Serial Changes in Cardiac Strain and Contractility After Hematopoietic Stem Cell Transplantation in Patients with Hematologic Malignancies

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Summary

Hematopoietic stem cell transplantation (HSCT) is occasionally associated with cardiac dysfunction during long-term follow-up. Global longitudinal strain (GLS) has emerged as an early predictor of cardiotoxicity associated with cancer therapy; however, the serial changes in GLS before and after HSCT have not been elucidated. To clarify the association between HSCT and GLS, we investigated serial changes in GLS before and after HSCT. We evaluated cardiac function before and 1, 3, and 6 months after HSCT in 38 consecutive HSCT patients enrolled in this study. Overall, GLS and left ventricular (LV) ejection fraction (EF) temporally decreased 1 month post-HSCT. LVEF completely recovered to baseline at 3 months after HSCT, whereas GLS partially recovered 6 months after HSCT. Except for five patients who died within 6 months, GLS values in the low EF group (LVEF ≤ 55% at 6 months post-HSCT, n = 6) were significantly and consistently lower than those in the normal EF group (LVEF > 55% at 6 months post-HSCT, n = 27) at any time during follow-up. These findings suggest that GLS before HSCT might be associated with a decrease in LVEF after HSCT in patients with hematologic malignancies. Further prospective and long-term data will be important for understanding the management of HSCT-associated cardiac dysfunction.

Key words: HSCT-associated cardiac dysfunction, LVEF, GLS
cardiotoxicity during follow-up periods of 6 and 12 months.\textsuperscript{11,12} In contrast, the effect of HSCT on cardiac function has not been extensively validated. Therefore, the current study analyzed serial changes in GLS in patients with hematologic malignancies before and after HSCT over a 6-month period to explore the ability of GLS to indicate subclinical HSCT-associated cardiac dysfunction.

**Methods**

This single-center observational study used an HSCT database consisting of prospectively collected data from the Osaka International Cancer Institute (OICI), Osaka, Japan. The study protocol and consent forms were approved by the local ethics committee (approval No. 1712079249), and written informed consent was provided by the patients.

**Patients:** Of 44 consecutive patients with hematologic malignancies who underwent HSCT between December 2017 and September 2018 at the OICI, 38 who met the inclusion criteria were enrolled (Figure 1). The inclusion criteria were a diagnosis of histologically and cytologically confirmed hematologic malignancies and a single HSCT treatment history. Exclusion criteria were receiving multiple HSCTs for any reason \textit{(n} = 2), insufficient echocardiographic data \textit{(n} = 3), and low initial LVEF (< 50\%) before HSCT \textit{(n} = 1) (Figure 1). Cardiac comorbidities, initial medications, history of conditioning chemotherapy and TBI, source of HSCT, hematopoietic cell transplantation comorbidity index (HCT-CI) score, cardiac troponin-I (TnI) and B-type natriuretic peptide (BNP) concentrations, and other data prior to and 1, 3, and 6 months following HSCT were obtained from the electronic medical records.

**Transthoracic echocardiography and cardiac strain:** Transthoracic echocardiography was performed using an IE 33 imaging device (Philips HealthCare, Amsterdam, The Netherlands). According to the HSCT database protocol, echocardiographic data were obtained before and 1, 3, and 6 months after HSCT. Images were obtained in the left lateral decubitus position, and two-dimensional images of at least three beats were digitally stored for offline analysis. LV end-diastolic dimension (LVDd), LV end-systolic dimension (LVDs), and LV wall thickness were measured in the parasternal long-axis view. Tissue Doppler-derived indices were measured using the apical four-chamber view, and the e’ was measured via the septal mitral annulus. Automatic tracking analysis by QLAB (v. 10.0; Philips HealthCare) was performed on apical four-chamber, two-chamber, and three-chamber views for GLS according to the manufacturer’s instructions. QLAB automatically obtained the endocardial and epicardial borders at the end-diastole to adjust the range of interest (ROI). The obtained ROI was fine-tuned by a cardiologist manually. GLS was obtained as the average of 17 segmental strains. QLAB automatically calculated LVEF obtained by the biplane modified Simpson method after manual adjustment of the ROI by a cardiologist.

