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# Multimodal therapy for urologic cancers

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Despite advances in surgery and radiotherapy, many genitourinary cancers recur after primary therapy. In the US, cancer is now the leading cause of death, surpassing cardiovascular disease. Single treatment modalities have limited capacity to optimize cure and minimize morbidity. In many cases, combined therapy can downstage locally advanced tumors to make radical resection feasible, improve local control and reduce distant metastases after radical surgery in high-risk patients. For one urologic cancer after another, multimodal treatment strategies have emerged as therapeutic options. How important are they? When should combined therapy be considered? Should urologists consult other specialists to help identify options and develop treatment plans?

Testicular cancers offer an instructive model. Forty years ago surgery (orchiectomy followed by retroperitoneal lymph node dissection) was the only effective therapy for nonseminomatous germ cell tumors. With the development of highly effective, cisplatin-based combination chemotherapy in the late 1970s, many oncologists declared the era of surgery for testicular cancer over; they argued that these cancers should be treated in the same way as lymphomas. As time passed, late recurrences of cancer in the retroperitoneum and elsewhere confirmed that complete retroperitoneal lymph node dissection is necessary in most patients, despite the response to chemotherapy. Today, surgery and chemotherapy are combined judiciously to achieve the greatest chance of long-term survival.

Urologists frequently treat superficial bladder cancer with transurethral resection followed by intravesical chemotherapy or bacillus Calmette–Guérin immunotherapy. However, many patients with invasive bladder cancer do not receive adjuvant chemotherapy before or after radical cystectomy. Prospective randomized trials have clearly documented the survival advantage of neoadjuvant chemotherapy followed by cystectomy, and adjuvant chemotherapy provides similar benefits. Nevertheless, it appears from national registry data that many eligible patients do not receive chemotherapy. While patients make their own medical decisions, a face-to-face consultation with a medical oncologist before cystectomy may alter a patient's perception of the risks and benefits of chemotherapy and lead to more frequent acceptance of a multimodal treatment plan.

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The management of kidney cancer has been revolutionized by the frequent detection of incidental masses, the development of minimally invasive surgery, and the discovery of systemic biologic agents that target the molecular pathways that drive the tumor. Truly effective systemic therapy for kidney cancer is finally available, and clinical trials have also demonstrated the benefit of nephrectomy in selected patients with metastases. An important challenge over the next decade will be to develop multimodal treatment strategies for kidney cancer that combine systemic, local and regional therapy to achieve much better cure rates with tolerable morbidity.

Is multimodal treatment always better? For patients with favorable prognostic factors and localized cancer, the additional burden of multiple therapies risks increased toxicity with no therapeutic gain (a single treatment should be effective). Successful multimodal strategies require effective systemic agents and accurate classification of risk. Better predictive models, based on validated prognostic characteristics (clinical, pathologic, molecular), are essential to distinguish high-risk patients who may benefit from combined treatment from low-risk patients for whom a single treatment has a good chance of success with little associated morbidity. Standard staging systems are not adequate to classify risk in this way. Advanced statistical models (nomograms and neural networks) enhance the clinician's and patient's ability to classify risk and choose combined treatment when most appropriate. Combined therapy holds great potential for prolonging life and improving the wellbeing of our patients, and should be embraced once the benefits are established by well-designed clinical trials.

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