

ANTICOAGULATION IN PATIENTS WITH LIVER CIRRHOSIS: CLINICAL INDICATIONS, SAFETY, AND THERAPEUTIC SELECTION

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ABSTRACT

Introduction: Patients with liver cirrhosis exhibit a complex coagulopathy, placing them at simultaneous risk for bleeding and thrombosis. The contemporary understanding of “rebalanced hemostasis” challenges the outdated concept of spontaneous anticoagulation and reframes anticoagulation as a potential therapeutic strategy.

Purpose: To analyze the clinical indications, selection criteria, and risks associated with anticoagulant use in patients with liver cirrhosis, emphasizing the safety, efficacy, and practical application of anticoagulation in various clinical contexts.

Methods: A narrative literature review was conducted using PubMed, SciELO, Embase, and LILACS databases to identify studies published between 2018 and 2025. Search terms included anticoagulation, liver cirrhosis, portal vein thrombosis, and atrial fibrillation. International guidelines, systematic reviews, and clinically relevant observational studies were prioritized.

Results and Discussion: Anticoagulation appears safe and effective in compensated cirrhosis (Child–Pugh A/B), especially in cases of portal vein thrombosis (PVT) and atrial fibrillation. Anticoagulant choice should consider liver function, bleeding risk, renal status, and presence of esophageal varices. Direct oral anticoagulants (DOACs), such as apixaban and edoxaban, are preferred in CP A/B, while low molecular weight heparin (LMWH) or vitamin K antagonists (VKAs) are favored in more advanced cases. Endoscopic variceal prophylaxis should be performed before starting anticoagulation when indicated. A multidisciplinary approach and close clinical monitoring are essential. The lack of randomized trials in decompensated cirrhosis (CP B/C) remains a major limitation.

Final Considerations: When appropriately indicated and monitored, anticoagulation can improve clinical outcomes in cirrhotic patients. Future research must focus on randomized

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clinical trials and context-adapted protocols, especially within public health systems such as Brazil's SUS and in vulnerable populations.

Keywords: Liver Cirrhosis. Direct Oral Anticoagulants. Portal Vein Thrombosis.

ANTICOAGULAÇÃO EM PACIENTES COM CIRROSE HEPÁTICA: INDICAÇÕES CLÍNICAS, SEGURANÇA E SELEÇÃO TERAPÊUTICA

RESUMO

Introdução: Pacientes com cirrose hepática apresentam uma coagulopatia complexa, colocando-os em risco simultâneo de sangramento e trombose. A compreensão contemporânea da "hemostasia reequilibrada" desafia o conceito ultrapassado de anticoagulação espontânea e reformula a anticoagulação como uma potencial estratégia terapêutica.

Objetivo: Analisar as indicações clínicas, os critérios de seleção e os riscos associados ao uso de anticoagulantes em pacientes com cirrose hepática, enfatizando a segurança, a eficácia e a aplicação prática da anticoagulação em diversos contextos clínicos.

Métodos: Foi realizada uma revisão narrativa da literatura utilizando as bases de dados PubMed, SciELO, Embase e LILACS para identificar estudos publicados entre 2018 e 2025. Os termos de busca incluíram anticoagulação, cirrose hepática, trombose da veia porta e fibrilação atrial. Diretrizes internacionais, revisões sistemáticas e estudos observacionais clinicamente relevantes foram priorizados.

Resultados e Discussão: A anticoagulação parece segura e eficaz na cirrose compensada (Child-Pugh A/B), especialmente em casos de trombose da veia porta (TVP) e fibrilação atrial. A escolha do anticoagulante deve considerar a função hepática, o risco de sangramento, o estado renal e a presença de varizes esofágicas. Anticoagulantes orais diretos (ACODs), como apixabana e edoxabana, são preferidos na PC A/B, enquanto heparina de baixo peso molecular (HBPM) ou antagonistas da vitamina K (AVKs) são preferidos em casos mais avançados. A profilaxia endoscópica de varizes deve ser realizada antes do início da anticoagulação, quando indicada. Uma abordagem multidisciplinar e monitoramento clínico rigoroso são essenciais. A falta de ensaios clínicos randomizados em cirrose descompensada (PC B/C) continua sendo uma limitação importante.

Considerações Finais: Quando adequadamente indicada e monitorada, a anticoagulação pode melhorar os desfechos clínicos em pacientes cirróticos. Pesquisas futuras devem se concentrar em ensaios clínicos randomizados e protocolos adaptados ao contexto, especialmente em sistemas de saúde pública como o SUS brasileiro e em populações vulneráveis.

