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Relationship between SUVmax in F-18 FDG PET/CT and serum YKL-40 levels in Breast Cancer

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ABSTRACT

This investigation aimed to study the differences in tumor maximum standardized uptake values (SUVmax) in breast cancer patients and compare serum levels of YKL-40, an inflammatory glycoprotein found at high levels in patients with different types of cancer, with healthy controls.

Fifty-one women who underwent 18F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET/CT) imaging for the staging of pathologically-confirmed breast cancer were included. The tumor SUVmax of each patient was calculated by 18F-FDG PET/CT. Serum YKL-40, ischemia modified albumin (IMA), carcinoembryonic antigen (CEA), and cancer antigen 15-3 (CA15-3) levels were assessed after the PET/CT imaging. A group of 38 healthy women were included as controls, from which serum YKL-40 and IMA levels were obtained.

Compared to healthy subjects, serum YKL-40 and IMA levels were significantly higher in patients with breast cancer ($p<0.001$ for both). Patients with a tumor size of 2-5 cm had significantly higher YKL-40 ($p=0.002$), SUVmax ($p=0.008$), CEA ($p=0.025$), and CA15-3 ($p=0.016$) measurements than patients with a tumor size of <2 cm. However, IMA levels did not vary ($p>0.05$) between the two groups of tumor sizes. While YKL-40 showed significant correlations with CA15-3 ($r=0.318$, $p=0.023$) and IMA ($r=0.257$, $p=0.016$), no correlation was found between SUVmax and the measured serum variables in the breast cancer group ($p>0.05$).

Our results indicate that serum IMA and YKL-40 levels were above average in breast cancer patients. Also, increasing SUVmax and serum YKL-40 levels may be separately observed related to tumor size. YKL-40 and SUVmax may be utilized in the evaluation and follow-up of breast cancer.

Keywords: Breast Cancer; PET/CT; Chitinase-3-Like Protein 1; YKL-40 Protein; Biochemical Tumor Markers

Introduction

Globally, breast cancer is the highest encountered cancer in women and among the top causes of cancer-related mortalities (1). According to data from Turkey, in the year 2015, breast cancer is the most common (43.8/100.000 women) type of cancer in women, accounting for about a quarter of all cancers in women (2).

Metabolic scanning using 18F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET/CT) is a long-known technique. It considers the high proportions of glucose influx into the tumor tissue. On the other hand, accurate initial staging in breast cancer is critical for precise prognostication and optimal choice of therapy. 18F-FDG PET/CT is currently employed for staging, checking for remaining malignant tissue after treatment, and screening for recurrences in breast cancers (3,4). It can semiquantitatively measure the functional metabolism in tumor cells (5). The most strong 18F-FDG uptake in the index lesion is computed as the maximum standardized uptake value (SUVmax), which is a semiquantitative measurement (6,7).

YKL-40 is a 40 kDa heparin- and chitin-binding glycoprotein, also referred as human cartilage glycoprotein 39 (HC-gp39) (8), 38-kDa heparin-binding glycoprotein (9), or chitinase-3-like protein 1 (CHI3L1) (10), it was discovered in 1993 by Hakala et al. (8). YKL-40 is released from activated microglia and exhibits inflammatory processes (11,12), but its function is not known entirely; it is considered as a product of the inherent immune system, which has some roles in

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remodeling in inflammatory conditions [13]. YKL-40 may be a promising indicator in cancer patients, for it may affect the growth and distinction of tumor cells. It was found that YKL-40 is present in many types of malignancies, including breast, colon, kidney, lung, glioblastoma, pancreas, and thyroid. Moreover, a relationship between high serum YKL-40 levels and worse survival outcome has been detected [14].

Ischemia modified albumin (IMA) indicates oxidative stress and is a product generated from albumin as a result of hypoxia [15]. Serum IMA levels were widely determined for different types of ischemic diseases. It is a modified protein generated during acute ischemic conditions [16]. Also, levels of serum IMA were found to be high in gastric, colorectal, prostate, soft tissue cancer, and neuroblastoma patients [17–20]. A few reports have mentioned serum IMA levels in breast cancer patients [21].

Cancer antigen 15-3 (CA15-3) and carcinoembryonic antigen (CEA) are routinely assayed serum tumor indicators in breast cancer patients.

We hypothesized that the SUVmax, YKL-40, CA15-3, CEA, and IMA levels may change with tumor size and can be used as markers of breast cancer.

