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Assessment of Target Volume Definition for Precise Radiotherapeutic Management of Locally Recurrent Biliary Tract Cancers: An Original Research Article

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ABSTRACT

Objective: Biliary tract cancer (BTC) refers to a heterogeneous group of tumors including intrahepatic, perihilar, and extrahepatic cholangiocarcinomas, along with gallbladder cancers. BTC originates from the biliary epithelium of small ducts in the periphery of the liver (intrahepatic) and from main ducts of the hilum (extrahepatic). Although comprising a small proportion of all cancers, BTC accounts for the second most frequent hepatic malignancy after hepatocellular carcinomas. Patients with BTC may be diagnosed at relatively advanced stages, and symptoms may deteriorate quality of life significantly. Currently, multidisciplinary management may be utilized for achieving optimal therapeutic outcomes. Radiation therapy (RT) may play a role in definitive, adjuvant, or palliative setting and also for management of recurrent disease. Target volume definition comprises a critical aspect of radiotherapeutic management for BTC. In this original research article, we shed light on this critical issue by assessment of multimodality imaging with incorporation of Magnetic Resonance Imaging (MRI) for RT target volume definition of locally recurrent BTC.

Materials and Methods: In this original research article, we undertook a comparative analysis of target definition for radiotherapeutic management of locally recurrent BTC based on Computed Tomography (CT) simulation images only or by incorporation of fused CT-MRI. Main outcome measure of the study was to investigate the utility of multimodality imaging for target definition.

Results: Ground truth target volume has been found to be identical with fused CT-MRI based target definition for patients with locally BTC as the primary endpoint of this original research article.

Conclusion: Consideration of multimodality imaging with incorporation of MRI in the RT planning procedure should be prioritized for optimal radiotherapeutic management of patients with locally recurrent BTC.

Introduction

Biliary tract cancer (BTC) refers to a heterogeneous group of tumors including intrahepatic, perihilar, and extrahepatic cholangiocarcinomas, along with gallbladder cancers. BTC originates from the biliary epithelium of small ducts in the periphery of the liver (intrahepatic) and from main ducts of the hilum (extrahepatic). Extrahepatic BTC includes the gallbladder cancers, ampullary cancers, and cancers of pancreatic biliary ducts. While extrahepatic cancers originate from similar epithelia, the etiology may differ due to their anatomy. Although comprising a small proportion of all cancers, BTC accounts for the second most frequent hepatic malignancy after hepatocellular carcinomas [1-5]. The subclassification includes intrahepatic cholangiocarcinomas arising from the biliary tree within the liver, and extrahepatic cholangiocarcinomas arising from the biliary tree outside the liver, and gallbladder carcinoma. Extrahepatic cholangiocarcinomas may be subcategorized into perihilar and distal cholangiocarcinomas. Gallbladder is a small and pear-shaped organ which lies underneath the liver with the main function of storing bile. Although the gallbladder is a small organ, it may be associated with cancer. There may be preponderance for early spread with resultant poor prognosis partly due to the lack of serosa layer and close proximity to critical surrounding structures along with extension to lymphatics [1-5].

Patients with BTC may be diagnosed at relatively advanced stages, and symptoms may deteriorate quality of life significantly. Currently, multidisciplinary management may be utilized for achieving optimal therapeutic outcomes [2-10]. Radiation therapy (RT) may play a role in definitive, adjuvant, or palliative setting and also for management of recurrent disease. Target volume definition comprises a critical aspect of radiotherapeutic management for BTC. Advances in surgery, RT, and systemic treatment offer improved life expectancies for patients suffering from BTC. Within this context, treatment induced toxicity has become an endpoint of increasing importance recently. With excellent integration of contemporary approaches in cancer management, radiotherapeutic strategies have demonstrated critical progress in the millenium era. Introduction of contemporary therapeutic concepts and techniques such as Intensity Modulated RT (IMRT), Image Guided RT (IGRT), molecular imaging methods, automatic segmentation techniques, stereotactic RT, and adaptive RT (ART) have clearly contributed to optimal radiotherapeutic management [11-50].

Integration of these relatively newer radiotherapeutic approaches led to more precise and accurate targeting of tumors by virtue of steeper dose gradients around the target volumes resulting in decreased normal tissue exposure. Reduced critical organ doses may allow for decreased adverse effects and treatment dose escalation which could pave the way for an improved therapeutic ratio. Admittedly, vigilance is warranted for clinical implementation of these state-of-the-art radiotherapeutic concepts in daily routine. Optimization of target volume determination has become an indispensable component of recent RT protocols for BTC. Currently, Computed Tomography (CT) simulation plays a significant role in RT planning at majority of treatment centers globally. CT serves as a plausible imaging modality for dose calculation purposes, nevertheless, inclusion of other imaging modalities for RT planning may clearly add to the accuracy and precision in target definition. In the literature, there have been many studies addressing the use of multimodality imaging for optimal target definition for RT [51-87]. Herein, we assess target definition for locally recurrent BTC by use of multimodality imaging and provide an extensive review of relevant literature.

Materials and Methods

Patients referred to Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences for radiotherapeutic management of BTC have been assessed for target definition by use of multimodality imaging in this original research article. A comparative analysis has been performed to evaluate target determination based on CT simulation images only or by incorporation of Magnetic Resonance Imaging (MRI). Ultimate goal of this study was to evaluate the utility of multimodality imaging for target definition, however, other factors such as contouring of critical organs, interobserver and intra observer variations have also been investigated. A ground target volume has been used for comparative analysis and for comparison purposes, and the ground truth target volume has been defined by our expert group of radiation oncologists following thorough consideration of all imaging and relevant data with meticulous colleague peer review and consensus. Decision making for RT was based on multidisciplinary assessment of patients by experts from surgical oncology, radiation oncology, and medical oncology. Patient, disease, and treatment related characteristics were considered individually by taking into account age, symptomatology, performance status, previously administered therapies, lesion size, localization and association with surrounding critical structures, expected results of suggested treatments, patient preferences and logistical issues.

