PULMONARY GAS EXCHANGE IN ACUTE MYOCARDIAL INFARCTION WITH LOW PULMONARY CAPILLARY WEDGE PRESSURE

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To evaluate the clinical characteristic of pulmonary gas exchange in patients with low pulmonary capillary wedge pressure (PCW < 18 mmHg) in the early phase of acute myocardial infarction, we investigated 48 patients admitted within 24h from the onset of chest pain. The alveolar-arterial oxygen tension difference (AaDO₂) and arterial blood gas parameters were obtained while breathing room air on admission. The disturbance of pulmonary gas exchange, as revealed by the high value of AaDO₂, existed without left ventricular dysfunction, and AaDO₂ had no significant relationship with any of the hemodynamic parameters including the difference between plasma colloid osmotic pressure and PCW. Multiple regression analysis was performed using 9 variables related to pulmonary gas exchange, to identify those which were important. As a result, QRS score ($p < 0.01$) and age ($p < 0.05$) were identified as significant variables related to AaDO₂. Thus, the disturbance of pulmonary gas exchange in patients with low PCW was caused by mechanisms other than left ventricular failure which may reflect the extent of ischemic myocardium.

ARTERIAL hypoxemia is often recognized during the first few days after acute myocardial infarction¹⁻⁸ and a significant relationship between pulmonary congestion and hypoxemia has been reported⁸. The major mechanisms of hypoxemia are pulmonary shunts and V/Q maldistribution due to pulmonary edema and congestion^{1-4,6,8}. Da Luz et al⁹ suggested that the difference between plasma colloid osmotic pressure (COP) and pulmonary capillary wedge pressure (PCW) is the critical determinant for the development of pulmonary edema after

acute myocardial infarction. On the other hand, pulmonary edema is observed without critical increase in left atrial pressure¹⁰ and several recent experimental studies have suggested that myocardial ischemia alters the vascular permeability of the lung¹¹⁻¹³. Furthermore, the reduction in lung volume and the presence of a small airways obstruction, which are thought to be due to pulmonary edema, have also been reported without critically increased PCW in patients with acute myocardial infarction^{14,15}. Based on these studies, we hypothesized that the disturbance of pulmonary gas exchange can exist without increased PCW. However, the clinical characteristics of pulmonary gas exchange in such cases are still unclear because earlier studies dealing with pulmonary gas

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TABLE I THE CLINICAL CHARACTERISTICS OF 48 PATIENTS WITH LOW PULMONARY CAPILLARY WEDGE PRESSURE

Variables		P-value
Age (Year)		60±11
Sex	Male	33
	Female	15
Location	Anterior	21
	Inferior	27
Smoking	(-)	11
	(+)	37
DM	(-)	34
	(+)	14
PrA	(-)	22
	(+)	26
QRS score		5.9±2.9
CI (L/min/m ²)		3.3±0.9
RA (mmHg)		4.1±3.7
PCW (mmHg)		9.8±3.4
COP (mmHg)		24.5±2.4
COP-PCW (mmHg)		14.7±4.3
PaO ₂ (mmHg)	Admission	71.5±13.4
	LHP	80.0±8.3
PaCO ₂ (mmHg)	Admission	33.9±5.0
	LHP	36.5±3.5
AaDO ₂ (mmHg)	Admission	36.8±13.0
	LHP	25.3±9.0

Values are mean±standard deviation. DM=diabetes mellitus; PrA=preinfarction angina; CI=cardiac index; RA=right atrial pressure; PCW=pulmonary capillary wedge pressure; COP=plasma colloid osmotic pressure; COP-PCW=difference between plasma colloid osmotic pressure and pulmonary capillary wedge pressure; LHP=late hospital phase; PaO₂=arterial oxygen tension; PaCO₂=arterial carbon dioxide tension; AaDO₂=alveolar-arterial oxygen tension difference.

exchange included patients with congestive heart failure. Therefore, the purpose of this study was to elucidate the clinical characteristics of pulmonary gas exchange in patients with low PCW (<18 mmHg) following acute myocardial infarction.

