EXPERT REVIEWS

Improving surgical outcomes in renal cell carcinoma involving the inferior vena cava

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Radical nephrectomy with tumor thrombectomy remains the mainstay of treatment in renal cell carcinoma with inferior vena cava extension. Despite the rapid improvements experienced in perioperative care in recent years, this intervention still often results in significant morbidity and mortality. A deeper understanding of salient features of this complex operation provides a valuable insight into the clinical mechanisms underlying the variations observed in surgical outcomes. The 'operation profile' serves not only as a basis for making an adequate prognostic assessment, but also creates a platform from which 'innovative' strategies for improving quality and safety can be made. The present review aims to set a 'profile' for radical nephrectomy and tumor thrombectomy, and to propose a number of strategies that may reduce the complication rates of this intervention.

Keywords: complications • inferior vena cava • morbidity • mortality • operation profile • quality • renal cell carcinoma • safety • surgical outcomes • tumor thrombus

Surgical care can prevent loss of life but it is also associated with a considerable risk of complications, which can be life-threatening and even lead to death. Although poorly characterized, surgical complications represent a substantial burden worthy of attention [1]. Potentially life-threatening surgical complication rates of 3–17% and inpatient perioperative death rates of 0.4–0.8% have been reported. Current data suggest that at least one-half of all surgical complications are avoidable when adequate perioperative changes are implemented [2,3].

Variations in morbidity and mortality rates among different surgical programs and even among individual surgeons have become increasingly apparent. Prompted by these differences, numerous surgical programs have made efforts to better understand these differences while improving surgical outcomes. The efforts of these programs have provided a valuable insight into the clinical mechanisms underlying these variations and have lead to more effective quality improvement strategies [4]. However, in spite of the rapid improvements experienced in perioperative care for the last 50 years, surgical complications remain as a major issue in the management of renal cell carcinoma (RCC) with inferior vena cava (IVC) extension.

The present review 'profiles' radical nephrectomy and tumor thrombectomy [5], aiming to capture all salient features of this complex operation as well as to provide a deeper understanding of its surgical outcomes. According to the profile obtained, some 'innovative' strategies to reduce the rate of perioperative complications are proposed.

Role of surgical outcomes in RCC with IVC tumor thrombus

In the urological oncology literature, traditional studies have focused on oncological outcomes. As a result, all of these end points have been reasonably well investigated [6–8]. At present, however, as the interest in outcomes research increases, a greater emphasis has been placed on measuring the operative results of our interventions [9]. Although the reasons for this are many (i.e., variations in clinical practice, and rising costs), a key reason is to determine the quality of our surgical management.

Classifying and evaluating the complications arising after surgical treatment would provide

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the adequate environment in which comparisons between individual surgeons, institutional experiences and different techniques can be accomplished in a systematic, objective and reproducible way [10]. With this approach, an earlier recognition of the pattern of complications may be achieved, thereby facilitating the adoption of changes in care in an effort to prevent and reduce morbidity and mortality.

Hence, when oncologic outcomes are utilized to evaluate the surgical approach to RCC with IVC invasion, it may be noted that nothing or little has improved for decades, falling into the 'terrible acknowledgement of our failure to change the natural history of this disease' [11]. Our ability to perceive this change is probably depleted because we surrogate the inadequate end points (i.e., oncological outcomes). The use of intermediate end points (i.e., surgical complications) would aid in determining how best is our surgical care in terms of safety and quality [12–15].

Setting an 'operation profile' for radical nephrectomy & tumor thrombectomy

The overwhelming determining factor in survival for RCC is the complete surgical removal of the tumor. Although the curative merit of radical nephrectomy is well established [16], the operative outcomes of the procedure are considerably worse when the vena cava is involved by malignancy [17].

Despite the encouraging outcomes obtained in selected patients, radical nephrectomy and tumor thrombectomy often results in significant morbidity and mortality [18]. Surgical morbidity is prevalent in this context, with complication rates exceeding 50% [19]. Likewise, postoperative mortality rates as high as 23.5% have been reported [20], rising up to 40% in cases of thrombus extending above the diaphragm [21].

Factors determining the development of complications in radical nephrectomy and tumor thrombectomy include: preoperative factors, operative factors, surgeon and team-related factors, postoperative factors and environmental factors (Figure 1).

Preoperative factors

Several studies have attempted to identify preoperative factors, which predispose patients to complications and poorer surgical outcomes. Major aspects include comorbidity status, disease features and ensuring an adequate decision-making process through accurate diagnosis [11,22]. Unfortunately, most of these factors cannot be modified before the intervention. Perhaps, they would provide more information for surgeons who can then better counsel patients and their relatives preoperatively regarding risks of perioperative complications and mortality.

Comorbidity

Patients who are at increased risk of complications have been found to have overall poorer health and functional status preoperatively. Status performance and Charlson Comorbidity Index have been outlined as important surgical outcome predictors [23,24].

Disease features

Postoperative prognostic factors for RCC invading the IVC include TNM stage, presence of necrosis, presence of sarcomatoid features and invasion of the renal sinus, perinephric fat, hepatic veins, collecting system or renal vein ostium [25,26]. Recently, Klatte *et al.* performed a multivariable analysis to identify prognostic factors for surgical outcomes in RCC extending into the venous system [23]. The presence of positive lymph nodes and distant metastasis at diagnosis were shown to be independent predictors of outcome in this study. Higher nuclear Fuhrman grades (III–IV) and tumor histology have been also reported as additional prognostic factors, being worse for papilar, unclassified and collecting duct carcinoma [27,28]. However, no difference in prognosis was observed among other histological subtypes, or different thrombus levels.

