

Study of baseline echocardiography and treatment endpoint in patients with acute lymphoblastic leukemia

Gholamreza Bahoush¹, Semira Mehralizadeh², Neda Tavakoli³,
Marzieh Nojoomi⁴

¹Pediatric Hematologist and Oncologist, Ali-Asghar Children Hospital, Department of Pediatrics, Faculty of Medicine, Iran University of Medical Sciences, ²Pediatric Cardiologist, Ali-Asghar Children Hospital, Iran University of Medical Sciences, ³Department of Pediatrics, Faculty of Medicine, Iran University of Medical Sciences, ⁴Department of Community Medicine, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran

ABSTRACT

Introduction: Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Anthracyclines are among the most common and effective drugs for the treatment of children ALL. However, long-term consumption and higher doses of these drugs may lead to toxic effects on the heart of children. For this purpose, in the present study, the baseline and posttreatment echocardiography status was evaluated in children with ALL during 7 years. **Materials and Methods:** This retrospective cross-sectional study was performed on 53 children with ALL who were under the age of 18 years. Different factors including risk groups, age, gender, white blood cells, dosage, and duration of treatment, as well as baseline and posttreatment echocardiography findings including EF, E/A, E/A', MVE/A were evaluated in all patients. **Results:** All enrolled patients had not any abnormalities in the baseline echocardiography preventing the beginning of chemotherapy. The results of this study did not show a significant difference in mean baseline echocardiography parameters after treatment including EF, E/A, E/A', MVE/A. In addition, there was no significant difference in mean EF, E/A, E/A', MVE/A, and E/E before and after treatment among SR, IR, and HR groups. Although there was no significant difference in the mean EF, E/A, and MVE/A before and after treatment between male and female sex, the mean E/E after chemotherapy in girls (8.5 ± 0.7) was significantly higher than the mean before treatment (6.85 ± 1.5) ($P < 0.001$). It was also higher than the mean in boys (7.04 ± 0.99) ($P = 0.019$). Although there was no significant relationship between the duration of chemotherapy and the mean of EF, E/A, E/A', MVE/A after treatment, high dose of the drug was found to be significantly associated with a gradual decrease of EF or systolic function of the heart ($P < 0.001$). There was no significant relationship between drug dose and other parameters of echocardiography including E/A, MVE/A, and E/E after treatment. **Conclusion:** It appears that chemotherapy should not be delayed by echocardiography. Based on the findings presented herein, increasing the dose of anthracycline can be considered as an effective factor in reducing the systolic function of the heart (EF reduction). On the other hand, chemotherapy in the period of 1 to 5.3 years does not seem to have a significant effect on the mean parameters of EF, E/E, E/A, and MVE/A although another study with higher sample size and follow-up is needed to confirm these results.

Keywords: Acute lymphoblastic leukemia, anthracycline, cardiac toxicity, conventional echocardiography, tissue Doppler echocardiography (TDE)

Introduction

Cancer is considered to be a chronic disease. Given the current treatment, many cancer patients are endangering life-threatening conditions; therefore, cancer can be considered as one of the

Address for correspondence: Dr. Semira Mehralizadeh,

Pediatric Cardiologist, Associate Professor, Ali-Asghar Children Hospital, Iran University of Medical Sciences, Tehran, Iran.

E-mail: mehralizadeh@sums.ac.ir

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most annoying diseases. Childhood cancer also includes a group of malignancies, each of which has its own pathology and mortality rate.^[1] Childhood cancer is one of the cancers that are diagnosed in children under the age of 15.^[2] Leukemia is a cancerous hematopoietic tissue that includes bone marrow and lymphatic system. Leukemias are generally divided into two acute and chronic categories and are classified into two major groups, acute myeloblastic leukemia (AML) and acute lymphoblastic (ALL), depending on the type of origin of the cell.^[3] ALL accounts for about 77% of all childhood leukemia and its prevalence has been attributed to the ages of 2–5 and is reported more commonly in boys than in girls.

