Volume 5 • Issue 1 • 2023

Research Article

Journal of Medical Research and Case Reports

Cardiac Echography Assessment for Cardiac Iron Overload among Thalassemia Patients: A Cross-sectional Study

Ahmad Abu Lamzi[1]*, Abdullah Abu Lamzi[2], Sohaib Abu Nasser[3], Aseel Abu Nada[4], Nour Abu AlHussein[4] and Ibrahim Owda[1]

[1]*Internal Medicine Department, Nasser Medical Complex, Ministry of Health, Khan Younis, Palestine*

[2]*Internal Medicine Department, An-Najah National University Hospital, Nablus, Palestine*

[3]*Family Medicine Department, Al-Rimal Primary Health Care Center, Gaza, Palestine*

[4]*Anesthesia and ICU Department, Shifa Medical Complex, Gaza, Palestine*

***Corresponding Author:** Ahmad Abu Lamzi, Internal Medicine Department, Nasser Medical Complex, Ministry of Health, Khan Younis, Palestine.

Received: May 19, 2022; **Published:** May 30, 2023

Abstract

Background and Objective: Many thalassemia patients don't have any symptoms until the disease has progressed to the point where the heart has been damaged by iron overload. Consequently, the prognosis of such individuals might be improved with early diagnosis of cardiac abnormalities at preclinical levels. We analyzed tissue Doppler echocardiography for its potential use in the preliminary diagnosis of iron overload in these individuals.

Methods: Two- and three-dimensional echocardiography were used to evaluate 52 thalassemic individuals with normal global LV function who were receiving frequent blood transfusions. The echo finding-serum ferritin level correlation was studied.

Results: This study included 52 asymptomatic thalassemic patients (23 females and 29 males) with global LVEF> 55%. They received periodic clinical exams, blood transfusions to maintain hemoglobin levels over 9.5, and chelation treatments (Deferoxamine or combination of Deferoxamine and Deferiprone). Patients averaged 23.75. Serum ferritin averaged 2584 19.3 ng/ml. Spearman's correlation coefficient connected cardio echography and serum ferritin levels. Ecocardiography did not correlate with blood ferritin levels (r = 0.14, p = 0.92). Table 1 details additional linkages. All other echocardiographic markers did not correlate with iron levels, although septal myocardial velocity and global strain did (P = 0.002, P 0.001).

Conclusion: Many thalassemia patients don't show symptoms until iron excess damages the heart. The aforementioned studies and our investigation showed a strong relationship between cardiac echography and iron accumulation. This approach should be tested as a screening tool for myocardial iron excess.

Citation: Ahmad Abu Lamzi, Abdullah Abu Lamzi, Sohaib Abu Nasser, Aseel Abu Nada, Nour Abu AlHussein and Ibrahim Owda. (2023). Cardiac Echography Assessment for Cardiac Iron Overload among Thalassemia Patients: A Cross-sectional Study . *Journal of Medical Research and Case Reports* 5(1). DOI: 10.5281/zenodo.8026172

Introduction

Caused by flaws in the mother's ability to produce hemoglobin, thalassemia is a kind of microcytic, hypochromic hemolytic anemia. The thalassemia gene is carried by around 9 percent of the world's population. According to many studies [1, 2], it has the highest prevalence of any genetic disorder. Blood transfusions may improve the symptoms of serious thalassemia patients who have severe anemia. Without regular blood transfusions, patients with thalassemia major would be in a severe state of anemia (hemoglobin less than 6 g/dL) [3]. Iron overload is a frequent medical issue for people with thalassemia major who are receiving transfusions for their disease. Chelation treatment is required since each blood unit contains between 200 and 250 mg of iron [4, 5].

The heart, liver, and endocrine glands are especially vulnerable to the toxic effects of iron excess. Chelation therapy has been effective in the treatment of this condition [6]. Patients with alpha thalassemia were the first to have iron overload-induced cardiomyopathy documented in 1964 [7]. Non-transferrin binding iron (NTBI) is released into the bloodstream as a result of secondary overload because iron metabolism is disrupted and the iron level in the circulation is higher than the transferrin capacity. NTBI is highly reactive and causes the production of oxygen free radicals. Finally, this leads to the development of membrane lipids peroxidation and oxidative damages to cellular proteins.

