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Research Article

Predictability of Bone Metastasis with the Monocyte/HDL-Cholesterol Ratio in Breast Cancer Patients

Fuzuli Tugrul,[1] Utku Donem Gundogdu[2]

[1]Department of Radiation Oncology, Eskişehir Acıbadem Hospital, Eskişehir, Türkiye
[2]Department of Medical Oncology, Afyonkarahisar Park Hayat Hospital, Türkiye

Abstract

Objectives: Monocyte/HDL-C is a marker of inflammation. One of the most common sites of metastasis by breast cancer is bone. This study was purposed to define the predictability of bone metastasis with the Monocyte/HDL-Cratio in breast cancer patients.

Methods: Study consisted of patients diagnosed with breast cancer. Patients with breast cancer bone metastasis detected by whole body bone scan and pet-CT were included.

Results: A comparison of monocyte/high-density lipoprotein was planned in patients with and without breast cancer bone metastases. Patients with hematological disease, using lipid-lowering drugs, and lipid metabolism disorders were excluded from the study. A statistically significant difference was determined between the patients' bone metastasis status and LDL values at 99% confidence level [t(207) = 1.899; p=0.049; p<0.05]. On the other hand, whether the patients have bone metastasis or not, no statistically significant difference was found in case of Monocyte/HDL (p = 0.878; p>0.05), Monocyte/Lymphocyte (p=0.239; p>0.05), HDL (p=0.235; p>0) 0.05), TG (p=0.819; p>0.05), and total cholesterol (p=0.285; p>0.05).

Conclusion: This study was applied to determine the predictability of bone metastasis with the monocyte/HDL-C ratio in breast cancer patient. Monocyte/HDL of the patients having breast cancer bone metastasis (BCBM) was compared with non-BCBM patients but there was no significant correlation between monocyte/HDL-C, monocyte/lymphocyte, HDL-C, TG, and total cholesterol.

Keywords: Bone Metastasis, Breast cancer, HDL-C, LDL- C

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Most widespread causes of death in the world are cardiovascular diseases and cancer. The etiopathogenesis of both shows similar features. The main mechanisms in the formation of both diseases are inflammation, uncontrolled cell proliferation and oxidative stress. The later causes deterioration of cell proliferation, development of atherosclerotic plaque, and formation of cancer.[1]

Atherosclerosis and cancer are considered as chronic inflammatory diseases. Pro-inflammatory and inflammatory cytokines (e.g., IL-6), C-reactive protein (CRP), and TNF-α have been found to be elevated in cardiovascular disease and cancer e.g., prostate, colon, ovary, lung.[2-6] High-density lipoprotein cholesterol (HDL-C) is a protective lipid for atherosclerosis. Studies have found its antioxidant, anti-

Address for correspondence: Fuzuli Tugrul, MD. Department of Radiation Oncology, Eskişehir Acıbadem Hospital, Eskişehir, Türkiye
Phone: +90 533 572 50 82 **E-mail:** tugruldrfuzuli@gmail.com

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inflammatory and anti-thrombotic effects.[7-9] It has been associated with decreased production of pro-inflammatory agents such as HDL-C, IL-6 and tumor necrosis factor receptors, and rised levels of anti-inflammatory cytokines such as interleukin 10 (IL-10), which induces apoptosis.[10]

Monocyte/HDL-C level was used as a marker of oxidative stress due to inflammation. HDLC counteracts the prooxidant and proinflammatory effects of monocytes by inhibiting the oxidation of LDL cholesterol and macrophage migration.[11,12] Therefore, features such as monocyte count (MHR) to HDL-C ratio may indicate the patient's inflammatory status. Coharent with this, the relate between increased MHR and case of atherosclerosis has been showned. MHR has arised as a new indication of inflammation in studies.

Inflammatory cytokines activate angiogenesis and have been found to be effective in drug resistance. Many studies have been carried out to determine the efficacy of anti-inflammatory agents targeting cytokines and chemokines, transcription factors or inflammatory cells in cancer treatment.[13]

Chronic inflammation of myeloid cells, including macrophages and neutrophils, contributes to tumor progression and metastasis. Once tumor cells begin to proliferate in the bone, inflammatory signals induced by cancer cells and their interaction with neighboring cells trigger enlargement steps involving virtually all components of the microenvironment in which immune cells have a fundamental role in allowing tumor colonization. Anti-inflammatory therapies have been successfully evaluated to target tumor progression and metastasis and have been found to be associated with deductibleinfiltration of bone marrow-derived myeloid cells and premetastatic macrophages.[14-16] Despite the new treatment modalities of breast cancer, mortality is still high. Inflammation is responsible for the etiopathogenesis and progression of many cancers. Monocyte/HDL-C is a marker of inflammation. One of the most common sites of metastasis by breast cancer is bone. This study was aimed to determine the predictability of bone metastasis with the Monocyte/HDL-C ratio in breast cancer patients.

