

Bölüm 46

KAS İNVAZİV OLMAYAN MESANE KANSERİNE YAKLAŞIM VE YÖNETİM

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GİRİŞ

Mesane kanserinde kas invazyonu surveyi çok etkileyen, tedaviyi tamamen değiştiren bir durumdur. Bunun için mesane kanserini kas invaze ve kas invaze olmayan şeklinde iki gruba ayırıyoruz. Bu bölümde kas invaze olmayan mesane kanserini ele alacağız.

Kas invaze olmayan mesane kanserini tanımlayacak olursak, TNM sınıflandırmasına göre Ta, Tis ve T1 tümörler bu gruptadır (1). Yani mukozaya sınırlı ya da lamina propriaya invaze papiller tümörler ve mukozaya sınırlı karsinoma in situ olarak adlandırılan flat tümörlerdir(1).

EPİDEMİYOLOJİ

Mesane kanseri, kanser sıralamasında dünyada onbirinci, erkek popülasyonunda ise yedinci sıradadır (2). İnsidansına baktığımızda ise erkeklerde yüz binde 9, kadınlarda yüz binde 2.2'dir (2). Erkeklerde sigara kullanımının ve çevresel etkenlere maruziyetin fazla olması sebep olarak gösterilebilir.

2012de yapılan bir çalışmada mortalite oranları erkekte yüz binde 3.2, kadında ise yüz binde 0.9 saptanmıştır (2).

Tanı anında hastaların yaklaşık %75'i kas invaziv olmayan grupta olup kanser spesifik mortalite oranları kas invaziv olan grupta kıyaslandığında belirgin düşüktür (2-4).

ETYOLOJİ

Etyolojide en sık suçlanan faktör sigara olup olguların %50'sinde sigara içimi mevcuttur (3, 5-7). Çevresel sigara dumanına maruziyet de kanser riskini artırmaktadır (3). Sigarada bulunan polisiklik hidrokarbonlar, aromatik aminler idrar yoluyla atıldığı için üriner sisteme kanserojenik etkisi vardır.

Aktif sigara içen grupta risk en fazla olup sigarayı bırakan grupta mesane kanseri riski düşer. Ancak hiç sigara içmeyen grup seviyesine düşmez (6).

İkinci sırada ise endüstriyel kimyasallara maruziyet suçlanmaktadır. Boya, metal ve petrol ürünleri ile temasa neden olan durumlar riskin artmasına yol açar (3, 5, 8, 9). Gelişmiş ülkelerde ise artan iş güvenliği tedbirleri ile bu risk normal popülasyon seviyesine inmiştir (3, 8, 9).

Günlük alınan su miktarı ve sıvı çeşidi tartışmalıyken sudaki klor ve arsenik gibi maddelerin mesane kanseri riskini arttırdığı gösterilmiştir (3, 10).

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BCG intoleransı: BCG tedavisini yarıda bırakacak ciddi yan etki.

Başarısız BCG tedavisi ya da BCG sonrası nüks durumunda radikal sistektomi gündeme gelmelidir.

KİOMK'da Radikal Sistektomi

Mesane kanserinde radikal sistektomi etkili bir yöntem olmasının yanında hayat kalitesini düşürmesi, çeşitli morbiditelere sebep olması nedeniyle kas invaze olmayan mesane kanserinde ilk planda düşünülmemektedir. Fakat bazı kas invaze olmayan mesane kanserlerinin progresyon göstererek invaze olduğu ve primer kas invaze kanserlerden daha kötü prognoza sahip olduğu (50, 51), T1 tümör nedenli radikal sistektomi yapılan hastaların patoloji sonucunun %27-51 oranında kas invaziv olarak raporlandığı gözlenmiştir (52-57). Dolayısıyla kar/zarar oranı göz önüne alınarak seçilmiş vakalarda(özellikle çok riskli grupta) radikal sistektomi de göz önüne alınmalıdır.

Takip

Takipte kullanılan temel yöntem sistoskopidir. Görüntüleme yöntemleri ve sitoloji ile desteklenebilir. 3. ayda kontrol sistoskopi mutlaka yapılmalı sonrasında ise hasta bazlı takibe devam edilmelidir.

Düşük dereceli tümörlerde 5 yıllık nüksüz takip sonrası nüks riski düşük olduğu için takip sonlandırılabilir (58, 59). Fakat orta ve özellikle yüksek riskli grupta 10 yıl sonrasında bile nüks gözlenebildiği için takip ömür boyu sürdürülmelidir (59)

SONUÇ

Sonuç olarak mesane kanseri hayatı tehdit eden önemli bir hastalıktır. Risk faktörlerinden uzak durulmalı, tedavi ve sonrasındaki takip aksatılmamalıdır. Progrese olarak mortalite ve morbiditesi daha yüksek olan kas invaze hale dönüştüğünde hayatta ciddi değişikliklere sebep olmaktadır.