**Statistical analyses:** Parametric comparisons of serial echocardiographic parameters and physiological biomarkers were performed using two-way analysis of variance (ANOVA), followed by Bonferroni post-hoc test for pairwise comparisons. Within- and between-group comparisons of changes in cardiac parameters were made and tested with the paired and unpaired \textit{t}-tests, respectively. Statistical analyses were performed using Prism software.
Table I. Patient Characteristics

|                      | All (n = 38) | Normal EF (n = 27) | Low EF (n = 6) |
|----------------------|-------------|--------------------|---------------|
| Age (median)         | 55 (44–61)  | 56 (46–61)         | 50.5 (48–55)  |
| Male (%)             | 22 (57.9)   | 15 (55.6)          | 4 (66.7)      |
| Hematologic malignancy (%) |
| AML                  | 9 (23.7)    | 7 (30.4)           | 1 (16.7)      |
| ALL                  | 3 (7.9)     | 2 (7.4)            | 1 (16.7)      |
| CML                  | 3 (7.9)     | 2 (7.4)            | 0 (0)         |
| MDS                  | 10 (26.3)   | 5 (18.5)           | 3 (50.0)      |
| Malignant lymphoma    | 13 (34.2)   | 11 (40.7)          | 1 (16.7)      |
| HSCT (%)             |             |                    |               |
| Unrelated BMT        | 10 (26.3)   | 8 (29.6)           | 1 (16.7)      |
| Related PBSCST       | 14 (36.8)   | 9 (33.3)           | 4 (66.7)      |
| Unrelated PBSCST     | 4 (10.5)    | 2 (7.4)            |              |
| CBT                  | 10 (26.3)   | 8 (29.6)           | 1 (16.7)      |
| Anthracyclines (%)   | 29 (76.3)   | 20 (74.1)          | 4 (66.7)      |
| Total dose, mg/m²     | 116 (6–207) | 120 (3–192)        | 124 (99–235)  |
| TBI (%)              | 29 (76.3)   | 21 (77.8)          | 5 (83.3)      |
| HCT-CI score         |             |                    |               |
| 0                    | 25 (65.8)   | 19 (70.4)          | 3 (50.0)      |
| 1                    | 6 (15.8)    | 5 (18.5)           | 1 (16.7)      |
| 2                    | 4 (10.5)    | 3 (11.1)           | 1 (16.7)      |
| 3                    | 0 (0)       | 0 (0)              | 0 (0)         |
| 4                    | 3 (7.9)     | 0 (0)              | 1 (16.7)      |
| Comorbidity (%)      | 21 (55.3)   | 15 (55.6)          | 4 (66.7)      |
| Hypertension         | 9 (23.7)    | 8 (29.6)           | 1 (16.7)      |
| Diabetes             | 8 (21.1)    | 5 (18.5)           | 1 (16.7)      |
| Dyslipidemia         | 11 (28.9)   | 9 (33.3)           | 2 (33.3)      |
| Smoking              | 6 (15.8)    | 3 (11.1)           | 2 (33.3)      |
| Drugs (%)            |             |                    |               |
| ß blocker            | 8 (21.1)    | 5 (19.2)           | 1 (16.7)      |
| ACEi/ARB             | 8 (21.1)    | 6 (22.2)           | 2 (33.3)      |
| Calcium blocker      | 5 (13.2)    | 4 (15.4)           | 1 (16.7)      |
| Diuretics            | 2 (5.3)     | 0 (0)              | 1 (16.7)      |

Age and total anthracycline dose are presented as median (interquartile range). ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BMT, bone marrow transplantation; CBT, cord blood transplantation; CML, chronic myelogenous leukemia; EF, ejection fraction; HCT-CI, hematopoietic cell transplantation comorbidity index; MDS, myelodysplastic syndrome; PBSCST, peripheral blood stem cell transplantation; and TBI, total body irradiation.

Results

Characteristics of HSCT patients and overall assessment of cardiac function following HSCT: Table I summarizes the characteristics of all patients with hematologic malignancies treated by HSCT. The median patient age was 55 years (IQR: 44.3-61.0 years), with 57.9% males and 55.3% carrying at least one cardiovascular risk factor and receiving cardioprotective drugs (Table I). Hematologic malignancies included acute myeloid leukemia (23.7%), acute lymphoblastic leukemia (7.9%), chronic myelogenous leukemia (7.9%), myelodysplastic syndrome (26.3%), and malignant lymphoma (34.2%). The sources of HSCT were unrelated bone marrow (26.3%), related peripheral blood stem cells (36.8%), unrelated peripheral blood stem cells (10.5%), and cord blood (26.3%), all of which were allogeneic (Table I). In the pre-transplantation course, 76.3% of the patients received anthracyclines as induction or consolidation chemotherapy at a median dose of 116 mg/m² (IQR: 6-207 mg/m²), and 76.3% of the patients received TBI. Patients previously received cardioprotective and anti-hypertensive drugs, including a ß blocker (21.1%), angiotensin-converting enzyme inhibitor (ACEi)/angiotensin II receptor blocker (ARB) (21.1%), calcium blocker (13.2%), and diuretics (5.3%), before HSCT (Table I). The HCT-CI score was 0 in 65.8% of the patients, 1 in 15.8%, 2 in 10.5%, and 4 in 7.9% (Table I), suggesting a relatively low risk for HSCT and cardiovascular diseases in this cohort.

