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ORIGINAL ARTICLE

# Necrotizing fasciitis in liver cirrhosis

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**KEYWORDS**
hypoalbuminemia;
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**Summary** *Background:* Necrotizing fasciitis (NF) is associated with a high mortality rate. Hepatitis is endemic in Taiwan, and liver cirrhosis is associated with the development of NF. The characteristics of these patients, however, have not been well documented or the predictors of mortality clearly identified. The purpose of this study is to identify predictors of mortality in patients with liver cirrhosis and necrotizing fasciitis.
*Methods:* This study was conducted at the Chi-Mei Medical Center in southern Taiwan. Demographic data, clinical characteristics, and the microorganisms responsible for NF in patients with liver cirrhosis were recorded. To identify independent predictors associated with mortality, univariate analysis followed by multivariate logistic regression modeling was performed.
*Results:* During the period 2003–2011, a total of 55 patients with liver cirrhosis and NF were treated at the Chi-Mei Medical Center. Most patients had infections by monomicrobial Gram-negative bacilli. Univariate analysis revealed that severity of liver cirrhosis, shock, band polymorphonuclear neutrophil (>10%), international normalized ratio (>1.5), serum creatinine (>2.0 mg/dL), serum albumin (<2.5 g/dL), and activated partial thromboplastin time (>60 seconds) were significantly associated with mortality. However, multivariate logistic regression analysis revealed that serum albumin of <2.5 g/dL was the only independent predictor of mortality in patients with liver cirrhosis and NF.
*Conclusion:* NF in the vast majority of cirrhotic patients was caused by Gram-negative bacilli. Hypoalbuminemia (serum albumin <2.5 g/dL) was associated with mortality in patients with

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liver cirrhosis and NF. Further studies are needed to assess whether resuscitation with albumin-containing solutions lowers the mortality rate in such patients.


## 1. Introduction

Necrotizing fasciitis (NF), first reported by Wilson in 1952,[1] is a soft tissue infection with fascial necrosis. It has an estimated incidence of 1000 cases/year in the USA. The predisposing conditions are mainly diabetes mellitus, alcoholism, end-stage renal disease, malignancy, liver cirrhosis (LC), malnutrition, gout, corticosteroid use, and trauma.[2] The most common initial sign is tender erythema in the infected area. Other common symptoms originating from the skin are edema of the limbs, induration of the skin, purulence, fluctuance, and local heat. NF is a severe disease of sudden onset requiring the administration of high doses of intravenous antibiotics as well as aggressive surgical debridement. Despite improved medical care and better understanding of this disease today, the mortality rate remains high (24–34%).[3] LC predisposes patients to serious bacterial infections. In fact, the incidence of infection is 5–7 times higher in these patients than in other hospitalized patients.[4] Infection in cirrhotic patients involves organisms that gain access to the gastrointestinal tract by escaping phagocytosis in the hepatic reticuloendothelial system.[5] Hepatitis is endemic in Taiwan and LC has been shown to be associated with NF.[6,7] However, the characteristics of this specific group of patients have not been well documented and the risk factors of mortality have not been clearly identified. The purpose of this study is to present our clinical experience in treating NF in patients with LC and identify risk factors of mortality.

## 2. Methods

This study was conducted at the Chi-Mei Medical Center in southern Taiwan. The medical records of patients with liver cirrhosis who were diagnosed to have NF from 2003 to 2011 were reviewed. This study was approved by the ethics committee of our hospital. The diagnosis of NF was established according to the International Classification of Diseases, 9th revision (NF, 728.86; in combination with LC, 571.2 or 571.5). The final diagnosis of LC was based on hepatosplenic ultrasonography findings and the definitive diagnosis of NF on operative findings of necrosis of the fascia.

