Lactate dehydrogenase as a prognostic marker of renal transplant recipients with severe community-acquired pneumonia: a 10-year retrospective study

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Background: Lactate dehydrogenase (LDH) is an easily accessible biological marker that has been associated with several pulmonary disorders. The aim of this study was to investigate the prognostic value of serum LDH in renal transplant recipients with severe community-acquired pneumonia (CAP).

Methods: A total of 77 renal transplant recipients with severe CAP admitted to the intensive care unit (ICU) were screened for eligibility in this retrospective study. Patient characteristics and laboratory tests, such as LDH on day 1 ($LDH_{day\ 1}$) and day 3 ($LDH_{day\ 3}$) were recorded. Cox regression models were used to assess the performance of LDH to predict 90-day mortality.

Results: Median LDH level was higher on day 1 in 90-day nonsurvivors (440 U/L, IQR, 362–1,055 U/L) than in survivors (334 U/L, IQR, 265–432 U/L; P<0.001); median LDH level on day 3 in nonsurvivors was 522.5 U/L (IQR, 457.5–1,058.5 U/L) and in survivors 290 U/L (IQR, 223–387.5 U/L; P<0.001). Analysis of LDH kinetics from day 1 to day 3 showed an increase in nonsurvivors and a decrease in survivors. Moreover, Multivariate Cox analysis showed that $LDH_{day\ 1}$ (increase per 100 U/L), $LDH_{day\ 3}$ (increase per 100 U/L) and LDH kinetics (increase per 10%) were independently associated with 90-day mortality.

Conclusions: Serum LDH levels and LDH kinetics early were independently associated with 90-day mortality in renal transplant recipients with severe CAP. In future, the prognostic role of LDH needs to be warranted.

Keywords: Community-acquired pneumonia (CAP); severe pneumonia; lactate dehydrogenase (LDH); renal transplantation; mortality

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Introduction

Community-acquired pneumonia (CAP) is a common and potentially serious entity that is associated with considerable morbidity and mortality, particularly in immunocompromised patients (1). Kidney transplant recipients, a vital subgroup of immunocompromised patients, may face an increased risk of community-acquired infection due to the long-term use of immunosuppressive therapy (2,3). Moreover, CAP is the most frequent cause of admission to ICU in kidney transplant recipients,

accounting for 50% to 60% of such cases (4-6). Severe CAP after kidney transplant is still associated with a high mortality rate, despite interdisciplinary approaches have been implemented in our center since 2009 (7-12). Although Scoring systems, such as the Pneumonia Severity Index (PSI) and CURB-65 score (confusion, blood urea nitrogen, respiratory rate, blood pressure, and age >65 years), and biomarkers, such as procalcitonin (PCT), are available to assess the severity and prognosis of CAP for immunocompetent patients (13-17).

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme present in all major organ systems (18). The extracellular existence of LDH is used to reflect cell damage or inflammation (19). Several studies have reported that elevated serum LDH levels were associated with several pulmonary disorders, such as CAP, pneumocystis jiroveci pneumonia (PJP), *Mycoplasma pneumoniae* pneumonia (20-26). However, the clinical value of LDH in renal transplant recipients with severe CAP remains unclear.

Therefore, the aim of this 10-year retrospective study was to assess the role of serum LDH levels early in ICU to predict outcome of renal transplant recipients with severe CAP.

Methods

Study population

Between January 1, 2009 and July 31, 2018, a total of 106 renal transplant recipients with dyspnea were admitted to the 10-bed mixed ICU of Zhongshan Hospital, Fudan University. CAP was defined as pneumonia acquired outside of a health care setting (27). Hospital-acquired pneumonia (HAP) was defined as pneumonia that occurred after 48 h or more in a healthcare setting (28). Severe pneumonia was defined according to the 2007 guidelines of the Infectious Diseases Society of America/American Thoracic Society (29). One of two major criteria (acute respiratory failure requiring intubation and mechanical ventilation and septic shock requiring vasopressor use) or at least three of nine minor criteria (respiratory rate ≥30 breaths/min; PaO_2/FiO_2 ratio ≤250 mmHg; multilobar infltrates; confusion; blood urea nitrogen level ≥20 mg/dL; white blood cell count <4,000 cells/mm^3; platelet count <100,000 cells/mm^3; core temperature <36 ℃; and hypotension requiring aggressive fluid resuscitation) were required for ICU admission. Any patient meeting the following criteria was excluded: cardiogenic pulmonary edema; complication of other site of infection, such as the urinary tract, abdomen, and intestinal tract; aspartate transaminase or alanine transaminase concentration of >500 U/L or bilirubin >34 μmol/L; do not intubate (DNI) order; readmission to ICU; and HAP.

