Perioperative Considerations in Metastatic Renal Cell Carcinoma

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Patients with metastatic renal cell carcinoma are complex, with the potential for significant complications, and require extensive pre-, peri-, and postoperative management. This article discusses, in depth, the necessary considerations in the treatment of these patients.

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KEY WORDS

Renal cell carcinoma • Radical nephrectomy • Cytoreductive nephrectomy • Metastasis • Perioperative care

Radical nephrectomy in the presence of metastatic disease (cytoreductive nephrectomy) may be indicated as part of an integrated management strategy. Patients most likely to benefit from cytoreduction are those with good cardiopulmonary reserve in whom the majority of the total tumor burden is within the kidney and the patient has minimal volume metastatic disease.[1] The other main consideration pertains to surgical resectability.

Patients with limited metastatic disease (approximately 2%-3% of cases) may be considered for metastasectomy. Favorable prognostic factors include complete resectability (eg, solitary lung metastasis) and an indolent course, supporting the assumption that this is a lone metastasis[2]; 5-year survival in this group of patients may reach 30% with metastasectomy.[3]

Preoperative Considerations

General

A thorough preoperative assessment should take place to assess physiologic status and cardiopulmonary reserve. Renal and hepatic function should be assessed and optimized if possible. Blood tests, including a complete blood count, renal and liver function tests, and a coagulation profile, should be performed. It is important to note that cancer surgery often cannot be postponed while lengthy investigation and interventions are carried out.

Cardiac complications are particularly relevant and electrocardiography and echocardiography should be performed, at minimum. Consideration should also be given to stress echocardiography and coronary angiography, if indicated.[4] Chest radiography should only be performed if clinically indicated.

Morbidity rates for open nephrectomy are high (approaching 30% in one study).[5,6] This impacts negatively upon hospital length of stay, need for critical care, and long-term outcomes. Identification of those patients at risk for complications and increased length of stay is important in preoperative risk stratification and in coordination of individualized postsurgical care. In an attempt to quantify the risk of perioperative morbidity and mortality, a number of scoring systems have been developed.[7]

The American Society of Anesthesiologists Physical Status score[8] is the most well known of these. This system uses a subjective assessment of preoperative physiologic fitness to categorize patients into one of five groups, but has been shown to be a poor predictor of postoperative complications.[7] To address some of these limitations, Copeland and colleagues[9] developed the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) scoring system; however, the inclusion of intra- and postoperative variables precludes validation for prediction of preoperative risk. Additionally, the system has been shown to exhibit significant inconsistencies in predictive accuracy in different surgical cohorts. Despite these limitations, POSSUM (and its more recent derivations) is now the most widely validated predictive scoring system used in perioperative medicine.[7]

Traditionally, anesthetists have assessed patients' cardiopulmonary fitness preoperatively using metabolic equivalents (METs), and four METs (the equivalent of climbing two flights of stairs) is generally accepted as a reasonable level of fitness. Cardiopulmonary exercise testing (CPET) is a far more objective indicator of patient suitability for surgery than risk assessment of fitness using METs. It is based on the premise that patients who are unable to increase cardiac output and oxygen delivery during CPET are more likely to have a poor postoperative outcome, as they are unable to meet the increased oxygen demand during this period. The anaerobic threshold (AT), the point at which anaerobic metabolism is needed to supplement aerobic metabolism, is used rather than the maximum aerobic capacity (VO_{2max}) for prognostication. AT is reached well before VO_{2max} and can, therefore, readily be attained independent of motivation and age. An AT of $<$ 11 mL/min/kg correlates with moderate to severe heart failure[10] and predicts increased postoperative mortality from cardiopulmonary causes.[11] It also has a high negative predictive value for detecting those patients not at increased risk.[12] However, there are little published data on the use of CPET in major urologic surgery.[13]

Studies in patients with esophageal and rectal cancer have shown that treatment with neoadjuvant chemotherapy is associated with markedly reduced physical fitness, as assessed using CPET.[14,15] It may be that this is as a result of anemia or reduced myoglobin levels. Certainly, decreased exercise capacity is a feature of anemia,[16] and AT has been shown to improve following blood transfusion in anemic patients.[17] Lean muscle mass has been demonstrated to be closely related to aerobic performance in patients with nondisseminated colorectal cancer and healthy subjects alike.[18] However, the same study showed no relationship in either group between plasma myoglobin concentration and lean muscle mass or aerobic fitness, despite myoglobin being most highly expressed in the muscle fibers associated with aerobic performance.[19]

Nausea

Patients with metastatic renal cancer may be nauseated prior to surgery as a result of metabolic abnormalities, including uremia and hypoxia, or as a side effect of chemotherapy or opioids.

