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Early Cardiac Complications in the First Month After Hematopoietic Stem Cell Transplantation: A Retrospective Analysis

Hematopoietik Kök Hücre Naklinden Sonraki İlk Ayda Gelişen Erken Kardiyak Komplikasyonlar: Retrospektif Bir Analiz

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ABSTRACT Objective: Cardiological evaluation before transplantation is extremely important in predicting cardiac complications in hematopoietic stem cell transplantation (HSCT) patients. In this study, our aim is to determine the incidence of post-HSCT early cardiac complications' mortality and morbidity and to identify the risk factors which act on the development of cardiac complications. **Material and Methods:** This study included 218 patients who had undergone HSCT during the time period between January 2014 and January 2020. Patient data were retrospectively retrieved from patient charts and internal electronic record database. **Results:** Fifty six % (n=122) were males and median age of the cohort was 55 (47-63) years. Eight (3.6%) patients developed Grade III-IV cardiac complications. Patients with ST-T alterations in the pre-transplant electrocardiogram (ECG) had a higher rate of cardiac complications (chi-square, p=0.019). Among the conditioning regimens, cardiac toxicity was determined at a higher rate the group who received melphalan 200 mg/m^2 (p=0.040). **Conclusion:** ST segment and T-wave alterations observed in ECG, pulmonary arterial pressure as measured by electrocardiography and particularly a reading over >25 mmHg, utilization of melpahalan 200 mg/m^2 as conditioning regimen feature out as the most important risk factors for cardiac complications which may develop subsequent to HSCT.

Keywords: Hematopoietic stem cell transplantation; cardiac toxicity; risk factors

ÖZET Amaç: Kardiyak toksisite, hematopoietik kök hücre nakli (HKHN) için en önemli sınırlayıcı faktörlerden biridir. HKHN hastalarında, pretransplant kardiyolojik değerlendirmenin kardiyak komplikasyonları öngörmedeki yararlılığı hâlen tartışmalıdır. Bu çalışmada amacımız, HKHN sonrası gelişen yaşamı tehdit edici ve fatal kardiyak komplikasyon insidansını saptamak ve kardiyak komplikasyon gelişimine etkili olan faktörleri belirlemektir. **Gereç ve Yöntemler:** Ocak 2014-Ocak 2020 yılları arasında HKHN yapılan 218 hasta çalışmaya dâhil edildi. Hasta sonuçlarına hasta dosyalarından ve elektronik kayıt sisteminden, retrospektif olarak ulaşıldı. **Bulgular:** Hastaların %56'sı (n=122) erkek, ortanca yaşları 55 (47-63) yıl idi. Sekiz (%3,6) hastada Grade III-IV kardiyak komplikasyon gelişti. HKHN öncesi değerlendirilen elektrokardiyogramda (EKG) ST-T değişiklikleri olan hastalarda, kardiyak komplikasyon gelişimi daha sık idi (ki-kare, p=0,019). Hazırlama rejimleri içerisinde melphalan 200 mg/m^2 kullananlarda kardiyak toksisite daha sık saptandı (p=0,040). **Sonuç:** EKG'deki ST segment ve T dalga değişiklikleri, elektrokardiyografide değerlendirilen pulmoner arteriyel basınç (PAB), özellikle de PAB değeri >25 mmHg olması ve hazırlık rejimi olarak melfalan 200 mg/m^2 kullanımı HKHN sonrası gelişebilecek kardiyak komplikasyonlar açısından en önemli risk faktörleridir.

