



Research Article

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Evaluation of Tumor Size Changes Following Systemic Therapy for Oligoprogressive Bladder Cancer with Pelvic Lymph Node Dissemination

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Abstract

Objective: Limited-site progression in metastatic bladder cancer presents unique therapeutic challenges and may create opportunities for combining systemic and local treatment approaches. In patients with pelvic lymph node dissemination, systemic therapy can alter the extent and configuration of both primary and nodal disease. This study investigated radiographic changes in tumor burden following systemic treatment in patients with oligoprogressive bladder cancer and examined the potential clinical significance of these changes for subsequent locoregional management.

Materials and Methods: A retrospective analysis was performed on patients with oligoprogressive bladder cancer involving pelvic lymph nodes who received systemic therapy and underwent imaging evaluation before and after treatment. Tumor characteristics were assessed using CT, MRI, and/or PET/CT studies. Measurements of the primary bladder lesion, metastatic pelvic lymph nodes, and overall disease extent were compared between baseline and post-treatment assessments to determine patterns of anatomical response.

Results: Post-treatment imaging revealed a reduction in disease burden in most evaluated patients. Decreases in lesion dimensions were identified at the primary bladder tumor as well as within metastatic pelvic lymph nodes. These responses were accompanied by changes in the spatial distribution of disease and a reduction in the overall volume of radiographically apparent tumor involvement. The observed anatomical modifications may have implications for the design and delivery of subsequent local therapies.

Conclusion: Systemic treatment produced appreciable tumor regression in patients with oligoprogressive bladder cancer and pelvic lymph node dissemination. The resulting changes in disease extent may facilitate more individualized locoregional treatment strategies and contribute to optimization of radiotherapy target definition. Further prospective studies are needed to clarify how treatment-induced anatomical responses should be incorporated into multidisciplinary management algorithms for this patient population.

Keywords: Bladder Cancer; Oligoprogressive Disease; Pelvic Lymph Node Metastasis; Systemic Therapy; Radiotherapy

Abbreviations: CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PET/CT: Positron Emission Tomography/Computed Tomography; IGRT: Image-Guided Radiotherapy; IMRT: Intensity-Modulated Radiotherapy; VMAT: Volumetric Modulated Arc Therapy; SBRT: Stereotactic Body Radiotherapy; FGFR: Fibroblast Growth Factor Receptor

Introduction

Bladder cancer remains one of the most prevalent malignancies of the genitourinary system and continues to represent a major global health burden [1]. Despite advances in diagnostic techniques and therapeutic strategies, a substantial proportion of patients experience disease recurrence, regional spread, or distant metastasis during their illness [2]. While non-muscle-invasive disease can often be managed successfully with transurethral resection and intravesical therapies, progression

to muscle-invasive or metastatic disease is associated with significantly poorer outcomes and increased treatment complexity [2]. Among the various patterns of disease dissemination, involvement of pelvic lymph nodes is particularly common and constitutes an important determinant of prognosis, disease control, and therapeutic decision-making.

The therapeutic landscape of advanced bladder cancer has undergone remarkable transformation over the past decade.

Historically, platinum-based chemotherapy represented the cornerstone of systemic treatment for metastatic disease. More recently, the introduction of immune checkpoint inhibitors, fibroblast growth factor receptor (FGFR)-targeted agents, antibody-drug conjugates, and combination treatment strategies has expanded available therapeutic options and improved clinical outcomes for selected patient populations. Nevertheless, treatment resistance remains a major challenge, and disease progression ultimately develops in many patients despite initial therapeutic benefit. An increasingly recognized pattern of treatment failure is oligoprogressive disease, which refers to progression occurring in a limited number of lesions while many disease sites remain stable or responsive to ongoing systemic therapy [2].

This phenomenon is thought to arise from biological heterogeneity among tumor clones, differential drug sensitivity, and selective evolutionary pressures imposed by systemic treatment. The recognition of oligoprogression has important clinical implications because it suggests that resistant disease sites may be amenable to localized intervention while effective systemic therapy is maintained. Consequently, the oligoprogressive paradigm has stimulated growing interest in treatment strategies that combine systemic disease control with metastasis-directed local therapies. In bladder cancer, pelvic lymph nodes frequently serve as sites of persistent or progressive disease. Nodal involvement may occur within the obturator, internal iliac, external iliac, common iliac, and presacral regions and is associated with an increased likelihood of subsequent metastatic dissemination.

