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【 CASE REPORT 】

Use of a Non-invasive Cardiac Output Measurement in a Patient with Low-output Dilated Cardiomyopathy

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Abstract:

A 49-year-old man was diagnosed with acute cardiac insufficiency based on evidence of congestive heart failure. The non-invasive measurement of the cardiac output using an AESCULON® mini showed low cardiac output (CO, 3.9 L/min). We administered an intravenous diuretic for cardiac edema and dobutamine drip for low cardiac output. Soon after starting dobutamine at 3.2 γ (microg/kg/min), the CO improved to 6.8 L/min. Combination therapy of diuretic and dobutamine resolved the heart failure. CO measurement by an AESCULON® mini was safe, cost-effective, and convenient. Data output correlates with the CO by Swan-Ganz catheterization. The non-invasive measurement of the CO permitted a smooth recovery without recurrence in this patient.

Key words: heart failure, cardiovascular medicine, clinical diagnostic tests, non-invasive measurement

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Introduction

The number of heart failure (HF) patients with ischemic heart disease, dilated cardiomyopathy (DCM), valvular diseases, and hypertension is growing worldwide. The cardiac output (CO) and cardiac index (CI) measured by Swan-Ganz catheterization (SGC) are important factors used to determine treatment strategies for managing HF. During HF treatment, the CI is measured to determine where the patient fits into Forrester's hemodynamic subsets. Each subset carries a unique prognosis that aids in the selection of HF therapy (1). However, SGC is invasive, expensive, and labor-intensive. Major risks of an SGC procedure include bruising at the site of insertion, excessive bleeding, and vein injury, and minor risks include blood clots, low blood pressure, arrhythmias, cardiac tamponade, and pulmonary artery rupture, a rare occurrence with a 50% mortality rate (2).

Therefore, the non-invasive measurement of the CO/CI is preferable. Recently, several medical instruments that measure bioimpedance and bioreactance (including electrical velocimetry, rebreathing, ultrasonic markers, and pulse wave velocity) have been developed (3). The CO determined by electrical velocimetry shows superior precision to other non-invasive measurements (4). Electrical velocimetry uses the increase in the conductance (due to orientation changes of red blood cells) to determine the velocity of the blood flow (5, 6).

Reports on the non-invasive measurement of CO in adults with HF are few (7, 8). We herein report the case of a DCM patient with severe HF who recovered successfully after the CO measurement by non-invasive electrical velocimetry to determine the treatment plan.

Case Report

A 41-year-old man with no family history of disease was treated with chemotherapy for non-Hodgkin's lymphoma. His therapeutic regimen included cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) alternating with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD). The total dose of anthracycline antibiotics was 250 mg/m^2. After eight years of complete remission from his lymphoma, he gradually felt fatigued, and his legs were ede-

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matous. His medications included a statin for dyslipidemia and proton pump inhibitor for chronic gastritis. His weight had gradually increased by 10 kg in the 8 years of remission since his previous chemotherapy treatment. When he finally sought medical help, he was unable to move due to pronounced shortness of breath (NYHA stage III). After X-ray examination by his attending doctor indicated the presence of HF, he was directed to our hospital.

Investigations

At his first consultation with our department, the patient had a high blood pressure (172/102 mmHg), increased heart rate with regular rhythm (113 bpm), and stable SpO_2 level on room air (99%). His legs had severe pitting edema. Both X-ray (Fig. 1) and elevated brain natriuretic peptide (BNP) (Fig. 2) of 5,934 pg/mL indicated acute HF. Serum levels of AST, ALT, and creatinine were slightly elevated at 43, 125 U/L, and 1.67 mg/dL, respectively. His electrocardiogram (ECG) showed sinus tachycardia without ST changes (Fig. 3). The ejection fraction (EF) by echocardiography was 20% with diffuse hypokinesis and severe mitral regurgitation (MR; Fig. 4). Coronary angiography indicated no ischemic heart disease (Fig. 5). Based on these findings, we performed a right ventricular biopsy and found myocardial rarefaction and slight interstitial fibrosis, but inflammatory cells and myocardial disarray were not detected (Fig. 6). Electron microscopy detected partially fragmented myocardial fibers but no mitochondrial morphological abnormalities (Fig. 7). This biopsy showed nonspecific findings, consistent with DCM, but could not rule out cardiomyopathy induced by chemotherapy.

