

Editorial

## Mortality prediction of cirrhotic patients admitted to the Intensive Care Unit

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Key words: Cirrhosis, chronic liver disease, epidemiology, Mexico.

## Commentary

Chronic liver diseases are a major health issue worldwide.<sup>1</sup> In Mexico, cirrhosis mortality is among the highest of the world, being the third cause of death in the general population and the second in young adults (15-64 years) during 2005.<sup>2,3</sup> Furthermore, a steady rise in the number of cases is expected up to 2050.<sup>4</sup>

Acute deterioration of chronic liver disease due to variceal bleeding, infection/sepsis, grade III/IV hepatic encephalopathy, hepatorenal syndrome, overlapped alcoholic or viral hepatitis represents a critical situation that frequently requires management in an Intensive Care Unit (ICU) setting. Although the term acute-on-chronic liver failure has been proposed to cover these situations, no clear definition or consensus are available at the moment, mainly due to the heterogeneity of causes, modes of presentation and prognosis.<sup>5</sup>

The admittance of a cirrhotic patient to the ICU brings several questions. *First*, does the patient *really* require admittance to the ICU? In other words: how sick should an endstage liver disease patient be, to get admitted to the ICU? *Second*, how much «residual liver function» does the patient have? Is the patient a candidate for liver transplantation? *Third*, what outcome is expected if the patient recovers from this event?

Type 1 hepatorrenal syndrome could serve as an example. Its mortality is high at mid-term; and although available therapies prolong survival, no resolution is ex-

Manuscript received and accepted: 28 December 2007 and January 14 2008

pected with medical therapy alone, which acts as a bridge to liver transplantation. Therefore, if the patient is not a candidate for liver transplantation, probably he will not be a candidate for ICU admittance. Intermediate examples are plenty: hypovolemic shock secondary to variceal bleeding, septic shock, grade IV hepatic encephalopathy, severe alcoholic hepatitis. In all of these circumstances the decision to admit a patient to the ICU can be difficult.

Around the world, the costs generated in the ICUs alone ascend to 20–30% of total hospital costs in developed countries.<sup>6,7</sup> The use of sophisticated technology (MARS, bioartificial livers, etc.) and expensive medical care in critically-ill cirrhotics has produced an increased awareness of the need to optimize the use of resources available. In addition, liver transplantation currently offers proven long-term survival.<sup>8</sup> This scenario requires reliable prognostic factors to construct algorithms for critically-ill cirrhotics. Furthermore, it is mandatory to have scientific basis to assess when ICU admission will be futile for a patient's outcome and quality of life.

Scoring systems to predict mortality have been validated in cirrhotics admitted to ICU; and even if they show similar performance compared with established scoring systems<sup>9,10</sup> to the date no study has compared every single scale in the same cohort of patients, rising the question if any is superior to the others.

For the intention of this commentary, scoring systems can be grouped in two categories: first, «specific» scoring systems created specifically for cirrhotic patients, such as Child-Turcotte-Pugh Scale (CTP) and the Model for End-stage Liver Disease (MELD);<sup>11,12</sup> and second, «general» scoring systems designed for any patient admitted to the ICU; such as Organ System Failure (OSF) scale,<sup>13</sup> Acute Physiology and Chronic Health Evaluation (APACHE) I, II and III scale,<sup>14-16</sup> Sequential Organ Failure Assessment scale (SOFA)<sup>17</sup> and the Risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function and end-stage renal disease (RI-FLE).<sup>18</sup>

Scales for cirrhotic population were created for its application in a specific setting; CTP was originally developed and later modified to predict mortality in patients undergoing esophageal surgery and MELD was developed to predict mortality in patients undergoing trans-

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jugular intrahepatic portosystemic shunt.<sup>11,12</sup> Both scales has been validated in a number of circumstances and modifications has been proposed, such as MELD-Na and Creatinine-modified CTP.<sup>19,20</sup> However, the evidence of its performance predicting mortality for patients admitted to the ICU is scarce.

Five studies (three from Taiwan and two from Germany) have compared the differences between ROC curves of «general» over «specific» scoring systems;<sup>21-25</sup> showing that «general» scoring system had better discrimination compared with CTP. The area under the curve (AUC) for OSF and SOFA is > 0.80 and it seems to be better than APACHE II and III alone; however, Aggarwal *et al.*,<sup>26</sup> showed that APACHE III combined with the use of adrenergic support and the presence of acute renal failure, had superior prognostic accuracy (AUC 0.91). Cholangitas et al.,<sup>10</sup> found that MELD score (AUC 0.81) have the same discrimination efficiency as SOFA (AUC 0.83). MELD is better than APACHE II and CTP scores (AUC 0.78 and 0.72, respectively).

At the moment, validated scoring systems have an adjuvant role for admittance decision-making to the ICU. Despite some differences proposing «general» scoring systems to be better than «specific» systems, we believe it is necessary to follow a large cohort of patients admitted to the ICU to prospectively evaluate all these predictive strategies, and to design an *ad hoc* scoring system that allows optimal resource allocation for cirrhotic population in the ICUs. Definitively, prospective, large multicenter efforts will yield better results than current single center studies.