Preoperative assessment

Improvements in perioperative assessment have decreased the morbidity and improved the decision-making process, and thus the surgical outcomes for patients with RCC and venous tumor thrombus [29]. Assessment of tumor source and extent is critical in determining the subsequent operative procedures, including the use of extracorporeal circulation maneuvers [30]. The ability of cross-sectional imaging to classify venous thrombus according to the anatomic level inside the IVC has improved with recent advancements in computed tomography (CT) technology [31]. The utility of preoperative MRI to predict vascular wall invasion, which carries adverse prognostic significance, has also been demonstrated [26]. Hence, the preoperative assessment of patients with RCC involving the IVC is currently made according to multidetector-CT or MRI findings, which provide an accurate depiction of the extent of the disease and surgical treatment options.

Operative factors

Technique-related complications, wound infections and postoperative bleeding produce nearly one-half of all postsurgical adverse events [5]. Radical nephrectomy and tumor thrombectomy is technically demanding and poses a challenge due to its potential for causing life-threatening complications, including massive hemorrhage, accidental injuries and pulmonary embolism (PE).

Hemorrhage

Uncontrollable hemorrhage leading to exsanguination has been reported in up to 7.5% of cases [32]. Potential for intraoperative bleeding depends mainly on the anatomic disposition of the surgical field. The intravascular burden of disease (i.e., level and the degree of occlusion), the presence and extent of collateral circulation in response to obstruction and the involvement of surrounding structures, may increase the difficulty of the surgical procedure, and thus, the possibility for massive hemorrhage.

As a general rule, the extent of dissection is predicated on the cephalad level of tumor thrombus, dictating the number

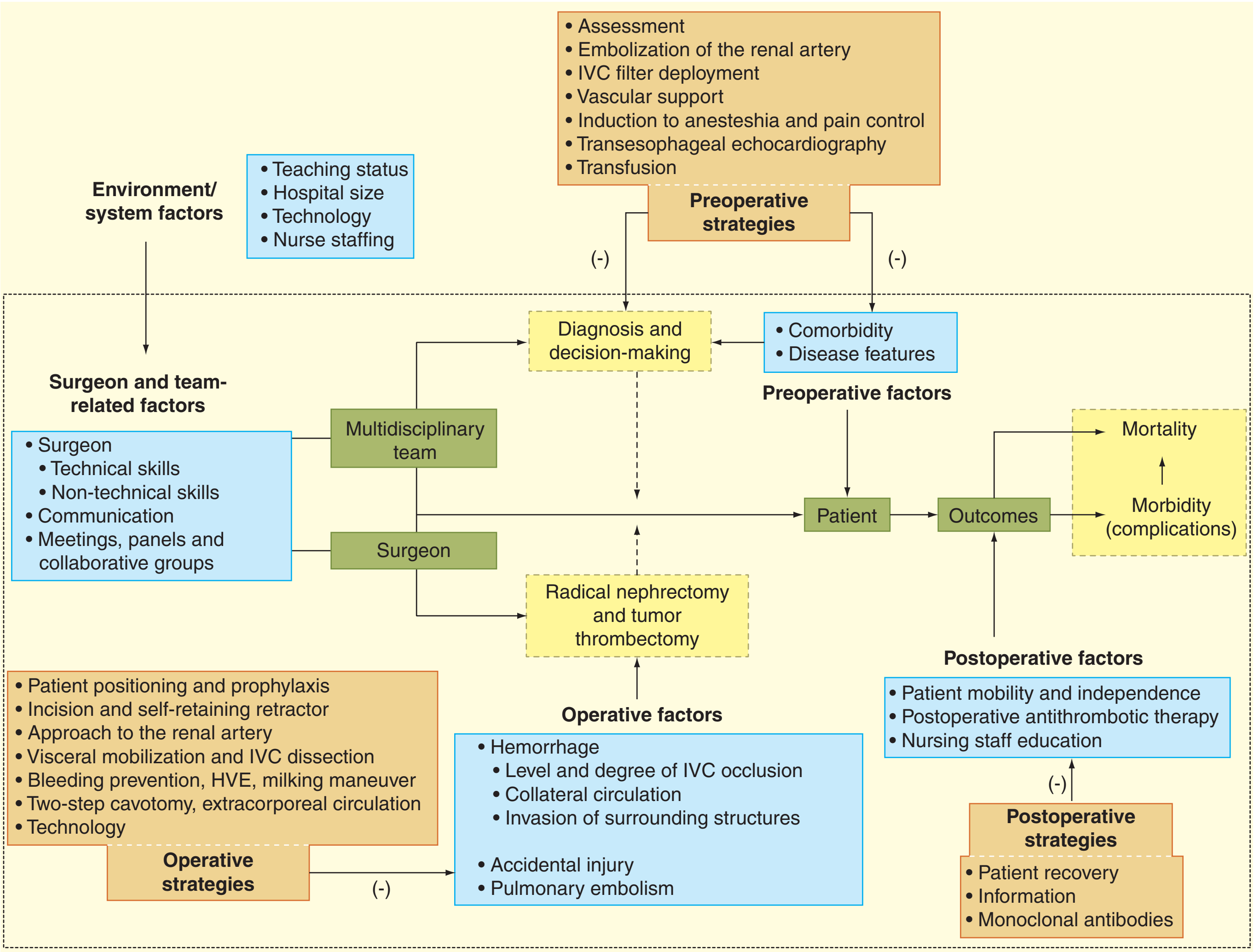

Figure 1. Operation profile for radical nephrectomy and tumor thrombectomy. Different innovative strategies have been implemented to decrease the number and severity of surgical complications.

and type of surgical techniques used for its successful removal. The successive addition of surgical maneuvers to handle increasing thrombus height also increases the risk of complications. For example, in a large series conducted by Blute *et al.* [18], it was noted that higher thrombus levels were associated with an increase in surgical complication rates (i.e., 8.6, 15.2, 14.1, 17.9 and 30.0%, respectively, for levels 0 to IV).

