either modified radical mastectomy or breast-conserving surgery) were considered eligible for evaluation of adjuvant systemic treatments according to the St Gallen risk classification. Eligible patients received adjuvant chemotherapy [EC 90 (epirubicine 90 mg/m^2 and cyclophosphamide 600 mg/m^2, IV, d1, q3w, 4 cycles) or FEC 100 (fluorouracil 500 mg/m^2, epirubicine 100 mg/m^2 and cyclophosphamide 500 mg/m^2, IV, d1, q3w, 6 cycles)], adjuvant hormonotherapy (Tamoxifen 20 mg/d, PO, qd, 5 years) and/or adjuvant radiotherapy, as indicated. Since the status of ovarian ablation was not fully available in the pre-menopausal patients at the time of the evaluation study, ovarian ablation was not part of the study protocol.

Efficacy parameters in the study were disease free survival (DFS) and distant disease free survival (DDSF) which were defined as the time interval from primary surgery to any relapse (loco-regional, contra-lateral and/or distant) and as

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Table 1. Distribution of patient characteristics according to adult BMI among women with invasive breast cancer [all values except P-values are represented as *n* (%), unless stated otherwise]

Characteristic	Normal (18.5≤BMI<25) *n* (%)	Overweight (25≤BMI<30) *n* (%)	Obese/ Morbid Obese (BMI≥30) *n* (%)	*P* value
Total patients (*n*)	77	110	79	
Age	45 (26–75)	52 (30–82)	55 (32–77)	0.000
[median (range)]				
<35 yrs	15 (19.5)	6 (5.5)	2 (2.5)	0.000
≥35 yrs	62 (80.5)	104 (94.5)	77 (97.5)	
Menopausal status				0.007
Pre/Peri	53 (68.8)	54 (49.1)	35 (44.3)	
Post	24 (31.2)	56 (50.9)	44 (55.7)	
Tumor size				0.042
≤2 cm	28 (36.4)	40 (36.4)	18 (22.8)	
>2 cm	49 (63.6)	70 (63.6)	61 (77.2)	
Nodal status				0.285
N (−)	25 (32.5)	48 (43.6)	33 (41.8)	
N (+)	52 (67.5)	62 (56.4)	46 (58.2)	
N ≥ 4	28 (36.4)	30 (28.3)	25 (31.8)	
Hormone receptor status				0.832
ER/PR (+)	52 (67.5)	76 (69.1)	52 (65.8)	
ER and PR (−)	25 (32.5)	34 (30.9)	27 (34.2)	
Tumor grade				0.358
Grade 1	14 (18.2)	24 (21.8)	11 (14)	
Grade 2–3	63 (81.8)	86 (78.2)	68 (86)	
Lymph vessel invasion				0.536
LVI (+)	58 (75.3)	77 (70)	58 (73.4)	
LVI (−)	7 (9.1)	14 (12.8)	10 (12.7)	
Unknown	12 (15.6)	19 (17.2)	11 (13.9)	
Vascular (blood vessel) invasion				0.011
VI (+)	12 (15.6)	20 (18.2)	27 (34.2)	
VI (−)	57 (74.0)	79 (71.8)	46 (58.2)	
Unknown	8 (10.4)	11 (10.0)	6 (7.6)	
cerbB-2 (IHC)				0.573
cerbB-2 (0–1)	56 (72.7)	76 (69.1)	49 (62)	
cerbB-2 (2–3)	13 (16.9)	19 (17.3)	17 (21.5)	
Unknown	8 (10.4)	15 (13.6)	13 (16.5)	
Surgery				0.052
BCS	44 (57.1)	54 (49.1)	39 (49.4)	
MRM	33 (42.9)	44 (57.1)	40 (50.6)	
ADJ CT	72 (93.5)	97 (88.2)	72 (91.1)	0.223
ADJ HT	52 (67.5)	76 (69.1)	52 (65.8)	0.933
ADJ RT	67 (87)	93 (84.5)	66 (83.5)	0.895

BMI, body mass index; ER, estrogen receptor; PR, progestron receptor; BCS, breast conserving surgery; MRM, modified radical mastectomy; ADJ CT, adjuvant chemotherapy; ADJ HT, adjuvant hormonotherapy; ADJ RT, adjuvant radiotherapy.

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the time interval from surgery to only distant metastases (bone and/or visceral organ) respectively. Patients who were lost to follow-up were not included in the study.