KAYNAKÇA

1. Sobin LH GM, Wittekind Ch. TNM classification of malignant tumors UICC International Union Against Cancer 7th edn 2009, Wiley-Blackwell.
2. Globocan W. Estimated cancer incidence, mortality and prevalence worldwide in 2012. Lyon: WHO. 2012.
3. Burger M, Catto JW, Dalbagni G, et al. Epidemiology and risk factors of urothelial bladder cancer. European urology. 2013;63(2):234-41.
4. Compérat E, Larré S, Roupret M, et al. Clinicopathological characteristics of urothelial bladder cancer in patients less than 40 years old. Virchows Archiv. 2015;466(5):589-94.
5. Chavan S, Bray F, Lortet-Tieulent J, et al. International variations in bladder cancer incidence and mortality. European urology. 2014;66(1):59-73.
6. Freedman ND, Silverman DT, Hollenbeck AR, et al. Association between smoking and risk of bladder cancer among men and women. Jama. 2011;306(7):737-45.
7. van Osch FH, Jochems SH, van Schooten F-J, et al. Quantified relations between exposure to tobacco smoking and bladder cancer risk: a meta-analysis of 89 observational studies. International journal of epidemiology. 2016;45(3):857-70.
8. Colt JS, Friesen MC, Stewart PA, et al. A case-control study of occupational exposure to metalworking fluids and bladder cancer risk among men. Occup Environ Med. 2014;71(10):667-74.
9. Pesch B, Taeger D, Johnen G, et al. Screening for bladder cancer with urinary tumor markers in chemical workers with exposure to aromatic amines. International archives of occupational and environmental health. 2014;87(7):715-24.
10. Steinmaus C, Ferreccio C, Acevedo J, et al. Increased lung and bladder cancer incidence in adults after in utero and early-life arsenic exposure. Cancer epidemiology and prevention biomarkers. 2014;23(8):1529-38.
11. Fernandes ET, Manivel JC, Reddy PK, et al. Cyclophosphamide associated bladder cancer--a highly aggressive disease: analysis of 12 cases. The Journal of urology. 1996;156(6):1931-3.
12. Travis L, Curtis R, Boice JJ, et al. Bladder cancer after chemotherapy for non-Hodgkin's lymphoma. The New England journal of medicine. 1989;321(8):544-5.
13. El-Bolkainy M, Mokhtar N, Ghoneim M, et al. The impact of schistosomiasis on the pathology of bladder carcinoma. Cancer. 1981;48(12):2643-8.
14. Tuccori M, Fillion KB, Yin H, et al. Pioglitazone use and risk of bladder cancer: population based cohort study. Bmj. 2016;352:i1541.