Approximately half of all cancer patients are cachexic, a state characterized by anorexia, weight loss, and impaired immune function. This means that patients are often nutritionally deplete, putting them at increased risk of nosocomial infection, poor wound healing, and pressure sores VO_{2max}.

Nutritional Status

Approximately half of all cancer patients are cachexic,[20] a state characterized by anorexia, weight loss, and impaired immune function.[21] This means that patients are often nutritionally deplete, putting them at increased risk of nosocomial infection, poor wound healing, and pressure sores. Infection in oncology patients can have an unfavorable effect on outcomes, and may be particularly challenging to treat.

Nutritional status should be optimized, if possible, either with nutritional supplements or by instituting enteral or parenteral feeding. Studies suggest that preoperative or early postoperative feeding in cancer patients produces a reduction in infectious complications and

protein catabolism.[22] Electrolyte imbalance should be corrected.

Anemia

Patients with metastatic renal cancer may be anemic for a number of reasons:

1. Anemia of chronic disease
2. Recurrent hematuria
3. Renal impairment, leading to reduced erythropoietin production

It may be necessary to optimize hemoglobin levels preoperatively using oral or intravenous iron, erythropoietin (EPO), and blood products.

Vascular Access

Peripheral and central vascular access may be troublesome if the patient has had multiple attempts or received intravenous chemotherapy previously. It may be necessary to conduct imaging such as a venogram to guide venous access.

Endocrinologic Paraneoplastic Syndromes

Hypertension. It is important to note that primary hypertension, as well as smoking and obesity, is an independent risk factor for the development of renal cell carcinoma (RCC).[23] This effect is more pronounced with increasing severity of both systolic and diastolic hypertension. However, Stojanovic and colleagues[24] demonstrated that, in patients with coexisting arterial hypertension and RCC, the hypertension resolved following nephrectomy.

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It may be that hypertension is a paraneoplastic phenomenon, occurring in 20% to 40% of all cases of RCC, and may occur through a variety of mechanisms.[25] These include hyperreninemia, vasculitis, polycythemia associated with increased EPO production, hypercalcemia possibly due to prostaglandin production, renal arteriovenous fistula, ectopic adrenocorticotropic hormone, and catecholamine production and ureteric obstruction.

Importantly, hypertension is a common side effect of the vascular endothelial growth factor (VEGF) inhibitor bevacizumab, and the tyrosine kinase inhibitors sunitinib, sorafenib, and, more recently, pazopanib, which are used in the medical management of metastatic RCC.[26]

It is important to determine whether there is any end-organ dysfunction, so an electrocardiogram and echocardiogram should be performed. The patient's hypertension should be controlled medically preoperatively. This may require multiple agents, especially in cases thought to be due to VEGF-inhibiting therapy.[27] Antihypertensive therapy should be closely monitored during the postoperative period.

Hypercalcemia. Hypercalcemia, defined as a total serum calcium of $>$ 2.55 mmol/L, affects up to 20% of patients with RCC.[28] It may be classified as metastatic and nonmetastatic or paraneoplastic.[29]

In approximately 50% of patients, hypercalcemia occurs secondary to osseous metastases,[30] which produce substances (thought to be prostaglandins) that promote osteoclastic activity, causing calcium release from bone. Local radiation therapy of bony lesions is often useful in alleviating bone pain. Medical treatment in the form of intravenous hydration, loop diuretics, and bisphosphonates may be beneficial in the symptomatic management of metastatic hypercalcemia.[28]

Paraneoplastic hypercalcemia accounts for the other 50% of cases. It is defined as hypercalcemia in the absence of osseous metastases and, by contrast, tends not to be associated with complaints of bony pain and is much less responsive to medical management.[28] The underlying pathophysiology involves the production of parathyroid hormone (PTH) and PTH-related peptide from the tumor cells. This produces a syndrome that is biochemically similar to primary hyperparathyroidism (hypercalcemia, increased serum PTH, reduced serum 1,25-dihydroxy-D_3, and renal phosphate wasting)[31]; however, patients with RCC and paraneoplastic hypercalcemia also exhibit decreased renal and intestinal calcium absorption.

