

Acute Pancreatitis Associated with Hemorrhagic Fever with Renal Syndrome: A Cohort Study of 346 Patients

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Abstract

Background: Acute pancreatitis is one of the rare complications of hemorrhagic fever with renal syndrome (HFRS), usually ending with high mortality rate and severe prognosis. In this study, we retrospectively analyzed to explore the risk factors, clinical characteristics, and outcomes in totally 346 patients with HFRS.

Methods: We retrospectively reviewed the 358 cases diagnosed with HFRS from January 2013 to July 2020, including 29 cases complicated with acute pancreatitis (AP). Clinical information and laboratory parameters were obtained by Hospital Information System. The characteristics and clinic outcomes between the HFRS group and HFRS-AP group were compared by multivariate analysis and a nested case-control study, respectively.

Results: 346 eligible patients diagnosed with HFRS, of which 29 (8.38%) developed acute pancreatitis. While 19 (65.5%) were male, 10 (34.5%) were female. The mean age was 44.38 years. For life style analysis, 11 (37.9%) of 29 exhibited a habit of smoking, and 9 (31.0%) exhibited drinking. The 90-day mortality was 7 (24.14%) for the HFRS+AP patients and 7 (2.21%) for the HFRS patients ($p < 0.001$). Multivariate analysis indicated that HFRS patients, who confirmed AP, were associated with increased mortality (aOR:17.60; 95% CI, 4.3–73.3) and other poor prognoses; the same trend was shown in propensity matched data. Liver function and inflammatory parameters (except procalcitonin) were expressed much worse in AP patients ($p < 0.05$, respectively). Serum calcium shown a negative correlated with AP patients ($p < 0.05$).

Conclusions: Our study indicates that patients with HFRS-AP are significantly associated with higher mortality and poor prognoses, it should be alert and complete necessary test for properly diagnosis on admission. In future, cohort study and randomized control trail are highly required for the best treatment of HFRS-AP.

Introduction

Hemorrhagic fever with renal syndrome (HFRS) is an acute infectious disease caused by Hantavirus mainly through inhalation of aerosols or dust particles contaminated by virus-containing rodent excreta [1]. Despite the vaccine were wildly used, HFRS remains endemic in Asia and Europe, while increased incidence have been reported in China [2][3], and selected areas of Europe, such as Germany [4].

Clinical characteristics of HFRS include hemorrhagic manifestations, renal failure, or even multiple organ dysfunction [5] Moreover, due to the lack of definitive therapy, treatment of HFRS remains supportive [6], with a mortality rate about 12% [7].

Acute pancreatitis (AP) is a rare but life-threatening complication of Hantavirus infection, with significant morbidity and mortality [8]. However, early detection of AP remains challenging, due to the high prevalence of abdominal pain (up to 64.6%) in HFRS patients even without AP [9].

Unfortunately, there have been very few reports of AP in cases of HFERS so far. As a result, we performed this retrospective cohort study to investigate the risk factors, clinical manifestations, laboratory abnormalities, and clinical outcomes in an endemic area of HFERS in China [10][11][12].

Methods

Study Population

We retrospectively reviewed the medical records of all adult patients with confirmed HFERS who were admitted to the First Affiliated Hospital of Xi'an Jiaotong University from January 2013 to July 2020. The diagnosis was based on compatible clinical manifestation and laboratory detection of serum IgG antibodies using indirect immunofluorescent antibody test or serum IgM antibodies by enzyme-linked immunosorbent assay (ELISA) method. This study was approved by the institutional review board. Informed consent was waived due to the retrospective nature of the study.

Study Design

The first part of this study was a retrospective cohort study that included all patients with confirmed HFERS. The outcome of patients with acute pancreatitis (case subjects) was compared with that of patients without acute pancreatitis (control subjects). The second part of the study was a matched (1:1) case-control study. For the purpose of this study, the patients with acute pancreatitis are designated as "case subjects", and those without acute pancreatitis as "control subjects". A schematic flow chart is shown in Fig. 1.

Definitions

Acute pancreatitis (AP) was diagnosed and graded according to the Atlanta criteria [13]. Shock was defined as hypotension requiring administration of vasopressors to maintain mean arterial pressure (MAP) > 65 mmHg [14]. Multidrug resistant organisms (MDROs) were microorganisms that were resistant to one or more therapeutic classes of antimicrobial agents [15]. Cardiovascular diseases included coronary heart disease, hypertension, and valvular heart disease, chronic liver diseases included chronic hepatitis and cirrhosis, whereas chronic respiratory disease referred to chronic obstructive pulmonary disease, bronchitis, and interstitial lung disease.

