What is low cardiac output syndrome? A report of two cases

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Abstract

***Background*: One of the diagnostic criteria of low cardiac output syndrome (LOS) is a cardiac index of less than 1.8 l/min/m^2. However, recognition of this syndrome differs among intensivists as to whether or not LOS is synonymous with cardiogenic shock.**

***Case reports*: Here, we present two cases of heart failure who were initially treated with diuretics and subsequently fell into a state of low cardiac output. We treated the patient with low blood pressure with inotropes and the patient with high blood pressure with a vasodilator according to their hemodynamics. We observed that cardiac power was the most significant hemodynamic change in response to these treatments. In this paper, we discuss the definition of LOS and show several criteria for determining LOS.**

***Conclusions*: Broadly, there are several conditions of determining LOS. Even with those conditions, we should still be aware of the pathophysiology of each patient with heart failure. We propose that the definition of LOS should be a state of low cardiac output with corresponding symptoms, even if their blood pressure is high.**

Key words: Low cardiac output syndrome, cardiogenic shock, cardiac power, blood pressure.

Introduction

The term low cardiac output syndrome (LOS) has a less well-established definition, and had originally spread among cardiovascular surgeons after surgical treatment. (1) Many intensivists and cardiologists have recently been using this term in various settings, from advanced end-stage chronic heart failure to acute-onset de novo heart failure frequently caused by acute coronary syndrome. There are also no consensus criteria for low cardiac output status, other than cardiogenic shock, as reported in 2013 ACCF/AHA, 2016 ESC, and 2017 JCS/JHFS Guidelines for Acute and Chronic Heart Failure. However, cardiogenic shock being a commonly reported feature of LOS has led to different opinions among intensivists as to whether LOS is the same pathogenetic condition as cardiogenic shock or if it should be considered a related, but different condition that may require treatment different than that of cardiogenic shock depending on the context.

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Case report

The two patients were admitted for treatment of decompensated heart failure with reduced ejection fraction (EF) with low cardiac output status. They were initially treated with diuretics for congestion and subsequently fell into LOS. One patient needed inotropes, whereas the other patient needed a vasodilator. Their clinical courses were very different. Patients' clinical characteristics and clinical outcomes are shown in **Table 1**. The most significant differences in hemodynamics between the two cases were blood pressure (BP) and cardiac power (the definition described later). Electrocardiograms

(ECGs), chest X-rays (CXRs), and transthoracic echocardiograms (TTEs) for the two cases are shown in **Figure 1**.

Case 1

A 37-year-old male patient who was diagnosed with dilated cardiomyopathy (left ventricular ejection fraction [LVEF] of 20%) four years ago was admitted due to exacerbation of chronic heart failure (New York Heart Association functional class [NYHA] III). Upon admission, his vital signs were as follows: BP 110/70 mmHg, pulse rate (P) 102/min, body temperature (BT) 36.0 ℃, respiratory rate (RR) 16/min, peripheral oxygen saturation (SpO2) 99% (room air). Laboratory data at admission showed chronic kidney disease (creatinine 1.23 mg/dl, estimated glomerular filtration rate [eGFR] 54.9 ml/min/1.73 m^2), mild liver dysfunction suggestive of a congestive liver (total bilirubin 1.1 mg/dl, aspartate aminotransferase [AST] 37 U/l, alanine aminotransferase [ALT] 87 U/l), and high B-type natriuretic peptide (BNP) level (1298 pg/ml).

A cardiologist administered furosemide for weight gain (+7 kg/2 weeks). After urination, the patient felt general fatigue and abdominal pain. He suffered from hypotension (BP 72/44 mmHg) and his clinical profile showed wet-cold.

His laboratory data showed worsening of renal function with hyponatremia (creatinine 1.83 mg/dl, eGFR 35.5 ml/min/1.73 m^2, Na 133 mmol/l). Echocardiography revealed severely left ventricular (LV) systolic dysfunction (LVEF 18%) with mild to moderate mitral regurgitation (MR), right ventricular systolic dysfunction, and low cardiac output (estimated cardiac index [CI] of 1.1 l/min/m^2 using a left ventricular outflow tract-velocity time integral [LVOT-VTI] of 5.0 cm by echocardiography). His systemic vascular resistance (SVR) was relatively high (SVR 1924 dyne.sec/cm^5) and cardiac power index (Cpi) was extremely low (0.15 W/m^2, normal range: 0.5-0.7 W/m^2). Cardiac power (index) can be calculated as mean arterial pressure x CO (CI) x 0.0022.

