Acute-on-chronic liver failure: A predictor of poor prognosis in patients with variceal bleeding or a risk factor for variceal bleeding?

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Acute-on-chronic liver failure (ACLF) is a dangerous condition defined by organ failure and increased short-term mortality. Therefore, it is not surprising that ACLF is associated with higher mortality after variceal bleeding in cirrhotic patients. However, limited direct data are available regarding this issue.

In this issue of Clinical and Molecular Hepatology, Shin et al. investigated whether the diagnosis of ACLF after variceal bleeding was associated with subsequent survival. The prevalence of ACLF was 13% among patients with acute deterioration of chronic liver disease following acute variceal bleeding. The overall survival of patients with ACLF was lower compared to those without ACLF, and a higher ACLF grade was related to lower overall survival. Recently, Trebicka et al. first reported that 17.8% of 2,138 patients with acute variceal bleeding had ACLF at admission, and that the presence of ACLF was independently related to rebleeding and mortality. Therefore, we assumed that 10–20% of cases involving acute variceal bleeding may experience ACLF at admission or during hospitalization, suggesting the need for careful evaluation of patients with variceal bleeding. The diagnosis of ACLF requires adequate management by physicians to reverse the clinical course.

According to Shin et al., the 28-day cumulative mortality was as high as 41% in patients with variceal bleeding and ACLF, which indicates a very high risk of mortality in this group. However, the mortality of patients with variceal bleeding in case of decompensated cirrhosis might be higher than that in the former. In the study population of Shin et al., these patients were excluded. Therefore, we could not compare the mortality between the two groups. Based on a clinical perspective, it is sometimes difficult to differentiate ACLF from aggravation of decompensated cirrhosis. Although ACLF is defined by acute aggravation in patients with reversible liver function, the prognosis of ACLF grade 3 is poor and may be irreversible. In this study, patients with variceal bleeding and ACLF grade 3 showed very poor overall survival (<10% in 90 days). Therefore, liver transplantation is imperative in such cases similar to aggravated decompensated cirrhosis.

Unfortunately, this study did not suggest the optimal treatment option for variceal bleeding in ACLF patients in their cohort due to
limited database. The clinical course may be changed if early tran-
jugular intrahepatic portosystemic shunt (TIPS) is used to control
active variceal bleeding or secondary prevention of rebleeding.
Several studies showed that patients with early or pre-emptive
TIPS had a lower rebleeding risk and higher overall survival, even
in ACLF patients. However, the aggravation of liver failure in se-
vere decompensated cirrhosis still remains a concern. Lv et al. re-
ported that early TIPS with covered stents improved transplantation-free survival in selected patients with advanced cirrhosis
Child B or C and acute variceal bleeding compared to standard
treatments, such as endoscopic band ligation and beta-blockers
following salvage TIPS as needed. The proportion of ACLF cases
in their study is unknown. Therefore, further studies are needed
to determine the indications for early TIPS in ACLF patients.

Finally, it is unclear whether ACLF induces variceal bleeding or
vice versa in each case. In patients with ACLF, hepatic venous
pressure gradient was elevated, which increases the risk of varice-
al bleeding. Also, in case of variceal bleeding, subsequent hypoxic
hepatitis may induce liver and renal failure and hepatic encepha-
lopathy in chronic liver disease. According to Joshi et al., variceal
bleeding was the most frequent morbidity accompanying ACLF
among 30% of the patients in their cohort. Both studies by Shin
et al. and Trebicka et al. did not reveal the temporal relationship
between variceal bleeding and ACLF. Therefore, we could not
compare the survival according to the order of the two pathologic
conditions. Generally, the baseline characteristics of patients with
underlying ACLF followed by variceal bleeding might be poorer
than those of patients manifesting ACLF after variceal bleeding.
However, the precise prognosis of both groups remains unknown,
and requires further analysis.

The greatest limitation of Shin’s study was the lack of informa-
tion related to technical issues involving endoscopic treatment.
Due to coagulopathy and cytopenia, variceal bleeding is some-
times difficult to control via endoscopic approach. Hemodynamic
instability in ACLF may interfere with endoscopy due to hypoten-
sion. Early access and advances in endoscopic approach might re-
duce the risk of mortality in ACLF associated with variceal bleed-
ing.

ACLF is probably a predictive factor of poor prognosis after vari-
ceal bleeding, based on the results of recent and current studies.
Regardless of the order of events, it is possible that ACLF and vari-
ceal bleeding may influence each other with negative synergism,
which facilitates the clinical monitoring of patients for possible
multi-organ failure or bleeding events.

Conflicts of Interest

The authors have no conflicts of interests to disclose.

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