

Swansea criteria score in acute fatty liver of pregnancy

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To the Editor: Acute fatty liver of pregnancy (AFLP) is an uncommon but potentially fatal disease unique to pregnancy that typically occurs in the third trimester and is one of the leading causes of maternal mortality in critically ill patients.^[1] The Swansea diagnostic criteria have been widely used in the diagnosis of AFLP worldwide since their proposal. The Swansea criteria include clinical symptoms and laboratory tests, imaging, and pathological examination results. Some studies have shown that the Swansea criteria score is a potential clinical tool for evaluating disease severity.^[2] The clinical symptoms lack specificity, and a pathological examination cannot be performed in most patients; therefore, the most important criteria are based on the laboratory examination results. In these criteria, the laboratory examination results mainly reflect dysfunction in the following: liver (total bilirubin $>14 \mu\text{mol/L}$, aspartate aminotransaminase [AST] or alanine aminotransferase [ALT] $>42 \text{ U/L}$, coagulopathy [prothrombin time $>14 \text{ s}$ or activated partial thromboplastin time $>34 \text{ s}$], low blood glucose $<4 \text{ mmol/L}$, elevated blood ammonia $>47 \mu\text{mol/L}$), kidney (serum creatinine $>150 \mu\text{mol/L}$), and blood (leukocyte count $>11 \times 10^9/\text{L}$). If the damage to a patient organ is aggravated, the Swansea criteria score will increase. However, it is unclear whether the Swansea criteria score could be useful for assessing maternal and fetal complications in patients with AFLP.

In this study, patients with AFLP admitted to Beijing Ditan Hospital, Capital Medical University from January 2008 to January 2018 were rescored using the Swansea criteria. We assessed the value of the Swansea criteria score for predicting maternal and fetal complications in Chinese patients with AFLP. Patient selection was based on the following criteria: (i) appearance of unexplained vomiting, anorexia, fatigue, abdominal pain, and progressive icterus in the third trimester of pregnancy; (ii) biochemical data showing decreased fibrinogen levels, increased coagulation time, elevated serum bilirubin (total bilirubin $>14 \mu\text{mol/L}$), and elevated serum transaminase activity (ALT

or AST, $300\text{--}500 \text{ U/L}$; normal value $<42 \text{ U/L}$); and (iii) the absence of another explanation such as hepatitis due to infection, drugs, poisoning, extra- or intra-hepatic cholestasis.^[3] The diagnosis of all selected cases was reassessed using the Swansea criteria. Meeting six or more criteria was required to diagnose AFLP. Postpartum hemorrhage, acute liver failure, acute renal impairment, and hypoglycemia were defined in accordance with the criteria. This study was approved by the local research Ethics Committee of Beijing Ditan Hospital, Capital Medical University including the entire study design, methods, and consent procedure used in this study (Approval number: PX 2017019). The data were collected anonymously.

Among the 24,054 pregnant patients admitted to the Department of Obstetrics and Department of ICU, Beijing Ditan Hospital from January 2008 to January 2018, 73 patients were diagnosed with AFLP (0.303%). Approximately, 11.0% (8/73) of these patients had signs of preeclampsia. Among these 73 cases, the mean gestational age at birth was 35.8 ± 2.3 weeks, and the mean maternal age was 27.6 ± 4.5 years. There were no cases of triplet pregnancy and there were eight cases of twin pregnancies. Fatality rates were 4.1% (3/73) for mothers and 17.3% (14/81) for fetuses.

As the 73 cases were reassessed using the Swansea criteria, only seven (9.6%) cases presented with fewer than six features and sixty-six (90.4%) cases were positive for six or more Swansea criteria features. The seven cases who did not fulfill the Swansea criteria were also diagnosed with AFLP in the absence of other explanations.

In this study, we found that the Swansea criteria scores were statistically significant for predicting major complications, such as acute liver failure, hepatic encephalopathy, coma, acute kidney injury, pulmonary edema, and gastrointestinal bleeding, in patients with AFLP ($P < 0.050$). We also found that the Swansea criteria scores had predictive value for the selection of specific treatment options for patients with AFLP, particularly

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Table 1: AUC of ROC and cutoff value of Swansea criteria in predicting maternal and fetal complications and treatment in AFLP patients (n = 73).

Maternal complications	n	AUC of ROC	P	Cut-off value	Sensitivity	Specificity
Acute liver failure	30	0.726 ± 0.062	0.001	8	0.767	0.674
Hepatic encephalopathy	18	0.773 ± 0.061	0.001	8	0.883	0.600
Coma	15	0.774 ± 0.069	0.001	7	0.923	0.583
Acute renal failure	13	0.796 ± 0.058	0.001	8	0.759	0.684
Acute renal injury	54	0.784 ± 0.063	≤0.001	8	0.605	0.971
Artificial liver treatment	16	0.733 ± 0.070	0.005	8	0.813	0.579
Continuous renal replacement therapy	12	0.805 ± 0.062	0.001	8	0.953	0.426
Intrauterine distress	19	0.694 ± 0.064	0.012	7	0.917	0.574
Fetal stillbirth	6	0.894 ± 0.044	0.001	10	0.833	0.866
Neonatal asphyxia	29	0.741 ± 0.058	0.001	7	0.833	0.866
Neonatal death	5	0.787 ± 0.058	0.033	9	0.956	0.632

AFLP: Acute fatty liver of pregnancy; ROC: Receiver operating characteristic; AUC: Area Under Curve.

artificial liver treatment and continuous renal replacement therapy ($P < 0.050$). We also used the receiver operating characteristic (ROC) curves to evaluate the value of the Swansea criteria in predicting fetal and neonatal complications in patients with AFLP [Table 1]. Studies have shown that the Swansea criteria scores are statistically significant for predicting major complications, such as intrauterine distress, intrauterine fetal death, neonatal asphyxia, and neonatal death, in fetuses and neonates ($P < 0.050$).