Methods

The blood lipid profile, hemogram profile and biochemical parameters of the cases over 18 years of age who were diagnosed with breast cancer histopathologically, were scanned and recorded between 01.06.2017 and 01.05.2021 at Afyon Private Parkhayat Hospital Medical Oncology Department and Eskişehir City Hospital Radiation Oncology Department. The ethics committee of the study was confirmed by Afyonkarahisar Health Sciences University, Clinical Research Ethics Committee with the number 399-2011-KAEK-2.

Patients with breast cancer bone metastasis detected by whole body bone scan and pet-CT were included. A comparison of monocyte/high-density lipoprotein was planned in patients with and without breast cancer bone metastases. Patients with hematological disease, using lipid-lowering drugs, and lipid metabolism disorders were excluded from the study.

Results

As seen in Table 1, a statistically significant difference was determined between the patients' bone metastasis status and LDL-C values at 99% confidence level [t(207) = 1.899; p=0.049; p<0.05].

According to this result, LDL-C levels of patients with bone metastases ($\bar{x}$=134.19) were found to be higher than patients without bone metastases ($\bar{x}$= 121.12). On the other hand, whether the patients have bone metastasis or not, no statistically significant difference was found in the case of monocyte/HDL-C (p=0.878; p>0.05), monocyte/lymphocyte (p=0.239; p>0.05), HDL (p=0.235; p>0) 0.05), TG (p=0.819; p>0.05), and total cholesterol (p=0.285; p>0.05).

As seen in Table 2, no statistically significant difference was determined between the bone metastasis subtypes of the patients Er (+) Pr (+) Cerbb (-), Er (+) Pr (-) Cerbb (-), Cerbb (+), Er (-) Pr (-)) Cerbb (-) with monocyte/HDL-C (p=0.722; p>0.05), monocyte/lymphocyte (p=0.778; p>0.05), HDL-C (p=0.940; p>.05), LDL-C (p=0.390; p>.05), TG (p=0.657; p>0.05), total cholesterol (p=0.308; p>0.05).

Discussion

Today, one out of every 8 women must struggle with breast cancer at some point in her life. Despite the difference in survival with newly developed treatment strategies and increased awareness in early diagnosis, treatment success has still not reached the desired level. One of the most common sites of metastasis and recurrence is bone. It has negative effects on the patient's standard of health. The fact that the treatment success is not at the desired level indicates that the disease mechanism is largely undetected.

The effect of cholesterol on carcinogenesis has been shown in many clinical and experimental studies.[17] There are studies that have found the LDL-C to be effective in metastasis and proliferation in breast cancer.[18] Whun-Lu et al.[19] found that L1 and L5 subfractions of LDL-C and VLDL in vitrosupport breast cancer progression and metastasis via Akt-induced EMT and angiogenesis, and dyslipoproteinemia promote breast cancer. High LDL-C values have been identified as a poor prognostic factor in esophageal cancer. High LDL-C values were found to be associated with lymph node metastasis.[20] In our study, LDL-C

Table 1. Analysis of the difference between the patients having bone metastases and the values

Values	Metastasis Group	Levene Test							
		n	$\bar{x}$	SD	F	p	t	df	p
Monocyte/HDL-C	Yes	47	0.01	0.01	0.188	0.665	-0.153	207	0.878
	No	162	0.01	0.01					
Monocyte/Lymphocyte	Yes	47	0.37	0.23	0.683	0.410	1.18		0.239
	No	162	0.32	0.28					
HDL-C	Yes	47	49.77	14.14	0.042	0.837	-1.19		0.235
	No	162	52.67	14.90					
LDL-C	Yes	47	134.19	57.70	3.811	0.052	1.899		0.049*
	No	162	121.12	35.61					
TG	Yes	47	167.23	77.08	1.284	0.258	-0.229		0.819
	No	162	170.84	99.65					
Total Cholesterol	Yes	47	213.21	55.00	2.507	0.115	1.072		0.285
	No	162	205.06	43.00					

*p<0.05; n=209.