Data Collection

Data collected included: (1) demographics (sex, age, and living habits); (2) comorbidities, such as biliary tract disease (cholecystitis, cholangitis, gallstones), diabetes, respiratory disease, tumor; (3) the course of HFERS: date of onset, symptoms at presentation, date of hospital admission, and complications (such as shock and infection with MDROs); (4) laboratory findings at hospital admission: complete blood count, blood chemistry, and inflammatory biomarkers (C-reactive protein [CRP], procalcitonin [PCT]), (5) treatment: intensive care unit (ICU) admission, mechanical ventilation, renal replacement therapy (RRT); and (6) outcome measures: 90-day all-cause mortality rate, and hospital length of stay (LOS).

Statistical Analysis

Results were analyzed with SPSS version 22.0K for Windows (SPSS Inc, Chicago, IL, USA) and STATA SE 14 (StataCorp LP, College Station, TX, USA). Categorical variables were examined by Fisher exact test or chi-square test, as appropriate, while continuous variables were compared by student t test or Mann-Whitney U test. All tests of significance were two-tailed and a P value of 0.05 was considered significant.

In order to account for potential confounding factors in this observational study, we developed a propensity score, using multivariate logistic regression analysis without regards to outcomes[16][17], to adjust for the differences in baseline characteristics between HFERS patients with and without AP. All prespecified covariates, as outlined above, were included in the final prediction model for AP among HFERS patients, by means of stepwise backward elimination with p value < 0.1. Model discrimination and calibration were assessment by *c*-statistics and Hosmer-Lemeshow statistics.

The effect of AP on 90-day mortality, as well as other clinical outcomes (i.e. ICU admission, RRT, mechanical ventilation, MDRO infection), was analyzed by stepwise backward logistic regression model by including any covariate with p value < 0.10 in univariate analysis. Moreover, individual propensity score was also included in the model to calculate the adjusted odds ratios (aOR) and 95% confidence intervals (CIs). In addition, we performed a nested case-control study (1:1 match) by matching case and control subjects using calipers of width equal to 0.2 of the standard deviation of the logit of the propensity score [18][19]. A nearest-neighbor matching algorithm was employed to form pairs of case and control subjects, once a match was made, previous matches were not reconsidered before making the next match. Survival curves for case and control subjects were analyzed by the Kaplan-Meier method and compared by long-rank test.

Results

Patient Enrolment and Clinical Characteristics

During the study period, 358 patients with the diagnosis of HFERS were admitted to the First Affiliated Hospital of Xi'an Jiaotong University. After exclusion of 12 patients due to withholding or withdrawal of life-sustaining therapies or accidental death, 346 patients (mean age 46.1, 255 men [73.7%]) were included in the final analysis (Fig. 1).

Among all these patients, some had comorbidities, such as cardiovascular disease (n = 45, 13.0%), diabetes (n = 25, 7.2%), chronic liver disease (n = 24, 6.9%), biliary tract disease (n = 11, 3.2%), and others. The most common presenting signs and symptoms included fever (n = 302, 87.3%), back/flank pain (n = 213, 61.6%), gastrointestinal symptoms (n = 118, 34.1%), and shock (n = 33, 9.5%). Of 118 patients with presenting gastrointestinal symptoms, 45 had abdominal pain, 13 had nausea/vomiting, 48 had diarrhea, and 12 had abdominal distention. A total of 25 patients (7.2%) were admitted to ICU, and 14 patients (4.0%) died at 90 days.

Patients with Acute Pancreatitis and Development of Propensity Score

A total of 29 patients (8.4%) developed AP on admission or during hospitalization, who were admitted to the hospital earlier than those without AP. Compared with HFERS patients without AP, patients with AP were more likely to be smokers and alcoholics (Table 1). There was no significant difference between patients with and without AP with regards to common risk factors (biliary tract disease, diabetes and other underlying diseases) and presenting signs/symptoms (fever, back/flank pain, and shock) other than gastrointestinal symptoms ($p < 0.001$) (Table 1).

Table 1

Baseline characteristics and clinical outcome of hemorrhagic fever renal syndrome patients with and without acute pancreatitis.

	Case Subjects (n = 29)	Control Subjects (n = 317)	P value
Age, yr (mean \pm SD)	44.4 \pm 16.4	46.2 \pm 17.3	0.63
Male sex	19 (65.5%)	236 (74.4%)	0.32
Smoking	11 (37.9%)	132 (41.6%)	0.02
Alcohol misuse	9 (31.0%)	40 (12.6%)	0.03
Comorbidities			
No comorbidities	14 (48.3%)	185 (58.4%)	0.33
Cardiovascular disease	6 (20.7%)	39 (12.3%)	0.24
Diabetes	2 (6.9%)	23 (7.3%)	> 0.99
Chronic liver disease	2 (6.9%)	22 (6.9%)	> 0.99
Biliary tract disease	3 (10.3%)	8 (2.5%)	0.06
Chronic respiratory disease	2 (6.9%)	9 (2.8%)	0.23
Pregnancy	1 (3.5%)	4 (1.3%)	0.36
Chronic renal disease	0 (0)	4 (1.3%)	> 0.99
Solid tumor	0 (0)	2 (0.6%)	> 0.99
Others	2 (6.9%)	37 (11.7%)	0.76
Days from symptom onset to hospitalization, d (mean \pm SD)	4.6 \pm 2.6	6.4 \pm 5.4	0.02
Presenting symptoms			
Fever	24 (82.8%)	278 (87.7%)	0.39
Back/Flank pain	14 (48.3%)	199 (62.8%)	0.16
Gastrointestinal symptoms	20 (69.0%)	98 (30.9%)	< 0.01
Nausea/vomiting	2 (6.9%)	11(3.5%)	0.30
Abdominal pain	8 (27.6%)	37 (11.7%)	0.04