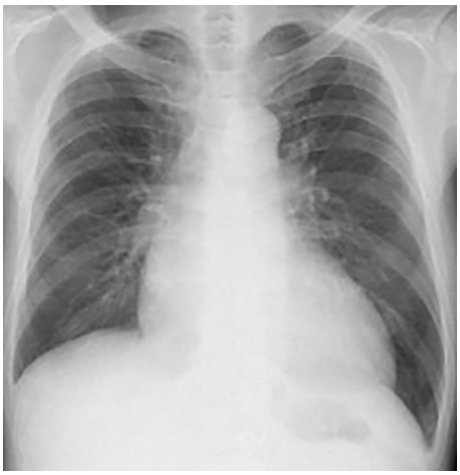

Figure 1. X-ray. X-ray findings indicated cardiac dilatation.

Results from SGC indicated high RVEDP (21 mmHg), normal PCWP (16 mmHg), low CO (3.18 L/min by thermodilution, 2.52 L/min by Fick), and a low CI (1.83 L/min/m^2 by thermodilution, 1.45 L/min/m^2 by Fick) at Day 1. In addition to invasive SGC, we performed the non-invasive measurement of the CO (AESCULON® mini; Osypka Medical, Berlin, Germany), which requires only a 4-lead ECG (Fig. 8). The CO and CI as measured by the AESCULON® mini were 3.9 and 2.3, respectively, upon starting treatment for HF (Fig. 2). Based on the data from both measurement techniques, we defined his HF stage as group III under the Forrester classification.

The treatment and outcome

Following the diagnosis of DCM with HF, we immediately initiated 2 L/min oxygen inhalation, intravenous loop

	Aesculon mini	SGC(Thermo)	SGC(Fick)	Echo	MRI
Day 1 CO/CI	3.9 / 2.3	3.18 / 1.83	2.52 / 1.45	2.4 / 1.5	-
Day 11 CO/CI	5.4 / 3.5	5.62 / 3.58	4.62 / 2.94	4.8 / 3.0	-
Day 21 CO/CI	5.3 / 3.3	-	-		5.44 / 3.48

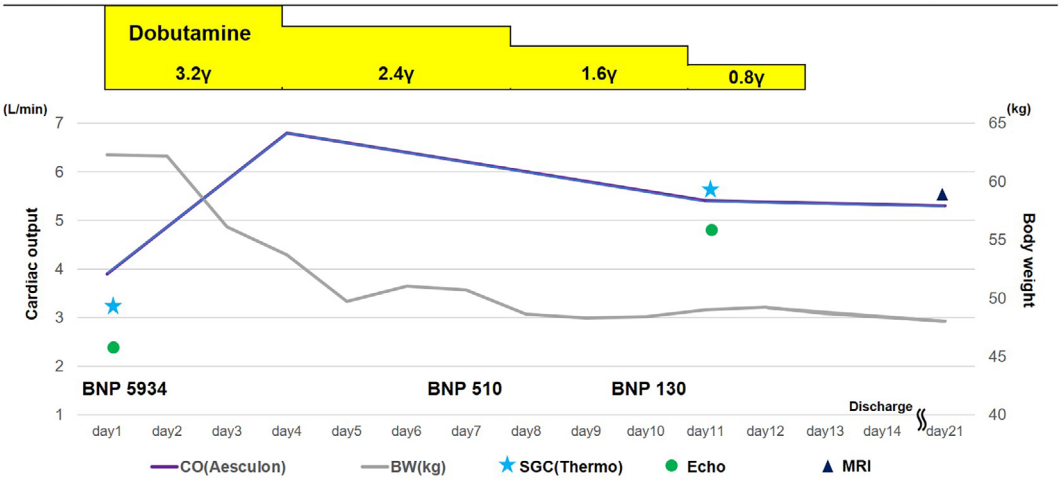

Figure 2. The clinical course of hospitalization. BNP: brain natriuretic peptide, Thermo: thermodilution, CO: cardiac output, CI: cardiac index, SGC: Swan-Ganz catheterization, MRI: magnetic resonance imaging

