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Ahmed Saadullah

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List of Abbreviations

ABC ..... Advanced Bladder Cancer Meta-analysis Collaboration Group.

AJCC ..... American Joint Committee on Cancer.

ANC..... Absolute Neutrophil Count.

BCG..... Bacillus Calmette Guerin.

CIS ..... Carcinoma In Situ.

CMV ..... Cisplatin, Methotrexate and Vinblastine.

CP..... Carboplatin.

CR..... Complete Remission.

CUETO ..... Club Urologico Espanol De Tratamiento Oncologico.

DHFR..... Dihydrofolate reductase.

ECOG ..... Eastern Co-operative Oncology Group.

LND..... Lymph Node Dissection.

LVI ..... Lymphovascular Invasion.

MTD ..... Maximum Tolerated Dose.

M-VAC ..... Methotrexate , Vinblastine , Adriamycin and Cisplatin.

PAC ..... Paclitaxel.

PSA..... Prostate Specific Antigen.

QOL..... Quality Of Life.

RTOG ..... Radiation Therapy Oncology Group.

SCC ..... Squamous Cell Carcinoma.

TCC ..... Transitional Cell Carcinoma.

TNM ..... Tumor, Node, Metastasis.

TURBT..... Transurethral Resection of Bladder Tumor.

TURT ..... Transurethral Resection of Tumor.

UICC ..... International Union Against Cancer.

UICC ..... Union International Contre Le Cancer.

U-PA..... Urokinase plasminogen activator.

USC ..... University of South California.

استئصال الورم بالمنظار للحفاظ على المثانة في علاج سرطان المثانة

رســـــــالـــــة

توطئة للحصول على درجة الماجستير في جراحة المسالك البولية

مقدمة من

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Bladder Preservation in Treatment of Muscle Invasive Bladder Cancer

An Essay

Submitted For Partial Fulfillment of the Master Degree **In Urology**

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الملخـــص العـــربـــي

مقـــدمة

يعتبر سرطان المثانة ثاني اشهر سرطان يصيب الجهاز البولي وهو يمثل ٧% من السرطانات التي تصيب الرجال و ٢% من السرطانات التي تصيب النساء.

ولقد تم تقسيم سرطان المثانة الى مراحل تبعا للعمق الذي يصيبه في جدار المثانة والاعضاء التي حولها وايضا حسب مدى انتشاره واصابته للغدد الليمفاوية.

وبالرغم من ان الاستئصال الجذري للمثانة ما يزال العلاج الاساسي للسرطانات العميقة الا انه وجد ان هذه الطريقه لها مضاعفات عدة.

ولهذا فقد تم تطوير طرق اخرى تعتمد على الحفاظ على المثانة من خلال استئصال الورم بالمنظار مع استخدام علاج كيماوي واخر اشعاعي، او بالاستئصال الجزئي للمثانة البولية.

ويتم استخدام هذه الطريقة لدى بعض المرضى الذين يتمتعون بمواصفات معينه من ضمنها الا يكون الورم قد اصاب اعضاء اخرى من جسم المريض.

وبالرغم من ان هذه الطريقة مازالت محل جدل علمي ،الا انه يتوجب ان يكون المريض على دراية وافية للبدائل المتاحة للتعامل مع السرطان وخاصة ما يتعلق بالطرق التي تتيح له الحفاظ على المثانة.

الهدف من الدراسة

دراسة الطرق البديلة لعلاج سرطان المثانة العميق والتي تستهدف الحفاظ على المثانة ، وتوضيح المواصفات الخاصة باختيار الحالات المناسبة لهذا النوع من العلاج وكيفية متابعة الحالات والنتائج المستخلصة.

INTRODUCTION

Bladder cancer is the second most common cancer of the genitourinary tract. Approximately 90% of all bladder cancers are transitional cell carcinomas. It accounts for 7% of new cancer cases in men and 2% of new cancer cases in women **(Canto and Chu, 2000).**

The main staging system of bladder cancer, which has been revised, is the one developed jointly by the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC) **(Sobin and Wittekind, 1997)**. It is also termed Tumor-Node-Metastasis (TNM).

