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1 Sequential speckle tracking imaging to detect early stage of 2 cancer therapeutics-related cardiac dysfunction in a patient 3 with breast cancer

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14 **Word counts:** 396

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22 Key Words: cancer therapeutics-related cardiac dysfunction, onco-cardiology,
23 echocardiography, speckle tracking method, global longitudinal strain.

1 A 69-year-old woman was diagnosed right breast cancer which was a stage III invasive
2 ductal breast carcinoma with high proliferative activity (**Ki-67 expression: 30%**
3 **positively-stained cell**), positive hormone receptor (androgen receptor) and HER2
4 overexpressed. Echocardiography before initial chemotherapy showed normal left
5 ventricular (LV) size and function. After the initial echocardiographic study, the patient
6 was given 4 cycles of epirubicin and cyclophosphamide, followed by 3 cycles of
7 trastuzumab and paclitaxel as neoadjuvant chemotherapy. The patient was performed
8 surgical resection of right breast cancer at 6 months later from initial chemotherapy.
9 After initial chemotherapy, global longitudinal strain (GLS) seemed to decrease from
10 the baseline values, **however** LV ejection fraction (EF) did not change within normal
11 limit during 15 months follow-up. After 15 months from initial chemotherapy, although
12 serum B-type natriuretic peptide is 30pg/ml and high sensitive troponin I is <5mg/dl,
13 she had mild exertional breathlessness. **Transthoracic echocardiography** after 15 months
14 from initial chemotherapy showed decreased LVEF of 33% (**FIGURE**), then she was
15 diagnosed chemotherapy-related cardiac dysfunction (CTCRD). We stopped
16 chemotherapy, and patient was provided heart failure pharmacological treatment with
17 enalapril 2.5mg, carvedilol 2.5mg, and azosemide 15mg/day (**SUPPLEMENT 1**). With
18 a slow pharmacological up-titration, LVEF **and GLS** had normalized.

19 This case shows two important insights. The first is that importance of regular
20 sequential follow-up examination. We can find the tiny change of LV systolic
21 dysfunction by performing regular follow-up examinations. CTCRD is occurred in 6-
22 9% of patients with chemotherapy within 12 months from the last administration [1].
23 **However**, many literatures reported that CTCRD also occurred in remote phase [2]. We
24 should perform sequential echocardiographic examination, cardiac **magnetic resonance**

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1 **imaging** or multigated acquisition scan because CTRCD is defined by the value of
2 LVEF. The second is to confirm that we can detect the early change of LV systolic
3 dysfunction due to chemotherapy by GLS rather than LVEF. Previous literature reported
4 that the patients with 11% decreased of Δ GLS after chemotherapy had more
5 development of CTRCD [3]. SUPPLEMENT 1 shows the measurements of LVEF and
6 GLS every 3 months during follow-up. The decrease of Δ GLS of 14% at follow-up
7 study 3 months later from initial chemotherapy may indicate the early impairment of LV
8 myocardium. According to our case, it is important to evaluate regularly cardiac systolic
9 function after chemotherapy, and GLS is more useful than conventional values such as
10 LVEF to detect early stage of myocardial impairment as pre-stage of CTRCD.

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3 **Compliance with ethical standards, Human rights statement**

4 All procedures followed were in accordance with the ethical standards of the
5 responsible committee on human experimentation (institutional and national) and with
6 the Helsinki Declaration of 1964 and later revisions.

7 **Informed consent**

8 Informed consent was obtained from the patient for being included in this case report.

9 **Conflict of interest**

10 Yoshihito Saijo, Kenya Kusunose, Nao Yamada, Hirotsugu Yamada, Susumu Nishio,
11 Yukina Hirata, and Masataka Sata declare that they have no conflict of interest.

1
2 **1 FIGURE LEGENDS**
3

4 **2 FIGURE.**
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6
7 3 This is the time course figure about global longitudinal strain (GLS) and left ventricular
8
9 4 ejection function (LVEF): Upper figures show the polar maps by using speckle tracking
10
11 5 method and lower figure shows time courses of Δ GLS and Δ LVEF. The decrease of
12
13 6 Δ GLS of 14% at follow-up study 3 months later from initial chemotherapy was shown
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15 7 (arrow).
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22 **9 SUPPLEMENT 1.**
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24 10 This is the flow diagram of chemotherapy and cardiac protection therapy.
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31 **12 REFERENCES**
32

- 33 13 1. Cardinale D, Colombo A, Lamantia G et al. Anthracycline-induced
34 14 cardiomyopathy: clinical relevance and response to pharmacologic therapy. *J Am*
35 15 *Coll Cardiol* 2010;55:213-20.
36
37 16 2. Pinder MC, Duan Z, Goodwin JS et al. Congestive heart failure in older women
38 17 treated with adjuvant anthracycline chemotherapy for breast cancer. *J Clin Oncol*
39 18 2007;25:3808-15.
40
41 19 3. Negishi K, Negishi T, Haluska BA et al. Use of speckle strain to assess left
42 20 ventricular responses to cardiotoxic chemotherapy and cardioprotection. *Eur*
43 21 *Heart J Cardiovasc Imaging* 2014;15:324-31.
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Figure
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