Palavras-chave: Cirrose Hepática. Anticoagulantes Orais Diretos. Trombose da Veia Porta.

ANTICOAGULACIÓN EN PACIENTES CON CIRROSIS HEPÁTICA: INDICACIONES CLÍNICAS, SEGURIDAD Y SELECCIÓN TERAPÉUTICA

RESUMEN

Introducción: Los pacientes con cirrosis hepática presentan una coagulopatía compleja, lo que los expone a un riesgo simultáneo de hemorragia y trombosis. La comprensión actual de la «hemostasia reequilibrada» cuestiona el concepto obsoleto de anticoagulación espontánea y replantea la anticoagulación como una posible estrategia terapéutica.

Objetivo: Analizar las indicaciones clínicas, los criterios de selección y los riesgos asociados al uso de anticoagulantes en pacientes con cirrosis hepática, destacando la seguridad, la eficacia y la aplicación práctica de la anticoagulación en diversos contextos clínicos.

Métodos: Se realizó una revisión narrativa de la literatura utilizando las bases de datos PubMed, SciELO, Embase y LILACS para identificar estudios publicados entre 2018 y 2025. Los términos de búsqueda incluyeron anticoagulación, cirrosis hepática, trombosis de la vena porta y fibrilación auricular. Se priorizaron las guías internacionales, las revisiones sistemáticas y los estudios observacionales clínicamente relevantes.

Resultados y discusión: La anticoagulación parece segura y eficaz en la cirrosis compensada (Child-Pugh A/B), especialmente en casos de trombosis de la vena porta (TVP) y fibrilación auricular. La elección del anticoagulante debe considerar la función hepática, el riesgo de sangrado, el estado renal y la presencia de varices esofágicas. Los anticoagulantes orales directos (ACOD), como apixabán y edoxabán, son los preferidos en la cirrosis pulmonar idiopática (CP A/B), mientras que la heparina de bajo peso molecular (HBPM) o los antagonistas de la vitamina K (AVK) se prefieren en casos más avanzados. Se debe realizar profilaxis endoscópica de varices antes de iniciar la anticoagulación cuando esté indicado. Un enfoque multidisciplinario y una monitorización clínica estrecha son esenciales. La falta de ensayos aleatorizados en cirrosis descompensada (CP B/C) sigue siendo una limitación importante.

Consideraciones finales: Cuando está adecuadamente indicada y monitorizada, la anticoagulación puede mejorar los resultados clínicos en pacientes cirróticos. La investigación futura debe centrarse en ensayos clínicos aleatorizados y protocolos adaptados al contexto, especialmente en sistemas de salud pública como el SUS de Brasil y en poblaciones vulnerables.

Palabras clave: Cirrosis Hepática. Anticoagulantes Orales Directos. Portal de Trombosis Venosa.

1 INTRODUCTION

Hepatic cirrhosis, the advanced stage of chronic liver disease, is characterized by a significant restructuring of the liver's architecture, resulting in metabolic, hemodynamic, and hematological dysfunctions. For a long time, these patients were considered at high risk for bleeding due to laboratory abnormalities such as prolonged prothrombin time (PT) and thrombocytopenia. (O'LEARY et al., 2019). However, recent studies challenge this perspective, showing that cirrhotic patients may present both bleeding and thrombotic risks simultaneously. This paradox arises from complex alterations, including a reduction in anticoagulant factors such as protein C and antithrombin, and an increase in procoagulant factors such as von Willebrand factor. (FERDINANDE et al., 2025).

In addition, bacterial infections in patients with cirrhosis can exacerbate coagulation disorders, increasing the risk of bleeding, including variceal hemorrhages. The presence of infection may trigger the release of endogenous anticoagulant substances, such as heparinoids, which interfere with blood coagulation. This effect is particularly concerning in patients who already have esophageal varices, as the combination of infection and anticoagulation can further increase the risk of bleeding. (TURCO et al., 2019).

Thus, anticoagulation in patients with cirrhosis represents a significant clinical challenge. The choice of an appropriate anticoagulant requires careful assessment of the severity of liver disease, presence of infections, bleeding risk, esophageal varices, and renal function. (BALLANTINE et al., 2021).