The characteristics of the patients were obtained from the medical records. Etiology of the disease, patient data, the cause and severity of LC, affected sites, clinical symptoms, laboratory examination results, and results of microbiologic testing comprised the primary variables. Hepatotropic viruses were identified using common serological techniques. The modified Child–Pugh classification system was used to grade the severity of LC at admission for each patient.[8] The modified Child–Pugh classification of the severity of liver disease was determined according to the degree of ascites, the plasma concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total score of 5–6 was considered Grade A, 7–9 was Grade B, and 10–15 was Grade C. Laboratory results were obtained in the emergency room or within 24 hours after admission to the hospital. The white blood cell (WBC), band polymorphonuclear neutrophil (PMN), and platelet counts, activated partial thromboplastin time (aPTT), international normalized ratio (INR), and levels of hemoglobin, C-reactive protein, serum creatinine, glucose, and albumin were dichotomized, with a cutoff point based on clinical experience and previous reports. Shock was defined as a systolic blood pressure of $<$90 mmHg. Wound cultures were obtained in the emergency room or during the initial surgery. Microbiologic results were recorded for patients with positive cultures for organisms. The primary study outcome was 30-day mortality.

To identify risk factors associated with mortality, we first performed a series of Chi-square or Fisher's exact tests. Variables with a $p < 0.05$ were considered potential risk factors and were therefore included in a stepwise multivariate logistic regression model to determine the most important independent predictors of 30-day mortality. Statistical significance was defined as a $p < 0.05$, unless specified otherwise. Data analyses were performed on a personal computer using the statistical software package SPSS for Windows (Version 17.0; SPSS Inc., Chicago, IL, USA).

## 3. Results

### 3.1. Etiology, patient characteristics, and affected sites

From January 2003 to December 2011, a total of 55 patients with liver cirrhosis and NF were treated at the Chi-Mei Medical Center. The overall mortality rate was 51% ($n = 28$) and all deaths occurred within 30 days of hospitalization. The patients comprised 42 men and 13 women with a mean age of 59.0 $\pm$ 12.4 years. The cause of NF was either unknown ($n = 27$, 49%) or trauma ($n = 10$, 18%), when added together, in more than half of the patients. Six of the patients (11%) had a history of exposure to dirty water or fish-fin injury and two patients (4%) had a history of seafood intake before the episodes (Table 1). All the six patients with a history of exposure to dirty water or fish-fin injury were infected by *Vibrio* species. One patient with a history of seafood intake was infected by *Vibrio* species and others by *Aeromonas* species. No association was noted between mortality and age $>$60 years. In addition, there were no differences in comorbidities including diabetes mellitus, cancer (by history), heart disease, and end-stage renal

**Table 1** Causes of necrotizing fasciitis in patients with liver cirrhosis.

| Cause | Number of patients ($n = 55$) |
|---|---|
| Idiopathic | 27 (49) |
| Trauma | 10 (18) |
| Dirty water exposure or fish-fin injury | 6 (11) |
| Diabetic foot infection | 2 (4) |
| Seafood intake | 2 (4) |
| Chronic ulcer/wound | 2 (4) |
| Surgical wound infection | 2 (4) |
| Pyomtositis | 2 (4) |
| Perianal abscess | 1 (2) |
| Burn injury | 1 (2) |

Values are expressed as *n* (%).

disease between survivors and nonsurvivors (Table 2). NF occurred in the extremities in most patients ($n = 53$, 96%). There was no significant association between mortality and affected sites in the univariate analysis.

### 3.2. The causes and severity of LC

Alcoholic hepatitis was noted in 24 (44%) patients, and was the major cause of LC, Other causes included chronic hepatitis B virus (HBV) infection ($n = 18$, 33%), chronic hepatitis C virus (HCV) infection ($n = 17$, 31%), coexistent HBV and HCV infection ($n = 2$, 4%), and combined alcoholic and viral hepatitis infection ($n = 1$, 2%). There was no significant association between mortality and the cause of LC (Table 3). According to the modified Child—Pugh classification, eight patients (15%) in our series had Grade A, 26 (47%) Grade B, and 21 (38%) Grade C LC. The results of univariate analysis revealed that the severity of LC differed significantly between survivors and nonsurvivors ($p = 0.035$; Table 3).

