Respiratory Collapse of the Inferior Vena Cava Reflects Volume Shift and Subsequent Fluid Refill in Acute Heart Failure Syndrome

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Background: Fluid redistribution rather than fluid accumulation plays an important role in the development of acute heart failure (HF) syndrome. Patients with fluid redistribution develop acute HF without prominent volume overload. We investigated volume status by measuring the diameter of the inferior vena cava (IVC) and examining variations in hemoglobin and hematocrit.

Methods and Results: Seventy-four consecutive patients admitted for acute HF syndrome were analyzed. Blood tests and measurement of IVC diameter after stabilization of respiratory distress were performed on admission and were repeated after 24 h. IVC collapsibility index (IVC-CI) was calculated as (maximum IVC-minimum IVC)/maximum IVC. According to the initial IVC-CI, the patients were divided into the collapse group (IVC-CI ≥0.5: n=34) and the non-collapse group (IVC-CI <0.5: n=40). Initial blood pressure was higher in the collapse group (P<0.001). Although 24-h urine volume did not differ between the groups, hemoglobin (P<0.001) and hematocrit (P<0.001) decreased significantly in the collapse group but not in the non-collapse group after 24 h. Furthermore, IVC-CI significantly decreased in the collapse group after 24 h (P=0.003).

Conclusions: In acute HF syndrome, IVC-CI ≥0.5 on admission suggests a volume shift from the central vein into the pulmonary vasculature. Fluid refill occurs within 24 h after admission. This observation could be helpful in selecting strategies for diuretic use. (Circ J 2016; 80: 1171–1177)

Key Words: Echocardiography; Heart failure; Hematocrit; Hemoglobin

In the management of patients with acute heart failure (HF) syndrome, the assessment of fluid status is essential. Traditionally, fluid accumulation was thought to be a major factor in the development of acute HF syndrome. Recent studies, however, have shown that fluid redistribution can also play an important role.1–3 This particular type of acute HF is characterized by an abrupt redistribution of existing fluid from the splanchnic and central circulation into the pulmonary vasculature.2 These patients are often said to be systemically euvoletic or hypovolemic, given that acute or worsening HF can occur in the absence of significant weight gain before admission4,5 and in the absence of significant weight reduction during admission.6 Studies on determination of euvoletic or hypovolemic state by the direct measurement of intravascular volume are limited.

Measuring the circulatory blood volume in patients with acute HF is not easy. The classical approach is via radioisotope dilution techniques, using 125I-labeled human albumin or 51Cr-labeled red blood cells,7,8 but this technique is complicated. Measuring the diameter of the inferior vena cava (IVC) is a simple and reliable method for evaluating intravascular volume in patients with congestive HF,9,10 as well as other disorders.11,12 It has thus far mainly focused on volume overload.

Short-term changes in intravascular substances such as hemoglobin and hematocrit have become a surrogate marker of volume changes. In fact, these are used in hemodialysis on a routine basis.13–15 The aim of this study was therefore to clarify fluid volume status in patients with acute HF syndrome by measuring IVC diameter and by examining the changes in hemoglobin and hematocrit.

Methods

Subjects
From January 2015 to August 2015, we enrolled 104 consecutive patients admitted to Naha City Hospital for new-onset HF...
or decompensated chronic HF without signs of acute coronary syndrome. The exclusion criteria were as follows: (1) inability to undergo echocardiography on admission or repeat blood tests after 24 h (n=15); (2) need for intubation or non-invasive positive pressure ventilation (NPPV; n=4); (3) use of hemodialysis or recombinant human erythropoietin shortly after admission for chronic kidney disease (n=5); (4) acute exacerbation of chronic pulmonary disease, presenting predominantly as right-side HF (n=4); (5) suspected bleeding (n=1); and (6) chronic anemia due to a hematological disorder (n=1). Thus, a total of 74 patients participated in this study, including 1 with acute-onset HF after percutaneous coronary intervention. The study was approved by the ethics review committee, and written informed consent was obtained from all patients.