Some studies indicate that the use of anticoagulants, such as low-molecular-weight heparin (LMWH) or vitamin K antagonists (VKAs), may promote portal vein recanalization and prevent the progression of thrombosis without significantly increasing the risk of bleeding. (NORONHA et al., 2019).

Direct oral anticoagulants (DOACs), such as apixaban and rivaroxaban, have been studied in patients with Child-Pugh A and B cirrhosis, demonstrating efficacy and safety comparable to VKAs in certain populations. However, in patients with advanced cirrhosis (Child-Pugh C), the use of DOACs is generally contraindicated due to the lack of safety data and impaired hepatic metabolism. (STEUBER et al., 2019).

Individualization of treatment, based on a comprehensive assessment of the patient, is essential to optimize clinical outcomes and minimize the risks associated with anticoagulation in this complex population. (COSTACHE et al., 2023).

2 PURPOSE

This narrative review aims to analyze the main indications for anticoagulation in patients with liver cirrhosis, discuss criteria for selecting the most appropriate anticoagulant, and evaluate the risk of bleeding in this complex clinical context.

3 MATERIALS AND METHODS

This is a narrative review of the literature, conducted through searches in the PubMed, SciELO, Embase, and LILACS databases using descriptors related to anticoagulation, liver cirrhosis, and portal vein thrombosis. Priority was given to studies published between 2018 and 2025, with a focus on clinical data and recommendations from international societies.

4 RESULTS AND DISCUSSION

4.1 HEMOSTASIS IN CIRRHOSIS: CONCEPT OF REBALANCING

Anticoagulation in patients with liver cirrhosis is based on the understanding of rebalanced hemostasis: despite traditional laboratory abnormalities such as elevated prothrombin time (PT) and thrombocytopenia, these individuals may simultaneously present risks of bleeding and thrombosis due to the consumption of anticoagulant factors (protein C, antithrombin) and increased procoagulant factors (factor VIII, von Willebrand factor) (LISMAN et al., 2021). This complex functional reorganization results in an ambivalent risk state, requiring a careful and individualized therapeutic approach. Thus, anticoagulation emerges not only as a method to prevent thrombotic events but also as a potential modulator of liver disease progression itself, with experimental data suggesting a positive impact on portal hypertension and fibrosis (LISMAN et al., 2021).

4.2 INDICATIONS FOR ANTICOAGULATION: PORTAL VEIN THROMBOSIS AND ATRIAL FIBRILLATION

The most recent guidelines, including those from the International Society on Thrombosis and Haemostasis/Scientific and Standardization Committee (ISTH/SSC) in 2024 and the American Gastroenterological Association (AGA) in 2021, consistently recommend anticoagulation in patients with Child–Pugh A and B cirrhosis who present with symptomatic or progressive portal vein thrombosis (PVT). The implementation of anticoagulation in this population aims to maximize hepatic recanalization, prevent complications related to portal

hypertension, and preserve vascular viability in potential liver transplant candidates (CARLIN et al., 2024; O'SHEA et al., 2021).

In cases of acute PVT with significant obstruction (more than 50% of the portal lumen) or mesenteric involvement, early initiation of anticoagulant therapy is strongly recommended, with a minimum duration of three to six months, potentially extending depending on persistent thrombotic risk or transplant indication (BOCCATONDA et al., 2024; XIAO et al., 2024). Vascular recanalization in this situation is crucial to reducing ischemic symptoms, stabilizing portal pressure, and improving quality of life. However, when PVT presents in a chronic, fibrotic form without significant hemodynamic risk (established cavernoma), anticoagulation is typically not indicated. In this context, the risk of gastrointestinal or uncontrolled variceal bleeding tends to outweigh the benefits, as stated by the AGA and American College of Gastroenterology (ACG) guidelines (O'SHEA et al., 2021; SIMONETTO et al., 2020).

In clinical practice, observational and meta-analytical evidence supports this strategy: in an analysis involving 6,005 patients, anticoagulation increased portal vein thrombosis (PVT) recanalization by approximately fourfold and reduced the extent of PVT by 74% compared to the untreated group. Both the risk of bleeding and mortality showed no statistically significant differences (DONG et al., 2021).

In the hospital setting—particularly in patients with prolonged immobilization, surgical procedures, infections, or hepatic decompensation—venous thromboembolism (VTE) prophylaxis with low-molecular-weight heparin (LMWH) or unfractionated heparin is widely recommended by the guidelines, with no specific contraindications for compensated cirrhosis (O'SHEA et al., 2021). This represents a low-risk prophylactic strategy with well-defined benefits.