Comparison of the characteristics of patients in three different categories of BMI were made by ANOVA. The Kaplan–Meier method was used to calculate the percentage of women alive with disease and distant disease free, while the log-rank test was used to compare survivals across three groups according to menopausal status and endocrine receptor status. Cox proportional hazards models for outcomes related to time variables was also performed in the overall study population according to menopausal status and the three main strata (normal, overweight and obese/morbid obese groups). To select those factors with independent significant influence on outcomes, multivariate analyses were carried out in a stepwise (Cox regression) fashion. Prior to the application of these methods, univariate analyses were performed for a preliminary exploration of marked associations. Statistical analysis and survival curves were obtained using the computer software SPSS 11.0 for Windows and all tests of statistical significance ($P < 0.05$) were two-sided.

RESULTS

Two hundred and forty patients were referred from the Aegean Region (Western Turkey) (90.4%), 64% of whom live in Izmir, as well as 26 cases (9.6%) referred from other regions of Turkey.

There were 77, 110 and 79 women in Group 1 (normal), Group 2 (overweight) and Group 3 (obese/morbid obese) respectively. The age of the overall group ranged from 26 to 82 years, with a median age of 52 years. The sample characteristics of the three groups were statistically compared. Table 1 shows the principal demographic, clinical, histopathological and treatment characteristics of all the patient study population. Demographic variables with a significance of $P < 0.05$ included age and menopausal status. Post-menopausal patients were in the higher quartile of BMI than pre-menopausal patients ($P = 0.007$). Regarding the tumor features, tumor size ($P = 0.042$) and vascular invasion ($P = 0.011$) were prominent in the obese/morbid obese women. Of women, 55–65% were node positive and 30–35% of them had $\geq$4 metastatic lymph nodes.

All the study groups including intermediate and high risk patients received adjuvant systemic treatment, approximately 90% chemotherapy and/or 65% hormonotherapy.

The median follow-up period has not yet been reached. The mean follow-up period after diagnosis was 60 (8–67) months. Seven patients (2.6%) had loco-regional recurrences and 44 patients (16.6%) had distant metastases [10 (3.8%) in bone, 16 (6%) in bone and viscera, 18 (6.8%) in viscera]. Twenty-eight patients (10.5%) had died.

Table 2 shows distribution of significant patient characteristics according to BMI and menopausal status. Tables 3, 4 and 5 show DFS and DDFS with 95% CI according to BMI, menopausal status and endocrine receptor status. The independent prognostic factors with respect to univariate and multivariate analyses are given in Table 6.

Survival curves of the pre-menopausal and post-menopausal patients according to BMI and the three BMI groups according to menopausal status are revealed in Figs 1 and 2, and 3 and 4 respectively.

Table 2. Distribution of significant patient characteristics according to body mass index and menopausal status

Characteristic	Normal (18.5≤BMI <25) *n* (%)	Overweight (25≤BMI <30) *n* (%)	Obese/ Morbid Obese (BMI≥30) *n* (%)	*P* value
T>2 cm				0.002
PostM	14 (58.3)	36 (67.9)	38 (86.4)	
PreM	35 (65.4)	34 (62.9)	23 (65.7)	
VI (+)				0.000
PostM	1 (4.8)	11 (20.8)	21 (47.7)	
PreM	11 (21.2)	9 (16.7)	6 (17.1)	

PreM, Premenopausal Status; PostM, Postmenopausal Status
T, Tumor Size; VI, Blood Vessel Invasion.

Table 3. DFS and DDFS with 95% CI in postmenopausal and premenopausal patients according to body mass index

	Postmenopause		Premenopause	
	DFS	DDFS	DFS	DDFS
Normal/ Overweight	55 (51–60)*	56 (52–60)	55 (52–59)	57 (54–61)
Obese/Morbid Obese	48 (43–54)	48 (43–54)	63 (60–67)	63 (60–67)
P value	0.034	0.026	0.018	0.056

DFS, Disease Free Survival (month); DDFS, Distant Disease Free Survival (month) *95% CI (months)

Table 4. DFS and DDFS with 95% CI according to BMI and menopausal status (95% CI) (months)

	Group 1 (18.5≤BMI<25)		Group 2 (25≤BMI<30)		Group 3 (BMI≥30)	
	DFS	DDFS	DFS	DDFS	DFS	DDFS
PreM	56 (50–61)	57 (52–62)	54 (49–59)	57 (52–61)	63 (60–67)	63 (60–67)
PostM	55 (48–63)	58 (51–64)	53 (48–59)	53 (48–59)	49 (43–55)	49 (43–55)
P value	0.970	0.830	0.624	0.714	0.001	0.001

BMI, Body Mass Index; DFS, Disease Free Survival; DDFS, Distant Disease Free Survival; PreM, Premenopause; PostM, Postmenopause.