15. Teleka S, Häggström C, Nagel G, et al. Risk of bladder cancer by disease severity in relation to metabolic factors and smoking: A prospective pooled cohort study of 800,000 men and women. *International journal of cancer*. 2018;143(12):3071-82.
16. Ramirez D, Gupta A, Canter D, et al. Microscopic haematuria at time of diagnosis is associated with lower disease stage in patients with newly diagnosed bladder cancer. *BJU international*. 2016;117(5):783-6.
17. Davis R, Jones JS, Barocas DA, et al. Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. *The Journal of urology*. 2012;188(6S):2473-81.
18. Hilton S, Jones LP. Recent advances in imaging cancer of the kidney and urinary tract. *Surgical Oncology Clinics*. 2014;23(4):863-910.
19. Choyke PL. Radiologic evaluation of hematuria: guidelines from the American College of Radiology's appropriateness criteria. *American family physician*. 2008;78(3).
20. Palou J, Rodriguez-Rubio F, Huguet J, et al. Multivariate analysis of clinical parameters of synchronous primary superficial bladder cancer and upper urinary tract tumor. *The Journal of urology*. 2005;174(3):859-61.
21. Yafi FA, Brimo F, Steinberg J, et al., editors. *Prospective analysis of sensitivity and specificity of urinary cytology and other urinary biomarkers for bladder cancer*. *Urologic Oncology: Seminars and Original Investigations*; 2015: Elsevier.
22. Cumberbatch MG, Foerster B, Catto JW, et al. Repeat Transurethral Resection in Non-muscle-invasive Bladder Cancer: A Systematic Review. *European urology*. 2018;73(6):925-33.
23. Naselli A, Hurler R, Paparella S, et al. Role of restaging transurethral resection for T1 non-muscle invasive bladder cancer: a systematic review and meta-analysis. *European urology focus*. 2018;4(4):558-67.
24. Grimm M-O, Steinhoff C, Simon X, et al. Effect of routine repeat transurethral resection for superficial bladder cancer: a long-term observational study. *The Journal of urology*. 2003;170(2):433-7.
25. Divrik RT, Yildirim Üt, Zorlu F, et al. The effect of repeat transurethral resection on recurrence and progression rates in patients with T1 tumors of the bladder who received intravesical mitomycin: a prospective, randomized clinical trial. *The Journal of urology*. 2006;175(5):1641-4.
26. Sfakianos JP, Kim PH, Hakimi AA, et al. The effect of restaging transurethral resection on recurrence and progression rates in patients with nonmuscle invasive bladder cancer treated with intravesical bacillus Calmette-Guerin. *The Journal of urology*. 2014;191(2):341-5.
27. Baltacı S, Bozlu M, Yıldırım A, et al. Significance of the interval between first and second transurethral resection on recurrence and progression rates in patients with high-risk non-muscle-invasive bladder cancer treated with maintenance intravesical Bacillus Calmette-Guérin. *BJU international*. 2015;116(5):721-6.
28. Soukup V, Čapoun O, Cohen D, et al. Prognostic performance and reproducibility of the 1973 and 2004/2016 World Health Organization Grading classification systems in non-muscle-invasive bladder cancer: a European Association of Urology non-muscle invasive bladder cancer guidelines panel systematic review. *European urology*. 2017;72(5):801-13.
29. Sylvester RJ, van der Meijden A, Witjes J, et al. High-grade Ta urothelial carcinoma and carcinoma in situ of the bladder. *Urology*. 2005;66(6):90-107.
30. Lamm D, Herr H, Jakse G, et al. Updated concepts and treatment of carcinoma in situ. *Urologic oncology*. 1998;4(4-5):130-8.
31. Palou J, Sylvester RJ, Faba OR, et al. Female gender and carcinoma in situ in the prostatic urethra are prognostic factors for recurrence, progression, and disease-specific mortality in T1G3 bladder cancer patients treated with bacillus Calmette-Guérin. *European urology*. 2012;62(1):118-25.
32. Cookson MS, Herr HW, Zhang Z-F, et al. The treated natural history of high risk superficial bladder cancer: 15-year outcome. *The Journal of urology*. 1997;158(1):62-7.
33. Sylvester RJ, van der Meijden AP, Oosterlinck W, et al. Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. *European urology*. 2006;49(3):466-77.
34. Lamm D. Carcinoma in situ. *The Urologic clinics of North America*. 1992;19(3):499-508.
35. Brausi M, Collette L, Kurth K, et al. Variability in the recurrence rate at first follow-up cystoscopy after TUR in stage Ta T1 transitional cell carcinoma of the bladder: a combined analysis of seven EORTC studies. *European urology*. 2002;41(5):523-31.
36. Soloway MS, Masters S. Urothelial susceptibility to tumor cell implantation influence of cauterization. *Cancer*. 1980;46(5):1158-63.
37. Pan JS, Slocum HK, Rustum YM, et al. Inhibition of implantation of murine bladder tumor by thiotepa in cauterized bladder. *The Journal of urology*. 1989;142(6):1589-93.
38. Brocks CP, BÜTTNER H, BÖHLE A. Inhibition of tumor implantation by intravesical gemcitabine in a murine model of superficial bladder cancer. *The Journal of urology*. 2005;174(3):1115-8.
39. Oosterlinck W, Kurth KH, Schröder F, et al. A prospective European Organization for Research and Treatment of Cancer Genitourinary Group randomized trial comparing transurethral resection followed by a single intravesical instillation of epirubicin or water in single stage Ta, T1 papillary carcinoma of the bladder. *The Journal of urology*. 1993;149(4):749-52.
40. Sylvester RJ, Oosterlinck W, Holmang S, et al. Systematic review and individual patient data meta-analysis of randomized trials comparing a single immediate instillation of chemotherapy after transurethral resection with transurethral resection alone in patients with stage pTa-pT1 urothelial carcinoma of the bladder: which patients benefit from the instillation?