Ten of the 74 patients had a history of re-hospitalization more than twice during this period. The analysis used the data from the first hospitalization, provided they were complete. All patients except 1 had similar clinical profiles and the same classification of IVC diameter at each hospitalization. Physician diagnosis of HF was based on clinical history, chest radiography, physical examination, and brain natriuretic peptide >100 pg/dl. The diagnosis was confirmed by the study group.

Measurements and Clinical Scenario (CS)

Blood tests were performed on admission and 24 h later. Blood pressure and the amount of oxygen supplementation were measured at the time of hospital arrival. The amount of oxygen supplied is the oxygen given according to peripheral oxygen saturation monitor or blood gas analysis. The amount of oxygen administered by nasal cannula or face mask is a key triage data point and could become a useful clinical indicator for lung congestion. The target oxygen saturation was determined by each individual physician, depending on patient condition and past history. The maximum amount of oxygen administered was 15 L/min. When respiratory condition was not stable on maximum oxygen, NPPV or intubation was applied. These patients were automatically excluded from the study because the IVC diameter could not be measured reliably.

CS was defined based on a previous report:

- CS1, dyspnea and/or congestion with systolic blood pressure (SBP) >140 mmHg; CS2, dyspnea and/or congestion with SBP 100–140 mmHg; CS3, dyspnea and/or congestion with SBP <100 mmHg.

Echocardiography and IVC Diameter

All echocardiography was performed by sonographers on admission and by sonographers or a physician (T.A.) after 24 h. The measurement of IVC diameter was performed with the patient in the supine position, after stabilization of respiratory distress. The transducer was placed in the subxiphoidal region, and long- and short-axis views of the IVC were obtained just below the diaphragm in the hepatic segment. IVC diameter was measured during expiration (maximum IVC) and deep inspiration (minimum IVC). The IVC collapsibility index (IVC-CI) was defined as (maximum IVC–minimum IVC)/maximum IVC. According to the initial IVC-CI, the patients were divided into the collapse group (IVC-CI ≥0.5) and the non-collapse group (IVC-CI <0.5).

Given that a cut-off of enlarged IVC diameter may be smaller in Japanese patients due to their smaller physique compared with Western patients, we calculated normal values from the age- and sex-matched subjects without heart disease as controls.

In the most recent 33 patients, repeat measurements of IVC diameter were performed after 24 h.

Statistical Analysis

All continuous variables are expressed as mean±SD. Unpaired Student’s t-test was used to compare continuous variables between the 2 groups. Factors that were not normally distributed were compared using Mann-Whitney U-test. Paired t-test was performed to compare data on admission with that at 24 h after admission. Differences in categorical variables were analyzed using chi-squared test. P<0.05 was considered to be statistically significant. All analyses were performed using IBM SPSS Statistics 22 (SPSS, Tokyo, Japan).

Results

IVC-CI

Figure 1 shows the distribution of IVC-CI in all patients. IVC-CI varied over a wide range from 0.20 to 0.92. Mean IVC-CI was 0.48±0.25 and the median was 0.48.

Patient Characteristics

Table 1 lists the patient characteristics. Mean age, prevalence of male sex, and body weight on admission did not differ between the groups. The prevalence of diabetes mellitus and coronary artery disease was higher in the collapse group than in the non-collapse group. In contrast, the prevalence of cardiomyopathy and atrial fibrillation was lower in the collapse group. Initial blood pressure was higher in the collapse group than in the non-collapse group. The amount of oxygen supplied was also higher in the collapse group, suggesting more severe pulmonary congestion. The duration from onset of symptoms to hospital visit was shorter and the prevalence of lower extremity edema was lower in the collapse group than in the non-collapse group. The prevalence of CS1 was higher and the prevalence of CS2 was lower in the collapse group than in the non-collapse group. With respect to laboratory data, there was no statistically significant difference between the 2 groups. Serum creatinine, hemoglobin, and hematocrit, however, had a tendency to be higher in the collapse group, suggesting hemoconcentration in this group.
IVC Collapse and Volume Shift in HF

Treatment and Clinical Parameters After Admission
During the 24 h after admission, all patients received 1 or more diuretics. There was no difference in 24-h urine volume between the 2 groups. Weight reduction from admission to discharge was significantly lower in the collapse group than in the non-collapse group (Table 3).

