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Research Article

# Monocyte-to-High Density Lipoprotein Cholesterol Ratio Correlates with the Presence of Cardiovascular Risk Factors in Patients Who Received Upfront Dexrazoxane During Anthracycline Treatment: A Single-Center Observation

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## Abstract

**Objectives:** In this study, we aimed to retrospectively analyze the baseline characteristics, blood parameters and cardiovascular risk factors of the patients who received dexrazoxane to prevent anthracycline-induced cardiotoxicity.

**Methods:** The data of patients who applied to our hospital's medical oncology clinic between March 2019 and August 2019, were treated with anthracycline due to various malignancies and received primary prophylaxis with dexrazoxane were retrospectively analyzed.

**Results:** A total of 75 patients included in the study. It was observed that 81.3% (n=61) of the cases had at least one risk factor for developing cardiac side effects. The risk factors of the cases ranged from 0 to 4, with a mean of 1.45. As of August 2019, none of the patients had any symptoms related with cardiac dysfunction A positive correlation between glucose (r=0.234; p=0.044), creatinine (r=0.380; p=0.001), monocyte (r=0.232; p=0.046), triglyceride (r=0.252; p=0.033) measurements of the subjects and the number of risk factors was found. A significant positive correlation analyses was found between the monocyte-to-HDL ratio (MHR) (r=0.233; p=0.048) of the subjects and the number of risk factors.

**Conclusion:** We suggest that dexrazoxane is an important cardioprotective agent that have a huge potential on preventing the long-term cardiotoxicity, and blood parameters especially those which represents the state of inflammation in the body such as MHR should be utilized when assessing the cardiovascular risks of each patient.

**Keywords:** Anthracycline, cardioprotection, cardiotoxicity, cardiovascular risk, dexrazoxane

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Remarkable progress in the cancer therapy has been achieved in the past two decades in the means of multiple combinations of drugs, new generation targeted drugs, radiation therapy, and surgery. Anthracyclines (antineoplastic antibiotics) still represent the base of the standard adjuvant chemotherapy for many solid cancers including breast and lung cancer, and hematological malignancies.[1] However, anthracycline-induced cardiotoxicity still remains as an important cause of chemotherapy-induced heart disease in the high-risk population. This cardiotoxicity usually appears when the administered doxorubicin cumulative dose is higher than 240 mg/m$^2$. However, it is reported that

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16% patients who received doxorubicin cumulative dose of 240 mg/m$^2$ shows the subclinical cardiac manifestations.[2] While cardiotoxicity might cause treatment discontinuation in some cases, the signs might appear years after completion of primary cancer treatment in others, which significantly impairs the patient's quality of life.[1, 3]

American Society of Clinical Oncology have described the criteria defining the population who are at increased risk for cardiac side effects.[4] They made a serious of recommendations including the use of cardioprotective agents such as dexrazoxane to minimize the potential risks. Dexrazoxane is an inhibitor of topoisomerase IIb and an intracellular iron chelator, which prevents the complex formation between metal ions and anthracyclines. This property interferes with the generation of anthracycline-dependent reactive oxygen species and inhibits DNA replication, which triggers the myocardial cell death and eventually, left ventricular systolic dysfunction.[5] Many studies demonstrated that the use of dexrazoxane significantly reduces the incidence of heart failure and cardiotoxicity in both adult and pediatric population.[2, 6] However, due to concerns regarding interference with anti-tumor efficacy or increased risk for second primary malignancies, dexrazoxane was not routinely used in clinical practice. Several trials have been published on benefit-risk of dexrazoxane since then, and they concluded that dexrazoxane is an effective cardioprotector agent and not associated with either reduction in anti-tumor efficacy or increased risk for second primary malignancies.[7] Currently, dexrazoxane is approved and being successfully used to reduce the cardiac side effects of anthracycline-based (e.g., doxorubicin, epirubicin) chemotherapy recipients for advanced breast cancer, soft tissue sarcomas, or small-cell lung cancer. It is used as a primary prophylaxis in conjunction with the anthracycline of choice to decrease the incidence of cardiomyopathy and systolic dysfunction.[7, 8]

Recent data has demonstrated that both cancer and cardiovascular disease share some risk factors including obesity, diabetes, dyslipidemia and older age.[1] It is known that even the patients who did not have any history of cardiovascular disease can show future cardiovascular events due to cardiotoxic side effects of anthracycline-based chemotherapies.[9] Therefore, the identification and approval of reliable blood parameters to better identify the patients who are at risk for future cardiovascular events are required to make the use of prophylactic cardioprotective agents as a part of the routine clinical practice. Cumulative research has focused on the investigation of the correlation between recently emerged markers such as peripheral blood derived ratios with inflammatory response in cardiovascular diseases.[10, 11]