Thrombus above the diaphragm may necessitate opening the right atrium to assure complete clearance [33]. Although cardiotomy under extracorporeal circulation has been traditionally axiomatic for all instances of supradiaphragmatic venous extension [18], this maneuver has been shown to be correlated with significant morbidity [34]. In a recent series by Lubahn *et al.* [35], it was shown that tumors requiring cardiovascular procedures were associated with an increased risk of perioperative complications, including hemorrhage.

Determinants of collateral circulation are the location of the obstructed venous segment, the length and degree of obstruction and number of veins involved in the process [36]. These elements, taken separately or in combination, determine venous redistribution to the heart. In general, more proximal and longer occlusions condition wider distribution of collateral vessels, and thus a greater risk of bleeding. In addition, complete IVC obstruction in intimate contact or invading the venous wall, may necessitate segmental caval resection for thrombus complete removal. Under these circumstances, collateral circulation is commonly present, making IVC reconstruction rarely necessary. However, in cases of insufficient collateral circulation (i.e., presence of lower extremity edema [LEE], or risk of venous return impairment), a vascular prosthesis may be needed to ensure adequate venous drainage.

Accidental injuries

Adjacent organ resection has been also associated with nonhemorrhagic complications including injuries to adjacent structures. Vascular and visceral injuries can also be life-threatening if they go unrecognized. Involvement of surrounding structures by tumor makes excision longer and more tedious. In a recent series by Zisman *et al.* adjacent organ resection due to locally advanced tumor and regional lymph node involvement was highlighted as an independent predictor of vascular injury and bleeding, thus, requiring transfusion. By contrast, the rate of surgical complications was not higher in the presence of locally advanced or metastatic disease, except for cases in which metastasectomy was attempted [37].

Pulmonary embolism

Probably, the most feared intraoperative complication in cases of RCC invading the IVC is the embolization of dislodged thrombus fragments to pulmonary circulation secondary to IVC surgical manipulation. This complication has been reported infrequently (i.e., 1.5–3.4% of cases), although when it occurs, mortality has been shown to be extremely high, reaching 60–75% of such cases [38]. Higher anatomic thrombus level and association with bland thrombus have been outlined as major factors increasing the rate of PE [39,40].

Surgeon & team-related factors

Contemporary treatment strategies rely on multidisciplinary care teams, channeling individual expertise through a unified healthcare process. Similarly, perioperative care has evolved from a surgical-nursing team to a broad interdisciplinary cooperative endeavor. Observational studies have identified the individual and team factors that seem to underlie surgical performance [41–45].

Surgeon

Clinical competence is a combination of cognitive factors (acquiring and applying knowledge, decision-making, using resources and learning from expertise), personality traits (communication skills) and psychomotor skills (technical skills) [46,47]. Once surgical outcomes have been adjusted for patient risk factors, the remaining variance in surgical outcomes is presumed to be explained by individual surgical skills. The training system introduced by Halsted in 1889 [48] remains the cornerstone of surgical training. However, advances in educational theory, as well as pressures in the clinical environment, have led to questions about the reliance on this approach to teaching technical skills. Those pressures include a move toward a shorter workweek for residents and an emphasis on operating room efficiency, both of which diminish teaching time. The increasing complexity of cases and a greater emphasis on mitigating medical error limit faculty surgical assistance. Sheer volume of exposure, rather than specifically designed curricula, is the hallmark of current surgical training [49].

In surgery, 'experts' have been defined as experienced surgeons with consistently higher volumes and better outcomes. However, volume alone does not account for the skill level among practitioners, since variations in performance have been shown among surgeons with high and very high volumes. Thus, 'deliberate practice' (i.e., focused on a defined task) has become a critical process for the development of mastery [50]. In the current model of surgical training the opportunities for deliberate practice are rare, thus, increasing the interest in directed fellowship trainings. Operations are complex in urologic oncology, and even more complex in the case of radical nephrectomy and tumor thrombectomy. Fellowship surgical training in urologic oncology tries to prepare future surgeons to deal with these cases, but RCC with tumor thrombus occurs infrequently, making surgical opportunities scarce. In our opinion, given that a number of specific technical skills are necessary for the performance of a safe procedure in this context, a 2-year fellowship in urologic oncology complemented with additional training in transplant surgery would be of interest for the potential surgeon, since with this approach a sound formation in abdominal visceral mobilization and difficult vascular procedures can be acquired.

Over the last decade, there has been increasing recognition that adverse events in surgery are more likely to originate from behavioral failures than a lack of technical expertise. Although technical skills are necessary for safe surgery, taken in isolation they are not sufficient to maintain high levels of performance over time. In addition, what are now commonly termed as non-technical skills [51] are as important as (and sometimes more important than) technical skills in ensuring an optimum outcome for the patient undergoing surgery.

Non-technical skills include interpersonal (i.e., communication, teamwork), cognitive (i.e., decision-making, situational awareness) and personal resource skills (i.e., coping with stress and fatigue). These non-technical skills probably remain key root causes of surgical errors worldwide [52–55] and to date have never been formally recognized, taught or assessed. We now understand and recognize these non-technical skills. The challenge in the future is to incorporate them into undergraduate teaching, postgraduate training, assessment and perhaps even selection.

Multidisciplinary team & communication

Different professional staff groups are responsible for unique aspects of surgical care in patients with RCC involving the IVC. The development of a multidisciplinary and experienced surgical team is nowadays an essential requirement in this type of surgery. Fluent, concise and effective communication between all members of the team will favor optimal perioperative outcomes [56].