Although radical cystectomy with pelvic lymph node dissection remains the standard treatment for muscle invasive bladder cancer, local or distant failure continues to be common reported in the range of 15% to 40% even for early stages of muscle infiltrating tumors (stage 2) **(Bochner et al., 2004)**.

An alternative approach is multimodality bladder preservation, which in modern series includes thorough TURBT, chemotherapy, and radiation therapy. This approach has been developed to improve quality of life for patients who want to maintain urinary function without a diversion, and also for patients who are

refusing surgery. Overall survival results from large centers using the multimodality conservative approach are similar to those for radical cystectomy (Shipley et al., 2002).

Another alternative treatment is partial cystectomy, which is a surgical method of removing a selected full-thickness portion of the bladder wall. Its primary indication is for solitary, primary, muscle-invasive, or high-grade bladder cancer that does not involve the bladder trigone, vesical neck, or posterior urethra and that can be resected with adequate surgical margins (minimum of 2 cm). Partial cystectomy has certain advantages over radical cystectomy, such as preserving a functional continent native urinary reservoir and sparing of potency in males (Kassouf et al., 2006).

General criteria for selective bladder preservation includes presence of muscle-invasive disease, absence of hydronephrosis, normal renal function, normal complete blood count, suitable candidate for cystectomy, and absence of metastatic disease on imaging studies. It is believed that this treatment regimen permits salvage cystectomy to be performed sooner for patients who are incomplete responders and before they have received full-dose radiation (Shipley et al., 2005).

As long as sustained curative responses are noted in many patients, they should be made aware of multimodal organ preservation strategies as an alternative treatment. Those most likely to benefit from organ preservation include individuals with significant medical comorbidity and small-to-moderate local tumor burdens who are also compelled by age or the utility value of avoiding the morbidity of major surgery to seek other treatment (Chatterjee et al., 2004).

AIM OF THE WORK

To revise and discuss the bladder preservation protocols applied for the management of muscle invasive TCC in comparison to standard radical cystectomy with urine diversion and possible effects of these modalities on radicality, with detailed discussion of the selection criteria. The follow up schedule and the result of each protocol will be discussed in details.

Pathology

Transitional cell carcinomas are the second most common urological malignancy in industrialized countries. Approximately 80% of the tumors are diagnosed as non muscle invasive tumors at first diagnosis. Disease-specific 5-year survival of patients with muscle-invasive bladder tumors ranges between 40 and 60% without significant changes in recent years **(Oosterlinck et al, 2002)**. The individual prognosis can be estimated with the use of nomograms **(Bochner, 2006)**.

In western countries, about 90% of bladder tumors are transitional cell carcinoma (TCC) **(Macvicar, 2000)**.

Staging:

Pathological staging of bladder cancer is the most important determinant of prognosis. In fact, it is the most potent predictor of survival in transitional cell carcinoma and it is critical in stratifying patients for therapy **(Lapham et al., 1997)**.

Accurate pathologic staging requires knowledge of the basic histology of the organ in question. In the urinary bladder, transitional epithelium (urothelium) overlies a basement membrane and lamina propria,

which is composed of connective tissue and vascular and neural structures. Until recently, few pathologists and urologists realized that adipose tissue may be present within the lamina propria and muscularis propria. The lamina propria, in turn, is enveloped by a muscularis propria, with its thick but poorly oriented muscle bundles. In transurethral biopsy material, the tissue chips are frequently poorly oriented (not cut perpendicular to the bladder wall). This fact by itself may make it difficult to establish depth of invasion. Also, it is evident that the urinary bladder wall thickness is not uniform. In fact, even in the bladder that is not distended, the lamina propria is much attenuated (and consequently, the muscularis propria is closer to the epithelial surface) in the area of the trigone and bladder neck and adjacent to the ureteral orifices **(Eble et al., 2004)**.

The American joint committee on cancer-union international contre le cancer (AJCC-UICC) TNM (tumor, node, metastasis) staging system (1997) proposed the currently used staging system. CIS comprises a flat neoplasm that is confined to basement membrane. Stage Ta tumors are lesions confined to the urothelial mucosa that extend papillary fronds surrounding a central fibrovascular stalk into the lumen of the bladder. Stage T1 are tumors penetrating