Usually, the primary manifestations of ALL are nonspecific and mild, including anorexia, fatigue, irritability, mild and intermittent fever, petechia or ecchymosis, lethargy, bone or joint pain, especially in the lower extremities, and history of an upper respiratory tract infection in the past 1–2 months.^[4,5]

This disease is heterogenic and the factors such as age of the patient at diagnosis, sex, liver and spleen enlargement, lymph nodes size, white blood cell count, immunophenotype, central nervous system involvement, and response to early treatment are important in determining the prognosis of disease.^[6]

Success in the treatment of patients with acute lymphoblastic leukemia is due to the progression of chemotherapy drugs, improvement of chemotherapy methods and protocols, and advancement in supportive care. Today, anthracyclines are one of the most common and effective chemotherapy drugs for ALL. Anthracyclines, such as adriamycin and daunomycin, are naturally occurring compounds that interact with the activity of the topoisomerase enzyme and, as a result, impair the reproduction and repair of cancer cells.^[7]

Although anthracyclines are widely used in chemotherapy against certain types of cancers, especially ALL, studies have shown that these compounds are the most common causes of cardiac toxicity in a dose-dependent manner.^[8] The prevalence of toxicity from these drugs has been attributed to 7%–15%, and has reached 36% even in cumulative doses.^[9] Heart failure following anthracycline treatment occurs when compensatory mechanisms fail to maintain normal myocardial function. As a result, patients treated with anthracyclines should be evaluated for the diagnosis of cardiac dysfunction.

These patients may have no symptoms of cardiac toxicity, and ECG changes, echocardiography, angiography, and serum levels of cardiac enzymes are effective in detecting chemotherapy-induced cardiac toxicity.^[10]

For this purpose, the evaluation of cardiac function using conventional echocardiography and tissue Doppler imaging (TDI) before and after treatment is important in preventing the risk of heart problems in children with ALL. Therefore, the aim of this study was to evaluate the status of

baseline echocardiography in ALL patients and to assess the end of treatment in these patients.

Materials and Methods

This retrospective, cross-sectional study was conducted on medical records of 60 children under the age of 18 years old with ALL under the anthracycline chemotherapy were selected during the years 2007 to 2013 in Ali Asghar Hospital, Tehran-Iran. Demographic information about patients including age, gender, and history of any familiar diseases was recorded and inclusion and exclusion criteria were investigated.

Inclusion criteria were: 1) age under 18 years and 2) having ALL disease. Exclusion criteria included: 1) use of chemotherapy drugs other than anthracyclines; 2) other cancerous diseases; 3) parental dissatisfaction; 4) incomplete information in the medical records; 5) lack of baseline echocardiography and posttreatment examination; and 6) congenital heart problems and abnormalities.

After assessing the patients' records, 53 patients eventually found the conditions for inclusion. Then, clinical and laboratory results were recorded for patients including WBC. According to IC-BFM 2009, patients were finally divided into three risk groups including SR (standard-risk), IR (intermediate-risk), and HR (high risk).

$$\text{Ejection fraction} = \frac{\text{LVEDV} - \text{LVESV} \times 100}{\text{LVEDV}}$$

LVEDV = Left ventricular end-diastolic volume

LVESV = Left ventricular end-systolic volume

In this study, the left ventricular ejection fraction (LVEF) was considered as normal if this value was equal to or higher than 55%, while value below 55% was defined as abnormal. After that, the mitral valve was examined. E and A waves were measured and then the E/A ratio was also calculated. In the next step, tissue Doppler echo was performed, in which the waves a', e', and s' septal of the mitral valve were examined and the ratios of e'/a' and E'/e' were calculated.

According to the Guideline published in the Journal of the American Society of Echocardiography in 2016, the test is considered diastolic dysfunction when E/e' >14 and e' <7, and if E/e' ≤14 and e' ≥7, it is considered as normal diastolic function.^[11] Then, the grading was done. Normal right atrial pressure and grade I diastolic dysfunction were classified when the following conditions are met: E/A ≤0.8 and E ≤50 cm/s, and E/A <0.8, E >50 cm/s or 0.8 <E/A >2 and E/e' >14 is reported as an increase in the right atrial pressure and Grade II diastolic dysfunction. The MV E/A index is related to the rate of fractional discharge of the mitral valve, in which its normal range is different in different age groups. According to the new guidelines, the normal value of MV E/A in age group of <1 year, 1–5 years, 6–9 years, 10–13 years, and 14–8 years of age was determined as 1.2 ± 0.03, 1.6 ± 0.5, 2 ± 0.5, 2 ± 0.6,

and 2.1 ± 0.7 .^[12] Finally, the relationship of the duration of chemotherapy and the dose of drug was evaluated and assessed by echocardiography. Furthermore, the relationship of echocardiographic findings with age, sex, and risk groups was also analyzed.