PATIENTS AND METHODS

Patients

Among the consecutive patients with acute myocardial infarction admitted to our coronary care unit, 48 patients fulfilled the following criteria: 1) no previous history of pulmonary diseases and myocardial infarction; 2) blood gas analysis and hemodynamic parameters measured within 24h from the onset of their chest pain (average delay from the onset 5.5±4.9h) with no treatment at the time of measurement; 3) PCW below 18

mmHg on admission; 4) QRS score obtained on the 7th hospital day from the Selvester's Complete 54-Criteria 32-point QRS Scoring System¹⁶ using the standard 12-lead electrocardiogram.

Patients with the following criteria were not included: 1) right or left bundle branch block, or nonspecific intraventricular conduction delay (QRS≥110 ms), 2) left anterior fascicular block (QRSaxis≤-30), 3) right ventricular and/or left ventricular hypertrophy, 4) non-q wave myocardial infarction, 5) revascularization performed by interventional therapy in acute phase, 6) extension of infarction or reinfarction during the first 7 days.

The diagnosis of acute myocardial infarction was established by a history of prolonged typical chest pain and ST-T wave changes with new Q-waves in serial electro-

Fig.1. Relation between the alveolar-arterial oxygen tension difference (AaDO₂) and pulmonary capillary wedge pressure (PCW) on admission. NS=not significant.

Fig.2. Relation between the alveolar-arterial oxygen tension difference (AaDO₂) and the difference between plasma colloid osmotic pressure and pulmonary capillary wedge pressure (COP-PCW) on admission.

cardiograms with enzymatic confirmation. History of diabetes mellitus, smoking and angina was recorded by interview.

Measurements

Arterial blood gas samples were obtained on admission and during the late hospital phase after leaving the coronary care unit in

Fig.3. Relation between arterial carbon dioxide tension (PaCO_2) and pulmonary capillary wedge pressure (PCW) on admission.

Fig.4. Relation between the alveolar-arterial oxygen tension difference (AaDO_2) on admission and QRS score obtained from the Selvester's QRS Scoring System on the 7th hospital day.

44 patients. Arterial oxygen tension (PaO_2) and arterial carbon dioxide tension (PaCO_2) were measured at 37°C with the standard electrode technique utilizing a Radiometer

system (Radiometer company, ABL2) while the patient was breathing room air. Alveolar-arterial oxygen tension difference (AaDO_2) was calculated by assuming a re-

TABLE II IMPORTANT VARIABLES RELATED TO AaDO₂

Variables	Age	Smoking	DM	PrA	QRS score	CI	RA	PCW	COP
Regression coefficient	0.314	5.036	2.807	-1.249	2.789	-0.705	-0.909	0.308	-0.913
Partial correlation coefficient	0.327	0.215	0.137	-0.069	0.651	-0.056	-0.285	0.095	-0.224
P-value	<0.05	NS	NS	NS	<0.01	NS	NS	NS	NS

AaDO₂=alveolar-arterial oxygen tension difference; DM=diabetes mellitus; PrA=preinfarction angina; CI=cardiac index; RA=right atrial pressure; PCW=pulmonary capillary wedge pressure; COP=plasma colloid osmotic pressure; NS=not significant.

spiratory quotient equal to 0.8. Right heart catheterization was performed by the flow-directed balloon-tipped catheter technique. The pressures were measured with a SIEMENS-ELEMA transducer positioned 5 cm below the sternal angle. Cardiac output was determined by the thermodilution technique with an EDWARDS 9520 computer. COP was obtained from Nitta-Staub's¹⁷ equation using the measured values for total protein content, serum albumin, and serum globulin on admission:

$$\text{COP} = a (2.8c + 0.18c^2 + 0.012c^3) + b (0.9c + 0.12c^2 + 0.004c^3)$$

Where a(%)=serum albumin; b(%)=serum globulin; c(g/dl)=total protein.

