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Evaluation of Tumor Size Changes Following Neoadjuvant Systemic Therapy for Muscle Invasive Carcinoma of the Bladder

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Abstract

Objective: Carcinoma of the bladder presents as a major public health concern with its critical incidence worldwide. As a matter of fact, both the disease itself and treatments used for management of bladder carcinoma may deteriorate quality of life. Neoadjuvant systemic therapy may be suggested for management bladder carcinoma. The rationale behind neoadjuvant systemic treatment may include reduction of the disease burden before administration of subsequent therapies. Also, neoadjuvant systemic treatment may prevent widespread dissemination of the disease. Selected groups of patients with bladder cancer may benefit from neoadjuvant systemic treatment. Herein, we assessed tumor size changes following neoadjuvant systemic therapy for muscle invasive carcinoma of the bladder.

Materials and methods: Patients with muscle invasive carcinoma of the bladder having available imaging data as part of initial workup have been studied. All included patients have received upfront neoadjuvant systemic treatment and then were referred for RT at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences. We performed a comparative analysis for tumor sizes at diagnostic CT scans of the patients and at CT-simulation for radiation treatment planning after neoadjuvant systemic treatment.

Results: As the primary outcome, we found a mean decrease of 27% in tumor sizes following neoadjuvant systemic treatment for patients with muscle invasive carcinoma of the bladder.

Conclusion: The results of our study may have implications for utilization of adaptive RT strategies, however, there is still need for further studies focusing on this critical issue.

Keywords: Muscle invasive carcinoma of the bladder; Radiation therapy (RT); Neoadjuvant systemic treatment; Molecular imaging methods; CT simulations

Abbreviations: RT: Radiation Therapy; IGRT: Image Guided RT; IMRT: Intensity Modulated RT; ART: Adaptive RT; LINAC: Linear Accelerator; ICRU: International Commission on Radiation Units and Measurements; AAPM: American Association of Physicists in Medicine

Introduction

Carcinoma of the bladder presents as a major public health concern with its critical incidence worldwide [1-3]. As a matter of fact, both the disease itself and treatments used for management of bladder carcinoma may deteriorate quality of life. In the meantime, optimal management of bladder cancer may be achieved by using a single treatment modality or by combined modality management with surgery, radiation therapy (RT), and systemic agents [2,3]. In terms of RT, several forms of irradiation may be utilized, and contemporary technologies including intensity modulation and adaptive RT techniques may lead to better RT outcomes. While the use of higher effective doses may lead to improved local control outcomes, toxicity profile of radiation delivery must be considered to maintain patients' quality of life. Recent years have witnessed critical advances in technology which contributed to improved radiotherapeutic results. Automatic segmentation techniques, Image Guided RT (IGRT), molecular imaging methods, Intensity Modulated RT (IMRT), stereotactic RT, and adaptive RT (ART) have been introduced for improved therapeutic efficacy [3-40].

In the real world, optimal therapeutic outcomes might solely be achieved by close collaboration among related disciplines for

cancer management. Within this context, tumor boards improve collaboration among surgical oncologists, radiation oncologists, and medical oncologists by providing a good platform for discussing patients, tumors, and treatment characteristics. Tumor boards may improve determining the individualized therapy for optimal patient management. Neoadjuvant systemic therapy may be suggested for management bladder carcinoma [41-43]. The rationale behind neoadjuvant systemic treatment may include reduction of the disease burden before administration of subsequent therapies. Also, neoadjuvant systemic treatment may prevent widespread dissemination of the disease. Admittedly, there may also be controversies regarding neoadjuvant systemic treatments such as the risk of delayed local treatments including RT or surgery. Nevertheless, selected groups of patients with bladder cancer may benefit from neoadjuvant systemic treatment [41-43]. Herein, we assessed tumor size changes following neoadjuvant systemic therapy for muscle invasive carcinoma of the bladder.

Materials and Methods

Our Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences serves as a tertiary cancer center for patients from Turkey and abroad for decades. Several benign and malignant tumors are irradiated here by using modernized equipment and contemporary technologies including IGRT, IMRT, ART, stereotactic RT, automatic segmentation techniques, and molecular imaging methods [3-40]. In the context of this study, we aimed at evaluating tumor size changes following neoadjuvant systemic therapy for muscle invasive carcinoma of the bladder. For this purpose, patients with muscle invasive carcinoma of the bladder having available imaging data as part of initial workup have been studied. All included patients have received upfront neoadjuvant systemic treatment and then were referred for RT at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences.