Meetings, panels & collaborative groups

An increasing number of national guidelines make regular multidisciplinary team meetings a prerequisite to the practice of oncological surgery. Indeed, a study of urological cancers found that management plans were altered in over one-third of patients discussed at such meetings [57].

Wise recommendations from expert panels [33] and the analysis of data from multi-institutional collaborative working groups are of outstanding value in the study of low frequency diseases (i.e., RCC with tumor thrombus), given that single institutional experiences may not be sufficiently representative. Recently, a multi-institutional initiative including 22 centers from Europe and the USA has been created for this purpose [24,28].

Postoperative factors

Patient mobility & independence

Efforts to promote the patient's autonomy are crucial, including avoidance or early removal of intravenous lines, drains and urinary catheter. Routine use of abdominal drainage [58,59] and nasogastric tubes [60] increases gastrointestinal and infectious morbidity, with no benefit for the patient. To our knowledge, no special recommendation on this issue is available for patients undergoing radical nephrectomy and thrombectomy; hence, it is preferable to avoid their use whenever possible. Urinary catheters should be removed on the first postoperative day after abdominal procedures. Recatheterization rates of 10% were found in randomized trials investigating early removal of bladder catheters, and urinary tract infections and length of stay were also significantly reduced [61,62]. Enforced mobilization, breathing exercises and preservation of the sleep pattern with nighttime sedation as needed are important.

Postoperative antithrombotic therapy

Venous thromboembolism (VTE) represents one of the most common preventable causes of death in patients with cancer undergoing surgery. The incidence of VTE increases with recent surgery, advanced malignancy and hospital admission [63]. Most institutions support in-hospital VTE prophylaxis and bridging treatment for patients receiving vitamin K antagonist or antiplatelet therapy based on updated, risk-stratified and evidence-based guidelines [64–66]. Recently, Woodruff *et al.* reviewed the literature regarding postoperative management of RCC with IVC surgical cases and provided specific recommendations on postoperative anticoagulation therapy, IVC filter use and imaging follow-up protocols [67].

Nursing staff education

An important aspect concerning postoperative care of patients with RCC involving the IVC regards nursing staff education. Recently, Klipfel *et al.* outlined the need for nurses to understand this surgical procedure and its inherent risks to proactively and successfully manage the patient's postoperative care and discharge plan [68].

Environment factors

The outcome of surgery is also dependent on the quality of care received throughout the patient's stay in hospital and the performance of a considerable number of health professionals, all of whom are influenced by the environment in which they work. The impact of systems of care on perioperative complications is an active area of interest, since it is clear that certain systems may manage complications more effectively and provide better overall patient support than others.

The complexity of the interventions for RCC invading the IVC makes tertiary referral hospitals the adequate environment to manage patients with this disease. However, good results have also been reported in the low volume setting [69]. Although optimal teaching status, hospital size, technology and nurse staffing have been associated with improved survival rates, many of the differences between hospital morbidity and mortality are not still well explained [70,71]. A better understanding of environmental variables which may contribute to these differences would allow for the institution of quality improvement programs in higher morbidity hospitals with the goal of improving patient outcomes.

Strategies to reduce the rate of complications in radical nephrectomy & tumor thrombectomy

Innovation is defined as the introduction of something new, whether an idea, method or device, aiming to obtain an improvement over the current standard that is applied. In the modern surgical era, this process ideally occurs via a graduated system of original thinking, surgical ingenuity and rigorous research. Whereas the best of these innovations have the potential to incite major shifts in surgical paradigms, most do not achieve this end point. Although they may not attract the same attention as true paradigm shifts, these other innovations are vitally important in the evolution of a surgical subspecialty. The following are some 'innovative' strategies that, according to the operation profile previously set, may decrease the number and severity of perioperative complications when dealing with such complex cases (Figure 1).

Preoperative strategies

Assessment

Commonly, the classification systems used to plan the surgical approach in RCC with IVC tumor thrombus cases have been based on the imaging depiction of intracaval extension. Probably, the most widely used system for surgical purposes is the one provided by Neves and Zincke [72]. However, in our opinion this system does not provide complete decision-making information regarding some retrohepatic and suprahepatic/infradiaphragmatic (i.e., level III) tumor thrombi. Conversely, the Miami classification system may provide additional information to improve decision-making in this particular setting [73].

Embolization of the renal artery

This maneuver aims to reduce blood supply, mass size and collateral blood flow around the tumor. Although isolated single institutional experiences support this procedure as a method to decrease the overall complexity of the intervention [74], this technique presents certain disadvantages, which may advise against its use. Subramanian *et al.* [75] showed that there is no significant advantage in preoperative embolization for the treatment of RCC with an IVC thrombus, and in fact, this procedure may increase the risk of complications and mortality probably by inducing a significant reaction around the kidney and surgical field. Hence, both the high frequency of postembolization syndrome and in many cases its severe clinical presentation, led experts to no longer recommend this maneuver [33].

IVC filter deployment

Possible migration of dislodged thrombus fragments into the pulmonary circulation favored the presurgical use of IVC filters as PE preventive strategy [76]. Currently, this recommendation remains also controversial, due in part to different reports on the rupture of the caval wall during the device deployment [77], not to mention the infrequent proximal migration of the filter into the right heart chambers causing a lethal cardiac tamponade [78].

In our opinion, if the patient presents an established PE at the time of diagnosis, there is no indication for IVC filter use. In most of these cases, if not all, PE is produced by a mix of tumor and bland thrombus fragments. Tumor thrombus fragments are completely insensitive to anticoagulant therapy. Under these circumstances, endarterectomy under cardiopulmonary bypass (CPB) is advisable for a complete tumor removal.

IVC filters are not capable of preventing tumor thrombus enlargement. Therefore, the device can be progressively entrapped within the neoplastic tissue after placement. If this occurs, the complexity of the procedure is multiplied exponentially, and what apparently would be a resectable case, may become almost unresectable.