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Table 5. DFS and DDFS data with 95% CI in premenopausal and postmenopausal patients according to ER/PR status and body mass index

	Normal (18.5≤BMI<25)				Overweight (25≤BMI<30)				Obese/Morbid Obese (BMI≥30)			
	PostM		PreM		PostM		PreM		PostM		PreM	
	DFS	DDFS	DFS	DDFS	DFS	DDFS	DFS	DDFS	DFS	DDFS	DFS	DDFS
ER/PR (+)	58 *(51–66)	58	56 (51–66)	58 (49–62)	55 (52–64)	55 (49–61)	55 (49–61)	58 (50–61)	48 (53–63)	48 (41–55)	67 (41–55)	67
ER-PR (−)	37 (22–51)	44 (34–54)	55 (45–64)	55 (45–64)	50 (40–60)	50 (40–60)	50 (41–60)	53 (44–62)	49 (38–60)	49 (38–60)	59 (50–66)	59 (50–66)
P value	0.146	0.570	0.986	0.664	0.426	0.426	0.518	0.430	0.788	0.788	0.188	0.188

DFS, Disease Free Survival (month); DDFS, Distant Disease Free Survival (month).
PreM, Premenopausal Status; PostM, Postmenopausal Status.
ER/PR, Estrogen Receptor / Progesterone Receptor.
*95% CI (months).

Table 6. P values from univariate and multivariate analyses: BMI ≥30 group

	Univariate		Multivariate	
	DFS	DDFS	DFS	DDFS
Tumor size	0.028	0.012	0.098	0.082
ER/PR status	0.044	0.036	0.344	0.212
Menopausal status	0.030	0.024	0.072	0.065
Vascular invasion	0.010	0.010	0.031	0.031
Lymph node (+)	0.050	0.048	0.570	0.496

BMI, Body Mass Index; ER/PR, Estrogen Receptor/Progesterone Receptor
DFS, Disease Free Survival; DDFS, Distant Disease Free Survival.

Post-menopausal women in the highest category of BMI had more breast cancer recurrences than the other post-menopausal (log-rank $P = 0.024$ for DFS and 0.036 for DDFS) and pre-menopausal women (log-rank $P = 0.001$ for both DFS and DDFS). Although univariate analysis revealed significance for tumor size, hormone receptor status, menopausal status, vascular invasion and lymph node involvement, multivariate tests confirmed significance for only vascular invasion as independent prognostic factor for both survival indices [log-rank $P = 0.031$ (HR 6.2, 95% CI: 1.18–11.76)] in the BMI ≥ 30 group. Regarding the overall study population, there was a trend towards poor relapse free survival for obese/morbid obese patients, but it did not reach statistical significance. Post-menopausal status