The indication for anticoagulation also extends to patients with atrial fibrillation (AF) and a high CHA₂DS₂-VASc score, provided they are classified as Child–Pugh A or B. The SSC/ISTH recommends the use of DOACs at standard doses, arguing that the risk of stroke far outweighs the potential risk of bleeding, although in Child–Pugh C patients, the evidence is either lacking or unfavorable (DONG et al., 2021; LISMAN et al., 2021; MOHAN et al., 2020).

These observational data provide strong support for the indication of anticoagulation in selected clinical scenarios, although large randomized trials with DOACs are still lacking. A study by Xiao et al. (2024) demonstrated that DOACs—especially edoxaban—were

associated with reduced progression of PVT, higher recanalization rates, and superior therapeutic response compared to VKAs, with similar safety profiles (XIAO et al., 2024).

4.3 CHOICE OF ANTICOAGULANT

In terms of agent selection, low-molecular-weight heparin (LMWH) offers advantages due to its ease of use and predictable response, making it particularly useful for hospitalized patients with stable renal function. On the other hand, vitamin K antagonists (VKAs), though traditional, present monitoring challenges due to unstable INR resulting from underlying coagulopathy, drug interactions, and variable vitamin K intake (LISMAN et al., 2021). Direct oral anticoagulants (DOACs) offer benefits such as rapid onset, oral administration, and reduced need for monitoring, in addition to a favorable pharmacokinetic profile in compensated cirrhosis. However, caution is advised in Child–Pugh B patients, and DOACs are not recommended in Child–Pugh C cases. Rivaroxaban has been associated with potential hepatotoxicity in patients with more advanced liver dysfunction, while apixaban and edoxaban appear to have a lesser hepatic impact. Apixaban, in particular, has a lower hepatic metabolism (25%) and reduced renal excretion, which supports its relative preference (STEUBER et al., 2019).

4.4 SAFETY AND RISK OF BLEEDING

In terms of safety, studies have shown that anticoagulation, when appropriately indicated, does not result in a significant increase in the risk of major bleeding compared to non-anticoagulated patients. A meta-analysis including DOACs, VKAs, and LMWH reported similar rates of major bleeding—between 7% and 9%—suggesting that careful use of these therapies does not significantly raise the risk of hemorrhagic events (MOHAN et al., 2020). Among the most concerning complications are variceal bleeds, particularly of gastrointestinal origin. In such cases, prior endoscopic variceal prophylaxis is crucial, substantially reducing the incidence of hemorrhage and underscoring the importance of a multidisciplinary approach before initiating anticoagulation.

The presence of active infection, in turn, warrants caution. Bacterial infections can destabilize the hemostatic system, increasing the propensity for bleeding, which may require suspension or immediate adjustment of anticoagulation, along with close monitoring of platelet count and renal function (QAMAR et al., 2018).

Among the most concerning complications are variceal bleeds, particularly of gastrointestinal origin. In such cases, prior endoscopic variceal prophylaxis is crucial, substantially reducing the incidence of hemorrhage and underscoring the importance of a multidisciplinary approach before initiating anticoagulation. The presence of active infection, in turn, warrants caution. Bacterial infections can destabilize the hemostatic system, increasing the propensity for bleeding, which may require suspension or immediate adjustment of anticoagulation, along with close monitoring of platelet count and renal function (CARLIN et al., 2024; DOUROS et al., 2022; HU et al., 2023). The HAS-BLED score may be useful for estimating bleeding risk, but it should not be used alone as a contraindication, as it is not validated in cirrhotic patients. Targeting modifiable risk factors—such as blood pressure control, improvement of renal function, and stabilization of platelet count—are more appropriate strategies. In liver transplant candidates with portal vein thrombosis (PVT), prolonged anticoagulation may promote venous recanalization and maintenance of portal flow, which are relevant criteria for transplant eligibility and graft success (CHEN et al., 2020; GUERRERO et al., 2023).

The minimum recommended duration of anticoagulation in these patients is generally six months, with continuation based on therapeutic response and persistence of thrombotic risk. Reassessment via imaging every two to three months is advised to guide further clinical decisions (O'SHEA et al., 2021). Laboratory follow-up should include liver and renal function tests, platelet count, INR when applicable, and, when needed, plasma levels of DOACs—especially in cases of uncertainty regarding efficacy or safety. Another advantage of using DOACs is the availability of specific reversal agents—such as idarucizumab for dabigatran and andexanet alfa for factor Xa inhibitors—which increases therapeutic safety in emergency settings (CHEN et al., 2020).