Definition of abbreviations: ICU, intensive care unit; RRT, renal replacement therapy.

Data are presented as the number (percentage) of patients unless indicated otherwise.

	Case Subjects (n = 29)	Control Subjects (n = 317)	P value
Diarrhea	7 (24.1%)	41 (12.9%)	0.09
Abdominal distention	3 (10.3%)	9 (2.8%)	0.06
Shock	5 (17.2%)	28 (8.8%)	0.18
Treatment			
Antibiotic combination therapy (mean ± SD)	1.7 ± 1.2	0.7 ± 0.8	0.01
ICU admission	13 (44.8%)	12 (3.8%)	< 0.01
ICU-free days at day 28, d (mean ± SD)	19.1 ± 10.2	27.1 ± 4.8	< 0.01
RRT	17 (58.6%)	69 (21.8%)	< 0.01
RRT-free days at day 28, d (mean ± SD)	18.6 ± 11.4	25.2 ± 6.5	< 0.01
Mechanical ventilation	9 (31.0%)	8 (2.5%)	< 0.01
Ventilator-free days at day 28, d (mean ± SD)	21.3 ± 11.5	27.4 ± 4.1	< 0.01
Clinical outcome			
90-day mortality	7 (24.1%)	7 (2.2%)	< 0.01
Hospital-free days at day 28, d (mean ± SD)	8.6 ± 8.4	16.4 ± 6.6	0.005
Definition of abbreviations: ICU, intensive care unit; RRT, renal replacement therapy.			
Data are presented as the number (percentage) of patients unless indicated otherwise.			

On hospital admission, compared with patients without AP, patients with AP were characterized by more pronounced inflammation (as suggested by higher white cell count, higher CRP), lower platelet count, hypocalcemia, and abnormal liver functions (as suggested by higher liver enzymes, higher bilirubin, and lower albumin) (Table 2). In addition, patients in both groups suffered from mild to moderate renal dysfunction, as indicated by elevated serum creatinine and BUN levels. Interestingly, there was no significant difference with regard to serum lipase and serum/urine amylase levels between the two groups.

Table 2
Laboratory results on hospital admission in hemorrhagic fever renal syndrome patients with and without acute pancreatitis.

	Case Subjects (n = 29)	Control Subjects (n = 317)	P value
WBC (x 10 ⁹ /L)	20.0 ± 15.2	11.9 ± 9.1	0.01
Platelet (x 10 ⁹ /L)	55.5 ± 84.0	110.3 ± 98.1	0.01
Neutrophil (%)	76.9 ± 27.2	63.9 ± 19.2	0.01
C-reactive protein (mg/L)	45.8 ± 31.4	30.9 ± 19.5	0.02
Procalcitonin (ng/ml)	12.9 ± 37.0	4.8 ± 11.8	0.20
Albumin (g/L)	29.5 ± 5.6	34.8 ± 7.0	0.01
Total bilirubin (µmol/L)	15.6 ± 6.9	11.2 ± 5.3	0.01
AST (U/L)	194.8 ± 261.6	67.2 ± 100.8	0.01
ALT (U/L)	83.0 ± 84.6	42.9 ± 24.5	0.02
ALP (U/L)	78.67 ± 53.9	99.7 ± 32.8	0.75
LDH (U/L)	1056 ± 1150	547.9 ± 280.8	0.04
Triglyceride (mmol/L)	3.21 ± 1.91	9.89 ± 75.2	0.93
Low density lipoprotein (mmol/L)	1.44 ± 1.05	1.8 ± 0.6	0.29
High-density lipoprotein (mmol/L)	0.6 ± 0.2	0.9 ± 0.8	0.14
Serum creatinine (µmol/L)	292.2 ± 260.6	217.5 ± 205.8	0.14
BUN (mmol/L)	15.1 ± 10.7	11.7 ± 9.0	0.12
Serum calcium (mmol/L)	1.8 ± 0.2	2.0 ± 0.2	0.01
Blood amylase (U/L)	257.9 ± 232.4	170.7 ± 97.8	0.39
Urine amylase (U/L)	200.2 ± 194.1	133 ± 26.1	0.65
Serum lipase (U/L)	1261.0 ± 1068.2	988.2 ± 899.1	0.39
Definition of abbreviations: ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; LDH, lactate dehydrogenase; WBC = white blood cell count.			
Data are presented as the mean ± SD.			