Data analysis

The results of this study were analyzed by SPSS software (version 19). Quantitative data were analyzed using the descriptive program and displayed as Mean \pm SD. Crosstabs and Chi-Square tests were used to compare the percentages or frequencies between the groups. The McNemar test has been used to compare the mean of normal and abnormal echo data before and after treatment. The comparison of the mean of parametric data between two groups, including two groups of women and men, was compared by independent sample-t test.

Comparison of mean echo data (i.e. EF, E/E', E'/A', and MVE/A) before and after treatment was performed by Paired-t-test. ANOVA test and Tukey test were used to compare the mean echo data, drug dosage, and duration of chemotherapy among SR, IR, and HR groups. Pearson correlation test was employed to examine the relationship between quantitative variables and Spearman's correlation test was used to evaluate the ranked variables. In addition, the effect of an independent variable on the level of dependent variables was investigated using multiple linear regression. In this study, the *P* value less than 0.05 was considered statistically significant.

Ethical considerations

All patient information is completely confidential. This project was approved at the Ethics Committee of the University of Medical Sciences.

Results

A total of 53 patients were enrolled on the basis of inclusion and exclusion criteria. The prevalence of risk groups among the patients showed that the IR group was the most common (60.4%) among the patients, as compared to two HR states (22.6%) and SR (17%) groups (*P* < 0.001).

Of all enrolled patients, 29 (54.7%) were male and 24 (45.3%) were female, the frequency of IR group was determined in girls (66.66%) and boys (55.17%). The frequency of HR risk in the female group (27.58%) and the boy (16.66%) was also reported, followed by the prevalence of risk in the SR group (female: 17.24% and male: 16.66%). According to the results, there was no significant difference in the percentage of each risk group between males and females (*P* = 0.61), and the frequency of IR risk group in both males and females was significantly higher than other HR and SR risk groups (*P* < 0.001).

In Table 1, mean normal range of EF (equal to or above 55%) and abnormal (<55%) was shown before and after treatment; there

was no significant difference in mean of normal and abnormal EF range before and after treatment (*P* > 0.05).

The percentage of patients with abnormal EF before treatment was 20.8%, which reduced to 15.1% after treatment, while the frequency of patients with normal EF before and after treatment was 79.2% and 84.9%, respectively. There was no significant difference in the percentage of normal or abnormal EF before and after treatment (*P* > 0.05).

Regarding the mean of echocardiographic parameters before and after chemotherapy, mean of EF before and after treatment in all patients was $61.54\% \pm 6.26\%$ and $63.09 \pm 5.9\%$, respectively. There was no significant difference in mean EF before and after treatment in all patients (*P* = 0.11).

The mean normal range of E/A (<0.8%) and abnormal (equal to or less than 0.8%) in the pre and posttreatment stage is shown in Table 2. Frequency of normal E/A before and after treatment was 92.9% and 90.5% after treatment, which was not significantly different (*P* > 0.05).

Furthermore, the frequency of abnormal E'/A'/patients before and after treatment was 7.1% and 9.5%, respectively; although it was slightly increased, this increase was not statistically significant (*P* > 0.05). In addition, the mean E'/A' before and after treatment was $1.82\% \pm 0.43$ and $1.83\% \pm 0.63$, respectively. No significant difference was found in mean E'/A' before and after treatment in all patients (*P* = 0.94).

