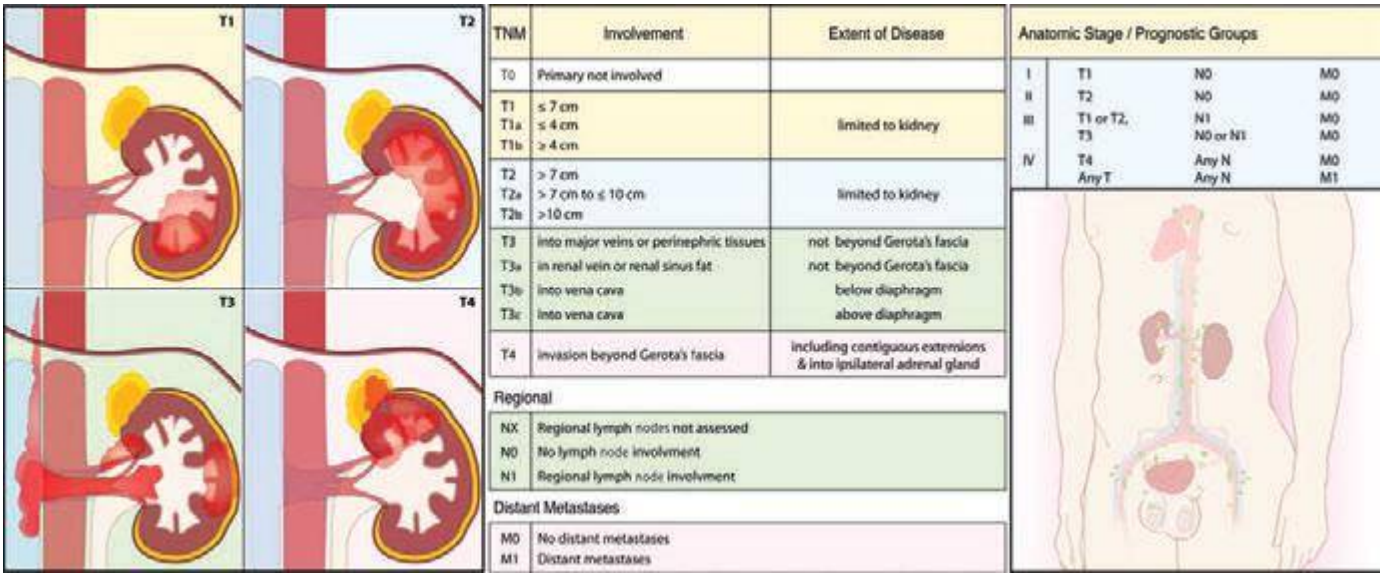

FIGURE 114-2 Renal cell carcinoma staging. TNM, tumor, node, metastasis.

its contents, including the kidney, the ipsilateral adrenal gland in some cases, and adjacent hilar lymph nodes. The role of a regional lymphadenectomy is controversial. Extension into the renal vein or inferior vena cava (stage III disease) does not preclude resection even if cardiopulmonary bypass is required. If the tumor is resected, half of these patients have prolonged survival.

Nephron-sparing approaches via open or laparoscopic surgery may be appropriate for patients who have only one kidney, depending on the size and location of the lesion. A nephron-sparing approach can also be used for patients with bilateral tumors. Partial nephrectomy techniques are applied electively to resect small masses for patients with a normal contralateral kidney. Adjuvant therapy following this surgery does not improve outcome, even in cases with a poor prognosis.

ADVANCED DISEASE

Surgery has a limited role for patients with metastatic disease. Long-term survival may occur in patients who relapse after nephrectomy in a solitary site that is removed. One indication for nephrectomy with metastases at initial presentation is to alleviate pain or hemorrhage of a primary tumor. Also, a cytoreductive nephrectomy before systemic treatment improves survival for carefully selected patients with stage IV tumors.

Metastatic renal cell carcinoma is refractory to chemotherapy. Cytokine therapy with IL-2 or interferon α (IFN-α) produces regression in 10–20% of patients. IL-2 produces durable complete remission in a small proportion of cases. In general, cytokine therapy is considered unsatisfactory for most patients.

The situation changed dramatically when two large-scale randomized trials established a role for antiangiogenic therapy, as predicted by the genetic studies. These trials separately evaluated two orally administered antiangiogenic agents, sorafenib and sunitinib, that inhibited receptor tyrosine kinase signaling through the VEGF and PDGF receptors. Both showed efficacy as second-line treatment following progression during cytokine treatment, resulting in approval by regulatory authorities for the treatment of advanced renal cell carcinoma. A randomized phase III trial comparing sunitinib to IFN-α showed superior efficacy for sunitinib with an acceptable safety profile. The trial resulted in a change in the standard first-line treatment from IFN to sunitinib. Sunitinib is usually given orally at a dose of 50 mg/d for 4 out of 6 weeks. Pazopanib and axitinib are newer agents of the same class. Pazopanib was compared to sunitinib in a randomized first-line phase III trial. Efficacy was similar, and there was less fatigue and skin toxicity, resulting in better quality of life scores for pazopanib compared with sunitinib. Temsirolimus and everolimus, inhibitors of the mammalian target of rapamycin (mTOR), show activity in patients with untreated poor-prognosis tumors and in sunitinib/sorafenib-refractory tumors. Patients benefit from the sequential use of axitinib and everolimus following progression to sunitinib or pazopanib first-line therapy.

The prognosis of metastatic renal cell carcinoma is variable. In one analysis, no prior nephrectomy, a KPS <80, low hemoglobin, high corrected calcium, and abnormal lactate dehydrogenase were poor prognostic factors. Patients with zero, one or two, and three or more factors had a median survival of 24, 12, and 5 months, respectively. These tumors may follow an unpredictable and protracted clinical course. It may be best to document progression before considering systemic treatment.

115 Benign and Malignant Diseases of the Prostate

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Benign and malignant changes in the prostate increase with age. Autopsies of men in the eighth decade of life show hyperplastic changes in >90% and malignant changes in >70% of individuals. The high prevalence of these diseases among the elderly, who often have competing causes of morbidity and mortality, mandates a risk-adapted approach to diagnosis and treatment. This can be achieved by considering these diseases as a series of states. Each state represents a distinct clinical milestone for which therapy(ies) may be recommended based on current symptoms, the risk of developing symptoms, or death from disease in relation to death from other causes within a given time frame. For benign proliferative disorders, symptoms of urinary frequency, infection, and potential for obstruction are weighed against the side effects and complications of medical or surgical intervention. For prostate malignancies, the risks of developing the disease, symptoms, or death from cancer are balanced against the morbidities of the recommended treatments and preexisting comorbidities.

ANATOMY

The prostate is located in the pelvis and is surrounded by the rectum, the bladder, the periprostatic and dorsal vein complexes and neurovascular bundles that are responsible for erectile function, and the urinary sphincter that is responsible for passive urinary control. The