When treated promptly with iron chelation treatment, iron-deposit-induced cardiomyopathy may be reversed. To avoid the development of heart failure, it is crucial to look for iron deposits in the heart as early as possible [8]. Subclinical cardiac involvement cannot be diagnosed with a standard electrocardiogram (ECG), physical examination (physical exam), standard echocardiogram, or serum ferritin level [9]. Unfortunately, this technique is not widely accessible because of its high price tag.

Typical echocardiography, which looks at things like ejection fraction (EF) and fractional shortening (FS), isn't reliable enough for early detection of cardiac iron overload. Previous studies have proven the advantages of modern echocardiographic methods such as Strain Imaging [10, 11] and Tissue Imaging [12] for the diagnosis of early and subclinical myocardial dysfunction syndromes. However, most of the studies have compared thalassemia patients with normal population and have omitted a comparison with cardiac MRI results as the noninvasive gold standard [13] and if this comparison is done just a correlation evaluation was done. A more pressing concern is how these echocardiographic results vary in individuals with cardiac MRI T2* values of less than 20 ms, which is indicative of myocardial iron deposition. Here, we are going to address this issue and to explain if advanced echocardiography may be beneficial in thalassemia patients as an available approach for detection of subclinical instances cardiac iron overload to identify individuals in need of additional clinical treatment [14].

Methods

Study Design and Participants

The research was conducted between December 22, 2022, and January 19, 2023. Cardiovascular disease, echocardiographic evidence of dysfunction, valvular disease, arrhythmia, coronary heart disease (CHD), endocrine disease (diabetes, hypothyroidism, hypertension), and the use of drugs known to affect cardiac function were all reasons for excluding patients from the study. As a result of echocardiographic indications of LV dysfunction, we had to exclude two individuals from the research, bringing the total number of participants to 50. All patients provided written informed permission after being provided with a short summary of the study's aims.

Echocardiographic Studies

All patients had echocardiograms taken on GE vivid 9 machines. Typical pictures were captured of patients at the left lateral, subcostal, apical, and para-sternal positions. Everyone who participated in the research had normal sinus rhythm. Modified Simpson methods were used to estimate LVESV and LVEDV based on two apical 2 chamber and apical 4 chamber views, respectively; from these measurements, the EF was derived. Tissue Doppler studies evaluated E (early diastolic) systolic s and diastolic velocities on the lateral and mitral septal annulus walls in apical 4 chamber view. Both septal and lateral strains were measured from the same vantage point. The global longitudinal strain was determined using the 2D specked tracking echocardiography (STE) technique [10] in three apical 2-chamber, 3-chamber, and 4-chamber perspectives. In all patients, ferritin levels were measured at the hospital laboratory anywhere from 2 days to 2 weeks after MRI and echo investigations were performed.

Statistical Analysis

The Spearman rank correlation test was performed to analyze the relationship, with significant results being found for p-values under 0.05. To determine a threshold for GLS based on the detection of myocardial iron overload, a receiver operating characteristic (ROC)

curve analysis was performed. The Statistical Software for the Social Sciences, version 23.0, was used for all analyses (SPSS Inc., Chicago, IL, USA).

Ethical Consideration

An ethical approval was gained from cardiology department administration as well as hospital's administration. Study objectives were explained to participants and parents or participant according to their age signed written informed consent.

Results

Among thalassemic patients admitted to the hospital, 52 asymptomatic individuals with thalassemia major (23 females and 29 males) with global LVEF> 55% (Global left ventricular ejection fraction) were chosen for this research. They had been subjected to frequent clinical examinations, blood transfusions to keep their hemoglobin levels over 9.5, and chelation treatments (Deferoxamine or combination of Deferoxamine and Deferiprone). The average age of the patients was 23.75 years. The mean serum ferritin concentration was 2584 19.3 ng/ml.

Cardio echography results association with serum ferritin levels parameters were correlated using Spearman's correlation coefficient. We found no statistically significant relationship between ecocardiography results and blood ferritin concentrations (r = 0.14, p = 0.92). Table 1 displays other relationships in more depth.