To assess the influence of HSCT on cardiac function, we serially analyzed cardiac parameters and physiological biomarkers before and after HSCT. BNP and cardiac TnI levels significantly increased from baseline to 73.8 ± 96.7
pg/mL and 0.016 ± 0.015 ng/mL after 1 month of HSCT, respectively ($P < 0.05$), and almost recovered to basal levels 6 months after HSCT (Table II). These results suggest that myocyte damage might have occurred at a relatively early stage after HSCT and recovered within 6 months. Although the overall LVEF slightly but significantly decreased at 1 month after HSCT, LVEF was almost stable during the observational period after HSCT (Figure 2A and Table III). In contrast, $e'$ significantly decreased and $E/e'$ increased at 3 months after HSCT, and both were significantly altered at 6 months post-HSCT compared to the pre-HSCT values (Table III). Additionally, overall GLS showed a significant reduction at 1 month post-HSCT (−18.8% ± 0.7%) relative to baseline (−19.3% ± 0.7%) ($P < 0.05$ versus pre-HSCT) and did not fully recover to the basal level but significantly increased from the nadir at 1 month to 6 months post-HSCT (−19.1% ± 0.8%, $P < 0.05$ versus pre-HSCT and 1 month post-HSCT) (Table III and Figure 2B). These findings indicated that LVEF was relatively stable during a 6-month follow-up period after HSCT, whereas GLS and diastolic function indicated by $e'$ and $E/e'$ displayed variability following HSCT, although the serial changes in GLS and $e'$ were unexpectedly small.

We assessed the relationship between patients’ pretransplantation course, e.g., anthracyclines, TBI, cardioprotective drugs, LVEF or GLS (Supplemental Tables I, II). We could not detect any significant effects of anthracyclines and/or TBI on LVEF and GLS (Supplemental Table I) in the analyzed groups at 6 months after HSCT. The proportions of patients receiving drugs increased after HSCT to 28.9% for ACEi/ARB, 36.8% for calcium blockers, and 26.3% for diuretics. The patients could be categorized into four groups: (1) no cardioprotective drug ($n = 22$), (2) drug(s) initiated after HSCT ($n = 2$), (3) receiving drugs before and after HSCT ($n = 6$), and (4) additional drugs and/or increased dose of drug(s) ($n = 3$) (Supplemental Table II). In groups (2) and (4), the drugs were started and increased with the intention of cardioprotection. Although LVEF and GLS tended to decrease after 6 months in group (4), in which reduction of LVEF was a reason for the increased number of drug(s), there was no difference in LVEF and GLS obtained pre-HSCT and 6 months after HSCT in each group.

**Reduction of LVEF after HSCT might be associated with low baseline GLS:** To predict HSCT-induced subclinical cardiac dysfunction, we analyzed LVEF at 6 months after HSCT with a cutoff LVEF of 55% according to a guideline of the Cardiac Review and Evaluation Committee. After excluding five patients who died due to the progression of the original disease within 6 months post-HSCT, we found 6 HSCT patients who showed LVEF ≤ 55% at 6 months post-HSCT (Figure 1). We then evaluated these 6 patients by classifying them into a low EF group (LVEF ≤ 55% at 6 months post-HSCT) and compared them with the remaining 27 patients in the normal EF group (LVEF > 55% at 6 months post-HSCT) (Figure 1 and Table I). Before HSCT, there was no obvious difference in cardiac risk factors and HCT-CI score. There was no significant difference in basal LVEF between the low and normal EF groups (57.4% ± 3.1% versus 59.8% ± 2.5%; $P = 0.056$) (Figure 3A and Table IV). However, LVEF in the low EF group showed significant continuous decreases at 3 and 6 months post-HSCT, whereas the normal EF group maintained the basal level until 6 months after HSCT (55.8% ± 3.5% versus 60.3% ± 2.6%, $P = 0.001$; and 53.6% ± 2.1% versus 59.6% ± 2.1%, $P < 0.001$; respectively) (Figure 3A and Table IV). These results suggest that HSCT might have subclinical detrimental effects on cardiac function in some patients with hematologic malignancies. However, it was still difficult to distinguish these two groups using the LVEF values before HSCT or 1 month post-HSCT (Figure 3A and Table IV).

