Clinical Study

Effect of Admission Time on the Outcomes of Liver Cirrhosis with Acute Upper Gastrointestinal Bleeding: Regular Hours versus Off-Hours Admission

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Background and Aims. Acute upper gastrointestinal bleeding (AUGIB) is a lethal complication of liver cirrhosis. We aimed to compare the outcomes of patients with liver cirrhosis and AUGIB who were admitted to hospital on regular hours and off-hours. Methods. This retrospective study screened all cirrhotic patients with AUGIB who were admitted to our hospital from January 2010 to June 2014 for the test cohort and from December 2014 to March 2018 for the validation cohort. A 1:1 propensity score matching analysis was performed to adjust the Child-Pugh and MELD scores. In-hospital mortality, 5-day rebleeding rate, length of stay, and total payment were primary outcomes. Results. Overall, 826 and 173 patients with liver cirrhosis and AUGIB were included in the test and validation cohorts, respectively. After propensity score matching, 226 and 40 patients were included in the test and validation cohorts, respectively. The overall analysis of the test cohort found significantly higher Child-Pugh score (P=0.006), 5-day rebleeding rate (18.69% versus 10.72%, P<0.001), and total payment (¥25,906.83 versus ¥22,017.42, P<0.001) in patients admitted on off-hours. By contrast, the overall analysis of the validation cohort did not find any difference in Child-Pugh score, 5-day rebleeding rate, in-hospital mortality, length of stay, or hospital payment between patients admitted during regular hours and off-hours. Similarly, the propensity score matching analyses of both test and validation cohorts found no difference in these primary outcomes between the two groups. Conclusions. Off-hours admission might not be negatively associated with the outcomes of patients with liver cirrhosis and AUGIB.

1. Introduction

Liver cirrhosis is the 13th major cause of death worldwide. Acute upper gastrointestinal bleeding (AUGIB) is a frequent medical emergency with a high incidence of 45-172/100,000 each year in the general population and is a lethal complication of liver cirrhosis leading to an in-hospital mortality of 10% [1, 2]. Due to the acute performance of AUGIB itself, early diagnosis and timely management are needed. Notably, there are general shortage of staff, a potentially lower professional level of staff, and delayed use of endoscopy during weekends and holidays, which may lead to worse outcomes [3, 4]. Previous studies evaluated the effect of admission time on the outcomes of patients with AUGIB, but their findings were inconsistent. Some authors supported the “weekend effect” that patients admitted during weekends had worse outcomes [5–9], such as higher mortality and rebleeding rate, longer length of stay, and increased cost. On the contrary, others suggested no significant difference in the mortality between patients admitted during weekends and weekdays [10–15].
A meta-analysis [16] reported that off-hours admission was significantly associated with an increased mortality and less timely endoscopy in patients with nonvariceal bleeding but not those with variceal bleeding. More recently, another meta-analysis [17] also had similar results. However, there were some limitations in previous studies.

First, meta-analyses have shown that geographical variation leads to different weekend effect on outcomes [16, 17]. A study, which included 571 patients suspected with upper gastrointestinal bleeding (UGIB) from 8 participating hospitals in the Netherlands [11], reported that patients admitted on weekends had higher mortality and rebleeding rate than those admitted on weekdays. By contrast, two prospective studies [14, 15] conducted in the United Kingdom found no significant difference in mortality of patients with UGIB between weekend and weekday admission groups. A retrospective study conducted in Korea [12], which included 294 cirrhotic patients with acute variceal bleeding, found no significant difference in the in-hospital mortality between weekend and weekday admission groups. Notably, all studies included in the two meta-analyses were not conducted in China mainland. Considering a geographical difference in the staff schedule and management and outcome of AUGIB, further studies should be performed in China mainland.

Second, meta-analyses have also shown that a variation in the source of bleeding leads to different weekend effect on outcomes. All of 4 studies conducted in the United States were based on Nationwide Inpatient Sample, but showed different results [5, 6, 8, 13]. The first study demonstrated that patients with UGIB regardless of source of bleeding admitted on weekends had significantly higher mortality and longer length of stay than those admitted on weekdays [5]. The second study also demonstrated that patients with peptic ulcer hemorrhage admitted on weekends had higher mortality and longer length of stay [6]. The third study further confirmed that patients with nonvarical UGIB admitted on weekends had higher mortality [8]. However, the fourth study found that the mortality in patients with acute variceal bleeding was similar between weekend and weekday admission groups [13].

Third, previous studies usually compared the effect of weekends versus weekdays on the mortality of AUGIB. But the nighttime during weekdays was often ignored from the definition of off-hours. Thus, further studies should refine the interval of off-hours.

Herein, we performed a retrospective study to compare the outcomes of patients with liver cirrhosis and AUGIB who were admitted to our department and underwent contrast-enhanced CT scans and endoscopy since December 2014. Thus, based on the data during the patients’ enrollment and follow-up, a validation cohort of cirrhotic patients with AUGIB between December 2014 and March 2018 was established for the present study. Age and sex were not limited. The source of bleeding was not limited. Patients with liver and other malignancies were excluded. Patients with incomplete case information and unavailable electronic medical records were also excluded. Data from repeated admission was not deliberately excluded. The outcomes we observed included 5-day rebleeding rate, in-hospital mortality, length of hospital stay, and total payment during hospitalizations. This study was approved by the Medical Ethical Committee of our hospital and the ethical approval number was k (2017)42. The patient’s informed consent was not required in the retrospective study.

2.2. Data Collection. The primary data collected were age, sex, admission time, etiology of liver disease, and laboratory tests (i.e., red blood cell, hemoglobin, white blood cell, platelet count, total bilirubin, direct bilirubin, indirect bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, blood urea nitrogen, creatinine, potassium, sodium, prothrombin time, activated partial thromboplastin time, and international normalized ratio [INR]). The severity of esophageal varices was also collected. Treatment options of AUGIB were collected as follows: endoscopic therapy (i.e., band ligation, sclerotherapy, and histoacryl), Sengstaken-Blakemore tube, somatostatin and/or octreotide, blood transfusion, proton pump inhibitors (PPIs), and surgery.

2.3. Definitions and Formulas. AUGIB was defined as hematemesis and/or melena within 5 days before our admission or positive occult blood test at the day of admission [18]. Regular hours referred to the interval from 8:00 AM to 17:00 PM at the weekdays (i.e., from Monday to Friday). Otherwise, off-hours were considered, and weekends and public holidays were also considered as off-hours. Child-Pugh score [19] was calculated according to hepatic encephalopathy, ascites, total bilirubin, albumin, and INR. Model for end-stage liver disease (MELD) score=9.57 × ln (creatinine [μmol/L]×0.01) + 3.78 × ln(bilirubin [μmol/L] × 0.05) + 11.2 × ln(INR) + 0.643 [20]. According to the study by Reverter et al. [21], recalibrated MELD score=5.312+0.207×MELD. Albumin-bilirubin (ALBI) score=−0.085 × albumin (g/L) + 0.66 × log_{10}bilirubin (μmol/L) [22, 23].