	Echo findings	Ferritin	
		Correlation coefficient (r)	P value
EF (%)	58.96 ± 4.96	0.12	0.38
Septal systolic Velocity (mm/sec)	5.67 ± 1.03	0.12	0.93
Septal early diastolic velocity (mm/sec)	9.63 ± 1.88	0.14	0.33
Lateral systolic Velocity (mm/sec)	6.10 ± 1.56	0.06	0.65
Lateral early diastolic Velocity (mm/sec)	12.60 ± 1.70	0.09	0.51
Septal systolic Strain (%)	1.05 ± 0.26	0.14	0.31
Lateral systolic Strain (%)	1.12 ± 0.32	0.19	0.18
Global Strain (%)	19.36 ± 3.24	0.26	0.06
Left Ventricular End Systolic Volume (mm^3)	21.85 ± 6.20	−0.11	0.42
Left Ventricular End Diastolic Volume (mm^3)	53.65 ± 12.68	−0.02	0.88

Table 1: *Echocardiographic findings and their correlation with serum ferritin level. Data are represented as mean ± SD*

Septal myocardial velocity and global strain were the only echocardiographic measures shown to have a statistically significant connection with iron levels (P = 0.002, P 0.001), whereas all others failed to do so.

Discussion

Here, we compared the results of echo Doppler and strain echo parameters in thalassemia patients. Serum ferritin level and ejection fraction were not substantially linked with MRI T2* results [15], indicating that they are not useful for predicting aberrant deposition of cardiac iron and for making an early diagnosis of heart failure in individuals with thalassemia. T2* was significantly associated with septal systolic myocardial velocity and global longitudinal strain, but not with the other echocardiographic data. With a sensitivity of 82.14% and specificity of 86.36%, a T2* level below 20 could be predicted by a global strain rate 19.5.

Multiple research have looked at how different echocardiographic characteristics in thalassemia patients compare to cardiac MRI readings. Aypar et al. [15] found a correlation between sepal SM (Septal systolic myocardial velocity) and septal EM (Septal early diastolic myocardial velocity) in a study of 33 thalassemia patients. Systolic RV free wall strain, septal wall strain, and lateral wall strain were all substantially linked with thalassemia trait 2* in a study of 30 thalassemia patients by Magri et al. [16]. There was also a significant correlation between T2* and RVEM (Right ventricular early diastolic myocardial velocity), septal EM (septal early myocardial velocity), septal SM (septal early myocardial velocity), and LVEM (Left ventricular lateral wall early diastolic myocardial velocity) from TDILVSM (Left ventricular lateral wall systolic myocardial velocity). Our results show that the T2* value correlates with septal systolic myocardial velocity, therefore their conclusions are consistent with ours. Variations in diastolic cardiac function between the septal wall and RV free wall and the Lat LV wall are likely due to higher iron accumulation at the septal wall and thinner RV free wall [16]. Since iron deposition occurs often in the LV septum, it stands

to reason that this region would experience less strain under cardiac iron overload [13].

Research has compared echocardiographic parameters in the general population to those in thalassemia patients. Hamdy conducted a research comparing 27 patients with thalassemia and 14 healthy controls, and found that thalassemic patients exhibited localized systolic dysfunction in the LV lateral wall and diastolic dysfunctions in the LV septal wall and RV free wall [17]. Vogel et al. studied 52 asymptomatic thalassemia patients with TDI and MRI T2* and found that thalassemic patients exhibited reduced systolic and diastolic cardiac velocities compared to the control group [18]. Eighty-seven percent of the participants in this research had regional systolic and diastolic dysfunctions, and seventy-three percent exhibited aberrant cardiac iron overload. When looking for anomalous iron deposits, the TDI had a sensitivity of 88 and a specificity of 65 [19]. Left ventricular end-systolic diameter, end-diastolic volume, end-systolic volume, left ventricular mass index, and mitral early/late diastolic flow velocity ratio were all shown to be significantly higher in children with thalassemia (p 0.05) in separate research by Bay et al. Patients had increased strain and strain rate in the left ventricle's basal lateral wall compared to healthy controls. As a result of their analysis, they came to the conclusion that, in children, LV volume and mass index measures may be more sensitive than the other traditional and strain/strain rate imaging parameters.