### 3.3. Clinical symptoms and signs and time of arrival to surgical intervention

Patients admitted to the hospital presented with pain, swelling, erythema, localized heat, fever, purulent discharge, blistering, general malaise, foul odor, skin discoloration or induration, altered mental status and shock. None of the clinical symptoms and signs with the exception of shock differed significantly between survivors and nonsurvivors in the univariate analysis (Table 4). Surgical intervention was performed in 31 patients (56%) within 24 hours of admission and in 24 patients more than 24 hours after admission. Results of the univariate analysis revealed that there was no significant association between mortality and time to surgical intervention (Table 4).

**Table 3** Effect of the cause and severity of liver cirrhosis on mortality.[a]

| | All patients ($n = 55$) | Survivors ($n = 27$) | Nonsurvivors ($n = 28$) | $p$* |
|---|---|---|---|---|
| Cause | | | | |
| Hepatitis B | 18 (33) | 9 (33) | 9 (32) | 0.925 |
| Hepatitis C | 17 (31) | 9 (33) | 8 (29) | 0.702 |
| Alcoholic hepatitis | 24 (44) | 12 (44) | 12 (43) | 0.906 |
| Grade | | | | |
| A | 8 (15) | 7 (26) | 1 (4) | 0.035 |
| B | 26 (47) | 13 (48) | 13 (46) | |
| C | 21 (38) | 7 (26) | 14 (50) | |

Values are expressed as *n* (%) of patients.
[a] There were two patients coinfected with hepatitis B and C. Another patient had combined alcoholic and viral hepatitis infection. *$p$ values are based on comparisons between survivors and nonsurvivors using the Chi-square test or Fisher's exact test.

### 3.4. Laboratory examinations

Nonsurvivors presented with significantly greater numbers of band PMNs (>10%) and significantly lower serum albumin levels (<2.5 g/dL) than survivors. Additionally, the nonsurvivors had higher aPTT values (>60 seconds), INR values (>1.5), and serum creatinine levels (>2.0 mg/dL) than the survivors (Table 5).

### 3.5. Microbiology

Wound cultures were obtained from all patients, and 53 patients had cultures positive for bacterial pathogens (96%). Of those with positive wound cultures, 43 (81%) had monomicrobial cultures. The causative organisms in the 43

**Table 2** Effect of demographic characteristics and comorbidities on mortality of patients with necrotizing fasciitis and liver cirrhosis.

| Variables | All patients ($n = 55$) | Survivors ($n = 27$) | Nonsurvivors ($n = 28$) | $p$ |
|---|---|---|---|---|
| Sex (male) | 42 (76) | 20 (74) | 22 (79) | 0.695 |
| Age > 60 y | 26 (47) | 11 (41) | 15 (54) | 0.341 |
| Diabetes mellitus | 18 (33) | 9 (33) | 9 (32) | 0.925 |
| Cancer history | 11 (20) | 5 (19) | 6 (21) | 0.787 |
| Heart disease | 4 (7) | 1 (4) | 3 (11) | 0.611 |
| End-stage renal disease | 4 (7) | 0 (0) | 4 (14) | 0.111 |

Values are expressed as *n* (%). $p$ values are based on comparisons between survivors and nonsurvivors using the Chi-square test or Fisher's exact test.

**Table 4** Effect of clinical symptoms and signs and time to surgical intervention on mortality.

| | All patients ($n$ = 55) | Survivors ($n$ = 27) | Nonsurvivors ($n$ = 28) | $p$* |
|---|---|---|---|---|
| Swelling | 50 (91) | 24 (89) | 26 (93) | 0.965 |
| Pain | 47 (85) | 23 (85) | 24 (86) | > 0.99 |
| Erythema | 38 (69) | 19 (70) | 19 (68) | > 0.99 |
| Fever | 26 (47) | 12 (44) | 14 (50) | 0.887 |
| Local heat | 24 (44) | 13 (48) | 11 (39) | 0.696 |
| Pus discharge | 17 (31) | 8 (30) | 9 (32) | > 0.99 |
| Shock | 16 (29) | 3 (11) | 13 (46) | 0.004 |
| Foul odor | 11 (20) | 5 (19) | 6 (21) | > 0.99 |
| General malaise | 9 (16) | 4 (15) | 5 (18) | > 0.99 |
| Skin discoloration or induration | 8 (15) | 3 (11) | 5 (18) | 0.747 |
| Blistering | 8 (15) | 4 (15) | 4 (14) | > 0.99 |
| Hemorrhagic bullae | 6 (11) | 3 (11) | 3 (11) | > 0.99 |
| Altered mental status | 5 (9) | 3 (11) | 2 (7) | 0.965 |
| Time to surgical intervention < 24 h | 31 (56) | 16 (59) | 15 (54) | 0.671 |