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Patients with hypercalcemia may show electrocardiographic changes, including a shortened QT interval and presence of J waves. They exhibit ventricular excitability and are predisposed to arrhythmias. They may have nephrogenic diabetes insipidus and be hypovolemic as a result.

Polycythemia. Up to 8% of patients with RCC have polycythemia.[28] This paraneoplastic phenomenon is believed to be mediated by the glycoprotein EPO, which stimulates differentiation of erythrocyte colony-forming units in the bone marrow, increasing erythrocyte production.[32] In the healthy kidney, EPO is produced by peritubular interstitial cells in

response to local tissue hypoxia. By contrast, in patients with RCC, EPO production occurs within the tumor cells. Interestingly, ectopic EPO production is found in 66% of RCC cases.[33] The disparity between this and the number of patients with erythrocytosis may be that the majority of the EPO produced in RCC is inactive. EPO levels fall to normal following nephrectomy in nonmetastatic RCC. This is not the case in metastatic disease.[28] Polycythemia is of concern to the anesthetist due to the potential for additional hypercoagulability in an already prothrombotic condition.

EPO levels fall to normal following nephrectomy in nonmetastatic RCC.

Nonmetastatic Hepatic Dysfunction

In 1961, Stauffer[34] described a syndrome of hepatic dysfunction associated with RCC in the absence of discernible hepatic metastatic disease. It is seen in up to 20% of patients with RCC, and resolves following nephrectomy in two-thirds of patients with localized disease.[35] Biochemically, this manifests as elevation of transaminases and alkaline phosphatase, prolonged prothrombin time, and frequently hyperbilirubinemia.[28] The mechanism of liver injury in Stauffer syndrome is poorly understood. Histologic examination of liver tissue in affected patients reveals generalized hepatitis with lymphocytic infiltration and hepatocellular degeneration in the absence of biliary obstruction.[36]

Patients may present with hepatosplenomegaly, fever, and weight loss.[36] Considerations for anesthesia in these patients are similar to those in patients with other causes of liver disease: malnutrition, hypoglycemia, and coagulopathy are important.[37] Involvement of the gastroenterology team may be of benefit in planning the perioperative care of these patients.

Inflammatory Syndrome

Fever is present in 20% to 30% of patients with RCC, and it may be the presenting symptom in 2% of cases.[38] A constitutional syndrome may be present in up to one-third of patients, with symptoms including fever, cachexia, and anorexia. It is thought to be mediated by cytokines produced by the tumor cells. Interleukin (IL)-6 and tumor necrosis factor-α are likely candidates, and IL-1, interferons (IFNs), and prostaglandins have also been postulated to be possible causative molecules.[28]

Other Rare Endocrine Syndromes

Cushing Syndrome. RCC has been shown to be the underlying malignancy in 2% of all neoplastic Cushing syndrome. It is postulated that this is secondary to conversion of pro-opiomelanocortin to adrenocorticotrophic hormone by an enzyme contained within the tumor cells.[28] This causes adrenal hyperplasia and cortisol production.[39] The Cushing syndrome resolves following nephrectomy and partial adrenalectomy in most cases.

At the preoperative assessment, the anesthetist should actively seek symptoms and signs of Cushing syndrome. These include hypertension with possible left ventricular hypertrophy, obesity, and obstructive sleep apnea, which may be associated with a potential difficult airway, impaired glucose tolerance, or frank diabetes and hypokalemia (due to the weak mineralocorticoid effect of cortisol).[40] Postoperatively, one must be vigilant for signs of an Addisonian crisis.[28]

Alterations in Glucose Homeostasis. There have been a number of case reports of deranged glucose metabolism in patients with RCC that have resolved following nephrectomy.[28] Insulin and glucagon have both been isolated from RCC tissue.[41]

Nonendocrine Paraneoplastic Syndromes

Secondary Amyloidosis. In 3% to 8% of cases, RCC is associated with amyloid A amyloidosis.[28] This condition is characterized by extracellular tissue deposition of fibrils that are composed of fragments of serum amyloid A protein, a major acute-phase reactant protein, produced predominantly by hepatocytes in response to proinflammatory cytokines.[42] RCC resection can lead to regression of the amyloidosis. The most common sites affected are the following:

1. Kidney (90%) – the patient may have proteinuria, progressive renal impairment, or full-blown nephrotic syndrome
2. Liver – may present as painful hepatomegaly, but is often asymptomatic despite a high hepatic amyloid load
3. Spleen – should be suspected if Howell-Jolly bodies are found in the blood smear of a nonsplenectomized patient, and may predispose to recurrent infection
4. Heart (10%) – echocardiography may reveal left ventricular hypertrophy with diastolic dysfunction, or left ventricular failure

Nephropathy. Rarely, paraneoplastic glomerulonephropathies attributed to immune complex deposition can be associated with RCC.[43] They are usually either membranous glomerulonephritis

or minimal-change membranous glomerulonephritis. Patients may present with nephrotic or nephritic syndrome. The glomerulonephropathy resolves in some cases following nephrectomy; however, the usual course is persistence of symptoms, suggesting that the other kidney is involved.[44]

Neuromyopathy. Rarely, neuromyopathies have been described in patients with RCC. They may be sensory or motor, and range in severity from nonspecific myalgia to diaphragmatic paralysis to bilateral phrenic neuropathy to amyotrophic lateral sclerosis.[28] There are reports of resolution following nephrectomy, but polymyositis and polyneuromyopathy have been known to recur with the development of metastatic disease.[44] The cause is unknown, but it is postulated that the tumor cells secrete substances that cause the neuropathy, or that they may have an autoimmune basis.[45] Any preexisting neurologic deficit should be carefully documented, and special care should be taken with positioning.

Coagulopathy. Various disorders of coagulation are seen in patients with RCC. It is likely that this represents malignancy-associated coagulopathy.[44]

Malignancy predisposes patients to both thrombosis and hemorrhage; moreover, advanced metastatic disease has been shown to convey more of an increased risk of venous thromboembolism (VTE) than localized cancer.[46] Patients taking antiangiogenic agents and those in the perioperative period are at additional risk.[47] Trousseau initially described an association between thrombotic events and occult malignancy in 1865. Now, Trousseau syndrome encapsulates any thromboembolic phenomenon occurring in a patient with cancer.[48] Deep vein thrombosis is the most common venous manifestation, followed by pulmonary embolism, cerebral sinus thrombosis, and migratory superficial thrombophlebitis. It has been shown that VTE prophylaxis with low molecular weight heparin for 4 weeks after surgery for major abdominal and pelvic cancers significantly reduces the risk of VTE when compared with prophylaxis for 1 week postoperatively.[49]

Importantly, patients with confirmed VTE may have inferior vena cava (IVC) filters in situ. There is no significant increase in risk of further thromboembolism if these patients are not anticoagulated perioperatively.[50] Their position should be noted by the surgeon, especially if IVC clamping is planned.

Arterial thromboembolism may occur peripherally or in the coronary or cerebral vasculature. This may contribute to increased risk of perioperative myocardial infarction or stroke. The mesenteric, renal, and hepatic vessels may be involved.

Bleeding may occur in metastatic RCC for a number of reasons, including thrombocytopenia, decreased synthesis of clotting factors due to liver dysfunction, and preexisting mild coagulation deficiencies.[48] Liaison with the hematology team is advisable in this instance.

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Site-specific Metastatic Effects

Lung. The lung is the most common site to which RCC metastasizes.[51] Patients with solitary pulmonary metastases have a better prognosis than those with spread to other sites, irrespective of whether they are treated with nephrectomy.[52] Clinically, the patient may complain of chest pain, dyspnea, cough, or hemoptysis, but they may be asymptomatic. The typical radiologic appearance is described as "cannonball" metastases, caused when showers of tumor emboli travel to the lungs via the IVC.[53] Tracheal or endobronchial lesions may also be present; as a result, there may be signs of airway obstruction, postobstructive atelectasis, consolidation, or air trapping. Pleural metastases have been reported in up to 12% of cases[54]; this may result in malignant pleural effusion, which can compromise respiratory function and may warrant drainage. Computed tomography can delineate lung lesions further. In addition, pulmonary function tests should be conducted preoperatively. It may be useful to discuss the case with a respiratory physician.