Strain and strain rate imaging results in adults, however, may be lower than normal [20, 21]. The detection of left ventricular dysfunction at an early stage in thalasemic patients may be aided by STI, as shown by Parsaee et al. [14]. Both global longitudinal strain (GLS; 20.9% 1.9 vs. 22.2 1.03) and longitudinal strain in the basal segments (17.4% 2.7 vs. -19.6% 1.2) were significantly lower in the study group compared to the normal subjects group. The researchers found no connection between circumferential strain and left ventricular dysfunction. On the other hand, as noted by Ari et al. [22], an abnormal strain value, particularly a circumferential one, may be the first discovery of aberrant iron load and is connected to T2* values.

Despite the significance of these discoveries, more research should focus on the associations between myocardial iron overload and cardiac MRI T2* values of fewer than 20 milliseconds. As can be shown in Table 2, only GLS demonstrated a significant connection with cardiac MRI T2* values of less than 20 milliseconds, out of all the parameters assessed in our investigation (including ferritin level). Consistent with our results, Silviarat et al. [19] found that blood ferritin levels were unable to detect iron accumulation in the myocardium in 31 thalassemic individuals with normal global LVEF. The global longitudinal strain may diagnose T2* under 20 with a sensitivity of 76% and specificity of 88% [23], according to a research conducted by Garceau et al. on 45 patients with thalassemia major or Diamond Blakfan anemia who were undergoing continuous blood transfusion. Furthermore, Pizzino et al. demonstrated that GLS substantially correlated with T2* values (R = 0.49; P = 0.001), and that it was considerably lower in individuals with a T2* value lower than 20 milliseconds (18.3 2 vs. 21.3 2.7, P = 0.02). Significant myocardial iron deposition was more likely to be seen in individuals with impaired GLS (19.5%) (Odds-ratio-OR = 17; 95% confidence interval [CI]). Using a threshold of 19.5 as a cut off value, our research found that GLS could detect Iron deposition with a sensitivity of 82.14 percent and a specificity of 86.3 percent. Therefore, it may be hypothesized that GLS evaluation might serve as a helpful and less costly method for screening myocardial iron overload, particularly in countries with a restricted MRI availability due to logistical or budgetary constraints.

Conclusion

Many thalassemia patients don't have any symptoms until the disease has progressed to the point where the heart has been damaged by iron overload. As shown by the findings of the aforementioned research and the substantial link we established in our study between cardiac echography and iron deposit. More prospective research is required to see whether this method may be used as a screening tool for the early diagnosis of myocardial iron overload.

References

1. Pizzino F, Meloni A, Terrizzi A, et al. (2018). Detection of myocardial iron overload by two-dimensional speckle tracking in patients with beta-thalassaemia major: a combined echocardiographic and T2* segmental CMR study. Int J Cardiovasc Imaging. ; 34: 263–271.
2. Hosseini SH, Khani H, Khalilian A, Vahidshahi K. (2007). Psychological aspects in young adults with Beta- Thalassemia major, control group. J Mazandaran Univ Med Sci. 17: 51–60.
3. Attar A, Khosravi Maharlooi M, Khoshkhou S, et al. (2013). (2001). Colony forming unit endothelial cells do not exhibit telomerase alternative splicing variants and activity. Iran Biomed J. 17:146–151.
4. Porter JB. Practical management of iron overload. Br J Haematol. 115: 239–252.