Statistical Analysis

Results are reported as mean±standard deviation. The paired t-test was used to test the change of arterial gas variables between admission and late hospital phase. The least squares linear regression analysis was used to obtain the relationship between blood gas and clinical variables. Multiple regression analysis was used to determine the important variables related to AaDO₂ based on the following 9 variables: cardiac index, right atrial pressure, PCW, COP, QRS score, age, smoking, diabetes mellitus and preinfarction angina. A p-value less than 0.05 was considered significant.

RESULTS

Clinical and Hemodynamic Parameters in Patients with Low PCW (Table I)

PaO₂ and PaCO₂ on admission were lower than those during late hospital phase

(71.5±13.4 vs 80.0±8.3 mmHg and 33.9±5.0 vs 36.5±3.5 mmHg, p<0.001 and p<0.005 respectively). Therefore, a significantly higher AaDO₂ was observed on admission than in late hospital phase (36.8±13.0 vs 25.3±9.1 mmHg, p<0.001). Hypoxemia and hyperventilation existed even in low PCW on admission. The average delay from admission to late hospital phase was 20±14 days.

Correlations between AaDO₂ and Clinical Variables (Fig. 1–4)

AaDO₂ had no significant correlations with any of the hemodynamic variables (cardiac index, right atrial pressure and PCW). Furthermore, the correlation between AaDO₂ and the difference between COP and PCW was not significant. However, there was a weak correlation between PaCO₂ and PCW (r=-0.30, p<0.05) and a fairly good correlation between AaDO₂ and QRS score (r=0.63, p<0.001).

Important Variables Related to AaDO₂ (Table II)

Multiple regression analysis was used to determine the important variables related to AaDO₂ (pulmonary gas exchange) using 9 variables. As a result, QRS score (p<0.01) and age (p<0.05) were identified as significant variables contributing to the disturbance of pulmonary gas exchange.

DISCUSSION

A PCW of 18 mmHg has been shown to be critical for the onset of radiologic signs of left ventricular failure¹⁸ and this value has also been used by Forrester et al¹⁹ for defin-

ing hemodynamic subsets in acute myocardial infarction. We investigated the patients with low PCW (<18 mmHg) and found that the disturbance of pulmonary gas exchange, as revealed by the high value of $AaDO_2$, existed without left ventricular dysfunction in the early phase of myocardial infarction. Our patients with low PCW following acute myocardial infarction had a reduced $PaCO_2$ without severe hypoxemia, and only a weak correlation existed between $PaCO_2$ and PCW ($r = -0.30$, $p < 0.05$). These data indicated that alveolar hypoventilation was not the mechanism of hypoxemia.^{1,4,5} Hyperventilation is attributed to stimulation of interstitial J-type receptors by the edema or to stretch receptors in the interstitium rather than to the hypoxemia.²⁰ Interstitial edema and pulmonary congestion are some of the important factors which can induce hyperventilation following acute myocardial infarction. Because hypoxemia can be compensated by hyperventilation, $AaDO_2$ was chosen in this study as an indicator of pulmonary gas exchange.

Earlier reports have described hypoxemia with pulmonary congestion,¹⁻⁸ and a significant relationship was observed between hypoxemia and pulmonary artery diastolic pressure.⁸ $AaDO_2$ in our patients with low PCW had no significant relationship with any of the hemodynamic parameters including the difference between COP and PCW. Furthermore, hemodynamic parameters and COP were not significant factors contributing to the change in $AaDO_2$ in the multiple regression analysis. These results suggest that hydrostatic pressure was not the major factor causing the disturbance of pulmonary gas exchange in our patients with low PCW. Several recent studies have demonstrated experimental evidence of pulmonary capillary disruption during myocardial infarction.¹⁻¹³ These studies found greater elevations in extravascular lung water levels after coronary artery ligation, despite stable microvascular pressure when compared with control dogs. They concluded that myocardial ischemia altered the vascular permeability of the lung, and speculated that prostaglandin and prostaglandin metabolites might have provoked this condition through direct and indirect effects.¹²⁻¹³ Furthermore, in several recent studies a number of mediators (cyclooxygenase

