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Use of initial distribution volume of glucose to determine fluid volume loading in pulmonary thromboembolism and right ventricular myocardial infarction

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Abstract
We report a case of acute right ventricular myocardial infarction (right AMI) following pulmonary thromboembolism (PTE). Following percutaneous coronary intervention, the patient was treated in our intensive care unit (ICU) with intraortic balloon pumping, anticoagulants, and plasma expansion. Fluid overload may cause a further leftward shift of the interventricular septum in patients with PTE, resulting in decreased cardiac output (CO). The initial distribution volume of glucose (IDVG) has been reported to indicate central extracellular fluid volume. As both PTE and right AMI affect cardiac filling pressures, such as central venous pressure (CVP) and pulmonary artery wedge pressure (PAWP), we measured IDVG in order to evaluate the patient's cardiac preload, comparing it with the cardiac filling pressures. Fluid volume loading over 12 h yielded an obvious increase in IDVG. However, low arterial blood pressure and CO, associated with high CVP, remained unchanged and were accompanied by deteriorating pulmonary oxygenation. Accordingly, volume loading was discontinued and the rates of infusion of catecholamines were increased instead. At 12 h thereafter, IDVG became normal, and both CO and blood pressure became improved. However, the cardiac filling pressures remained increased. Although the patient died on the subsequent day, this case report could support the usefulness of IDVG as a fluid volume marker in critically ill patients, especially those with right AMI.

Key words Right ventricular infarction · Pulmonary thromboembolism · Distribution volume · Glucose

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Introduction

We report a case in which a patient suffered acute right ventricular myocardial infarction (right AMI) following pulmonary thromboembolism (PTE). In the management of this patient we evaluated fluid volume status by measuring the initial distribution volume of glucose (IDVG). IDVG has been reported to indicate central extracellular fluid (ECF) volume without modification of glucose metabolism and peripheral fluid accumulation [1,2], and to display good linear correlation with cardiac output (CO) during hypovolemia and subsequent fluid volume loading [3]. IDVG has potential to act as an indirect marker of cardiac preload, even though the concept of dilution volumetry is different from that of cardiac preload, namely, ventricular end-diastolic volume, and IDVG is not proportionally larger than cardiac preload. The measurement of IDVG was originally based on four repeated blood samples taken over 7 min following glucose (5 g) administration, but an approximation can be made with two blood samples taken before and at 3 min postinjection [4]. While there have been no reports on IDVG in patients with apparent right ventricular dysfunction, IDVG measurement could be clinically useful if it reliably mirrors fluid volume status in this critical condition.

Case report

An 81-year-old woman (height, 152 cm; weight, 48 kg) presented to her general practitioner with palpitations and dyspnea. On ECG examination, negative T waves in $V_{1–5}$ were noted, and an echocardiographic examination was scheduled. About 1 month later, a transthoracic echocardiographic examination revealed a dilated right ventricle, paradoxical motion of the interventricular septum, moderate tricuspid regurgitation, pulmonary valve regurgitation, and pulmonary

hypertension. PTE or primary pulmonary hypertension (PH) was suspected. A few hours following the examination she complained of chest pain. The ECG showed elevated S-T segment in II, III, aV_F, and V_{3-6}. Acute myocardial infarction was strongly suspected and she underwent an emergency cardiac catheter examination. Total occlusion of segment 2 of the right coronary artery was found, and catheter intervention, including stent insertion, was performed for the right coronary artery. After the application of intraaortic balloon pumping (IABP) the patient was transferred to the intensive care unit (ICU).

Immediately after admission to the ICU her arterial blood pressure (ABP) was 80/45 mmHg and heart rate was 120 bpm, associated with central venous pressure (CVP) of 7 mmHg. She presented a low CO of around 2.2 l·min^{-1} and PH with pulmonary arterial pressure (PAP) of 41/25 mmHg. In addition, she had poor pulmonary oxygenation. Pa_{O_2} was 51 mmHg ($F_{I_{O_2}}$: approximately 0.6) with an oxygen mask, even though her consciousness was clear and she was not agitated. She was treated with the application of IABP, the administration of heparin (600 U·h^{-1}), antiplatelet agents (100 mg aspirin, 100 mg ticlopidine and 100 mg cilostazol), nicorandil (6 mg·h^{-1}), olprinone (0.2 μg·kg^{-1}·min^{-1}) and fluid volume loading with colloids and crystalloids. As right AMI affected cardiac filling pressures such as CVP, we measured IDVG several times by measuring the difference in plasma glucose concentration between immediately before and at 3 min after 5-g glucose administration to assess changes in fluid volume status following fluid loading. The approximate IDVG was obtained according to a following formula [4]:

$$\text{IDVG (l)} = 24.4 \times e^{-0.03 \times \Delta\text{Gl-3 min}} + 2.7$$

where ΔGl-3 min (mg·100 ml^{-1}) = incremental plasma glucose concentration at 3 min postinjection. Assuming that her basal body weight was 48 kg, as measured on admission to the ICU, her IDVG on admission was low (4.8 l; 100 ml·kg^{-1}), compared to the normal value (110–130 ml·kg^{-1}) [5]. Fluid loading with either 10% dextran in Ringer's solution or lactated Ringer's solution was continued and her IDVG became normal (5.7 l; 119 ml·kg^{-1}) 6 h after admission, and this was associated with increased PAP and CVP (Table 1). However, her pulmonary oxygenation deteriorated at that time (Table 1). Commencement of mechanical ventilation was required, which was followed by an unexpected cardiac arrest (pulseless electrical activity) immediately after the administration of sedatives such as ketamine (100 mg), midazolam (4 mg), and morphine (3 mg). She was resuscitated by cardiac massage and administration of adrenaline (0.2 mg). Transesophageal echocardiography detected a thrombus in right main trunk of the pulmonary artery (Fig. 1). PTE was diagnosed as the trigger for the AMI. However, neither thrombolytic therapy nor surgical treatment was planned, taking into consideration that the onset of the PTE had been about 1 month previously in this elderly patient. Conservative therapeutic measures, including anticoagulants and mechanical and pharmacological cardiac support associated with fluid volume loading, were continued, according to strong recommendations by cardiologists. Twelve hours following her admission, the patient's IDVG became apparently large (7.1 l; 148 ml·kg^{-1}) and this was associated with high cardiac filling pressures, but low ABP and CO (Table 1). Furthermore, deteriorated pulmonary oxygenation became more evident. Considering these measurement results, further fluid volume loading was discontinued and a maintenance dose of crystalloid solution (approximately 2 ml·kg^{-1}·h^{-1}) was administered thereafter. Additionally, a dobutamine infusion was started, combined with an increased infusion rate of noradrenaline. Twenty-four hours after admission, her ABP and CO were improved and IDVG became normal (5.7 l; 119 ml·kg^{-1}). In contrast, both

Table 1. Physiological variables, inotrope infusion, and measurements of IDVG during the first 24 h in the ICU

Time in ICU (h)	0	6	12	24
ABP (mmHg)	80/45	80/40	65/30	95/35
HR (bpm)	120	120	115	112
CO (l·min^{-1})	2.2	2.4	2.0	2.8
PAP (mmHg)	41/25	59/26	46/24	51/23
CVP (mmHg)	7	12	13	15
Fluid balance (ml) [colloid volume]	0	960 [500]	2700 [500]	3840
$Pa_{O_2}/F_{I_{O_2}}$	85	59	52	47
Noradrenaline (μg·kg^{-1}·min^{-1})		0.05	0.4	0.2
Dobutamine (μg·kg^{-1}·min^{-1})			10	10
IDVG (l)	4.8	5.7	7.1	5.7
[ΔGl-3 min (mg·dl^{-1})]	[81]	[70]	[57]	[70]

Fluid balance, infused fluid volume-urine out put, measured from the time of admission to the ICU; IDVG, initial distribution volume of glucose; ΔGl-3 min, incremental glucose concentration at 3 min postinjection

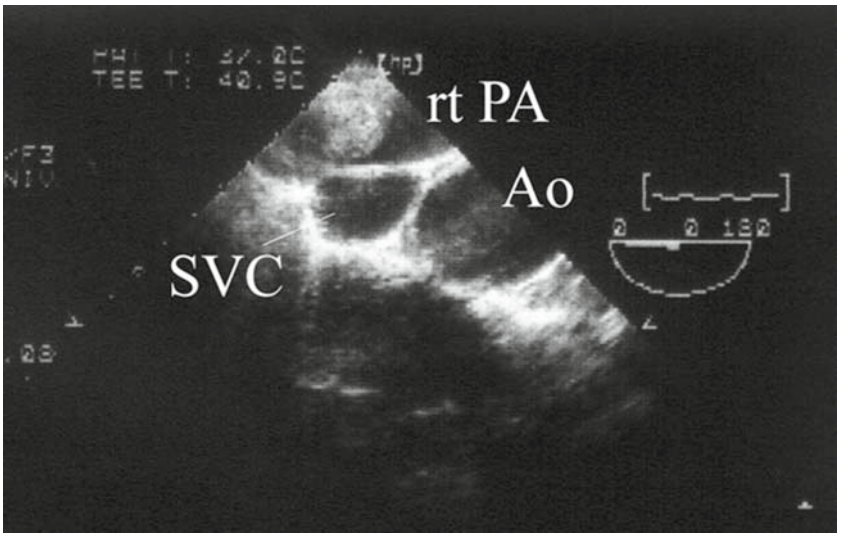

Fig. 1. Mid-esophageal ascending aortic; short axis view. A thrombus is shown in the right main trunk of the pulmonary artery. *Rt PA*, Right pulmonary artery; *Ao*, ascending aorta; *SVC*, superior vena cava

cardiac filling pressures remained increased and apparent edema formation was seen in her face and extremities. Thirty-six hours after admission to the ICU she suffered another arrest from which we were unable to resuscitate her. Massive thrombus in the right pulmonary artery was confirmed at postmortem examination.

