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Effect of Pericardial Effusion on Right Ventricular Functions in Oncology Patients Receiving Chemotherapy

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ABSTRACT

Introduction: Pericardial effusion is an indicator of poor prognosis in patients with cancer. We investigated the effect of pericardial effusion development on right ventricular function in oncology patients receiving chemotherapy for malignancy.

Methods: A total of 90 patients who were followed up in the oncology clinic and who applied to our outpatient clinic for routine cardiac examination were included in the study. Echocardiography was performed on the patients, and they were divided into two groups: patients with and without pericardial effusion. Demographic characteristics and, clinical and laboratory findings of the patients were recorded. The right ventricular functions of the patients were then evaluated.

Results: Pericardial effusion was in 30 (33.3%) of 90 patients included in the study. The mean age of patients without pericardial effusion was 57.33±15.59, and the mean age of patients with effusion was 60.27±13.51, and it was similar between the groups (p=0.36). No statistically significant difference was detected between the groups in right ventricular (RV) fractionated area change, RV-early peak, tricuspid annular plane systolic excursion, pulmonary artery pressure, E/E', and heart failure with preserved ejection fraction values, which are parameters that indicate right ventricular functions and diastolic dysfunction. However, RV systolic velocity and RV-AM, which are indicators of diastolic dysfunction, were found at higher rates in the patient group with pericardial effusion (p-value 0.041 and 0.001, respectively). In addition, Mitral E velocity was found to be lower in the patient group with pericardial effusion (p=0.032).

Conclusion: In malignancy patients who develop pericardial effusion, we recommend that diastolic parameters be checked and close clinical follow-up of the patients be performed before overt heart failure clinic develops. It should be kept in mind that the development of pericardial effusion in oncology patients receiving chemotherapy does not mean right ventricular failure.

Keywords: Chemotherapy, pericardial effusion, diastolic heart failure, right ventricular failure

Introduction

Death rates due to cancer have begun to decrease significantly in recent years, thanks to technological developments and newly developed drugs. However, cardiotoxic effects continue to frequently occur because of the effects of some chemotherapeutic drugs (1-3). Pericardial effusion occurs because of the inflammatory effect of pericardial fluid or disorders in lymphatic drainage. Among the most common causes of pericardial effusions, they are; they can be counted as 27% infection, 25% malignancy, 14% post-radiation inflammation, and 12% collagen tissue diseases (4,5). Pericardial effusion develops in approximately 15% of malignant patients, and this is mostly due to lung and breast cancer (6,7). The development of pericardial effusion in patients with malignancy is among the common complications and is associated with poor prognosis (8). Patients with malignant pericardial effusion usually die within 1 year of diagnosis (9). Cardiotoxicity that develops in patients receiving chemotherapy affects their treatment process of the patients and causes the development of heart failure, which is a significant cause of morbidity and mortality (10). In the literature, although there are many studies on left ventricular functions after chemotherapy, the number of studies on right ventricular functions is extremely low. In this study, we aimed to show the difference between the right ventricular functions of oncology patients who developed pericardial effusion after chemotherapy and those of patients who did not develop pericardial effusion.

Methods

Between June 2020 and October 2023, 90 patients who were followed up in the oncology clinic, received chemotherapy, and applied to our outpatient clinic for routine cardiac examination were included in the study. The patients included in the study were selected from patients

