Organ Failures Due to Low Cardiac Output Syndrome Following Open Heart Surgery

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During the period from August, 1977 to December, 1984, a total of 3003 patients who received open heart surgery were treated postoperatively at the ICU of National Cardiovascular Center. Low cardiac output syndrome (LOS) developed in 669 (22.3%) patients. Organ failures due to LOS were studied in these patients. Although the overall mortality of postoperative patients was 5.6% and improved to around 4% in the later years, death rate of patients with LOS was persistently high (22.8%) and showed no tendency to improve even in the latest year. Moreover, the clinical results of those LOS patients who developed organ failure were extremely poor; the mortality of patients with respiratory failure (RF) accounted for 36.8% and that of patients with other organ failure exceeded 50%. The incidence of impaired organs in LOS patients was 49.9% in RF, 29.9% in acute renal failure (ARF), 18.4% in hepatic failure (HF), 16.4% in disseminated intravascular coagulation (DIC), 15.5% in central nervous system failure (CNSF), and 11.1% in gastrointestinal bleeding (GIB). Pathophysiological mechanisms as well as the management of these major complications caused by LOS are also discussed. Some patients developed multiple organ failure (MOF). Plasma exchange (PE) was performed on 16 patients who developed MOF. Improvement of various organ functions was obtained and consequently three patients were successfully treated by means of PE. Removal of various substances toxic to organs, supplement of deficient substances and cessation of the vicious cycle produced by the interaction of impaired organs in patients with MOF are major roles of PE in the treatment of MOF.

THE low output syndrome (LOS) following cardiac surgery is defined as the imbalance of oxygen demand and supply in tissues as the result of impaired cardiac function.¹ Deteriorated hemodynamic conditions and insufficient oxygen delivery in the status of LOS cause various type of organ failures, which subsequently lead to an unsatisfactory results.² In this paper, the organ failures caused by LOS in postoperative patients who received open heart surgery are analyzed, the pathophysiological mechanisms are described and patient management is discussed.

Key Words:

Cardiac surgery
Low cardiac output syndrome
Multiple organ failure
Plasma exchange

SUBJECTS

From August, 1977 to December, 1984, a total of 3003 patients were operated on for cardiac disorders and were treated postoperatively at the ICU of the National Cardiovascular Center. The classification of underlying diseases were: congenital heart disease (1396 patients); acquired heart disease (1192 patients) and coronary disease (415 patients). LOS was defined here as a decrease of cardiac index less than 2.2 L/min/m^2 with evidence of peripheral vasoconstriction and reduced tissue perfusion, and necessitated to administer a large dosages of inotropic agents with or without the assistance of intra-aortic balloon pumping to maintain stable hemodynamic conditions. With this definition, LOS

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TABLE I PATIENTS WHO RECEIVED OPEN HEART SURGERY AND THEIR CLINICAL RESULTS

Year	Open heart surgery patients (mortality)	LOS patients (mortality)	Incidence of LOS (%)
1977	42 (19.0%)	10 (70.0%)	23.8
1978	208 (9.6%)	86 (18.6%)	41.3
1979	296 (11.5%)	114 (29.8%)	38.5
1980	371 (4.6%)	142 (12.7%)	38.3
1981	479 (5.2%)	116 (19.8%)	24.2
1982	446 (3.6%)	94 (14.9%)	21.1
1983	531 (4.3%)	64 (32.8%)	12.1
1984	630 (3.8%)	43 (46.5%)	6.8
Total	3003	669	
Mean	(5.6%)	(22.8%)	22.3

Abbreviation: LOS = low output syndrome

TABLE II THE CRITERIA FOR ORGAN FAILURES

Respiratory failure (RF):	Respiratory index ($A-a\text{Do}_2/P\text{ao}_2$) greater than 1.5 or necessitated prolonged mechanical ventilation
Acute renal failure (ARF):	Serum creatinine greater than 2.0 mg/dl or necessitated dialysis
Hepatic failure (HF):	Serum bilirubin greater than 3.0 mg/dl
Disseminated Intravascular coagulation (DIC):	FDP above 20 $\mu\text{g/ml}$ and platelet count less than $7.0 \times 10^4/\text{mm}^3$ or rapid fall
Central nervous system failure (CNSF):	Altered levels of consciousness and/or seizures
Gastro-intestinal bleeding (GIB):	Necessitated transfusion

Abbreviations: FDP = fibrin or fibrinogen degradation product; $A-a\text{Do}_2$ = alveolar-arterial oxygen tension difference