2.4. Statistical Analyses. Continuous variables were reported as median (range) and were compared using the nonparametric Mann-Whitney U test. Categorical variables were reported as frequency (percentage) and were compared using the chi-square test. Subgroup analyses were also conducted based on the presence of varices on endoscopy (AUGIB with endoscopically confirmed varices and without varices on endoscopy). A 1:1 propensity score matching analysis was performed to adjust the effect of gender, age, Child-Pugh score, MELD score, and recalibrated MELD score on the
outcomes. A two-tailed $P<0.05$ was considered statistically significant. All statistical analyses were performed with IBM SPSS 20.0 (IBM Corp.) statistical package and Stata/SE 12.0 (Stata Corp, College Station, TX) software.

3. Results

3.1. Test Cohort

3.1.1. Patients’ Characteristics. Between January 2010 and June 2014, a total of 826 patients with liver cirrhosis and AUGIB were included. Baseline patient characteristics are described in Table 1. Median age was 55.27 years (range: 6.28 to 95.13). Among them, 564 (68.3%) patients were male. Major etiology of liver diseases included hepatitis B virus infection (n=208, 25.2%) and alcohol abuse (n=219, 26.5%). A majority of patients had Child-Pugh class B (339/776, 51.4%). Median MELD score at admission was 6.37 (-7.52 to 38.22). Five hundred and twenty-two patients underwent endoscopy. No, mild, moderate, and severe esophageal varices were observed in 32 (6.1%), 24 (4.6%), 54 (10.3%), and 412 (78.9%) patients, respectively. As for the treatment of AUGIB, 508 (61.5%) patients underwent endoscopic therapy, 20 (2.4%) patients underwent Sengstaken Blackmore tube placement, 750 (90.8%) patients received somatostatin and/or octreotide, 544 (65.9%) patients received blood transfusion, 813 (98.4%) patients received PPIs, and 8 (1.0%) patients underwent surgery. Information regarding 5-day rebleeding was unavailable in 4 patients, because some of their medical records were missing. Five-day rebleeding rate was 14.0% (113/822). In-hospital mortality was 5.7% (47/826). Median length of hospital stay was 11.23 days (range: 0.06 to 100.55). Total payment was ¥23,120.87 (range: 1,287.54 to 226,872.93).

3.1.2. Outcome. Patients admitted on off-hours had lower serum albumin ($P<0.001$) and higher white blood cell ($P<0.001$), blood urea nitrogen ($P<0.001$), potassium ($P<0.001$), prothrombin time ($P=0.034$), INR ($P=0.040$), Child-Pugh score ($P=0.006$), and ALBI score ($P<0.001$) than those admitted on regular hours (Table 1). As for the interventions, patients admitted on off-hours had a higher proportion of blood transfusion than those admitted on regular hours (73.3% versus 60.7%, $P<0.001$). Among the different departments of our hospital, there was no significant difference in the selection of most treatment options for AUGIB between patients admitted on regular hours and off-hours (Supplementary Table 1). As for the outcomes, patients admitted on off-hours had a higher 5-day rebleeding rate (18.7% versus 10.7%, $P=0.001$) and a larger amount of payment ($¥25,906.83$ versus $¥22,017.42$, $P<0.001$). In-hospital mortality was not significantly different between the two groups ($P=0.418$). Length of stay was not significantly different between the two groups ($P=0.830$).

3.1.3. Subgroup Analyses. The origin of bleeding could be evaluated in 611 patients in the test cohort. They included 591 patients with endoscopically confirmed esophageal and/or gastric varices and 20 patients without varices at endoscopy (Supplementary Table 2).

Among the patients with endoscopically confirmed varices, patients admitted on off-hours were older ($P=0.015$) and had lower red blood cell ($P=0.026$) and serum albumin ($P<0.001$) and higher white blood cell ($P<0.001$), blood urea nitrogen ($P<0.001$), potassium ($P=0.001$), prothrombin time ($P=0.027$), INR ($P=0.04$), Child-Pugh score ($P<0.001$), MELD score ($P=0.023$), recalibrated MELD score ($P=0.023$), and ALBI score ($P<0.001$) than those admitted on regular hours. As for the interventions, patients admitted on off-hours had a higher proportion of blood transfusion (75.5% versus 59.5%, $P<0.001$) and surgery (2.1% versus 0.3%, $P=0.027$) than those admitted on regular hours. As for the outcomes, patients admitted on off-hours had a higher 5-day rebleeding rate (16.5% versus 10.6%, $P=0.038$) and a larger amount of payment ($¥29,361.51$ versus $¥23,864.24$, $P<0.001$). In-hospital mortality and length of stay were not significantly different between the two groups ($P=0.094$ and $P=0.856$, respectively).

Among the patients without varices at endoscopy, no significant difference in demographics, etiology of liver disease, laboratory tests, Child-Pugh score, MELD score, recalibrated MELD score, ALBI score, and treatment options was observed between patients admitted on regular hours and off-hours ($P>0.05$, in all comparisons). As for the outcomes, none died. Five-day rebleeding rate, length of stay, and total payment were not significantly different between the two groups ($P=0.117$, $P=0.869$, and $P=0.187$, respectively).

3.1.4. Patients’ Characteristics after Propensity Score Matching. After a 1:1 propensity score matching analysis, a total of 226 patients with liver cirrhosis and AUGIB were included. Baseline patient characteristics are described in Table 2. Median age was 54.51 years (range: 6.28 to 81.62). Among them, 144 (63.7%) patients were male. Major etiology of liver diseases included hepatitis B virus infection (n=58, 25.7%) and alcohol abuse (n=50, 22.1%). A majority of patients had Child-Pugh class B (n=121, 53.5%). Median MELD score at admission was 6.12 (-7.14 to 21.56). No, mild, moderate, and severe esophageal varices were observed in 11 (4.9%), 19 (8.4%), 23 (10.2%), and 182 (80.5%) patients, respectively. As for the treatment of AUGIB, 191 (84.5%) patients underwent endoscopic therapy, 8 (3.5%) patients underwent Sengstaken Blackmore tube placement, 218 (96.5%) patients received somatostatin and/or octreotide, 159 (70.4%) patients received blood transfusion, 750 (90.8%) patients received PPIs, and 8 (1.0%) patients underwent surgery. Information regarding 5-day rebleeding was unavailable in 4 patients, because some of their medical records were missing. Five-day rebleeding rate was 14.2% (143,048.30). In-hospital mortality was 2.2% (n=5). Median length of hospital stay was 12.83 days (range: 2.76 to 78.00). Median total payment was ¥28,633.075 (range: 2,776.55 to 226,872.93).