Based on above data, we developed a propensity score using a multivariate logistic regression model with an area under the receiver operating characteristics curve of 0.71 (95%CI 0.62 to 0.81), indicating

good discrimination of HFRS patients developing AP (Fig. 2).

Acute Pancreatitis as Risk Factor for Clinical Outcome

Compared with patients without AP, patients with AP were more severe, as indicated by more antibiotic combination therapy, more life-sustaining therapies (i.e. mechanical ventilation, RRT), more ICU admissions (44.8% vs. 3.8%, OR 20.7, 95%CI 8.4 to 53.5, $p < 0.001$), and longer hospital and ICU LOS (length of stay), as well as higher 90-day mortality rate (24.1% vs. 2.2%, OR 14.1, 95%CI 4.8 to 40.4, $p < 0.001$) (Table 1 and Table 3).

Table 3

Analysis of acute pancreatitis associated with 90-day mortality rate and supportive treatment in 346 patients with hemorrhagic fever renal syndrome

	Crude		Adjusted ^{&}		Propensity-matched [#]	
	OR (95% CI)	<i>P</i> Value	OR (95% CI)	<i>P</i> Value	OR (95% CI)	<i>P</i> Value
90-day mortality	14.1 (4.8–40.4)	< 0.001	17.6 (4.3–73.3)	< 0.001	8.9 (1.3-103.4)	0.045
ICU admissions	20.7 (8.4–53.5)	< 0.001	22.8 (7.8–66.4)	< 0.001	22.8 (3.3-249.6)	0.0004
Treated with RRT	5.1 (2.3–11.3)	< 0.001	4.3 (1.9–9.6)	< 0.001	3.2 (1.1–8.7)	0.06
Treated with mechanical ventilation	17.4 (6.1–52.4)	< 0.001	32.5 (7.9-134.4)	< 0.001	12.6 (1.64–142.4)	0.01
MDRO	7.8 (1.3–38.8)	0.06	5.02 (0.5–46.9)	0.16	2.07 (0.2–31.0)	> 0.999

Definition of abbreviations: CI = Confidence Interval; OR = Odds Ratio; ICU = Intensive Care Unit; RRT = Renal Replacement Therapy; MDRO = Multiple Drug Resistant Organism.

[&]Adjusted for variables (age, gender, life style, underlying diseases and onset of symptoms prior to admission to hospital) associated with 90-day mortality, treated in ICU, treated with CRRT, treated with mechanical ventilation, infected with MDRO, and the propensity score of each patient's likelihood of being diagnosed with acute pancreatitis.

[#]Of 346 patients, 29 pairs were matched.

In multivariate regression analysis adjusted for potential confounders with propensity score, AP was associated with increased 90-day mortality rate (adjusted odds ratio [aOR], 17.6; 95% confidence interval [CI], 4.3 to 73.3, $p < 0.001$). In addition, AP was an independent risk factor of ICU admission (aOR, 22.8; 95%[CI], 7.8 to 66.4, $p < 0.001$), mechanical ventilation (aOR, 32.5; 95% CI, 7.9 to 134.4, $p < 0.001$), and RRT (aOR, 4.3; 95% CI, 1.9 to 9.6, $p < 0.001$) (Table 3).

Matched Case–Control Study

In propensity score-matched case control study, 29 pairs of HFERS patients with and without AP were successfully matched. Case subjects were more likely to receive mechanical ventilation (OR, 12.6; 95% CI, 1.64 to 142.4, $p = 0.01$), ICU admission (OR, 22.8; 95% CI, 3.3 to 249.6, $p < 0.01$), but not RRT (OR, 3.2; 95% CI, 1.1 to 8.7, $p = 0.06$). Compared with control subjects, case subjects had a significantly higher 90-day mortality rate (24.1% vs. 3.5%, OR 8.9, 95% CI 1.3 to 103.4, $p = 0.045$) (Table 3 and Table 4), and significantly shorter duration of therapy free-days to 28 day such as RRT and mechanical ventilation free days ($p < 0.05$, respectively). Figure 3 shows the survival curves of this matched case–control study.

Table 4

Comparison of baseline characteristics and outcomes between HFERS-AP group and HFERS group in the propensity-score matched sample.

