SUPERFICIAL BLADDER CANCER: CURRENT CONCEPTS TO PREVENT DISEASE RECURRENT AND PROGRESSION

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Bladder cancer is the fifth most common solid human cancer with an estimated number of 54,200 new cases in the United States in 1999. Approximately 70–80% of these tumors are confined to the mucosa or invade the lamina propria at the time of initial diagnosis. However, 50–80% of patients with superficial bladder cancer experience disease recurrence and about 5–20% will eventually progress to muscle invasive disease.

Since common genetic alterations in metachronous tumors have been demonstrated, suggesting a single progenitor cell, it is conceivable that intraluminal tumor cell seeding and/or incomplete resection are major factors contributing to disease recurrence. The latter is further supported by the observation that up to 75% of recurrences develop at the site of initial resection. Alternatively, multifocal tumor initiation due to independent transforming events has been suggested. Based upon these hypotheses currently applied measures to reduce recurrence and progression after transurethral resection (TURB) of superficial bladder cancer include intravesical chemo-or immunotherapy, repeated transurethral resection (ReTURB) and the use of fluorescence endoscopy.

Instillation of various chemotherapeutic agents has been studied extensively. No single agent seems to be superior with regard to improvement of recurrence rates. A recent meta-analysis of 3703 patients undergoing intravesical chemoprophylaxis found a 30 to 80% decrease in recurrence rate thus contradicting prior analyses suggesting only modest efficacy. Several authors favour a single early (within 24 hours after TURB) instillation as it provides similar results compared with late initiated maintenance therapy. While intravesical chemotherapy is best suited for moderate and low grade mucosally confined transitional cell carcinoma immunotherapy with BCG is indicated for carcinoma in situ and high grade disease. BCG significantly reduces recurrence rates; prevention of disease progression has been discussed but remains unproven. However, treatment with BCG is not generally accepted due to the fear of (severe) side effects.

Retrospective studies consistently show a high frequency of tumor detection ranging from 30–75% of the cases if a ReTURB is performed 2–8 weeks after initial treatment of superficial bladder cancer. This kind of retrospective data have been criticized since (i) only a few studies distinguish between incomplete and complete TURB and (ii) accumulation of patients at risk (e. g. with high stage, grade or multifocal disease) undergoing ReTURB has been assumed. However, in our own prospective study again tumor was detected in 33% of patients undergoing ReTURB for Ta or T1 bladder cancer.

In an attempt to decrease the number of incomplete resections and overseen tumors during TURB 5-aminolevulinic acid induced fluorescence endoscopy (AFE) is increasingly applied. A significant decreased incidence of cases with residual tumor after TURB using AFE compared to white light cystoscopy has been reported. Regardless of this advantage ReTURB will still demonstrate tumor in one third of patients undergoing initial AFE based TURB.

As an alternative measure to intravesical instillation and AFE based TURB we have investigated the impact of routine application of ReTURB on the long term outcome of superficial bladder cancer with regard to recurrence and progression. 83 patients undergoing ReTURB in our prospective trial were followed until recurrence, death or for a minimum of five years. Estimated mean recurrence-free survival was 62 months (median 87 months) resulting in an excellent 5-year recurrence-free survival rate of 63%. Only 1% of patients progressed to muscle invasive disease probably due to better risk stratification. Our findings suggest that routine ReTURB must be considered a true alternative treatment option to minimize the risk for recurrence and progression.