We diagnosed him as having LOS and treated him with dobutamine (3 μg/kg/min). Although his condition was stabilized with dobutamine infusion, he developed catecholamine-dependent heart failure. Implantation of a left ventricular assist device was performed eight months later and a heart transplantation was performed 3.5 years later.

Case 2

A 70-year-old male patient was admitted due to acute decompensated heart failure (ADHF) and bronchopneumonia (NYHA IV, BP 180/116 mmHg, P 116/min, BT 38.8 ℃, RR 24/min, SpO2 92% [room air]). His laboratory data at admission showed renal dysfunction (creatinine 1.41 mg/dl, eGFR 39.4 ml/min/1.73 m^2), slight liver dysfunction (total bilirubin 1.0 mg/dl, AST 38 U/l, ALT 35 U/l), high BNP level (1974 pg/ml), and slightly elevated inflammatory markers (white blood cells [WBC] 9400/μl, C-reactive protein 1.29 mg/dl).

A physician administered furosemide, antibiotics, and oxygen to the patient. On the 3rd day of hospitalization, the patient's laboratory data showed acute kidney injury with hyperkalemia (creatinine 4.32 mg/dl, eGFR 11.6 ml/min/1.73 m^2, kalium 6.4 mmol/l) and significant liver dysfunction (total bilirubin 1.4 mg/dl, AST 4942 U/l, ALT 2467 U/l) with elevated lactate (2.7 mmol/l). The patient was transferred to our hospital with high BP (BP 156/106 mmHg and P 72/min) and was diagnosed with LOS (clinical profile: wet-cold, LVOT-VTI 7.7 cm, estimated CI 1.4 l/min/m^2, LVEF 23%, MR mild to moderate). His SVR was extremely high (4102 dyne.sec/cm^5) and Cpi was relatively low (0.38 W/m^2).

We treated the patient with nitroglycerin infusion and continuous hemodialysis. Eventually, we diagnosed him as having hypertensive heart disease and silent myocardial ischemia. We prescribed antihypertensive agents and performed percutaneous coronary intervention. He was subsequently discharged ambulatory without maintenance dialysis.

Criteria of low cardiac output syndrome

Table 2 shows several criteria of LOS and cardiogenic shock, which were used in major trials or guidelines. (2-7) In all of those trials and guidelines for cardiogenic shock, low cardiac output status (cardiac index of less than 1.8 to 2.2 l/min/m^2 with or without catecholamine or mechanical support) or symptoms related to low cardiac output were part of the criteria for all of those publications. Low BP was also a necessary condition to meet the criteria in most of those publications.

Discussion

LOS is characterized by the inability of the heart to pump a sufficient quantity of blood to meet the needs of tissue for oxygen and nutrients, along with signs of tissue hypoperfusion (cold periphery, clammy skin, confusion, oliguria, elevated lactate level) in the absence of hypovolemia. (1,8) Despite multiple mentions of LOS in recent publications, there is no established definition of what constitutes a low cardiac output status. There are some commonalities between publications, such as the use of hemodynamic parameters and criteria. An example of one of these criteria is a cardiac index of less than 1.8 $l/min/m^2$, or less than 2.2 $l/min/m^2$ if inotropic agents are being administered. (9) However, the definitions in clinical trials vary (**Table 2**), and among intensivists and cardiovascular surgeons, LOS seems to be synonymous or used interchangeably with cardiogenic shock. The common definition of LOS or cardiogenic shock among those specialists includes not only a decrease in CI, but also a systolic blood pressure of less than 90 mmHg. (8) According to this definition, the use of inotropic agents or mechanical circulatory support is required to improve the hemodynamics of patients. (5,7,8) However, even though blood pressure is one of the most important signs of hypoperfusion, it is not a necessary or sufficient condition for LOS. If the definition of LOS is considered to be synonymous with cardiogenic shock, that would overlook vital organ failure of critically ill patients who have maintained their BP, which might lead to the administration of diuretics instead of vasodilators.