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who had been receiving chemotherapy for at least 3 months. Patients with known heart failure, active infection, hematological malignancy, severe valve disease, chronic renal failure, rheumatological disease, hematological disease, pulmonary hypertension, history of pericardial disease, history of acute coronary syndrome within the last month, and patients with inadequate image quality were not included in the study. Patients with solid organ tumors, without a tamponade clinic, and regardless of the type of chemotherapeutic drug they received were included in the study. A voluntary consent form was obtained from the patients participating in the study, and the Necmettin Erbakan University Ethics Committee approval was obtained for the study (approval number: 2023/4541, date: 15.09.2023). Among the patients included in the study, those without an effusion on echocardiography before chemotherapy but developed an effusion after chemotherapy were included in the group of patients who developed an effusion. The clinical, demographic, and laboratory findings of all patients were recorded. In addition to routine echocardiographic evaluation, all patients underwent detailed echocardiography, including right ventricular function. Echocardiography was performed using two-dimensional imaging, M-mode, and tissue Doppler techniques, in accordance with the recommendations of the American Society of Echocardiography (11). The fluid remaining between the pericardium and epicardium at the end of diastole was considered to be pericardial effusion. To prevent the appearance of suspicious effusion in patients with prominent epicardial fat pads, these patients were not included in the study. The right ventricular fractionated area change (RV-FAC), right ventricular systolic velocity (RV-SM), right ventricular early peak (RV-EM), and late peak (RV-AM) diastolic parameters of the patients were examined. In addition, the tricuspid annular plane systolic excursion (TAPSE) and pulmonary artery pressure (PAP) were measured. The patients' left ventricular mitral E velocity, septal E velocity, epicardial fat thickness, and E/E' parameters were examined. Then, the diastolic characteristics of the patients were recorded by examining their heart failure with preserved ejection fraction (H 2 FPEF) score.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics version 20.0 for Windows (SPSS Inc, Chicago, IL). Data are presented as mean and standard deviation, median and interquartile range, or numbers and proportions. Continuous variables were evaluated using the Student's t-test or Mann-Whitney U test after their suitability for normal distribution was checked using the Kolmogorov-Smirnov test, and categorical variables were evaluated using the chi-square test. A value of $p<0.05$ was considered significant.

Results

Pericardial effusion was in 30 (33.3%) of the 90 patients included in the study. The mean age of patients without pericardial effusion was 57.33±15.59, and the mean age of patients with effusion was 60.27±13.51, and it was similar between the groups (p=0.36) (Table 1). There was no statistically significant difference between the groups and patients with additional diseases such as diabetes mellitus, hypertension, coronary artery disease, chronic obstructive pulmonary disease, and hyperlipidemia (Table 2). No statistically significant difference was detected between the groups in RV-FAC, RV-EM, TAPSE, PAP, E/E', and H 2 FPEF values, which are parameters that indicate right ventricular functions and diastolic dysfunction (Table 1). However, RV-SM and RV-AM, which are indicators of diastolic dysfunction, were found at higher rates in the patient group with pericardial effusion (p-value 0.041 and 0.001, respectively). In addition, mitral E velocity was found to be lower in the patient group with pericardial effusion (p=0.032).

Table 1. Distribution of the clinical, demographic, echocardiographic, and laboratory characteristics of patients according to the pericardial effusion status

	Without pericardial effusion	Pericardial effusion	p-value
Age	57.33±15.59	60.27±13.51	0.36
Size	162.82±7.866	165.53±8.025	0.133
BMI	27.24±5.11	26.56±7.01	0.636
Alb/CRP	1.63±2.49	1.52±2.39	0.842
RV-FAC	42.73±9.40	42.63±9.09	0.960
RV-SM	13.88±3.35	15.25±2.69	**0.041**
RV-EM	10.94±3.13	11.51±3.65	0.473
RV-AM	14.26±4.25	17.28±3.50	**0.001**
Septal E	8.83±2.39	8.45±2.24	0.466
Mitral E	73.53±19.05	63.73±20.17	**0.032**
TAPSE	2.22±0.41	2.25±0.49	0.812
PAP	27.95±6.04	29.37±8.10	0.402
Epicardial fat	0.45±0.18	0.46±0.21	0.717
H 2 FPEF	33.15±20.85	32.77±20.08	0.934
E/E'	8.53±3.07	9.53±7.21	0.470