	Case Subjects (n = 29)	Control Subjects (n = 29)	Standardized difference
Propensity score (mean \pm SD)	0.1 \pm 0.1	0.1 \pm 0.08	0.01
Age, yr (mean \pm SD)	44.4 \pm 16.4	45.3 \pm 18.1	0.047
Male sex	19(65.5%)	18 (62.1%)	0.07
Smoking	11(37.9%)	8 (27.6%)	0.22
Alcohol misuse	9 (31.0%)	7 (24.1%)	0.15
Comorbidities			
No comorbidities	14 (48.3%)	15 (51.7%)	0.07
Cardiovascular disease	6 (20.7%)	5 (17.2%)	0.09
Diabetes	2 (6.9%)	1 (3.4%)	0.16
Chronic liver disease	2 (6.9%)	5 (17.2%)	0.32
Biliary tract disease	3 (10.3%)	3 (10.3%)	0.01
Chronic respiratory disease	2 (6.9%)	1 (3.4%)	0.16
Pregnancy	1 (3.4%)	0 (0%)	0.27
Chronic renal disease	0 (0%)	1 (3.4%)	0.27
Solid tumor	0 (0%)	0 (0%)	0.00
Others	2 (6.9%)	2 (6.9%)	0.00
Days from symptom onset to hospitalization, d (mean \pm SD)	4.6 \pm 2.6	4.5 \pm 2.1	0.06
Treatment			
Antibiotic combination therapy (mean \pm SD)	1.7 \pm 1.2	0.9 \pm 0.8	0.78
ICU admission	13 (44.8%)	1 (3.5%)	1.10
ICU-free days at day 28, d (mean \pm SD)	19.1 \pm 10.2	27.0 \pm 5.2	0.97
RRT	17 (58.6%)	9 (31.0%)	0.58
Definition of abbreviations: CI = Confidence Interval; OR = Odds Ratio; ICU = Intensive Care Unit; CRRT = Continuous Renal Replacement Therapy.			
Data are presented as the number (percentage) of patients unless indicated otherwise.			

	Case Subjects (n = 29)	Control Subjects (n = 29)	Standardized difference
RRT-free days at day 28, d (mean ± SD)	18.6 ± 11.4	23.8 ± 8.4	0.52
Mechanical ventilation	9 (31.0%)	1 (3.5%)	0.78
Ventilator-free days at day 28, d (mean ± SD)	21.3 ± 11.5	27.0 ± 5.2	0.64
Clinical outcome			
90-day mortality	7 (24.1%)	1 (3.5%)	0.63
Hospital-free days at day 28, d (mean ± SD)	8.6 ± 8.4	15.3 ± 7.2	0.86
Definition of abbreviations: CI = Confidence Interval; OR = Odds Ratio; ICU = Intensive Care Unit; CRRT = Continuous Renal Replacement Therapy.			
Data are presented as the number (percentage) of patients unless indicated otherwise.			

Discussion

The major findings of our study

Diverse clinical manifestations had been reported in HFRS patients, ranging from mild and acute influenza-like illness to more severe shock syndrome. Apart from acute renal insufficiency, up to one-third of HFRS patients exhibited extrarenal organ involvement, with pancreatobiliary diseases as the most common manifestation, including acalculous cholecystitis, pancreatitis, and cholangitis [9]. In 1950s, Hullinghorst and Steer reported pathological evidence of pancreatitis in one-third of HFRS autopsies during the Korean conflict [20]. The reported prevalence of AP among HFRS patients was highly variable in observational studies, with a pooled prevalence of 6.8% (36/529) [9][21][22][23][24][25]. We found that 8.4% of HFRS patients in our cohort developed AP. The observed difference in prevalence of AP among HFRS patients might be related, at least in part, to the causative viruses [9], geographic region [24], male-to-female ratio [8], prevalence of risk factors (such as alcohol misuse and history of gallstones), and time course during disease progression. For example, the highest prevalence of AP was reported by Bui-Mansfield and colleagues in a group of 13 male patients with HFRS [22], whereas the lowest prevalence of AP was reported by Zhu and coworkers in 218 HFRS patients (150 males and 68 females) [23].

Another major finding of our study was that AP was an independent risk factor for 90-day mortality in HFRS patients, which had never been studied in the above-mentioned observational studies, possibly due to the limited number of AP cases (3 to 12) in the individual study [8][9][21][22][23][24][25]. However, pooled results from these studies suggested similar mortality rates [8.3% (3/36) in HFRS patients with AP vs 4.9% (24/493) in HFRS patients without AP, $p = 0.3618$]. In comparison, the 29 cases in our cohort represented the largest number of AP cases among HFRS patients ever reported, which allowed us to investigate the impact of AP on mortality in univariate and multivariate analyses. The significantly higher

mortality rate in HFERS patients with AP (24.1% vs. 2.2%) could be explained by the severity of acute illness, as demonstrated by more pronounced inflammation (higher white cell count and CRP levels), liver dysfunction, more life-sustaining therapies (including mechanical ventilation and RRT), and more ICU admissions (44.8% vs. 3.8%).

