Tumor Thrombus in the Inferior Vena Cava: Prognostic Implications, Surgical Complexity, and Approaches

Trombo Tumoral na Veia Cava Inferior: Implicações Prognósticas, Complexidade Cirúrgica e Abordagens

Trombo Tumoral en la Vena Cava Inferior: Implicaciones Pronósticas, Complejidad Quirúrgica y Enfoques

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RESUMO

Objetivo: O trombo tumoral na veia cava inferior (TTVCI) é uma complicação rara, associada ao carcinoma de células renais (CCR) e hepatocelular (CHC), caracterizada por invasão intraluminal que pode se estender ao átrio direito. Está relacionada a pior prognóstico, maior risco cirúrgico e sobrevida limitada. O tratamento principal é cirúrgico, incluindo nefrectomia ou hepatectomia com trombectomia, sendo a extensão e morfologia do trombo determinantes para a complexidade operatória e desfechos. Terapias neoadjuvantes, como inibidores de tirosina-quinase e imunoterapia, mostram potencial para reduzir o trombo e viabilizar cirurgias menos invasivas. O manejo deve ser individualizado e multidisciplinar, destacando a necessidade de novas pesquisas para melhorar prognóstico e opções terapêuticas.

Palavras-chave: trombo tumoral, veia cava inferior, carcinoma de células renais, carcinoma hepatocelular, trombectomia.

ABSTRACT

Objective: Inferior vena cava tumor thrombus (IVCTT) is a rare complication associated with renal cell carcinoma (RCC) and hepatocellular carcinoma (HCC), characterized by intraluminal invasion that may extend to the right atrium. It is linked to poor prognosis, higher surgical risk, and limited survival. Surgical treatment, including nephrectomy or hepatectomy with thrombectomy, remains the mainstay, with thrombus extent and morphology determining complexity and outcomes. Neoadjuvant therapies, such as tyrosine kinase inhibitors and immunotherapy, may reduce thrombus and allow less invasive surgery. Management should be individualized and multidisciplinary, highlighting the need for further research to improve prognosis and therapeutic options.

Keywords: tumor thrombus, inferior vena cava, renal cell carcinoma, hepatocellular carcinoma, thrombectomy.

RESUMEN

Objetivo: El trombo tumoral en la vena cava inferior (TTVCI) es una complicación rara asociada al carcinoma de células renales (CCR) y hepatocelular (CHC), caracterizada por invasión intraluminal que puede extenderse al atrio derecho. Se asocia con peor pronóstico, mayor riesgo quirúrgico y supervivencia limitada. El tratamiento principal es quirúrgico, incluyendo nefrectomía o hepatectomía con trombectomía, siendo la extensión y morfología del trombo determinantes de la complejidad y los resultados. Las terapias neoadyuvantes, como inhibidores de tirosina quinasa e inmunoterapia, pueden reducir el trombo y permitir cirugías menos invasivas. El manejo debe ser individualizado y multidisciplinario, destacando la necesidad de nuevas investigaciones para mejorar el pronóstico y las opciones terapéuticas.

Descriptores: trombo tumoral, vena cava inferior, carcinoma de células renales, carcinoma hepatocelular, trombectomía.

REVISÃO

Introduction

Tumor Thrombus in the Inferior Vena Cava (TTIVC) corresponds to intraluminal invasion by neoplastic cells, forming an obstructive mass extending from the renal vein or hepatic venous system. It is a rare and challenging complication, frequently associated with renal cell carcinoma (RCC) and hepatocellular carcinoma (HCC). Its presence carries significant prognostic and therapeutic implications, being related to higher surgical morbidity and mortality and limited survival.[1–3]

The treatment of choice for TTIVC is predominantly surgical, involving simultaneous resection of the primary tumor and the thrombus (thrombectomy), since systemic therapies alone—such as chemotherapy or radiotherapy—show limited efficacy in this context.[1–3] In RCC, the extent of the tumor thrombus (TT) is a crucial prognostic factor, with surgery considered potentially curative for low-level thrombi, while more extensive ones require advanced techniques and entail higher perioperative risk.[1,4]

The morphological pattern of the thrombus also influences the therapeutic approach, potentially increasing surgical complexity and directly affecting prognosis. The survival rate of patients undergoing radical nephrectomy with complete thrombectomy can exceed 50% at five years, while incomplete resections are associated with less than 10% survival in the same period.[4] In HCC, invasion of the inferior vena cava (IVC) is a rare and severe condition, associated with a median survival of only 2 to 5 months in the absence of treatment.[2–3]

In recent years, advances in TTIVC management have included the use of neoadjuvant therapies. Recent studies suggest that tyrosine kinase inhibitors (TKIs) and immunotherapy, either alone or in combination, can reduce the length and level of the thrombus, allowing less invasive surgeries and, in some cases, avoiding the use of cardiopulmonary bypass.[6] Despite encouraging results, the heterogeneity of studies and the limited number of clinical trials still preclude definitive conclusions.