Table 2. Analysis of the difference between subgroups and values.

Values	Alt Groups	n	$\bar{x}$	SD	df	F	p
Monocyte/HDL-C	Er(+)Pr(+)Cerbb(-)	120	0.01	0.01	3 - 200	0.443	0.722
	Er(+)Pr(-)Cerbb(-)	16	0.01	0.01			
	Cerbb(+)	47	0.01	0.01			
	Er(-)Pr(-)Cerbb(-)	21	0.01	0.00			
Monocyte/Lymphocyte	Er(+)Pr(+)Cerbb(-)	120	0.34	0.32	3 - 200	0.365	0.778
	Er(+)Pr(-)Cerbb(-)	16	0.31	0.12			
	Cerbb(+)	47	0.32	0.16			
	Er(-)Pr(-)Cerbb(-)	21	0.39	0.24			
HDL-C	Er(+)Pr(+)Cerbb(-)	120	52.30	13.79	3 - 200	0.133	0.940
	Er(+)Pr(-)Cerbb(-)	16	50.44	15.47			
	Cerbb(+)	47	52.09	17.08			
	Er(-)Pr(-)Cerbb(-)	21	50.62	15.77			
LDL-C	Er(+)Pr(+)Cerbb(-)	120	121.76	37.51	3 - 200	0.1009	0.390
	Er(+)Pr(-)Cerbb(-)	16	140.50	75.62			
	Cerbb(+)	47	124.19	32.97			
	Er(-)Pr(-)Cerbb(-)	21	128.76	51.23			
TG	Er(+)Pr(+)Cerbb(-)	120	171.15	101.37	3 - 200	0.538	0.657
	Er(+)Pr(-)Cerbb(-)	16	160.88	87.64			
	Cerbb(+)	47	179.00	94.30			
	Er(-)Pr(-)Cerbb(-)	21	148.76	64.15			
Total Cholesterol	Er(+)Pr(+)Cerbb(-)	120	208.17	45.14	3 - 200	1.208	0.308
	Er(+)Pr(-)Cerbb(-)	16	210.06	34.38			
	Cerbb(+)	47	197.30	43.53			
	Er(-)Pr(-)Cerbb(-)	21	219.10	64.57			

p>0.05; n=204.

rates were found to be statistically significantly higher in patients with bone metastases compared to patients without bone metastases.

Low HDL-C has been identified as a risk factor in cardiovascular diseases as well as in some cancers.[21] Low HDL-C increases the risk of breast cancer in postmenopausal pa-

tients as reported earlier.[22] In the study by Anna et al.,[23] low HDL-C was identified as a risk factor for the development of premenosal breast cancer. A study found found low HDL-C level as a poor prognostic factor in breast cancer in their study on breast cancer patients.[24] In our study, there was no difference in HDL-C levels between patients with and without breast cancer bone metastases.

There are studies on MHR as an inflammatory marker associated with atherosclerosis in coronary artery disease. Inflammation and inflammatory cytokines play a critical role in the metastasis. Epithelial mesenchymal transition (EMT) is associated with carcinogenesis and confers metastatic properties on cancer cells by increasing motility, invasion, and resistance to apoptotic stimuli. Various mechanisms of inflammation-induced tumor progression. Metastases induce infiltration and activation of myoloid cells. Myeloid cells cause immunosuppression, ensuring tumor cell survival and promoting angiogenesis, thereby preparing distant sites for tumor cells to grow. Cytokines and chemokines are involved in the accumulation, survival and proliferation of these cells.Some studies with NLR used as an inflammatory indication that is prognostic in many cancers. It has been identified as a poor prognostic factor in patients with bone metastases.

In the study although it is clearer that the NLR value is associated with an increase in NLR in other organ metastases, a slight increase in NLR was found only in patients with bone metastases.[25] Our hypothesis was to determine the effect of monocyte/HDL-C ratio used as an inflammatory marker in predicting bone metastasis. It has been studied for the first time in the literature. In our study, no bone metastasis relationship was found between the monocyte/HDL-C ratio. In the literature, the relationship between monocyte metastasis and HDL –C metastasis is controversial. We think that there is a need for more extensive research by increasing the number of patients.

Disclosures

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