WebCafé report by

{niftybox width=180px,float=right,textalign=left}

Organizer:

{/niftybox}Wendy Sheridan

November, 2003

The objective of the 2 day course was to present and evaluate the most recent developments in the management of bladder cancer and extravesical transitional cell carcinoma.

Lectures and presentations given by expert urologists, oncologists, and pathologists from the USA and Europe focused on techniques and cost-efficacy of screening, intravesical therapy, the management of muscle invasive bladder cancer, the role of radiation and chemotherapy, new drug regimens and innovative approaches on the horizon.

Also discussed were the differences and similarities of treatment approaches between countries and the need for a universal standardization defining the many different types of bladder tumors that present.

Index of the presentations

Session 1: Diagnosis of bladder cancer

Chair- Mark.S.Soloway, University of Miami School of Medicine, Florida, USA

MRI of urinary bladder cancer

J.O. Barentsz MD, PhD, University Medical Center, Nijmegen, Netherlands

Tumor Markers in Bladder Cancer: Where are we?

J.A. Witjes MD, PhD, University Medical Center, Nijmegen, The Netherlands

Review Pathology: Why it is critical

F. Algaba MD, PhD, Fundacio Puigvert Universdad Autonoma de Barcelona; Barcelona, Spain

Analyzing p53 status and other markers to determine management strategies

J. Schalken, MD, PhD, University Medical Center Nijmegen, The Netherlands

Flourescence in Situ Hybridization as a tool for early detection of bladder cancer P.F. Bassi, MD, Clinica Urologica, Universita di Padova, Italy

Session 2: How to Treat Low-Risk Tumors

Chair:A.P.M. van der Meijden, MD, PhD Jeroen Bosch Hospital, s-Hertogenbosch, The Netherlands

Chemoresection for superficial bladder cancer

W.Oosterlinck, MD, PhD, Ghent University Hospital, Belgium

A meta-analysis of randomized trials investigating transurethral resection plus one immediate instillation of chemotherapy

R.J. Sylvester, ScD, European Organization for Research and Treatment of Cancer, Brussels, Belgium

Observation of TaGI bladder tumors: Acceptable?

Mark.S.Soloway, University of Miami School of Medicine, Florida, USA

Results from Finn bladder group in low risk Tumors,

E. Rintala, MD, Helsinki University Central Hospital, Finland

Session 3: How Do I Treat Intermediate and High-Risk Tumors? Chair:A.P.M. van der Meijden, MD, PhD Jeroen Bosch Hospital, s-Hertogenbosch, The Netherlands

Chemotherapy for intermediate risk and BCG for high risk

E.Solsona, MD, Valencia Institute of Oncology, Spain

Which patients treated with BCG do better: Those with or without side-effects? A.P.M. van der Meijden, MD, PhD Jeroen Bosch Hospital, s-Hertogenbosch, The Netherlands

New Agents in the Treatment of superficial bladder cancer M.A. O Donnell, MD, University of Iowa Health Care, Iowa, United States

Session 4: Advanced Bladder Cancer

Chair: P.G.Harper, MD, Guy s

Hospital, London, United Kingdom

What
to do when radical cystectomy is not radical,

D.P.Petrylak, MD, PhD, Colombia Uinversity, NY, NY, USA

Current treatment approaches in
advanced bladder cancer

P.G.Harper, MD, Guy s Hospital, London, United Kingdom

Adjuvant chemotherapy in muscle invasive
bladder cancer: Current concepts D.F. Bajorin,MD, Memorial
Sloan-Kettering Cancer Center, NY, NY, USA

Overview of novel agents

Ch.Sweeney, MD, MBBS, Indiana University, Indianapolis, Indiana, USA

Future management of advanced bladder
cancer

D. Raghavan, MD, PhD, University of Southern California Norris Comprehensive
Cancer Center Los Angeles, California, USA

Session 1: Diagnosis of bladder cancer

Chair- Mark.S.Soloway, University of Miami School of Medicine,
Florida, USA

MRI of urinary bladder cancer

J.O. Barentsz MD, PhD, University Medical Center, Nijmegen, Netherlands

Magnetic resonance imaging (MRI) is
the best modality for visualizing bladder cancer, however, due to limited resources this technique should only be used to obtain information which directly influences therapy and outcome. In order to achieve this, continuous education of urologists on the use of MR imaging and radiologists on the clinical handling of patients is needed. Communications between these two specialties is a necessity.

