Surgical Treatment of Renal Cell Carcinoma With Cavoatrial Involvement: A Systematic Review of the Literature

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The treatment of renal cell carcinoma (RCC) with cavoatrial involvement represents a major surgical challenge. To date, many surgical strategies have been proposed. However, general agreement on the best approach does not yet exist.

Deep hypothermic circulatory arrest (DHCA) is the most commonly used method and allows complete tumor resection without increasing operative risk. Cardiopulmonary bypass (CPB) without circulatory arrest and methods using no CBP were also proposed, without a clear evidence of superiority of 1 technique over the others. Further studies are needed to evaluate the possible role of alternative techniques compared with deep hypothermic circulatory arrest.

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Renal cell carcinoma (RCC) with cavoatrial involvement represents a major surgical challenge. Several surgical techniques for the treatment of these tumors have been proposed, but because of a small number of patients and limited follow-up, substantial controversy about the best operative management still exists.

In this review, we analyze the results of the most commonly used surgical strategies (cardiopulmonary bypass [CPB] with deep hypothermic circulatory arrest [DHCA], CPB without circulatory arrest, vascular occlusion without CPB, and venovenous bypass [VVBP] and summarize the current evidence on the perioperative management of this complex pathologic condition.

Material and Methods

In July 2015, a systematic literature search was performed in MEDLINE using the keywords "renal cell carcinoma," "right atrium tumor thrombus," "cardiopulmonary bypass renal carcinoma," "deep hypothermic circulatory arrest renal carcinoma," "tumor thrombus evaluation," and "tumor thrombus prognosis." The searches were limited to articles published in English. All relevant abstracts were reviewed, and the function "related articles" was used for all included articles. A manual reference cross-check was performed for all selected studies. When the same patient population was reported in more than 1 publication, only the 1 with the most updated and complete data was included. To give an overview of the contemporary surgical results, only the series published after 1990 were included; single case reports were excluded from the analysis.

Results

Incidence, Classification, and Prognosis of RCC With Cavoatrial Involvement

RCC is 1 of the most common genitourinary malignancies, and it accounts for 3% of all solid neoplasms [1]. RCC has a biological propensity toward intravascular invasion of the renal vein and extension into the inferior vena cava (IVC). It is estimated that 4% to 10% of patients with RCC have a tumor thrombus extending into the IVC [2–4], and in almost 1% of cases this intraluminal thrombotic extension reaches the right atrium (RA). A small portion of these thrombi will further extend through the tricuspid valve into the right ventricle [5, 6].

Based on its cephalic extension, many staging systems for RCC with venous tumor thrombus have been proposed. According to the Neves and Zincke classification [7], level I tumors extend less than 2 cm above the renal vein, level II tumors extend more than 2 cm above the renal vein while remaining infrahepatic, level III tumors extend into the retrohepatic IVC, and level IV tumors extend above the diaphragm into the RA.

The prognostic significance of the cephalad extent of IVC thrombi is still unclear. Sosa and coauthors [8] compared the 2-year survival rate in patients with suprahepatic versus intrahepatic thrombi and found a

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
DHCA = deep hypothermic circulatory arrest
IBS = intraoperative blood salvage
IVC = inferior vena cava
MRI = magnetic resonance imaging
NT = neoadjuvant therapy
RAE = renal artery embolization
RCC = renal cell carcinoma
TOT = total operative time
VVBP = venovenous bypass

better outcome in the latter (21% versus 80%). Similarly, Skinner and colleagues [9] reported a 5-year survival rate of 0% versus 18% for patients with right atrial versus intrahepatic tumors, respectively. Further reports have failed to prove a statistically significant correlation between tumor thrombus level and survival [10, 11]. However in a large retrospective study on a total of 1,192 patients, the overall survival was statistically better for patients with a tumor thrombus in the renal vein (52 months) compared with those with IVC involvement (25.8 months for subdiaphragmatic involvement and 18 months for supradiphragmatic extension; $p < 0.001$). No significant difference in survival was noted for the subdiaphragmatic versus the supradiaphragmatic groups ($p = 0.613$) [12]. A recent multiinstitutional retrospective study of 1,122 patients followed for a median period of 24 months reported a statistically significant correlation between survival and tumor level. The 5-year survival was 43.2% for renal vein involvement, 37% for IVC involvement below the diaphragm, and 22% for IVC involvement above the diaphragm. On multivariate analysis, tumor thrombus level correlated independently with survival (hazard ratio, 2.10 [range, 1.53–3.0]; $p = 0.00$) [13].