BMI: Body mass index, Alb: Albumin, CRP: C-reactive protein, RV-FAC: Right ventricular fractionated area change, RV-SM: Right ventricular systolic velocity, RV-EM: Right ventricular early peak, RV-AM: Right ventricular late peak, TAPSE: Tricuspid annular plane systolic excursion, PAP: Pulmonary artery pressure, H 2 FPEF: Heart failure with preserved ejection fraction

Table 2. Distribution of clinical, demographic, and laboratory characteristics of patients according to the pericardial effusion status

	Without pericardial effusion	Pericardial effusion	p-value
Sex			
Female	41 (68.3%)	16 (53.3%)	0.164
Male	19 (31.7%)	14 (46.7%)	
DM	9 (15.0%)	6 (20.0%)	0.549
HT	17 (28.3%)	8 (26.7%)	0.868
AF	1 (1.7%)	0 (0.0%)	0.477
HL	3 (5.0%)	4 (13.3%)	0.164
Smoke	10 (16.9%)	6 (20.0%)	0.892
Alchol	3 (5%)	2 (6.7%)	0.340
CAD	8 (13.3%)	2 (6.7%)	0.343
COPD	4 (6.7%)	4 (13.3%)	0.295

DM: Diabetes mellitus, HT: Hypertension, AF: Atrial fibrillation, HL: Hyperlipidemia, CAD: Coronary arterial disease, COPD: Chronic obstructive pulmonary disease

Discussion

This study is important because it shows that the development of pericardial effusion in patients with oncological malignancies receiving chemotherapy does not cause right ventricular failure or diastolic heart failure.

In clinical studies, pericardial effusion was detected in 5-20% of cancer patients (12). The development of pericardial effusion in patients with cancer is considered an indicator of poor prognosis. These patients are more likely to develop pericardial tamponade, especially those receiving cardiotoxic chemotherapy. There are several different mechanisms of pericardial effusion development in patients with malignancy. The most common is the spread of the tumor to the pericardium. In addition, chemotherapeutic drugs, radiotherapy, heart failure, and renal failure are among other conditions that are effective in the development of effusion. In a study conducted in 35 patients with pericardial effusion, Pradhan et al. (13) showed that the patients had improvement in both right and left ventricular functions after pericardiocentesis (14-16). This situation is important because pericardial effusion indicates right ventricular dysfunction. Cardiac dysfunction associated with cancer treatment can be classified into two ways. Type 1 effusion begins as soon as the drug is started and increases with the cumulative effect of the drug. It is more common in anthracycline-like chemotherapeutic areas. When the effect of the drug reaches its maximum, myofibrils become disorganized and apoptosis occurs (17). This results in ventricular failure and irreversible cardiac damage. In type 2, the myocardium becomes hibernated without cell death and cardiac contractility decreases. This condition is a reversible process, and the likelihood of cardiac failure is low (18). Many studies in the literature have been conducted on left ventricular failure, but there are almost no studies on right ventricular failure and diastolic failure. Pericardial effusion causes insufficient relaxation of the pericardium and impairs diastolic filling in patients. In a meta-analysis by Theetha Kariyanna et al. (10), they found a decrease in RV radial systolic functions and RV-FAC values in patients receiving anthracycline and trastuzumab treatment (19). In addition, a significant decrease was detected in the RV free wall longitudinal strain value, which is an indicator of diastolic dysfunction. Results similar to those of Theetha Kariyanna et al. (10) were obtained in the literature (1,20,21). In our study, different results were obtained from the study of Theetha Kariyanna et al. (10) While there was no statistically significant difference in the RV-FAC value, which was among the parameters we examined, a statistically significant difference was detected in the RV-SM, RV-AM, and mitral E speed, which indicate diastolic dysfunction. However, the effectiveness of these parameters in indicating diastolic dysfunction is low. In studies, the development of right ventricular failure is less common than that of left ventricular failure. If right ventricular failure develops, it causes serious symptoms that impair the quality of life of patients and is a significant cause of morbidity and mortality (22,23). Echocardiographic evaluations of the right ventricle have become more important in recent years as an important indicator of mortality (24,25). Because two-dimensional echocardiographic evaluation of the right ventricle is difficult, it is necessary to evaluate both systolic and diastolic functions with tissue Doppler echocardiography. In our study, it was observed that there was no significant change in the right ventricular functions of patients with pericardial effusion after chemotherapy. Although statistically significant changes were detected in some diastolic parameters and right ventricular tissue Doppler parameters, these parameters are insufficient to indicate heart failure. For this, advanced examinations such as strain echocardiography are required. Right ventricular functions are expected to be suppressed because of the development of serious effusion, both in patients receiving chemotherapy and in those not receiving chemotherapy. However, in our study, it was observed that there was no significant suppression of right ventricular functions in patients who developed effusion after chemotherapy compared with patients who did not develop effusion. This can be explained by the fact that the patients did not have serious pericardial effusion. If deterioration in diastolic parameters can be detected at the beginning in patients who develop effusion, precautions can be taken and undesirable events can be prevented before the clinical picture of heart failure appears in the patients. This is especially important in oncology patients. Because ventricular functions are important for patient treatment continuity. The H 2 FPEF score is a scoring system developed for the diagnosis of HFpEF. This score consists of body mass index >30 kg/m^2, use of two or more anti-hypertensive drugs, paroxysmal or persistent AF, pulmonary artery systolic pressure >35 mmHg by echocardiography, age >60, E/E.