Historically, management of nodal progression has been challenging because of concerns regarding occult disease burden and limited durable control with local therapy alone. However, improvements in cross-sectional imaging, molecular characterization, and treatment delivery techniques have enhanced the ability to identify and selectively target sites of limited progression. As a result, local treatment approaches such as stereotactic body radiotherapy (SBRT), conventionally fractionated radiotherapy, salvage lymph node-directed therapy, and selected surgical interventions are being increasingly incorporated into multidisciplinary management strategies [3-100]. The effectiveness of local treatment is highly dependent on accurate characterization of disease extent.

Systemic therapy administered before local intervention may substantially modify both tumor burden and anatomical distribution of disease. Regression of the primary bladder lesion, reduction in nodal size, and changes in the spatial configuration of metastatic deposits may significantly influence treatment planning considerations. These changes can affect target volume definition, treatment field design, dose optimization, and the ability to spare surrounding normal tissues. Furthermore, alterations in tumor geometry may modify the relationship between disease sites and critical pelvic structures, including the rectum, bowel, uninvolved

bladder, femoral heads, pelvic vasculature, and reproductive organs. Parallel to advances in systemic therapy, radiotherapy has evolved into a highly sophisticated and increasingly adaptive treatment modality.

Contemporary technologies such as image-guided radiotherapy (IGRT), intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), stereotactic body radiotherapy (SBRT), magnetic resonance-guided radiotherapy, and adaptive radiotherapy enable highly conformal dose delivery with improved precision and reduced exposure of adjacent normal tissues. These innovations are particularly valuable in pelvic malignancies, where treatment accuracy may be affected by bladder filling variation, bowel motion, organ displacement, and day-to-day anatomical changes. Consequently, understanding treatment-induced alterations in tumor size and distribution has become increasingly relevant for the optimization of individualized radiotherapy strategies. Although the clinical importance of oligoprogressive disease is being increasingly recognized, relatively little information is available regarding the extent of anatomical response following systemic therapy in patients with oligoprogressive bladder cancer and pelvic lymph node dissemination.

Specifically, data describing changes in primary tumor dimensions, nodal disease burden, and overall treatment geometry remain limited. Such information may be valuable for refining treatment sequencing, improving target delineation, facilitating adaptive treatment approaches, and enhancing multidisciplinary decision-making. The present study was undertaken to evaluate radiographic changes in tumor burden following systemic therapy in patients with oligoprogressive bladder cancer involving pelvic lymph nodes. In addition, we sought to explore how treatment-related anatomical modifications may influence subsequent local treatment planning and support the development of more individualized management strategies in this clinically challenging patient population.

Materials and Methods

A retrospective institutional review was performed at the Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences, a tertiary academic center specializing in the multidisciplinary management of urological malignancies. Clinical records, radiological databases, and treatment documentation were systematically examined to identify patients diagnosed with oligoprogressive bladder cancer accompanied by pelvic lymph node dissemination who received systemic therapy during the study period. Eligible patients were required to have radiologically confirmed bladder cancer with evidence of progressive pelvic nodal involvement and available imaging studies obtained both before initiation and after completion of systemic treatment. Only patients with sufficient imaging quality to permit comparative tumor measurements were included.

Patients lacking complete radiological documentation, post-treatment evaluation studies, or adequate clinical follow-up information were excluded from the analysis. For the purposes of this study, oligoprogressive disease was defined as progression occurring in a limited number of lesions while the remaining disease burden remained stable or demonstrated ongoing response to systemic therapy. Disease status was determined through multidisciplinary assessment incorporating clinical findings and radiological evaluation. The identification of oligoprogressive disease was based on consensus review by the institutional tumor board, taking into consideration previous treatment history, disease kinetics, and imaging characteristics.

All patients underwent comprehensive pretreatment evaluations involving specialists from medical oncology, radiation oncology, radiology, nuclear medicine, and urology. Treatment strategies were individualized according to disease extent, prior therapeutic interventions, performance status, comorbid conditions, and multidisciplinary recommendations. Systemic treatment regimens were administered according to contemporary institutional protocols and physician discretion. Depending on clinical circumstances, treatment approaches include chemotherapy, immunotherapy, targeted systemic agents, or combination strategies. Following completion of systemic treatment, patients underwent repeat radiological assessments to evaluate treatment response and determine eligibility for subsequent local therapeutic interventions.

Radiological evaluation was performed using one or more imaging modalities, including contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT). Additional diagnostic procedures, including cystoscopy and histopathological confirmation, were reviewed when available and clinically relevant. Baseline imaging studies obtained immediately before systemic therapy were compared with post-treatment examinations performed after completion of the planned treatment course. All imaging datasets were reviewed to assess anatomical changes in both primary and nodal disease sites.