3.1.5. Outcomes after Propensity Score Matching. After a 1:1 propensity score matching analysis, 113 patients were matched on each group (Table 2). No significant difference in demographics, etiology of liver disease, laboratory tests, Child-Pugh score, MELD score, recalibrated MELD score, ALBI score, and treatment options was observed between the two groups ($P>0.05$, in all comparisons). As for the outcomes, 5-day rebleeding rate, in-hospital mortality, length of stay,
Table 1: Characteristics of patients with liver cirrhosis and AUGIB in test cohort.

| Variables                      | No. Pts | Overall | No. Pts | Regular hours | No. Pts | Off-hours | P value |
|--------------------------------|---------|---------|---------|---------------|---------|-----------|---------|
| Age (years)                    | 826     | 55.27(6.28-95.13) | 486     | 54.54(20.88-95.13) | 340     | 55.95(6.28-84.56) | 0.074   |
| Sex (male)                     | 826     | 564(68.3%) | 486     | 337 (69.3%)    | 340     | 227 (66.8%)    | 0.434   |
| Etiology of Liver Diseases     | 826     |          |         |                |         |           | 0.387   |
| HBV                            | 208     | 25.2%    | 126     | 25.9%          | 82      | 24.1%     |         |
| HCV                            | 51      | 6.2%     | 32      | 6.6%           | 19      | 5.6%      |         |
| HBV + HCV                      | 6       | 0.7%     | 2       | 0.4%           | 4       | 1.2%      |         |
| Alcohol Abuse                  | 219     | 26.5%    | 125     | 25.7%          | 94      | 22.7%     |         |
| HBV + Alcohol Abuse            | 64      | 77%      | 42      | 8.6%           | 22      | 6.5%      |         |
| HCV + Alcohol Abuse            | 13      | 16%      | 7       | 1.4%           | 6       | 1.8%      |         |
| HBV + HCV + Alcohol Abuse      | 2       | 0.2%     | 1       | 0.2%           | 1       | 0.3%      |         |
| Drug Related                   | 35      | 4.2%     | 23      | 4.7%           | 12      | 3.5%      |         |
| Autoimmune Liver Diseases      | 56      | 6.8%     | 26      | 5.4%           | 30      | 8.8%      |         |
| Other or Unclear Etiology      | 172     | 20.8%    | 102     | 21%            | 70      | 20.6%     |         |
| Laboratory Tests               |         |          |         |                |         |           |         |
| Red Blood Cell (10^12/L)       | 822     | 2.56(0.93-5.49) | 482     | 2.61(0.93-5.49) | 340     | 2.49(1.05-5.10) | 0.250   |
| Hemoglobin (g/L)               | 822     | 72.00(23.00-180.00) | 482     | 73.00(23.00-164.00) | 340     | 71.00(23.00-180.00) | 0.512   |
| White Blood Cell (10^5/L)      | 822     | 4.70(0.40-46.10) | 482     | 4.20(0.80-33.50) | 340     | 5.30(0.90-46.10) | <0.001  |
| Platelet Count (10^5/L)        | 822     | 75.00(9.00-842.00) | 482     | 74.00(9.00-842.00) | 340     | 77.50(17.00-775.00) | 0.429   |
| Total Bilirubin (umol/L)       | 820     | 20.30(3.30-679.10) | 480     | 20.10(3.30-679.10) | 340     | 20.50(3.30-250.80) | 0.598   |
| Direct Bilirubin (umol/L)      | 820     | 8.30(0.50-413.80) | 480     | 8.20(1.30-413.80) | 340     | 8.50(0.50-195.20) | 0.916   |
| Indirect Bilirubin (umol/L)    | 820     | 11.75(1.30-265.30) | 480     | 11.50(1.30-265.30) | 340     | 12.05(2.00-126.60) | 0.436   |
| Albumin (g/L)                  | 796     | 30.40(9.60-49.30) | 469     | 31.00(9.60-49.30) | 327     | 29.30(10.00-48.00) | <0.001  |
| Alanine Aminotransferase (U/L) | 818     | 23.00(5.00-1064.00) | 479     | 23.00(5.00-730.00) | 339     | 24.00(5.00-1064.00) | 0.403   |
| Aspartate Aminotransferase (U/L)| 818     | 31.00(7.00-1487.00) | 479     | 31.00(7.00-1399.00) | 339     | 32.00(8.00-1487.00) | 0.255   |
| Alkaline Phosphatase (U/L)     | 818     | 73.00(1.30-889.00) | 479     | 74.00(1.30-889.00) | 339     | 72.00(1.30-888.00) | 0.535   |
| Gamma-glutamyl Transferase (U/L)| 818   | 35.00(5.00-1168.00) | 479     | 35.00(5.00-1168.00) | 339     | 37.00(6.00-755.00) | 0.945   |
| Blood Urea Nitrogen (mmol/L)   | 792     | 7.71(1.58-42.83) | 465     | 7.06(1.58-42.83) | 327     | 8.21(19.6-3677)  | <0.001  |
| Serum Creatinine (mmol/L)      | 792     | 61.00(20.00-999.00) | 465     | 60.00(20.00-999.00) | 326     | 61.00(24.00-32700) | 0.284   |
| Potassium (mmol/L)             | 810     | 4.06(2.13-7.87) | 473     | 4.00(2.13-7.07) | 337     | 4.12(2.79-7.76) | <0.001  |
| Sodium (mmol/L)                | 810     | 138.80(83.00-160.80) | 473     | 138.80(83.00-160.80) | 337     | 138.80(83.00-160.80) | 0.055   |
| PT (seconds)                   | 794     | 16.20(10.80-62.80) | 465     | 15.90(10.80-62.80) | 329     | 16.50(11.00-49.50) | 0.034   |
| APTT (seconds)                 | 791     | 40.30(25.70-180.00) | 463     | 40.50(25.70-180.00) | 328     | 39.95(27.30-97.20) | 0.452   |
| INR                            | 791     | 1.31(0.77-796)   | 463     | 1.28(0.77-796)   | 328     | 1.35(0.79-5.94) | 0.040   |
| Child-Pugh Score               | 776     | 7.00(5.00-15.00) | 455     | 7.00(5.00-15.00) | 321     | 7.00(5.00-15.00) | 0.006   |
| Child-Pugh A/B/C               | 776     | 234(30.2%)/339 | 455     | 160(35.2%)/216 | 321     | 74 (23.1%)/183 | 0.001   |
Table 1: Continued.

| Variables                              | No.          | Overall                        | Regular hours        | Off-hours        | P value |
|----------------------------------------|--------------|--------------------------------|----------------------|------------------|---------|
| MELD Score                             | 772          | 6.37 (-7.52-38.22)             | 453 5.87 (-7.52-38.22) | 319 7.06 (-7.44-37.65) | 0.067   |
| Recalibrated MELD Score                | 772          | -4.00 (-6.87-2.60)             | 453 -4.10 (-6.87-2.60) | 319 -3.85 (-6.85-2.48) | 0.067   |
| ALBI Score                             | 793          | -1.70 (-3.31-0.22)             | 467 -1.77 (-3.31-0.03) | 326 -1.59 (-3.13-0.22) | <0.001  |
| Esophageal Varices (No/Mild/Moderate/Severe) | 522          | 32 (6.1%)/24 (4.6%)/20 (6.5%)/17 (5.5%)/22 (10.3%)/240 (77.6%) | 309 (10.4%)/240 (77.6%) | 213 (10.3%)/172 (80.8%) | 0.650   |
| Treatment                              |              |                                |                      |                  |         |
| Endoscopic Treatment                   | 826          | 508 (61.5%)                    | 486 310 (63.8%)      | 340 198 (58.2%)  | 0.107   |
| Sengstaken Blakemore                   | 826          | 20 (2.4%)                      | 486 12 (2.5%)        | 340 8 (2.4%)     | 0.915   |
| Somatostatin and/or Octreotide         | 826          | 750 (90.8%)                    | 486 435 (80.5%)      | 340 315 (92.7%)  | 0.124   |
| Blood Transfusion                      | 826          | 544 (65.9%)                    | 486 295 (60.7%)      | 340 249 (73.3%)  | <0.001  |
| PPIs                                   | 826          | 813 (98.4%)                    | 486 477 (98.2%)      | 340 336 (98.8%)  | 0.443   |
| Surgery                                | 826          | 8 (1.0%)                       | 486 2 (0.4%)         | 340 6 (1.8%)     | 0.051   |
| 5-day Re-bleeding After Treatment      | 822          | 115 (14.0%)                    | 485 52 (10.7%)       | 337 63 (18.7%)   | 0.001   |
| Death During Hospitalization           | 826          | 47 (5.7%)                      | 486 25 (5.1%)        | 340 22 (6.5%)    | 0.418   |
| Length of Stay (days)                  | 826          | 11.23 (0.06-100.55)            | 486 11.27 (0.06-78.00)| 340 11.13 (0.09-100.55) | 0.830   |
| Total Payment (¥)                      | 826          | (1,287,542-226,872.93)         | 486 (1,683,37-241,538)| 340 (1,287,54-226,872.93) | <0.001  |