Detecting bladder cancer is done by cystoscopy and histology [microscopic
investigation of tumor cell characteristics]. Once diagnosed, staging follows. For the clinical staging of superficial tumors transurethral resection is the best technique. A CTU
or MRU should be performed to rule
out spread to other parts of the urinary tract such as ureters or renal pelvis.

Tumors staged Ta, carcinoma in situ (CIS) or T1 may be treated with local
endoscopic resection with or without adjuvant intravesical instillations.

No further radiological imaging is necessary. Follow up cystoscopy may be done every 3 or 6 months.

In the case of muscle invasive tumors stages T2-T4, further staging should be performed by MRI. Cystectomy plus curative or palliative chemo-radiotherapy may be given.

MRI is valuable in diagnosing bone marrow metastasis, local and nodal tumor involvement and for visualizing the bladder wall. However, up to 24% of involved lymph nodes may be missed, and MRI does not differentiate between TUR defects or tumor.

Contrast dye improves the quality of MRI, and MR-lymphography improves detection of node metastases.

CT-urography, a new technique used in the Europe, provides a 3 dimensional image of the urinary tract, and has been shown to be more accurate in staging of upper urinary tract and multi-focal disease than the RVP, 97.6% to 79% respectively. The drawbacks are; lack of equipment and training and a rather high dose of radiation with this modality. Pregnancy or young age would be considered contra-indicative for doing CTU, considering lifetime exposure to radiation and its cumulative risks.

RVP and IVP's, the currently used diagnostic tests, will probably be replaced by CTU.

index

Tumor Markers in Bladder Cancer: Where are we?

J.A. Witjes MD, PhD, University Medical Center, Nijmegen, The Netherlands

Tumor markers can potentially detect primary bladder cancer, be used for early detection of high risk tumors or follow up.

The Gold Standard -

Cystoscopy is still the gold standard for detecting bladder tumors. Unfortunately, [white light] cystoscopes, either flexible or rigid, miss up to 45% of multiple tumors, 20% of single tumors and around 30% of CIS disease.

Gold Standard Becomes Platinum

Used in Europe, photodynamic cystoscopy (see Hexvix) utilizing florescent light improves overall accuracy, detection of multi-focal disease and is able to find CIS 97% of the time. This diagnostic tool has been shown to be a considerable improvement over white light cystoscopy with NO side effects beyond those normally occurring during routine cystoscopy.

[Phase III clinical trial: Cystoscopy and Hexyl 5-Aminolevulinate in Detecting Carcinoma In Situ in Patients With Bladder CancerThis study is currently recruiting patients]

Gold Standard #2-Cytology

Cytology tests investigate the urine for cancerous cells, are standard procedure when bladder cancer is suspected, and may be given before cystoscopy. As with most pathology reporting, it is a subjective test and results may vary between laboratories and pathologists. As a tumor marker it is not sensitive enough to replace cystoscopy. Both CIS and low grade lesions are most often missed. A false positive is not predicative of recurrence.

Other markers used:

NMP22: This urine marker marketed by Matritech detects more tumors than cytology alone

Immunocyt: This test can be used for all tumors and helps detect low grade tumors up to (61%), but is best combined with cytology.

Confounding factors Bladder cancer diagnostics and treatments are often invasive and may induce scarring, inflammation, urinary tract infections and other damage which may influence the results of any urine marker test.

The Future

*DNA microarrays such as the (urine) FISH test, marketed for use in bladder cancer by Vysis

*Combining more than one urine marker test

*Serum markers (blood tests) Markers mentioned by Dr. Witjes included TPA and TPS.

*Prognostic markers Ki-67 and p53, both potential guides on how to treat bladder tumors.

[When Dr. Witjes polled the audience of approximately 200 uro-oncologists if any of the experts present used the p53 marker, very few participants raised their hand. In the opinion of Dr. Witjes, it's time to begin.

WebCafe has more information on urine markers, including an explanation of the sensitivity vs. specificity issues pertaining to cytology and other urine marker tests.