Synergy (Elekta, UK) linear accelerator (LINAC) has been used in delivery of irradiation with integration of IGRT techniques. After robust immobilization of the patients, CT simulation images have been acquired at the CT simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) for RT planning. Thereafter, these acquired RT planning images were sent to the contouring workstation (SimMD, GE, UK) through the network for generation of individualized structure sets including target volumes and critical structures. For the purpose of this study, we have performed a comparative

analysis to evaluate target and critical organ determination based on either CT simulation images only or fused CT-MR images.

Results

Multimodality imaging by integration of MRI for target volume determination has been evaluated for patients referred for radiotherapeutic management of locally recurrent BTC in this original research article. All treatments were administered at Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences and included patients underwent thorough multidisciplinary assessment by experts from surgical oncology, radiation oncology, and medical oncology. We undertook a comparative analysis for assessment of target and critical organ definition by use of either CT only imaging or by fused CT-MRI in an attempt to reveal the role of multimodality imaging. Tumor related parameters which were taken into account in management were lesion size, localization and association with surrounding critical structures. Also, individual characteristics such as patient symptomatology, age, performance status have been evaluated along with logistical factors. RT planning has been performed by expert radiation physicists by consideration of reports by American Association of Physicists in Medicine (AAPM) and International Commission on Radiation Units and Measurements (ICRU). Electron density, tissue heterogeneity, CT number and HU values in CT images were considered in precise RT planning. Main objective of RT planning has been to achieve optimal target volume coverage with minimal exposure of nearby critical organs. Ground truth target volume was individually determined for every patient by board certified radiation oncologists following detailed assessment, rigorous colleague peer review procedure, and consensus to be utilized for actual treatment and for comparison purposes. In addition, IGRT techniques have been used for accurate setup verification. Synergy (Elekta, UK) LINAC was used for treatment delivery. The ground truth target volume has been found to be identical with fused CT-MRI based target determination for patients with locally recurrent BTC as the endpoint of the study.

Discussion

BTC may be considered as a heterogeneous group of tumors. BTC originates from the biliary epithelium of small ducts in the periphery of the liver (intrahepatic) and from main ducts of the hilum (extrahepatic). Extrahepatic BTC includes the gallbladder cancers, ampullary cancers, and cancers of pancreatic biliary ducts. While extrahepatic cancers originate from similar epithelia, the etiology may differ owing to their anatomy. Although comprising a small proportion of all cancers, BTC accounts for the second most frequent hepatic malignancy after hepatocellular carcinomas [1-5]. The subclassification includes intrahepatic cholangiocarcinomas arising from the biliary tree within the liver, and extrahepatic cholangiocarcinomas arising from the biliary tree outside the liver, and gallbladder carcinoma. Extrahepatic cholangiocarcinomas may be subcategorized into perihilar and distal cholangiocarcinomas. The gallbladder is a small and pear-shaped organ which lies underneath the liver with the main function of storing bile. Although the gallbladder is a small organ, it may be associated with cancer. There may be predilection for early spread with resultant grim prognosis partly due to the lack of serosa layer and close proximity to critical surrounding structures along with extension to lymphatics [1-5].

Patients with BTC may be diagnosed at relatively advanced disease stages, and symptoms may profoundly deteriorate quality of life. In the meantime, multidisciplinary management may be used to achieve improved treatment results [2-10]. RT may play a critical role in definitive, adjuvant, or palliative setting and also for management of recurrent BTC. Target determination comprises a considerable aspect of precise RT for BTC. Improvements in surgery, RT, and systemic treatment offer improved life expectancies for patients suffering from BTC. Within this context, adverse radiation effects became an endpoint of increasing importance in recent years. By virtue of excellent integration of contemporary strategies in cancer management, RT concepts have shown dramatical progress in the millenium era. Incorporation of sophisticated technologies and techniques including IGRT, IMRT, automatic segmentation techniques, stereotactic RT, ART, and molecular imaging methods have obviously contributed to optimal RT strategies [11-50].

Integration of these relatively newer RT approaches resulted in more precise and accurate targeting of tumors by virtue of steeper dose gradients around the target volumes which led to decreased exposure of normal tissues. Reduced critical organ doses may allow for decreased adverse radiation effects and also treatment dose escalation could be achieved which might pave the way for an improved therapeutic ratio. Clearly, vigilance is required for clinical implementation of these excellent radiotherapeutic approaches in daily routine. Optimization of target definition has recently become an indispensable component of contemporary RT protocols for BTC. In the meantime, CT simulation plays a critical role in RT planning at majority of treatment centers on a global scale. While CT may be considered as a plausible imaging modality for dose calculation purposes, integration of other imaging modalities for RT planning may add to the accuracy and precision of target definition. There are several studies addressing the use of multimodality imaging for optimal target definition for RT [51-87]. In this context, we consider that our study may have implications for routine implementation of multimodality imaging-based target definition for radiotherapeutic management of BTC.

We conclude that multimodality imaging through integration of MRI in the RT planning process may be considered for improving the accuracy and precision of target definition for radiotherapeutic management of locally recurrent BTC.

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