Data are expressed as median (range) or frequency (percentage).

Abbreviations: AUGIB: acute upper gastrointestinal bleeding; HBV: Hepatitis B virus; HCV: Hepatitis C virus; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; MELD: model for end-stage liver disease; ALBI: albumin-bilirubin; PPIs: proton pump inhibitors; ¥: Renminbi.
Table 2: Characteristics of patients with liver cirrhosis and AUGIB after propensity matching in test cohort.

| Variables                              | Overall (n=226) | Propensity matching patients | Off-hours (n=113) | P value |
|----------------------------------------|----------------|-----------------------------|------------------|---------|
|                                        |                | Regular hours (n=113)       |                  |         |
|                                        |                | Off-hours (n=113)           |                  |         |
| Age (years)                            | 54.51 (6.28-81.62) | 54.41 (29.85-81.62)       | 54.60 (6.28-78.66) | 0.829   |
| Sex (male)                             | 144 (63.7%)    | 73 (64.6%)                 | 71 (62.8%)       | 0.782   |
| Etiology of Liver Diseases             |                |                             |                  | 0.612   |
| HBV                                    | 58 (25.7%)     | 29 (25.7%)                 | 29 (25.7%)       |         |
| HCV                                    | 14 (6.2%)      | 7 (6.2%)                   | 7 (6.2%)         |         |
| HBV+ HCV                               | 1 (0.4%)       | 1 (0.9%)                   | 0 (0%)           |         |
| Alcohol Abuse                          | 50 (22.1%)     | 26 (23.0%)                 | 24 (21.2%)       |         |
| HBV+ Alcohol Abuse                     | 26 (11.5%)     | 15 (13.3%)                 | 11 (9.7%)        |         |
| HCV+ Alcohol Abuse                     | 3 (1.3%)       | 0 (0%)                     | 3 (2.7%)         |         |
| HBV+ HCV+ Alcohol Abuse                | 1 (0.4%)       | 0 (0%)                     | 1 (0.9%)         |         |
| Drug Related                           | 10 (4.4%)      | 5 (4.4%)                   | 5 (4.4%)         |         |
| Autoimmune Liver Diseases              | 12 (5.3%)      | 5 (4.4%)                   | 7 (6.2%)         |         |
| Other or Unclear Etiology              | 51 (22.6%)     | 25 (22.1%)                 | 26 (23.0%)       |         |
| Laboratory Tests                       |                |                             |                  |         |
| Red Blood Cell (10^12/L)               | 2.54 (0.98-5.49) | 2.60 (0.98-5.49)       | 2.53 (1.15-4.68) | 0.989   |
| Hemoglobin (g/L)                       | 71.50 (23.00-157.00) | 72.00 (23.00-157.00) | 71.00 (23.00-133.00) | 0.901   |
| White Blood Cell (10^3/L)              | 4.30 (1.00-26.30) | 4.10 (1.10-26.30)       | 4.40 (1.00-17.50) | 0.239   |
| Platelet Count (10^9/L)                | 74.00 (17.00-435.00) | 72.00 (27.00-303.00) | 79.00 (17.00-435.00) | 0.538   |
| Total Bilirubin (umol/L)               | 18.80 (3.30-187.40) | 9.00 (6.10-90.40)       | 18.40 (3.30-187.40) | 0.669   |
| Direct Bilirubin (umol/L)              | 7.50 (0.50-151.60) | 750 (1.30-56.30)        | 7.20 (0.50-151.60) | 0.384   |
| Indirect Bilirubin (umol/L)            | 11.35 (2.40-56.80) | 11.20 (3.20-41.10)      | 11.40 (2.40-56.80) | 0.771   |
| Albumin (g/L)                          | 30.10 (10.00-49.30) | 30.48 (10.50-49.30)     | 29.40 (10.00-45.60) | 0.580   |
| Alanine Aminotransferase (U/L)         | 23.00 (5.00-234.00) | 23.00 (6.00-234.00)     | 23.00 (5.00-154.00) | 0.896   |
| Aspartate Aminotransferase (U/L)       | 31.00 (9.00-263.00) | 31.00 (12.00-263.00)    | 31.00 (9.00-175.00) | 0.872   |
| Alkaline Phosphatase (U/L)             | 74.00 (17.44-707.00) | 77.00 (17.44-707.00) | 71.00 (21.00-685.00) | 0.282   |
| Gamma-glutamyl Transpeptidase (U/L)    | 35.00 (8.00-168.00) | 45.00 (8.00-168.00)     | 33.00 (9.00-737.00) | 0.354   |
| Blood Urea Nitrogen (mmol/L)           | 762 (1.96-34.00) | 766 (2.04-34.00)         | 761 (1.96-28.10) | 0.989   |
| Serum Creatinine (umol/L)              | 60.00 (28.00-234.00) | 60.00 (28.00-225.70) | 59.00 (30.50-234.00) | 0.655   |
| Potassium (mmol/L)                     | 4.06 (2.90-5.50) | 4.05 (3.00-5.50)         | 4.08 (2.90-5.50) | 0.285   |
| Sodium (mmol/L)                        | 138.50 (128.00-150.00) | 138.30 (130.40-148.00) | 138.50 (128.00-150.00) | 0.773   |
| PT (seconds)                           | 15.80 (11.00-46.30) | 15.60 (12.10-36.10)    | 16.00 (11.00-46.30) | 0.912   |
| APTT (seconds)                         | 39.55 (27.30-66.80) | 40.10 (28.20-66.80)     | 38.50 (27.30-63.90) | 0.253   |
| INR                                    | 1.28 (0.79-4.77) | 1.26 (0.90-3.57)         | 1.29 (0.79-4.77) | 0.950   |
| Variables                        | Overall (n=226) | Regular hours (n=113) | Off-hours (n=113) | P value |
|---------------------------------|----------------|-----------------------|-------------------|---------|
| Child-Pugh Score                | 7.00 (5.00-13.00) | 7.00 (5.00-12.00)     | 7.00 (5.00-13.00) | 0.891   |
| Child-Pugh A/B/C                | 72 (31.9%)/121  | 35 (31.0%)/64         | 37 (32.7%)/57     | 0.544   |
| MELD Score                      | 6.12 (-7.14-21.56) | 6.12 (-5.03-20.16)    | 5.68 (-7.14-21.56)| 0.733   |
| Recalibrated MELD Score         | -4.05 (-6.79 - -0.85) | -4.04 (-6.35 - -1.14)| -4.14 (-6.79 - -0.85)| 0.733   |
| ALBI Score                      | -1.70 (-3.23 -0.22) | -1.70 (-3.23 -0.43)  | -1.69 (-3.06-0.22) | 0.767   |
| Esophageal Varices              | 11 (4.9%)/10 (4.4%)/23 (10.2%)/92 (81.4%) | 5 (4.4%)/5 (4.4%)/II (10.2%)/92 (81.4%) | 6 (53%)/5 (4.4%)/12 (10.2%)/90 (79.7%) | 0.984   |
| Treatment                       |                |                       |                   |         |
| Endoscopic Treatment            | 191 (84.5%)     | 96 (85.0%)            | 95 (84.1%)        | 0.854   |
| Sengstaken Blakemore            | 8 (3.5%)        | 5 (4.4%)              | 3 (2.7%)          | 0.472   |
| Somatostatin and/or Octreotide  | 218 (96.5%)     | 107 (94.7%)           | 111 (98.2%)       | 0.150   |
| Blood Transfusion               | 159 (70.4%)     | 80 (70.8%)            | 79 (69.9%)        | 0.884   |
| PPIs                            | 226 (100%)      | 113 (100%)            | 113 (100%)        | NA      |
| Surgery                         | 1 (0.4%)        | 1 (0.9%)              | 0 (0%)            | 0.316   |
| 5-day Re-bleeding After Treatment| 32 (14.2%)     | 14 (12.4%)            | 18 (15.9%)        | 0.445   |
| Death During Hospitalization    | 5 (2.2%)        | 2 (1.8%)              | 3 (2.7%)          | 0.651   |
| Length of Stay (days)           | 12.835 (2.76-78.00) | 12.97 (3.91-78.00)  | 12.41 (2.76-15.26) | 0.229   |
| Total Payment (¥)               | (2,776.55-143,048.30) | (2,776.55-143,048.30) | (2,776.55-143,048.30) | 0.390   |