Clinical trial using Hexvix-cystoscopy: Phase III Diagnostic Study of Blue Light Fluorescent Cystoscopy With Reconstituted Hexyl 5-Aminolevulinate (Hexvix®) Versus White Light Cystoscopy for the Detection of Carcinoma in Situ in Patients With Bladder Cancer

index

Review Pathology: Why it is critical
F. Algaba MD, PhD, Fundacio Puigvert Universdad Autonoma de Barcelona; Barcelona, Spain

Knowing the level of invasion and the grade of the cells is essential to tumor evaluation. In the field of pathology, a major drawback is the subjectivity, or interpersonal variations when interpretating specimens. These variations can have major consequences affecting the choice of treatment approaches made available to the patient.

The problem lies partly with the subjectivity of human beings and human error, and partly with the quality of specimens taken during surgery. Second opinions are common before radical treatment, but education and co-operation between specialists is essential for improving the accuracy of pathology. Most urologists have no knowledge of pathology, yet are totally dependent on the results.

T Category variation

According to the literature, an initial T1 tumor is downstaged to Ta between 35-53% of cases, while between 3 and 10% of them a T2 or higher is considered.

Anatomical bladder wall variations

The walls of the individual bladder are irregular; specimens providing clear muscle tissue are difficult to discern. The bladder neck detrusor muscle has fibers to the mucosa, and irregular muscularis mucosae is found between the outer and inner layers of the bladder lining, both of which can be confused with muscularis propria in specimens.

Effect of sample quality

Information regarding TUR specimens that cannot be evaluated by the pathologist because of poor quality is rarely provided, but some papers reported the lack of muscularis propria in the TUR specimen to be from 37-66%.

In practice tumor specimens must be diagnosed under difficult conditions such as poor tissue orientation, thermal and crush artifacts or inadequate samples. Accordingly, urologists must be aware of the limits.

Strict subepithelial Invasion criteria

Over-staging can be a consequence of using frivolous criteria&pathologists should focus mainly on invasion changes such as isolated cordonal growth, small nests, high grade and stromal reaction. Dr. Algaba advocates for improvement in staging through T1 stratification (T1a, T1b, T1c, according to depth of sub-epithelial tissue invasion) because identifying the different between major and minor invasion can be an important prognostic factor.

Grading

A similar variation of pattern can be observed in the grade.

Grade III and some grade II tumors can impact prognosis dramatically. Detailed definitions of various grades of tumor will hopefully lead to greater inter-observer agreement, guidelines must be considered, and followed by pathologists and urologists with the realization that the quality of the evaluation rests on them.

Keys for accurate pathological interpretations:

*Urologists must avoid sampling thermal and crush artifacts

*Specimens of tumor and deep bladder wall should be sent in different containers with clear anatomic identification

*Pathologists must be sure of the origin of muscle in the specimen (muscularis mucosa vs. musluaris propria)

*If there is no muscle contained in specimens, pathologists and urologists must confer about the consequences following lack of a clear diagnosis.

*Pathologists must use strict application of the invasion criteria to avoid overstaging

*For grading, strict criteria for high-grade is the most important aspect

Recommendation for review -

Second opinions are useful in the case of:

*Uncertainty by the pathologist (especially in cases of suspected T1 tumors)

*If the artifact is very important

*In cases of invasion between isolated muscle fibers

*In cases of clinical-pathological discordance

*In big tumors

Although immuno-histochemical staining which look at tumor markers such as p53 or CK20 can be helpful, the testing is not yet universally standardized and interpretations are still subjective. In Dr. Algaba s opinion they weren t much better than clinical diagnoses.

A big problem is the lack of muscle tissue in specimens due to insufficient biopsy. High quality specimens are needed to detect invasion at different levels.

Grading is the expression of progressive genetic aberrations. Even between the most experienced uro-pathologists, a second review produced an agreement only 75.4% of the time.

Biopsy specimens taken post TUR may harbor fibrosis or coagulation, making them too hard to read and thus must be staged at Tx.

index

Analyzing p53 status and other markers to determine management strategies, J. Schalken, MD, PhD, University Medical Center Nijmegen, The Netherlands

In the US, bladder cancer is the fourth most common malignancy in men and the seventh in women. More than 90% of bladder cancers are urothelial cell carcinomas (UCC), although the incidence varies widely between countries. About 2/3 of UCC s will present initially as superficial (Ta, T1 or CIS/carcinoma in situ), with remaining 1/3 muscle invasive (T2-T4) or with metastatic disease.