The results demonstrated that a predicted cutoff value of seven in the Swansea criteria was useful for predicting coma, intrauterine distress, and neonatal asphyxia, and a cutoff value of eight was useful for predicting acute liver failure, hepatic encephalopathy, acute renal failure, acute renal injury, artificial liver treatment, and continuous renal replacement. The results showed that cutoff values of nine and ten could predict neonatal death and fetal death, respectively [Table 1].

AFLP is an uncommon, but potentially fatal disease occurring in the late stage of pregnancy or in the early puerperium with micro-vesicular fatty infiltration of the liver, which can induce maternal multiorgan failure or even death of the mother and fetus. Prospective and retrospective studies suggest an incidence ranging from 1/7000 to 1/20,000 pregnancies.^[4] The prevalence in this study was 1/330 which was much higher than previous studies, which may be because our hospital is a liver disease specialty hospital in North China. In this cohort, the maternal and fetal mortality rates were 4.1% and 17.3%, which is similar to a previous report.^[4]

Among the 73 patients who were initially diagnosed using the Williams Obstetrics criteria, 66 patients (90.4%) were confirmed using the Swansea criteria. The gold standard for AFLP diagnosis is liver biopsy; however, it is rarely performed in pregnant patients because of the risk of bleeding. In this cohort, patients were usually diagnosed on the basis of clinical and laboratory findings. The most common features in our study were elevated serum ALT or AST (97.3%), elevated

serum bilirubin (93.2%), leukocytosis ($>11 \times 10^9/L$; 84.9%), and subsequent coagulopathy (82.2%).

A large national cohort study showed that there was substantial agreement between the clinical diagnosis of cases and the Swansea criteria, and the authors suggested that these diagnostic criteria may be adopted as an objective measure in future studies.^[4] Knight and Goel demonstrated a high level of agreement between clinical assessment and the Swansea criteria and a high level of agreement between the Swansea criteria and histological diagnosis of hepatic micro-vesicular steatosis, respectively.^[5,6] This study verified the relevance of the Swansea criteria for maternal and neonatal complications.

In this study, we used the diagnostic criteria proposed by Ch'ng *et al*^[7] in Swansea. In this study, we found that the Swansea criteria score was not only significantly associated with maternal complications and fetal complications, but also the treatment required for the mother. Our study shows that the Swansea criteria score could predict major complications in patients with AFLP such as acute liver failure, hepatic encephalopathy, coma, acute renal injury, and pulmonary edema. The cutoff score to predict liver and kidney complications was eight points. Although pulmonary edema is not a direct complication of AFLP, the incidence of pulmonary edema in patients with AFLP is increased because of the fluid overload after pregnancy and the presence of acute renal failure.

This study also found that the Swansea criteria score was insufficient for predicting some of the rarer complications of AFLP, such as postpartum hemorrhage, placental abruption, and acute pancreatitis. This study found that the Swansea criteria score has predictive value for the choice of treatment options for major complications, especially plasma exchange and continuous renal replacement therapy, which both had cutoff values of eight points. This suggests that in patients with a score $>$ eight points, it is necessary to actively evaluate the complications of liver and renal failure and take targeted treatment in a timely manner.

This study shows that Swansea criteria scores have good predictive value for intrauterine distress, intrauterine fetal death, neonatal asphyxia, and neonatal death. In patients with a score >seven points, clinicians need to be alert to the possibility of various fetal and neonatal complications. In patients with a score >nine points, it is necessary to assess the potential for fetal death in a timely manner and be alert to the possibility of neonatal death. Wang *et al*^[2] reported that patients who were positive for seven or more criteria had a significantly higher risk of stillbirth and a higher rate of continuous blood purification treatment. Our findings are similar. Wang *et al*^[2] also found that the area under the ROC curve for postpartum hemorrhage was 0.670, which reached statistical significance ($P = 0.040$). We did not find the same result, which may be related to the difference in the number of samples in the two studies.

The Swansea criteria are still in the process of continuous improvement. If a patient has serious postpartum hemorrhage due to coagulopathy but does not have liver and kidney failure as the main manifestation, it can be seen from the results of this study that the score may not play an early warning role.

Other studies showed that when using the Swansea criteria for the diagnosis of AFLP, using pregnancy-specific and/or laboratory-specific reference intervals is recommended.^[8] Therefore, we suggest that the subjective symptom score in the Swansea criteria can be appropriately reduced in order to more reasonably judge the patient's condition changes.

In conclusion, this study shows that the Swansea criteria score may be useful for assessing disease severity in patients with AFLP, and it can partially predict maternal and fetal complications. The diagnostic criteria can be applied in clinical practice and should be continuously improved.

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Conflicts of interest

None.

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