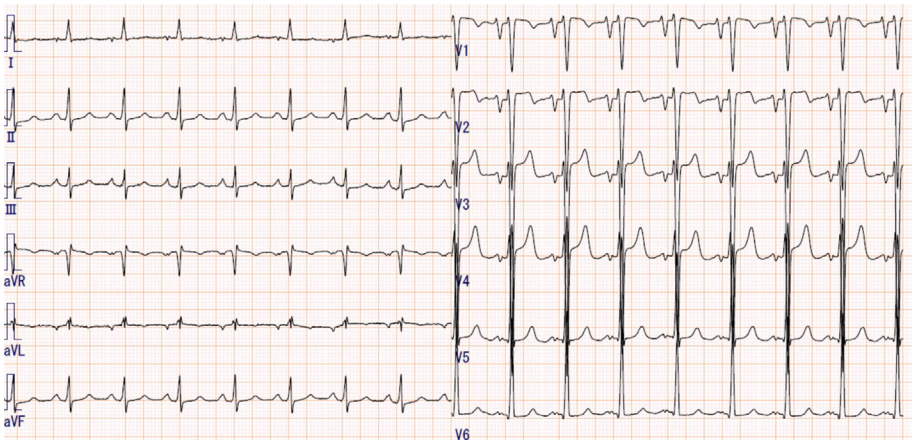

Figure 3. **The electrocardiogram. The electrocardiogram showed sinus tachycardia without ST changes.**

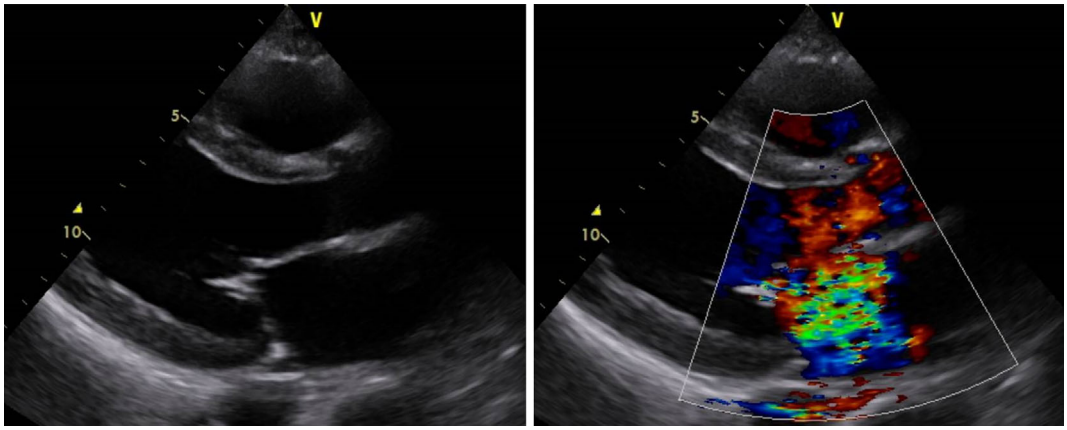

Figure 4. **Echocardiography. The ejection fraction was 20% with diffuse hypokinesis and severe mitral regurgitation.**

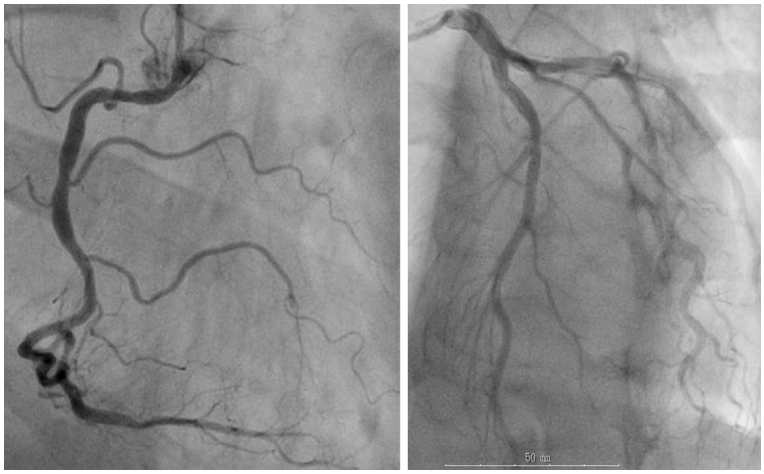

Figure 5. **Coronary angiography. Coronary angiography indicated no significant coronary stenosis.**