Anahtar Kelimeler: Hematopoietik kök hücre naklî; kardiyak toksisite; risk faktörleri

Hematopoietic stem cell transplantation (HSCT) is a treatment modality employed in a variety of diseases, malignant hematological disorders at the first place, which is capable of providing cure or long-term remission but also bringing in procedure-related morbidity and mortality. Cardiac and pulmonary comorbidities are important limiting factors for HSCT. It is very important to optimize pre-transplant risk as-

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sessment in order to improve HSCT decision making. The hematopoietic cell transplantation (HCT) comorbidity index, which includes arrhythmia, cardiovascular, diabetes and cerebrovascular comorbidities, provides a better prediction of HCT-related morbidity and mortality compared to other non-HCT-specific indices.[1] Cardiac complications including congestive heart failure (CHF), fatal arrhythmia, pancarditis, and cardiac tamponade induced by high-dose cyclophosphamide, total body irradiation (TBI), and other conditioning regimens have been well documented in HSCT recipients.[2-4] Besides the incidents associated with cytotoxic agents, cardiac arrhythmias including myocardial infarction and cardiac arrest have been reported during the acute phase of HSCT due to cryopreserved stem cell infusion.[5] When the studies in the literature were examined, it is seen that the incidence of major cardiac complications varies between 1% and 9%.[2-4,6,7] It remains controversial as to whether it helps predicting cardiac complications to conduct cardiological assessment prior to transplantation. While certain studies suggest a low ejection fraction (EF) value, which is a part of pre-transplant assessment, is predictive of development of severe cardiac complications, there are also other studies which did not determine any correlation between pre-transplant cardiac functions and post-HSCT life-threatening cardiac complications.[3,8]

The aim of our study is to reveal the frequency, mortality and morbidity, and effective factors of early cardiac complications associated with transplantation in our patients who underwent HSCT.

MATERIAL AND METHODS

PATIENT SELECTION

This study included 218 patients who had undergone HSCT in Bone Marrow Transplant Unit of Eskişehir Osmangazi University, Faculty of Medicine, Department of Hematology. Our study covered the time period of January 2014 to January 2020 when 218 patients underwent HSCT, of whom 56% (n=122) were males and median age was 55 (47-63) years. Autologous HSCT and allogeneic HSCT were performed in 85.3% (n=186) and 14.7% (n=32) of the patients, respectively. Patient data were retrospectively retrieved from patient charts and internal electronic record database. The study protocol was approved from Eskişehir Osmangazi University Non-interventional Clinical Research Ethics Committee (reference 2020/19). This study was conducted in accordance with the World Medical Association's 2000 Declaration of Helsinki. Informed written consent was obtained from all the patients.

METHODS

From this data, the following information were deduced: patient age, gender, primary diagnosis, past cardiac disease history, pre-transplant serum ferritin level, type of stem cell transplantation, pre-transplant findings from routine 12-lead electrocardiogram (ECG) (rate, rhythm, ST-T alterations, QT/QTc intervals), and echocardiogram (ECHO) [EF, left atrial dimension (LAD), left ventricular end-diastolic dimension (LVDd), left ventricular end-systolic dimension (LVDs), end-diastolic intraventricular septal thickness (IVSth), left ventricular posterior wall thickness (PWth), E/A ratio, and mean systolic pulmonary artery pressure (PAP)], anthracycline usage and cumulative anthracycline dose exposure, whether anthracycline was used within 60 days before transplantation, prior history for mediastinal radiotherapy, occurrence of any cardiac involvement, type of stem cell transplantation mobilization regimen and conditioning regimen, and existence of any cardiac complications. PAP values were evaluated by ECHO. Pulmonary hypertension was defined as PAP of >25 mmHg at rest.

