

Survival Drops When Bladder Cancer Surgery Is Deferred

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ANN ARBOR, Mich., March 28, 2006 - In patients with muscle invasive bladder cancer, surgery delayed is survival denied, reported researchers here.

Among 214 patients with muscle-invasive bladder cancer, those who had surgery within three months of diagnosis had a 51% survival rate at three years, compared with only 38% for those whose surgery was delayed past three months, reported Cheryl Lee, M.D., and colleagues of the University of Michigan's Comprehensive Cancer Center.

The most common reason for delaying surgery was because of physician scheduling problems, they reported in the April issue of the Journal of Urology. Only a few patients took extra time to seek multiple opinions, were misdiagnosed, or were reluctant to undergo the radical procedure, the researchers found.

"Most of these causes for delaying surgery are potentially reversible, and physicians -- despite busy schedules and the need for second opinions -- need to be diligent about coordinating appointments and information in a timely way," Dr. Lee said.

She and her colleagues sought to determine whether delay in the treatment of patients diagnosed with stage T2 bladder could affect survival by allowing the cancer to progress locally to a more difficult-to-treat stage, or whether other pathologic factors might be involved.

To do this, they followed a contemporary cohort of 214 consecutive patients who presented with clinical T2 bladder cancer and who eventually underwent radical cystectomy as primary therapy.

The analysis included time from diagnosis to cystectomy, pathologic stage, disease-specific survival, and overall survival. The authors also used univariate and multivariate modeling to explore the relationships between various factors contributing to survival and to reasons for delay.

They found that the mean time to surgery for all patients was 60 days, ranging from four days after diagnosis to as long as 175 days, or nearly six months. The majority of patients (107) had surgery from 43 to 84 days after diagnosis, but 43 had delays of anywhere from 85 to 175 days.

Among all patients treated within 93 days (3.1 months) of diagnosis, there were significant advantages in disease-specific survival ($P=0.05$) and overall survival ($P=0.02$) compared with those whose radical cystectomies were delayed for longer than 93 days. An analysis of disease burden showed that pathologic staging was similar among the patients treated before and after the 93-day cutpoint ($P=0.15$).

"In the multivariate survival models, patients with cystectomy delays of more than 93 days had a 96% increased risk of death from any cause ($P=0.04$) and a 112% increased risk of death from bladder cancer ($P=0.08$) compared with patients with cystectomy delays of 93 days or fewer," the authors wrote.

A total of 87 patients died, 39% in the group who had surgery within 93 days, and 54% of those for whom surgery was delayed for longer. In all, 55 patients died from bladder cancer. The disease killed 25% of all patients who had surgery within 93 days, compared with 35% of those who had surgery later than that.

The median disease-specific survival for those patients treated in a more timely fashion has not been reached, the authors noted, but for those treated after 93 days it was one year. Three year disease-specific survival was 62% among patients treated promptly, compared with 49% of those whose surgery was delayed past 93 days.

The median overall survival for patients in the group treated in 93 days or fewer was 3.4 years, compared with 0.9 years for those in the group treated after 93 days. In all 51% of patients who waited 93 days or less for surgery survived three years, compared with 38% of those who waited longer.

Among the 26 patients who didn't have cystectomies until more than 3.1 months after diagnosis, 12 (46%) had to wait because of scheduling delays related to clinical or research appointments, the authors found. One patient sought multiple opinions, one had social reasons for delay, one was misdiagnosed, and one was reluctant to undergo treatment.

An additional four patients had comorbidities that needed to be resolved, three had difficulty with decision-making, and the remainder had unknown reasons for delays.

The researchers wrote that the survival differences between the early and late treatment groups was probably because of micrometastatic spread rather than local tumor progression.

"Micrometastases are not detectable by contemporary imaging and are thus not readily quantifiable by this study," they wrote. "However, a delay in primary local control might ultimately lead to an increased rate of micrometastases, similar to what has been experienced with testis cancer."

"The striking difference in median survival between patients with a 93 or fewer days' delay (not reached yet) and those with a delay of more than 93 days (one year) may be consistent with this hypothesis," they continued. "The very short (one year) median disease-specific survival for patients with cystectomy delay of more than 93 days is consistent

with the median survival of bladder patients with known metastatic disease."

The authors noted an important limitation of the study. "This retrospective dataset is limited in that patient factors and comorbidity may be underestimated," they wrote. "If patients delayed their cystectomy because of indecision or treatment fear, they may have ultimately opted for an alternative treatment and thus would not be included in this study. Similarly, if comorbidities resulted in a lack of medical clearance or high-risk medical clearance, patients again may have sought non surgical treatments." Primary source: Journal of Urology Source reference: Lee CT et al. "Cystectomy Delay More Than 3 Months From Initial Bladder Cancer Diagnosis Results in Decreased Disease Specific and Overall Survival" J Urol. 175;4: 1262-1267