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The paradox of thromboembolic events in trauma patients with cirrhosis

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Abstract

Only ca.1% of trauma patients are cirrhotic but they have a very long hospital stay, and a very high complication rate and mortality rate especially if they need to undergo surgery. Cirrhosis is therefore viewed as an independent risk factor for mortality. Cirrhosis and trauma are a deadly combination. Cirrhosis is still thought to be a prototype of acquired hemorrhagic coagulopathy and as a result cirrhotic trauma patients are often given prophylactic transfusions of blood and blood products although this practice no longer has a scientific basis. It is clear that hemostasis in cirrhotic trauma patients is a "dynamic equilibrium" which can pass from a prothrombotic phase to a frankly hemorrhagic phase without any guarantee that one excludes the other. The standard laboratory tests should no longer be used to monitor the coagulation status of these patients since they do not provide entirely reliable results. Monitoring of the coagulation status of cirrhotic trauma patients should be carried out with the viscoelastic tests ROTEM ® and TEG® which can be used forpoint-of-care testing so that prompt and appropriate treatment is possible not only with transfusions of blood and blood products but with procoagulants or anticoagulants..

Keywords: Cirrhosis and trauma, Cirrhotic coagulopathy, New protocols

Introduction

Although the number of deaths due to liver disease has been declining in some countries, including Italy[1], cirrhosis is the 11th most common cause of death worldwide[2], The number of deaths due to cirrhosis is rising in most areas of the world, notably the USA ,where in 1999-2016 cirrhosis -related mortality increased from 20,661 to 34,174,and it is expected that the number of deaths will triple in the next 20 years[3].In the USA cirrhotic patients account for about 100,000 visits to the Emergency Department per year[4].

Cirrhosis is a very dangerous condition which not only causes dysfunction of the liver parenchyma but affects the function of other organs and body systems. Patients with decompensated cirrhosis can develop various serious complications and cirrhosis has be shown to be an independent risk factor for mortality (5)

Cirrhosis and trauma

Only ca.1% of all trauma patients are cirrhotic but their mortality rate is more than twice that of trauma patients without cirrhosis. If they require emergency surgery the mortality rate can rise to 40-56%. This is directly related to the severity of the traumatic injury (as established by the Revised Trauma Score (RTS) or the Injury Severity Score (ISS) and increases in direct proportion the severity of the patient's cirrhosis as established by the Child-Turcotte-Pugh score. Cirrhotic coagulopathy, anemia and acidosis favor a further increase in the mortality rate [6]

It is important to note that within the first 24 hours after surgery, especially emergency surgery, 33% of cirrhotic patients require blood transfusions, but transfusing more than 6 units of plasma or platelets increases the risk of death. In fact, the postoperative complication rate in cirrhotic trauma patients can exceed 70% and their postoperative stay in the intensive care unit can be very long. This is why cirrhosis and trauma are considered to be a deadly combination [7].

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Therefore, these patients must be very carefully monitored right from the start to ensure that homeostasis is maintained and that they are hemodynamically stable.

Every effort must be made to avoid aggressive treatment associated with a high mortality risk and choose a conservative approach [8]. This sometimes means avoiding invasive methods; surgery, catheterization, percutaneous interventional radiologic or endoscopic procedures, or even a combination, all of which inevitably expose the patient to additional risks especially the risk of bleeding [9].

Cirrhosis has long been regarded as the prototype of acquired bleeding disorders, and this leads surgeons and other medical professionals to give cirrhotic trauma victims prophylactic blood or platelet transfusions [10]. There is, however, no scientific basis for this practice. On the contrary, the literature shows that the risk of hemorrhage in cirrhotic patients who undergo surgery is less than 3% in case of minor surgery, with less than 1% being massive hemorrhage, and that mortality rate of these patients is less than 0.16% [9].