Data are expressed as median (range) or frequency (percentage).

Abbreviations: AUGIB: acute upper gastrointestinal bleeding; HBV: Hepatitis B virus; HCV: Hepatitis C virus; PT, prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; MELD: model for end-stage liver disease; ALBI: albumin-bilirubin; PPIs: Proton pump inhibitors; ¥, Renminbi.
and total payment were not significantly different between the two groups (P=0.445, P=0.651, P=0.229, and P=0.390, respectively).

3.1.6. Subgroup Analyses after Propensity Score Matching. After a 1:1 propensity score matching analysis, 140 patients with endoscopically confirmed varices were matched on each group (Supplementary Table 3). Patients admitted on off-hours had higher white blood cell (P=0.007), blood urea nitrogen (P=0.01), and potassium (P=0.001) than those admitted on regular hours. As for the interventions, patients admitted on off-hours had a higher proportion of blood transfusion (77.1% versus 58.6%, P=0.001) and surgery (2.9% versus 0%, P=0.044) than those admitted on regular hours. As for the outcomes, 5-day rebleeding rate, in-hospital mortality, length of stay, and total payment were not significantly different between the two groups (P=0.306, P=0.409, P=0.421, and P=0.058, respectively).

3.2. Validation Cohort

3.2.1. Patients’ Characteristics. Between December 2014 and March 2018, a total of 173 patients with liver cirrhosis and AUGIB were included. Baseline patient characteristics are described in Table 3. Median age was 56.60 years (range: 20.57 to 88.73). Among them, 121 (69.9%) patients were male. Major etiology of liver diseases included hepatitis B virus infection (n=47, 27.2%) and alcohol abuse (n=55, 31.8%). A majority of patients had Child-Pugh class B (94/169, 55.6%). Median MELD score at admission was 7.22 (-3.16 to 23.19). One hundred and fifty-one patients underwent endoscopy. No, mild, moderate, and severe esophageal varices were observed in 2 (5%), 5 (12.5%), and 27 (67.5%) patients, respectively. As for the treatment, 88 (50.9%) patients received blood transfusion, 173 (100%) patients received somatostatin and/or octreotide, 21 (52.5%) patients received blood transfusion, all patients received PPIs, and no patient underwent surgery.

3.2.2. Outcomes. Information regarding 5-day rebleeding was unavailable in one patient. Five-day rebleeding rate was 7.6% (13/172). In-hospital mortality was 5.82 (range: -2.38 to 23.19). One hundred and fifty-one patients underwent endoscopy. No, mild, moderate, and severe esophageal varices were observed in 2 (5%), 5 (12.5%), and 27 (67.5%) patients, respectively. The origin of bleeding could be evaluated in 162 patients, of whom only 4 did not have esophageal and/or gastric varices. As for the treatment of AUGIB, 139 (80.3%) patients underwent endoscopic therapy, 1 (0.6%) patients underwent Sengstaken Blackmore tube placement, 160 (92.5%) patients received somatostatin and/or octreotide, 88 (50.9%) patients received blood transfusion, 173 (100%) patients received PPIs, and 0 (0%) patients underwent surgery. Information regarding 5-day rebleeding was unavailable in one patient. Five-day rebleeding rate was 7.6% (13/172). In-hospital mortality was 2.3% (4/173). Median length of hospital stay was 10.10 days (range: 0.12 to 32.94). Total payment was ¥24,328.31 (range: 3,427.24 to 98,215.78).

3.2.3. Patients’ Characteristics after Propensity Score Matching. After a 1:1 propensity score matching analysis, a total of 40 patients with liver cirrhosis and AUGIB were included. Baseline patient characteristics are described in Table 4. Median age was 56.86 years (range: 20.57 to 75.64). Among them, 28 (70%) patients were male. Major etiology of liver diseases included hepatitis B virus infection (n=9, 22.5%) and alcohol abuse (n=14, 35%). A majority of patients had Child-Pugh class B (n=22, 55%). Median MELD score at admission was 5.82 (range: -2.38 to 23.19). No, mild, moderate, and severe esophageal varices were observed in 2 (5%), 5 (12.5%), 6 (15%), and 27 (67.5%) patients, respectively. As for the treatment of AUGIB, 38 (95%) patients underwent endoscopic therapy, no patient underwent Sengstaken Blackmore tube placement, 39 (97.5%) patients received somatostatin and/or octreotide, 21 (52.5%) patients received blood transfusion, all patients received PPIs, and no patient underwent surgery.