Although the use of dexrazoxane was approved by FDA, this drug is recently approved and become available to be used in Turkey. Therefore, there was no data available regarding the baseline characteristics of the population receiving dexrazoxane and measurability of this data with the current guideline. Here, we retrospectively analyzed a cohort of our hospital database to assess the baseline demographical and laboratory characteristics and cardiovascular risk factors of the patients who received dexrazoxane as a primary prophylaxis during anthracycline treatment. The secondary objective of this study was to assess if there is any correlation between the initial blood parameters, peripheral blood count-derived ratios and presence of cardiovascular risk factors exists.

## Methods

### Study Group

The data of 75 patients who applied to our hospital's medical oncology outpatient clinic between March 2019 and August 2019, were treated with anthracycline due to various malignancies and received primary prophylaxis with dexrazoxane at the time of anthracycline treatment were retrospectively analyzed. Since one of the aims of the study to assess the characteristics of the study population, all the patients who received dexrazoxane during the aforementioned time period was included in the study. The study was approved by local institutional review board and the informed consent was waived due to the retrospective nature of the study. All patients received at least four cycles of doxorubicin and all adjuvant chemotherapy treatments were initiated within 2 months after surgery. The decision to use dexrazoxane as a primary prophylaxis was made according to concerns arising from clinician's considerations. Dexrazoxane was administered to patients who meet at least one criterion to be at increased risk for developing cardiac dysfunction based on American Society of Clinical Oncology 2016 clinical practice guidelines. To the patients who do not have any risk factor, the decision to use dexrazoxane was made on the basis of physician's decision based on the concern to avoid any cardiac toxicity. Dexrazoxane was infused intravenously over 15 minutes at a 10:1 dose ratio, 30 minutes prior to each cycle of doxorubicin.

### Study Design

A data record form consisting of a total of questions, including demographic characteristics of patients, anthracycline treatment and dosage, non-anthracycline chemotherapeutic agents, other oncological treatments such as radiotherapy and surgical procedures, biochemical parameters at the time of treatment initiation for the patients, data on cardiac

functions and cardiovascular risk parameters, retrospectively filled in for each patient based on patient files and hospital records. Evaluation of the baseline blood parameters and cardiac functions were performed before the first cycle of doxorubicin. Each patient received a full-cardiac examination and a baseline echocardiogram was performed prior to anthracycline treatment. MHR was calculated as the ratio of monocyte-to-HDL, LMR was calculated as the ratio of lymphocyte-to-monocyte lastly NLR was calculated as the ratio of neutrophil-to-lymphocyte. All of the blood parameters were obtained from the same automated blood sample at the same time. Descriptive criteria identifying a patient with increased risk for developing cardiac dysfunction is defined based on American Society of Clinical Oncology 2016 clinical practice guidelines (Table 1). After filling-in all required information, patients were classified into groups according to number of criteria they had.

### Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. The suitability of quantitative data to normal distribution was tested by Shapiro-Wilk test and graphical analysis. Mann-Whitney U test was used for comparisons of quantitative variables that did not show normal distribution between two groups. Spearman correlation analysis was used to evaluate the relationships between quantitative variables. A $p<0.05$ was accepted as statistically significant.

## Results

The study included a total of 75 cases (92% (n=69) female and 8% (n=6) male) that were treated in our oncology department between March 2019 and August 2019. The demographical characteristics of the patients are shown in Table 2. The ages of the subjects included in the study ranged from 25 to 75, and the mean age was 52.76. The height of the subjects included in the study ranged from 146 to 184 cm, with an average of 159.27 cm, weight measurements ranging from 44 to 108 kg with an average of 76.88, and body mass index(BMI) measurements ranged from 18% to 43% kg/m$^2$, and the average was found as 30.38%.