TABLE III THE INCIDENCE OF IMPAIRED ORGANS IN LOS PATIENTS AND THEIR CLINICAL RESULTS

Impaired organ	Incidence	Mortality
Respiratory failure	49.9%	36.8%
Acute renal failure	29.9%	54.5%
Hepatic failure	18.4%	52.8%
DIC	16.4%	59.1%
Gastro-intestinal Bleeding	11.1%	66.2%
CNS failure	15.5%	62.5%

Abbreviations: LOS = low output syndrome; DIC = disseminated intravascular coagulation; CNS = central nervous system

TABLE IV THE INCIDENCE OF IMPAIRED ORGANS IN LOS PATIENTS WITH MULTIPLE ORGAN FAILURE (MOF) AND THEIR CLINICAL RESULTS

No.*	Patients (mortality)	Incidences of impaired organ (%)					
		RF	ARF	HF	DIC	GIB	CNSF
0	244 (7.0%)	0	0	0	0	0	0
1	197 (14.7%)	64.0	15.2	7.6	3.6	1.5	8.1
2	83 (27.7%)	91.6	44.6	16.9	19.3	9.6	18.1
3	43 (48.8%)	83.7	72.1	48.8	32.6	18.6	44.2
4	41 (53.7%)	95.1	82.9	58.5	56.1	41.5	65.9
5	33 (69.7%)	100.0	97.0	78.8	81.8	60.6	65.9
6	23 (95.7%)	100.0	100.0	100.0	100.0	100.0	100.0

Abbreviations: LOS = low output syndrome; RF = respiratory failure; ARF = acute renal failure; HF = hepatic failure; DIC = disseminated intravascular coagulation; GIB = gastro-intestinal bleeding; CNSF = central nervous system failure.

* = Number of impaired organ

TABLE V THE CRITERIA FOR EACH TYPE OF RESPIRATORY FAILURES AND VENTRICULAR FAILURES

<i>Respiratory failures</i>	
<i>Lung edema and congestion type:</i>	<i>respiratory index > 1.5 and chest X-ray findings</i>
<i>Hypercapnia type:</i>	<i>Paco₂ > 50 torr associated with tachypnea and stressed respiration without findings of lung edema in chest X-ray</i>
<i>Combined type:</i>	<i>Hypercapnia type with findings of lung edema in chest X-ray</i>
<i>Ventricular failures</i>	
<i>Left ventricular failure:</i>	<i>LOS with LAP > RAP or LAP > 15 mmHg</i>
<i>Right ventricular failure:</i>	<i>LOS with LAP < RAP or RAP > 15 mmHg</i>
<i>Bilateral ventricular failure:</i>	<i>LOS with LAP $\div$ RAP or LAP $\div$ RAP 15 > mmHg</i>

Abbreviations: LOS = low cardiac output syndrome; LAP = left atrial pressure; RAP = right atrial pressure

developed in 669 patients (22.3%).

The clinical results of LOS patients

The incidence of LOS in open heart surgery and mortality is summarized in Table I. The rate has gradually decreased in recent years. The overall mortality rate was 5.6% which has been decreased nearly to 4% in the latest year. On the other hand, the mortality of patients who developed LOS postoperatively has been persistently high and the rates show no tendency to improve even in the later years.

The organ failures in LOS patients

The criteria for organ failures used in this study are listed in Table II. The incidence of

impaired organs in LOS patients and clinical results are summarized in Table III. Respiratory failure (RF) and acute renal failure (ARF) were the most common complications. The clinical results of LOS patients associated with an organ failure were extremely poor; the mortality of patients with RF was 36.8% and of patients with other organ failures exceeded 50%. Some patients developed multiple organ failure (MOF). Their clinical results, as well as the incidences of the impaired organs in MOF patients, are given in Table IV. The mortality elevates inevitably as the number of organ failure increase, consequently all but one patient that developed 6 organ failures died. However, when only LOS occurred without associated organ failure,

TABLE VI THE RELATIONSHIP BETWEEN THE TYPE OF RESPIRATORY FAILURES AND VENTRICULAR FAILURE Patients (mortality)

	Lung edema	Hypercapnia	Combined	Total
LVF	48 (41.7%)	1 (0.0%)	5 (60.0%)	54 (42.6%)
RVF	1 (100.0%)	28 (17.9%)	1 (100.0%)	30 (23.3%)
BVF	11 (90.9%)	23 (56.5%)	15 (33.3%)	49 (57.1%)
Total	60 (51.7%)	52 (34.6%)	21 (42.9%)	133 (43.6%)

Abbreviations: L(R,B)VF = left (right, bilateral) ventricular failure

Fig.1. Postoperative mean pulmonary and systemic pressure ratio (Pp/Ps), and pulmonary arteriolar and systemic vascular resistance ratio (PARI/SVRI) in patients associated with respiratory failure.

the mortality remained in the lowest range (Table IV). Therefore, it could be said that the organ failure caused by LOS has been playing vital role in mortality of the syndrome. In patients with LOS, MOF usually begins with impaired lung and kidney function, and other organ failures follow in the delayed periods either from the onset of LOS or of the initial organ failure. These are accelerated by infection, shock, cardiac arrest, malnutrition and other aggravating conditions?