Pleural metastases have been reported in up to 12% of cases; this may result in malignant pleural effusion, which can compromise respiratory function and may warrant drainage.

Bone. Metastasis to bone from RCC is common, ranging from 30% to 40%.[55] Pain from bony lesions is likely to produce high baseline analgesic requirements. It is important to be aware of any preexisting pathologic fractures, and, given that there is a potential for further fractures perioperatively, positioning should be meticulous.

Approximately 15% of bone metastases from RCC are in the spine.[56] Cord compression occurs in 5% to 14% of cases.[57] Neurologic deficit is almost universally preceded by back pain, but the condition is often diagnosed late. It is important to be vigilant for the development of neurologic symptoms and signs in the perioperative period, and to differentiate nerve compression that may occur as a result of poor intraoperative positioning from spinal cord compression.

Bone marrow invasion or compression by bony metastases may result in pancytopenia or isolated anemia, leucopenia, or thrombocytopenia. These findings each present their own problems for the anesthetist, and should be investigated and, if possible, corrected prior to surgery.

Liver. Liver metastases seem to be associated with a particularly poor prognosis.[52] Spread may occur either by contiguous extension or by the hematogenous route, the latter being more common. Interestingly, although the patient may be symptomatic with right upper quadrant pain from capsular distension, the liver function is usually normal.[58] Nonetheless, preoperative assessment of liver biochemistry and synthetic function should be performed.

Brain. Patients with cerebral metastatic disease require fastidious perioperative management. Preoperatively, they may have neurologic symptoms and signs including sensory, motor, or visual field deficits (all of which should be documented carefully). They may have seizure disorders and be taking one or more antiepileptic medications, the side effects and drug interactions of which are vast.[59] Patients with preexisting cognitive or physical impairment have increased propensity for postoperative cognitive dysfunction.[60]

Induction and maintenance of anesthesia should be smooth and undertaken in such a way as to minimize risk of surges in intracranial pressure. This can be achieved with intravenous or inhalational techniques. Remifentanil may be used intraoperatively but can lower mean arterial pressure in a dose-dependent fashion, resulting in reduced cerebral perfusion pressure.[61] Care should be taken to avoid indiscriminate fluid therapy, and the anesthetist should be mindful of any activity that may increase the intracranial pressure. This may include head down positioning, patient/ventilator dyssynchrony, coughing and high intra-abdominal pressure (such as with pneumoperitoneum). Normothermia, normoxia, normocapnia, and normoglycemia should be maintained. As such, it makes sense that these patients have an open procedure and be paralyzed and ventilated throughout and, if possible, extubated while in a deep plane of anesthesia to minimize coughing. Additionally, attention should be paid to maintaining adequate cerebral perfusion pressure. Treatment with steroids to reduce localized cerebral edema may be beneficial,[61] and discussion with neurologists, neurosurgeons, and oncologists may assist in the preoperative planning of such complex patients.

Adrenal. The incidence of ipsilateral adrenal metastases from RCC varies from 1.1% to 10%.[62] This is viewed as locally advanced tumor. Patients with RCC and a single contralateral adrenal metastasis should be considered as having solitary metastases. The ipsilateral adrenal should only be removed if there is any suspicion of metastasis.[63] Clearly, these patients should be managed expectantly to avoid perioperative Addisonian crisis.

Thyroid. Metastases from RCC may develop in the thyroid gland many years after the primary renal tumor, or prior to the diagnosis of RCC.[64] Interestingly, thyroid metastatic disease is noted in 5% to 12% of cases of RCC at postmortem examination.[65] It generally presents as a cold nodule—a painless mass that demonstrates decreased uptake of iodine-131. Patients are usually clinically and biochemically euthyroid,[44] and, as such, should not cause a problem for the anesthetist; however, larger masses may distort the airway, making endotracheal intubation difficult. Histologic examination is required to differentiate between primary thyroid malignancy and metastatic disease. If the thyroid lesion is found to be a solitary metastatic deposit, resection in combination with cytoreductive nephrectomy may provide an opportunity for long-term control of the disease.