Details about the patients' histories are shown in Table 3. Of the cancer types included in the study, 86.7% (n=65) was breast cancer, 5.4% (n=2) was sarcoma, 2.7% (n=2) was lung cancer, 2.7% (n=2) was Hodgkin lymphoma, 1.3% (n=1) was non-Hodgkin lymphoma and 1.3% (n=1) was malignant mesenchymal tumor. It was observed that 74.7% (n=56) of the cases had non-metastatic disease, while 18.6% (n=14) had metastatic and 6.7% (n=5) had locally advanced disease. Adjuvant anthracycline treatment was received by

**Table 2.** Demographical characteristics of the patients

| | |
|---|---|
| Age | |
| Min-Max (Median) | 25–75 (53) |
| Average±SD | 52.76±11.79 |
| Gender, n (%) | |
| Female | 69 (92.0) |
| Male | 6 (8.0) |
| Height (cm) | |
| Min-Max (Median) | 146–184 (159) |
| Average±SD | 159.27±7.45 |
| Weight (kg) | |
| Min-Max (Median) | 44–108 (77) |
| Average±SD | 76.88±12.70 |
| Body-Mass Index (kg/m$^2$) | |
| Min-Max (Median) | 18–43.8 (30.10) |
| Average±SD | 30.38±5.29 |

SD: Standard deviation.

**Table 1.** Descriptive criteria to define a patient with increased risk for developing cardiac dysfunction according to American Society of Clinical Oncology 2016 clinical practice guidelines

| |
|---|
| High dose anthracycline (doxorubicin≥250 mg/m$^2$) |
| Presence of high dose radiotherapy (RT≥30 Gy) where the heart is in the treatment field |
| Lower-dose anthracycline (doxorubicin<250 mg/m$^2$)+Presence of lower dose radiotherapy (RT<30 Gy) |
| Lower-dose anthracycline (doxorubicin<250 mg/m$^2$)+Presence of multiple (≥2) cardiovascular risk factor |
| Lower-dose anthracycline (doxorubicin<250 mg/m$^2$)+older age(≥60) |
| Lower-dose anthracycline (doxorubicin<250 mg/m$^2$)+compromised cardiac function (*Borderline EF 50-55%, history of myocardial infarction, history of moderate valvular heart disease*) |
| Trastuzumab+Presence of multiple (≥2) cardiovascular risk factor |
| Trastuzumab+older age(≥60) |
| Trastuzumab+compromised cardiac function (*Borderline EF 50–55%, history of myocardial infarction, history of moderate valvular heart disease*) |
| Lower-dose anthracycline (doxorubicin<250 mg/m$^2$)+Sequential therapy with trastuzumab |

**Table 3.** Patient's characteristics and details of treatment regimen

| | |
|---|---|
| Primary diagnosis, n (%) | |
| Breast cancer | 65 (86.7) |
| Sarcoma | 4 (5.4) |
| Hodgkin lymphoma | 2 (2.7) |
| Non-Hodgkin lymphoma | 1 (1.3) |
| Lung cancer | 1 (1.3) |
| Malign mesenchymal tumor | 1 (1.3) |
| Presence of metastasis, n (%) | |
| Non-Metastatic | 56 (74.7) |
| Metastatic | 14 (18.6) |
| Locally advanced | 5 (6.7) |
| History of surgery before oncological treatment, n (%) | |
| No | 29 (38.7) |
| Yes | 46 (61.3) |
| Other agents used in anthracycline-containing, n (%) chemotherapy regimen | |
| Cyclophosphamide | 65 (86.7) |
| Cyclophosphamide+Mesna | 5 (6.7) |
| R-Chop | 2 (2.7) |
| Vinblastine+Dacarbazine | 1 (1.3) |
| Bleomycin+Vinblastine+Dacarbazine | 1 (1.3) |
| Cyclophosphamide+Vincristine | 1 (1.3) |
| Planned anthracycline dose (mg/m$^2$) | |
| Min-Max (Median) | 105–300 (240) |
| Average±Standard deviation | 243.20±18.61 |
| Presence of radiotherapy containing heart, n (%) | |
| No | 53 (70.7) |
| Yes | 22 (29.3) |