Respiratory failure in LOS

Respiratory failure due to LOS is divided into three types: lung edema and congestion caused by increased pulmonary capillary pressure in LOS which resulted in a reduction of P_{aO_2} (LE type); an elevation of P_{aCO_2} associated with tachypnea and stressed respiration (hypercapnia type); and the combination of both types of respiratory failures (combined type). LOS was also classified into three groups according to the characteristics of cardiac failure such as left ventricular failure (LVF), right ventricular failure

(RVF) and bilateral ventricular failure (BVF). The criteria for each type of respiratory failures and ventricular failures are listed in Table V.

The relationship between the type of respiratory failure and those of ventricular failure are summarized in Table VI. It was clear that the

TABLE VII TREATMENTS FOR RESPIRATORY FAILURE

<i>Lung edema – LVF type</i>	
1.	PEEP or HFOV
2.	Inotropic supports & IABP
3.	Systemic vasodilators
4.	Diuretics
<i>Hypercapnea – RVF type</i>	
1.	PEEP or HFOV: not recommended
2.	Carefully and slowly weaning from mechanical ventilation after recovery from RVF
3.	Inotropic supports
	Isoproterenol or dobutamine: recommended
	Epinephrine or norepinephrine: not recommended
4.	Pulmonary vasodilator
	Trazoline, nitroglycerin, calcium antagonist
5.	Nutritional supports
6.	Anticoagulation

Abbreviations: L(R)VF = left (right) ventricular failure; PEEP = positive endoexpiratory pressure; HFOV = high frequency oscillatory ventilation; IABP = intra-aortic balloon pumping

close relationships existed between LE and LVF and between hypercapnia type of respiratory failure and RVF, respectively. Moreover, the majority of patients with RVF had pulmonary hypertension (PH). All the patients except one patient did not develop LE in spite of LOS when postoperative mean pulmonary and systemic pressure ratio (Pp/Ps) was greater than 0.42 and pulmonary arteriolar and systemic vascular resistance ratio (PARI/SVRI) was greater than 0.35 (as shown in Fig. 1). It is speculated, therefore, that RVF with PH had thickened pulmonary capillary walls as a result of long-term preoperative pressure stress to the walls which provided a mechanism for the reduction of water filtration in the pulmonary capillary walls. These patients develop the hypercapnia type of respiratory failure which causes the uneven ventilation-perfusion ratio due to decreased pulmonary blood flow in LOS and results in an elevation of $Paco_2$. Treatment for these respiratory failures are summarized in Table VII. Positive end expiratory pressure (PEEP) and high frequency ventilation (HFV) were effective in the LE type of respiratory failure but were not recommended for the hypercapnia type because the pulmonary blood flow was reduced considerably in peep and HFV.

Acute renal failure in LOS

The incidence of acute renal failure (ARF)

TABLE VIII THE ANNUAL INCIDENCES AND CLINICAL RESULTS OF ACUTE RENAL FAILURE (ARF)

	Incidences			Mortality (%)	
	Overall (%)	LOS patients (%)	PD (%)	Overall	PD
1977	9.5	40.0	75.0	75.0	66.7
1978	16.3	39.5	41.2	44.1	85.7
1979	11.3	28.9	60.6	54.5	90.0
1980	7.3	19.0	51.9	44.4	64.3
1981	5.4	17.8	61.5	53.8	68.8
1982	5.8	27.7	57.7	50.0	73.3
1983	4.7	39.1	88.0	68.0	72.7
1984	3.5	51.2	77.3	77.3	88.2
Total mean	6.6	29.9	61.4	54.5	77.2

Abbreviations: LOS = low output syndrome; PD = peritoneal dialysis

are listed in Table VIII. Although the overall incidence of ARF has decreased to less than 4% in the latest year, that of LOS patients remain high. The ARF in LOS patients develops according to the following process: first, a reduction of renal blood flow due to LOS leads to oliguria or anuria, then reduced blood flow allows ischemic damage of the parenchyma and finally leads to acute tubular necrosis. This is facilitated by a compression of swollen renal cells of the intercellular renal capillaries because of Na-K pump failure in the cell membranes, secondary to the impaired productions of ATP in mitochondria that is induced by ischemic damage.³