The cumulative dose of pre-HSCT anthracycline exposure was then categorized as none, low (0-99 mg/m^2), medium (100-399 mg/m^2) and high (>400mg/m^2). These upper limit cumulative doses were 150 mg/m^2 for idarubisin and 160 mg/m^2 for mitoxontrone which was compared to a generally accepted safe upper limit, cumulative dose of doxorubicin of 450 mg/m^2.[9,10] For daunorubicin conversion, doxorubicin is computed as two-thirds of the daunorubicin dose with respect to cardiotoxicity.[11]

All cardiac events were reviewed and categorized using previously published grading systems for cardiac toxicity after HSCT. Regimen-related cardiac toxicity was graded according to Bearman grade.[1]

The scale scores Grade I as: [I] cardiomegaly on chest X-ray without symptoms, [II] mild ECG changes not requiring treatment, [III] asymptomatic pericardial effusion; Grade II as: [I] moderate ECG changes requiring and responding to medical intervention, [II] CHF requiring and responding to afterload reduction, diuretics and digitalis, [III] pericarditis; Grade III as: [I] severe ECG abnormalities with no or only partial response to medical intervention, [II] CHF requiring inotropic support, [III] cardiogenic shock, [IV] decrease in QRS voltage by >50%, [V] pericardial tamponade; and Grade IV as fatal toxicity. Only cardiac complications that developed within 28 days after transplantation were considered regimen-related cardiac toxicity. Grade III-IV cardiac complications were defined to be severe.

STATISTICAL ANALYSIS

Continuous data were depicted as median (Q1; Q3), while categorical data were depicted as percentage (%). Shapiro-Wilk test was used to compare the conformity of the data to normal distribution. In the analysis of cross tables, Pearson chi-square, Pearson Exact chi-square, Yate's chi-square, Fisher's Exact chi-square analyses were applied. p value≤0.05 was considered statistically significant. Analyses were performed using IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) program.

RESULTS

Autologous HSCT and allogeneic HSCT were performed in 85.3% (n=186) and 14.7% (n=32) of the patients, respectively. The ECOG performance of 205 (94%) patients was 0, 11 (5%) patients was 1, 1 (0.5%) patient was 2, and 1 (0.5%) patient was 3. All 218 patients were exposed to dimethyl sulfoxide. Most frequently used conditioning regimens were melphalan 200 mg/m^2 (n=126, 57.8%), carmustine+etoposide+cytarabine+melphalan (140 mg/m^2) (n=41, 18.8%), and busulfan+cyclophosphamide (n=32, 14.7%) (Demographic features and clinical findings of patients are given in Table 1). Eight (3.6%) patients developed Grade III-IV cardiac complications from the conditioning regimen up to 28 days after transplantation. None of the patients de-

TABLE 1: Demographic characteristics and clinical findings of patients undergoing HSCT.

	n (%)
Age, year (median, Q1-Q3)	55 (47-63)
Sex, male/female	122/96 (56/44)
Primary diagnosis	
MM	107 (49.1)
Primary amyloidosis	2 (0.9)
Others PCD	3 (1.4)
Lymphoma	74 (33.9)
Acute leukemia	23 (10.6)
CML-blastic phase	3 (1.4)
Aplastic anemia	1 (0.5)
High risk MDS	3 (1.4)
Hypocellular MDS	1 (0.5)
PMF	1 (0.5)
Stem cell	
Peripheral blood/bone marrow	215/3 (98.6/1.4)
Mobilization regimens	
Cyclophosphamide	127 (68.3)
DHAP	27 (14.5)
EPOCH	2 (1.1)
ICE	8 (4.3)
Vepesid	6 (3.2)
CHOEP	1 (0.5)
HyperCVAD	8 (4.3)
G-CSF	4 (2.2)
MTX-C-ARA	1 (0.5)
G-CSF+Pleriksafor	1 (0.5)
IGEV	1 (0.5)
Conditioning regimens	
Melphalan	126 (57.8)
BEAM	41 (18.8)
Busulfan+Cyclophosphamide	32 (14.7)
Bu/Cy/E	10 (4.6)
CBV	3 (1.4)
Fludarabine+Melphalan	3 (1.4)
Thiotepa/Bu/Cy	3 (1.4)
Cumulative anthracycline dose (mg/m^2)	
None	71 (32.6)
Low	57 (26.1)
Medium	88 (40.4)
High	2 (0.9)
Cardiac complications*	38 (17.4)
Grade 1	18 (8.2)
Grade 2	12 (6)
Grade 3	6 (2.8)
Grade 4	2 (0.9)

