M.N. Luu[a,b], D.T. Quach[a,b,*]

[a] *Departamento de Medicina Interna, Universidad de Medicina y Farmacia de la Ciudad de Ho Chi Minh, Ho Chi Minh City, Vietnam*
[b] *Departamento de Gastroenterología, Hospital Nhan Dan Gia Dinh, Ho Chi Minh City, Vietnam*

* Corresponding author at: Department of Internal Medicine, University of Medicine and Pharmacy at Ho Chi Minh City. 217 Hong Bang Street, District 5, Ho Chi Minh 700000, Vietnam. Tel.: +84918080225.
E-mail address: drquachtd@gmail.com (D.T. Quach).

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Periprocedural and perioperative anticoagulation management strategies in liver cirrhosis

Estrategias de manejo perioperatorio y periprocedimiento de la anticoagulación en la cirrosis hepática

Dear Editors,

We have read the consensus statement by Velarde-Ruiz Velasco et al.[1] with great interest and would like to share the following thoughts and questions. It is important to emphasize that there is a significant prevalence of comorbid cardiovascular conditions, such as non-valvular atrial fibrillation, venous thromboembolism, and splanchnic venous thromboembolism of 5%, 7%, and up to 24%, respectively, according to epidemiological data.[2] Moreover, in a cohort study conducted within the time frame of 2012 and 2019, the prescription and use of direct oral anticoagulants (DOACs) increased from 20 to 77%, showing a significant increase in prescription trends with DOACs in the liver cirrhosis population.[2]

Given the above, we strongly believe that special and meticulous care, in a multidisciplinary fashion (e.g., the inclusion of a hematologist or vascular medicine specialist with expertise in thrombosis and hemostasis) should be considered, and reasonable recommendations should be provided within the Velarde-Ruiz Velasco consensus paper,[1] not only for thromboprophylaxis, but also for patients currently taking DOACs for the abovementioned clinical cardiovascular indications. Recently, different medical societies have published clinical practice guidelines with their own recommendations regarding the perioperative and periprocedural management of diverse antithrombotic therapies, including DOACs and antiplatelet therapies. Such recommendations apply to our liver cirrhosis population.[3,4]

Importantly, Velarde-Ruiz Velasco et al.[1] failed to provide detailed recommendations on how to approach significant adverse effects of anticoagulants, including DOACs, such as the occurrence of major life-threatening bleeding events. This encompasses knowing the *what, when, which, and how*, when considering potential clinical indications for rapid and appropriate reversal strategies in a cirrhotic patient taking DOACs; for example, in the setting of intracranial bleeding, life-threatening GI bleeding with hemorrhagic shock, or the need of urgent/emergency surgical intervention that cannot be delayed (e.g. acute cholecystitis or appendicitis). How do the consensus authors tackle these challenging clinical scenarios? Would they consider nonspecific or specific reversal agents, like 4-factor prothrombin concentrates (4F-PCC) or andexanet alfa (AA)?[5] When should 4F-PCCs be considered over AA and vice versa? Does the high-risk baseline hypercoagulable/prothrombotic status of our patients (e.g. non-valvular atrial fibrillation with a CHA2DS2-VASc score > 7 points or recent severe venous thromboembolism within 90 days) need to be better screened or risk stratified, before making such tough decisions in a multidisciplinary manner? The International Society on Thrombosis and Haemostasis recently published an updated guidance document for DOAC reversal strategies.[5]

Lastly, Velarde-Ruiz Velasco et al.[1] recommended low molecular weight heparin over unfractionated heparin for thromboprophylaxis. We disagree with this recommendation, especially in clinical scenarios in which advanced chronic kidney disease (CKD stage 4 or 5 according to the KDIGO classification, defined by a GFR < 30 ml/min × 1.73 m^2) and advanced liver cirrhosis coexist (e.g. Child-Pugh class C or MELD score > 20 points). Furthermore, there is a scarcity of randomized, prospective data addressing these clinically relevant caveats.[6,7] We prefer unfractionated heparin due to its excretion through the reticuloendothelial system, including the liver, thus avoiding bioaccumulation and bleeding complications.

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Conflict of interest

The authors declare that there is no conflict of interest to disclose.