3.2.4. Outcomes after Propensity Score Matching. After a 1:1 propensity score matching analysis, 20 patients were matched on each group (Table 4). No significant difference in demographics, etiology of liver disease, laboratory tests, Child-Pugh score, MELD score, recalibrated MELD score, ALBI score, and treatment options was observed between the two groups (P>0.05, in all comparisons). As for the outcomes, 5-day rebleeding rate, in-hospital mortality, length of stay, and total payment were not significantly different between the two groups (P=0.633, P=0.311, P=0.441, and P=0.829, respectively).

4. Discussion

Traditionally, a worse outcome in patients with UGIB during the weekend was potentially attributed to lower staffing levels and relatively younger and inexperienced staff [11]. Indeed, both overall analyses and subgroup analyses of patients with endoscopically confirmed varices in the test cohort demonstrated a significantly higher 5-day rebleeding rate and a larger amount of payment in patients admitted on off-hours. This might be primarily due to worse liver dysfunction in patients admitted on off-hours, such as lower albumin and higher prothrombin time, INR, Child-Pugh score, and ALBI score. As the Child-Pugh score was matched, the propensity score matching analyses of both test and validation cohorts showed no significant effect of admission time on the rebleeding rate, in-hospital mortality, length of stay, and total payment of cirrhotic patients with AUGIB. These findings suggested that the weekend effect might not be an independent risk factor for worse outcomes of cirrhotic patients with AUGIB.

A meta-analysis [16] found that off-hours admission was not associated with a higher risk of rebleeding rate (OR=1.06, 95%CI=0.83-1.35, and P=0.66) and longer length of stay (WMD 0.06 day, 95%CI= -0.30 - 0.42, P=0.747). These previous findings were consistent with our results regarding 5-day rebleeding rate and length of stay. Notably, our study focused on the 5-day rebleeding rate after treatment during
Table 3: Characteristics of patients with liver cirrhosis and AUGIB in validation cohort.

| Variables                        | No. Pts | Overall          | No. Pts | Regular hours | No. Pts | Off-hours | P value |
|----------------------------------|---------|------------------|---------|---------------|---------|-----------|---------|
| Age (years)                      | 173     | 56.60 (20.57-88.73) | 131     | 56.60 (20.57-75.73) | 42      | 56.56 (33.42-88.73) | 0.683   |
| Sex (male)                       | 173     | 121 (69.9%)      | 131     | 91 (69.5%)    | 42      | 30 (71.4%) | 0.809   |
| Etiology of Liver Diseases       | 173     |                  |         |               |         |           | 0.830   |
| HBV                              | 47      | 27.2%            | 37      | 28.2%         | 10      | 23.8%     |         |
| HCV                              | 17      | 9.8%             | 12      | 9.2%          | 5       | 11.9%     |         |
| Alcohol Abuse                    | 55      | 31.8%            | 41      | 31.3%         | 14      | 33.3%     |         |
| HBV + Alcohol Abuse              | 3       | 1.7%             | 2       | 1.5%          | 1       | 2.4%      |         |
| HCV + Alcohol Abuse              | 1       | 0.6%             | 1       | 0.8%          | 0       | 0%        |         |
| Drug Related                     | 1       | 0.6%             | 1       | 0.8%          | 0       | 0%        |         |
| Autoimmune Liver Diseases        | 3       | 1.7%             | 3       | 2.3%          | 0       | 0%        |         |
| Other or Undetermined Etiology   | 46      | 26.6%            | 34      | 25.9%         | 12      | 28.6%     |         |
| Laboratory Tests                 |         |                  |         |               |         |           |         |
| Red Blood Cell (10^12/L)         | 173     | 2.70 (1.32-5.11) | 131     | 2.70 (1.32-5.11) | 42      | 2.62 (1.56-4.14) | 0.372   |
| Hemoglobin (g/L)                 | 173     | 73.00 (31.00-156.00) | 131     | 73.00 (31.00-156.00) | 42      | 73.50 (38.00-130.00) | 0.575   |
| White Blood Cell (10^9/L)        | 173     | 4.20 (1.00-23.10) | 131     | 4.10 (1.00-23.10) | 42      | 4.35 (1.70-14.90) | 0.368   |
| Platelet Count (10^9/L)          | 173     | 71.00 (18.00-457.00) | 131     | 73.00 (18.00-377.00) | 42      | 68.50 (23.00-457.00) | 0.980   |
| Total Bilirubin (umol/L)         | 172     | 20.80 (5.20-210.00) | 131     | 21.60 (5.20-210.00) | 41      | 18.30 (6.70-106.30) | 0.587   |
| Direct Bilirubin (umol/L)        | 172     | 8.70 (2.00-146.90) | 131     | 9.00 (2.00-146.90) | 41      | 8.30 (2.50-60.10)  | 0.643   |
| Indirect Bilirubin (umol/L)      | 172     | 10.65 (2.60-79.90) | 131     | 11.40 (2.60-69.20) | 41      | 9.80 (4.20-79.90)  | 0.801   |
| Albumin (g/L)                    | 171     | 29.40 (17.00-50.70) | 130     | 29.65 (17.00-50.70) | 41      | 29.40 (17.00-41.00) | 0.693   |
| Alanine Aminotransferase (U/L)   | 172     | 20.70 (5.00-275.36) | 131     | 20.98 (6.00-140.00) | 41      | 17.17 (5.00-275.36) | 0.504   |
| Aspartate Aminotransferase (U/L) | 172     | 27.00 (9.63-310.39) | 131     | 27.50 (9.63-278.00) | 41      | 26.11 (10.00-310.39) | 0.801   |
| Alkaline Phosphatase (U/L)       | 172     | 78.23 (24.02-378.66) | 131     | 75.66 (24.02-378.66) | 41      | 79.75 (46.24-197.00) | 0.981   |
| Gamma-glutamyl Transpeptidase (U/L) | 172   | 31.98 (7.54-1227.00) | 131     | 29.65 (7.54-1227.00) | 41      | 40.53 (7.69-295.00) | 0.346   |
| Blood Urea Nitrogen (mmol/L)     | 172     | 27.60 (2.17-47.25) | 131     | 7.40 (2.17-47.25) | 41      | 7.96 (2.47-20.18)  | 0.993   |
| Serum Creatinine (umol/L)        | 172     | 69.145 (34.40-267.63) | 131     | 67.03 (34.40-267.63) | 41      | 74.21 (34.90-144.98) | 0.116   |
| Potassium (mmol/L)               | 173     | 3.95 (2.48-5.54)  | 131     | 3.95 (2.48-5.54) | 42      | 3.97 (3.12-5.49)  | 0.876   |
| Sodium (mmol/L)                  | 173     | 138.50 (124.00-152.90) | 131     | 138.40 (130.40-152.90) | 42      | 138.80 (124.00-145.70) | 0.544   |
| PT (seconds)                     | 171     | 16.10 (10.50-27.40) | 130     | 16.10 (11.60-27.40) | 40      | 16.05 (10.50-27.20) | 0.606   |
| APTT (seconds)                   | 170     | 37.85 (19.40-59.70) | 131     | 37.90 (27.50-59.70) | 39      | 37.40 (19.40-52.10) | 0.542   |
| INR                              | 170     | 1.32 (0.91-2.55)  | 130     | 1.33 (1.01-2.55) | 39      | 1.31 (0.91-2.50)  | 0.681   |
### Table 3: Continued.