ICU management

Treatment protocols for renal transplant recipients with severe pneumonia were based on the interdisciplinary approach as previously described (7). All patients received high-resolution computed tomography examinations before and during ICU stay. Oxygen therapy at ICU admission via a conventional face mask or noninvasive mechanical ventilation (NIV) or high-flow nasal cannula (HFNC) was administered at the discretion of the treating physicians. Patients who met the following criteria were considered for endotracheal intubation: unable to clear airway secretions; unable to protect the airway; unable to maintain a PaO_2/FiO_2 ratio >100 mmHg or PaO_2 <60 mmHg despite optimal oxygen management with NIV or HFNC; artery blood gas pH of <7.3 within 4–8 h; and hemodynamic instability.

On day 1 (at ICU admission), methylprednisolone (1–2 mg/kg every 12 h) was initiated followed by gradual discontinuation of all immunosuppressants. Once the methylprednisolone dose was reduced to 1.0 mg/kg body weight/day, low-dose calcineurin inhibitors were added (11). Antibiotic therapy was administrated at the discretion of the treating physicians. Usually, empirical antibiotic therapy included tigecycline, moxifloxacin, or meropenem, ganciclovir, and trimethoprim/sulfamethoxazole. Antifungal drugs were used for suspected or confirmed fungal infections.

Microbiological diagnostic approach

Diagnostic tests to identify the cause of severe pneumonia included invasive diagnostic procedures (fiberoptic bronchoscopy with bronchoalveolar lavage), noninvasive procedures (blood, urine, and sputum cultures, as well as serum antibodies against Epstein–Barr virus, cytomegalovirus, *Legionella*, and *Mycoplasma*, as determined by polymerase chain reaction analyses of blood, serum, and nasopharyngeal aspirates), or both according to the established protocol for each situation. Besides, the 1,3-β-D glucan test (G test), galactomannan antigen detection (GM test) and T cells spot test of tuberculosis infection test (T-SPOT) were performed. Tuberculin testing was

performed as an indirect diagnosis.

Data collection

The following information was collected: patient demographics, prior immunosuppressive regimens, clinical characteristics, including the Acute Physiology and Chronic Health Evaluation II (APACHE-II) score, PSI score, CURB-65 score, PaO_2/FiO_2 ratio, acute rejection history, vasopressor use within 24 h after ICU admission, renal replacement therapy, invasive mechanical ventilation (IMV), and microbiological identifications. Baseline laboratory testing of hemoglobin, platelet count, white blood count, creatinine, bilirubin, N-terminal pro-brain natriuretic peptide, troponin T, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyl transpeptidase (γ-GT), fibrinogen, D-dimer, PCT, LDH on day 1 and day 3, as well as clinical outcomes, including ICU mortality, 90-day mortality, length of ICU stay and hospital stay were also recorded. LDH change (LDHc) from day 1 to day 3 was calculated using the following formula: LDHc (%) = $(LDH_{day\ 3} - LDH_{day\ 1})/LDH_{day\ 1} \times 100\%$. 90-day mortality evaluation was performed via electronic medical system or telephone interview by a certified physician.

Statistical analysis

Patient characteristics were compared using the chi-square test or Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Receiver operating characteristic (ROC) curves were used to examine the performance of variables to predict mortality in the ICU. The area under the curve (AUC) and Youden's index to maximize the sum of the sensitivity and specificity were calculated from ROC curves. The optimal cut-off value was based on Youden's index. Survival curves for mortality in the ICU were plotted and compared across different LDH levels using the log rank test. We performed an analysis using Cox proportional hazards regression to evaluate prognostic values of LDH. Univariate models were fitted and those associated with the outcome with a probability (P) value of <0.1 were introduced into multivariable models (stepwise variable-selection method). To account for the possible influence of LDH on 90-day mortality, multivariable models were constructed. Correlations between variables and LDH level were analyzed through Spearman correlation tests. A P value of <0.05 was considered statistically significant. All statistical analyses were performed using the SPSS software package, version 13.0 (SPSS, Inc., Chicago, IL, USA).