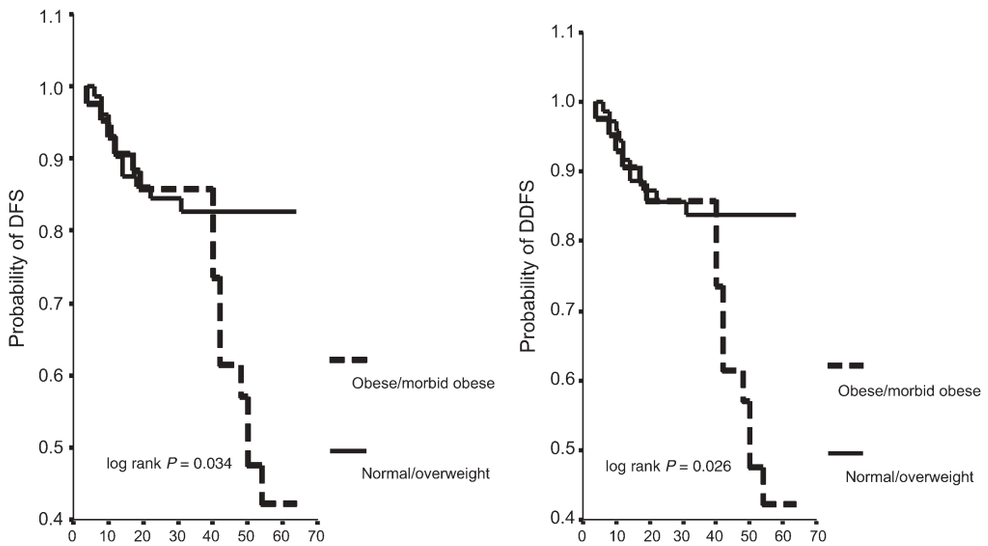


Figure 1. Distant disease free survival (DDFS) and disease free survival (DFS) of post-menopausal patients according to body mass index.

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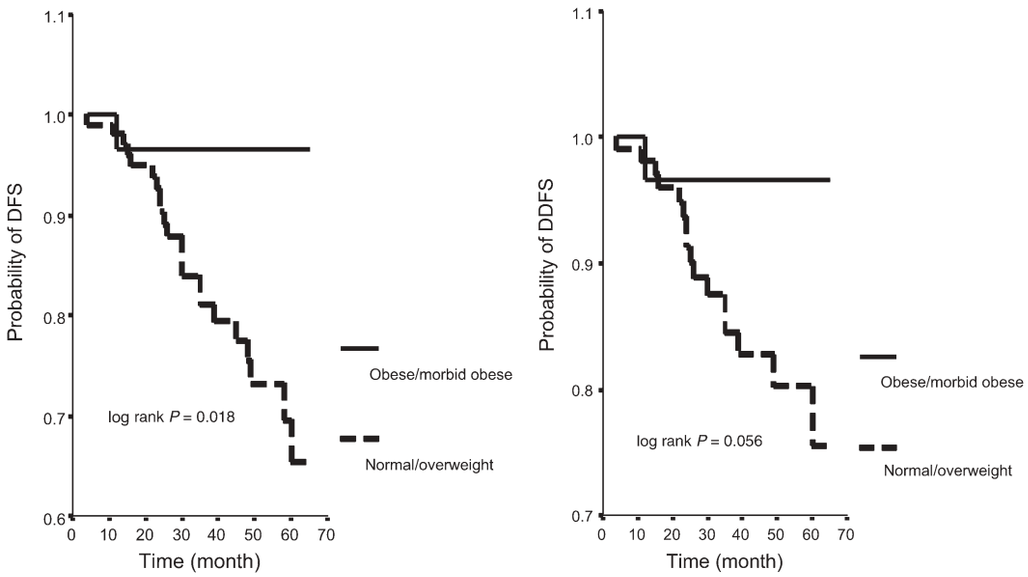


Figure 2. Disease free survival (DFS) and distant disease free survival (DDFS) of pre-menopausal patients according to body mass index.

[log-rank $P = 0.042$ (HR 2.46, 95% CI: 1.04–5.80)] and lymph node involvement [log-rank $P = 0.005$ (HR 1.6, 95% CI: 0.40–5.76)] were the independent negative predictors of DSF and DDSF for all of the patients.

DISCUSSION

Excess body weight is the sixth most important risk factor contributing to the overall burden of diseases worldwide. It leads to many comorbidities. This association is profoundly important for the affected individuals, but the associated morbidity is also economically damaging for society. Many factors such as age, gender, ethnicity, educational, economical and marital status, parity, dietary and smoking habits, alcohol consumption and physical activity influence the development of obesity besides genetic factors (25–27). High prevalence of obesity and metabolic syndrome, particularly among women, is one of the major public-health problems in Turkey (28–30). In developing countries such as Turkey, lifestyle changes following modernization and urbanization bring the increment in obesity prevalence (31–34). Education levels are also shown to play a role in the prevalence of obesity. According to a population-based study in Istanbul, a higher level of education was associated with a lower prevalance of obesity [low (high school and below) versus high (university and post-graduate studies) education in 2003: obesity prevalance for males, 34% versus 26% and for females, 45% versus 15% respectively] (35).

In another population-based study, it is reported that the onset of menopause in Turkish women living in the west Anatolian rural region is earlier on average than women living in western or industrialized countries (36).