Figure 2 shows the speculative hemodynamic differences between our two cases illustrated in a pressure-volume relationship. Case 1 had low LV pressure and a decreased slope of maximum elastance (Emax) (contractility) compared with the normal subject (**Figure 2A**). On the other hand, case 2 had high LV pressure and a steep slope of effective arterial elastance (Ea) (afterload) compared with the normal subject (**Figure 2B**). Both cases had small stroke volumes, nevertheless, each case had quite different LV pressures, contractility, and afterload. Since both patients' heart rates were similar, both of them were in low cardiac output status. The "excessive" volume reduction for both cases could cause a further reduction in stroke volume and cause them to fall into LOS.

Cardiac output is dependent on heart rate and stroke volume, which are influenced by three interdependent components: preload, afterload, and contractility. There are various indexes of contractility including LVEF, LV cardiac work (LVCW), slope of the end systolic pressure volume relationship (ESPVR), maximum elastance (Emax), max dP/dt, and cardiac power (index). However, LVEF is highly dependent upon afterload and causes a significant misinterpretation of the actual contractility. Although the determination of max dP/dt, LVCW, and Emax needs an invasive procedure using left heart catheterization, cardiac power can be estimated non-invasively using blood pressure and an echocardiogram. Cardiac power (index) can be calculated as mean arterial pressure x CO (CI) x 0.0022. Mean arterial pressure is calculated from blood pressure cuff measurements using the following empirical formula: diastolic BP + (1/3 [systolic BP - diastolic BP]). In addition to its relative ease of measurement, cardiac power is also the strongest hemodynamic parameter correlated with outcome in critically ill patients. (10)

Clinical scenarios (CS) based on systolic BP are used in prehospital and early in-hospital management of patients with ADHF. About 50% of patients with CS 1 have reduced LVEF and are at risk of low cardiac output during treatment.

Cardiac power would be a more appropriate indicator for identifying the pathophysiology and treatment for LOS. Actual contractility should be taken into consideration when treating LOS patients with low EF and high blood pressure.

Here, we propose that LOS should refer to a tissue hypoperfusion status leading to organ failure due to low cardiac output, regardless of hypotension. At the very least, the concept, definition, and criteria of LOS should be clarified and standardized among experts instead of being used interchangeably with cardiogenic shock.

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Table 1. Patients' clinical characteristics and clinical outcomes

	Case 1		Case 2	
Age (years)	37		70	
Gender	Male		Male	
Etiology of heart failure	Dilated cardiomyopathy		Hypertensive, ischemic	
	At admission	At LOS	At admission	At LOS
NYHA	III	IV	IV	IV
Blood pressure (mmHg)	110/70	72/44	180/116	156/106
Heart rate/min	102	72	116	72
Hemoglobin (g/dl)	14.5	14.8	11.5	11.6
Sodium (mmol/l)	140	133	136	137
Creatinine (mg/dl)	1.23	1.83	1.41	4.32
Total bilirubin (mg/dl)	1.1	1.2	1.0	1.4
AST (U/l)	37	14	38	4942
ALT (U/l)	87	28	35	2467
BNP (pg/ml)	1298	1045	1974	767
LVEF (%)	18		23	
CO (CI) [l/min (l/min/m^2)]	1.9 (1.1)		2.1 (1.4)	
SVR (dyne*sec/cm^5)	1,924		4,102	
CP (Cpi) [W (W/m^2)]	0.25 (0.15)		0.57 (0.38)	
Treatment	Dobutamine		Nitroglycerine	
Clinical course	Heart transplant		Discharge	