nase pathway products, lipoxygenase pathway products, platelet activating factor, tumor necrosis factor, etc) reported in adult respiratory distress syndrome²¹ were also found in ischemic myocardium.²²⁻²⁷ Moreover, a recent clinical study reported that extensive myocardial infarction induces the release of tumor necrosis factor into the circulation, and that this was associated with pulmonary edema.²⁷ Based on these studies, we can assume that acute pulmonary edema in the early phase of acute myocardial infarction may be associated with the extent of ischemic myocardium. In our study, QRS score had the best correlation with $AaDO_2$ in the multiple regression analysis. QRS score obtained by the Selvester's QRS scoring system is reported to be one of the indicators of infarct size.^{28,29} Therefore, the disturbance of pulmonary gas exchange without critically increased PCW might be due to interstitial edema caused by increased permeability of the capillary endothelium, caused in turn by mediators released from the infarcted myocardium.

We found that aging was an important factor contributing to disturbance of pulmonary gas exchange in patients without critically increased PCW, but neither smoking nor diabetes mellitus was an independent factor. Several studies established that aging of the lung results in a progressive reduction in arterial oxygen tension in healthy adults.³⁰⁻³² Thus, an impairment in gas exchange which occurs with aging of the lung may be the reason aging appears in the multivariate analysis to be an important factor affecting $AaDO_2$. Smoking has been recognized to alter pulmonary function and gas exchange, but Kelly et al.³³ analyzing data from 2955 patients with myocardial infarction, found that smokers were more than 10 years younger than nonsmokers. As in the earlier study, smokers in the present study were younger than nonsmokers (57 ± 11 vs 67 ± 7 years, $p < 0.01$). The unexpected result that smoking was not a significant factor associated with pulmonary gas exchange could be due to the difference in the age distribution.

Diabetic patients with initial myocardial infarction of modest extent have been reported to have a significantly higher incidence of pulmonary congestion than their nondiabetic counterparts.³⁴ Earlier studies

indicated that left ventricular function is compromised by the pathogenetic processes of diabetes mellitus in the myocardium,^{35,36} which may lead to higher incidences of pulmonary congestion. However, it is not clear that diabetes mellitus affects pulmonary gas exchange or the incidence of pulmonary edema in patients with low PCW. Considering our results from the multivariate analysis, diabetes mellitus may not be associated with the disturbance of pulmonary gas exchange in patients without critically increased PCW.

Two limitations of our study should be addressed. First, the high value of AaDO₂ on admission may not be caused by only pulmonary edema but by other factors: drugs (vasodilators, diuretics), age and posture. Drug administration can not have affected AaDO₂ on admission because the measurement was performed before the treatment. Age was established as the second factor in multiple regression analysis. Since we measured all blood gas parameters in supine posture, a significant improvement of arterial gas parameters from admission to late hospital phase indicates the existence of a transient disturbance of pulmonary gas exchange in the acute phase of myocardial infarction. Therefore, we believe that the disturbance of pulmonary gas exchange in the early phase of acute myocardial infarction exists even in low PCW which may be due to transient interstitial pulmonary edema.

Second, we used QRS score as the indicator of infarct size. QRS score may not independently provide a definitive measure of infarct size. On the electrocardiogram, myocardial infarction on opposing walls of the heart may "cancel" electrical changes, and intraventricular conduction delays or ventricular hypertrophy can either simulate or mask acute myocardial infarction. Moreover, the time lag between the onset and the measurement of QRS score may not be accurate in evaluating the infarct size because of re-infarction, extension of infarct and reduction of infarct by interventional therapy. Therefore, we carefully excluded such patients in this study.

In conclusion, the disturbance of pulmonary gas exchange existed even in low PCW, which did not correlate with any of the hemodynamic parameters but did correlate with infarct size. We believe that the distur-

ance of pulmonary gas exchange in patients without critically increased PCW may be caused by interstitial pulmonary edema reflecting the extent of ischemic myocardium.

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