diuretic, and dobutamine at 3.2 γ. The CO/CI by AESCULON® mini was 6.8/4.3, respectively, after dobutamine infusion; we considered this response to cardiac stimulant treatment sufficient and decided against additional therapy for the low output. For hypertension and preservation of the cardiac function, an ACE inhibitor and spironolactone were additionally prescribed. Gradually, his weight decreased, and we tapered the dose of dobutamine to 1.6 γ (Fig. 2). After

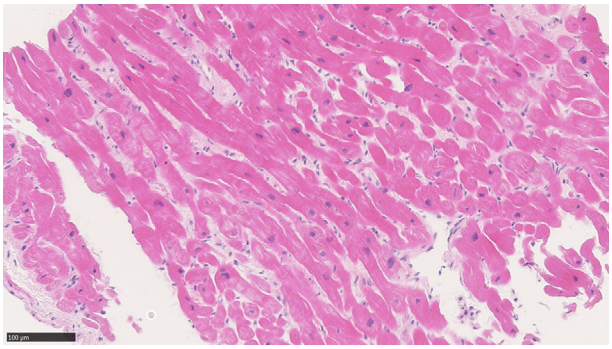

Figure 6. **Hematoxylin and Eosin staining of cardiac tissue on microscopy. A microscopic examination showed myocardial rarefaction and slight interstitial fibrosis, but inflammatory cells and myocardial disarray were not detected.**

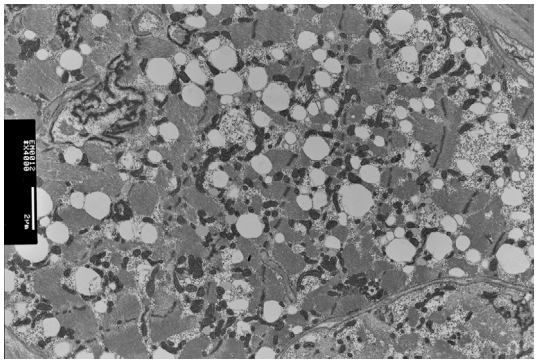

Figure 7. **Cardiac tissue on electron microscopy. Electron microscopy detected partially fragmented myocardial fibers but no mitochondrial morphological abnormalities from the myocardial tissue.**

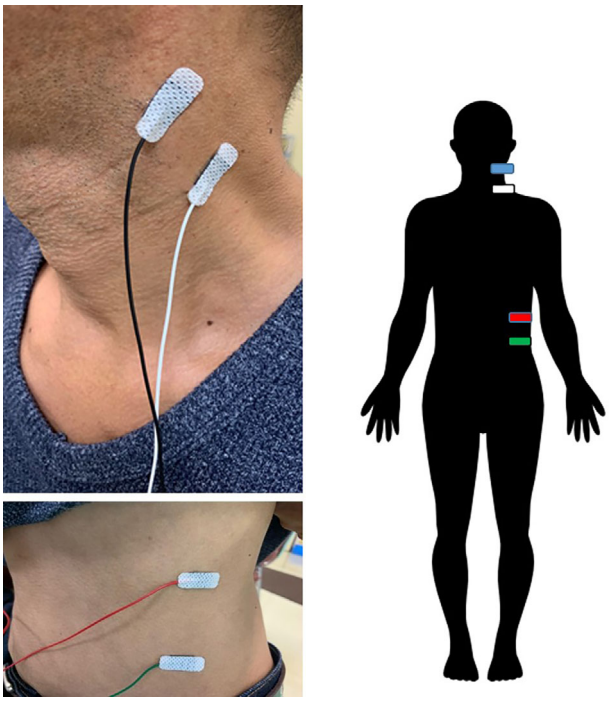

Figure 8. **Measurement by the AESCULON® mini. The AESCULON® mini requires a 4-lead electrocardiogram (2 leads at the neck and 2 at the flank).**

dobutamine tapering, SGC showed improved PCWP (13 mmHg). In addition, his CO/CI was 5.62/3.58, respectively, by thermodilution, 4.62/2.94 by Fick, and 5.4/3.5 by AESCULON® mini at Day 11. We therefore added a beta-blocker and stopped dobutamine (Fig. 2).