Cirrhotic coagulopathy

Coagulopathy is still a much feared feature of cirrhosis especially in trauma patients, because of the concept of auto-anticoagulation in cirrhotic patients, particularly the "heparin -like effect"

In these patients, endothelial dysfunction results in high levels of thrombomodulin, and is also responsible for the release of heparan sulfate and phosphates due endothelial glycocalix degradation and for a significant increase in interstitial fluid volume. Thus, in addition to auto-heparinization there is hemodiluition which further aggravates the coagulopathy [11, 12].

Moreover, in cirrhotic trauma patients both platelet count and platelet aggregation are reduced. This is another factor predictive of mortality [13].

Another well-known problem is the deficit of vitamin K found in 15% of cirrhotic trauma patients, and especially, the deficit vitamin K dependent clotting factors (VKCFD). Serum levels of antithrombin, protein C and protein S, that are 30-65% of normal further compromises the coagulation system [5].

Hyperfibrinolysis is another potential problem. Early onset hyperfibrinolysis (within the first hour post-trauma) is associated with a mortality rate of up to 88% (14)

In addition these patients are at high risk of developing disseminated intravasxular coagulation (DIC) [15]

However, it should be kept in mind that hemostasis in cirrhotic trauma patients is in what has been defined as a "dynamic equilibrium" [16[. Although 20% are in a hypocoagulable state, 35% have hypercoagulation [5]. The latter have a reduced hepatic ability to clear activated procoagulant factors and at the same time the capacity to produce thrombin, fibrinogen, factor VII and von Willebrand factor for adequate blood coagulation

Moreover it is known that in these patients systemic inflammation can trigger hypercoagulability [17]. In fact, at autopsy undiagnosed thrombotic events are discovered in 50%of cirrhotic patients, especially those with Child-Pugh grade C disease.

However it is essential to keep in mind that the presence of a hypercoagulable state in this type of patient does not exclude the possibility of unexpected bleeding and vice versa [5].

New protocols for monitoring cirrhotic coagulopathy

Old certainties about are crumbling and many dogmas are being challenged. For instance, the widespread practice of using the partial thromboplastin time (PTT), prothrombinn time (PT), the international normalized ratio (INR) and the platelet count to evaluate coagulation in cirrhotic trauma patients continues although these laboratory tests are carried out at up to 0.7 ° C below body temperature and therefore the results are not accurate enough to indicate whether transfusion of blood or blood products is required.

Besides, the literature has demonstrated that transfusions brings the INR back into the normal range in only 0.8% of cirrhotic patients and in 99% of cirrhotic trauma patients cannot normalize the PT [6]

It is therefore essential to avoid errors when treating these patients. Prophylactic transfusions put patients at risk of developing adverse reactions, even transfusion-associated acute lung injury (TRALI) without ensuring any benefits. Transfusions of fresh frozn plasma, cryoprecipitates, prothrombin complex concentrate, vitamin K, and especially recombinant factor VII a should not be given without clearly defined clinical indications because of the risk of thromboembolic events (2).

Currently the best approach is to use viscoelastic tests. Rotational thromboelastometry (ROTEM®) and thromboelastography (TEG®) are carried out at body temperature, around 37°C, with a 5ml sample of venous blood. Since results are available after 15-30 minutes, less time is lost than with laboratory tests, and more importantly the results give a comprehensive picture of the coagulation status of the patient, including the activation or inhibition of the coagulation cascade, fibrinolytic activity and a partial evaluation of platelet function [18].

Viscoelastic tests can be used for reliable point-of-care coagulation testing in all patients and as predictors of mortality in cirrhotic patients. These tests are expensive but can reduce the overall cost of treatment of these high-risk patients. They can help guide blood/blood product transfusion and treatment with vitamin K, tranexamic acid etc [19].

Moreover, these tests, by rapidly identifying hypercoagulability and the risk of thromboembolism, help us to realize when it is necessary to start anticoagulation therapy, which is a real paradox in the management of cirrhotic trauma patients.

Conflict of Interest

Authors have no conflict of interest to disclose

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