*Grade 1 and Grade 2 minor cardiac complications; sinus bradicarda, pericarditis, myopericarditis, atriyal fibrillation, supraventricular premature beat, congestive heart failure, bigemine ventricular ectopics, cardiomegaly, supraventricular tachycardia, ST segment and T-wave changes. HSCT: Hematopoietic stem cell transplantation; MM: Multiple myeloma; PCD: Plasma cell dyscrasia; CML: Chronic myeloid leukemia; MDS: Myelodysplastic syndrome; PMF: Primary myelofibrosis; DHAP: Cisplatine, cytarabine, dexametazone; EPOCH: Etoposide, vincristine, doxorubicine, cyclophosphamide, methylprednisolone; ICE: Ifosfamide, carboplatine, etoposide; CHOEP: Vincristine, doxorubicine, etoposide, cyclophosphamide, methylpredniso lone; HyperCVAD: Cyclophosphamide, doxorubicine, vincristine, dexametazone, methotrexate, cytarabine; G-CSF: Granulocyte-colony stimulating factor; MTX-C-ARA: Methotrexate, cytarabine; IGEV: Ifosfamide, gemcitabine, vinorelbine, methylprednisolone; BEAM: Carmustine, etoposide, cytarabine, melphalan; Bu/Cy/E: Busulfan, cyclophosphamide, etoposide; CBV: Carmustine, etoposide, cyclophosphamide.

TABLE 2: Major cardiac complications during the first 28 days post HSCT (n=8).

	Age/sex	Diagnosis	Cumulative anthracycline dose (mg/m²)	Cardiac disease	Pre-HSCT EF (%)/PAP	Conditioning regimens/HSCT type	Onset of toxicity (day HSCT)	Cardiac toxicity (Bearman grade)/outcome
1	66/M	MM	144	DM, HT	65/29	Melphalan 200 mg/m²/auto	Day 13	Severe CHF, AF (Grade III)/alive
2	54/F	HL	450	-	64/40	BEAM protocol/auto	Day 8	Severe CHF, AF (Grade III)/alive
3	69/F	MM	184	DM, HT	64/27	Melphalan 200 mg/m²/auto	Day 1	Atriyal flutter, SVT, requiring cardioverison (Grade III)/alive
4	63/M	NHL	None	HT	60/29	Thiotepa/Bu/Cy/ auto	Day 4	Sudden cardiac arrest (Grade IV)/died on day 4
5	62/M	NHL	475	CABG	62/25	Bu/Cy/E protocol/auto	Day 1	Cardiogenic shock, fatal (Grade IV)/died on day 1
6	55/M	NHL	510	-	65/25	Bu/Cy/E protocol/auto	Day 9	Hemodynamically significant AF, requiring cardioverison (Grade III)/alive
7	52/F	MM	122	HT, arrhythmia	62/30	Melphalan 200 mg/m²/auto	Day 6	SVT, requiring cardioverison (Grade III)/alive
8	68/F	MM	124	HT, CRF, CAD	65/25	Melphalan 200 mg/m²/auto	Day 14	Acute coronary syndrome (Grade III)/alive

HSCT: Hematopoietic stem cell transplantation; PAP: Pulmonary arterial pressure; EF: Ejection fraction; M: Male; F: Female; MM: Multiple myeloma; DM: Diabetes mellitus; HT: Hypertension; CHF: Congestive heart failure; AF: Atriall fibrillation; HL: Hodgkin lymphoma; BEAM: Carmustine, etoposide, cytarabine, melphalan; Bu/Cy/E: Busulfan, cyclophosphamide, etoposide; SVT: Supraventricular tachycardia; NHL: Non-Hodgkin lymphoma; CABG: Coronary artery bypass graft; CRF: Chronic renal failure; CAD: Coronary artery disease.