In our study, post-menopausal Turkish women had significantly higher body mass index than pre-menopausal Turkish women. Adult weight gain is an established risk factor for breast cancer in post-menopausal women. The exact mechanism for this increased risk of breast cancer in obese women is not fully understood. However, it is hypothesized that this is a function of lifetime exposure to oestrogen, because the oestrogen milieu is important in the initiation and the progression of breast cancer. Obese women have higher levels of circulating oestrogens than leaner women. In post-menopausal women, the main source of oestrogen is from the conversion of androgen precursor androstenedione in the peripheral adipocytes to oestrogen; thus the greater the amount of adipose tissue, the greater the conversion and hence the greater the exposure of breast cells to oestrogen. Lower levels of sex hormone-binding globulins which increase the bioavailability of oestrogen in post-menopausal obese women and insulin resistance associated with hyperinsulinemia are other suggested mechanisms. Oestrogen levels in pre-menopausal women do not vary by BMI and ovarian-derived oestrogen in pre-menopause is the main source of endogenous oestrogen rather than adipose tissue. According to a meta-analysis, there is a significant trend for a decreased relative risk (RR) for breast cancer in pre-menopausal women in association with increasing BMI (1,37–39). In a recent study, post-menopausal obese breast cancer survivors (BMI ≥ 30) had 35% higher concentrations of estrone and 130% higher concentrations of estradiol compared with post-menopausal lighter-weight survivors (BMI < 22.0), as well as concentrations of free estradiol and free testosterone that were two to three times greater in overweight and obese survivors compared with lighter-weight ones (40).

As it was reported in the literature, our study patients in the highest category of BMI did not only have greater tumor size but also aggressive phenotype with vascular (blood vessel) invasion. The metabolic consequences of obesity act

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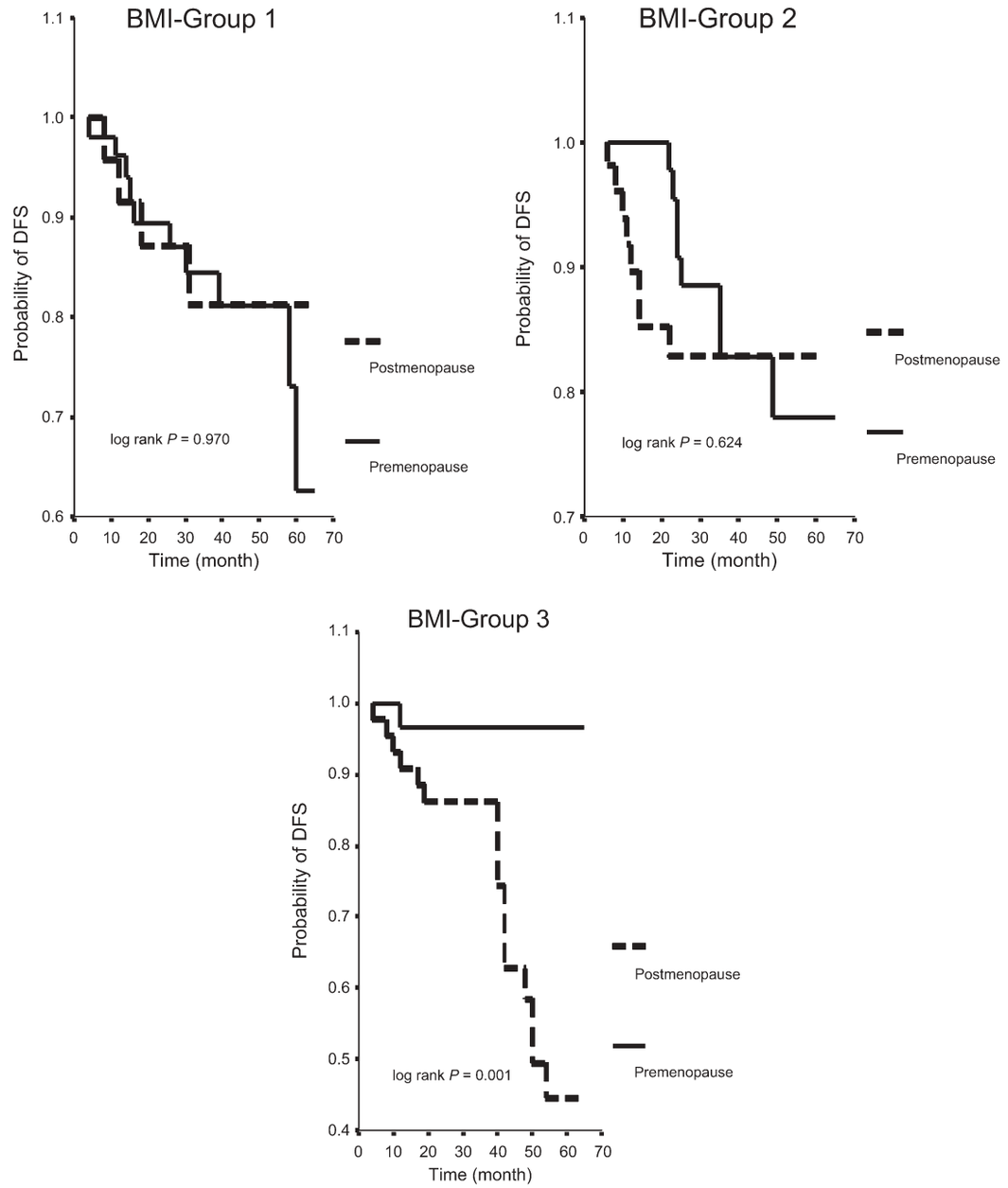