We performed a comparative analysis for tumor sizes at diagnostic CT scans of the patients and at CT-simulation for radiation treatment planning after neoadjuvant systemic treatment. CT simulations have been performed at CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) available at our tertiary cancer center. Tumor size changes after neoadjuvant systemic treatment were documented for comparative evaluation. A Linear Accelerator (LINAC) which had the capability of incorporating state of the art IGRT techniques has been utilized for RT. After rigid patient immobilization, planning CT images have been acquired at the CT simulator for RT planning. Thereafter, acquired RT planning images were sent to the contouring workstation through the network. Target volumes and critical structures were contoured on these images and structure sets were generated. All patients were treated by using sophisticated RT techniques at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences.

Results

Our original research article has aimed at investigating tumor size changes following neoadjuvant systemic therapy for muscle invasive carcinoma of the bladder. Irradiation procedures were executed at our Radiation Oncology Department of Gulhane Medical Faculty at University of Health Sciences, Ankara. Before irradiation, all patients included were individually assessed by a multidisciplinary team of experts from surgical oncology, medical oncology, and radiation oncology. Patients with muscle invasive carcinoma of the bladder having available imaging data as part of initial workup were included. Selected patients initially received upfront neoadjuvant systemic treatment and were referred for RT at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences. We have carried out a comparative analysis for tumor sizes at diagnostic CT scan of the patients and at CT-simulation for RT planning following neoadjuvant systemic treatment. CT simulations of the patients were performed at CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) available at our tertiary cancer center. Tumor size changes after neoadjuvant systemic treatment have been documented for comparative evaluation. As the main outcome of the current study, we found a mean decrease of 27% in tumor sizes after neoadjuvant systemic treatment for patients with muscle invasive carcinoma of the bladder.

Optimal RT planning processes included consideration of lesion sizes, localization and association with surrounding critical organs. Radiation physicists took part in RT planning procedures with consideration of reports by American Association of Physicists in Medicine (AAPM) and International Commission on Radiation Units and Measurements (ICRU). Precise RT planning procedure included consideration of electron density, tissue heterogeneity, CT number and HU values in CT images. Main objective of RT planning has been to achieve optimal coverage of treatment volumes along with minimized exposure of surrounding critical structures. All patients were treated by using sophisticated RT techniques at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences.

Discussion

Carcinoma of the bladder presents as a critical public health concern with its trending incidence worldwide [1-3]. Conceptually, both the disease itself and therapies administered for management of bladder carcinoma may deteriorate quality of life. Currently, optimal management of bladder cancer may be achieved by using either a single treatment modality or by combined modality management with surgery, radiation therapy (RT), and systemic agents [2,3]. From the perspective of RT, several forms of irradiation may be used, and sophisticated technologies such as intensity modulation and adaptive RT techniques may lead to improved radiotherapeutic results. The administration of higher irradiation doses may lead to improved treatment outcomes;

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however, the toxicity profile of radiation delivery should also be considered to maintain patients' quality of life. Clearly, there have been unprecedented advances in technology which contributed to improved radiotherapeutic results in the millennium era. Automatic segmentation techniques, Image Guided RT (IGRT), molecular imaging methods, Intensity Modulated RT (IMRT), stereotactic RT, and adaptive RT (ART) have been introduced for improved therapeutic efficacy [3-40].

In the real world, optimal therapeutic outcomes might solely be achieved by close collaboration among related disciplines for cancer management. Within this context, tumor boards improve collaboration among surgical oncologists, radiation oncologists, and medical oncologists by providing a good platform for discussing about patient, tumor, and treatment characteristics. Tumor boards may improve determining the individualized therapy for optimal patient management. Neoadjuvant systemic therapy may be suggested for management bladder carcinoma [41-43]. The rationale behind neoadjuvant systemic treatment may include reduction of the disease burden before administration of subsequent therapies. Also, neoadjuvant systemic treatment may prevent widespread dissemination of the disease. Admittedly, there may also be controversies regarding neoadjuvant systemic treatments such as the risk of delayed local treatments including RT or surgery. Nevertheless, selected groups of patients with bladder cancer may benefit from neoadjuvant systemic treatment [41-43]. Herein, we assessed tumor size changes following neoadjuvant systemic therapy for muscle invasive carcinoma of the bladder. As the main outcome of the current study, we found a mean decrease of 27% in tumor sizes after neoadjuvant systemic treatment for patients with muscle invasive carcinoma of the bladder.

Optimal treatment volume definition and normal tissue sparing may be considered among the most critical aspects of RT in the millennium era. While definition of larger treatment volumes could lead to excessive radiation induced toxicity, determination of smaller treatment volumes may ultimately result in therapeutic failures. Adaptive RT approaches and multimodality imaging-based target determination have been proposed for achieving improved results [44-91]. In the current study, we have documented tumor size changes following neoadjuvant systemic treatment with comparative assessment. As the primary result, we found a mean decrease of 27% in tumor sizes after neoadjuvant systemic treatment for patients with muscle invasive carcinoma of the bladder. While the results of our study may have implications for implementation of adaptive RT strategies, there is still need for further studies focusing on this critical issue.

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