The anatomical location of the proximal thrombus limit and the degree of IVC occlusion may also contraindicate the deployment of a filter. Filter placement may not be warranted in higher thrombus level cases (i.e., levels III–IV) due to a space conflict above the major hepatic veins (MHVs). Obviously, the filter cannot be placed in the right atrium. In addition, the use of a distal (i.e., femoral) instead of a proximal (i.e., transjugular) percutaneous approach for filter deployment may potentially induce a partial dislodgement of the thrombus with devastating consequences.

In cases of complete IVC flow interruption, filter deployment may be unnecessary since the thrombus would act as a filter itself (i.e., completely occluding the lumen of the IVC). In addition, as a result of complete IVC occlusion, venous flow redistributes through a secondary network of variable size collaterals. The diameter of these vessels is occasionally wide enough to permit the passage of thrombus fragments. Placing a filter in the IVC would not prevent an eventual PE under these circumstances. Nevertheless, if the filter is thought to be strongly indicated (i.e., level II, not completely obstructing, tumor thrombus cases, with or without associated bland thrombus), it should be deployed <48 h before surgery to reduce the incidence of thrombus entrapment [67].

Vascular support

Each case should be discussed with the anesthesiologist in order to decide on the appropriate types of invasive vascular access lines to be placed [79–82]. There are numerous types of catheters that play an important role in the management of these complex cases [82–89]. For routine resection of tumors involving the IVC and potentially other major vascular structures, a minimum of an arterial line, pulmonary artery catheter and a large bore central line have been recommended [90]. However, one of the strategic targets in perioperative care is to avoid iatrogenic harm [91]. Cancer patients with central catheters have higher rates of thrombosis and infection as part of their disease process [92]. In addition, a jugular line placed inside the right atrium may induce thrombus dislodgement before adequate vascular control; hence, we prefer not to use these devices in order to eliminate or minimize the possibility of iatrogenic PE. Likewise, the early withdrawal of invasive catheters in the recovery room after the intervention has been shown to avoid potential thrombotic and infectious complications related to these devices [93–95].

Induction & pain control

The surgeon should carefully observe the induction, ventilation and intubation of the patient. In most instances, inhalation anesthetic agents combined with intravenous narcotics provide the most satisfactory anesthesia management scheme [90]. Epidural anesthesia should be avoided as the risk of coagulopathy and epidural hematomas is high when significant blood loss is expected. However, for lower level tumor thrombi, in patients having a normal coagulation profile, a single opioid intrathecal injection may provide improved perioperative pain control.

Transesophageal echocardiography

Softer and higher level thrombi, and those associated with bland thrombus, present a higher risk of PE [40]. Transesophageal echocardiography (TEE) permits an excellent assessment of the shape, mobility and size of the proximal thrombus limit [96]. TEE real-time imaging not only aids in the characterization of the proximal thrombus limit but also allows access to any potential tissue detachment at this level during the intervention, especially when a 'milking' maneuver is required. Indirect visual information provided by TEE permits the management of most cases exclusively from the abdominal field [97]. In our opinion, the anesthesiologist committed to these cases should be familiar with the use of the TEE technique, since it can be of great value throughout the intervention.

Transfusion

Anemia is a common finding in patients undergoing surgery for RCC with venous involvement. However, a widely held dogma in oncology is that blood transfusion should be avoided whenever possible in these patients due to its immunosuppressive potential [98]. Despite a large number of experimental publications, the mechanism of transfusion-related immunomodulation remains poorly understood. Nevertheless, patients undergoing surgery for cancer, including RCC, who receive blood products remain prone to worse outcomes in terms of tumor growth and recurrence [99]. Meticulous and gentle techniques using electrosurgical dissection and acute hemodilution are effective in reducing the need for blood transfusion [100]. A pulmonary artery catheter would be of help in cases of massive transfusion [90].

To minimize transfusion requirements a cell-saver device can be used, since a recent meta-analysis suggested that cancer outcomes were not inferior when blood cells lost during surgery were transfused back [101]. In this study, cell salvage was recommended in all cases where estimated blood loss was above 1000 ml. Nevertheless, blood products should be reserved timely in the blood bank if important blood loss is anticipated and a cell-saver device is not available [90].

Operative strategies

Patient positioning

Long procedures under general anesthesia, with complete paralysis, place nerves under special risk of injury. Any significant abduction, extension or external rotation of the arm can stretch the brachial plexus and cause a nerve injury. Placing both arms by the side with the arms pronated and with gel pads placed near the ulna, beneath the elbow and tucked loosely by the side, can prevent ulnar nerve and brachial plexus injuries. This also gives the surgeon access and mobility to operate by the patient's side.

Prophylaxis

No specific guidelines on surgical-site infections are available to date for radical nephrectomy and tumor thrombectomy. However, the administration of a single dose of a broad-spectrum antibiotic is advisable before making the incision. Redosing of antibiotic prophylaxis in procedures longer than 4 h or when major blood loss occurs is also recommended [102–106].

Compression stocking devices have been shown to reduce the risk of DVT in patients with cancer undergoing surgery. They should be used for at least 30 min prior to the start of surgery. Is advisable to keep the stocking in place until the patient has started ambulation [63,64].

Incision

A large number of different incisions have been used in the treatment of RCC with caval involvement. Usually, the use of a particular type of incision is in relation to the volume of the renal mass, its relationship to the surrounding structures and the anticipated level of tumor thrombus. Thoraco-abdominal and flank approaches were frequently used in the past [107]. Midline xiphopubic and transverse subcostal incisions are now preferred by most surgeons, since they avoid the postoperative need for a thoracic tube. In addition, both types of incision can be combined with a midline sternotomy if CPB is required.