Discussion

Massive PTE produces anatomical obstruction of the pulmonary artery and neurohumoral vasoconstriction, resulting in PH [6]. PH leads to right ventricular dysfunction, which can be worsened by right ventricular ischemia due to decreased right coronary perfusion secondary to decreased ABP, elevated right ventricular wall tension and increased oxygen demand. Furthermore, right ventricular infarction can occur secondary to PTE.

One of the major therapeutic measures for right ventricular infarction is plasma volume expansion [7]. However, fluid volume loading may not translate into an increase in right ventricular output due to an excessive increase in afterload with PTE. Fluid volume loading to the already pressure-overloaded and damaged right ventricle may cause a further shift of the interventricular septum to the left. Mittal and Arora [8] suggested that volume loading would produce a further elevation in left ventricular filling pressure and a decrease in output. Therefore, careful plasma volume expansion is required for patients with right ventricular infarction and PTE. However, cardiac filling pressures such as pulmonary artery wedge pressure and CVP have been demonstrated as unreliable for making decisions regarding fluid volume loading in critically ill patients [9]. In retrospect, as both PTE and right AMI affected pulmonary circulation and thus the values of CVP and PAP, we could not advocate the use of cardiac filling pressures as a marker of cardiac preload in this pathological state.

We have proposed IDVG as an indicator of fluid volume [5]. IDVG indicates the central extracellular fluid volume, which consists of the plasma volume and the interstitial fluid volume of highly perfused tissues. IDVG was correlated well with CO during and after subsequent fluid volume loading in our experimental studies [1,2]. Additionally, IDVG rather than plasma volume, or blood volume, displays a better correlation with CO after major abdominal surgery, suggesting that IDVG has potential as an indicator of cardiac preload [10], even though glucose administered intravenously cannot stay in the intravascular compartment and is rapidly distributed into the extravascular space; thus, the concept of dilution volumetry is different from "true" cardiac preload.

It has been demonstrated that normal IDVG is 110–130 $ml \cdot kg^{-1}$ based on basal body weight, according to our experience of more than 4000 IDVG determinations in our ICU. A small IDVG of less than 100 $ml \cdot kg^{-1}$ generally requires volume loading and a large IDVG of more than 140 $ml \cdot kg^{-1}$ generally requires volume restriction. In our patient, IDVG increased from 4.81 (100 $ml \cdot kg^{-1}$) on admission to the ICU to 5.71 (119 $ml \cdot kg^{-1}$) at 6 h after admission and, further, to 7.11 (148 $ml \cdot kg^{-1}$) at 12 h after admission, with the rapid infusion of either colloidal or crystalloid solution, but ABP and CO remained low despite the high cardiac filling pressures associated with deteriorating pulmonary oxygenation. Accordingly, we found no beneficial effects of further fluid volume loading at 12 h after admission. We therefore changed the fluid infusion rate of crystalloid

solution to the maintenance rate and increased the noradrenaline infusion rate. In retrospect, however, we could have discontinued further rapid fluid volume loading and started an infusion of dobutamine at 6 h after admission when IDVG became normal, although CO and ABP remained low associated with high cardiac filling pressures. A reduction in the fluid infusion rate would have affected fluid volume status and cardiac function in this patient. The apparent large IDVG had returned to normal at the following 12 h, and ABP and CO levels had improved, accompanying with a decrease in the noradrenaline dose (Table 1). Presumably, a large amount of the fluid volume of both crystalloid and colloidal solution administered after admission to the ICU would have mostly moved from the central to the peripheral compartment during this 12-h period, resulting in apparent peripheral edema formation, as observed in this patient. This fluid redistribution would have produced the observed decrease in IDVG, because IDVG is not influenced by peripheral fluid accumulation [11,12]. However, cardiac filling pressures in our patient remained elevated even after fluid restriction. Thus, we believe that IDVG, but neither of the parameters of cardiac filling pressure was useful as a marker of fluid volume therapy in this patient.