This study aimed to analyze the differences in tumor SUVmax of patients with breast cancer and to compare serum YKL-40 levels with healthy controls. In addition, differences in SUVmax, serum YKL-40, IMA, CEA and CA15-3 levels in the patient group according to tumor diameter were investigated.

Methods and Materials

This study was carried out in a case-control plan at the department of nuclear medicine between July 2012-July 2013. During the study period, the department was serving monthly around 150 patients. A written informed agreement was obtained from all participants, and ethical permission was taken from the hospital's local ethics board.

Fifty-one women who underwent PET/CT imaging for initial staging were included in the study. The interval between PET/CT imaging and breast biopsy was minimum two weeks. The patients were confirmed to have breast cancer per pathological examination. No patients had any connective tissue or other systemic disease or received any treatment before PET-CT scanning. Among the patient relatives, 38 healthy adult women agreed to join the study as controls without any age restriction. The control participants did not have any history of previous cancer, chemotherapy, other chronic or inflammatory conditions, or chronic medication use. (Figure 1).

The independent study variable was patients and healthy women groups. Dependent study variables were YKL-40 levels and IMA. Additionally, SUVmax, CA15-3, and CEA levels were assessed in the patient group. Depending on the tumor size, the participants were split into two groups as <2 cm and 2-5 cm. Ages of the patients, lymphovascular invasion, presence of metastasized nodes, or distant tumor spread were recorded.

Post hoc sample size estimation was done centered on the primary outcome variable mean YKL-40 levels. A total sample size of 89 participants (51 study cases and 38 healthy controls) provides a power of 80% to entirely mean YKL-40 levels using the Student's t-test with an effect size of 0.61 (sufficient to compare $mean_1=32$ and $mean_2=38$ given a standard deviation of 10) and an alpha error of 0.05 [22].

18F-FDG PET/CT protocol: All patients fasted for minimally 6 hours, and their serum glucose was analyzed before 18F-FDG injection to ascertain that the level was less than 200 mg/dL. An intravenous injection of 444–555 MBq (12–15 mCi) 18F-FDG was applied to the patients and 60–90 minutes of resting was requested after the injection. PET/CT scans were done using a Siemens Biograph PET/CT system (Siemens, Knoxville, TN, USA). A low-dose CT scan was taken from the vertex to the thigh. Then, PET imaging was performed (7-9 beds, 3 min/bed) in the supine position. Increased 18F-FDG uptake compared to the background behavior was identified as unnatural, and CT images were used for anatomical information. In each case, the region of interest was taken manually from the PET/CT images that displayed the most extreme 18F-FDG uptake in the primary breast lesion, and the SUVmax was automatically measured.

Biochemical analysis: Before PET/CT scanning, blood samples from 51 breast cancer patients were taken, serum samples were obtained, and then the sera were kept at a deep freeze (-80 ºC) till the day of analysis. Serum YKL-40, IMA, CEA, and CA15-3 values were measured. Additionally, YKL-40 and IMA levels were analyzed in healthy volunteer serum samples. YKL-40 serum levels were measured with a commercially available YKL-40 Quantikine ELISA Kit (Cat DC3L10, R&D Systems, Inc. Minneapolis,

Table 1. Descriptive Presentation of The Tumor-Related Characteristics

		n	%
Tumor size	<2 cm	18	35.3
	2-5 cm	33	64.7
Pathological examination	Invasive ductal	45	88.2
	Invasive lobular	3	5.9
	Mixed	3	5.9
Lymphovascular invasion	No	8	21.6
	Yes	29	78.4
Metastatic lymph nodes	No	10	28.6
	Yes	25	71.4
Metastatic lymph nodes in PET/CT	No	21	41.2
	Yes	30	58.8
Distant metastasis	No	46	90.2
	Yes	5	9.8

Table 2. Comparison of SUVmax and Some Biochemical Variables According To Tumor Size

	Tumor size					
	<2 cm		2-5 cm			
	Median	IQR	Median	IQR	Z	p
SUVmax	3.21	4.19	6.65	6.68	2.661	0.008
YKL-40 (ng/ml)	32.26	15.38	53.58	38.76	3.134	0.002
CA15-3 (ng/ml)	13.55	8.64	20.40	13.90	2.415	0.016
CEA (U/ml)	1.56	0.67	2.28	2.46	2.237	0.025
IMA (U/mL)	0.84	0.10	0.86	0.15	0.195	0.846

IQR: Interquartile Range, Z: Mann-Whitney U test value

MN, USA). Serum samples were diluted at 1:50 with the assay buffer. Serum IMA was measured using the albumin cobalt binding assay. The findings were reported as absorbance unit (ABSU). Serum CEA levels were measured in a DXI analyzer using the chemiluminescence method (Beckman Coulter, USA). Serum CA15-3 was measured by commercially available EIA kits (CanAg CA15-3, Fujirebio Diagnostics, Inc. Malvern, PA, United States).