Preoperative evaluation of the proximal extent of the thrombus is essential for planning the appropriate surgical strategy. Magnetic resonance imaging (MRI) has traditionally been considered the gold standard for this purpose [14], but many studies have shown that computed tomography has comparable accuracy [15]. Given that a variation in proximal extension can influence the surgical strategy considerably, many groups have stressed the importance of the timing of imaging. MRI or computed tomography is ideally recommended within 14 days of the surgical procedure and definitely no longer than 30 days before the operation [16] because of the risk of further tumor extension in the interim between imaging and the surgical procedure. Transesophageal echocardiography also has reasonable accuracy in determining the presence and extent of tumor thrombus, and it may be a valuable tool when MRI findings are not definitive [17].

Radical surgical intervention has been universally accepted as the only curative treatment, because conventional chemoradiotherapy alone is not effective [18]. Previous reports have shown that complete surgical resection offers 40% to 70% 5-year survival in the absence of metastases or lymph node involvement. Survival is significantly lower (0%–20%) if metastases are present [6, 9, 13]. However, surgical treatment is associated with substantial perioperative risk. Even in the current era, in-hospital mortality can be up to 40% [18], and major or minor complications occur in up to 47% of cases, depending on the patient's comorbidities and the surgical approach [6].

Neoadjuvant Therapy

Neoadjuvant therapy (NT) with tyrosine kinase inhibitors has been shown to be an effective treatment for advanced RCC [19]. In 2007, Motzer and colleagues [20] reported a decrease in tumor size in 36% of cases and a better progression-free survival in 375 patients treated with sunitinib. However, this finding has more recently been tempered by a case series showing a decrease in the thrombus size in 44% of patients, a downstaging of the tumor level in only 12% of patients, and substantial modification of the operation originally planned after NT in only 4% [21]. Similar results were reported by Bigot and coworkers [22] who specifically investigated the effect of molecular therapies (sunitinib or sorafenib) on size and level of tumor thrombi. These authors found a significant regression of tumor thrombus level in only 1 patient (7%) without modification of the surgical strategy. Furthermore, besides its specific toxicity, NT has been associated with increased surgical morbidity, especially with regard to wound dehiscence and infections [23].

In the absence of conclusive results, it seems that NT should not be systematically proposed but rather considered on a selected basis after multidisciplinary discussions.

Preoperative Renal Artery Embolization

Preoperative renal artery embolization (RAE) has been shown to shrink the size of the tumor along with the cephalad extent of the thrombus [24]. Moreover, significant reduction in blood loss and operative time, together with improved survival, has been reported [25]. However, RAE has an overall complication rate of 5%, and up to 75% of patients experience symptoms related to the angioinfarction syndrome [26]. Subramanian and coauthors [27] recently reported greater perioperative mortality and longer operative times after RAE. May and associates [28] found a lack of benefit when RAE was used before surgical intervention.

To summarize, further studies are needed to clarify the role of RAE in the preoperative management of RCC.

Surgical Techniques

DEEP HYPOTHERMIC CIRCULATORY ARREST. First described by Marshall [29] in 1984, DHCA has been extensively used in the treatment of RCC with tumor thrombus extending above the diaphragm (Table 1).

This surgical technique allows direct visual inspection of the vena caval lumen and enables safe and exact removal of the entire tumor thrombus in a completely bloodless operative field [30, 31]. Additionally, DHCA provides complete vascular control and can decrease the