- European urology. 2016;69(2):231-44.
41. Malmström P-U, Sylvester RJ, Crawford DE, et al. An individual patient data meta-analysis of the long-term outcome of randomised studies comparing intravesical mitomycin C versus bacillus Calmette-Guérin for non-muscle-invasive bladder cancer. *European urology*. 2009;56(2):247-56.
 42. Losa A, Hurle R, Lembo A. Low dose bacillus Calmette-Guerin for carcinoma in situ of the bladder: long-term results. *The Journal of urology*. 2000;163(1):68-72.
 43. Griffiths T, Charlton M, Neal D, et al. Treatment of carcinoma in situ with intravesical bacillus Calmette-Guerin without maintenance. *The Journal of urology*. 2002;167(6):2408-12.
 44. Takenaka A, Yamada Y, Miyake H, et al. Clinical outcomes of bacillus Calmette-Guérin instillation therapy for carcinoma in situ of urinary bladder. *International journal of urology*. 2008;15(4):309-13.
 45. Gofrit ON, Pode D, Pizov G, et al., editors. The natural history of bladder carcinoma in situ after initial response to bacillus Calmette-Guérin immunotherapy. *Urologic Oncology: Seminars and Original Investigations*; 2009: Elsevier.
 46. LAMM DL, BLUMENSTEIN BA, CRISSMAN JD, et al. Maintenance bacillus Calmette-Guerin immunotherapy for recurrent TA, T1 and carcinoma in situ transitional cell carcinoma of the bladder: a randomized Southwest Oncology Group Study. *The Journal of urology*. 2000;163(4):1124-9.
 47. Jakse G, Hall R, Bono A, et al. Intravesical BCG in Patients with Carcinoma in situ of the Urinary Bladder: Long-Term Results of EORTC GU Group Phase II Protocol 30861. *European urology*. 2001;40(2):144-50.
 48. Solsona E, Iborra I, Dumont R, et al. The 3-month clinical response to intravesical therapy as a predictive factor for progression in patients with high risk superficial bladder cancer. *The Journal of urology*. 2000;164(3 Part 1):685-9.
 49. Lerner SP, Tangen CM, Sucharew H, et al., editors. Failure to achieve a complete response to induction BCG therapy is associated with increased risk of disease worsening and death in patients with high risk non-muscle invasive bladder cancer. *Urologic Oncology: Seminars and Original Investigations*; 2009: Elsevier.
 50. Moschini M, Sharma V, Dell'Oglio P, et al. Comparing long-term outcomes of primary and progressive carcinoma invading bladder muscle after radical cystectomy. *BJU international*. 2016;117(4):604-10.
 51. Schrier BP, Hollander MP, van Rhijn BW, et al. Prognosis of muscle-invasive bladder cancer: difference between primary and progressive tumours and implications for therapy. *European urology*. 2004;45(3):292-6.
 52. Huguet J, Crego M, Sabate S, et al. Cystectomy in Patients with High Risk Superficial Bladder Tumors Who Fail Intravesical BCG Therapy:: Pre-Cystectomy Prostate Involvement as a Prognostic Factor. *European urology*. 2005;48(1):53-9.
 53. Fritsche H-M, Burger M, Svatek RS, et al. Characteristics and outcomes of patients with clinical T1 grade 3 urothelial carcinoma treated with radical cystectomy: results from an international cohort. *European urology*. 2010;57(2):300-9.
 54. Turker P, Bostrom PJ, Wroclawski ML, et al. Upstaging of urothelial cancer at the time of radical cystectomy: factors associated with upstaging and its effect on outcome. *BJU international*. 2012;110(6):804-11.
 55. May M, Bastian PJ, Brookman-May S, et al. Pathological upstaging detected in radical cystectomy procedures is associated with a significantly worse tumour-specific survival rate for patients with clinical T1 urothelial carcinoma of the urinary bladder. *Scandinavian journal of urology and nephrology*. 2011;45(4):251-7.
 56. Svatek RS, Shariat SF, Novara G, et al. Discrepancy between clinical and pathological stage: external validation of the impact on prognosis in an international radical cystectomy cohort. *BJU international*. 2011;107(6):898-904.
 57. Shariat SF, Palapattu GS, Karakiewicz PI, et al. Discrepancy between clinical and pathologic stage: impact on prognosis after radical cystectomy. *European urology*. 2007;51(1):137-51.
 58. Mariappan P, Smith G. A surveillance schedule for G1Ta bladder cancer allowing efficient use of check cystoscopy and safe discharge at 5 years based on a 25-year prospective database. *The Journal of urology*. 2005;173(4):1108-11.
 59. Soukup V, Babjuk M, Bellmunt J, et al. Follow-up after surgical treatment of bladder cancer: a critical analysis of the literature. *European urology*. 2012;62(2):290-302.