Changes in Hemoglobin, Hematocrit and IVC-CI After 24 h
Although diuretics were used in all patients and urine volume did not differ between the 2 groups (Table 3), hemoglobin and hematocrit decreased significantly in the collapse group, but...
Recent studies, however, have shown that fluid redistribution, also termed “vascular failure”, rather than fluid accumulation, plays an important role in the development of acute HF. Given that some patients develop HF despite no significant weight gain before admission and no significant weight reduction during admission, reports demonstrating euvolemia or hypovolemia by the direct measurement of intravascular volume in patients with HF are limited. Figueras and Weil measured blood volume in patients with acute cardiogenic pulmonary edema using a radioisotope dilution technique. They showed that plasma volume decreased not in the non-collapse group, after 24 h (Figure 2). In the 33 patients who underwent repeat measurement of IVC diameter 24 h after admission, IVC-CI significantly decreased, suggesting volume expansion in the collapse group (n=15); and significantly increased, suggesting volume reduction in the non-collapse group (n=18; Figure 3).

**Discussion**

In this study, we demonstrated that IVC-CI was distributed over a wide range in patients with acute HF syndrome. When we divided the patients into 2 groups according to initial IVC-CI ≥ 0.5, we found differences in clinical profile on admission and clinical course thereafter. In addition, hemoglobin and hematocrit and IVC-CI decreased significantly after 24 h in patients with IVC-CI ≥0.5, suggesting fluid refill into a large vein.

Congestive HF has been considered as the result of fluid accumulation; this is also termed “cardiac failure”, in which the excess volume accumulation overwhelms the Starling mechanism. Recent studies, however, have shown that fluid redistribution, also termed “vascular failure”, rather than fluid accumulation, plays an important role in the development of acute HF. These patients are often said to be systemically euvolemic or hypovolemic. Given that some patients develop HF despite no significant weight gain before admission and no significant weight reduction during admission, reports demonstrating euvolemia or hypovolemia by the direct measurement of intravascular volume in patients with HF are limited. Figueras and Weil measured blood volume in patients with acute cardiogenic pulmonary edema using a radioisotope dilution technique. They showed that plasma volume decreased...
at the time of onset, and subsequently increased concomitantly with decreases in hematocrit, plasma protein, and colloid osmotic pressure during the 24h after admission when the patient was treated with oxygen, furosemide, and morphine sulfate. Similar results were reported by Vreim et al in an animal model.6 In patients with acute pulmonary edema, it appears that hemoconcentration occurs at the time of onset as a result of volume shift into the pulmonary vasculature, and is followed by fluid return into the intravascular space. Typically, those who have mainly redistribution etiology have unique clinical features, such as acute onset, high blood pressure, severe pulmonary congestion, and minimum weight reduction during admission.1 The present collapse group patients had findings exactly consistent with the characteristics of fluid redistribution.

In the present study, the prevalence of coronary artery disease and its powerful risk factor diabetes mellitus was higher in the collapse group than in the non-collapse group. This is not easy to explain on the basis of the currently available evidence. When we reanalyzed the data based on the presence or absence of coronary artery disease, the only difference was in the IVC diameter. This is clearly a field for further investigation in the future. In contrast, the prevalence of cardiomyopathy and atrial fibrillation was lower in the collapse group than in the non-collapse group. This is possibly because the chamber size was more enlarged and the ejection fraction more reduced in these patients.