Primary superficial tumors tend to recur after transurethral resection, around 70%, most often during the first year of follow up. About 3-4% of these tumors progress to invasive or metastatic disease.

The p53 suppressor gene is the most commonly mutated gene in all human malignant tumors. Research on p53 in bladder cancer is aimed at diagnosis, predicting treatment outcomes after intravesical therapy, predicting the risk of tumor progression and determining the benefits of adjuvant chemo or radiotherapy. Molecular markers like p53 may lead to a better approach in the management of patients with bladder cancer in the 21st century.

Other relevant markers:

ras p21

Epidermal growth factor receptors (EFGR) HER2

Cell adhesion molecules, ie: E-cadherin.

In the 3-5% of the bladder cancer population who do experience progression in stage, survival is poor, with 37% alive at 3 years compared to 67% of those diagnosed with primary, muscle-invasive bladder cancer. It is important to identify those at risk. Identifying abnormal P53 and decreased E cadherin (cell adhesion) can be useful tools. Approximately 30% of high risk bladder tumors will have abnormal p53.1

People who abnormally expressed both the p21 and p53 oncogenes had a progression rate of 85%.

High risk groups: T1 tumors, CIS, high grade and positive p53

In one study, of the 30% whose tumors had abnormal p53, 68% progressed in 2 years, 15% did NOT progress, and 2/3 die within 3 years.

Over-expressed, mutated p53 accurately predicts progression however there is no standardization of either scoring or detection. Furthermore, the cost/benefit ratio has not been established. Other obstacles are lack ofeducation on the subject and lack of promotion regarding its use.

See also: biomarkers

1.Multifocal transitional cell cancer and p53 mutation analysis.Van Der Poel HG, Hessels D, Van Leenders GJ, Bussemakers MJ, Schalken JA, Witjes JA, Debruyne FM.Department of Urology, University Hospital, Nijmegen, The Netherlands.PMID: 9628622 J Urol. 1998

Jul;160(1):124-5

index

Flourescence in Situ
Hybridization as a tool for early detection of bladder cancer
P.F. Bassi, MD, Clinica Urologica, Universita di Padova, Italy

There are many urine marker tests available
commercially (BTA, NMP22, Telomerase, FDG) for bladder cancer detection, but the accuracy of these tests is still unclear; none of the current tests is sensitive enough to be recommended for routine practice.

A newer assay known as UROVYSION is now available
for clinical evaluation. The improvement in this assay is the combination of four probes into a single probe, which increases sensitivity and perhaps specificity over that obtained with single or dual-probe sets.

The Urovysion FISH assay provides higher sensitivity and similar specificity
at detected TCC in urine samples as compared to cytology, BTA stat, telomerase and hemoglobin dip stick.

Urovysion s FISH assay is a promising new
assay for bladder cancer and further studies are needed to explore its definitive role.

-Only 5 cells are needed to perform this test.

-The specificity of the test is equal to cytology.

-The sensitivity of cytology is 24% compared to FISH s 78%.

-FISH picked up low grade tumors 56% of the time

-Is accurate in BCG treated patients

Is good for predicting tumor recurrence

index

Session 2: How to Treat Low-Risk
Tumors

Chair:A.P.M. van der Meijden, MD, PhD Jeroen Bosch Hospital, s-Hertogenbosch, The Netherlands

Chemoresection for
superficial bladder cancer W.Oosterlinck, MD, PhD, Ghent University Hospital, Belgium; Member of EORTC, EUA

The concept of chemoresection-using an intravesical drug against bladder
tumors instead of transurethral surgery- goes back to the early 1960 s, when Thiotepa was first used to treat bladder cancer (TCC). Other drugs were compared to this standard. It became standardized to leave a marker

lesion after TUR of all other papillary tumors. When the drug had no effect, the patient could be spared useless treatments. High risk people were excluded from this approach, and the marker lesion had to be less than 1 cm, but at least 0.5 cm. In case of a good response, a large disease-free interval could be expected.