It is a common belief that early recognition of patients with AP might be very important to improve clinical outcome of this potentially life-threatening condition. However, early diagnosis of AP among HFERS patients might be difficult, as both diseases shared some common clinical signs/symptoms, such as nausea/vomiting and abdominal pain. For example, abdominal pain was a presenting symptom in 30–90% of HFERS patients, which might explain the observed high misdiagnosis rate (up to 90%) [8]. As a result, HFERS patients with abdominal pain should be subject to further laboratory (i.e. pancreatic and/or liver enzymes) and imaging (i.e. abdominal CT scan or ultrasonography) investigations[9][24], in order to determine the presence and severity of pancreatobiliary complications.

The major strength of our study was the robustness of the study result (i.e. AP as an independent risk factor for mortality), which was supported by univariate analysis, multivariate regression analysis adjusted for PS, and PS-matched case-control analysis. Our study was also subject to limitations. First, this was a retrospective single-center study, the result of which might not be generalized to other settings and required further validation by prospective multicenter studies. Nonetheless, the number of AP cases as well as HFERS patients in our cohort was significantly higher than that in previous studies. Second, the prevalence of AP might be underestimated, because laboratory (serum amylase or lipase) and abdominal imaging investigations were only performed in selected but not all HFERS patients.

In conclusion, our study indicated that AP was independently associated with higher mortality in HFERS patients. While considering the difficulty of early recognition of AP among HFERS patients with similar signs and/or symptoms, further laboratory and imaging studies might help identify these patients at risk of poor clinical prognosis.

Declarations

Conflict of Interest

All the authors have fulfilled all conditions required for authorship and have approved the submission. None of the authors has any conflicts of interest to disclose.

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Ethical Approval

Institutional review board approval was obtained for this project.

We affirm that the content of this manuscript is not under consideration for publication elsewhere nor has the information been previously published.

All the authors have fulfilled all conditions required for authorship and have approved the submission.

Institutional review board approval was obtained for this project.

Authors' contributions

Qinyue Guo and Bin Du had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Qinyue Guo and Bin Du. Acquisition, analysis, or interpretation of data: Jing Xu and Qindong Shi. Drafting of the manuscript: Qinyue Guo. Critical revision of the manuscript for important intellectual content: Bin Du. Statistical analysis: Qinyue Guo, Bin Du. Supervision: Bin Du.