Values are expressed as $n$ (%). *$p$ values are based on the Chi-square or Fisher's exact test.

monomicrobial infections were aerobic Gram-positive cocci ($n$ = 15, 35%), Gram-negative bacilli ($n$ = 27, 63%), and anaerobic Gram-negative bacilli ($n$ = 1, 2%). Oxacillin-sensitive *Staphylococcus aureus* ($n$ = 10, 19%) was the most commonly isolated Gram-positive cocci and *Vibrio* species were the most commonly isolated Gram-negative bacilli ($n$ = 14, 26%), followed by *Escherichia coli* ($n$ = 5, 9%), *Aeromonas* species ($n$ = 5, 9%), and *Pseudomonas aeruginosa* ($n$ = 5, 9%; Table 6). All patients with infection due to *Aeromonas* species died. However, there was no significant association between the organism and mortality (Table 7).

Significant predictors in univariate analysis [severity of LC, shock, band PMNs (>10%), INR (>1.5), serum creatinine (>2.0 mg/dL), serum albumin (<2.5 g/dL), and aPTT (>60 seconds)] were included in a stepwise multivariate analysis to identify the most important risk factors for mortality. The results revealed that only serum albumin <2.5 g/dL was significantly associated with mortality in patients with LC and NF (odds ratio = 18.52, 95% confidence interval = 1.04–333.33, $p$ = 0.047).

## 4. Discussion

NF is a life-threatening disease with a reported mortality rate ranging from 24% to 34%. Patients with liver cirrhosis usually have chronic edema in the lower limbs, which predisposes them to bacterial infection.[9] However, NF can also occur in cirrhotic patients without an obvious lesion on the body surface. Bacteremia can occur via the intestinal–portal route because LC weakens the barrier that protects the patient against passage of bacteria from the intestine to the systemic circulation. Bacteria in the bloodstream may subsequently seed in the edematous soft tissue of the lower limbs, thereby causing necrotizing fasciitis. The mortality rate among patients with LC ranges from 33% to 65%.[10–12] In this study, we found that patients with liver cirrhosis and necrotizing fasciitis had poor outcomes, with an overall mortality rate of 51%. This high mortality rate may be due to abnormal defensive mechanisms including impaired monocyte function, decreased phagocytic activity of the reticuloendothelial system, defective chemotaxis, and low serum levels of complements.[13]

The clinical characteristics of cirrhotic patients with NF have not been well documented and the risk factors for mortality not accurately understood.[10,12,14] Cheng et al[10] reviewed 17 patients with LC and NF and found that underlying diabetes mellitus and Child–Pugh grade C LC were significant predictors of poor outcomes. Liu et al[12] reported that hemorrhagic bullae and Child–Pugh Grade C were independent risk factors for mortality in a series of 118 episodes of soft tissue infection in cirrhotic patients. In our series, 21 patients (38%) had Grade C LC; however, it was not an independent predictor of mortality in cirrhotic patients with NF. Liu et al[12,14] also demonstrated that hemorrhagic bullae represented an ominous sign of development of NF in patients with LC. In their series, the common pathogens isolated from cirrhotic patients with hemorrhagic bullae were Gram-negative bacteria including *Aeromonas hydrophila*, *Vibrio vulnificus*, and *Klebsiella pneumoniae*. However, neither microbiologic pathogens