5. Attar A, Aghasadeghi K, Parsanezhad ME, Namavar Jahromi B, Habibagahi M. (2015). Absence of correlation between changes in the number of endothelial progenitor cell subsets. Korean Circ J. 45: 325–332.
6. Wood JC, Ghugre N. (2008). Magnetic resonance imaging assessment of excess iron in thalassemia, sickle cell disease and other iron overload diseases. Hemoglobin. 32:85–96.
7. Walker JM, Nair S. (2010). Detection of the cardiovascular complications of thalassemia by echocardiography. Ann N Y Acad Sci. 1202: 165–172.
8. Murphy CJ, Oudit GY. (2010). Iron-overload cardiomyopathy: pathophysiology, diagnosis, and treatment. J Card Fail. 16: 888–900.
9. Kolnagou A, Economides C, Eracleous E, Kontoghiorghes GJ. (2006). Low serum ferritin levels are misleading for detecting cardiac iron overload and increase the risk of cardiomyopathy in thalassemia patients. The importance of cardiac iron overload monitoring using magnetic resonance imaging T2 and T2*. Hemoglobin. 30: 219–227.
10. Maharlooei MK, Attar A, Goran A, et al. (2017). Hydatid cyst of ovary: a case report. Iran J Med Sci. 34: 76–79.
11. Mirzaee F, Attar A, Mohammadianpanah M, Abtahi F, Amirmoezi F, Moaref A. Speckle tracking echocardiography for detection early myocardial changes in patients treated with anthracyclines. Int Cardiovasc Res J. 11: 55–59.
12. Abtahi F, Zibaeenezhad MJ, Shafazadeh F, Tahamtan M. (2016). Tissue Doppler findings in patients with pulmonary arterial hypertension. Int Cardiovasc Res J. 10: 113–117.
13. Ramazzotti A, Pepe A, Positano V, et al. (2009). Multicenter validation of the magnetic resonance T2* technique for segmental and global quantification of myocardial iron. J Magn Reson Imaging. 30: 62–68.
14. Parsaee M, Saedi S, Joghataei P, Azarkeivan A, Alizadeh SZ. (2017). Value of speckle tracking echocardiography for detection of clinically silent left ventricular dysfunction in patients with β-thalassemia. Hematology. 22: 554–558.
15. Aypar E, Alehan D, Hazirolan T, Gümrük F. (2010). The efficacy of tissue Doppler imaging in predicting myocardial iron load in patients with beta thalassemia major: correlation with T2* cardiovascular magnetic resonance. Int J Cardiovasc Imaging. 26: 413–421.
16. Magrì D, Sciomer S, Fedele F, et al. (2008). Early impairment of myocardial function in young patients with beta thalassemia major. Eur J Haematol. 80: 515–522.
17. Hamdy AM. (2007). Use of strain and tissue velocity imaging for early detection of regional myocardial dysfunction in patients with beta thalassemia. Eur J Echocardiogr. 8: 102–109.
18. Vogel M, Anderson LJ, Holden S, Deanfield JE, Pennell DJ, Walker JM. (2003). Tissue Doppler echocardiography in patients with thalassaemia detects early myocardial dysfunction related to myocardial iron overload. Eur Heart J. 24: 113–119.
19. Silvilairat S, Sittiwangkul R, Pongprot Y, Charoenkwan P, Phornphutkul C. (2008). Tissue Doppler echocardiography reliably reflects severity of iron overload in pediatric patients with beta thalassemia. Eur J Echocardiogr. 9: 368–372.
20. Bay A, Başpınar O, Leblebisatan G, Yalçın AS, İrdem A. (2013). Detection of left ventricular regional function in asymptomatic children with beta-thalassemia major by longitudinal strain and strain rate imaging. Turk J Haematol. 30: 283–289.
21. Zibaeenezhad MJ, Farhadi P, Attar A, Mosleh A, Amirmoezi F, Azimi A. (2017). Effects of walnut oil on lipid profiles in hyperlipidemic type 2 diabetic patients: a randomized, double-blind, placebo-controlled trial. Nutr Diabetes. 7: e259.
22. Ari ME, Ekici F, Çetin İİ, et al. (2017). Assessment of left ventricular functions and myocardial iron load with tissue Doppler and speckle tracking echocardiography and T2* MRI in patients with β-thalassemia major. Echocardiography. 34: 383–389.
23. Garceau P, Nguyen ET, Carasso S, Ross H, et al. (2011). Quantification of myocardial iron deposition by two-dimensional speckle tracking in patients with β-thalassaemia major and Blackfan-diamond anaemia. Heart. 97: 388–333.

Citation: Ahmad Abu Lamzi, Abdullah Abu Lamzi, Sohaib Abu Nasser, Aseel Abu Nada, Nour Abu AlHussein and Ibrahim Owda. (2023). Cardiac Echography Assessment for Cardiac Iron Overload among Thalassemia Patients: A Cross-sectional Study . *Journal of Medical Research and Case Reports* 5(1). DOI: 10.5281/zenodo.8026172

Citation: Ahmad Abu Lamzi, Abdullah Abu Lamzi, Sohaib Abu Nasser, Aseel Abu Nada, Nour Abu AlHussein and Ibrahim Owda. (2023). Cardiac Echography Assessment for Cardiac Iron Overload among Thalassemia Patients: A Cross-sectional Study . *Journal of Medical Research and Case Reports* 5(1). DOI: 10.5281/zenodo.8026172