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M. Porres-Aguilar[a,*], R. Izaguirre-Ávila[b], M. Uribe[c]

[a] *Departamento de Medicina Interna, Divisiones de Medicina Trombótica Clínica y Hospitalaria, Texas Tech University HSC, El Paso, Texas, United States*
[b] *Departamento de Hematología, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico*
[c] *Unidad de Obesidad y Enfermedades Digestivas, Clínica y Fundación Medica Sur, Mexico City, Mexico*

* Corresponding author at: Departamento de Medicina Interna, Divisiones de Medicina Trombótica Clínica y Hospitalaria, Texas Tech University HSC, 4800 Alberta Ave, El Paso, TX 79911, United States. Tel. +(915) 215 5647.
E-mail address: maporres@ttuhsc.edu (M. Porres-Aguilar).

Response to Porres-Aguilar et al., on ''Periprocedural and perioperative anticoagulation management strategies in liver cirrhosis''

Respuesta a Porres-Aguilar et al. «Estrategias de manejo perioperatorio y periprocedimiento de la anticoagulación en la cirrosis hepática»

We appreciate the comments and reflections of Porres-Aguilar, et al., in which they emphasize the existence of a significant prevalence of cardiovascular comorbidities in patients with cirrhosis, and the resulting increase in the prescription and use of direct oral anticoagulants (DOACs) from 20 to 77% between 2012 and 2019. Indeed, there are original studies on DOAC use in patients with cirrhosis and atrial fibrillation (AF) as a prophylactic strategy for preventing a cerebrovascular event that included: dabigatran, 24 patients; rivaroxaban, 32 patients (8 Child-Pugh A and 16 Child-Pugh B; Child-Pugh C was not included); and apixaban 32 patients (8 Child-Pugh A and B and 16 controls without cirrhosis). Based on that information, our guidelines recommend considering anticoagulation for cerebrovascular event prevention in patients with Child-Pugh A or Child-Pugh B cirrhosis that present with AF and a CHA_2DS_2-VASc score of 2 or more in men and 3 or more in women. There is no evidence for making recommendations regarding Child-Pugh C cirrhosis. Standard dose DOACs are suggested in patients with Child-Pugh A or B cirrhosis, instead of vitamin K antagonists (VKAs). Anticoagulation for pulmonary thromboembolism and deep vein thrombosis as treatment, but not as prophylaxis, is also mentioned. In addition, the guidelines underline the fact that patients with cirrhosis are excluded in the AMPLIFY, RECOVER, EINSTEIN, and HOKUSAI pivotal trials. Likewise, they recommend using DOACs in patients with Child-Pugh A or B cirrhosis, and enoxaparin in patients with Child-Pugh C cirrhosis, as a bridge to VKAs (in patients with a normal international normalized ratio).[1]

We should also clarify that there is a special section in our position paper that discusses anticoagulation in the cirrhosis population that has AF, and draws the following conclusions:[2,3]

a) In patients with Child-Pugh A or B cirrhosis and AF, oral anticoagulation is recommended in the absence of significant coagulopathy induced by liver failure or severe thrombocytopenia.
b) It is reasonable to prescribe DOACs (apixaban, dabigatran, or edoxaban), rather than warfarin, in patients with Child-Pugh A or B cirrhosis.
c) In patients with Child-Pugh B cirrhosis, rivaroxaban is contraindicated due to the potentially increased bleeding risk.

Porres-Aguilar, et al. also say they consider that special and meticulous multidisciplinary care (e.g., including a hematologist or a specialist in vascular medicine with experience in thrombosis and hemostasis) should be put forward in the position document, and that reasonable recommendations should be provided, not only with respect to thromboprophylaxis but also for patients currently taking DOACs for different cardiovascular indications. We agree that patients indicated for anticoagulation or those that are already taking anticoagulants should have a comprehensive evaluation by the vascular cardiologist, hematologist, and internist. As statement 4 of the scientific position paper says: ''Conducting a preoperative evaluation of non-hepatic comorbidities is recommended. It should include the habitual preoperative evaluation (electrocardiogram for estimating cardiovascular disease and the American Society of Anesthesiologists scale and Goldman index determinations)''. Likewise, statement 6 affirms: ''In patients with cirrhosis that require an elective surgical procedure, a