**Table 5** Effect of laboratory variables on mortality.

| | All patients ($n$ = 55) | Survivors ($n$ = 27) | Nonsurvivors ($n$ = 28) | $p$* |
|---|---|---|---|---|
| Hemoglobin <11 mg/dL | 27 (49) | 13 (48) | 14 (50) | 0.891 |
| White blood cell count > 15 × $10^9$/L | 9 (16) | 3 (11) | 6 (21) | 0.469 |
| Band PMNs > 10% | 20 (36) | 4 (15) | 16 (57) | <0.001 |
| Platelets < 100 × $10^9$/L | 37 (67) | 19 (70) | 18 (64) | 0.631 |
| INR > 1.5 | 24 (44) | 8 (30) | 16 (57) | 0.04 |
| aPTT > 60 s | 12 (22) | 1 (4) | 11 (39) | <0.001 |
| Creatinine > 2 (mg/dL) | 24 (44) | 5 (19) | 19 (68) | <0.001 |
| Albumin <2.5 (g/dL) | 38 (69) | 12 (44) | 26 (93) | <0.001 |

Values are expressed as $n$ (%).
*$p$ values are based on the Chi-square or Fisher's exact test.
aPTT = activated partial thromboplastin time; INR = international normalized ratio; PMN = polymorphonuclear neutrophil.

**Table 6** Microorganisms isolated from patients with liver cirrhosis and necrotizing fasciitis.[a]

| Microbiology | Positive wound culture, 53 |
|---|---|
| **Gram positive** | |
| Oxacillin-sensitive *Staphylococcus aureus* | 10 |
| *Viridans Streptococcus* | 4 |
| Oxacillin-resistant *Staphylococcus aureus* | 4 |
| *Streptococcus pyrogens* | 2 |
| *Enterococcus* | 2 |
| Group B *streptococcus* | 1 |
| **Gram negative** | |
| *Vibrio* spp. | 14 |
| *Escherichia coli* | 5 |
| *Aeromonas* spp. | 5 |
| *Pseudomonas aeruginosa* | 5 |
| *Klebsiella pneumoniae* | 4 |
| *Acinetobacter* spp. | 3 |
| *Enterobacter cloacae* | 2 |
| *Morganella* spp. | 1 |
| *Serratia* spp. | 1 |
| **Anaerobic bacteria** | |
| *Bacteroides* spp. | 2 |

CoNS = coagulase-negative *Staphylococcus*; ORSA = oxacillin-resistant *Staphylococcus aureus*.

[a] Wound cultures were collected from all patients; there were 53 positive wound cultures.

nor hemorrhagic bullae were independent risk factors for mortality in our series.

NF is essentially polymicrobial, deriving significant contributions from both Gram-negative and Gram-positive bacteria. In a recent study from southeast Taiwan, *Streptococcus pyogenes* was the most common single pathogen isolated in patients with NF and *Vibrio* species accounted for 1.8% (2/106) of infections.[2] However, in our previous report,[3] *Vibrio* species accounted for 10.8% (51/472) of infections. The Chi-Mei Medical Center is situated in southern Taiwan where agriculture and aquaculture are prevalent. People living in that region, therefore, are more likely to be exposed to fish-fin injury or dirty water, which can lead to such microbiological variations. Moreover, seven of 14 episodes caused by *Vibrio* species were associated with a history of contact with dirty water, fish-fin injury or consumption of seafood. It is worth mentioning that there were five patients with *Aeromonas* species infections in our study and all of those patients died. Nevertheless, results of multivariate analysis failed to reveal significant correlation between infection due to *Aeromonas* species and mortality. In addition, we also found that NF in the vast majority of cirrhotic patients was caused by Gram-negative bacilli, β-hemolytic streptococci, oxacillin-sensitive *S. aureus*, and oxacillin-resistant *S. aureus*. The results were similar to those reported by Lee et al,[11] who suggested that cefotaxime or levofloxacin should be considered as the initial antimicrobial agent for cirrhotic patients with NF.