Serial changes in GLS for each group showed different patterns. Basal GLS in the low EF group was significantly lower than that in the normal EF group (−18.5% ± 0.8% versus −19.5% ± 0.6%; $P = 0.0024$) (Figure 3B and Table IV). GLS decreased slightly at 1 month post-HSCT in the normal EF group and recovered to baseline levels up to 6 months post-HSCT. In contrast, the low EF group showed continuous reductions in GLS at 3 and 6 months post-HSCT, with these levels significantly lower than those in the normal EF group (−18.1% ± 0.8% versus −19.3% ± 0.7%, $P < 0.001$; and −17.9% ± 0.5% versus −19.3% ± 0.6%, $P < 0.001$) (Figure 3B and Table IV). In both groups, $e'$ tended to decrease from pre-HSCT to 6 months post-HSCT, and $e'$ in the low EF group remained continuously low during the study period. On the other hand, the pre-HSCT $E/e'$ was higher in the low EF group than in the normal EF group, and remained almost equivalent at 6 months after HSCT. However, there were no significant differences in both $e'$ and $E/e'$ between these groups at any time point (Table IV). BNP level in the low EF group was slightly but significantly higher than that in the normal EF group pre-HSCT, and it returned to the basal level at 3 and 6 months after HSCT, even though LVEF decreased at 6 months (Table IV). BNP values var-

### Table II. Serial Change in Blood Analyses in HSCT Patients

|                | Pre-HSCT       | 1 month         | 3 months        | 6 months        |
|----------------|---------------|----------------|----------------|----------------|
| BNP, pg/mL     | 18.4 ± 19.7   | 73.8 ± 96.7*   | 38.8 ± 48.3*   | 29.0 ± 34.4*   |
| Troponin-I, ng/mL | 0.010 ± 0.002 | 0.016 ± 0.015* | 0.012 ± 0.009* | 0.010 ± 0.0002* |
| Hb, g/dL       | 9.42 ± 2.05   | 9.48 ± 1.06    | 10.71 ± 1.71** | 10.85 ± 1.60** |
| Creatinine, mg/dL | 0.72 ± 0.23   | 0.68 ± 0.49    | 0.89 ± 0.36†   | 0.88 ± 0.40†   |
| eGFR, mL/minute/1.73 m² | 89.3 ± 27.7 | 104.5 ± 36.9* | 73.6 ± 29.8†   | 74.3 ± 28.7†   |
| Cystatin C, mg/L | 0.90 ± 0.23   | 1.13 ± 0.48*   | 1.23 ± 0.43*   | 1.16 ± 0.37*   |

*$P < 0.05$ versus pre-HSCT; †$P < 0.05$ versus 1-month post-HSCT. BNP indicates B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; and HSCT, hematopoietic stem cell transplantation.
Figure 2. Serial changes in LVEF and GLS in patients during a 6-months follow-up. A: LVEF (%) did not significantly change before or after 1/3/6 months of HSCT. B: GLS (%) significantly decreased at 1 month post-HSCT and partially recovered 3 and 6 months post-HSCT relative to baseline. *P < 0.05 versus pre-HSCT; †P < 0.05 versus 1 month after HSCT. 1/3/6M indicates 1, 3, and 6 months; GLS, global longitudinal strain; HSCT, hematopoietic stem cell transplantation; and LVEF, left ventricular ejection fraction.