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Figures

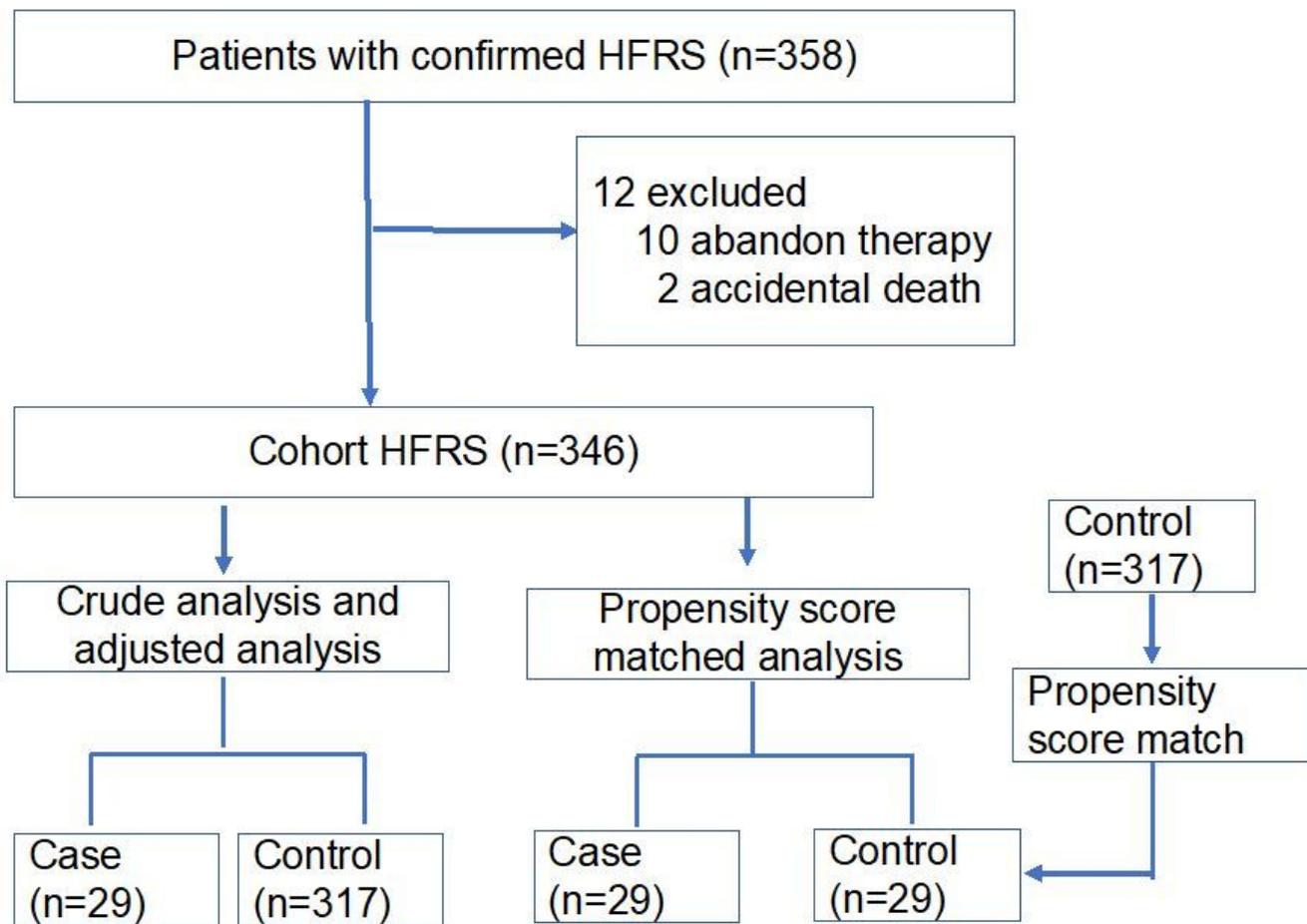


Figure 1

Schematic flow chart for a cohort study and matched case-control study.

