The Effectiveness and Role of Adapted Proton Beam Therapy for Hepatocellular Carcinoma

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Background

- Hepatocellular Carcinoma (HCC) patients have poor function reserves resulting from underlying liver cirrhosis (LC), and primary tumors and/or tumor vascular thrombosis (TVT) are often located near radiosensitive tissues, such as the gastrointestinal (GI) organs, and thus, when RT is performed in HCC patients with or without TVT, it is important to spare both the remaining normal liver and GI organs.
- The proton beam therapy (PBT) using simultaneous integrated boost (SIB) technique, which simultaneously delivers different doses to different targets, can potentially reduce irradiated doses to surrounding normal tissues and small time fractionation and improve the therapeutic ratio compared to conventional fractionated PBT.
- Based on this rationale, risk-adapted PBT using the SIB technique has been used for HCC patients with or without TVT at our institution since June 2012.
- The purpose of this study was to evaluate the long-term efficacy and safety of risk-adapted PBT in these patients.

Methods and Materials

- Patients who treated with PBT for primary or recurrent HCC from June 2012 to April 2017 were registered and the database was reviewed.
- Three dose-fractionation regimens were used according to the proximity of the GI organs:
  1. regimen A: the prescribed doses to PTV1 and PTV2 were 50 GyE (EQD2, 62.5 GyE) and 30 GyE (EQD2, 32.5 GyE) in 10 fractions, respectively, for the patients with GTV-V2 cm from the GI organs
  2. regimen B: the prescribed doses to PTV1 and PTV2 were 60 GyE (EQD2, 80 GyE) and 30 GyE in 10 fractions, respectively, for the patients with GTV within 1.1-1.9 cm from the GI organs
  3. regimen C: the prescribed doses to PTV1, identical to PTV2, was 66 GyE (EQD2, 91.3 GyE) in 10 fractions, respectively, for the patients with GTV-V2 cm from the GI organs

Results

- Overall Survival according to dose-fractionation regimens and BCLC stage

Clinical outcomes of PBT according to BCLC stage

Toxicity

- Acute adverse effects within 3 months after PBT were easily manageable and did not cause discontinuation of the treatment course.
- Of the 243 patients, 10 (4.1%) and 1 (0.4%) experienced grade 1 and 2 elevated alanine aminotransferase without disease progression, respectively, and 215 (87.7%) had no change in their Child-Pugh scores. 19 (7.8%) had a point decrease, 10 (4.1%) had a 1-point increase, and 1 (0.4%) had a 2-point increase due to biliary obstruction by tumor progression.
- Late GI toxicity

In regimens A=261, late GI toxicities were observed in 5 (12.5%) patients, including 1 (2.3%), 5 (1.5%), and 1 (2.5%) with grades 1, 2, and 3, respectively.

In regimens B and C, no patient experienced GI bleeding and ulcer

Conclusion

- Risk-adapted PBT using three dose-fractionation regimens could achieve long-term tumor control with minimal toxicity
- These outcomes of PBT suggested that PBT can have a role as a complementary or alternative therapeutic option in all staging of HCC that are unsuitable or ineffective with other locoregional treatments (LRTs).