Thus, TTIVC represents a complex condition that requires an individualized and multidisciplinary approach. The advancement of surgical techniques and the emerging role of neoadjuvant therapies highlight the clinical relevance of the topic and its importance for developing new therapeutic strategies.

Objective

This study aims to review the current literature on tumor thrombus in the inferior vena cava, both in cases of renal cell carcinoma and hepatocellular carcinoma. It seeks to explore the pathophysiology, the most widely used classification systems, the available surgical and nonsurgical therapeutic alternatives, and the clinical outcomes associated with each management strategy. Additionally, it aims to discuss recent developments, such as the role of thrombus morphology in surgical complexity, minimally invasive treatment possibilities, and the impact of neoadjuvant and combined therapies on patient survival.

Methods

This is a narrative literature review, developed from the evaluation of scientific articles published in journals indexed in PubMed, Scopus, Embase, and Web of Science. The following English terms and their Portuguese equivalents were used: *inferior vena cava tumor thrombus*, *renal cell carcinoma*, *hepatocellular carcinoma*, *onco-vascular surgery*, *surgical complexity*, *tumor thrombus morphology*, *presurgical treatment.*

Articles published in the last ten years were included, covering original studies—retrospective or prospective—systematic reviews, narrative reviews, and comparative analyses relevant to the topic. Studies addressing diagnosis, classification of tumor thrombus in the inferior vena cava, and surgical or multimodal therapeutic strategies—including radiotherapy, chemoembolization, targeted therapy, and immunotherapy—were selected. Case reports were included only when illustrating innovative management strategies or rare manifestations with clinical relevance.

Studies lacking proper methodological description, those without relevant clinical or prognostic data, and isolated case reports without a substantive discussion aiding understanding of TTIVC management were excluded.

After initial screening by titles and abstracts, full-text articles were read and included according to their relevance to the topic. In total, six studies were selected, forming the basis for comparative analysis, which considered aspects such as morbidity, overall survival, impact on quality of life, and technical improvement of surgical and multimodal approaches.

Results

TTIVC primarily affects patients with RCC and HCC. In RCC, invasion of the renal vein with progression to the IVC occurs in 4–10% of cases, reaching the right atrium (RA) in about 1%.[1] In HCC, invasion of the IVC is observed in 1.4–4.9% of patients, with progression to the RA in 2.4–6.3%.[2]

From a pathophysiological standpoint, TT forms through endothelial invasion by tumor cells, creating an environment favorable for cellular proliferation and centripetal progression within the vessel. This process promotes tumor extension from the renal or hepatic vein to the IVC and, in advanced cases, to the RA, increasing clinical severity..[3]

Several classifications help define management. In RCC, the most widely used is the Mayo classification[1]:

- **Class 0:** Thrombus confined to the renal vein.
- **Class I:** Extension into the IVC < 2 cm from the renal vein.
- **Class II:** Extension > 2 cm from the renal vein but below the diaphragm.
- **Class III:** Thrombus extending above the renal vein up to the diaphragm level.
- **Class IV:** Thrombus above the diaphragm, including the RA..

For HCC, the **Li et al. classification**[2] is often applied:

- **Class I:** Infradiaphragmatic.
- **Class II:** Supradiaphragmatic.
- **Class III:** Involving the RA.

In RCC, the standard treatment is radical nephrectomy combined with thrombectomy, performed either via open or laparoscopic approach. In Mayo III and IV cases, cardiopulmonary bypass and deep hypothermia may be necessary, increasing complication risk.[1] Average survival without surgery is around 5 months, while post-nephrectomy with thrombectomy, 5-year survival ranges between 40% and 60%, even in systemic disease.[5]

Neoadjuvant therapies have shown encouraging results. TKIs reduced TT size in about 40% of patients and downgraded Mayo classification in 30%. Immune checkpoint inhibitors reduced thrombus size by 42% and classification by 46%. Combination therapy (TKI + ICI) was effective in reducing size (84%) but less so in lowering thrombus level (14%).[6]

