What happens to the patients with muscle-invasive bladder cancer who refuse cystectomy after neoadjuvant chemotherapy?

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Herr HW. Outcome of Patients Who Refuse Cystectomy after Receiving Neoadjuvant Chemotherapy for Muscle-Invasive Bladder Cancer. Eur Urol 2008;54:126-32.
SUMMARY

This is a prospective study carried out to determine the outcome of patients who refuse cystectomy after receiving neoadjuvant chemotherapy for muscle-invasive bladder cancer. Sixty-three patients were evaluated between 1995 and 2001 who declined to undergo a planned cystectomy because they achieved a complete clinical response to neoadjuvant cisplatin-based chemotherapy. Herr assessed patient, tumor and treatment features for a median follow-up of 86 months, all patients being followed-up for more than 5 years. Forty patients (64%) survived, with 54% of them having an intact functioning bladder. The number and size of invasive tumors were strongly associated with the overall survival. The most significant treatment variable predicting better survival was complete resection of the invasive tumor on restaging transurethral resection (TUR) before starting chemotherapy. Of 23 patients (36%) who subsequently died of disease, 19 (30%) relapsed with invasive cancer in the bladder. Over 90% of the surviving patients had solitary, small and low-stage invasive tumors completely resected and 83% survived without relapses in the bladder.[1]

COMMENTS

Radical cystectomy and pelvic lymph node dissection is an excellent treatment for organ-confined disease. Many patients with extravesical or lymph node-positive bladder cancer will develop recurrent disease, often with distant metastases, and will ultimately die of their disease. Given the lethality of muscle-invasive bladder cancer, there is a definite need for effective systemic chemotherapy. Neoadjuvant chemotherapy has been extensively investigated in muscle-invasive bladder cancer. When taken together, the randomized controlled trials of neoadjuvant cisplatin-based combination chemotherapy demonstrate an improved survival over cystectomy alone. In addition, neoadjuvant chemotherapy can result in downstaging of primary tumors.[2]

The Advanced Bladder Cancer Metaanalysis Collaboration concluded that platinum-based combination neoadjuvant chemotherapy and cystectomy continues to show a clear and modest benefit for survival and disease-free survival of patients with muscle-invasive bladder cancer over radical surgery alone.[3] Downstaging after neoadjuvant chemotherapy was associated with improved survival in patients with muscle-invasive, extravesical (T > 3a) disease at presentation. Chemotherapy aims to treat undetected metastasis and radical cystectomy provides the best control of the primary tumor. Most survivors achieve major response to chemotherapy and have an increased likelihood of having no residual tumor (pT0) in the cystectomy specimen. [4] The author has analyzed whether patients who have pathological pT0 tumors after chemotherapy would have survived without subsequent cystectomy.

In the present study, 64% of the patients survived, with 54% of them having an intact functional bladder (35% of total cohort). Relapse occurred in the majority of the patients (64%), resulting in an additional disease-related mortality of 30%. The patients most likely to relapse had multiple or large tumors that were not clinically confined to the bladder. Delayed cystectomy salvaged fewer than half of the patients relapsing with persistent or new invasive bladder cancers.

Few other studies have dealt on conservative, bladder-sparing management of muscle-invasive transitional cell carcinoma (TCC) bladder using multimodality treatment.[5] These authors have used chemoradiotherapy for tumor control. Perdonà et al., have reported 121 patients with T2, T3 or T4 bladder cancer who underwent induction by TUR of the tumor and received two cycles of neoadjuvant chemotherapy followed by radiotherapy (RT) or radiochemotherapy (RCT). Six weeks after RT or RCT, responses were evaluated by restaging TUR. Patients who achieved a complete response were observed at regular intervals. In patients who had persistent or recurrent invasive tumor, further treatment was recommended. Treatment modality, tumor classification and resection status after initial TUR had an impact on survival rates ($P = 0.04, 0.02$ and $0.02$, respectively).

These studies highlight the fact that patients refusing cystectomy after chemotherapy are at high risk for disease-related mortality. At the same time, patients with small, clinically confined single tumors, which can be visibly and microscopically completely resected before neoadjuvant chemotherapy, are most likely to survive without cystectomy. They need a close follow-up as they remain at risk for new tumors in the bladder.

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