Hypoalbuminemia (serum albumin $<2.5$ g/dL) was the only independent predictor of mortality in cirrhotic patients with NF in our study. Patients with advanced LC almost always have hypoalbuminemia, which is caused by decreased synthesis of albumin in hepatocytes as well as water and sodium retention, which dilutes the content of albumin in the extracellular space.[15] Delaney et al[16] found that the use of albumin-containing solutions for the resuscitation of patients with sepsis was associated with lower mortality as compared with other fluid resuscitation regimens. There are a number of possible mechanisms by which albumin could have beneficial effects in patients with sepsis. As many of the beneficial effects of albumin in resuscitation were noted in comparison with those of crystalloids, it is possible that the effects are due to the additional intravascular volume expansion that albumin provides, as compared with that of crystalloids, even with similar resuscitation targets. In addition to volume expansion effects, albumin has important physiologic roles as a transporter of biologically active molecules, as a drug binder in the maintenance of both colloid osmotic pressure and the permeability of the capillary membrane in the inhibition of platelet aggregation, and as a free-radical scavenging antioxidant.[17,18] Restoration of physiologic levels of serum albumin may allow these functions to continue and provide benefits to patients with sepsis; the antioxidant function in particular may be crucial in the

**Table 7** Effects of microorganisms on mortality.[a]

| | All patients ($n = 53$) | Survivors ($n = 25$) | Nonsurvivors ($n = 28$) | $p$* |
|---|---|---|---|---|
| Monomicrobial infection | 43 (81) | 19 (76) | 24 (86) | 0.488 |
| *Vibrio spp* | 14 (26) | 6 (24) | 8 (29) | 0.706 |
| *Oxacillin-sensitive Staphylococcus aureus* | 10 (19) | 7 (28) | 3 (11) | 0.162 |
| *Klebsiella pneumoniae* | 4 (8) | 2 (8) | 2 (7) | $>0.99$ |
| *Pseudomonas aeruginosa* | 5 (9) | 3 (12) | 2 (7) | 0.658 |
| *Streptococcus pyrogens* | 2 (4) | 0 (0) | 2 (7) | 0.492 |
| *Enterococcus* | 2 (4) | 2 (8) | 0 (0) | 0.218 |
| *Escherichia coli* | 5 (9) | 1 (4) | 4 (14) | 0.355 |
| *Aeromonas* spp. | 5 (9) | 0 (0) | 5 (18) | 0.053 |

Values are expressed as $n$ (%).

*$p$ values are based on the Chi-square or Fisher's exact test.

[a] Wound cultures were collected from all patients; there were 53 positive wound cultures in total, and there were 25 positive wound cultures in the survivor group.

pathophysiology of sepsis. Guevara et al[19] reported that, compared with standard antibiotic therapy alone, treatment with albumin together with antibiotics has beneficial effects on renal and circulatory function and showed a potential survival benefit in cirrhotic patients with bacterial infections other than spontaneous bacterial peritonitis. However, no studies have investigated the effects of albumin resuscitation in cirrhotic patients with NF. Therefore, further studies are needed to assess whether resuscitation with albumin-containing solutions lowers the mortality rate in such patients.

The major limitation of this study is the small number of patients. The results of multivariate analysis showed that there was a significant, albeit weak, association between hypoalbuminemia (albumin <2.5 g/dL) and mortality ($p = 0.047$, 95% confidence interval = 1.04—333.33). This weak association may be due to chance or to the small number of patients in the study. Further studies with more patients will help to assess whether hypoalbuminemia (albumin <2.5 g/dL) is associated with higher mortality rates in patients with LC and NF.

In conclusion, NF in the vast majority of cirrhotic patients was caused by Gram-negative bacilli, β-hemolytic streptococci, oxacillin-sensitive *S. aureus*, and oxacillin-resistant *S. aureus*. NF in patients with LC was significantly associated with a high mortality rate, and hypoalbuminemia (serum albumin <2.5 g/dL), with high mortality. Further studies are needed to assess whether resuscitation with albumin-containing solutions lowers the mortality rate in these patients.