Table III. Serial Changes in Echocardiographic Parameters in HSCT Patients

|                      | Pre-HSCT | 1 month | 3 months | 6 months |
|----------------------|----------|---------|----------|----------|
| HR, bpm              | 76.7 ± 13.6 | 80.4 ± 12.7 | 79.8 ± 13.2 | 78.8 ± 11.7 |
| LVDD, mm             | 46.5 ± 4.9 | 46.1 ± 4.5 | 44.9 ± 4.7* | 45.8 ± 4.4 |
| LVDS, mm             | 30.7 ± 3.9 | 29.5 ± 3.8* | 28.9 ± 3.7* | 29.8 ± 3.7 |
| E/A                  | 1.1 ± 0.3 | 1.1 ± 0.3 | 1.0 ± 0.3 | 1.0 ± 0.3 |
| E, cm/s              | 71.3 ± 18.1 | 72.0 ± 14.8 | 66.4 ± 18.2 | 68.7 ± 17.0 |
| e’, cm/s             | 8.1 ± 2.4 | 7.8 ± 1.7 | 6.6 ± 1.9† | 6.8 ± 1.7*† |
| E/e’                 | 9.3 ± 2.7 | 9.7 ± 2.2 | 10.4 ± 3.1* | 10.4 ± 2.6* |
| Dct, ms              | 210.6 ± 24.1 | 208.1 ± 29.9 | 220.3 ± 26.6 | 218.3 ± 28.8 |
| TRPG, mmHg           | 21.0 ± 4.2 | 20.8 ± 2.8 | 23.7 ± 4.2 | 23.5 ± 5.7 |
| IVC, mm              | 11.2 ± 2.5 | 12.2 ± 3.1 | 10.9 ± 2.4 | 10.8 ± 2.9 |
| GLS, %               | −19.3 ± 0.8 | −18.9 ± 0.7* | −19.0 ± 0.8† | −19.1 ± 0.8*† |
| LVEF, %              | 59.3 ± 2.8 | 58.2 ± 2.9* | 59.5 ± 3.2 | 58.5 ± 3.1 |

LVEF was derived from the biplane modified Simpson method. *P < 0.05 versus pre-HSCT; †P < 0.05 versus 1-month post-HSCT. bpm indicates beats per minute; Dct, deceleration time; e’, peak early diastolic velocity of the mitral annulus; E, peak early diastolic velocity of transmitral flow; GLS, global longitudinal strain; HR, heart rate; HSCT, hematopoietic stem cell transplantation; IVC, inferior vena cava; LV, left ventricular; LVDD, LV end-diastolic dimension; LVDS, LV end-systolic dimension; LVEF, LV ejection fraction; and TRPG, tricuspid regurgitation peak gradient.

Discussion

To the best of our knowledge, this is the first study of cardiac strain in adult Japanese patients with hematologic malignancies before and after HSCT. According to LVEF at 55% at 6 months post-HSCT, classification revealed the possibility that low baseline GLS might be associated with reductions in LVEF after HSCT. Due to the limited number of patients, the relationships among low GLS, low LVEF, cardiovascular risk factors, and outcomes are still unclear. However, functional assessments of cardiac strain such as GLS as well as LVEF might help predict the subclinical risk of cardiac dysfunction after HSCT during long-term follow-up.

Cardiac strain as a marker for detecting LV dysfunction related to cardiotoxicity: Detection of cardiotoxicity associated with cancer treatment is based on evaluation of cardiac contractility over an extended period by echocar-
diography, cardiac magnetic resonance, nuclear cardiac imaging (MUGA), and cardiac biomarkers. Echocardiographic LVEF assessment is the most popular method; however, LVEF is recognized as a late-occurring detector of cardiotoxicity with a low predictive ability for future symptomatic heart failure. Notably, LVEF is not always the ideal index for predicting cardiotoxicity not only due to its load dependency, but also its inability to detect subclinical changes in cardiac function, which would allow timely intervention to slow the progression of cardiac dysfunction. In this study, we found that HSCT patients showing impaired LVEF at 6 months post-HSCT also displayed low GLS before and 6 months after HSCT; however, these patients showed highly similar LVEF as the normal EF group at baseline. Although the cutoff value of LVEF 55% was relatively high relative to several guidelines, we considered this high cutoff value appropriate for early detection based on other guidelines. Evaluation of GLS is also recommended for detecting cardiotoxicity associated with various cancer therapies. The guidelines indicate that a relative GLS reduction of > 15% from baseline might suggest a risk of cardiotoxicity.
In the present study, changes in GLS at all time points were < 8%; however, HSCT patients with impaired LVEF at 6 months post-HSCT showed a relatively low absolute GLS value accompanied by a downward trend. Paraskievaidis, et al. demonstrated that GLS, especially the subendocardial longitudinal strain, was impaired at 1 month after bone marrow transplantation (BMT), and that a cutoff GLS of −18.4% at 1 month after BMT showed high sensitivity and specificity for the identification of abnormal LVEF at 12 months post-BMT.21) At 6 months after HSCT, the cutoff LVEF value of 55% clearly indicated GLS less than −18.5%, which was coincidentally the same as in a previous report (Figure 4B). Although the low EF group was not divided at the pre-HSCT stage (Figure 4A), 3 (50.0%) and 5 (83.3%) patients in the low EF group showed GLS < −18.5% at baseline and 1 month post-HSCT, respectively. Our study demonstrated that low GLS at baseline might predict subsequent subtle LV impairments after HSCT. This finding suggested that the rate of change and the absolute value of GLS could be an early parameter for predicting changes in cardiac contractility after HSCT in patients with hematologic malignancies.