veloped cardiac toxicity during administration of preparative regimen, all incidents were post-HSCT. Severe cardiac toxicity (Grade III and Grade IV) was experienced by 8 patients, 2 of them died. Detailed clinical and laboratory features of the patients who had severe cardiac toxicity are given in Table 2. Grade I and II cardiac complications that can be detected by retrospective evaluation are given in Table 1. Sinus bradycardias resolved without intervention, digoxin and beta-blockers were used for Grade II atrial fibrillation, beta-blockers were used for atrial flutter and supraventricular tachycardia (SVT), and diuretics were used for CHF, and all Grade I and Grade II cardiac complications resolved. Regarding development of cardiac complications, there were no difference in terms of gender, serum ferritin level, anthracycline usage and whether anthracycline was used within 60 days before HSCT, mediastinal radiotherapy, whether autologous or allogeneic HSCT was performed, pre-HSCT ECG and ECHO findings (rate, rhythm, QT/QTc interval, EF, LAD, LVDd, LVDs, IVSth, PWth, and E/A) ($p>0.05$, comparative results of two groups are shown in Table 3). Patients with cardiac complications were found to have a significantly higher PAP as measured by ECHO (30.5 vs. 28.5, $p=0.029$). Out of 218 patients, 74 (33.9%) had a pre-HSCT history of cardiac comorbidity, such as coronary artery disease (CAD) and arrhythmia. The comorbidities in the patients were 16.6% (n=35) hypertension, 12.8% (n=27) diabetes mellitus, 7.1% (n=15) chronic renal failure, 3.8% (n=8) CAD, 1.4% (n=3) hyperlipidemia, 1% (n=2) arrhythmia, 1% (n=2) cerebrovascular disease and 0.5% (n=1) chronic obstructive pulmonary disease, respectively. Cardiac complications subsequent to HSCT occurred in 22 (15.2%) of 144 patients who had no prior cardiac comorbidity and in 16 (21.6%) of 74 patients who had a prior cardiac comorbidity. Presence of a prior history of cardiac comorbidity was not identified as a risk acting on development of post-HSCT cardiac complications (two-sample Kolmogorov-Smirnov test, $p=0.919$). Anthracycline was used by 146 patients. Likewise, no association was found between the cumulatively used dose of anthracycline and development of cardiac toxicity ($p>0.05$).

When patients were stratified into 2 as EF <55% and EF ≥55%, there was no difference between the 2 subgroups in terms of cardiac complication development ($p>0.05$).

Patients with ST-T alterations in the pre-transplant ECG had a higher rate of cardiac complications (chi-

TABLE 3: The relationship between possible confounding factors and the development of severe cardiac complications in hematopoietic stem cell transplantation patients.

	Severe cardiac complications		
	Positive (n=8)	Negative (n=210)	p value
Sex, (male/female), n	4/4	118/92	0.933
Age, years	57.5 (20-71)	54.5 (19-71)	0.347
History of cardiac disease, n	6/8	68/210	0.919
Ferritin level, median (Q1-Q3), ng/mL	309.5 (117.5-1665)	293.6 (22.8-7498)	0.325
Cumulative dose of anthracyclines	6	140	0.312
Low	2	55	
Medium	4	83	
High	0	2	
Anthracyclin within 60 days	0	2	>0.99
ECG			
QT interval (ms), median (Q1-Q3)	0.34 (0.24-0.48)	0.32 (0.20-0.40)	0.303
QTc interval (ms), median (Q1-Q3)	0.37 (0.29-0.52)	0.38 (0.31-0.52)	0.386
ECHO findings, median (Q1-Q3)			
EF, %	62 (50-65)	63 (50-77)	0.292
LAD (mm)	37 (20-47)	35 (23-46)	0.164
LVDd (mm)	46.5 (38-55)	46 (25-59)	0.624
LVDs (mm)	30 (20-39)	29 (20-47)	0.178
IVSth (mm)	10 (8-14)	10 (7-24)	0.569
PWth (mm)	10 (8-15)	10 (7-13)	0.704
E/A ratio	0.65 (0.25-2.6)	0.52 (0.02-8)	0.585
PAP mm/Hg	30.5 (25-58)	28.5 (20-55)	0.029*
Stem cell transplantation			
Auto/allo	8/0	178/32	0.969
Bone marrow/peripheral blood	0/8	3/207	

