Decreased serum level of lipoprotein cholesterol is a poor prognostic factor for patients with severe community-acquired pneumonia that required intensive care unit admission

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ABSTRACT

Purpose: The purpose of this study is to investigate the prognostic values of the serum levels of lipids in patients with severe community-acquired pneumonia (CAP) that required intensive care unit (ICU) admission.
Materials and methods: Patients who had severe CAP that required ICU admission were included. Serum lipid level was collected on the days 1 and 7 of ICU stay. Clinical outcome, including length of ICU stay, hospital stay, and death, were monitored prospectively.
Results: A total of 40 patients were enrolled in this study. Lower high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were found in nonsurvival group on ICU admission day 7 (survivors vs nonsurvivors; mean HDL, 41.8 vs 13.0 mg/dL, $P = .002$; LDL, 62.3 vs 30.3 mg/dL, $P = 0.006$, respectively). High-density lipoprotein cholesterol level of less than or equal to 17 mg/dL on day 7 (odds ratio, 1.23) and LDL cholesterol level of less than or equal to 21 mg/dL on day 7 (odds ratio, 1.10) could be a predictor of hospital mortality. The mean change in levels of HDL cholesterol in nonsurvivors decreased significantly than those in survivors from days 1 to 7 (8.5 vs -17.4 mg/dL, $P = .04$) but not LDL cholesterol.
Conclusions: Decreased serum HDL cholesterol level from days 1 to 7 may be of prognostic value.

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1. Introduction

Severe community-acquired pneumonia (CAP) is now recognized as an entity of its own requiring a specific management approach [1-8]. Approximately 10% of all hospitalized patients with CAP required admission to the intensive care unit (ICU) [9], and the mortality of these patients reaches 20% to 50% [1-7]. The epidemiology, etiology, and prognosis of severe CAP have repeatedly been investigated in the last decade [1-11], with the increasing data about the risk factors in the studies worldwide.

There is a growing body of evidence linking lipid metabolism to the host innate immune response to infection and acute injury. Significant changes in the distribution of circulating lipoproteins in septic patients had been reported [12,13]. High-density lipoprotein (HDL) and other lipoproteins may contribute to host homeostasis in ways other than the transport of fatty acids and cholesterol. Therefore, circulating lipids might support the body's defense against infection by binding and neutralizing bacterial toxins [14-18]. Chien et al [19] present additional data

in support of a protective role for HDL during life-threatening infections. Decreased serum HDL cholesterol and apolipoprotein A-I levels were associated with an increased mortality rate among severely septic patients [19]. However, the correlation of serum cholesterol and outcome of severe CAP has not been well investigated.

Although the reduction in lipid and lipoprotein levels is well known in critically ill patients [20,21], their prognostic implications in patients with severe CAP remain unclear. The aim of this study was to investigate the association between lipid kinetics and clinical outcome in patients with severe CAP. We hypothesize that there is a negative correlation between serum HDL concentrations and clinical outcome [20]. Hypocholesterolemia could be an independent predictor of mortality for severe CAP patients.

2. Material and methods

2.1. Patients

From November 2006 to January 2009, patients who were older than 18 years and admitted to medical ICU in National Taiwan University Hospital due to severe CAP were evaluated. Patients with permit sheet were enrolled in this study. The diagnosis of CAP was established, if chest radiographs presented with new infiltration combined with 2 of

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Table 1
Baseline characteristics

	Total (n = 40)	Survivors (n = 25)	Nonsurvivors (n = 15)	P
Sex (male)	27 (67.5%)	15 (60.0%)	12 (80.0%)	.30
Age	75.1 ± 14.0	74.4 ± 13.7	76.3 ± 14.8	.70
BMI	18.8 ± 3.8	19.7 ± 3.1	17.4 ± 4.5	.06
Diabetics mellitus	14 (35.0%)	10 (40.0%)	4 (26.7%)	.50
Hypertension	18 (45.0%)	15 (60.0%)	3 (20.0%)	.02
CHF	6 (15.0%)	6 (24.0%)	0 (0.0%)	.07
COPD	15 (37.5%)	13 (52.0%)	2 (13.3%)	.02
Old CVA	13 (32.5%)	10 (40.0%)	3 (20.0%)	.30
Liver cirrhosis	1 (2.5%)	0 (0.0%)	1 (6.7%)	.38
CKD	5 (12.5%)	3 (12.0%)	2 (13.3%)	1.00
Malignancy	7 (17.5%)	3 (12.0%)	4 (26.7%)	.40

CHF indicates congestive heart failure; CVA, cerebral vascular accident; CKD, chronic kidney disease.

the following criteria: (1) fever with body temperature greater than 38°C, (2) leukocytosis with white blood cell greater than 11 000/mm^3 or neutropenia with neutrophil less than 3500/mm^3, (3) cough with or without purulent sputum, (4) chest pain, and (5) abnormal physical findings of breathing sounds with crackles or rales. Severe CAP was defined to meet 1 of major criteria or 2 of minor criteria as followed [22,23]. Major criteria include need of mechanical ventilation, increased infiltration over chest radiographs within 48 hours, septic shock or need of vasopressor more than 4 hours, and acute renal failure (urine output <80 mL within 4 hours or serum creatinine >2 mg/dL without chronic renal insufficiency). Minor criteria include respiratory rate more than 30 breaths per minute, ratio of Pao$_2$ to fraction of inspired oxygen less than 250, bilateral infiltration or multiple lobar pneumonia over chest radiographs, systolic blood pressure less than or equal to 90 mm Hg, and diastolic blood pressure less than or equal to 60 mm Hg. Patients would be excluded, if they had following conditions: previous admission within 14 days; ICU admission after arriving in the hospital more than 48 hours; long-term mechanical ventilator dependence; pregnancy; and severe immunosuppression, including HIV infection, solid organ or bone marrow transplantation with immunosuppressant agents, and active malignancy under chemotherapy. Patients with hospital death were defined as poor outcome. The Institutional Review Board of the National Taiwan University Hospital approved the study.