4.5 CURRENT RECOMMENDATIONS AND GAPS IN THE LITERATURE

Despite the progress and encouraging results, there remains a lack of randomized clinical trials directly comparing DOACs and traditional anticoagulants in patients with varying degrees of hepatic dysfunction. This data gap is especially significant in individuals with decompensated cirrhosis (Child–Pugh B and C), in whom clinical outcomes such as morbidity, mortality, and quality of life remain poorly studied. Moreover, different degrees within Class B (e.g., B7 vs. B9) also carry important practical implications, yet are scarcely explored in studies. In this context, the guidelines from the European Association for the

Study of the Liver (EASL) recommend caution: they support the use of DOACs in compensated cirrhosis for the treatment and prophylaxis of venous thromboembolism (VTE), but emphasize that, in the specific case of portal vein thrombosis (PVT), evidence is still insufficient and more robust studies are needed to support clinical decision-making (VILLA et al., 2022).

Currently, the safest strategy involves a combination of imaging assessment, endoscopy for variceal detection, selection of anticoagulant based on Child–Pugh classification (preferably DOACs in A/B and LMWH or VKAs in more advanced cases), and rigorous dynamic clinical monitoring. This model aims to reduce complication risks while maximizing clinical benefits. The future of anticoagulation in cirrhosis should incorporate prospective studies with risk stratification, biomarker evaluation for thrombotic and hemorrhagic predisposition, and development of clinical algorithms to support individualized therapeutic decisions (CHEN et al., 2020; QAMAR et al., 2018; STEUBER et al., 2019).

In the context of Brazil's Unified Health System (SUS), the safe implementation of anticoagulation in cirrhotic patients faces several challenges, including the scarcity of specific laboratory tests for monitoring, limited availability of DOACs in the public health network, and restricted access to imaging and endoscopy for pretreatment evaluation (SILVA, et al. 2024). The lack of standardized national protocols on anticoagulation in cirrhotics worsens the heterogeneity of medical approaches and increases reliance on local experience and interdisciplinary collaboration (GUERRERO et al., 2022). The implementation of evidence-based clinical algorithms, validated for use in high-complexity and resource-limited populations, is essential to enhance care safety. Furthermore, strengthening multidisciplinary teams—including hepatologists, hematologists, cardiologists, and radiologists—can optimize management, reduce complications, and promote more equitable access to effective therapies. National studies are needed to characterize the clinical outcomes of anticoagulation in cirrhotics within SUS and to support public policies that ensure safe and rational access to anticoagulants.

Therefore, anticoagulation in patients with liver cirrhosis represents a promising approach, provided it is conducted with technical rigor and individualized management. Accumulated evidence suggests consistent clinical benefits, especially in portal vein thrombosis, atrial fibrillation, and VTE prevention (GUERRERO et al., 2023; MOHAN et al., 2020). However, the safety of therapy depends on careful selection of anticoagulants, continuous clinical monitoring, and the involvement of an experienced multidisciplinary team,

ensuring better outcomes for this population (O'SHEA et al., 2021; SIMONETTO et al., 2020; VILLA et al., 2022).

5 CONCLUSION

Current evidence demonstrates that, when carefully indicated and monitored, anticoagulation in patients with liver cirrhosis—particularly those classified as Child–Pugh A and B—is a safe and effective intervention. Clinical benefits include portal vein recanalization, prevention of venous thromboembolism, and reduction of thrombotic events in atrial fibrillation, without a substantial increase in major bleeding. The choice of anticoagulant should take into account the degree of hepatic dysfunction, the presence of esophageal varices, the overall bleeding risk, renal function, and the feasibility of monitoring. Whenever possible, prior endoscopic prophylaxis of varices is recommended before initiating anticoagulation.

Therapeutic decision-making should ideally occur within a multidisciplinary care setting, involving hepatology, hematology, cardiology, and interventional radiology. Although DOACs have shown to be practical and safe in compensated patients, significant gaps in the literature remain—especially in advanced cirrhosis—that hinder the standardization of treatment strategies. There is an urgent need for randomized clinical trials including representative populations with Child–Pugh B/C, as well as prospective studies applicable to the context of the Brazilian Unified Health System (SUS), aiming to optimize anticoagulant selection and expand access to evidence-based therapies for this complex and often neglected population.

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