*Statistically significant; ECG: Electrocardiography; ECHO: Echocardiogram; LAD: Left atrial dimension; LVDd: Left ventricular end-diastolic dimension; LVDs: Left ventricular end-systolic dimension; IVSth: End-diastolic intraventricular septal thickness; PWth: Left ventricular posterior wall thickness; PAP; Pulmonary arterial pressure.

square, p=0.019). When patients with systolic PAP ≤25 mmHg (n=55) vs. >25 mmHg (n=80) as measured by ECHO were compared, cardiac complications were significantly more common in those with higher pressure (chi-square, p=0.031). Although patients of advanced age more frequently had severe cardiac complications, the difference had borderline statistical significance (binary logistic regression analysis, p=0.061). When the patients were classified as using high-dose cyclophosphamide and those using low-dose cyclophosphamide, there was no difference in the development of cardiac complications between the two subgroups (p>0.05). Among the conditioning regimens, the group who received melphalan 200 mg/m^2 had significantly more cardiac toxicity (p=0.040).

DISCUSSION

Cardiovascular complications are one of the most common complications associated with HSCT.[12] Cardiac complications which may occur subsequent to HSCT usually include arrythmia, CHF, cardiac tamponade, and ventricular arrythmia. The incidence of severe cardiac complications has varied among studies, from less than 1% to more than 9%.[2-4,6,7,13] In our study, rate of HSCT-associated cardiac complications including arrythmia, CHF, cardiogenic shock within the first 28 days of transplantation was 3.6%. In our cohort, incidence of severe cardiac complications was at a comparable rate to that mentioned in the previous literature.

The most important risk factors for post-HSCT cardiac toxicity have been listed priorly as: cumulative pre-transplant anthracycline dose exposure and the use of anthracyclines within the 60 days before transplantation, administration of high dose cyclophosphamide, other intensive conditioning regimen, TBI, low EF, advanced age, female gender, and QTc interval in pre-HSCT ECG.[2,3,7,14-16] In our study, on the other hand, neither cumulative anthracycline dose nor use of anthracyclines within the 60 days before transplantation were found to be associated with severe cardiac toxicity. Corroborating the results of Hertenstein et al., EF was not identified as associated with severe cardiac toxicity, implying that pre-transplant EF could not be the sole determinant for cardiac toxicity.[7] In our comparison of patients with EF lower than 55% vs. greater than 55%, cardiac toxicity was not more common among those with lower EF. A likely explanation for this could be because we did not perform HSCT on any patients who had pre-transplant EF value lower than 50%, therefore we had no patients with EF values less than 50%. Although we also did not identify gender as a risk factor for cardiac toxicity, a finding in line with the previous literature was that cardiac toxicity was more frequently encountered in older patients.