Between 1980 and 2002, 19 chemo-resection studies using Mitomycin C were published, with a mean complete resection rate of 45.6%. When partial remissions were included the number jumped to 60%. BCG studies using marker lesions delivered a complete resection rate of 65%.

There have been several studies published since 1994 using this approach not in the clinical trial context, but as an actual treatment for superficial bladder cancer in order to avoid TUR. The most remarkable of these was published in 1999, and reported a 46% complete resection/response rate after one single instillation of Epirubicine.1 Akaza reported 66% complete response after 8 weeks of intravesical BCG, along with an 84% complete response for those with CIS, however, the study was too small to allow for definite conclusions. 2

Chemical resection of tumors can be cheaper and more comfortable for the patient than TUR, avoiding hospitalization, anesthesia and surgery. It can prolong the disease free interval.

There are several data demonstrating that TUR is often less complete than we hope for, the high recurrence rate at 3 months, the high variability of these recurrences between institutions, the high number of positive findings during a second TUR and the number of tumors detected by florescence are all an incitement for the EORTC to study this in a randomized, controlled clinical trial comparing chemoresection to TUR. Furthermore, TUR may enhance tumor growth as trauma activates cellular changes in the epithelium. Perhaps laser (non touch) surgery would be better.

Although this precludes knowing the pathology of the tumor, the reliability of the judgment of urologists regarding papillary tumors was very high, 93% of cases agreed with pathology (EORTC data on 1469 cases). Recurrent grade I tumors are the same pathologically as the initial tumor 90% of the time. The risk of leaving a marker lesion has been shown to be 0% for low risk, 2% for intermediate risk, and 7%for high risk.

Low risk tumors are often treated too aggressively, routine TUR for recurrences is riskier than appreciated, and before we begin calling it gold , it needs further study.

Thanks to these arguments, the EORTC (European Organization for Research and Treatment of Cancer) feels it s safe to begin the trial comparing TUR+ one immediate instillation of Mitomycin C against chemoresection with 4 weekly instillations with Mitomycin C. Health economics and quality of life study measuring possible additional advantages in one arm have been incorporated in the study.

Dr. Oosterlinck is the head author of the European Ass. of Urology's: Guidelines for treatment of bladder cancer

1 .Intravesical chemotherapy with epirubicin: a dose response

study. Masters JR, Popert RJ, Thompson PM, Gibson D, Coptcoat MJ, Parmar MK. Institute of Urology and Nephrology, University College and Department of Urology, King's College Hospital, London, United Kingdom. J Urol. 1999 May;161(5):1490-3. PMID: 10210379

2. Bacillus Calmette-Guerin treatment of existing papillary bladder cancer and carcinoma in situ of the bladder. Four-year results. The Bladder Cancer BCG Study Group .Akaza H, Hinotsu S, Aso Y, Kakizoe T, Koiso K.Department of Urology, University of Tsukuba, Japan. Cancer. 1995 Jan 15;75(2):552-9. PMID 7812924

index

A meta-analysis of randomized trials investigating transurethral resection plus one immediate instillation of chemotherapy R.J. Sylvester, ScD, European Organization for Research and Treatment of Cancer, Brussels, Belgium

70-80% of bladder tumors initially present as Ta, T1 or CIS. After TUR, BCG is the treatment of choice for high risk tumors, however, it is considered to be over-treatment in patients with low risk tumors.

Although intravesical chemotherapy delays the time to first recurrence after TUR, there is no consensus on whether single, low risk tumors should receive intravesical chemotherapy or just be followed up with cystoscopy alone after TUR. Likewise, there is still doubt about the value of one immediate instillation after TUR for patients with multiple tumors who are at a higher risk for recurrence.

The European Association of Urology guidelines recommend one immediate instillation after TUR for ALL superficial bladder tumors. The objective is to determine if one immediate instillation reduces risk of recurrence in those with Ta, grade 1 bladder cancer.

Materials and Methods

A meta-analysis was carried out which looked at randomized studies comparing TUR alone to TUR+one post-operative instillation of chemotherapy in people with primary or recurrent, stage Ta, T1 bladder cancer without carcinoma in situ.

Results

Seven trials with 1476 patients were indentified. Based on a median follow up of 3.4 years and a maximum of 14.5 years, 267 of 728 patients (36%) of those receiving one post-op instillation of epirubicin, mitomycin C, thiotepa or pirarubicin experienced a recurrence, as compared to 362 of 748 (48.4%) with TUR alone. This shows a reduction of 39% in the odds of recurrence with chemotherapy.