**Table 4.** Descriptive features and risk factors of the patients

| | |
|---|---|
| Pre-treatment ejection fraction (EF) | |
| Min-Max (Median) | 55–65 (60) |
| Average±SD | 62.05±2.58 |
| Use of G-CSF after anthracycline therapy, n (%) as primary prophylaxis | 75 (100.0) |
| Presence of an event of febrile, n (%) neutropenia during treatment | 1 (1.3) |
| High dose anthracycline, n (%) (doxorubicin ≥250 mg/m$^2$) | 9 (12.0) |
| Presence of high dose radiotherapy (RT ≥30 Gy), n (%) | 22 (29.3) |
| Cardiovascular risk factors: | |
| History of smoking, n (%) | 8 (10.7) |
| Hypertension | 15 (20.0) |
| Diabetes | 15 (20.0) |
| Dyslipidemia | 30 (40.0) |
| Obesity | 35 (46.7) |
| Presence of multiple (≥2) cardiovascular risk factor, n (%) | 34 (45.3) |
| Older age (≥60) | 24 (32.0) |
| Compromised cardiac function: | |
| Borderline EF 50–55% | 1 (1.3) |
| History of myocardial infarction | 2 (2.7) |
| History of moderate valvular heart disease | 1 (1.3) |
| Treatment with trastuzumab | 17 (22.7) |
| Number of patients who had at least one high-risk feature, n (%) | 61 (81.3) |
| Number of risk factors | |
| Min-Max (Median) | 0–4 (1) |
| Average±SD | 1.45±1.09 |

SD: Standard deviation.

61.3% (n=46) of the cases who had a surgical history. Radiotherapy including the heart area was applied in 29.3% of the cases (n=22). The planned anthracycline dose of the cases ranged from 105 to 300 mg/m$^2$, and the mean dose was found as 243.20±18.61 mg/m$^2$. Details of other agents used in anthracycline-containing chemotherapy regimen are shown in Table 3.

The distribution of the patients according to their cardiovascular risk factors is shown in Table 4. The mean baseline LVEF was 62.05% (ranging from 55%–65%). In all cases, G-CSF was used as a primary prophylaxis against febrile neutropenia after anthracycline treatment. An event of febrile neutropenia was observed only in one case during the treatment. High dose anthracycline (doxorubicin >250mg/m$^2$) was used in 12% (n=9) of the cases. Sequential therapy with trastuzumab was observed in 22.7% (n=17) of the cases.

A total of 15 (20%) and 15 patients (20%) had hypertension and DM, respectively. The frequency of overweight status or hyperlipidemia was 46.7% (n=35) and 40% (n=30), respectively. A total of 8 patients (11.4%) had a history of smoking. 32% (n=24) of the patients were over the age of 60. While 1.3% (n=1) of cases had an EF percentage of 50–55, 2.7% (n=2) had a history of myocardial infarction, and 1.3% (n=1) had a history of moderate-severe valvular heart disease. It was observed that 81.3% (n=61) of the cases had at least one risk factor for developing cardiac side effects. The risk factors of the cases ranged from 0 to 4, with a mean number of risk factors as 1.45±1.09.

The data of the laboratory findings of patients are presented in Table 5. The relationship between the number of risk factors and biochemistry results of the patients is evaluated in Table 6. A positive correlation between glucose (r=0.234; p=0.044), creatinine (r=0.380; p=0.001), monocyte (r=0.232; p=0.046), triglyceride (r=0.252; p=0.033), vitamin D (r=0.242; p=0.043) measurements of the subjects and the number of risk factors was found (meaning that the number of risk factors increases as the value increases). The correlation analyses between the monocyte-to-HDL ratio (r=0.233; p=0.048) of the subjects and the number of risk factors was significantly positive. There was no statis-

**Table 5.** Laboratory parameters of the patients

| | Min-Max (Median) | Average±SD |
|---|---|---|
| Glucose (mg/dl) | 74.8–211 (105) | 111.37±25.63 |
| Creatinine (mg/dl) | 0.38–1.16 (0.71) | 0.73±0.15 |
| Hemoglobin (g/dl) | 9.1–15.6 (12.7) | 12.68±1.36 |
| WBC (x10$^3$ µL) | 4.31–20.36 (7.65) | 7.84±2.63 |
| Neutrophil (x10$^3$ µL) | 2.12–15.78 (4.59) | 4.91±2.14 |
| Lymphocyte (x10$^3$ µL) | 1.02–5.04 (2.04) | 2.14±0.66 |
| Platelet (x10$^3$ µL) | 69–548 (287) | 291.49±87.68 |
| Monocyte (x10$^3$ µL) | 0.28–5.3 (0.54) | 0.64±0.58 |
| Eosinophil (x10$^3$ µL) | 0–1.33 (0.13) | 0.17±0.19 |
| Total cholesterol(mg/dl) | 58.9–275 (203) | 201.96±37.19 |
| LDL (mg/dl) | 70–221 (131) | 134.13±28.9 |
| HDL (mg/dl) | 28.3–77 (48) | 48.39±9.89 |
| Triglyceride(mg/dl) | 44–374 (136) | 159.91±79 |
| Vitamin D (ng/ml) | 3–80 (12.69) | 16.71±15.24 |
| hSCRP (mg/L) | 0–22.44 (0.29) | 1.11±2.87 |
| Monocyte to HDL ratio | 0.01–0.11 (0.01) | 0.01±0.01 |
| Neutrophil to lymphocyteratio | 1.06–10.01 (2.16) | 2.41±1.2 |
| Platelet to lymphocyte ratio | 38.31–256.62 (144.55) | 144.31±48.55 |
| Lymphocyte to monocyte ratio | 0.88–7.5 (4) | 3.91±1.34 |