Transverse incisions are based on better physiological principles and should be recommended, as there are fewer complications in the early postoperative period and a lower incidence of late incisional hernia [108]. A recent systematic review has shown that both analgesic use and pulmonary compromise may be reduced with a transverse incision. However, this does not appear to be clinically significant, as complication rates and recovery times are the same as with a midline incision [109].

Although the approach through the midline can provide excellent exposure, in our opinion this incision entails a typical telescopic effect, which increases with depth in the surgical field. This fact may put at risk the adequate control of 'deep' areas, and thus, the overall safety of the procedure [110]. Conversely, the trirradiate Chevron incision properly combines the advantages of midline and subcostal approaches without increasing the rate of incision-related complications. Nevertheless, the optimal incision for abdominal surgery still remains the preference of the surgeon [109].

Self-retaining retractor

In case a Chevron incision is used, a retractor designed for liver surgery is preferable (i.e., Rochard and Thompson). In fact, one of the main problems in the excision of higher-level thrombi is how to gain enough exposure in the upper abdominal quadrants. Liver retractors take the advantage of moving the costal margins toward the axilae. This movement flattens diaphragmatic domes, thereby increasing exposure at this level [111].

Approach to the renal artery

Access to the main renal artery can be obtained through two different planes of dissection: anterior and posterior. Each plane has specific advantages which may facilitate arterial vascular control under particular situations.

The posterior approach [112] requires the division of all adhesions between Gerota's fascia and the posterior abdominal wall. Although it may seem more complex, this approach avoids potential engorged vessels in the anterior surface, providing quick and safe access to the main renal artery near its take-off in the aorta. In our opinion, this access represents the best option in cases of marked venous collateral circulation or in cases of hampered renal hilum by bulky lymphadenopathy.

On the contrary, the anterior approach [113] may be the best option when the renal mass cannot be mobilized because of its large size. This access is perhaps faster and provides vascular control of both renal units at the same time, although it requires a relatively free anterior plane and extensive dissection on the great vessels, which may result in more injury.

Visceral mobilization

Anterior access to the kidney is achieved through mobilization of the ipsilateral colon segment. Bilateral peritoneal incision on the avascular line of Toldt is mandatory to gain this access. Medial colon rotation progressively exposes the anterior surface of Gerota's fascia. Both the Kocher maneuver and liver mobilization [114] complete right renal exposure, while the dissection of the complex formed by the stomach, spleen and pancreas allows a full inspection of the left anterior renal plane [115].

IVC dissection

Control of the obstructed IVC involves surgical steps at three different caval segments: infrahepatic/renal, retrohepatic/suprahepatic-infradiaphragmatic and supradiaphragmatic [110].

Infrahepatic IVC segment & renal veins

Every vestige of lymphatic tissue must be cleared from the anterior aspect of infrahepatic IVC segment. Both renal veins are encircled to be clamped before opening the IVC. The posterior surface of the IVC is detached from the abdominal wall by ligating and dividing all of the lumbar veins found at this level, thus gaining complete circumferential control. Circumferential control aims to limit the bleeding from the engorged collateral vessels at the time of cavotomy.

Retrohepatic/suprahepatic-infradiaphragmatic IVC segment

Exposure of this segment requires liver mobilization. In 1989, Tzakis *et al.* [116] described the so-called 'piggy-back' technique, which is based on a tangential clamping of IVC at the level of the MHVs avoiding complete caval occlusion. The liver is fully mobilized by dividing all its posterior attachments until it lies in a 'piggy-back' fashion only attached to the IVC by the MHVs. If this is done, the right bare area can be broadly entered. By so doing, it becomes possible to elevate the right lobe into the wound and to retract it toward the left freely, thus, facilitating full control of the entire retro- and suprahepatic IVC segments [110]. By using the 'piggy-back' technique, better hemodynamic stability, shorter anhepatic phase, operative times, ICU and hospital stay, lower blood product usage as well as reduced costs are obtained [117]. However, this maneuver can inadvertently be followed by the dislodgement of the proximal thrombus burden, thus causing a PE [118].

Supradiaphragmatic IVC segment

Diaphragmatic caval release, by opening the central tendon of the diaphragm and encircling the IVC, allows access to the intrathoracic IVC segment from the abdominal field [110]. Thereafter, the pericardium can be opened, and the right atrium can be gently pulled through the diaphragm to be controlled inside the abdomen. This maneuver permits the resection of most level III–IV tumor thrombi without the need for extracorporeal circulation.

Bleeding prevention

Before attempting the cavotomy, it is essential to check all possible sources of venous bleeding. Commonly, thrombi confined to the renal vein require only one vascular clamp partially occluding the IVC lumen, while in some level I cases, tumor thrombus can be repositioned manually inside the renal vein. In most cases, partially occluding level I–II tumor thrombi can be completely resected with the help of a vascular clamp placed on the IVC in an oblique fashion that preserves venous flow.

By contrast, completely occluding level II or higher tumor thrombi require the sequential clamping of the infrarenal portion of the IVC, the contralateral renal vein and the right adrenal vein. In these cases, the upper thrombus limit determines the location of the proximal clamp. Ideally, natural venous bypass through the liver should be preserved, since potential complications secondary to hepatic vascular exclusion (HVE) can be avoided. This maneuver is particularly important in cases of incomplete collateral circulation, in which cardiac preload is maintained by residual flow still circulating through the IVC. A trial of cross-clamping allows checking hemodynamic tolerability permitting the anesthesiology team to be ready for a sudden cardiac collapse [110,119,120]. A rapid infuser can be used under these circumstances to restore the volume required to obtain a critical cardiac input, thus avoiding hypotension and hypoperfusion [36].