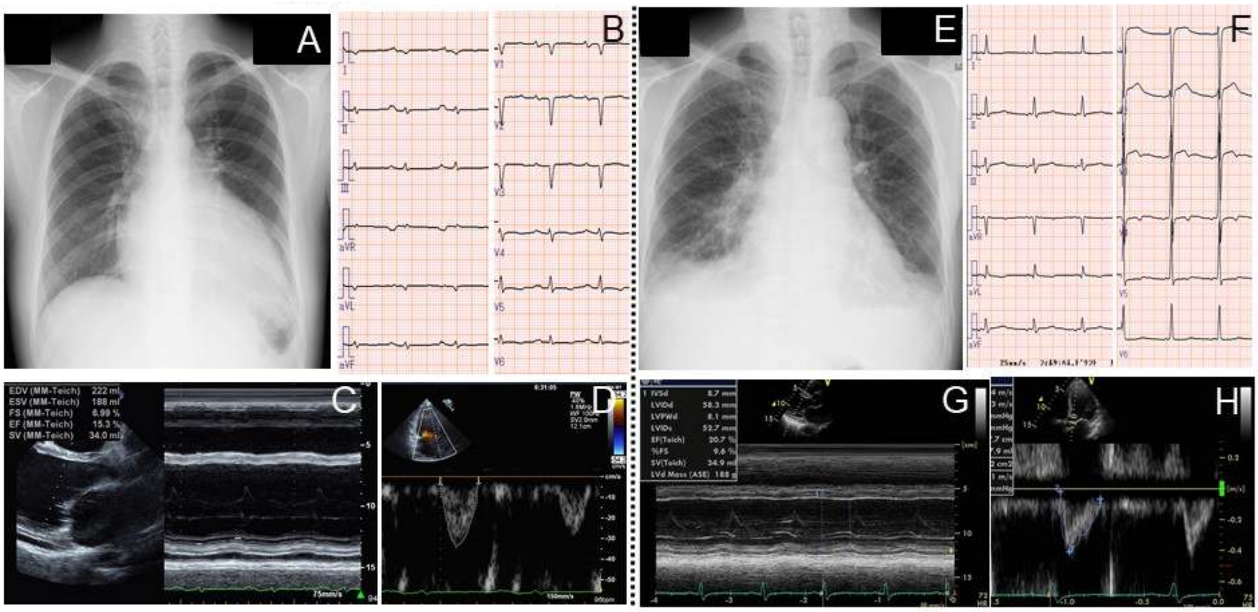
Legend: NYHA=New York Heart Association functional class; AST=aspartate aminotransferase; ALT=alanine aminotransferase; BNP=B-type natriuretic peptide; LVEF=left ventricular ejection fraction; CO=cardiac output; CI=cardiac index; SVR=systemic vascular resistance; CP=cardiac power; Cpi=cardiac power index; LOS=low cardiac output syndrome.

Table 2. Definitions of LOS or cardiogenic shock

	CI (l/min/m^2)	PAWP (mmHg)	sBP (mmHg)	Support	Duration (min)	Sign/setting
Rao, et al, 1996 (Ref. 5) (LOS)	<2.2	Not defined	<90	(+) IABP or catecholamine	≥30	Post CABG
SHOCK Trial, 1999 (Ref. 6) (Cardiogenic shock)	<2.2	≥15	<90 ≥90	(-) (+)	≥30	Acute myocardial infarction End-organ hypoperfusion (urine output <30 ml/h or cool extremities)
Algarni, et al, 2011 (Ref. 7) (LOS)	<2.2	Not defined	<90	(+) IABP or catecholamine		Post CABG After optimizing preload and afterload as well as correcting all electrolyte and blood gas abnormalities
IABP-SHOCK II, 2012 (Ref. 8) (Cardiogenic shock)	Not defined	Not defined	<90 >90	(-) (+) Catecholamine	≥30	Acute myocardial infarction Impaired end-organ perfusion (altered mental status, cold/clammy skin and extremities, urine output <30 ml/h or lactate >2.0 mmol/l)
SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement, 2015 (Ref. 9) (Cardiogenic shock)	<1.8 <2.2	>15	<90 or mBP >30 below baseline	(-) (+)	>30	
ESC Heart Failure Guidelines, 2016 (Ref. 3) (Cardiogenic shock)	Not defined	Not defined	<90	(-)	≥30	Adequate volume and clinical or laboratory signs of hypoperfusion Clinical hypoperfusion: Cold extremities, oliguria, mental confusion, dizziness, narrow pulse pressure Laboratory hypoperfusion: Metabolic acidosis, elevated serum lactate, elevated serum creatinine
Our suggestion (LOS)	<1.8 <2.2	Not defined	Not defined	(-) (+)	≥30	Adequate volume and clinical or laboratory signs of hypoperfusion: Cold periphery, clammy skin, confusion, oliguria, elevated lactate

Legend: LOS=low cardiac output syndrome; CI=cardiac index; PAWP=pulmonary artery wedge pressure; sBP=systolic blood pressure; mBP=mean arterial blood pressure; IABP=intra aortic balloon pump; CABG=coronary artery bypass grafting.