2.2. Data collection

Clinical characteristics, including age, sex, history of coexisting disease, presenting symptoms, disease severity, ventilator use, complications in ICU, and outcomes, were recorded within 24 hours after meeting the criteria for severe CAP in ICU admission. Severity of the disease was assessed using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score [24], and dysfunction of organ systems was defined as previously described [25]. Microbiological culture results were assessed daily from the start of observation until death or discharge.

Serum lipid proteins level including triglyceride, cholesterol, HDL, and low-density lipoprotein (LDL), and other inflammatory biomarker such as C-reactive protein (CRP) were collected on the days 1 and 7 of ICU admission.

Total cholesterol and HDL cholesterol concentrations were measured enzymatically using kits (Denka Seiken, Tokyo, Japan). Low-density lipoprotein cholesterol concentrations were measured by the homogeneous method using kits (Denka Seiken). Albumin concentrations were measured Bromocresol green using kits (Denka Seiken). Triglyceride concentrations were measured enzymatically using kits (Sentinel, Milan, Italy). C-reactive protein concentrations were measured by the immunoturbidimetric method using kits (Denka Seiken).

2.3. Statistical analysis

All continuous data were expressed as mean and SD. Categorical variables were analyzed by means of Fisher exact and χ^2 tests. Numerical variables were compared by using independent t test. Paired-samples t test was used to compare the change of serum cholesterol between days 1 and 7. Multivariate logistic regression analysis was performed for variables if P was less than .05. Receiver operating characteristic (ROC) curve was used to examine the capacity of serum HDL and LDL cholesterol level in differentiating the status of survival. The area under curve (AUC) and 95% confidence interval (CI) were reported. Statistical calculations were performed using SPSS version 16.0 (SPSS, Inc, Chicago, IL).

3. Results

3.1. Patient characteristics

From November 2006 to January 2009, 40 patients with severe CAP were enrolled in the study. There were 10 patients who died in ICU and 5 patients who died in hospital. The overall mortality rate was 37.5%. The baseline characteristics of the patients were presented as Table 1. There were 67.5% male patients (n = 27), and the mean age was 75.0 ± 14 years old. The body mass index (BMI) was relative low, especially in the nonsurvival group. More hypertensive patients and chronic obstructive pulmonary disease (COPD) patients were noted in the

Table 2
Initial clinical presentation on ICU admission

	Total (n = 40)	Survivors (n = 25)	Nonsurvivors (n = 15)	P
CURB-65	2.5 ± 1.1	2.1 ± 1.1	3.1 ± 0.7	.01
Pneumonia severity index	123.7 ± 33.0	117.7 ± 36.3	136.4 ± 20.8	.12
APACHE II score	21.2 ± 8.6	19.2 ± 8.4	24.5 ± 8.2	.06
Glasgow Coma Scale	9.8 ± 3.6	10.8 ± 3.4	8.1 ± 3.4	.02
Septic shock	13 (32.5%)	5 (20.0%)	8 (53.3%)	.04
Fever	18 (45.0%)	13 (52.0%)	5 (33.3%)	.33
Cough	22 (55.0%)	16 (64.0%)	6 (40.0%)	.20
Dyspnea	36 (90.0%)	23 (92.0%)	13 (86.7%)	.62
Altered mental status	13 (32.5%)	6 (24.0%)	7 (46.7%)	.18
Bilateral lung infiltration (CXR)	21 (52.5%)	11 (44.0%)	10 (66.7%)	.20
MAP (mm Hg)	84.8 ± 19.3	85.0 ± 18.7	84.6 ± 21.0	.95
Pao$_2$/Fio$_2$	191.7 ± 115.0	200.9 ± 109.3	176.9 ± 126.1	.53
WBC (/μL)	13836.3 ± 15717.5	15989.7 ± 19208.0	10247.3 ± 5798.2	.27
Hemoglobin level (g/dL)	11.6 ± 2.8	12.0 ± 2.8	11.0 ± 2.8	.30
Platelet (K/μL)	224.1 ± 127.8	222.1 ± 148.1	227.3 ± 88.8	.90
PT INR	1.0 ± 0.0	1.13 ± 0.2	1.30 ± 0.2	.02
Albumin (g/dL)	3.0 ± 0.7	3.3 ± 0.5	2.6 ± 0.6	<.0001
AST (U/L)	93.0 ± 140.6	60.5 ± 45.0	147.3 ± 215.8	.06
BUN (mg/dL)	34.4 ± 23.0	27.8 ± 16.6	45.4 ± 28.1	.02
Creatinine (mg/dL)	2.0 ± 2.0	1.5 ± 1.0	2.7 ± 2.9	.09
Positive blood culture	9 (22.5%)	6 (24.0%)	3 (20.0%)	1.00
Pneumonia-causing microorganism				
Gram-negative microorganism	19 (47.5%)	12 (48.0%)	7 (46.7%)	1.00
Gram-positive microorganism	3 (7.5%)	2 (8.0%)	1 (6.6%)	1.00
Mixed	7 (17.5%)	3 (12.0%)	4 (26.7%)	.39
Culture negative	11 (27.5%)	8 (32.0%)	3 (20.0%)	.50

CXR indicates chest x-ray; MAP, mean arterial pressure; Fio$_2$, fraction of inspired oxygen; WBC, white blood cell; AST, aspartate aminotransferase; BUN, blood urea nitrogen; PT INR, prothrombin time international normalized ratio.