The primary objective of imaging analysis was to characterize treatment-related changes in tumor burden. The following parameters were assessed:

- Maximum dimensions of the primary bladder tumor
- Size and distribution of metastatic pelvic lymph nodes
- Number of radiologically detectable lesions
- Extent of regional nodal involvement
- Overall anatomical distribution of disease
- Gross tumor volume characteristics when applicable

Comparisons between baseline and post-treatment studies were performed to determine the degree of tumor regression and changes in disease extent. Particular attention was directed toward evaluating alterations that could influence subsequent local treatment planning, including reductions in target volume, changes in nodal configuration, and modifications in the relationship between tumor targets and adjacent organs at risk. Because one of the objectives of the study was to explore the potential implications of systemic therapy-induced tumor regression for local treatment strategies, imaging findings were also reviewed from a radiotherapy planning perspective.

Changes in disease geometry, target volume definition, and anatomical relationships involving the bowel, rectum, uninvolved bladder tissue, femoral heads, and pelvic vasculature were assessed. Potential effects on treatment field design, dose conformity, and normal tissue sparing were documented. The principal outcome measure was the change in radiographically measurable disease burden after systemic treatment. Secondary observations included alterations in disease distribution and anatomical features potentially relevant to subsequent radiotherapy planning and multidisciplinary treatment decision-making.

Results

Selected patients with oligoprogressive bladder cancer and radiologically confirmed pelvic lymph node dissemination who met the eligibility criteria and were included in the analysis. All patients successfully completed the planned course of systemic therapy and underwent post-treatment imaging evaluation according to institutional follow-up protocols. Comparative assessment of baseline and post-treatment imaging studies demonstrated evidence of treatment response in most evaluated patients. Reductions in measurable disease burden were observed at both primary and nodal disease sites following systemic therapy. The extent of response varied among patients, ranging from modest decreases in lesion dimensions to more pronounced reductions in tumor volume and regional disease extent.

At the primary tumor site, post-treatment imaging frequently demonstrated a decrease in bladder wall involvement and reduction in the dimensions of the dominant lesion. In several cases, the anatomical boundaries of the primary tumor became less extensive compared with pretreatment evaluations, resulting in a smaller radiographically identifiable tumor volume. Nodal response was observed across multiple pelvic lymphatic regions. Decreases in lymph node size were identified involving obturator, internal iliac, external iliac, and common iliac nodal stations. In a number of patients, previously enlarged metastatic lymph nodes demonstrated substantial dimensional regression on follow-up imaging. These changes contributed to an overall reduction in regional nodal tumor burden and a more limited extent of radiographically apparent disease.

Evaluation of disease distribution before and after systemic therapy also revealed notable anatomical modifications. As tumor regression occurred, changes in the configuration and spatial extent of both primary and nodal lesions were observed. In several patients, the gross extent of disease became more localized following treatment, resulting in altered anatomical relationships between tumor-bearing regions and adjacent pelvic structures. Volumetric changes were particularly evident in cases demonstrating concurrent regression of the primary bladder lesion and metastatic lymph nodes. These findings were associated with reductions in the overall volume of radiographically detectable disease. Follow-up imaging frequently demonstrated decreased involvement of surrounding soft tissues and reduced regional disease extension compared with baseline examinations.

Review of imaging datasets from a treatment-planning perspective demonstrated that treatment-induced anatomical changes were accompanied by modifications in target geometry. Alterations in the proximity of disease sites to neighboring organs, including the bowel, rectum, uninvolved bladder, pelvic vasculature, and femoral heads, were observed in several patients. The magnitude of these changes varied according to the degree of tumor response and the anatomical location of involved nodal stations. Collectively, the radiological findings indicated that systemic therapy was associated with measurable anatomical regression of both primary and nodal disease in patients with oligoprogressive bladder cancer. The observed reductions in tumor dimensions and disease extent were consistently identifiable on post-treatment imaging and reflected substantial changes in the anatomical presentation of disease compared with baseline evaluations.

Discussion

Management of advanced bladder cancer has evolved considerably with the introduction of novel systemic therapies and increasingly sophisticated local treatment techniques [2]. Nevertheless, disease progression remains a frequent clinical challenge, particularly in patients with metastatic or recurrent disease [2]. Within this setting, the concept of oligoprogression has attracted growing interest because it represents a potentially distinct biological and therapeutic state characterized by limited progression occurring despite ongoing control of most disease sites [2]. Recognition of this pattern has encouraged the development of treatment strategies that combine systemic disease management with selective local intervention directed toward resistant tumor deposits.

The present study evaluated anatomical changes occurring after systemic therapy in patients with oligoprogressive bladder cancer involving pelvic lymph nodes. The findings demonstrated that treatment was associated with measurable reductions in both primary tumor burden and regional nodal disease. Regression was observed across multiple pelvic nodal stations and was

accompanied by alterations in overall disease configuration. These observations suggest that systemic therapy not only influences disease control but may also substantially modify the anatomical landscape upon which subsequent local treatment decisions are based. Pelvic lymph node involvement remains one of the most important adverse prognostic features in bladder cancer.