## References

- Bosetti C, Levi F, Lucchini F, Zatonski WA, Negri E, La Vecchia C. Worldwide mortality from cirrhosis: an update to 2002. J Hepatol 2007; 46: 827-39.
- National System of Health Information. [Bases de datos en formato de cubo dinámico]. http://sinais.salud.gob.mx/.
- Mendez-Sanchez N, Villa AR, Zamora-Valdes D, Morales-Espinosa D, Uribe M. Worldwide mortality from cirrhosis. Ann Hepatol 2007; 6: 194-5.
- Mendez-Sanchez N, Villa AR, Chavez-Tapia NC, Ponciano-Rodriguez G, Almeda-Valdes P, Gonzalez D, Uribe M. Trends in liver disease prevalence in Mexico from 2005 to 2050 through mortality data. *Ann Hepatol* 2005; 4: 52-5.
- 5. Sen S, Williams R, Jalan R. The pathophysiological basis of acuteon-chronic liver failure. *Liver* 2002; 22 Suppl 2: 5-13.
- Schroeder SA, Sandy LG. Specialty distribution of U.S. physicians—the invisible driver of health care costs. *N Engl J Med* 1993; 328: 961-3.
- Szalados JE. Intensive care unit resource utilization by Medicare patients: margin and mission meet public policy and practice economics. *Crit Care Med* 2004; 32: 2351-2.
- Busuttil RW, Farmer DG, Yersiz H, Hiatt JR, McDiarmid SV, Goldstein LI, Saab S, et al. Analysis of long-term outcomes of 3200 liver transplantations over two decades: a single-center experience. *Ann Surg* 2005; 241: 905-16; discussion 16-8.
- 9. Zauner CA, Apsner RC, Kranz A, Kramer L, Madl C, Schneider B, Schneeweiss B, et al. Outcome prediction for patients with cirrhosis of the liver in a medical ICU: a comparison of the

APACHE scores and liver-specific scoringsystems. *Intensive Care Med* 1996; 22: 559-63.

- 10. Cholongitas E, Senzolo M, Patch D, Kwong K, Nikolopoulou V, Leandro G, Shaw S, et al. Risk factors, sequential organ failure assessment and model for end-stage liver disease scores for predicting short term mortality in cirrhotic patients admitted to intensive care unit. *Aliment Pharmacol Ther* 2006; 23: 883-93.
- Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg* 1973; 60: 646-9.
- Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, D'Amico G, et al. A model to predict survival in patients with end-stage liver disease. *Hepatology* 2001; 33: 464-70.
- 13. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. Prognosis in acute organ-system failure. Ann Surg 1985; 202: 685-93.
- Knaus WA, Zimmerman JE, Wagner DP, Draper EA, Lawrence DE. APACHE-acute physiology and chronic health evaluation: a physiologically based classification system. *Crit Care Med* 1981; 9: 591-7.
- Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985; 13: 818-29.
- Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG, Sirio CA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest* 1991; 100: 1619-36.
- Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, Reinhart CK, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996; 22: 707-10.
- 18. Abosaif NY, Tolba YA, Heap M, Russell J, El Nahas AM. The outcome of acute renal failure in the intensive care unit according to RIFLE: model application, sensitivity, and predictability. *Am J Kidney Dis* 2005; 46: 1038-48.
- 19. Heuman DM, Abou-Assi SG, Habib A, Williams LM, Stravitz RT, Sanyal AJ, Fisher RA, et al. Persistent ascites and low serum sodium identify patients with cirrhosis and low MELD scores who are at high risk for early death. *Hepatology* 2004; 40: 802-10.
- 20. Giannini E, Botta F, Fumagalli A, Malfatti F, Testa E, Chiarbonello B, Polegato S, et al. Can inclusion of serum creatinine values improve the Child-Turcotte-Pugh score and challenge the prognostic yield of the model for end-stage liver disease score in the short-term prognostic assessment of cirrhotic patients? *Liver Int* 2004; 24: 465-70.
- Wehler M, Kokoska J, Reulbach U, Hahn EG, Strauss R. Shortterm prognosis in critically ill patients with cirrhosis assessed by prognostic scoring systems. *Hepatology* 2001; 34: 255-61.
- 22. Tsai MH, Chen YC, Ho YP, Fang JT, Lien JM, Chiu CT, Liu NJ, et al. Organ system failure scoring system can predict hospital mortality in critically ill cirrhotic patients. *J Clin Gastroenterol* 2003; 37: 251-7.
- 23. Tsai MH, Peng YS, Lien JM, Weng HH, Ho YP, Yang C, Chu YY, et al. Multiple organ system failure in critically ill cirrhotic patients. A comparison of two multiple organ dysfunction/failure scoring systems. *Digestion* 2004; 69: 190-200.
- 24. Ho YP, Chen YC, Yang C, Lien JM, Chu YY, Fang JT, Chiu CT, et al. Outcome prediction for critically ill cirrhotic patients: a comparison of APACHE II and Child-Pugh scoring systems. J Intensive Care Med 2004; 19: 105-10.
- 25. Rabe C, Schmitz V, Paashaus M, Musch A, Zickermann H, Dumoulin FL, Sauerbruch T, et al. Does intubation really equal death in cirrhotic patients? Factors influencing outcome in patients with liver cirrhosis requiring mechanical ventilation. *Intensive Care Med* 2004; 30: 1564-71.
- Aggarwal A, Ong JP, Younossi ZM, Nelson DR, Hoffman-Hogg L, Arroliga AC. Predictors of mortality and resource utilization in cirrhotic patients admitted to the medical ICU. *Chest* 2001; 119: 1489-97.