Table 1: Mean of normal and abnormal EF in the pre and posttreatment stage

Parameters	EF-before		EF-after	
	Normal ($\geq 55\%$)	Abnormal (<55%)	Normal ($\geq 55\%$)	Abnormal (<55%)
EF Mean \pm SD	63.85 \pm 4.6	52.72 \pm 3.03	64.71 \pm 4.77	54 \pm 1.92
Frequency (%)	42 (79.2%)	11 (20.8%)	45 (84.9%)	8 (15.1%)

Table 2: Mean of normal and abnormal E'/A' in the pre and posttreatment stage

Parameters	E'/A'-before		E'/A'-after	
	Normal (>0.8)	Abnormal (≤ 0.8)	Normal (>0.8)	Abnormal (≤ 0.8)
E'/A'/Mean \pm SD	1.91 \pm 0.29	0.63 \pm 0.15	1.96 \pm 0.48	0.55 \pm 0.28
Frequency (%)	39 (92.9%)	3 (7.1%)	38 (90.5%)	4 (9.5%)

Table 3: Average normal and abnormal E/E' in the pre and posttreatment stage

Parameters	E/E'-before		E/E'-after	
	Normal (≤ 14)	Abnormal (>14)	Normal (≤ 14)	Abnormal (>14)
E/E'/Mean \pm SD	7.09 \pm 1.45	-	7.65 \pm 1.13	-
Frequency (%)	34 (100%)	-	34 (100%)	-

Moreover, the mean MV E/A was determined as 1.6 ± 0.35 before treatment in all patients, while the rate was set to be $1.49 \pm 0.28\%$ after treatment. There was no significant difference in the mean MV E/A before and after treatment in all of the patients ($P = 0.06$). The frequency of patients with normal MV E/A before and after treatment was 42 (79.2%) and 39 (73.6%) respectively; although the percentage was reduced, this was not statistically significant ($P > 0.05$). Furthermore, the frequency of abnormal MV E/A patients before and after treatment was 11 (20.8%) and 14 (26.4%), respectively; although this frequency showed a mild increase after treatment, this was not statistically significant ($P > 0.05$).

Table 3 shows the mean of normal E/E' (equal to or <14) and abnormal (above 14) range in the pre and posttreatment stage. All patients had normal E/E' range before and after treatment. No significant difference was found in the prevalence of normal E/E' in pre and posttreatment ($P > 0.05$). Frequency of patients with normal E/E' before and after treatment was determined as 100%. There was no significant difference in the prevalence of normal E/E' before and after treatment ($P = 1.0$). In addition, the frequency of patients with abnormal E/E' before and after treatment was 0%. There was no significant difference in this regard ($P = 1.0$).

The mean of E/E' before and after treatment in all patients was determined as $7.9 \pm 1.29\%$ and $7.21 \pm 1.2\%$, but no significant difference was observed in mean E/E' before and after treatment in all patients. ($P = 0.39$).

In terms of EF before and after chemotherapy in both male and female groups, the mean score of EF before and after treatment in all patients was $61.54 \pm 6.26\%$ and $63.09 \pm 5.9\%$. There was no significant difference in mean EF before and after treatment in all patients ($P = 0.11$). The mean of EF before and after treatment in both male and female groups is shown in Table 4.

Table 5 shows the mean of EF before and after chemotherapy in each risk group, in which the results showed no significant difference in the mean of EF before ($P = 0.88$) and after chemotherapy ($P = 0.87$) in each risk group.

The mean of E'/A' before and after chemotherapy was evaluated in each risk group [Table 6]. The obtained data indicated no significant difference in the mean E'/A' before ($P = 0.42$) and after chemotherapy ($P = 0.2$) in each risk group.

In Table 7, the mean E'/A' before and after chemotherapy was evaluated in both sexes and the results were as follows: there was a significant difference in the mean E'/A' before ($P = 0.53$) and after chemotherapy ($P = 0.69$), between male and female. Table 7 shows the mean E'/A' before and after chemotherapy in each sex group.