For the treatment of ARF in LOS, various types of cardiac support (inotropic agents, vasodilators, volume load and intra-aortic balloon pumping) are used initially to increase renal blood flow. Administration of dopamine and aminophirine, which selectively increase renal blood flow, are also recommended. When oliguria or anuria persists in spite of these treatments and

in the presence of diuretics, dialysis should be started in the early period. Peritoneal dialysis (PD) or continuous hemofiltration is preferred because of their relative little influence on hemodynamics.⁴

PD was carried out in 61.4% of patients with ARF. The mortality in this group was extremely high (77.2%) compared to that of patients who did not receive PD (54.5%) (Table VIII). These results were attributable to the severity of LOS but probably not to ARF itself.

Hepatic failure in LOS

Hepatic failure in LOS patients is classified into two types, ischemic type and intrahepatic cholestatic type. The ischemic type is caused by low perfusion to liver tissue leading to the centrilobular necrosis, where serum levels of enzymes such as GOT and GPT are increased initially and followed by both direct and indirect bilirubin as seen in laboratory findings. These Clinical signs usually seen in the delayed periods after the initial onset of LOS because reserved liver cells will compensate for the impaired parts for a short while. Therefore, when this type of hepatic failure is clinically observed, the degree dysfunction of the liver is quite severe.

The second type of hepatic failure is initially caused by congestion of the liver due to right ventricular failure in LOS, which is considered to be an obstruction of the intrahepatic small biliary tract. The laboratory findings consist of elevation of the serum level of direct bilirubin and alkali-phosphatase without concomitant increases of enzymes. Liver cell swelling due to Na-K pump failure in the cell membranes, infection and overloading of intravenous hyperalimentation may contribute to the exacerbation of hepatic dysfunction.

Disseminated intravascular coagulation (DIC) in LOS

The incidences of DIC are listed in Table IX.

TABLE IX THE INCIDENCES OF DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

	Overall (%)	LOS patients
1977	2.4	10.0
1978	3.8	9.3
1979	10.5	27.2
1980	7.0	18.3
1981	2.9	9.6
1982	2.5	11.7
1983	2.1	17.2
1984	1.7	25.6
Total mean	3.7	16.4

TABLE X ROLES OF PLASMA EXCHANGE IN MOF

1. Removal of organ toxic substances
<i>Bilirubin, Bile acids, Enzymes released, Endotoxin, Urea nitrogen, Lipid peroxides, Free hemoglobin, Unknown</i>
2. Supplement of deficient substances
<i>Antithrombin III, Coagulation factors, Complement, etc.</i>
3. Cessation of the vicious cycle produced by interactions of impaired organs

DIC after cardiac surgery is induced by low tissue perfusion and associated infection. Ischemic organ damage by microembolisms, increased vascular permeabilities due to released vasoactive substances such as FDP, and bleeding tendency lead to various organ failures. Moreover, the XIIth coagulation factor is easily activated when a prosthesis is implanted or with atrial fibrillation after open heart surgery leading to thrombus formation. The best therapy for DIC is to control underlying disorders; however, anticoagulant therapy is essential, not only for the prophylaxis and the treatment of DIC but also for the prevention of thrombus formation in implanted prostheses and in the cardiac chambers. In our experience we find that the patient in DIC is easily apt to develop MOF.

As an intravenous anticoagulant, low doses of heparin at the rate of 10 U/kg/hour is effective in patients with LOS. Since prophylactic anticoagulant therapy using heparin has been used in patients with implanted prostheses following open heart surgery, the incidence of DIC has markedly decreased to 2% in recent years. However, the antithrombic action of heparin is dependent on circulating levels of antithrombin III (AT-III). Long-term heparin administration will reduce the circulating AT-III levels by accelerating the consumption of AT-III. In such cases, administration of gabexate mesilate or MD-805, which have anticoagulant activities without influencing AT-III, are recommended⁵

Plasma exchange for MOF in LOS patients^{2,6}

Plasma exchange by centrifugalization using fresh frozen plasma were performed on 16 patients with LOS who developed MOF with 6 other impaired organs. Improvement in various organ functions was obtained in these patients by

means of plasma exchange. Consequently, three patients were successfully treated and recovered from MOF. Although one of them died from paroximal brain bleeding 25 days after the recovery from MOF, the other two patients were discharged from hospital and are leading normal lives. The purpose of plasma exchange for MOF was to remove various circulating organ toxic substances, supplement deficient substances and to stop the vicious cycle produced by the interaction of impaired organs (Table X).

In the current state of medical technology, which has no essential management for MOF, plasma exchange is considered to be one of the most efficacious methods in the treatment of MOF.

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