Side Effects From Chemotherapeutic Agents

The collective experience with chemotherapeutic agents in metastatic RCC has been shown to have an overall objective response rate of 5% to 6%.[66] Combinations of treatments may modestly increase response rates up to 15%,[67] and combining chemotherapeutic treatments with immunotherapy has not produced any benefit over the use of immunotherapy in isolation.[68] Chemotherapy currently has only a trivial role in the management of metastatic RCC.[3]

Research into the underlying biologic mechanisms pertaining to the pathogenesis of RCC has determined that the VEGF and mammalian target of rapamycin pathways play an important role and, as such, may represent

important therapeutic targets.[3] Several novel agents have been approved as front-line treatments, and are now the standard of care in metastatic RCC.

Inhibitors of Vascular Endothelial Growth Factor. Sunitinib is a small-molecule inhibitor of tyrosine kinase element of the VEGF receptor. It is associated with fatigue, hand and foot syndrome, gastrointestinal disturbance,[3] hypothyroidism,[69] hypertension, and decline in left ventricular ejection fraction.[70] All patients on sunitinib should receive regular thyroid function tests, blood pressure checks, and echocardiography. These investigations should be performed preoperatively.

Sorafenib is a small-molecule inhibitor of VEGF, and is less efficacious than sunitinib, and has a similar, although less severe, toxicity profile.[3]

Bevacizumab is a monoclonal antibody directed at circulating VEGF molecules, and has been shown to improve objective response rate and progression-free survival in combination with interferon, when compared with interferon therapy alone.[71] The toxicity profile of this combination is greater than when either drug is used as monotherapy, and includes fatigue, anorexia, hypertension and proteinuria.[3]

Pazopanib is a multityrosine kinase inhibitor with effects comparable with sunitinib monotherapy and bevacizumab in combination with IFN-α. The most frequently occurring side effects are gastrointestinal disturbances (52%), hypertension (40%), transaminitis (53%), electrolyte disturbance (11%-33%), and blood dyscrasias (31%-37%).[72] These patients should have their full blood count, biochemistry, and blood pressure monitored regularly.

Inhibitors of Mammalian Target of Rapamycin. Temsirolimus has shown promise as an antitumor agent, particularly in patients with a number of adverse risk factors in treatment-refractory metastatic disease, both in combination with IFN and as monotherapy.[73,74] Common toxic effects include asthenia, rash, mucositis, anemia, electrolyte and glucose imbalance, and hyperlipidemia.

Intraoperative Considerations

It is important to discuss the anatomy of the tumor and intended surgical approach before induction of anesthesia. A multidisciplinary meeting involving the anesthetic, surgical, and oncologic teams may facilitate this.

Unlike uncomplicated laparoscopic nephrectomy, which carries no further risk than a standard laparoscopic procedure, it is prudent to utilize invasive blood pressure monitoring in these complex nephrectomies (whether open or laparoscopic). Large tumors may demand extensive dissection, and tumors that involve the IVC may necessitate cross-clamping of the vessel to permit resection.[75] Locally advanced tumors are typically managed with radical nephrectomy, which occasionally necessitates *en bloc* resection of adjacent organs, temporary occlusion of the regional vasculature, and venous thrombectomy.[3] These situations can result in profuse bleeding and significant cardiovascular instability, and it is sensible to secure central and large-bore peripheral venous access, ensure availability of appropriate blood products, and prepare level 1 infusion equipment and vasopressor medications in these cases. Additionally, veno-venous bypass may be required in cases of IVC infiltration, and a perfusionist should be involved in the planning of the case.

Common surgical practice in the United Kingdom is either a laparoscopic approach or a loin incision and retroperitoneal approach, which requires that the patient be positioned in the "kidney position." This involves the patient lying lateral, extended over a break in the table to separate the lower costal margin and the iliac crest.[22] A marked fall in blood pressure is not uncommon in this position, due to reduced venous return from the lower limbs. This is compounded in laparoscopic surgery by the introduction of the pneumoperitoneum. Further compression by the surgical team intraoperatively may produce a severe reduction in cardiac output.

As stated previously, extra care should be taken in positioning these patients, who are often cachexic, to ensure pressure areas are protected adequately. Appropriate thromboprophylaxis should be undertaken.

Large tumors may demand extensive dissection, and tumors that involve the IVC may necessitate cross-clamping of the vessel to permit resection.