Both single and multiple tumors were successfully treated, however, after one instillation, 65.2% of those with multiple tumors recurred as compared to 35.8% of single tumors, showing that one instillation is insufficient as adjuvant treatment in people with multiple tumors.

The assumption is that the chemotherapy kills any remaining cancer cells. Thiotepa was shown to be of no benefit, with a higher risk of systemic side effects occurring.

Conclusions

One immediate intravesical instillation of chemotherapy significantly reduces the risk of recurrence after TUR in patients with single and multiple, stage Ta T1 bladder cancer. It is the treatment of choice in patients with a single, low risk papillary tumor and is recommended as the initial treatment after TUR in patients with higher risk turmors.

Reference

The EAU Working Group on Oncological Urology: Guidelines on bladder cancer; Oosterlinck, W, LobelB, Jakse G, et al. . Eur. Urol.2002; 41:105

index

Observation of TaGI bladder tumors: Acceptable?

Mark.S.Soloway, University of Miami School of Medicine, Florida, USA

Fifty percent of newly diagnosed cases of bladder cancer are low grade, non-invasive and papillary. Extensive evidence has shown that people who present with these tumors rarely have a life-threatening subsequent tumor. Most urologists treat these patients with TUR and general anesthesia, and many cauterize these tumors in the office. Resection of these tumors in the operating room is a low risk procedure, however there can be morbidity and it is expensive. Is it necessary to remove these tumors when they are detected?

Dr. Soloway felt that it was acceptable to observe small, recurrent, low grade tumors in a select group of patients who were willing to accept conservative disease management. Beginning in 1992 and over a period of ten years, 32 patients with a history of G1, Ta TCC were considered for observation with the plan to eventually remove the tumor when it reached a certain size or hematuria occurred. An observation period ended when the tumor was resected or fulgurated or no longer apparent (which occurred in eight instances).

-Mean age of the patient: 72 (39 to 88)

-Mean duration of the 56 observation periods in the 32 pts: 10.1 month (range from 3-28 months)

-Mean tumor growth based upon the size determined by the endoscopist: 1.77mm per month (range from 0 to 5.83mm based on 37 tumors)

Only three of the 45 tumors observed (which were preceded by a low grade non-invasive tumor) were high grade Ta or T1 when removed. The high grade T1 tumors showed minimal invasion (T1a) only and the remaining 42 tumors were either low grade, non invasive or could not be excised because the

observation period (mean of 1 year) was not yet over, the tumor was fulgurated without a biopsy, or the tumor was no longer seen at the follow up endoscopy. Eight patients had a high grade Ta tumor prior to the observation, and when six of these had their tumors resected, none had invaded the mucosa of the lamina propria.

During this 10 year period not one of the 32 patients have experienced invasion of mucosa of the lamina propria or progressed to a muscle invasive tumor.

The rationale for observation is to avoid repeated TUR trauma, reduce its morbidity, and avoid risk associated with anesthesia. The approach could spare many useless cystoscopies. However, selection criteria seem to be very strict; Dr. Soloway writes: During this ten year interval I performed 419 TURBT s during this same time and only 32 patients were felt appropriate for this observation program. His study concluded:

Small, recurrent, low grade appearing bladder tumors are slow growing and pose minimal risk. Therefore, as an alternative to in office fulguration to minimize morbidity and cost associated with repeat transurethral resection it may not be necessary to remove these tumors promptly at new tumor occurrence or recurrence.1

References:

1. Expectant management of small, recurrent, noninvasive papillary bladder tumors. Soloway MS, Bruck DS, Kim SS. Department of Urology, University of Miami, Florida 33101, USA. J Urol. 2003 Aug;170(2 Pt 1):438-41 PMID: 12853794

Treated history of noninvasive grade 1 transitional cell carcinoma. The National Bladder Cancer Group.Prout GR Jr, Barton BA, Griffin PP, Friedell GH.Massachusetts General Hospital, Boston. J Urol. 1992 Nov;148(5):1413-9. PMID: 1433540