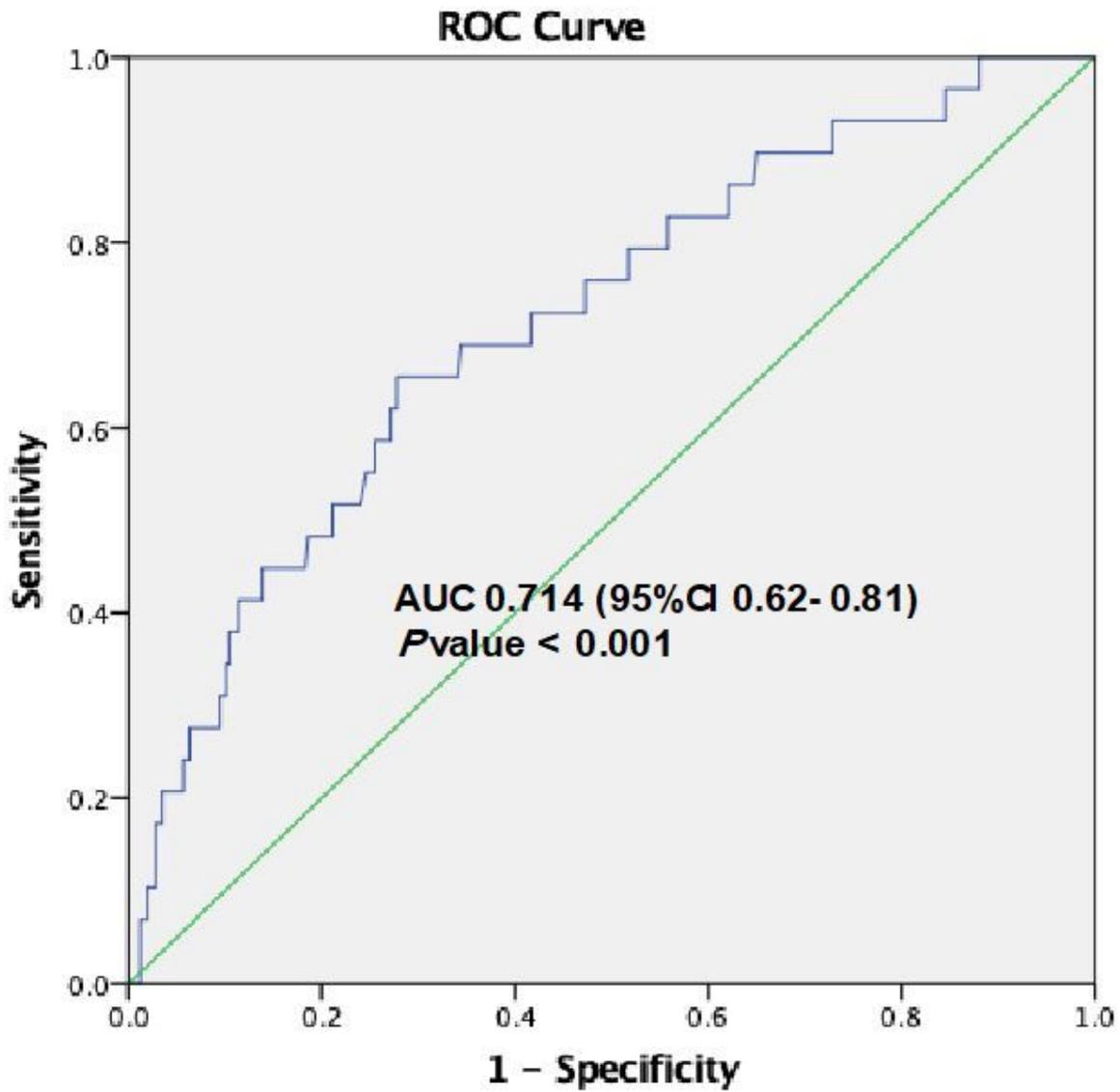


Figure 2

Receiver operating characteristics (ROC) curve for the propensity score for a HFERS patient's likelihood of diagnosed with acute pancreatitis. AUC, area under ROC curve.

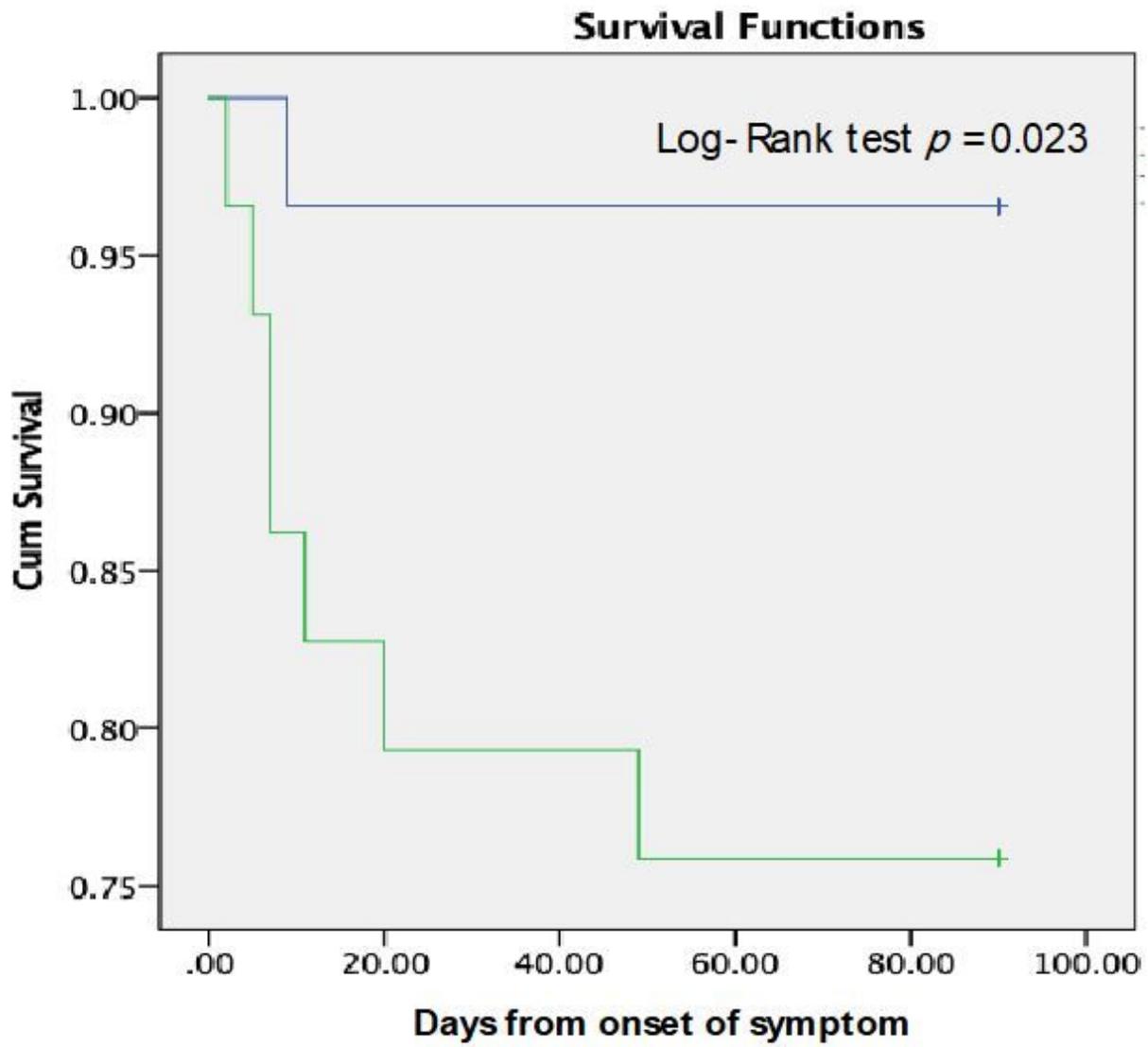


Figure 3

Survival curves stratified by all 29 patients with confirmed acute pancreatitis were compared with 29 matched subjects who without.