Results

Patient characteristics

Between January 1, 2009 and July 31, 2018, a total of 106 renal transplant recipients with dyspnea were admitted to the ICU. Of those, 29 patients were excluded, including 10 with cardiogenic pulmonary edema at ICU admission, 11 with multiple sites of infection, 3 who were readmitted to the ICU, 3 with HAP, one with hepatic dysfunction, and 1 with a DNI order. Finally, 77 patients with severe CAP were included for analysis (*Figure 1*).

The baseline characteristics are shown in *Table 1*. The median APACHE II score and PaO_2/FiO_2 ratio were 12 points and 197 mmHg, respectively. As compared with survivors (*Table 1*), nonsurvivors had higher APACHE II scores {17.5 [14–26] *vs.* 11 [9–14], respectively, P<0.01} and lower PaO_2/FiO_2 ratios {127 [103–203] *vs.* 213 [150–274] mmHg, respectively, P<0.01}. The PSI and CURB-65 scores were comparable between 90-day survivors and nonsurvivors. The baseline immunosuppressive regimens included cyclosporine A (CsA), tacrolimus (TAC), mycophenolate mofetil (MMF), rapamycin (Rapa), and prednisone (Pred), which were used in different combinations; specifically, CsA + MMF + Pred in 32 patients, TAC + MMF + Pred in 39, and Rapa + MMF + Pred in 6. There was no difference in the use of the three immunosuppressive regimens between 90-day survivors and nonsurvivors (*Table 1*).

The laboratory tests at ICU admission are shown in *Table S1*. The median LDH was 360 U/L (IQR, 278–465 U/L) on day 1 and 334 U/L (IQR, 241–464.5 U/L) on day 3. Median LDH was higher on day 1 in 90-day nonsurvivors (440 U/L, IQR, 362–1,055 U/L) than in survivors (334 U/L, IQR, 265–432 U/L; P<0.001); median LDH on day 3 in nonsurvivors was 522.5 U/L (IQR, 457.5–1,058.5 U/L) and in survivors 290 U/L (IQR, 223–387.5 U/L; P<0.001). Analysis of LDH kinetics from day 1 to day 3 showed an increase in nonsurvivors (18.02%, IQR, 6.59–42.14%) and a decrease in survivors (–10.79%, IQR, –24.36–2.83%; P<0.001). The levels of γ-GT was higher in nonsurvivors than in survivors (all P<0.05, *Table S1*). Also, there were no significant differences in the median levels of hemoglobin, platelets, white blood cells, ALT, AST, ALP, serum creatinine, glomerular filtration rate, troponin T, N-terminal pro-

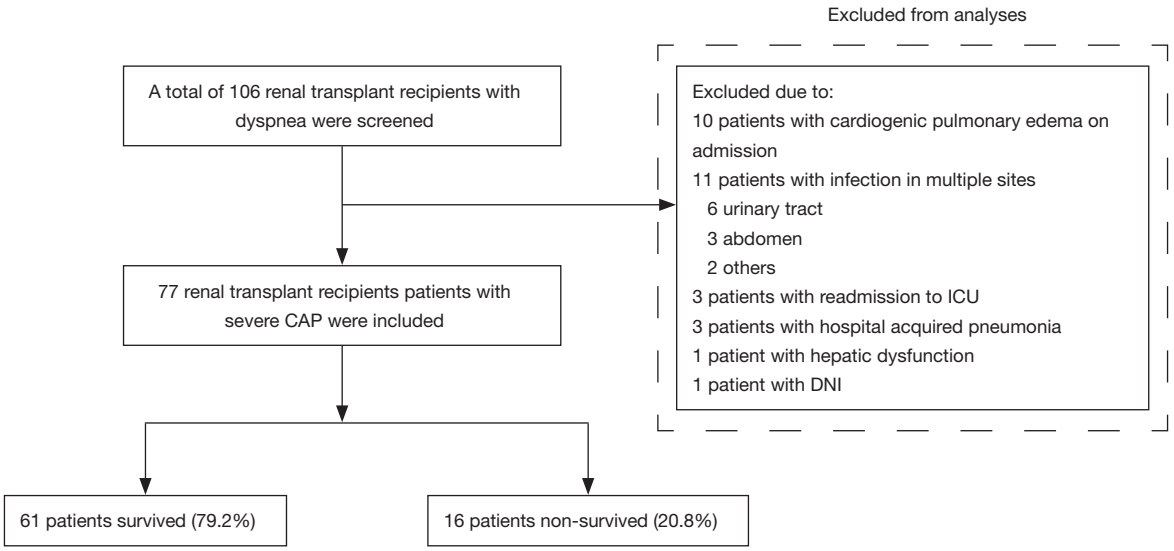

Figure 1 The enrollment of the study subjects. DNI, do not intubate; CAP, community-acquired pneumonia.