SD: Standard deviation; WBC: White blood cell; LDL: Low-density lipoprotein; HDL: high-density lipoprotein; hSCRP: High sensitivity c-reactive protein.

**Table 6.** Evaluation of the correlation between the number of risk factors and laboratory results

| | Number of risk factors | |
|---|---|---|
| | r | p |
| Glucose | 0.234 | 0.044* |
| Creatinine | 0.380 | 0.001** |
| Hb | –0.090 | 0.443 |
| WBC | 0.038 | 0.748 |
| Neutrophil | –0.001 | 0.996 |
| Lymphocyte | 0.080 | 0.496 |
| Platelet | –0.012 | 0.916 |
| Monocyte | 0.232 | 0.046* |
| Eosinophil | 0.166 | 0.154 |
| Total cholesterol | 0.004 | 0.974 |
| LDL | 0.051 | 0.672 |
| HDL | –0.065 | 0.589 |
| Triglyceride | 0.252 | 0.033* |
| Vitamin D | 0.242 | 0.043* |
| hSCRP | 0.135 | 0.252 |
| Monocyte to HDL ratio | 0.233 | 0.048* |
| Neutrophil to lymphocyte ratio | –0.155 | 0.183 |
| Platelet to lymphocyte ratio | –0.178 | 0.126 |
| Lymphocyte to monocyte ratio | –0.113 | 0.332 |

r: Spearman's Correlation Coefficient; *p<0.05; **p<0.01; Hb: Hemoglobine; WBC: White blood cell; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; hSCRP: High sensitivity c-reactive protein.

tically significant correlation between the Hb, WBC, neutrophil, lymphocyte, platelet, eosinophil, total cholesterol, LDL, HDL, hSCRP, NLR, PLR and LMR measurements and the number of risk factors (p>0.05). The association between presence of any risk factor and MHR, NLR, PLR and LMR measurements are evaluated in Table 7. None of the peripheral blood-count-derivative ratios show statistically significant difference between the patients who had no risk factors (n=14) and the patients who had at least one risk factor (n=61) (p>0.05). During the follow-up time, none of the patients had cardiac problems and as of August 2019, all patients survived.

## Discussion

Dexrazoxane is an iron chelator and DNA-topoisomerase II inhibitor which is utilized as a cardioprotective agent for patients receiving doxorubicin chemotherapy who are at an increased risk for cardiotoxicity. In recent years, concerns related to decreased anti-tumor efficacy of doxorubicin and increased risk for second primary cancers raised from dexrazoxane when administered along with doxorubicin. [2] This issue limited the utilization of dexrazoxane in the routine clinical practice. However, numerous articles have demonstrated that concomitant use of dexrazoxane with anthracycline therapy resulted in cardioprotectant successful course of treatment without symptomatic cardiac decompensation.[7] Since dexrazoxane is recently approved to be used in Turkey, there was no data available regarding the baseline characteristics of the population receiving dexrazoxane and measurability of this data with the current guidelines. To fill this gap, we retrospectively analyzed a cohort of our hospital database to assess the baseline demographical and laboratory characteristics and cardiovascular risk factors of the patients who received dexrazoxane as a primary prophylaxis during anthracycline treatment.