Statistical methods: Data was entered into the computer and analyzed using the SPSS 25.0 software (SPSS, Chicago, Illinois, USA). The results were presented as frequencies, percentages, mean, standard deviations (SD), median, and interquartile range (IQR). All numerical data were tested for normality using the Shapiro-Wilk test. The comparison of two independent groups for a numerical variable was performed by the Mann-Whitney *U* test. Correlations were assessed using the Spearman's rank correlation. Logistic regression analysis was performed to check the independent effects of IMA and YKL-40 on classifying breast cancer. A p-value of <0.05 was regarded as statistically significant.

Results

Results for 51 patients with breast cancer and 38 healthy women are reported. The median age of the participants was 50.55±10.94 years (min. 30, max. 72). Of the 51 women with cancer, 18 had a tumor size <2 cm, while 33 had a tumor size of 2-5 cm. The pathological examination showed invasive ductal carcinoma as the most common tumor type (88.2%; n=45). On the other hand, a lymphovascular invasion was present in 78.4% (n=29) of the patients. The majority had no distant metastasis (Table 1).

Outcome Data: The mean SUVmax, YKL-40, CEA, and CA15-3 levels of patients with a 2-5 cm tumor diameter were significantly elevated than those with a tumor size of <2 cm, but IMA levels in the two groups were not different (Table 2).

In patients with breast cancer, higher serum YKL-40 and IMA levels were seen compared to the healthy subjects (Table 3, Figure 2).

YKL-40 showed significant correlations with CA15-3 (r=0.318, p=0.023) and IMA (r=0.257,

Table 3. Comparison of IMA and YKL-40 Levels In Patient and Control Groups

	Groups					
	Breast cancer		Healthy controls			
	Median	IQR	Median	IQR	Z	p
IMA (U/mL)	0.84	0.12	0.70	0.12	4.145	<0.001
YKL-40 (ng/ml)	44.96	43.25	31.36	16.72	3.724	<0.001

IQR: Interquartile Range, Z: Mann-Whitney U test value

Table 4. Logistic Regression Analysis Computer Output

						95% CI for EXP (B)	
	B	SE	Wald	p	Exp (B)	Lower	Upper
IMA	3.634	1.648	4.863	0.027	37.855	1.498	956.542
YKL-40	0.045	0.014	9.819	0.002	1.046	1.017	1.077
Constant	-4.293	1.401	9.386	0.002	0.014		