In order to shorten the follow-up course and facilitate his familial obligations, the patient was discharged, and outpatient cardiac rehabilitation was scheduled. The HF marker of BNP improved to 130 pg/mL from 5,934 pg/mL, and his weight recovered to 48.8 kg from 62.3 kg during hospitalization (Fig. 2). Pulmonary congestion improved, and at discharge (Day 14), he had normal blood pressure (110/60 mmHg) and heart rate (80 bpm). The echocardiac findings (EF; left ventricular diastole dimension, systole dimension, and end-diastolic volume) at Day 14 were slightly improved compared to the values obtained at Day 1 (20% to 31%, 57 mm to 55 mm, 52 mm to 48 mm, and 220 mL to 203 mL, respectively). The patient's severe MR had improved to moderate MR by Day 14. The CO/CI improved with dobutamine intravenous infusion, indicating recovery from HF. The CO/CI as measured by the AESCULON® mini was 5.3/3.3, respectively, and that by magnetic resonance imaging (MRI) was 5.44/3.48, respectively, on Day 21. The CO/CI obtained by the AESCULON® mini was consistent with that assessed by thermodilution and MRI in this case. In the course of acute HF treatment, the patient had no sustained VT or VF.

Discussion

A 49-year-old man suffered from acute HF with reduced EF and smoothly recovered with medication using the non-invasive measurement of CO/CI. This case highlights the potential role of the non-invasive measurement of CO/CI in treating DCM with HF. Not only did this system allow us to manage the HF more efficiently, but measuring at the bedside in a general ward (where we could not easily perform SGC) in the acute phase allowed him to return home quickly in order to care for his elderly mother.

In 1929, at 24 years old, Werner Forssmann introduced a catheter directly into his own heart through his left brachial vein (9). Cournand and Richards later showed that catheterization could be used to study the pathophysiology of heart disease (10). In 1969, measurement of right heart pressures using a flow-directed right heart catheter was reported (11). Finally, in 1970, Drs. Swan and Ganz reported a balloon flotation flow-directed catheter (the 'Swan-Ganz' catheter) that could be used easily and rapidly without fluoroscopy (12). With their technique, SGC became routine for patients with cardiac shock after acute myocardial infarction, acute HF, and pulmonary hypertension and has become invaluable for hemodynamic monitoring to facilitate decision-making in cardiac treatment.

However, for patients with acute coronary syndrome and

Table. Methods of Cardiac Output Measurement.

	AESCULON® mini	SGC	Echo	MRI
Accuracy	low	high	low	low
Cost	low	very high#	low	high
Convenience	high	very low	moderate	low
Risk	very low	high	low	moderate
Pacemaker/ICD	OK	OK	OK	NO*
Infant	OK	OK	OK	OK

#The costs of hospitalization is included. *Some pacemaker/ICD are possible for undergoing MRI.

SGC: Swan-Ganz catheterization, Echo: echocardiography, MRI: magnetic resonance imaging, ICD: implantable cardioverter defibrillator

non-coronary high-risk patients, randomized clinical trials have shown that the routine use of SGC is not recommended due to the high risk of complications (13, 14). One meta-analysis concluded that the combination of bedside SGC and careful clinical assessment did not affect the overall mortality or hospitalization (15). Furthermore, another meta-analysis found that SGC-guided management did not improve the mortality rate or cost-effectiveness for adult HF patients in intensive care (16). However, we cannot ignore the complications associated with SGC (2), and the advantages of monitoring circulation by SGC are weakened by those complications. Following the publication of these SGC meta-analyses, Chatterjee reviewed the indications for the use of SGC and determined that routine SGC in high-risk cardiac and noncardiac patients is not recommended (17).