Does cystoscopy correlate with the histology of recurrent papillary tumours of the bladder? Herr HW.Department of Urology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.BJU Int. 2001 Nov;88(7):683-5. PMID: 11890237

Phase II trials in Ta, T1 bladder cancer. The marker tumour concept. van der Meijden AP, Hall RR, Kurth KH, Bouffioux C, Sylvester R.Bosch Medical Center, 's Hertogenbosch, Netherlands, Br J Urol. 1996 May;77(5):634-7.PMID: 8689102

Outpatient flexible cystoscopy and fulguration of recurrent superficial bladder tumors. Herr HW. Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York. PMID: 2231928

index

Results from Finn bladder group
in low risk Tumors, E. Rintala, MD, Helsinki University Central Hospital, Finland

The Finn Bladder (FB) Group has been studying the treatment of superficial bladder cancer since 1985. Most of the clinical studies involved those with frequently recurring superficial tumors, at an intermediate or high-risk for future recurrence. The group s experience with strictly Ta, G1 tumors is limited.

In their series of long term studies, multiple tumors were predicative of future recurrence, regardless of the treatment approach used.

The policy of the FinnBladder Group regarding low to intermediate risk superficial tumors is to do a TUR followed immediately by one intravesical instillation of epirubicin 100mg or mitomycin C 40mg for two hours, as long as no perforation is feared. For infrequent recurs, a single instillation may be given again, and in case of frequent recurrences a maintenance instillation regimen for six to twelve months is recommended.

FB Study I

We compared an intensive two year BCG monotherapy to a similar Mitomycin C monotherapy. BCG therapy was significantly better than MMC regarding recurrence after median follow-up of 95 months

The effect of BCG and Mitomycin C instillation treatment in recurrent superficial bladder carcinoma. 15 year follow up of a randomized prospective FinnBladder study. Taipale L, Permi J, Viitanen J, et al. Eur. Urol. 2002;1:101

FB Study II

2 years of Mitomycin C mono-therapy was compared to alternating instillations of BCG and MMC. No difference between the two treatment arms was found regarding recurrence or progression.

Alternating mitomycin C and bacillus Calmette-Guerin instillation prophylaxis for recurrent papillary (stages Ta to T1) superficial bladder cancer. Finnbladder Group. Rintala E, Jauhiainen K, Kaasinen E, Nurmi M, Alfthan O. Department of Urology, Helsinki University Central Hospital, Finland. J Urol. 1996 Jul;156(1):56-9; discussion 59-60.Comment in: J Urol. 1996 Jul;156(1):61-2. PMID: 8648837

FB Study III

CONCLUSIONS: A single perioperative instillation of 100 mg. epirubicin causes a significant and sustained decrease in primary superficial bladder cancer recurrence, whereas a single dose of 50 milliunits interferon-alpha2b is ineffective for prophylaxis&We found a 2-fold relative risk of recurrence in the TUR alone group compared with the group who also received epirubicin

Perioperative single dose instillation of epirubicin or interferon-alpha after transurethral resection for the prophylaxis of primary superficial bladder cancer recurrence: a prospective randomized multicenter study--FinnBladder III long-term results.Rajala P, Kaasinen E, Raitanen M, Liukkonen T, Rintala E; Finnbladder Group.Divisions of Urology, Turku University Hospital, Turku, Finland. J Urol. 2002 Sep;168(3):981-5 PMID: 12187204

FB Study IV

The timing of the first instillation was a significant predictor for further recurrences with more than a 2-fold relative risk for a new recurrence if the first Mitomycin C instillation was given later than on day zero after TUR. CONCLUSION: Preceding recurrence rate, most accurately reflects, in patients with frequently recurring tumors, the inherent risk for new recurrences. This risk can be considerably reduced by use of an effective chemo-immunotherapy regimen, and in addition, by inclusion of an early peri-operative chemotherapy instillation in such a regimen.

Factors explaining recurrence in patients undergoing chemoimmunotherapy regimens for frequently recurring superficial bladder carcinoma.Kaasinen E, Rintala E, Hellstrom P, Viitanen J, Juusela H, Rajala P, Korhonen H, Liukkonen T; FinnBladder Group.Hyvinkaa Hospital, Hyvinkaa, Finland. Eur Urol. 2002 Aug;42(2):167-74. PMID: 12160589

index