brain natriuretic peptide, fibrinogen, and D-dimer between survivors and nonsurvivors.

Microbiological findings

Forty-seven (61.0%) patients had definitive microbiological findings based on non-invasive and/or invasive diagnostic tests (*Table S2*). Bacterial infection (29.9%) was the leading cause of severe pneumonia in renal transplant recipients, followed by viral infection (23.4%) and fungal infection (23.4%). No pathogens were isolated in the remaining 30 (39.0%) patients. As compared with survivors (*Table S2*), nonsurvivors had a higher incidence of bacterial infection (75.0% *vs.* 18.0%, respectively, P<0.001) and lower proportion of cases with an undetermined etiology (12.5% *vs.* 46.0%, respectively, P=0.02). The incidences of viral and fungal infections were comparable between survivors and nonsurvivors.

Clinical course

Concerning the clinical course, IMV was required in 16 (20.8%) patients. The requirement for vasopressors within 24 h after ICU admission, renal replacement therapy, and IMV were more common in nonsurvivors than survivors (all P<0.001, *Table S2*). The ICU mortality was 18.2%. The hospital and 90-day mortality were 20.78%. The median length of ICU stay and hospital stay were longer in nonsurvivors compared to survivors {16.5 [5.5–30] *vs.* 6 [3.5–10.5] days, P=0.01 and 21 [13–29] *vs.* 33 [20–46], P=0.04, respectively}.

Value of indicators to predict 90-day mortality

ROC curves were constructed to evaluate the performance of indicators to predict 90-day mortality (*Figure 2*). The AUC, optimal cutoff value, sensitivity, and specificity of each indicator are shown in *Table 2*. The APACHE II score (AUC 0.84±0.06), $LDH_{day\ 1}$ (AUC 0.78±0.06), $LDH_{day\ 3}$ (AUC 0.93±0.03) and LDH kinetics (AUC 0.85±0.06) had a good power for prediction of 90-day mortality (all P <0.001). A LDH cutoff value of ≥375 U/L on day 1 had a sensitivity of 75% and a specificity of 63.3%. A LDH threshold of ≥453 U/L on day 3 had a sensitivity of 94% and a specificity of 87%. LDH increase ≥9.2% from day 1 to day 3 had a sensitivity of 75% and a specificity of 90%. PSI score had a poor power for prediction of 90-day mortality as suggested by the AUC of 0.65±0.08 (P=0.07), which was similar to that of the CURB-65 score (AUC 0.64±0.09, P=0.09).

Indicators for prediction of 90-day mortality

Survival curves for 90 day mortality are shown in *Figure 3*. Based on the ROC curves, the cut-off value of LDH levels on day 1 and day 3 were set at 375 and 453 U/L, respectively. Patients with higher LDH levels on day 1 (≥375 U/L) and day 3 (≥453 U/L) were at significantly higher risks of mortality (all P<0.01, log-rank test).