Hepatic vascular exclusion

HVE may facilitate thrombus excision, since potential bleeding from the liver is prevented. A small orifice practiced in the lesser omentum permits the control of the vascular inflow to the liver (Pringle maneuver), while a vascular clamp applied at the level of the MHVs controls the liver venous outflow [110,114].

'Milking' maneuver

In case of IVC involvement at the level or beyond the MHVs, and depending on the particular situation, the cranial thrombus limit may be 'milked-down' below the MHVs to preserve the natural liver bypass [73,110]. TEE permits optimal control over the thrombus cranial end during this maneuver. However, in many other cases, the thrombus cannot be 'milked-down' below this level, and a 'two-step' cavotomy would become the best option.

Two-step cavotomy

This maneuver requires temporary HVE. When complete IVC control is achieved, the first step is started. The IVC wall is opened to a level below the MHVs. The IVC lumen is completely cleared of thrombus fragments up to this level, and flushed with heparin. The proximal clamp is then repositioned below the MHVs, and the IVC wall is sutured closed with a double 4-0 running polypropylene suture. Pringle maneuver [114] is released thereafter, and natural liver bypass is restored. Afterward, in a second step, the cavotomy is continued downward to the renal veins, and every vestige of neoplastic tissue is withdrawn from the IVC lumen. Commonly, the caval wall containing the renal vein ostium involved by tumor is also excised to ensure a safe resection margin (i.e., tangential resection).

Inferior vena cava resection

Clinical conditions requiring IVC resection are rare and include complete obstruction of the caval lumen, densely adherent intracaval tumor, encasement of the great vessels by bulky disease and direct caval wall invasion [36]. Although most commonly, CT is used for this purpose, one distinct advantage of MRI in this context is its high sensitivity for detecting caval wall invasion.

Masses involving less than half of the IVC may be managed with tangential resection. Conversely, IVC interruption with circumferential resection either by ligation, stapling or oversewing may be necessary in the following scenarios: lesions involving more than half the circumference of the IVC, presence of complete chronic obstruction in the absence of clinical symptoms suggestive of venous stasis, high risk of postoperative PE due to the presence of unresectable bland thrombus, and successful thrombectomy attempt complicated by vascular intima layer damage resulting in an increased risk for new clot development [36].

Venous reconstruction

IVC interruption can be accomplished below the level of the MHVs without any major consequences. IVC resection without reconstruction is feasible in cases of complete IVC obstruction, extensive bland thrombus without a clear depicted limit and no preoperative evidence of LEE. The clinical changes observed after this procedure are transient, and resolve by the time of discharge.

By contrast, acute resection without preexisting chronic obstruction is poorly tolerated because of the absence of sufficient collateral circulation. As such, IVC reconstruction should be considered in patients with preoperative LEE, inadequate collaterals or intraoperative disruption of preexisting collateral circulation [36]. However, the decision to reconstruct the IVC must be balanced by concern for complications such as graft occlusion/thrombosis, infection or enterocaval fistula formation.

While small cavotomies may be closed primarily, extensive caval incisions may result in luminal narrowing. In this setting, an autologous patch may be utilized to bridge the gap, thus minimizing the risk of venous thrombosis formation. Interposition grafting is typically necessary in the absence of enough collateral circulation when *en bloc* IVC resection is planned. Extended polytetrafluoroethylene (ePTFE) is the preferred synthetic material when replacement is considered, as it has low thrombogenic potential and a high reported patency rate.

Veno-venous bypass

During the phase of HVE for higher thrombus level excision, there are hemodynamic issues that affect morbidity, mortality and the entire postoperative course. Veno-venous bypass (VVBP) was originally described to give response to the interruption of blood flow back to the heart, which in turn, is associated with a decrease in cardiac output and arterial pressure by up to 50% [116]. This interruption leads to critical organ hypoperfusion, damage in the intestinal capillary bed, increase in systemic vascular resistance and extensive bleeding from venous collaterals [121,122]. In addition, two cases of splenic rupture during Pringle maneuver due to vascular congestion were described [16]. However, some complications have been described when VVBP is used, and some hemodynamic alterations cannot be completely avoided [123].

Experience in liver surgery has demonstrated that the hemodynamic changes observed during HVE restore promptly after hepatic reperfusion, with renal function remaining stable and the requirement for blood transfusion is comparable with procedures with VVBP. Thus, two main conclusions can be drawn from this experience. First, the theoretical benefits of VVBP on renal function during HVE are of little clinical relevance. Second, perioperative blood loss and transfusion requirements are similar in patients with or without VVBP, indicating that there is no clear advantage for routine use of VVBP [122,123].

Cardiopulmonary bypass

CPB sparked a monumental advance in surgery in recent years that would otherwise be impossible, given the operative difficulty and poor operative outcomes obtained with classic approaches to procedures involving the heart [124]. CBP with or without deep hypothermic circulatory arrest (DHCA) brings relative technical ease by providing continuous blood return to the heart in order to preserve cardiac output, thus, being used in the past in all cases with suprahepatic and supradiaphragmatic thrombus extension.

Unfortunately, in so doing it induces a whole-body inflammatory response that is capable of causing devastating morbidity and mortality. This response has the potential of engendering a constellation of clinical, biochemical and radiological manifestations of multi-organ dysfunction with tremendous prognostic implications. In the field of cardio-thoracic surgery, prospective randomized trials have failed to find any significant differences between on-pump and off-pump procedures. However, both prospective and retrospective studies have reported a reduction in the need for mechanical ventilation, postoperative blood loss and need for transfusion, postoperative complications, length of intensive care and hospital stay and consequently the cost of treatment when CBP is not used [124]. Avoidance of CBP therefore, has the potential of obviating the clinical manifestations of CBP-related morbidity, and it is this appeal that has impelled the renaissance of off-pump procedures. Off-pump approaches to tumor thrombus are currently undergoing greater scrutiny, and thus, the medical literature contains an increasing amount of research on this issue [97,125].