The accuracy of using IDVG data in severely ill patients, such those with a low CO may be criticized, because the initial distribution volume for several drugs is determined by CO, regional blood flow, and the characteristics of the particular drug [13]. Based on the capillary permeability of glucose, the rate at which glucose molecules diffuse through the capillary membrane is approximately 50 times greater than the rate at which plasma itself flows linearly along the capillary [14]. Presumably, CO itself has a minimal effect on glucose distribution and, thus, IDVG determination may not be affected in a low CO state. Our experimental fluid volume challenge study [11] and our clinical study of congestive heart failure and fluid overload, including a low CO state [15] failed to show IDVG and CO moving consistently together in the same direction. Considering the result of the clinical study [15] and our clinical experience with IDVG determination, we assume that CO greater than 2.0 l·min^{-1} would yield adequate mixing of administered glucose within 3 min postinjection and, thus, have no significant impact on IDVG. However, further detailed studies are mandatory to determine whether or not IDVG measurement remains accurate when CO is extremely low. Additionally, we restrict the use of IDVG measurement in patients with ischemia of the central nervous system and in those with an extremely high plasma glucose level (greater than 300 mg·dl^{-1}) to avoid apparent glucose toxicity.

While we were unable to resuscitate our patient because of the double fatal complications of PTE and AMI, this case report could support the usefulness of IDVG, and not cardiac filling pressures, as a fluid volume marker even in critically ill patients with a low CO state.

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References

1. Shimodate Y, Koh H, Ishihara H, Matsuki A. Comparison of glucose and sucrose as an indicator for dilution volumetry in haemorrhagic shock. Eur J Anaesthesiol. 1995;12:397–401.
2. Iwakawa T, Ishihara H, Takamura K, Sakai I, Suzuki A. Measurements of extracellular fluid volume in highly perfused organs and lung water in hypo- and hypervolaemic dogs. Eur J Anaesthesiol. 1998;15:414–21.
3. Ishihara H, Nakamura H, Okawa H, Yatsu Y, Tsubo T, Hirota K. Comparison of initial distribution volume of glucose and intrathoracic blood volume during hemodynamically unstable states early after esophagectomy. Chest. 2005;128:1713–9.
4. Ishihara H, Nakamura H, Okawa H, Takase H, Tsubo T, Hirota K. Initial distribution volume of glucose can be approximated using a conventional glucose analyzer in the intensive care unit. Crit Care. 2005;9:144–9.
5. Ishihara H, Giesecke AH. Fluid volume monitoring with glucose dilution. Heidelberg Berlin New York Tokyo: Springer; 2007.
6. Stratmann G, Gregory GA. Neurogenic and humoral vasoconstriction in acute pulmonary thromboembolism. Anesth Analg. 2003;97:341–54.
7. Antman EM. ST-Elevation: myocardial infarction management. In: Zipes DP, Libby P, Bonow R, Braunwald E, editors. Braunwald's heart disease. A textbook of cardiovascular medicine. 7th ed. Philadelphia: Elsevier Saunders; 2004. p. 1202–4.
8. Mittal SR, Arora H. Pulmonary embolism with isolated right ventricular infarction. Indian Heart J. 2001;53:218–20.
9. Vincent JL, Weil MH. Fluid challenge revisited. Crit Care Med. 2006;34:1333–7.
10. Ishihara H, Suzuki A, Okawa H, Sakai I, Tsubo T, Matsuki A. The initial distribution volume of glucose rather than indocyanine green derived plasma volume is correlated with cardiac output following major surgery. Intensive Care Med. 2000;26:1441–8.
11. Miyahara A, Ohkawa H, Ishihara H, Matsuki A. Changes in the initial distribution volume of glucose and plasma volume following volume challenge in dogs. Infusionsther Transfusionsmed. 1995;22:274–9.
12. Ishihara H, Suzuki A, Takamura K, Yatsu Y, Kimura N, Otomo N, Tsubo T, Matsuki A. Does the initial distribution volume of glucose reflect the shift of the central extracellular fluid volume after major surgical procedures? (in Japanese). J Jpn Intensive Care Med. 1998;5:203–10.
13. Ghoneim M, Pearson K. Pharmacokinetics of drugs administered intravenously. In: Scurr C, Feldman S, Soni N, editors. Scientific foundations of anaesthesia. 4th ed. Chicago: Year Book Medical; 1990. p. 559–71.
14. Guyton AC, Hall JE. Textbook of medical physiology. 10th ed. Philadelphia: Saunders; 2000. p. 162–83.
15. Ishihara H, Takamura K, Koh H, Iwakawa T, Matsuki A. Does the initial distribution volume of glucose reflect the central extracellular fluid volume status in critically ill patients? Infusionsther Transfusionsmed. 1996;23:196–201.