Among the preparative regimens of HSCT, melphalan, either used alone for autologous HSCT or in combination with fludarabine within reduced-intensity conditioning, was reported to cause cardiac complications including arrhythmia in 9% of the cases.[17-19] The most common arrhythmias after HSCT include atrial fibrillation, atrial flutter, and SVT. Risk factors for the development of arrhythmias include the following; older age, prior anthracycline use, lower baseline EF, history of arrhythmias, baseline renal dysfunction, and the presence of premature supraventricular complexes on baseline screening ECG.[13,17] Our analysis of HSCT conditioning regimens in association with cardiac toxicities revealed melphalan 200 mg/m^2 used in conditioning regimen was a significant risk factor compared to other regimens in HSCT recipient patients. Types of arrhythmia experienced by our patients who had received melphalan often took place in the forms of SVT, atrial fibrillation, and atrial flutter which was consistent with the previous findings in literature. In our cohort, all of 4 patients who had received a conditioning regimen consisting of melphalan 200 mg/m^2 and then developed cardiac toxicity had a prior history of cardiac disorder, with one of them also had a prior history of arrhythmia. When a conditioning regimen consisting of melphalan 200 mg/m^2 is intended or in the event of patients with pre-HSCT history of arrhythmia or ST segment and T-wave alterations observed in ECG, closer attention should be paid to cardiac adverse event follow-up.

In literature, there is a scarce number of studies on pulmonary arterial hypertension-related cardiac mortality over the first 100 days of HSCT, and most studies have focused on analysis of PAP impact on late-term mortality.[20,21] In their study, Özdöver et al. compared the HSCT recipients with pre-transplant PAP higher than 25 mmHg vs. lower than 25 mmHg regarding mortality, with no difference over the first 100 days or 12 months, but afterwards in late-term, 5-year mortality was significantly higher in HSCT recipients with pre-transplant PAP value was higher than 25 mmHg.[20] In this study, we have evaluated the cardiac complications over the first 28 days after HSCT when not only PAP was identified as a prognostic parameter affecting cardiac complications but also patients with pre-transplant PAP value >25 mmHg had a higher rate of cardiac toxicity. On contrary to previous studies, our findings suggest PAP value of measured by ECHO may hold a place as a prognostic variable to estimate post-HSCT acute cardiac complication, particularly those ranked as Grade III-IV by severity.

The main limitation of this study is its retrospective design. Second, it includes both allegoneic and autologous HSCT patients. Third, it lacks some ECHO findings as they could not be investigated in detail. Moreover, this work is restricted by the extent of complications evaluated; Grade 1 and Grade 2 cardiac toxicities which remained asymptomatic and/or did not require any treatment as well as other cardiovascular complications such as de novo hypertension and exacerbation of hypertension episodes were not addressed here. Fourth, the patients treated with allogeneic HCST is limited and the data seem skewed due to the limited proportion of patients who were

treated with allogeneic HSCT. The group is also heterogenous in terms of primary diagnosis and conditioning regimen.

CONCLUSION

Cardiac and pulmonary complications are more important limiting factors for HSCT. Cardiac toxicity in HSCT was heterogeneous. Arrhythmias, severe CHF, cardiogenic shock and sudden cardiac arrest have been documented. EF value in the pre-transplantation period is not sufficient to predict cardiac toxicity in HSCT patients. In addition to the EF value, pre-transplant cardiac assessment warrants an ECG exam and PAP measurement by ECHO. ST segment and T-wave alterations observed in pre-transplant ECG, PAP as measured by ECHO and particularly a reading over >25 mmHg, and utilization of melpahalan (200 mg/m^2) as conditioning regimen feature out as the most important risk factors for cardiac complications which may develop subsequent to HSCT.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Hava Üsküdar Teke, Deniz Teke;* ***Design:*** *Hava Üsküdar Teke, Eren Gündüz;* ***Control/Supervision:*** *Cengiz Bal, Hava Üsküdar Teke;* ***Data Collection and/or Processing:*** *Hava Üsküdar Teke, Eren Gündüz;* ***Analysis and/or Interpretation:*** *Hava Üsküdar Teke, Deniz Teke, Cengiz Bal;* ***Literature Review:*** *Hava Üsküdar Teke, Deniz Teke, Eren Gündüz;* ***Writing the Article:*** *Hava Üsküdar Teke, Deniz Teke;* ***Critical Review:*** *Hava Üsküdar Teke, Eren Gündüz, Deniz Teke.*

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