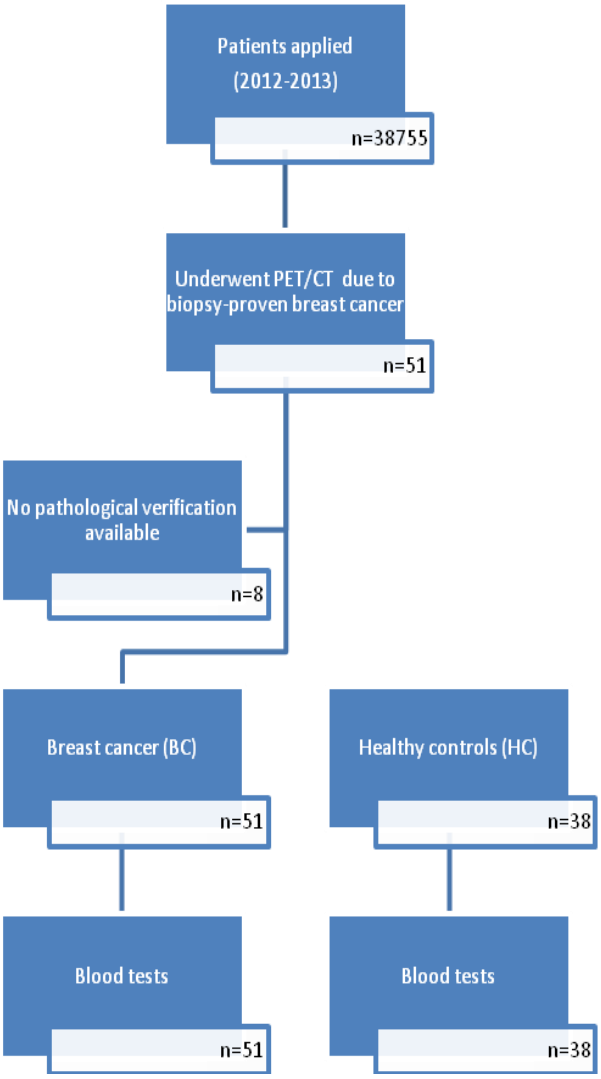

Fig. 1. Participant Flow Chart

p=0.016). However, there were no correlations with SUVmax and the other measured serum variables in the breast cancer group (p>0.05). When a logistic regression analysis was performed, the combined use of IMA and YKL-40 had a sensitivity of 74.0% and a specificity of 78.9% in correctly classifying breast cancer patients (overall percentage: 76.1%). Both variables had significant effects on the outcome (Table 4).

Discussion

The serum YKL-40 levels and IMA values were higher in breast cancer patients compared to healthy participants. The mean SUVmax, YKL-40, CA15-3, and CEA measurements of women with larger tumors were considerably larger than those with smaller tumor sizes. Combined, YKL-40 and IMA measurements have an overall 76.1% predictive capacity for detecting breast cancer.

The results should be interpreted in in light of the fact that our sample size allows for a relatively large effect size. On the other hand, among the studied variables, only YKL-40 and IMA were studied both in cancer and control groups. Another limitation is the time gap between study conduction and reporting, which was due to the personal problems of the primary author. However, the relationships of YKL-40 and IMA with breast cancer are still not sufficiently elaborated.

The advantages of PET/CT in malignant condition diagnoses made this imaging modality more preferable for patients and health professionals. PET/CT scans are increasingly ordered in breast cancer patients before or after surgery [14]. Furthermore, increased YKL-40 levels in the circulation were found in many solid tumors including breast, endometrial cancer, lung, ovarian cancer, colon, prostate, bladder, squamous cell cancer of the esophagus, melanoma, and glioblastoma, which was suggested as a predictor of poor outcome or short disease-free survival [23]. Large-sample clinical research performed in Danish people indicated that

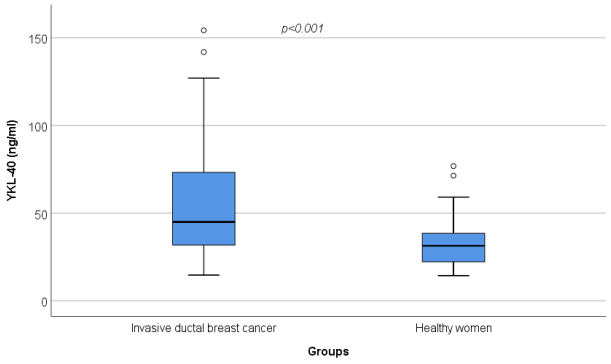

Fig. 2. Comparison of YKL-40 levels in patient and control groups

higher levels of plasma YKL-40 increase the risk of early mortality from cancer, cardiovascular disease, and other health conditions [24]. Our results demonstrate that serum YKL-40 levels are higher in invasive ductal carcinoma patients compared to healthy controls.

Studies investigating IMA and breast cancer are scarce. IMA Ma et al. [25] reported that there was a significant difference in IMA levels before and after each cycle of doxorubicin chemotherapy, and the IMA levels positively correlated with the cumulative doses in patients with breast cancer. Also, Abusoglu et al. [21] reported that the IMA level was higher in patients than in control subjects. Similarly, in our study, the IMA level was higher in cancer patients than in the control group.

Çiledağ et al. [26] reported that tumor size was not related to the blood YKL-40 values in individuals with lung cancer. On the contrary, Wang et al. [27] mentioned that a significantly higher percentage of breast cancer patients with YKL-40 positive tumors had a bigger tumor size. Our results show that a positive relationship is present between YKL-40 and tumor size. On the other hand, although we found an association between tumor size and CA15-3 as well as CEA levels, Fujimoto et al. [28] showed that tumor size was not associated with serum CA15-3 and CEA values in women having breast malignancies. However, this issue needs further clarification with other studies.

Karam et al. [29] showed that SUVmax of non-small cell lung cancer patients had a substantial correlation with tumor size. Besides, Ozgul et al. [30] published the same figures before, in people with non-small cell lung malignancy. Our results show that a positive relationship was founded between SUVmax and tumor size. The literature lacks any report in patients with breast cancer showing significant differences of SUVmax for different patient groups categorized based on the tumor size.