The mean E/E' before and after chemotherapy in each risk group is shown in Table 8, indicating a significant difference in the

Table 4: Mean EF before and after chemotherapy in male and female

	Gender	Mean	Std. Deviation	P
EF before	Male	62.17	6.61	0.43
	Female	60.79	5.86	
EF after	Male	63.75	5.55	0.37
	Female	62.29	6.31	

Table 5: Mean of EF before and after chemotherapy in each risk group

		Mean	Std. Deviation	P
EF before	IR	61.53	6.05	0.88
	HR	62.16	5.81	
	SR	60.77	8.08	
EF after	IR	63.43	5.41	0.87
	HR	62.50	6.96	
	SR	62.66	6.68	

Table 6: Mean E'/A' before and after chemotherapy in each risk group

		Mean	Std. Deviation	P
E'/A' before	IR	1.83	0.333	0.42
	HR	1.80	0.424	
	SR	2.13	0.305	
E'/A' after	IR	1.80	0.510	0.2
	HR	1.61	0.967	
	SR	2.15	0.407	

Table 7: E'/A' mean before and after chemotherapy in each sex group

	Gender	Mean	Std. Deviation	P
E'/A' before	Male	1.83	0.35	0.53
	Female	1.95	0.33	
E'/A' after	Male	1.86	0.67	0.69
	Female	1.79	0.58	

Table 8: Mean E/E' before and after chemotherapy at each risk group

		Mean	Std. Deviation	P
E/E' before	IR	7.07	1.36	0.75
	HR	6.90	1.87	
	SR	7.66	0.577	
E/E' after	IR	7.88	1.24	0.6
	HR	7.06	0.92	
	SR	7.50	.	

mean E/E' before ($P = 0.75$) and after chemotherapy ($P = 0.6$) in each risk group.

The mean E/E' before and after chemotherapy in each sex group was indicated in Table 9. Our results revealed no significant difference in mean E/E' before chemotherapy between the two sex groups ($P = 0.44$), while the mean E/E' after chemotherapy

in girls ($8.5 \pm 0.7\%$) was significantly higher than that of boys ($7.04 \pm 0.99\%$; $P = 0.019$). Furthermore, the mean E/E' after chemotherapy in girls was significantly higher than the mean before treatment ($P < 0.01$). However, there was no significant difference in mean E/E' before and after treatment in boys.

In Table 10, the mean MV E/A before and after chemotherapy was investigated in each risk group. According to the results, a significant difference was not seen in the mean MV E/A before ($P = 0.71$) after chemotherapy ($P = 0.96$), in each risk groups.

The mean of MV E/A before and after chemotherapy in each sex group was shown in Table 11. Based on the results, no significant difference was seen in the mean MV E/A before ($P = 0.31$) and after chemotherapy ($P = 0.59$) between two groups.

According to Table 12, the average duration of chemotherapy and the dose of the drug in all patients was 2.5 ± 1 years and 178.63 ± 145.65 mg/g, respectively, and no significant difference was found in the mean duration of chemotherapy ($P = 0.62$) and drug dose ($P = 0.69$) between two groups, indicating that this dosage and the duration of chemotherapy did not affect the improvement of patients.

The average duration of chemotherapy and the dose of a drug used in each of the risk groups is shown in Table 13. Regarding

the findings, there was no significant difference in the mean duration of chemotherapy (P -pain = 0.72) between groups, indicating that chemotherapy did not affect the improvement of patients, while a significant difference was observed in the mean dose of the drug ($P = 0.005$). The dosage of the drug in the HR group was significantly greater than the two groups of IR ($P = 0.002$) and SR (P -pain = 0.006), which indicates that this dosage was better in patients with HR where increased their health; however, there was no significant difference in the dosage of the drug between the IR and SR groups ($P = 0.62$).

Regarding the relationship between the duration of chemotherapy and echocardiographic factors, there was a significant relationship between the duration of chemotherapy and EF ($P = 0.89$), E/A ($P = 0.88$), MVE/A ($P = 0.69$), and E/E' ($P = 0.85$), indicating that although the duration of chemotherapy was accompanied by a slight increase in E/E', this relationship was not statistically significant.

The relationship between drug dosage and echocardiography was evaluated and there was no significant correlation between E/A (P -pain = 0.99), ($P = 0.24$) E/E', and MV E/A ($P = 0.94$). However, a significant relationship was found between the dose of EF and EF ($P = 0.003$), indicating that the dose of EF decreased by increasing dosage.