The measurement of IVC diameter is a simple and reliable method for evaluating total body fluid volume.9-12 In patients with HF, IVC diameter and collapsibility index have been widely used to estimate right atrial pressure.20 Research interest, however, has focused mainly on volume overload rather than volume depletion. Kajimoto et al reported an algorithm in which IVC-CI >0.5 could rule out the cardiogenic causes of dyspnea in the emergency department.21 They performed ultrasound within 30 min after admission, with the patient in a supine or sitting position. In the present study, we did not measure IVC diameter until the patient was able to lie in a supine position for an adequate time after initial treatment, given that IVC diameter and IVC-CI vary with posture.20,22 Under these conditions, 46% of the present patients had respiratory collapse. In the collapse group, only 3 patients (9%) had IVC diameter >21 mm, which is the criterion for enlarged IVC recommended by the American Society of Echocardiography,20 on admission. The maximum and minimum IVC diameter on admission in this group, however, were larger than in the control group, suggesting that elevated right atrium pressure exists even after stabilization of respiratory distress.

Short-term changes in hemoglobin and hematocrit have been widely used as an indicator of changes in intravascular volume. In the field of hemodialysis, changes in hematocrit are advocated as a tool for maintaining an adequate volume of the intravascular compartment in order to avoid dialysis hypotension.13-15 In HF, there has been a great deal of recent discussion about the relationship between anemia and prognosis,23,24 and the relationship between hemoconcentration and worsening renal function.25,26 Use of excessive diuretics causes hemoconcentration, deteriorating renal function, and worsening of the prognosis of HF.26 Kanhere and Bersten reported that hematocrit decreased significantly after 24-h treatment, while the calculated blood and plasma volumes significantly increased in patients with acute cardiogenic pulmonary edema compared with those with acute exacerbation of chronic obstructive pulmonary disease, who seem to experience similar stress.27 Konishi et al also reported that patients who required immediate airway intervention for acute pulmonary edema had higher hemoglobin on admission and a subsequent decrease in hemoglobin 24h after admission despite the use of diuretics.28 This supports the concept of the movement of intravascular volume into the pulmonary vasculature in patients with acute pulmonary edema, followed by fluid refill into the intravascular space as a result of treatment.

It is generally accepted that diuretics are not necessary for the initial treatment of CS1 patients. Diuretics, however, were used in all patients including those with CS1 in the present study. This is because treatment decision-making for acute HF
was made by physicians, especially in the emergency room. In Japan, diuretics tend to be used in almost all patients with acute HF; Konishi et al reported that furosemide or carperitide were used in 97.9% of patients, and Matsushita et al reported that furosemide was used in 94% of patients. In this study, it became possible to estimate the changes in intravascular volume by the changes in hemoglobin and hematocrit because urine volume after treatment was almost the same. Nevertheless, we believed that it was important to find differences in the changes in hemoglobin and hematocrit between the groups.

In patients in the non-collapse group, hemoglobin and hematocrit did not change after 24 h. IVC-CI, however, significantly increased, suggesting volume reduction in a large vein. It is not easy to explain this discrepancy, but it is possible that hemoglobin and hematocrit tend to decrease as part of an acute phase response in patients admitted to hospital for acute HF.

**Study Limitations**

There are some limitations to this study. First, given that it was a single-center study and the number of patients was small, the patient characteristics might be unrepresentative of the more general HF population. The present patients tended to have a higher ejection fraction compared with those in large clinical studies. This might have affected the results, making patients more likely to be allocated to the collapse group, given that patients with vascular failure often have a preserved ejection fraction. Second, although we inferred the changes in intravascular volume from the changes in IVC diameter and hemoglobin and hematocrit, these are indirect findings. Essentially, it would have been better to make measurements using radioisotope dilution techniques, but this method imposes a large burden on patients. We think that there are valid clinical reasons for using ultrasound and blood tests, which can be easily performed in every institute, for the estimation of blood volume. Third, we repeated the measurements of IVC diameter only in the last 33 patients and not in all study patients, but we believe that the results would have been no different even if repeat measurement of IVC diameter had been performed in all patients.

**Conclusions**

Patients with respiratory collapse of the IVC on admission have a pathophysiology of fluid redistribution, and intravascular volume will return within 24 h after admission. These findings provide valuable information that could be used for selection of diuretic use strategy in the management of acute HF syndrome.

**Disclosures**

None.

**References**

25. Peacock WF, Costanzo MR, De Marco T, Lopatin M, Wynne J,