Figure 3. Disease free survival (DFS) according to body mass index (BMI) and menopausal status.

to increase generalized tumor growth, but they promote the selection and growth of more aggressive cells in addition. There is some evidence that the metabolic changes associated with insulin resistance and, in particular, the related alteration in cytokine production by adipose tissue defined as adipocytokines—vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), leptin, tumor necrosis factor-alpha (TNF-α), heparin-binding epidermal growth factor-like growth factor (HBEGF), and interleukin-6 (IL-6) are major contributors to the aggressive behavior of breast cancers that develop in obese women through their effects on angiogenesis and stimulation of invasive capacity of cancer cells (41–50). In early stage development of adipose tissue, adipogenesis is tightly associated with angiogenesis. Adipose tissue, unlike other organs, grows and develops continuously throughout life. The adipocyte-derived cytokine, leptin, has been shown to control metabolism by affecting the metabolic, neuroendocrine, reproductive, immune and hematopoietic systems. Although initially thought to be exclusively expressed in and secreted by adipocytes, leptin has been identified in additional tissues, such as placenta, gastric and colonic mucosa, as well as mammary epithelial cells. Serum leptin levels has been shown to be significantly correlated with BMI. Leptin exerts its effects through the

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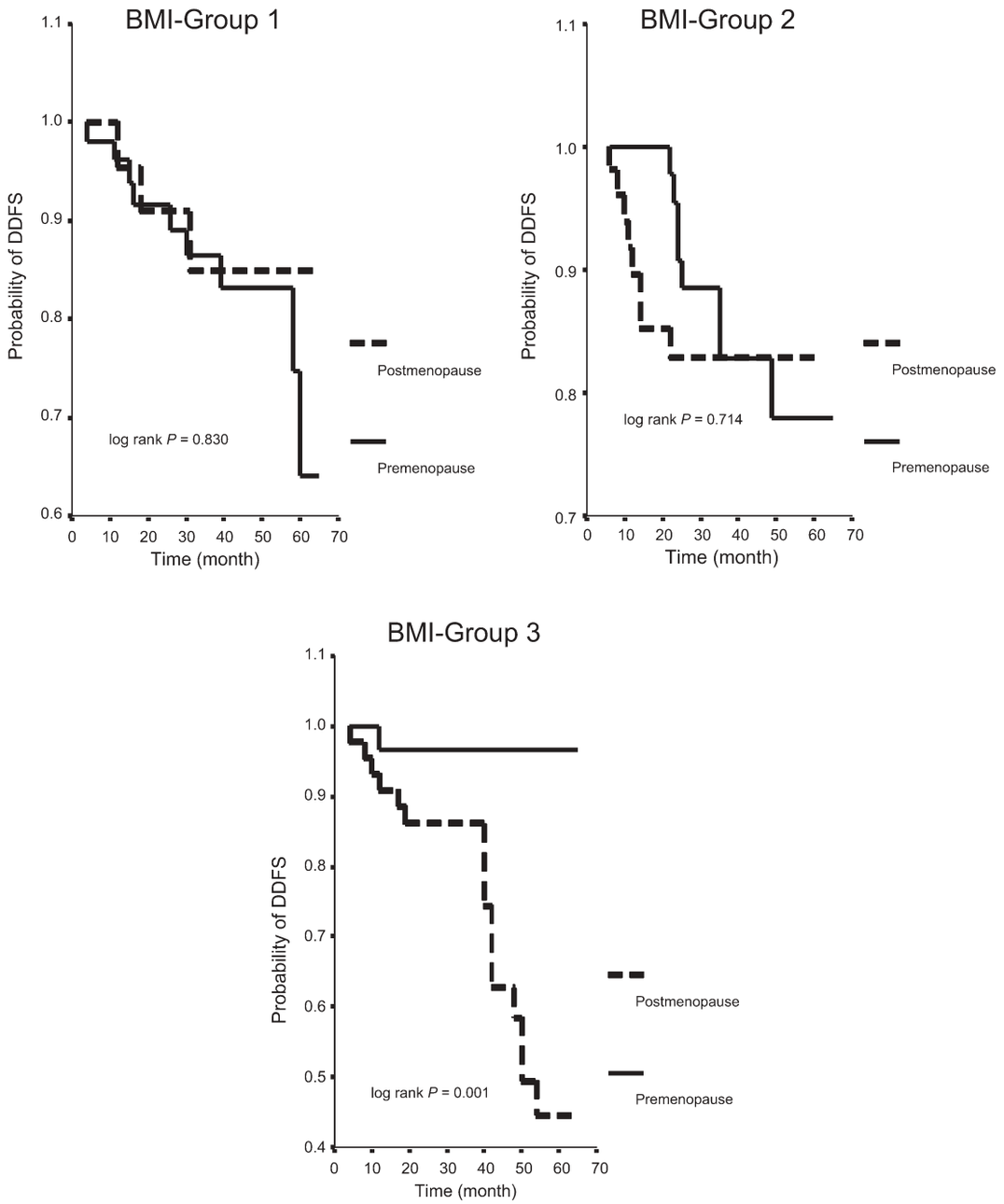


Figure 4. Distant disease free survival (DDFS) according to body mass index (BMI) and menopausal status.

transmembrane leptin receptor [Lep-R (OB-Rb)], which is similar to class I cytokine receptors. Leptin may have a promoting effect on the carcinogenesis and metastasis of breast cancer, possibly in an autocrine manner, by stimulation of normal and tumor cell growth, tumor migration and invasion, enhancement of angiogenesis and enhanced aromatase activity. An epidemiological study has indicated that breast cancer in obese women is more aggressive, with a poor prognosis. Very recently, it has been reported that high expression of both leptin and Lep-R in breast cancer tissue, high serum leptin levels, leptin and leptin receptor polimorphisms were associated with poor prognosis of breast carcinoma (51–56).