Table 1 Clinical characteristics of patients grouped by 90-day mortality

Characteristics	All patients (N=77)	90-day survival (n=61)	90-day mortality (n=16)	P value
Gender (male), n (%)	57 (74.0)	44 (72.1)	13 (81.2)	0.54
Age (years)	52 [40–59]	51 [38–59]	55 [49.25–61.5]	0.38
Comorbidities				
Diabetes mellitus, n (%)	9 (11.7)	5 (8.2)	4 (25.0)	0.08
Hypertension, n (%)	57 (74.0)	45 (73.8)	12 (75.0)	1.00
Immunosuppression regimens before admission				
CsA + MMF + Pred, n (%)	32 (41.6)	25 (41.0)	7 (43.8)	1.00
TAC + MMF + Pred, n (%)	39 (50.6)	31 (50.8)	8 (50.0)	1.00
Rapa + MMF + Pred, n (%)	6 (7.8)	5 (8.2)	1 (6.3)	1.00
Median time from transplantation to ICU admission, months	8 [3–54]	8 [3–54.5]	5.5 [2.25–45.5]	0.47
Median time from fever onset to hospital admission, days	6 [3–7]	6 [3–7]	5.5 [1.8–7.3]	0.55
Median time from fever onset to ICU admission, days	7 [4–11]	7 [4–11]	8.5 [4–15.3]	0.58
Acute rejection history, n (%)	13 (16.9)	9 (14.75)	4 (25.0)	0.45
APACHE II score at ICU admission	12 [9–16]	11 [9–14]	17.5 [14–26]	<0.01
PSI score at ICU admission	114 [99–134]	110 [98.5–128.5]	131 [102.75–155]	0.07
CURB-65 score at ICU admission	2 [2–3]	2 [2–2]	2.5 [2–3]	0.05
PaO_2/FiO_2 ratio (mmHg) at ICU admission	197 [131–264]	213 [150–274]	127 [103–203]	<0.01
LDH (U/L)				
$LDH_{day\ 1}$ (U/L)	360 [278–465]	334 [265–432]	440 [362–1,055]	<0.001
$LDH_{day\ 3}$ (U/L)	334 [241–464.5]	290 [223–387.5]	522.5 [457.5–1,058.5]	<0.001
LDHc (%)	–4.71 [–21.09–7.66]	–10.79 [–24.36–2.83]	18.02 [6.59–42.14]	<0.001
Outcome				
Median length of ICU stay, days	7 [4–13]	6 [3.5–10.5]	16.5 [5.5–30]	0.01
Median length of hospital stay, days	23 [14.5–31]	21 [13–29]	33 [20–46]	0.04
ICU mortality, n (%)	14 (18.2)	0 (0)	14 (87.5)	<0.01
Hospital mortality, n (%)	16 (20.8)	0 (0)	16 (100.0)	<0.01

Values are median [interquartile range (IQR)] for continuous variables and percentages for categorical variables. The baseline immunosuppressive regimens included: CsA, cyclosporine A; TAC, tacrolimus; MMF, mycophenolate mofetil; Rapa, rapamycin; Pred, prednisone; APACHE-II, Acute Physiology and Chronic Health Evaluation II; PSI, Pneumonia Severity Index; ALT, alanine aminotransferase; LDH_{day1}, LDH level at ICU admission; LDH_{day3}, LDH level on day 3; LDHc, LDH change from day 1 to day 3 [calculated using the following formula: LDHc (%) = $(LDH_{day3} - LDH_{day1})/LDH_{day1} \times 100\%$].

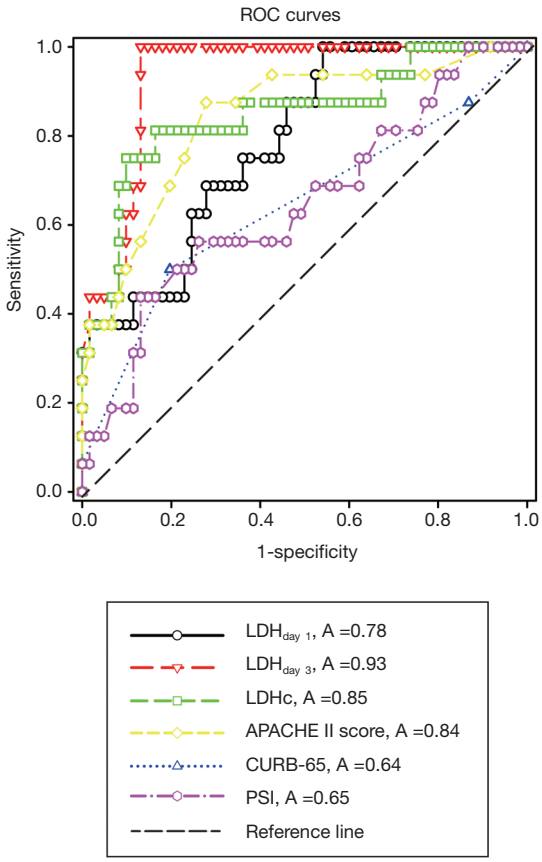

Figure 2 Receiver operating characteristic curves for APACHE II score, $LDH_{day\ 1}$, $LDH_{day\ 3}$, LDHc, PSI and CURB-65 score. APACHE-II, Acute Physiology and Chronic Health Evaluation II; LDH, lactate dehydrogenase; PSI, Pneumonia Severity Index; $LDH_{day\ 1}$, LDH level on day 1; $LDH_{day\ 3}$, LDH level on day 3; LDHc, LDH change from day 1 to day 3 [calculated using the following formula: LDHc (%) = ($LDH_{day\ 3}$ – $LDH_{day\ 1}$)/$LDH_{day\ 1}$ ×100%].