Today, CPB is among the most used surgical adjuncts in RCC with tumor thrombus surgery, and it continues to evolve through research. Techniques to minimize morbidity associated with the use of CPB and DHCA include: the use of antegrade cerebral perfusion, a minimally invasive approach to CPB instauration and the use of CBP under mild hypothermia [34,126,127]. The new scene provided by off-pump procedures has also ignited a keen enthusiasm in the refinement of CPB techniques. In most practices, the off-pump approach is paradoxically dependent on, and guaranteed by the presence of the CBP machine. Therefore, the two techniques should be regarded as complimentary, and the advance of one technique will tend to improve the practice of the other [124].

Technology

Consistent benefits have been established for laparoscopic and robotic assisted approaches compared with laparotomy: earlier resumption of a normal diet, reduced blood loss, halved short-term morbidity and decreased postoperative pain and analgesic use. These benefits have translated into a reduction of hospital stay, less need for skilled nursing facility utilization and improved quality of life and recovery [128]. The application of advanced techniques has allowed the management of RCC with IVC extension in a purely minimally invasive fashion. However, the standard approach to RCC with intracaval extension remains open surgery, because the long-term benefits of minimally invasive approaches are still unknown. Further experience will be necessary to decide whether these benefits justify the new approaches [129,130].

Postoperative strategies

Patient recovery

Most patients are extubated if surgery was uneventful at the conclusion of the case. Uncomplicated cases typically recover routinely. By contrast, complex cases may need ventilation support for at least 12–24 h after the procedure. Consultation with a critical care physician is recommended to ensure safe and immediate perioperative care [90].

Information

Information about the care process is paramount, starting in the preoperative visit and extending to post-discharge management. Written information about the procedure and related expectations should be provided in plain language, including discharge criteria and follow-up arrangements. The patient, relatives and all healthcare providers involved should share a common understanding of the expected care pathway [131].

Conclusion

Contemporary perioperative care is a multidisciplinary endeavor. By capturing all relevant features of an intervention, a more adequate assessment is made, and a deeper understanding of its surgical outcomes is obtained. This is particularly important in an era of enhanced scrutiny of healthcare practice, constrained resources and rising medical needs – nowhere more pertinent than in RCC with tumor thrombus surgery.

Surgeons must continue to pursue 'innovative' thinking, make technological advances, improve training and systematic research in order to be able to better deal with perioperative variables and technical difficulties that may be potentially fatal in this context. In surgical procedures, complications can arise at any time, from initial evaluation of the patient to the post-operative period. Anticipation and appropriate preparedness for surgery are crucial to limiting complications. Knowing how to manage complications is important, but knowing how to avoid them is prudent and intelligent. The ultimate objective of the 'innovative' strategies addressed in this review is to obtain an improvement in patient care manifested as a decrease in morbidity and mortality.

Expert commentary

The present review has outlined important factors in the surgical care of patients with RCC and IVC extension. Although they are not all directly effective against RCC *per se*, they aim to make a difference in outcomes when applied. Many of these elements belong to surgical routine and may be influenced by tradition. Uptake of innovations can be a daunting task, sometimes requiring a huge collection of research in its favor prior to the whole surgical community implementing its use. This review should aid to reinforce those changes that collectively make a difference to patients with RCC and IVC extension.

Five-year view

Awareness and enhancement of the culture of perioperative care safety is increasing in the mind of surgeons. Over the next 5 years, we will be spectators of an unprecedented growth in the number and quality of innovative strategies implemented to achieve this purpose. This is particularly the case for the management of a unique form of locally advanced RCC so-called tumor thrombus and many others. Implementing improved strategies into daily surgical practice will allow our patients, despite their ominous prognosis, to expect the best care that we can provide to increase not only their hope for a potential cure, but also their quality of life.

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Key issues

- Improvements in surgical management have placed us in a vantage position of judging the potential of our treatment modalities to cause harm.
- Classifying and evaluating the complications arising after surgical treatment would provide the adequate environment in which comparisons between individual surgeons, institutional experiences and different techniques can be accomplished in a systematic, objective and reproducible way, thereby, facilitating the adoption of preventive changes in care in an effort to decrease morbidity and mortality.
- Radical nephrectomy and tumor thrombectomy still often result in significant morbidity and mortality, with complication rates exceeding 50% and postoperative mortality rates as high as 23.5%.
- The radical nephrectomy and tumor thrombectomy 'operation profile' tries to capture all relevant features of this operation to: provide a deeper understanding of surgical outcomes; provide a basis for assessing the intervention; expand operative assessment beyond patient factors and technical skills of the surgeon and extend assessment of surgical skills beyond bench models to the operating room.
- This profile provides a valuable insight into the clinical mechanisms and the detection of underlying variations in outcomes and possible mishaps in care that occur, and to develop effective quality improvement strategies.
- Factors influencing surgical complications in renal cell carcinoma with inferior vena cava invasion include: preoperative factors (comorbidity status, disease features and accurate diagnosis); operative factors (hemorrhage, accidental injuries and pulmonary embolism); surgeon and team-related factors; postoperative factors (patient independence, antithrombotic therapy and nursing staff education) and environment factors.
- Rarely, surgical 'innovations' have the potential to incite major shifts in surgical paradigms, but the vast majority do not achieve this end point. Although they may not attract the same attention as true paradigm shifts, they are still vitally important in the evolution of a surgical subspecialty.
- Some of the 'innovations' or strategies provided in this review may decrease the number and severity of perioperative complications when dealing with renal cell carcinoma and inferior vena cava extension.

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