Comparison of the frequency of tricuspid valve regurgitation in patients before and after treatment was shown in Figure 1. A significant difference was found in the frequency of tricuspid valve regurgitation before and after treatment ($P = 0.0001$). Before treatment, 42.1% of the patients had no tricuspid valve regurgitation, followed by mild regurgitation (26.3%) and trivial regurgitation (31.6%). After treatment, 2.6% of the patients exhibited tricuspid valve regurgitation. The mild tricuspid valve regurgitation and trivial regurgitation were attributable to 21.1% and 76.3% of the subjects.

Table 9: Average E/E' before and after chemotherapy in each sex group

	Gender	Mean	Std. Deviation	P
E/E' before	Male	7.32	1.43	0.44
	Female	6.85	1.50	
E/E' after	Male	7.04	0.99	0.019
	Female	8.50	0.70	

Table 10: Mean MV E/A before and after chemotherapy at each group risk

		Mean	Std. Deviation	P
MV E/A before	IR	1.59	0.31	0.71
	HR	1.67	0.39	
	SR	1.55	0.43	
MV E/A after	IR	1.49	0.27	0.96
	HR	1.51	0.36	
	SR	1.50	0.22	

Table 11: Mean MV E/A before and after chemotherapy between two sex groups

	Gender	Mean	Std. Deviation	P
MV E/A before	Male	1.64	0.39	0.31
	Female	1.55	0.28	
MV E/A after	Male	1.51	0.32	0.59
	Female	1.47	0.24	

Table 12: Mean duration of chemotherapy and drug dosage based on the gender

	Gender	Mean	Std. Deviation	P
Chemotherapy duration (year)	Male	2.44	0.77	0.62
	Female	2.58	1.23	
Drug dose (mg)	Male	186.07	155.26	0.69
	Female	169.95	136.36	

Table 13: Average chemotherapy duration and drug dose for each of the risk groups

		Mean	Std. Deviation	P
Chemotherapy duration (year)	IR	2.46	1.13	0.72
	HR	2.70	0.86	
	SR	2.38	0.65	
Drug dose (mg)	IR	149.64	105.03	0.005
	HR	294.16	215.49	
	SR	124.44	58.60	

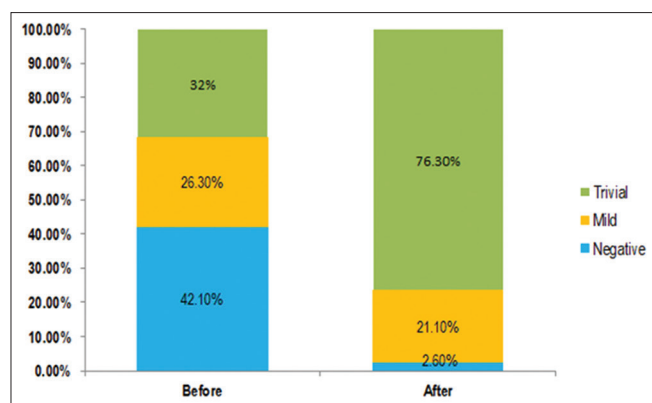


Figure 1: Frequency of tricuspid valve regurgitation before and after treatment

Discussion

Leukemia is one of the malignant diseases of the hematopoietic system, which is associated with an increase in the production of abnormal white blood cells and causes mortality in a very short time.^[13] Leukemia accounts for about 8% of all cancers and is the fifth most common cancer in the world.^[14]

In this study, the baseline and posttreatment echocardiography status was evaluated in 53 children with ALL. The relationship between echocardiographic findings with dose and duration of drug use in the sex and risk groups was also compared. The results of this study showed that more than half of patients (60.40%) were in moderate risk or IR group, while the frequency of HR and SR risk groups was 60.20% and 17%, respectively. There was no significant difference in the distribution of risk groups between boys and girls.

The results of comparison of mean baseline echocardiographic parameters and posttreatment in all patients did not show a significant difference in the mean of EF, E/A', MV E/A, and E/E/ϕ. Therefore, our findings showed that chemotherapy with anthracycline has no significant effect on systolic and diastolic activity of the heart in children with ALL, which was not consistent with the results of Horacek, 2009,^[15] as the results of his research showed that chemotherapy with anthracycline is associated with changes in electric activity of the myocardium, QRS voltage reduction, and left ventricular dysfunction in ALL patients.

