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European Association of Urology

Editorial – referring to the article published on pp. 1176–1182 of this issue

Thoughts on Delaying Cystectomy

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The literature review of Fahmy et al. [1] reveals that the majority of studies on bladder cancer confirm that pretreatment delays are associated with worse outcome. The studies suggested a window of opportunity of less than 12 wk from diagnosis of invasive disease to radical cystectomy.

1. Types of delay

1. Delay can occur when a tumour is treated late in the course of the disease. While it is obvious that a pT2a tumour has a better prognosis than a pT3a, it is unclear whether a primary tumour of any stage has the same tumour-specific survival as a progressive tumour of the identical stage. Currently patients with primary and progressive muscle-invasive bladder cancer are treated equally, assuming a similar cancer-specific survival for both groups. However, the study of Schrier et al. [2] showed that patients with muscle-invasive disease and a history of superficial bladder cancer have a worse prognosis than patients with primary muscle-invasive bladder cancer. Their study shows a large and clinically significant difference in disease-specific survival between primary and progressive muscle-invasive cancer patients, favouring the primary group. The disease-specific survival appears to be approximately twice as high in the primary group at all times during follow-up. The 3- and 5-yr survival rates are 67% and 55%, respectively, for patients with a primary invasive tumour, and 37% and 28%, respectively, for patients with a progressive invasive tumour. This trend in survival difference between the two study groups was observed in the Nijmegen population as well as in the Rotterdam patients: in both centers patients with progressive invasive tumours had a significantly worse prognosis than patients with primary invasive tumours.
2. ''Delay'' also means late after the diagnosis of invasive bladder cancer has been made. Known reasons for this form of delay are
   - factors linked to the health care system in which the patient is treated.
   - Patient-related factors for treatment delay such as the wish for a second or third opinion, clearance from comorbid disease, attempted less-invasive procedures, and lastly patient's personal choice.

The greatest reason for delay in definitive treatment for bladder cancer is a lack of patient and physician education. All too often patients are not aware of the association between cigarette smoking and bladder cancer. Patients do not seek medical attention after noticing gross hematuria. Family physicians or internists treat patients with gross hematuria with antibiotics for presumed urinary tract infections without seeing and evaluating the patients with urinalysis, urine cultures, radiologic imaging, or referral for urologic consultation. Many patients have a history of episodes of gross hematuria for months before the internist refers the patient to a urologist, who promptly makes the diagnosis.

DOI of original article: 10.1016/j.eururo.2006.05.046
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 doi:10.1016/j.eururo.2006.05.047

Another cause for delay is patient reluctance to lose the bladder and have an ileal conduit and external drainage device. As urologists, we must inform patients about and perform continent urinary diversions.

Patients should be encouraged to obtain a second opinion. There is not so much urgency about getting on with the treatment that they should be pressured to schedule surgery immediately. On the other hand, most individuals clearly understand that moving ahead with treatment in a timely fashion is important, as underscored by the 90% of patients in this series who underwent surgery within 12 wk of diagnosis.

Treatment related factors are as follows:

- In a recent study Lambert et al. [3] showed that the increasing use of intravesical therapies for T1 bladder cancer coincides with decreased survival after cystectomy.
- In the past 15 years, their experience indicates that patients with T1 superficial bladder cancer are now more likely to receive intravesical therapy. In addition, they noted that disease-free survival was better before 1998 in this group. In very few other cancers has disease-free survival decreased over time. The authors postulate that the decrease in survival may be related to the increase in intravesical therapy.
- We also have to acknowledge that neoadjuvant treatment (chemotherapy, radiation) does not benefit every patient and is a significant delay of curative treatment for a significant percentage of patients with muscle-invasive disease.
- Patients might receive chemotherapy unnecessarily because a more-complete operation may have indicated a greater likelihood of surgical cure. It is also unlikely that preoperative chemotherapy will compensate for a poor operation in which significant tumour volume has been left behind in the pelvis.

2. Why is it so difficult to demonstrate an impact of cystectomy delay on survival?

There can be no doubt that muscle-invasive bladder cancer is a potentially lethal disease. Studying the Kaplan-Meier plots of any major cystectomy series reveals that overall a cystectomy delay of 12 wk will at best result in a 3–5% survival disadvantage, if at all [4].

The vast majority of authors who looked at delaying cystectomy picked less ideal cohorts, as shown by the following examples:

1. For almost all M+ and N+ patients, a cystectomy delay of several months probably will have no further impact on survival, because this oncologic situation is likely to have existed for a longer period of time.
2. Progressing from pT3a to pT3b or from pT3b to pT4a will have little impact on survival.
3. A pT1 tumour should still be in a curable stage after 3 mo have elapsed.
4. The staging error of up to 50% and the unknown micrometastasis rate and time point further complicate the issue.

The ideal tumour stage to study the impact of delaying cystectomy on survival is a pT2a tumour, because progression from pT2a to pT2b has the most dramatic effect on survival plots, apart from N0 to N+ [4].

3. Conclusions

Patients diagnosed with cancer often want to schedule an operation as soon as possible, even the next day. Others may delay surgery while they obtain additional opinions, search the Internet, and try to decide about treatment. How long does the window of opportunity to cure a cancer remain open?

In patients with muscle invasion at diagnosis, a delay in surgery is associated with a more-advanced pathologic stage, especially when the delay is longer than 90 days. Although an appropriate time should be given for consideration of options and pretreatment evaluation, undue delay may compromise cancer control.

Once the diagnosis of muscle-invasive disease is made, proceeding with radical cystectomy expeditiously would seem to be in the patient's best interest.

References

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