The predictive indicators of 90-day mortality were analyzed using Cox regression and the results are listed in *Table 3*. In univariable analysis, APACHE II score, $LDH_{day\ 1}$ (per 100 U/L), $LDH_{day\ 3}$ (per 100 U/L), LDH kinetics (increase per 10% from day 1 to day 3), white blood cell count (per 10^9/L), PaO_2/FiO_2 ratio (per 100 mmHg) and PCT were significantly associated with 90-day mortality .

To account for the possible influence of LDH on 90-day mortality, multivariable models were constructed (*Table 3*). As the APACHE II score have repeated items of PaO_2/FiO_2 ratio and white blood cell count, APACHE II score was entered into the multivariable analysis only. In multivariable analysis, $LDH_{day\ 1}$ (per 100 U/L), $LDH_{day\ 3}$ (per 100 U/L), LDH change (per 10%) and the APACHE II score were independently associated with 90-day mortality (*Table 3*).

Discussion

In the present study, we found that $LDH_{day\ 1}$ (increase per 100 U/L) and LDH_{day3} (increase per 100 U/L) were independently associated with 90-day mortality, and LDH_{day3} had more predictive power relatively. Additional, changes of LDH early also have predictive value, which might evaluate the effectiveness of early therapy. To the best of our knowledge, this is the first study to evaluate the risk factors of severe CAP in renal transplant recipients.

LDH is a cytoplasmic enzyme that is widely expressed in major organs, including the brain, kidney, liver, lung, lymph nodes, myocardium, skeletal muscle, and spleen, as well as various cell types, such as erythrocytes, leucocytes, and platelets (18,30). Due to the widespread distribution in the body, high LDH levels are abnormal in a majority of

Table 2 Performance of variables in predicting 90-day mortality

Variable	AUC ROC	95% CI	P	Cut-off	Sensitivity (%)	Specificity (%)
APACHE II score	0.84±0.06	0.73–0.95	<0.001	≥13.5	87.5	72.1
$LDH_{day\ 1}$	0.78±0.06	0.66–0.90	<0.001	≥375	75	63.3
$LDH_{day\ 3}$	0.93±0.03	0.88–0.98	<0.001	≥453	94	87
LDHc	0.85±0.06	0.73–0.97	<0.001	≥9.2	75	90
PSI score	0.65±0.08	0.49–0.81	0.07	≥109.5	68.8	48.3
CURB-65	0.64±0.09	0.47–0.81	0.09	≥2.5	50	80

AUC ROC, area under the receiver operating characteristic curve; CI, confidence interval; APACHE-II, Acute Physiology and Chronic Health Evaluation II; PSI, Pneumonia Severity Index; LDH_{day1}, LDH level at ICU admission; LDH_{day3}, LDH level on day 3; LDHc, LDH change from day 1 to day 3 [calculated using the following formula: LDHc (%) = (LDH_{day3} – LDH_{day1})/LDH_{day1} ×100%].