Moreover, there were no significant differences in the mean EF, E/A', and MV E/A before and after treatments between male and female sex groups. However, mean E/E/ϕ, after treatment in female patients (8.5 ± 0.7) was significantly higher than males (7.04 ± 0.99). Furthermore, the mean E/E/ϕ after chemotherapy (8.5 ± 0.7) in girls was significantly higher than the mean before treatment (6.85 ± 1.5), which indicates the effect of chemotherapy on the E/E/ϕ, parameter in the girls in comparison with boys. These findings were more or less in agreements with a Dr. Kang and their colleagues in 2018 study that evaluated

the subclinical left ventricular dysfunction after anthracycline treatment. They indicated that echocardiography did not show significant changes in cardiac function parameters (systolic and diastolic activity), while subendocardial deformity was evident in these patients.^[16] In the present study, the relationship between the results of baseline echocardiography and posttreatment parameters in all three risk groups was compared. The results of statistical analysis showed no significant difference in the mean of EF, E/A', MV E/A, and E/E/ϕ, before and after treatment among SR, IR, and HR groups. This result suggests that there is no relationship between risk groups and heart disease in these patients.

The average duration of chemotherapy and the dose of the drug used in all patients was 2.5 ± 1 years and 178.63 ± 145.65 mg. There was no significant difference in the mean duration of chemotherapy and the dose of the drug used between the two groups. Furthermore, no significant difference was found in the mean duration of chemotherapy between risk groups. But, the dose of anthracycline in the HR group was significantly more than the IR and SR groups.

Dr. Keihanian and their colleagues evaluated 46 breast cancer patients who underwent anthracyclines-containing chemotherapy. As their results showed that EF after the third period of chemotherapy in 89.2% of patients was equal to or greater than 50%, while one year after the onset of chemotherapy, this frequency decreased to 84.7%.

The mean EF before chemotherapy in patients was determined as $64.5 \pm 5.3\%$; it was recorded as $54.1 \pm 5.6\%$ after the third chemotherapy period and one year after the onset of chemotherapy, it reached to $52.2 \pm 4.8\%$, and these changes were statistically significant. Therefore, Dr. Keihanian and their colleagues stated that anthracycline chemotherapy resulted in a decrease in the mean EF,^[17] which was not consistent with the findings of our study. In the current study, there was no significant change in the mean EF before and after chemotherapy in patients, which is probably due to the duration of the follow-up and even the dose of the drug. A study indicated that the effect of echo application prior to anthracycline-based therapy on 120 AML patients, in which 97% of the patients had an LVEF of more than 50%. In 4 patients (3%), the baseline EF was less than 40%. The results of this study showed that LVEF does not correlate with the survival rate of patients. On the other hand, 4 of the patients with EF <40% received anthracycline and only one patient had cardiac disorders. Therefore, the researchers stated that the results of echocardiography were normal in 99% of AML patients undergoing chemotherapy with anthracycline. Therefore, they conclude that it is not clear whether echocardiography, especially in younger patients, provides valuable results in identifying cardiac injuries from chemotherapy.^[18] Although in our study, echocardiography has been assessed in children with ALL, the results of this research are largely in line with our findings.

In the present study, 42.1% of the patients had not tricuspid valve regurgitation before treatment, followed by mild

regurgitation (26.3%) and trivial regurgitation (31.6%). After treatment, 2.6% of the patients exhibited tricuspid valve regurgitation. The mild tricuspid valve regurgitation and trivial regurgitation were attributable to 21.1% and 76.3% of the subjects. These results indicate that chemotherapy leads to an increased tricuspid valve regurgitation after treatment.

Conclusion

Increasing the dosage of anthracycline can be considered as an effective factor in reducing systolic cardiac function (EF reduction). On the other hand, chemotherapy in the period of 1 to 5.3 years does not seem to have a significant effect on the mean parameters of EF, E/A×, MV E/A, and E/E/although another study with higher sample size and follow-up is needed to confirm these results. On the other hand, it appears that chemotherapy should not be delayed by echocardiography.

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Conflicts of interest

There are no conflicts of interest.

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