PET/CT combines anatomical and functional imaging, which has been shown to increase the accuracy of the detection of recurrences and metastases [31]. SUVmax has been shown to be correlated with tumor size and invasion [32,33]. Our findings support the knowledge that higher SUVmax values may indicate higher malignancy of the tumor and worse treatment outcomes. In light of our findings, it may be claimed that PET/CT SUVmax values associate well with the immunohistochemical YKL-40 results and tumor size.

To the best of our knowledge, there is no investigation on the combined effects of YKL-40 and IMA in patients with breast cancer. We believe that our report can contribute to the medical literature by guiding researchers focusing on novel diagnostic methods for detecting and classifying breast cancer.

Conclusion

The combined analysis of serum YKL-40 and IMA levels can contribute to the diagnosis of breast cancer. Furthermore, higher SUVmax, YKL-40, CA15-3, and CEA values in women having breast malignancies indicate larger tumor sizes. Studies with bigger sample sizes and more predictive variables can suggest cheap, fast, and non-invasive methods in the diagnosis of breast cancer.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018. doi:10.3322/caac.21492.
2. İlter H, Keskinkılıç B. [Turkey Cancer Statistics 2015]. 1st ed. Ankara: [General Directorate of Public Health, Ministry of Health]; 2018.
3. Cochet A, Dygai-Cochet I, Riedinger JM, et al. 18F-FDG PET/CT provides powerful prognostic stratification in the primary staging of large breast cancer when compared with conventional explorations. Eur J Nucl Med Mol Imaging 2014. doi:10.1007/s00259-013-2595-4.
4. Groheux D, Hindié E, Delord M, et al. Prognostic impact of 18FDG-PET-CT findings in clinical stage III and IIB breast cancer. J Natl Cancer Inst 2012. doi:10.1093/jnci/djs451.
5. Fuster D, Duch J, Paredes P, et al. Preoperative staging of large primary breast cancer with [18 F] fluorodeoxyglucose positron emission tomography/computed

tomography compared with conventional imaging procedures. J Clin Oncol 2008. doi:10.1200/JCO.2008.17.1496.