| Variables                             | No. Pts | Overall     | No. Pts | Regular hours | No. Pts | Off-hours | P value |
|---------------------------------------|---------|-------------|---------|---------------|---------|-----------|---------|
| Child-Pugh Score                      | 169     | 8.00 (5.00-15.00) | 130     | 8.00 (5.00-12.00) | 39      | 7.00 (5.00-12.00) | 0.603   |
| Child-Pugh A/B/C                      | 169     | 51 (30.2%)/94 (55.6%) | 130     | 37 (28.5%)/75 (57.7%) | 39      | 14 (35.9%)/19 (48.7%) | 0.596   |
| MELD Score                            | 170     | 7.22 (-3.16-23.19) | 131     | 7.26 (-3.16-20.70) | 39      | 7.22 (-2.38-23.19) | 0.671   |
| Recalibrated MELD Score               | 170     | -3.82 (-5.97 -0.51) | 131     | -3.81 (-5.97 -1.03) | 39      | -3.82 (-5.80 -0.51) | 0.671   |
| ALBI Score                            | 171     | -1.63 (-3.40 -0.11) | 130     | -1.62 (-3.40 -0.11) | 41      | -1.68 (-2.70 -0.19) | 0.675   |
| Esophageal Varices                    | 151     | 9 (6.0%)/23 (15.2%)/26 | 116     | 6 (5.2%)/18 (15.5%)/20 | 35      | 3 (8.6%)/5 (14.3%)/6 | 0.965   |
| Treatment                             |         |             |         |               |         |           |         |
| Endoscopic Treatment                  | 173     | 139 (80.3%) | 131     | 104 (79.4%) | 42      | 35 (83.3%) | 0.576   |
| Sengstaken Blakemore                  | 173     | 1 (0.6%)   | 131     | 0 (0%)       | 42      | 1 (2.4%)  | 0.077   |
| Somatostatin and/or Octreotide        | 173     | 160 (92.5%) | 131     | 119 (90.8%) | 42      | 41 (97.6%) | 0.447   |
| Blood Transfusion                     | 173     | 88 (50.9%) | 131     | 62 (47.3%)  | 42      | 26 (61.9%) | 0.100   |
| PPIs                                  | 173     | 173 (100%) | 131     | 131 (100%)  | 42      | 42 (100%) | NA      |
| Surgery                               | 173     | 0 (0%)     | 131     | 0 (0%)       | 42      | 0 (0%)    | NA      |
| 5-day Re-bleeding After Treatment     | 172     | 13 (7.6%)  | 130     | 9 (6.9%)    | 42      | 4 (9.5%)  | 0.579   |
| Death During Hospitalization          | 173     | 4 (2.3%)   | 131     | 3 (2.3%)    | 42      | 1 (2.4%)  | 0.973   |
| Length of Stay (days)                 | 173     | 10.10 (0.12-32.94) | 131     | 10.10 (0.12-32.94) | 42      | 10.28 (5.02-31.06) | 0.335   |
| Total Payment (¥)                     | 173     | 24,328.31 (3,427.24-98,215.78) | 131     | 22,685.20 (3,427.24-98,215.78) | 42      | 25,213.81 (9,970.37-81,125.52) | 0.166   |

Data are expressed as median (range) or frequency (percentage). 

**Abbreviations.** AUGIB: acute upper gastrointestinal bleeding; HBV: Hepatitis B virus; HCV: Hepatitis C virus; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; MELD: model for end-stage liver disease; ALBI: albumin-bilirubin; PPIs: proton pump inhibitors; ¥: Renminbi.
Table 4: Characteristics of patients with liver cirrhosis and AUGH after propensity matching in validation cohort.

| Variables                                         | Overall (n=40) | Propensity matching patients | P value |
|---------------------------------------------------|----------------|-------------------------------|---------|
|                                                   |                | Regular hours (n=20)          |         |
|                                                   |                | Off-hours (n=20)              |         |
| Age (years)                                       | 56.86 (20.57-75.64) | 60.64 (20.57-75.64) | 55.52 (35.18-74.33) | 0.160 |
| Sex (male)                                        | 28 (70%)       | 13 (65%)                      | 15 (75%) | 0.490 |
| Etiology of Liver Diseases                        |                |                               |         |
| HBV                                               | 9 (22.5%)      | 4 (20%)                       | 5 (25%)  | 0.622 |
| HCV                                               | 4 (10%)        | 2 (10%)                       | 2 (10%)  |         |
| Alcohol Abuse                                     | 14 (35%)       | 7 (35%)                       | 7 (35%)  | 0.997 |
| Drug Related                                      | 2 (5%)         | 0 (0%)                        | 2 (10%)  |         |
| Autoimmune Liver Diseases                         | 1 (2.5%)       | 1 (5%)                        | 0 (0%)   |         |
| Other or Undeclared Etiology                      | 10 (25%)       | 6 (30%)                       | 4 (20%)  |         |
| Laboratory Tests                                  |                |                               |         |
| Red Blood Cell (10^12/L)                          | 2.625 (1.65-3.89) | 2.58 (1.69-3.89) | 2.705 (1.65-3.78) | 0.968 |
| Hemoglobin (g/L)                                  | 74.50 (38.00-126.00) | 77.00 (53.00-122.00) | 72.50 (38.00-126.00) | 0.473 |
| White Blood Cell (10^3/L)                         | 4.40 (1.80-14.90) | 4.40 (2.20-11.70) | 4.35 (1.80-14.90) | 0.839 |
| Platelet Count (10^9/L)                           | 72.50 (2700-301.00) | 72.50 (2700-301.00) | 72.00 (32.00-145.00) | 0.978 |
| Total Bilirubin (umol/L)                          | 18.10 (5.50-106.10) | 16.85 (5.50-50.90) | 18.10 (8.50-106.10) | 0.256 |
| Direct Bilirubin (umol/L)                         | 7.85 (2.20-60.10) | 7.10 (2.20-41.50) | 7.95 (3.00-60.10) | 0.675 |
| Indirect Bilirubin (umol/L)                       | 9.50 (2.80-46.00) | 8.55 (2.80-22.10) | 10.00 (5.40-46.00) | 0.148 |
| Albumin (g/L)                                     | 30.65 (18.00-39.20) | 30.85 (19.00-38.60) | 30.00 (18.00-39.20) | 0.117 |
| Alanine Aminotransferase (U/L)                    | 21.805 (6.79-88.77) | 21.805 (9.44-72.47) | 20.415 (6.79-88.77) | 0.756 |
| Aspartate Aminotransferase (U/L)                   | 25.635 (10.74-136.00) | 28.38 (11.00-88.79) | 25.635 (10.74-136.00) | 0.978 |
| Alkaline Phosphatase (U/L)                        | 80.10 (40.34-234.00) | 80.94 (40.34-234.00) | 78.245 (46.24-149.45) | 0.705 |
| Gamma-glutamyl Transpeptidase (U/L)               | 41.245 (7.69-295.00) | 40.48 (13.71-254.00) | 42.765 (7.69-295.00) | 0.955 |
| Blood Urea Nitrogen (mmol/L)                      | 7.395 (2.98-18.83) | 7.055 (2.98-18.83) | 8.40 (4.65-18.72) | 0.245 |
| Serum Creatinine (umol/L)                         | 70.11 (3.90-143.10) | 66.68 (42.60-95.20) | 74.235 (34.90-143.10) | 0.177 |
| Potassium (mmol/L)                                | 3.95 (3.10-4.66) | 3.88 (3.10-4.66) | 3.98 (3.27-4.59) | 0.330 |
| Sodium (mmol/L)                                   | 139.10 (124.00-145.70) | 138.50 (135.00-141.40) | 139.45 (124.00-145.70) | 0.279 |
| PT (seconds)                                      | 15.80 (13.30-24.50) | 15.40 (13.30-23.90) | 16.05 (13.50-24.50) | 0.417 |
| APTT (seconds)                                    | 36.25 (30.80-47.50) | 35.90 (30.80-45.20) | 37.15 (32.20-47.50) | 0.351 |
| INR                                               | 1.275 (1.02-2.19) | 1.255 (1.08-2.08) | 1.31 (1.02-2.19) | 0.516 |
| Child-Pugh Score                                  | 8.00 (5.00-12.00) | 8.00 (5.00-12.00) | 7.00 (5.00-12.00) | 0.836 |
| Child-Pugh A/B/C                                  | 14 (35%)/22 (55%)/4 | 7 (35%)/12 (60%)/1 | 7 (35%)/10 (50%)/3 | 0.544 |
| MELD Score                                        | 5.82 (-2.38-23.19) | 5.51 (-1.04-14.75) | 6.51 (-2.38-23.19) | 0.245 |
Table 4: Continued.