**HSCT and cardiac dysfunction:** The precise underlying mechanism associated with cardiac dysfunction in patients who receive HSCT remains unclear; however, a multifactorial etiology related to anthracyclines, TBI, and other HSCT-associated factors as well as patient-specific cardiovascular risks, should be considered. We evaluated the effects of anthracyclines and TBI on cardiac function (Supplemental Table I); however, further long-term follow-up is necessary. Armenian et al. reported that lymphoma survivors treated with relatively modest doses of anthracyclines (1-249 mg/m²) had a 5-fold higher risk of cardiac dysfunction than controls.22) Furthermore, another study reported that rare variants of cardiomyopathy-associated genes increased the risk of cardiac adverse events in patients receiving anthracyclines.23) These findings suggest that screening should not be limited to survivors treated with high-dose anthracyclines alone, and that cardiac dysfunction might occur even at doses < 250 mg/m². Also, the decreased GLS occurred 1 month post-HSCT even in patients not receiving anthracyclines, TBI, or carrying cardiovascular risk factors, suggesting that the entire HSCT process or other factors might exert a suppressive effect on GLS. Cyclophosphamide, especially at high doses, has also been reported to show cardiotoxicity.24) We found 12 patients (44.4%) in the normal EF group and 3 patients (50.0%) in the low EF group that involved cyclophosphamide administration around HSCT. High-dose cyclophosphamide for posttransplant cyclophosphamide (PTCy) was administered to 3 patients (11.1%) and 1 patient (16.7%) in the normal and low EF groups, respectively. The distribution of these patients suggested that cyclophosphamide, even at high doses, did not seem to have a marked effect on cardiac dysfunction in this study cohort.

**Figure 4.** Relationship between LVEF and GLS before HSCT and 6 months post-HSCT. A: Overlapping distributions of the normal (blue triangles) and low (red circles) EF groups before HSCT. B: At 6 months post-HSCT, the low EF group (red circles) distributed LVEF ≤ 55% and GLS < −18.4%. Blue lines indicate LVEF 55% and GLS −18.5%, respectively. The dotted blue line indicates GLS −17.5%. GLS indicates global longitudinal strain; HSCT, hematopoietic stem cell transplantation; and LVEF, left ventricular ejection fraction.
EF group. The GVHD rate seemed to be higher in the low EF group than in the high EF group. However, the association between LV dysfunction and GVHD was still unclear. We could not conclude the influence of high-dose cyclophosphamide or GVHD on cardiac function in our study. Further observation is necessary to clarify cyclophosphamide- or GVHD-associated cardiac dysfunction.

Limitations of this study: The limitations associated with this study were as follows: it was a single-center study, involved a small sample size and short observational period, and lacked a control group. During the observational period, cardiac adverse events, such as symptomatic heart failure, hospitalization due to heart failure, or depression of LVEF within 6 months post-HSCT were not observed.

Conclusion
Serial cardiac strain and contractility changes revealed an association between sustained low GLS detected pre-HSCT and reductions of LVEF at 6 months post-HSCT in patients with hematologic malignancies. GLS may have the ability to predict LV dysfunction after HSCT in patients with hematologic malignancies. Further investigations are necessary to clarify the cutoff value of GLS and the association between GLS and cardiac adverse events during long-term follow-up of HSCT. Because HSCT is the only radical treatment for hematologic malignancies and improves these diseases’ prognoses, additional research on the associations among treatment exposure, comorbidities, and cardiac function should contribute to further improvement.

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Conflicts of interest: The authors declare no conflicts of interest.

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Supplemental Files

Supplemental Tables I, II

Please see supplemental files; https://doi.org/10.1536/ihj.20-434