According to the 2013 ACCF/AHA Guidelines for the Management of Heart Failure (18), invasive SGC is recommended in most acute HF patients (Class I or IIa) but is not recommended in normotensive patients with acute HF and congestion who experience symptomatic relief with diuretics and vasodilators (Class III). The case presented here was indicated for SGC (i.e., acute HF with hypertension) and experienced only a small complication of hematoma at the puncture site. While close monitoring of hemodynamics benefits almost all HF patients, a non-invasive alternative that eliminates complications is preferable.

The introduction of non-invasive measurement of CO/CI is a viable alternative to invasive right heart catheterization. In 2007, bioimpedance and bioreactance methods were successfully introduced as non-invasive methods to measure CO (19). However, bioimpedance has not proven accurate enough to estimate the CO in the intensive-care unit (ICU) due to the electrical noise from ICU monitors. The bias of the CO measured by bioimpedance is reported to be up to 20% (20). In other words, the CO in HF patients may be measured within a bias of 20%. In comparison with the bioimpedance method, the CO measured by the AESCULON® mini, which uses electrical velocimetry, shows a superior correlation ($r=0.97$, $p<0.001$) to the CO measured by Fick during SGC (4). Thoracic electrical bioimpedance reflects well the changes in electrical conductivity of the aortic arch blood flow. Electrical velocimetry methods have been shown to be able to estimate the CO based on the change in the erythrocyte orientation monitored from the thoracic skin surface (4, 7). In the present case, the CO measured by the AESCULON® mini correlated well with that measured by thermodilution. We were unable to achieve the extreme accuracy ($r=0.97$) of the previous report (4) when using the AESCULON® mini, but we were able to measure the value within a bias of 20% compared to SGC (Fig. 2).

A recent review of the electrical velocimetry method mentioned that this method was unable to demonstrate high accuracy when measuring the CO (21); however, it was useful for monitoring trends in the CO, as in our case. According to comparisons made among the other non-invasive methods, including echocardiography and MRI in this case, the echocardiography method tended to underestimate the CO/CI, as the calculation assumes a perfect circle for the left ventricular outflow instead of the actual elliptical shape. The CO as measured by MRI was almost the same as that measured by the AESCULON® mini (Fig. 2). All methods of non-invasively measuring the CO require further improvements in order to acquire high precision (3, 21) (Table). Clinical research on the correlation among CO values measured by different methods is needed.

No case reports have evaluated the utility of the non-invasive CO measurement for HF patients in a general (i.e., non-critical) care ward. The AESCULON® mini using only four leads to measure the CO at the bedside over a couple of minutes (Fig. 8) was the most convenient method of measuring CO among all modalities (Table).

In the present case, the non-invasive CO measurement accurately reflected the CO value obtained by invasive SGC. This may be because we measured the CO at the bedside, where the electrical noise generated by monitoring equipment was lower than that in an ICU. The AESCULON® mini carries no risk of medical complications; it is a safe, rapid, and cost-effective method. While the initial cost is sizable (suggested retail price 2,000,000-3,000,000 yen), it costs approximately 200 yen per examination and does not require the subject's hospitalization. SGC, by contrast, costs 36,000 yen per examination according to National Health Insurance system of Japan. Furthermore, patients who undergo SGC must be hospitalized, which incurs further costs.

The monitor can also be used in infants for simple measurement protocols in the neonatal ICU and in patients with pacemakers. The potential utility of this device by general practitioners would increase when a patient is hesitant to go to the hospital and for outpatient monitoring because the AESCULON mini requires only a short period of time to perform the necessary calculations.

However, one disadvantage of the AESCULON mini is the low accuracy of measuring the absolute value of the CO. Female, higher height, and an increasing CO were reported to be associated with increased bias (8). The monitor sometimes fails to function correctly if a patient moves a lot during the measurement process or if the electrode patch is moved from its placement by sweat. Furthermore, measurement errors can occur due to a low voltage of the R wave, concurrent use of other electronic monitors, and the use of a deteriorated adhesive electrode patch.

There is currently no mention of non-invasive CO measurements in the HF guidelines. If the measurement of the CO by non-invasive methods continues to prove accurate, we have no choice but to move toward the non-invasive measurement of the CO for HF patients.

The authors state that they have no Conflict of Interest (COI).

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