Survival of patients with cirrhosis after acute variceal bleeding

E d i t o r i a l

Acute bleeding from ruptured esophagogastric varices is one of the most serious complications of cirrhosis. In the last few decades mortality in this setting has decreased from 42% in 1981, the year when the classic study by Graham and Smith was published, to 15-20% in present day (1-4). This improvement reflects the effectiveness of standard therapy, which consists of combined vasoactive drugs since admission, early endoscopic therapy, and prophylactic antibiotic therapy, with a failure rate of 15% (3-6). Mortality occurs precisely in patients with hemorrhage refractory to standard treatment, either because of failed bleeding management or as a result of early rebleeding, which may occur in nearly 70% of cases (3).

On assessing the prognosis of a bleeding episode, any demise occurring within 6 weeks (42 days) after said episode is considered to be related to it, since death risk returns to baseline values subsequently (7). In these 6 weeks, the most critical period includes the initial 5 days, where nearly 40% of deaths occur and during which rescue therapies are attempted and resource use increases. During these initial 5 days, 60% of deaths result from rebleeding and the remaining 40% from liver failure and hepatorenal syndrome, whereas these numbers are transposed for days 5 to 42.

The prognosis of cirrhotic patients with acute variceal hemorrhage depends on the severity of liver disease and on bleeding volume. The extent of liver failure conditions both long-term survival and the patient's ability to endure the additional damage entailed by acute hemorrhage. The latter puts the patient at risk of exanguination and compromises the liver's functional reserve and renal perfusion. This explains why liver failure markers (such as the Child-Pugh stage) and hemorrhage severity indicators (active bleeding at endoscopy, hematocrit, transfusional needs, and blood pressure) are among the factors that predict an early failure of bleeding control. In turn, mortality predictors from week 6 on are associated with liver failure extent rather than bleeding severity.

There is currently a growing interest in identifying predictors for failed hemorrhage control and early rebleeding in order to stratify patients with acute variceal bleeding into different risk groups. This would allow individualized patient treatment according to risk. In this respect, Abraldes et al. have published a study where they demonstrate that a model based on Child-Pugh staging, systolic blood pressure at admission, and cirrhosis etiology is highly effective to screen patients with a high risk of uncontrolled hemorrhage, early rebleeding and/or death within the first 5 days (8).

In other models, as in the one published by Sempere et al. in this issue of *Revista Española de Enfermedades del Aparato Digestivo,* the goal is focused on assessing the long-term prognosis of cirrhotic patients suffering from acute variceal bleeding (9). Sempere et al. studied the ability of various variables to foretell survival at 3 and 12 months (short and long term, respectively) for patients with cirrhosis who had an acute variceal bleeding event. The authors used data from a cohort of 215 patients who had a

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total of 270 variceal bleeding episodes, and who were cared for in their Unit between 1996 and 2003. Of all 215 patients included, 46 (48%) died within 6 weeks and 50 (52%) died at a later time. In the multivariate analysis independent mortality variables included age ≥ 65 years, presence of hepatocellular carcinoma, Child-Pugh ≥ 10, and MELD ≥ 18. In the short term variables with the highest predictive power included the presence of hepatocellular carcinoma and MELD, whereas in the long term age was the one variable increasing between-group differences. The discriminative power of MELD was always higher than that of the Child-Pugh system, but differences were attenuated for long-term prediction. On the other hand survival predictors change with cirrhosis stage, and in a cohort of decompensated patients, as is the case with this study, Child-Pugh and MELD scores, besides age and presence of liver carcinoma, are the factors most commonly included in survival models (10,11).

An added value of the study by Sempere et al. is the absence of selection regarding the analyzed cohort, which allowed for instance the identification of hepatocellular carcinoma as a prognostic factor. This is in contrast to results from a similar study by Bambah et al., where the analyzed cohort was part of a randomized study on the use of vasoactive drugs for patients with variceal bleeding from which subjects with known liver carcinoma were excluded (12). Age is another predictor identified in the study by Sempere et al., and its robustness has already been noted by a number of studies regardless of cirrhosis stage (10). Another added value of the study by Sempere et al. is having tested the usefulness of MELD to predict survival at 36 months.

The results from the study by Sempere et al. are consistent with those reported by other authors, which reveal a link between liver disease severity (as defined by Child-Pugh or MELD scores) and mortality at 6 weeks after a bleeding event (3,10,12). The superiority of MELD over the Child-Pugh scale is likely related to the creatinine index, which allows assessing the prognostic significance of renal failure (13). It is not by chance that the predictive power of both indices was demonstrated in this setting if we bear in mind that both were initially designed to estimate the prognosis of patients with variceal bleeding undergoing portosystemic shunt – surgically for Child-Pugh, percutaneously for MELD.

Major limitations of the study by Sempere et al. include retrospective data collection, and potential treatment changes during the analyzed period of time, which is not mentioned in the study's description. Prognostic models for variceal bleeding must be based on patient cohorts with standard treatment, including early administration of vasoactive drugs and prophylactic antibiotic therapy. On the other hand, having data available on the severity of bleeding episodes, which strongly conditions survival and allows prognostic estimates at 5 days and 6 weeks, would have been most interesting.

MELD has proven an accurate, objective tool for cirrhosis severity assessment. The study by Sempere et al. shows that estimates at 24 hours after admission are also useful to predict mortality in patients with cirrhosis and acute variceal bleeding. In addition, the study identified two factors with relevant prognostic value – presence of hepatocellular carcinoma and age. A MELD score ≥ 18 and a diagnosis of hepatocarcinoma identify patients with a poorer prognosis at 12 weeks, and who may benefit from a rapid assessment of their eligibility for liver transplantation. In the longer term age ≥ 65 years is the factor making a significant difference between groups.

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Supervivencia de pacientes con cirrosis tras la primera hemorragia aguda por varices esofágicas

La hemorragia aguda por rotura de varices esofagogástricas es una de las complicaciones más graves de la cirrosis. En las últimas décadas, su mortalidad ha disminuido desde el 42% en 1981, fecha en la que se publica el estudio clásico de Graham y Smith, hasta el 15-20% actual (1-4). Esta mejoría refleja la eficacia del tratamiento estándar consistente en la combinación de fármacos vasoactivos desde el momento del ingreso, terapia endoscópica precoz y antibioterapia profiláctica, cuya tasa de fracaso es del 15% (3-6). La mortalidad se produce precisamente en los pacientes en los que la hemorragia es refractaria al tratamiento estándar, bien por falta de control de la hemorragia o por resangrado precoz, en los que puede alcanzar una cifra cercana al 70% (3).