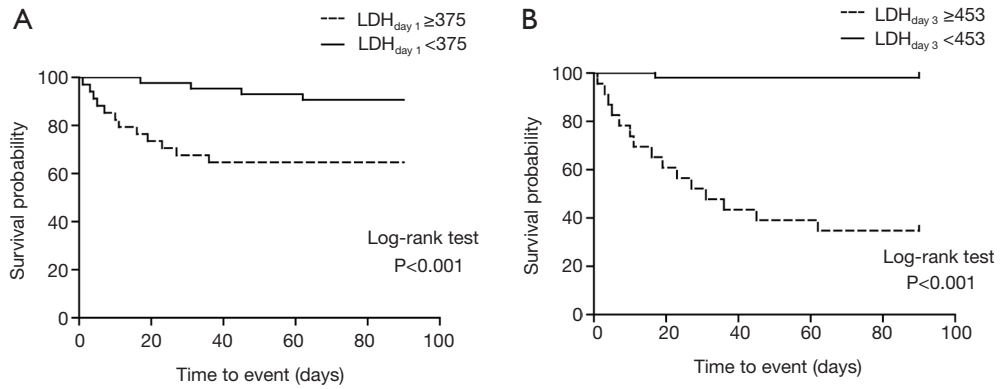

Figure 3 Kaplan-Meier curve for survival. Survival probability in patients with low and high LDH levels. A significant difference was observed with higher risk of survival events in patients with $LDH_{day\ 1}$ ≥375 U/L and $LDH_{day\ 3}$ ≥453 U/L. Log-rank P value shown on graphs. LDH, lactate dehydrogenase; $LDH_{day\ 1}$, LDH level on day 1; $LDH_{day\ 3}$, LDH level on day 3.

Table 3 Independent predictors of 90-day mortality by multivariate Cox regression analysis

Variable	Hazard ratio (95 % CI)	P value
Model 1		
APACHE II score at ICU admission (per point)	1.11 (1.03–1.19)	<0.001
$LDH_{day\ 1}$ (per 100 U/L)	1.43 (1.21–1.69)	<0.001
LDHc (per 10%)	1.31 (1.13–1.52)	<0.001
Model 2		
APACHE II score at ICU admission (per point)	1.11 (1.03–1.19)	<0.01
$LDH_{day\ 3}$ (per 100 U/L)	1.36 (1.17–1.57)	<0.001
LDHc (per 10%)	1.16 (1.00–1.34)	0.04

Model 1 adjusted for APACHE II score at ICU admission, $LDH_{day\ 1}$, LDHc, procalcitonin and platelet count at ICU admission. Model 2 adjusted for APACHE II score at ICU admission, $LDH_{day\ 3}$, LDHc, procalcitonin and platelet count at ICU admission (stepwise variable-selection method). As the APACHE II score have repeated items of PaO_2/FiO_2 ratio and white blood cell count, APACHE II score was entered into the multivariable analysis only. APACHE-II, Acute Physiology and Chronic Health Evaluation II; LDH_{day1}, LDH level at ICU admission (day 1); $LDH_{day\ 3}$, LDH level on day 3; LDHc, LDH change from day 1 to day 3 [calculated using the following formula: LDHc (%) = ($LDH_{day\ 3}$ – $LDH_{day\ 1}$)/$LDH_{day\ 1}$ ×100%].

diseases (18), as levels are normally low in peripheral blood. Leakage of the enzyme from damaged tissues or cells can significantly increase serum LDH levels. Therefore, serum LDH is a sensitive, but nonspecific marker (19).

Several literatures reported that elevated serum LDH levels have been associated with severe pulmonary disorders, including CAP, PJP, mycoplasma pneumoniae pneumonia, pandemic flu, and ARDS (20-26). Cell damage, inflammation, or both may be involved in pulmonary pathogenesis in these studies (19). Elevated serum LDH levels may mainly result from damage to lung parenchymal cells or local inflammatory cells, such as alveolar macrophages and polymorphonuclear neutrophils (19). Our study revealed that renal and cardiac tests were comparable between nonsurvivors and survivors. Hence, we inferred that elevated serum LDH levels were associated with pneumonia and not attributed to renal, cardiac and hepatic dysfunction. With comprehensive suppression of the innate and adaptive immune responses by immunosuppressive agents, it is relatively difficult for renal transplant recipients to mount an effective immune response (31). This may partially explain the higher mortality of these patients with severe CAP. However, the pathophysiological mechanism underlying the association between LDH level and poorer

outcomes of renal transplant recipients with severe CAP has not been fully elucidated.

Other clinical scores such as PSI and CURB-65 scores were not able to discriminate between nonsurvivors and survivors, which were the most frequently used scoring systems to predict CAP severity and related mortality (15,32). This discrepancy can be attributed to the following reasons. First, scoring systems available to assess CAP severity and prognosis are derived from immunocompetent patients, but may not be generalizable to immunocompromised patients. Second, the PSI score usually overestimates age and can underestimate severity, particularly in patients with no comorbidity (15,33).