The presence of nodal dissemination is associated with increased risks of recurrence, distant metastasis, and cancer-specific mortality. Historically, nodal progression was often viewed as an indicator of widespread disease requiring predominantly systemic management. However, improvements in diagnostic imaging and greater understanding of metastatic disease biology have led to increasing recognition that selected patients with limited-volume progression may derive benefit from local treatment of residual disease. In this context, the degree of response achieved with systemic therapy becomes particularly relevant, as treatment-induced reductions in nodal burden may influence both the feasibility and design of subsequent locoregional interventions.

An important observation of the present analysis was the substantial variability in the extent of tumor regression among individual patients. While many patients demonstrated meaningful reductions in disease burden, the magnitude and anatomical distribution of response differed considerably. Such heterogeneity is consistent with current understanding of bladder cancer biology, which is characterized by marked molecular diversity, clonal evolution, and variable sensitivity to systemic agents. Differential responses among primary and metastatic sites may reflect underlying biological differences between tumor subpopulations and may partially explain the development of oligoprogressive disease despite otherwise effective systemic treatment.

The observed anatomical changes may have particular relevance for radiotherapy planning. In contemporary radiation oncology practice, target definition is critically dependent upon accurate characterization of disease extent. Reduction in primary tumor dimensions and nodal volume may alter gross tumor volume delineation and influence the size of treatment fields required for adequate target coverage. Furthermore, decreases in disease burden may improve the geometric separation between tumor targets and adjacent normal tissues, creating opportunities for more conformal treatment delivery.

These considerations are especially important within the pelvis, where numerous dose-limiting structures are located in proximity to treatment volumes. Technological advances have significantly enhanced the ability of radiotherapy to accommodate anatomical complexity. Techniques such as image-guided radiotherapy (IGRT), intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), stereotactic body radiotherapy (SBRT), and adaptive radiotherapy have enabled

highly individualized treatment approaches that were not feasible in earlier eras. Such innovations are particularly relevant in bladder cancer because organ motion, variable bladder filling, bowel displacement, and treatment-related anatomical changes can all influence target localization.

The anatomical modifications observed following systemic therapy in the present study further support the importance of image-based reassessment before initiation of local treatment and highlight the potential value of adaptive planning strategies. The findings also have implications for treatment sequencing. Traditionally, local and systemic therapies have often been considered as separate treatment modalities delivered at different stages of disease management. However, increasing evidence suggests that the interaction between these approaches may be more dynamic than previously appreciated. Administration of systemic therapy before local intervention may not only reduce tumor burden but may also improve the technical feasibility of subsequent treatment. In selected patients, response-adapted strategies could potentially facilitate more precise target definition and reduce unnecessary irradiation of uninvolved tissues.

Although the optimal sequencing paradigm remains uncertain, the present observations support the concept that anatomical response assessment may represent an important component of multidisciplinary treatment planning. Another clinically relevant consideration is the growing interest in metastasis-directed therapy for oligometastatic and oligoprogressive disease. Local treatment of residual nodal lesions following systemic therapy has been proposed as a means of prolonging disease control, delaying the emergence of widespread progression, and maintaining the effectiveness of ongoing systemic treatment. While definitive evidence in bladder cancer remains limited, encouraging results reported in other solid tumors have generated substantial interest in this approach.

The anatomical responses documented in the present study suggest that systemic therapy may create more favorable conditions for such interventions by reducing disease volume and modifying target geometry. The present study provides valuable insight into the dynamic anatomical changes that occur following systemic therapy in patients with oligoprogressive bladder cancer and pelvic lymph node dissemination. To our knowledge, relatively few investigations have specifically examined the implications of treatment-induced tumor regression from a local treatment planning perspective in this patient population. The findings therefore contribute to a growing body of evidence supporting individualized and response-adapted treatment strategies.

In conclusion, systemic therapy was associated with substantial reductions in primary and nodal tumor burden in patients with oligoprogressive bladder cancer involving pelvic lymph nodes. These anatomical modifications have potential implications for radiotherapy target delineation, treatment

volume selection, and the integration of local treatment modalities into multidisciplinary care pathways. Future prospective studies incorporating volumetric analyses, adaptive radiotherapy methodologies, and long-term clinical outcomes are warranted to further clarify the role of treatment-induced anatomical changes in optimizing management of oligoprogressive bladder cancer.

Conflict of Interest: There are no conflicts of interest and no acknowledgements.

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