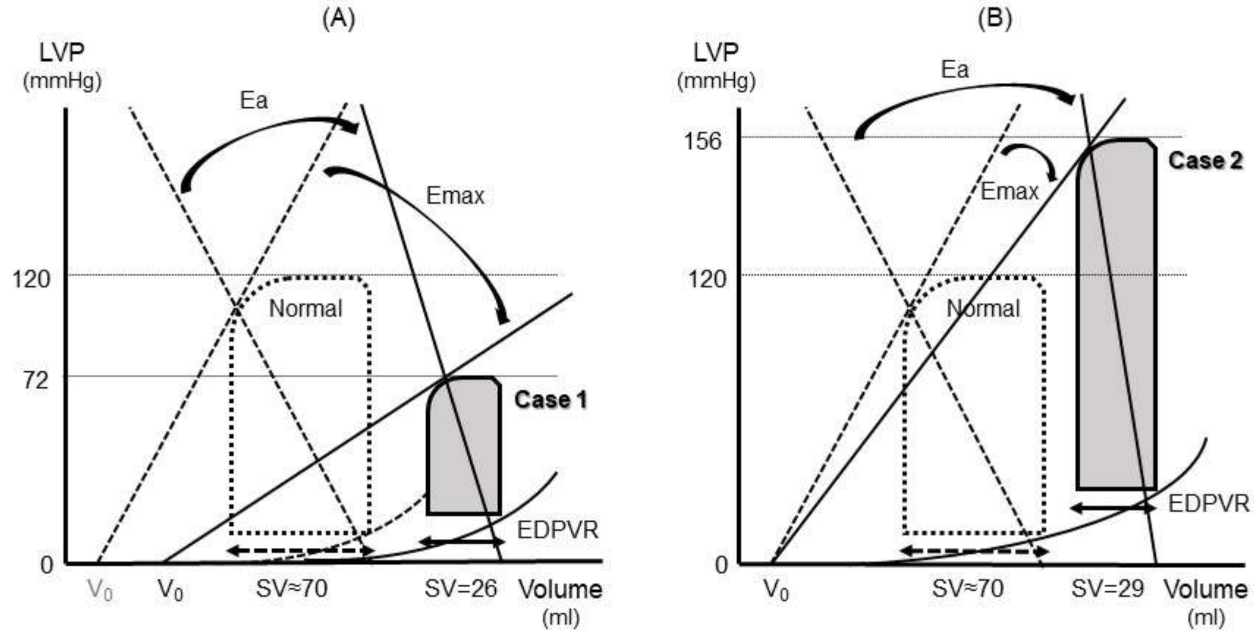
Figure 1. Electrocardiograms, chest X-rays, and transthoracic echocardiograms in two cases



Legend: Case 1: A-D; Case 2: E-H

A. The chest X-ray shows cardiomegaly, bilateral pleural effusion, and slight lung congestion.
B. The electrocardiogram shows left atrial overload, low voltage, and poor r progression in V1-V4.
C. The transthoracic echocardiogram (M-mode) shows left ventricle (LV) dilatation (LV end-diastolic dimension [LVDd] 66 mm, LV end-systolic dimension [LVDs] 61 mm) and severely reduced systolic function (LV ejection fraction [LVEF] 18%).
D. Pulse wave shows that LV outflow tract-velocity time integral (LVOT-VTI) is 5.0 cm, estimated cardiac output (CO) is 1.9 l/min and cardiac index (CI) is 1.1 l/min/m^2.
E. The chest X-ray shows cardiomegaly, lung congestion, and bilateral pleural effusion.
F. The electrocardiogram shows left ventricular hypertrophy with ST-T change.
G. The transthoracic echocardiogram (M-mode) showed LV dilatation (LVDd 58 mm, LVDs 53 mm) and severely reduced systolic function (LVEF 23%).
H. Pulse wave shows that LVOT-VTI is 7.7 cm, estimated CO is 2.1 l/min and CI is 1.4 l/min/m^2.

Figure 2. Hemodynamic differences shown in schematic pressure-volume loop in two cases



Legend: LVP=left ventricular pressure; BP=blood pressure; Emax=maximum elastance; Ea=effective arterial elastance; SV=stroke volume; EDPVR=end-diastolic pressure-volume relationship.

A. The dotted loop and lines represent normal subject and the solid loop and lines represent case 1. Case 1 has low LVP (BP), decreased slope of Emax, and relatively steep slope of Ea.
B. The dotted loop and lines represent normal control and the solid loop and lines represent case 2. Case 2 has high LVP (BP), relatively decreased slope of Emax, and steep slope of Ea.

Case 1 and case 2 have similar and small SV.

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