## References


1. Wilson B. Necrotizing fasciitis. *Am Surg*. 1952;18:416—431.
2. Bair MJ, Chi H, Wang WS, Hsiao YC, Chiang RA, Chang KY. Necrotizing fasciitis in southeast Taiwan: clinical features, microbiology, and prognosis. *Int J Infect Dis*. 2009;13:255—260.
3. Huang KF, Hung MH, Lin YS, et al. Independent predictors of mortality for necrotizing fasciitis: a retrospective analysis in a single institution. *J Trauma*. 2011;71:467—473.
4. Thulstrup AM, Sørensen HT, Schønheyder HC, Møller JK, Tage-Jensen U. Population-based study of the risk and short-term prognosis for bacteremia in patients with liver cirrhosis. *Clin Infect Dis*. 2000;31:1357—1361.
5. Caly WR, Strauss E. A prospective study of bacterial infections in patients with cirrhosis. *J Hepatol*. 1993;18:353—358.
6. Cheng NC, Tsai JL, Kuo YS, Hsueh PR. Bacteremic necrotizing fasciitis caused by *Vibrio cholerae* serogroup O56 in a patient with liver cirrhosis. *J Formos Med Assoc*. 2004;103:935—938.
7. Ho PL, Tang WM, Yuen KY. *Klebsiella pneumoniae* necrotizing fasciitis associated with diabetes and liver cirrhosis. *Clin Infect Dis*. 2000;30:989—990.
8. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Brit J Surg*. 1973;60:646—649.
9. Anaya DA, McMahon K, Nathens AB, Sullivan SR, Foy H, Bulger E. Predictors of mortality and limb loss in necrotizing soft tissue infections. *Arch Surg*. 2005;140:151—157. discussion 158.
10. Cheng NC, Tai HC, Tang YB, Chang SC, Wang JT. Necrotising fasciitis: clinical features in patients with liver cirrhosis. *Br J Plast Surg*. 2005;58:702—707.
11. Lee CC, Chi CH, Lee NY, et al. Necrotizing fasciitis in patients with liver cirrhosis: predominance of monomicrobial Gram-negative bacillary infections. *Diagn Microbiol Infect Dis*. 2008;62:219—225.
12. Liu BM, Chung KJ, Chen CH, et al. Risk factors for the outcome of cirrhotic patients with soft tissue infections. *J Clin Gastroenterol*. 2008;42:312—316.
13. Foreman MG, Mannino DM, Moss M. Cirrhosis as a risk factor for sepsis and death: analysis of the National Hospital Discharge Survey. *Chest*. 2003;124:1016—1020.
14. Liu BM, Hsiao CT, Chung KJ, Kung CT, Hung SC, Liu PP. Hemorrhagic bullae represent an ominous sign for cirrhotic patients. *J Emerg Med*. 2008;34:277—281.
15. Henricksen JH, Siemssen O, Krintel JJ, Malchow-Møller A, Bendtsen F, Ring-Larsen H. Dynamics of albumin in plasma and ascitic fluid in patients with cirrhosis. *J Hepatol*. 2001;34:53—60.
16. Delaney AP, Dan A, McCaffrey J, Finfer S. The role of albumin as a resuscitation fluid for patients with sepsis: a systematic review and meta-analysis. *Crit Care Med*. 2011;39:386—391.
17. Lang Jr JD, Figueroa M, Chumley P, et al. Albumin and hydroxyethyl starch modulate oxidative inflammatory injury to vascular endothelium. *Anesthesiology*. 2004;100:51—58.
18. Quinlan GJ, Margarson MP, Mumby S, Mumby S, Evans TW, Gutteridge JM. Administration of albumin to patients with sepsis syndrome: a possible beneficial role in plasma thiol repletion. *Clin Sci (Lond)*. 1998;95:459—465.
19. Guevara M, Terra C, Nazar A, et al. Albumin for bacterial infections other than spontaneous bacterial peritonitis in cirrhosis. A randomized, controlled study. *J Hepatol*. 2012;57:759—765.