This study had several limitations that should be addressed. First, this was a retrospective study. Second, the study was restricted by the small sample size, which might have impacted the statistic power. Third, LDH isoenzyme levels were not detected because of the restriction of local conditions, which may provide additional information for prognostic evaluation. Finally, as the cohort excluded patients with cardiogenic pulmonary edema, multiple infection sites, hepatic dysfunction, and HAP, the prognostic value of LDH in those patients should be applied with caution.

Conclusions

The results of this 10-year retrospective study showed that serum LDH levels early and LDH kinetics were independently associated with 90-day mortality in renal transplant recipients with severe CAP. The prognostic role of LDH needs to be confirmed by further studies.

Acknowledgments

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The protocol of this retrospective study was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (Shanghai, China) and conducted in accordance with the tenets of the Declaration of Helsinki. All laboratory indices were regularly measured for all patients in the ICU, thus the need for written informed consent was waived by the Ethics Review Board.

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Supplementary

Table S1 Laboratory tests at ICU admission

Variable	All patients (N=77)	90-day survival (n=61)	90-day mortality (n=16)	P value
Hemoglobin (g/L)	105 [91–122]	102 [91–120.5]	107 [92.5–127.3]	0.47
Platelet (10^9/L)	197 [148–230]	198 [158–246]	172.5 [101.5–220.8]	0.19
White blood cell count (10^9/L)	7 [5.0–10.3]	6.95 [4.3–10.1]	8.21 [5.3–13.6]	0.13
ALT (U/L)	21 [11–41.5]	21 [11–38.8]	31.5 [11.5–51]	0.47
AST (U/L)	25 [18.5–33]	25 [18–31.3]	28 [19–45]	0.33
ALP (U/L)	69 [54–99]	68.5 [54.5–89.5]	82 [51–118]	0.50
γ-GT (U/L)	35 [22–61.5]	31.5 [20–50.25]	67 [31–103]	0.03
Total bilirubin (μmol/L)	6.5 [4.9–9.17]	6.5 [4.9–9.2]	6.35 [4.7–11.3]	0.96
Troponin T (ng/mL)	0.024 [0.0125–0.083]	0.02 [0.01–0.08]	0.03 [0.02–0.12]	0.40
NT-proBNP (pg/mL)	600 [355.3–1,879]	593.35 [344.1–2,290.3]	600 [381–1,879]	0.99
Creatinine (μmol/L)	121 [93–177]	117 [92–171]	149 [101.5–312.3]	0.22
Procalcitonin (ng/mL)	0.16 [0.07–0.45]	0.16 [0.08–0.35]	0.11 [0.07–0.67]	0.78
GFR (CKD-EPI) (mL/min/1.73 m^2)	52.0 [36.7–76.7]	52 [37.6–76.9]	45.5 [16.9–74.8]	0.34
Fibrinogen(mg/dL)	436 [344–547]	436 [344–517]	441.5 [254.5–623.8]	0.80
D-dimer (mg/L)	1.72 [1.1–4.2]	1.6 [0.9–4.3]	1.9 [1.1–8.2]	0.51

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; γ-GT, γ-glutamyl transpeptidase; GFR, glomerular filtration rate.

Table S2 Clinical characteristics of patients during ICU stay

ICU management	All patients (N=77), n (%)	90-day survival (n=61), n (%)	90-day mortality (n=16), n (%)	P value
Vasopressors within 24 h after ICU admission	14 (18.2)	3 (4.9)	11 (68.8)	<0.01
Renal replacement therapy	15 (19.5)	6 (9.8)	9 (56.2)	<0.01
Need for IMV	16 (20.8)	2 (3.3)	14 (87.5)	<0.01
Microbiological identifications				
Bacterial infection	23 (29.9)	11 (18.0)	12 (75.0)	<0.01
Viral infection	18 (23.4)	12 (19.7)	6 (37.5)	0.18
Fungal infection	18 (23.4)	14 (23.0)	4 (25.0)	1.00
Pneumocystis jirovecii	8 (10.4)	8 (13.1)	0 (0)	0.19
Non-Pneumocystis jirovecii	10 (13.0)	6 (9.8)	4 (25.0)	0.20
Mycobacterium species	1 (1.3)	1 (1.6)	0 (0)	1.00
Mycoplasma	7 (9.1)	6 (9.8)	1 (6.2)	1.00
Undetermined	30 (39.0)	28 (46.0)	2 (12.5)	0.02

IMV, invasive mechanical ventilation.