Tahover et al.[2] stated that dexrazoxane should be considered as a cardioprotective agent in mostly healthy population with long life expectancy to ensure the maximal preservation of cardiac reserve. Ganatra et al.[7] also recommended the consideration of dexrazoxane from the initiation of anthracycline therapy for each patient, regardless of the type of cancer.Therefore, since March 2019, the date when the dexrazoxane became available in Turkey, our oncology department carefully investigates each patient for possible risk of cardiotoxicity and potential benefits of utilization of dexrazoxane. Since then, all patients were informed during their appointments about their option to off-label use of dexrazoxane. Out of 75 patients who

**Table 7.** Evaluation of the association between MHR, NLR, PLR and LMR and the presence of risk factors

| | Presence of risk factor | | |
|---|---|---|---|
| | None (n=14) | Yes (n=59) | p |
| Monocyte to HDL ratio | | | |
| Min-Max (Median) | 0.01–0,02 (0.01) | 0.01–0.11 (0.01) | [a]0.149 |
| Average±SD | 0.01±0.002 | 0.01±0.01 | |
| Neutrophil to lymphocyte ratio | | | |
| Min-Max (Median) | 1.4–3.34 (2.30) | 1.06–10.01 (2.08) | [a]0.245 |
| Average±SD | 2.41±0.56 | 2.42±1.30 | |
| Platelet to lymphocyte ratio | | | |
| Min-Max (Median) | 101.49–207.24 (158.28) | 38.31–256.62 (142.93) | [a]0.280 |
| Average±SD | 153.70±34.74 | 142.15±51.19 | |
| Lymphocyte to monocyte ratio | | | |
| Min-Max (Median) | 2.15–5.76 (4.02) | 0.88–7.50 (3.88) | [a]0.591 |
| Average±SD | 4.02±0.90 | 3.88±1.42 | |

[a]Mann Whitney U Test; SD: Standard deviation; MHR: Monocyte-to-HDL ratio; NLR: Neutrophil-to-lymphocyte ratio; PLR; Platelet-to-lymphocyte ratio; LMR: Lymphocyte-to-monocyte ratio; HDL: High-density lipoprotein.

agreed to receive dexrazoxane, as of August 2019, none of them had any symptoms related with cardiac dysfunction.

Consistent with the literature, we found a positive correlation between cardiovascular risk factors and glucose, creatinine, monocyte, and triglyceride counts. We believe that increased inflammatory state of the patients was responsible for this result, since both cardiovascular diseases and cancer is a state of inflammation affecting the whole-body mechanism.[10–15] Interestingly, increased vitamin D levels were also associated with increased cardiovascular risk factors. However, since the mean vitamin D value of the patients were found as 16.71, which is considered as severely insufficient, we believe that this increment should be considered for the values lower than the sufficient threshold.

While circulating monocytes are the source of various proinflammatory cytokines in the body, high-density lipoprotein (HDL) counteracts this proinflammatory and prooxidant effects of monocytes by inhibiting their proliferation and migration to the tissues.[16] Therefore, monocyte-to-HDL ratio emerged as a recent inflammatory and oxidative stress marker and a predictor of cardiovascular diseases(circulation). Recently, Ekiz et al.[16] suggested that MHR can be used to establish the patients at high risk for adverse cardiac events and to guide the selection for prophylactic therapy. Our results were supporting the literature, suggesting that MHR can be utilized to establish a baseline which represents the inflammatory state and the need for cardioprotective therapy.

The present study has some limitations including the retrospective design, single-center experience, relatively small patient cohort. Also, the choice to administer dexrazoxane was not random and no detailed long-term follow-up analysis existed regarding the effects of dexrazoxane on cardiovascular system. Further studies with control groups are required to claim the MHR as a reliable parameter to assess the cardiovascular risk of the patients.

As a conclusion, we believe that dexrazoxane is an important cardioprotective agent that have a huge potential on preventing the long-term cardiotoxicity and improving the patients' quality of life. The use of dexrazoxane as a primary prophylaxis is recommended according to certain criteria in the American Society of Clinical Oncology Clinical Practice Guideline, and the use of dexrazoxane was highly compliant with these criteria in the cohort we examined. Especially in recent years, since anthracycline-induced cardiotoxicity can be seen in patient populations with low risk of cardiac dysfunction, randomized studies including this patient population will lead us about how to behave these patients. We lastly suggest that blood parameters especially those which represents the state of inflammation in the body such as MHR should be utilized when assessing the cardiovascular risks of each patient.

### Disclosures

**Ethics Committee Approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards and with the Helsinki Declaration and its later amendments or comparable ethical standards within our institute. This study was performed in keeping with the principles outlined in the Declaration of Helsinki and approved by institutional ethics committee.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – D.E.; Design – D.E.; Supervision – D.E.; Materials – D.E., I.K.; Data collection &/or processing – D.E., I.K.; Analysis and/or interpretation – D.E., I.K.; Literature search – I.K.; Writing – I.K., D.E.; Critical review – D.E., I.K.

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