| Variables                                      | Overall (n=40) | Regular hours (n=20) | Off-hours (n=20) | P value |
|------------------------------------------------|----------------|----------------------|-----------------|---------|
| Recalibrated MELD Score                        | -4.11 (-5.80--0.51) | -4.17 (-5.53--2.26) | -3.96 (-5.80--0.51) | 0.245   |
| ALBI Score                                     | -1.67 (-2.62--0.49) | -1.73 (-2.44--0.49) | -1.67 (-2.62--0.60) | 0.787   |
| Esophageal Varices (No/Mild/Moderate/Severe)   | 2 (5%)/5 (12.5%)/6 | 1 (5%)/3 (15%)/3 | 1 (5%)/2 (10%)/3 | 0.971   |
| Treatment                                      |                |                      |                 |         |
| Endoscopic Treatment                           | 38 (95%)       | 19 (95%)             | 19 (95%)        | 1       |
| Sengstaken Blakemore                           | 0 (0%)         | 0 (0%)               | 0 (0%)          | NA      |
| Somatostatin                                   | 39 (97.5%)     | 20 (100%)            | 19 (95%)        | 0.311   |
| Blood Transfusion                              | 21 (52.5%)     | 9 (45%)              | 12 (60%)        | 0.342   |
| PPIs                                           | 40 (100%)      | 20 (100%)            | 20 (100%)       | NA      |
| Surgery                                        | 0 (0%)         | 0 (0%)               | 0 (0%)          | NA      |
| 5-day Re-bleeding After Treatment              | 5 (12.5%)      | 2 (10%)              | 3 (15%)         | 0.633   |
| Death During Hospitalization                   | 1 (2.5%)       | 0 (0%)               | 1 (5%)          | 0.311   |
| Length of Stay (days)                          | 11.95 (5.73-31.06) | 11.95 (5.73-21.95) | 11.28 (7.52-31.06) | 0.441   |
| Total Payment (¥)                             | 24,961.33      | 25,985.45            | 24,961.33       | 0.829   |

Data are expressed as median (range) or frequency (percentage).

Abbreviations. AUGIB: acute upper gastrointestinal bleeding; HBV: Hepatitis B virus; HCV: Hepatitis C virus; PT: Prothrombin time; APTT: activated partial thromboplastin time; INR, International normalized ratio; MELD: model for end-stage liver disease; ALBI: albumin-bilirubin; PPIs: proton pump inhibitors; ¥: Renminbi.
hospitalization. However, the interval of rebleeding was not specified in the meta-analysis. As we have known, the length of stay was usually associated with the severity of illness [24]. In addition, as well known, liver dysfunction as estimated by Child-Pugh score and MELD score were risk factors for mortality of cirrhotic patients with AUGIB [25–27].

Two of the published meta-analyses [16,17] demonstrated a significant weekend effect on the mortality in patients with nonvariceal UGIB, but not those with variceal bleeding. This finding seemed to be consistent with our results regarding mortality. Notably, our study focused on the outcomes during hospitalization, but not those after discharge. The fact is readily understood that admission time mainly influenced the in-hospitalization outcomes but marginally influenced the outcomes after discharge. Indeed, a meta-analysis also suggested that off-hours admission negatively influenced inhospital mortality (P=0.009), rather than 30-day mortality (P=0.116).

Our study has the following advantages. First, we refined the definitions of off-hours admission. Second, we included a test cohort and a validation cohort which can reduce the sampling bias to some extent. Third, we employed a propensity score matching analysis. Thus, the patient characteristics, especially Child-Pugh and MELD scores which are significantly associated with prognosis of liver cirrhosis, are comparable between the two groups. Our results become more stable. However, the major drawback of our study should be that not all patients undergo endoscopy to evaluate the source of bleeding. Additionally, the sample size is not adequate in the validation cohort. Finally, a potential selection bias could not be neglected due to the retrospective nature of this study.

In conclusion, off-hours admission might not be associated with outcomes in patients with liver cirrhosis and AUGIB. However, the geographical difference should not be neglected to extrapolate our findings.

Abbreviations
AUGIB: Acute upper gastrointestinal bleeding
UGIB: Upper gastrointestinal bleeding
INR: International normalized ratio
PPIs: Proton pump inhibitors
MELD: Model for end-stage liver disease
ALBI: Albumin-bilirubin.

Data Availability
The data used to support the findings of this study are available from the corresponding author upon request.

Disclosure
Yingying Li and Bing Han are co-first authors.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Authors’ Contributions
Yingying Li reviewed and searched the literature, wrote the protocol, collected the data, performed the statistical analysis, interpreted the data, and drafted the manuscript. Bing Han and Tingxue Song performed the statistical analysis and critical revision of the manuscript for important intellectual content. Wenchun Bao, Ran Wang, Zhaohui Bai, Kexin Zheng, and Qianqian Li collected the data and revised the manuscript. Hongyu Li and Xiaozhong Guo checked the data and gave critical comments. Xingshun Qi conceived the work, wrote the protocol, performed the statistical analysis, interpreted the data, and revised the manuscript. All authors have made an intellectual contribution to the manuscript and approved the submission. This work was partially presented at the 18th Congress of Gastroenterology China that was held in Dalian, China on September 2018.

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Supplementary Materials
Supplementary Table 1. Treatment of cirrhotic patients with AUGIB at different departments from our hospital in test cohort. Supplementary Table 2. Subgroup analyses of patients with liver cirrhosis and AUGIB based on the origin of bleeding in test cohort. Supplementary Table 3. AUGIB patients with endoscopically confirmed varices after propensity matching analysis in test cohort. (Supplementary Materials)

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