Although all of the study patients received appropriate adjuvant systemic treatments as indicated, a potential explanation for negative outcome of post-menopausal obese women may be the possible effect of obesity on the metabolism of drugs used or on the efficacy. Nowadays, aromatase inhibitors are recommended for adjuvant endocrine treatment of hormone responsive post-menopausal breast cancer patients, so there is possibility of drug resistance or insufficiency owing to obesity (57–59).

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Our study was subject to some limitations. First of all, there was a limited number of patients available for retrospective analysis because the study was carried out in a single institution. However, an advantage was that our case group was homogeneous with safety data. An additional limitation was the lack of information on possible prognostic or confounding factors occurring after breast cancer diagnosis such as post-diagnosis weight change.

It is suggested that reduction of obesity can decrease the cases of breast cancer by one-tenth in Europe with a consequent reduction in mortality. It is feared that increasing prevalence of obesity in women will not only manifest its effect of increased incidence of breast cancer but also other obesity-related disorders such as metabolic syndrome, diabetes mellitus and cardiovascular diseases in both western populations and Turkey in the coming years (25,26,60). As striking data, there is also a constant increase in BMI of Turkish children towards adulthood, especially during the pubertal years, in both sexes (61,62).

Since obesity is one of the few risk factors for breast cancer and poor prognosis which can be modified throughout life, a public-health policy, planning, health education and public awareness campaigns are urgently required to address the rising problems and reduce mortality in developing countries such as Turkey with limited financial resources.

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Conflict of interest statement

None declared.

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