6. Pujara AC, Raad RA, Ponzo F, et al. Standardized uptake values from PET/MRI in metastatic breast cancer: An organ-based comparison with PET/CT. Breast J 2016. doi:10.1111/tbj.12569.
7. Lucignani G, Paganelli G, Bombardieri E. The use of standardized uptake values for assessing fdg uptake with pet in oncology: A clinical perspective. Nucl Med Commun 2004. doi:10.1097/01.mnm.0000134329.30912.49.
8. Hakala BE, White C, Recklies AD. Human cartilage gp-39, a major secretory product of articular chondrocytes and synovial cells, is a mammalian member of a chitinase protein family. J Biol Chem 1993;268:25803–10.
9. Shackelton LM, Mann DM, Millis AJ. Identification of a 38-kDa heparin-binding glycoprotein (gp38k) in differentiating vascular smooth muscle cells as a member of a group of proteins associated with tissue remodeling. J Biol Chem 1995;270:13076–83.
10. Rehli M, Krause SW, Andreesen R. Molecular characterization of the gene for human cartilage gp-39 (CHI3L1), a member of the chitinase protein family and marker for late stages of macrophage differentiation. Genomics 1997;43:221–5. doi:10.1006/geno.1997.4778.
11. Rolstad S, Jakobsson J, Sellgren C, et al. Cognitive performance and cerebrospinal fluid biomarkers of neurodegeneration: a study of patients with bipolar disorder and healthy controls. PLoS One 2015;10:e0127100. doi:10.1371/journal.pone.0127100.
12. Hellwig K, Kvartsberg H, Portelius E, et al. Neurogranin and YKL-40: independent markers of synaptic degeneration and neuroinflammation in Alzheimer's disease. Alzheimers Res Ther 2015;7:74. doi:10.1186/s13195-015-0161-y.
13. Bonneh-Barkay D, Bissel SJ, Kofler J, Starkey A, Wang G, Wiley CA. Astrocyte and macrophage regulation of YKL-40 expression and cellular response in neuroinflammation. Brain Pathol 2012;22:530–46. doi:10.1111/j.1750-3639.2011.00550.x.
14. [Wan G, Xiang L, Sun X, et al. Elevated YKL-40 expression is associated with a poor prognosis in breast cancer patients. Oncotarget 2017;8:5382–91. doi:10.18632/oncotarget.14280.
15. [Kocaoglu C, Erdem SS, Ozel A. Is Level of Serum Ischemia-Modified Albumin A Useful Biomarker in Carbon Monoxide Poisoning Cases? Pediatr Emerg Care 2017. doi:10.1097/PEC.0000000000000587.
16. Sbarouni E, Georgiadou P, Voudris V. Ischemia modified albumin changes - Review and clinical implications. Clin Chem Lab Med 2011. doi:10.1515/CCLM.2011.037.
17. Stachowicz-Stencel T, Synakiewicz A, Owczarzak A, et al. Ischemia-modified albumin as a biochemical marker in children with neuroblastoma and soft tissue sarcomas. J Clin Lab Anal 2011. doi:10.1002/jcla.20469.
18. Da Silveira RA, Hermes CL, Almeida TC, et al. Ischemia-modified albumin and inflammatory biomarkers in patients with prostate cancer. Clin Lab 2014. doi:10.7754/Clin.Lab.2014.131018.
19. Satoh M, Kotani K, Gugliucci A, Horie H, Caccavello R, Takeuchi M. Correlation of ischemia-modified albumin with sofa and apache ii scores in preoperative patients with colorectal cancer. Sci World J 2014. doi:10.1155/2014/959075.
20. Huang QX, Ma J, Wang YS. Significance of preoperative ischemia-modified albumin in operable and advanced gastric cancer. Cancer Biomarkers 2018. doi:10.3233/CBM-171090.
21. Abusoglu S, Eryavuz D, Bal C, et al. Assessment of Serum Ischemia-modified albumin, Prolidase and Thiol-Disulphide Levels in Subjects With Breast Cancer. Rev Rom Med Lab 2019. doi:10.2478/rrlm-2019-0013.
22. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3:A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007.
23. Kzhyshkowska J, Yin S, Liu T, Riabov V, Mitrofanova I. Role of chitinase-like proteins in cancer. Biol Chem 2016. doi:10.1515/hsz-2015-0269.
24. Johansen JS, Bojesen SE, Tybjærg-Hansen A, Mylin AK, Price PA, Nordestgaard BG. Plasma YKL-40 and total and disease-specific mortality in the general population. Clin Chem 2010. doi:10.1373/clinchem.2010.146530.
25. Ma Y, Kang W, Bao Y, Jiao F, Ma Y. Clinical significance of ischemia-modified albumin in the diagnosis of doxorubicin-induced myocardial injury in breast cancer patients. PLoS One 2013. doi:10.1371/journal.pone.0079426.
26. Çiledağ A, Kabalak PA, Çelik G, et al. High serum YKL-40 level is associated with poor prognosis in patients with lung cancer. Tuberk Toraks 2018. doi:10.5578/tt.67319.
27. Wang D, Zhai B, Hu F, Liu C, Zhao J, Xu J. High YKL-40 Serum Concentration Is Correlated with Prognosis of Chinese Patients with Breast Cancer. PLoS One 2012. doi:10.1371/journal.pone.0051127.

28. Fujimoto Y, Higuchi T, Nishimukai A, et al. High levels of serum CA15-3 and residual invasive tumor size are associated with poor prognosis for breast cancer patients with non-pathological complete response after neoadjuvant chemotherapy. J Surg Oncol 2018. doi:10.1002/jso.25125.
29. Karam MB, Doroudinia A, Behzadi B, Mehrian P, Koma AY. Correlation of quantified metabolic activity in nonsmall cell lung cancer with tumor size and tumor pathological characteristics. Med (United States) 2018. doi:10.1097/MD.0000000000011628.
30. Ozgul MA, Kirkil G, Seyhan EC, Cetinkaya E, Ozgul G, Yuksel M. The maximum standardized FDG uptake on PET-CT in patients with non-small cell lung cancer. Multidiscip Respir Med 2013;8:69. doi:10.1186/2049-6958-8-69.
31. Yararbas U, Avci NC, Yeniay L, Argon AM. The value of 18F-FDG PET/CT imaging in breast cancer staging. Bosn J Basic Med Sci 2018;18:72.
32. Sanli Y, Kuyumcu S, Ozkan ZG, et al. Increased FDG uptake in breast cancer is associated with prognostic factors. Ann Nucl Med 2012;26:345–50.
33. Groheux D, Cochet A, Humbert O, Alberini J-L, Hindié E, Mankoff D. 18F-FDG PET/CT for staging and restaging of breast cancer. J Nucl Med 2016;57:17S-26S.