In HCC, management depends on the Child–Pugh score. In Child A (Class I) patients, hepatectomy with thrombectomy is generally indicated. In Class II, vascular occlusion and diaphragmatic opening may be required; in Class III, a combined hepatobiliary, thoracic, and cardiac approach with cardiopulmonary bypass is necessary.[2] Despite advances, perioperative mortality may reach 15%, and median survival after complete resection ranges from 19 to 30.8 months.[3]

For nonsurgical candidates, options include radiotherapy, transarterial chemoembolization (TACE) (complete response in 53.8% and median survival of 4.2 months), and systemic therapies such as sorafenib and thalidomide, still under investigation.[2]

Discussion

The presence of TTIVC, with or without extension into the right atrium (RA), represents one of the most complex oncologic scenarios, in both HCC and RCC. Vascular involvement is associated with poor prognosis and high risk of severe complications, such as pulmonary embolism, right heart failure, and sudden death.[2,3]

In RCC, TTIVC occurs in 4–10% of patients, reaching the RA in up to 1%.[1] Radical nephrectomy with thrombectomy remains the standard treatment, with the technique adapted according to the thrombus level. While level I and II thrombi can be managed with mobilization and temporary IVC clamping, levels III and IV often require cardiopulmonary bypass and, in selected cases, circulatory arrest under deep hypothermia.[1] Laparoscopic and robotic approaches have shown benefits such as less surgical trauma and faster recovery, although they still depend on highly specialized centers.[1]

Beyond extension, thrombus morphology plays an important prognostic role. Filled morphology thrombi are associated with greater bleeding, longer operative time, and higher postoperative complication risk compared to floating

morphology thrombi.[4] Therefore, detailed preoperative assessment, including advanced imaging and multidisciplinary planning, is essential to optimize outcomes. When properly managed, complete resection still represents the best chance of survival, achieving 40–60% at five years.[5]

In recent years, neoadjuvant therapies have emerged as strategies to reduce thrombus length and level, enabling less extensive surgeries. TKIs, immunotherapy, and TKI–ICI combinations have demonstrated significant thrombus reduction in early studies, with responses up to 84% in combined protocols.[6] Despite promising outcomes, prospective trials are still needed to confirm these benefits and establish standardized protocols.

In HCC, TT in the IVC/RA is rarer (1.4–4.9%) but carries an extremely poor prognosis, with median survival of 2–5 months without treatment.[2,3] Vascular invasion may result in Budd–Chiari syndrome, systemic congestion, arrhythmias, and thromboembolic complications.[2] When feasible, hepatectomy with thrombectomy can extend survival to 19–30 months in well-selected (Child–Pugh A) patients, though it remains associated with high morbidity and perioperative mortality (~15%).[3]

Adjuvant modalities such as TACE, stereotactic radiotherapy, and targeted therapies (e.g., sorafenib) have been employed mainly in patients unsuitable for resection.[2] TACE, in particular, has shown meaningful objective responses and may serve as a palliative or bridge therapy to surgery in selected cases.

Comparatively, in RCC, surgery offers substantial survival gains (40–60% at 5 years), and neoadjuvant therapies appear promising in reducing surgical complexity. In HCC, however, even in resectable cases, survival rarely exceeds 30 months, and adjuvant strategies remain largely palliative. In both tumors, individualized management, detailed assessment of thrombus extension/morphology, and multidisciplinary collaboration remain essential.[1-6]

Conclusion

TTIVC represents a rare but clinically significant condition with major prognostic and therapeutic implications in RCC and HCC. Its presence indicates a highly complex scenario, marked by diagnostic challenges, substantial surgical risk, and direct impact on patient survival. In RCC, radical surgical resection with thrombectomy remains the most effective strategy, achieving significant survival rates when complete. In HCC, although prognosis is poorer, resection in selected patients can prolong survival, particularly when combined with adjuvant therapies.[2,3,5]

Additionally, factors such as thrombus extent and morphology are key determinants not only for surgical planning but also for clinical outcomes. In this context, the incorporation of neoadjuvant therapies—including TKIs, immunotherapy, and TKI–ICI combinations—emerges as a promising approach to reduce thrombus extension and enable less invasive surgeries. However, the heterogeneity of available studies and the scarcity of robust clinical trials highlight the need for further research to validate these strategies.[6]

Therefore, TTIVC management should rely on an individualized, multidisciplinary approach integrating surgical advances, oncologic support, and emerging therapies. While surgery continues to offer significant survival gains in RCC, options remain more limited in HCC, underscoring the urgency for new research to improve prognosis and expand therapeutic possibilities in this highly lethal condition.[1-6]

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