Temperature monitoring and patient warming should be routine, as inadvertent perioperative hypothermia (temperature ≤ 36°C) will contribute to intraoperative bleeding, perioperative cardiac events, and increased length of stay in hospital, and would be detrimental for wound healing.[76–79]

Postoperative Considerations

Critical Care Admission

Given the complex nature of these patients, it is sensible to arrange

elective admission to the critical care unit to facilitate close monitoring of cardiovascular and renal physiology postoperatively.

Postoperative Renal Impairment

It has been shown that, even in the presence of a normal contralateral kidney and normal preoperative serum creatinine concentration, chronic kidney disease is more common after radical nephrectomy than after partial nephrectomy.[80] Increased rates of both mild (glomerular filtration rate < 60 mL/min) and moderate (glomerular filtration rate < 45 mL/ min) chronic kidney disease were noted after radical surgery when compared with partial nephrectomy. It is therefore sensible, wherever possible, to use drugs that do not undergo renal excretion or metabolism in the perioperative period, regardless of preoperative serum creatinine concentration.

Analgesia

Standard practice in our institution is to perform intercostal blocks at T6-T12 and a transversus abdominis plane block under laparoscopic vision following completion of laparoscopic nephrectomy. Regular paracetamol is prescribed and can be supplemented with systemic opioids (usually fentanyl or oxycodone patient-controlled analgesia unless postoperative renal function is normal). Clearly, nonsteroidal anti-inflammatory drugs are avoided in all but the most straightforward cases in euvolemic patients. Thoracic epidural analgesia is another option, particularly in open surgery, and although a high block (to T6/T7) will be necessary postoperatively it is wise to use it cautiously intraoperatively until hemostasis is secured.

Chronic Pain

Chronic pain is commonplace in this group of patients (as with other oncology cases), and they are often on established regimens of numerous different classes of drugs. They may be opioid-tolerant, and careful liaison with the acute and chronic pain teams, the oncologists, and even the palliative care team may be useful in titrating dosages and optimizing analgesia in these complex cases. It is important to note that surgery in these patients may actually relieve some of their pain attributable to local pressure effects of the tumor on surrounding structures, or change the nature of the pain.[81]

It is sensible to continue the patient's usual medications, although patients using transdermal patches should remove them preoperatively and equianalgesic doses of immediate-release oral preparations should be used.[82] This avoids problems with delayed absorption. Short-acting opioids should be used as required to supplement this background analgesia. Often, one-sixth of the total daily opioid requirement is prescribed as a starting breakthrough dose. It may also be helpful to convert the patient's opioids into an equianalgesic parenteral dose and run this as a continuous infusion.

Care should be taken to avoid both toxicity and withdrawal as well as the common side effects of opioid therapy, including constipation, nausea, and vomiting, although these tend not to be as problematic as in opioid-naive patients. Useful adjuncts in the management of acute chronic pain include clonidine (providing the patient is intravascularly replete), ketamine, and gabapentin.

It has been shown that, even in the presence of a normal contralateral kidney and normal preoperative serum creatinine concentration, chronic kidney disease is more common after radical nephrectomy than after partial nephrectomy.

Conclusions

Patients with metastatic renal cell carcinoma are complex with the potential for significant complications, and require extensive pre-, peri-, and postoperative management. The perioperative care of these patients requires a multidisciplinary approach, with input from anesthetists, surgeons, intensivists, nephrologists, oncologists, dietitians, physiotherapists, and specialist nurses. ■

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MAIN POINTS

- A thorough preoperative assessment should take place to assess physiologic status and cardiopulmonary reserve of patients with metastatic renal cell carcinoma. Renal and hepatic function should be assessed and optimized if possible. It is important to note that cancer surgery often cannot be postponed while lengthy investigation and interventions are carried out. Patients with limited metastatic disease (approximately 2%-3% of cases) may be considered for metastasectomy.
- It is important to discuss the anatomy of the tumor and intended surgical approach before induction of anesthesia.
- Unlike uncomplicated laparoscopic nephrectomy, which carries no further risk than a standard laparoscopic procedure, it is prudent to utilize invasive blood pressure monitoring in these complex nephrectomies (whether open or laparoscopic). Large tumors may demand extensive dissection, and tumors that involve the inferior vena cava may necessitate cross-clamping of the vessel to permit resection.

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