The higher this score, the higher the morbidity and mortality rates in the patients. In a study conducted by Suzuki et al. (26) suggested that the H 2 FPEF score is an independent predictor of future heart failure-related events. In our study, we examined the H 2 FPEF score of patients with and without pericardial effusion and did not detect a statistically significant difference between the results. This is important because it shows that it does not pose an extra risk of heart failure in patients who do not develop serious pericardial effusion after chemotherapy. Even in untreated cancer patients, increased pro-inflammatory markers, hormonal effects, and reactive oxygen radicals have negative effects on right ventricular functions (4,27,28). In a study by Oliveira et al. (16) they revealed that more support devices were needed in patients who developed chemotherapy-related right ventricular failure. This reveals that the prognosis is worse in patients receiving chemotherapy if right ventricular failure develops. In a study by Milano et al. (29), they found a decrease in both right and left ventricular wall thickness in patients receiving doxorubicin and trastuzumab. In the same study, they showed that fibrosis developed in the right ventricular free wall. The results of this study are different from those of our study. The development of pericardial effusion in patients after chemotherapy does not directly mean right ventricular failure and diastolic dysfunction. Although the development of pericardial effusion in cancer patients is considered a poor prognostic indicator, there is no need to change treatment if there is no suppression of right ventricular functions in the patients.

Study Limitations

Our limitations include not evaluating the basal right heart functions of the patients and not separately classifying the type of chemotherapeutic drug. Because the main purpose of our study was to evaluate right ventricular diastolic function parameters, even if the effusion was mild, patients were recruited regardless of the type of chemotherapeutic drug. Conducting studies in more homogeneous patient groups may provide additional information regarding cardiotoxicity.

Conclusion

Pericardial effusion is an indicator of poor prognosis in patients with cancer. In malignancy patients who develop pericardial effusion, we recommend that diastolic parameters be examined and close clinical follow-up of the patients is performed before the clinical picture of overt heart failure develops. It should be noted that the development of pericardial effusion in oncology patients receiving chemotherapy does not mean right ventricular failure.

Ethics Committee Approval: the Necmettin Erbakan University Ethics Committee approval was obtained for the study (approval number: 2023/4541, date: 15.09.2023).

Informed Consent: A voluntary consent form was obtained from the patients participating in the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions: Concept - S.T.; Design - Y.A.; Data Collection or Processing - N.A., İ.O., Y.E.Y.; Analysis or Interpretation - A.İ.; Literature Search - Y.A.; Writing - S.T.

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