Clinical and Translational Radiation Oncology 12 (2018) 34–39

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.elsevier.com/locate/ctro

Original Research Article

A neuropathic pain component as a predictor of improvement in pain interference after radiotherapy for painful tumors: A secondary analysis of a prospective observational study

Tetsuo Saito [a,b,*], Etsushi Tomitaka [c], Ryo Toya [a], Tomohiko Matsuyama [a], Satoshi Ninomura [a], Takahiro Watakabe [a], Natsuo Oya [a]

[a] Department of Radiation Oncology, Kumamoto University Hospital, Kumamoto, Japan
[b] Department of Radiation Oncology, Hitoyoshi Medical Center, Hitoyoshi, Japan
[c] Department of Radiation Oncology, Kumamoto Medical Center, Kumamoto, Japan

ARTICLE INFO

Article history:
Received 1 August 2018
Accepted 9 August 2018
Available online 13 August 2018

Keywords:
Palliative radiotherapy
Neuropathic pain
Painful tumors
Pain interference

ABSTRACT

Background and purpose: We previously demonstrated that patients with a tumor-related neuropathic pain component were more likely to experience a pain response after radiotherapy (RT) than those without. It is unknown whether the presence of a neuropathic component also favorably influences pain interference. In a secondary analysis of our previous prospective observational study, we investigated if the presence of a neuropathic component of the index pain caused by the irradiated tumors predicts greater reduction in pain interference.

Material and methods: For patients scheduled for RT for painful tumors, Brief Pain Inventory data were collected at initiation of RT and 1, 2, and 3 months thereafter. Multivariable linear regression analyses were performed to investigate the effects of the presence of a neuropathic component on the changes in pain interference scores (i.e., follow-up minus baseline). We used 10 covariates as potential confounders.

Results: Of the 302 analyzable patients, 93 (31%) were diagnosed as having a neuropathic component of the index pain. Multivariable linear regression analyses revealed that all the point estimates of regression coefficients at 1-, 2-, and 3-month follow-up were negative values; some were statistically significant. At 2-month follow-up, patients with a neuropathic component experienced greater reductions in their pain interference scores for walking ability ($p = 0.048$), normal work ($p = 0.021$), sleep ($p = 0.001$), and enjoyment of life ($p = 0.010$) than those without it.

Conclusions: The presence of a neuropathic pain component predicted a greater reduction in pain interference after RT. Patients with neuropathic tumor-related pain should be offered the option of receiving palliative RT.

Neuropathic pain occurs in 19% to 39% of cancer patients [1–3]; it may be challenging therapeutically and have a substantial impact on patients' quality of life [4]. Neuropathic cancer pain may be directly caused by tumors or be treatment-related. Although pharmacotherapy is the mainstay of neuropathic pain management [3], it is important not to miss the opportunity to reverse the cause of the pain with appropriate oncological management, including radiotherapy (RT) [4]. A few studies have investigated the effects of RT on neuropathic tumor-related pain and have demonstrated that it can effectively palliate this type of pain [5,6].

When selecting patients to receive palliative RT for painful tumors, it is important to predict which patients would benefit from this treatment. In our previous study, we demonstrated that patients with a neuropathic component of the index pain caused by the irradiated tumors were more likely to experience a pain response after RT than those without it [7]. It is not known whether the presence of a neuropathic component also favorably influences pain interference. When assessing interventions for pain, reduced

* Corresponding author at: Department of Radiation Oncology, Kumamoto University Hospital, 1-1-1, Honjo, Chuo-ku, Kumamoto-shi, Kumamoto 860-8556, Japan.
E-mail addresses: tsaito@kumamoto-u.ac.jp (T. Saito), tomitaka@kumamed.jp (E. Tomitaka), ryo108@kumamoto-u.ac.jp (R. Toya), matsutomo_llp@yahoo.co.jp (T. Matsuyama), n-oya@kumamoto-u.ac.jp (N. Oya).

https://doi.org/10.1016/j.ctro.2018.08.002

interference in daily activity rather than a simple reduction in pain intensity is a relevant endpoint that reflects the true benefits for patients [8]. Therefore, in a secondary analysis of our previous prospective observational study, we investigated if the presence of a neuropathic component of the index pain predicts a greater reduction in pain interference after RT for painful tumors.

Material and methods

Patients and study design

The present study is a secondary analysis of our previously published prospective observational study that was conducted at three medical centers [7]. In the primary study, we analyzed 302 patients (enrolled between July 2013 and September 2017) who were scheduled to receive RT for painful tumors (Fig. 1); we evaluated the characteristics of the patients, their tumors, and their pain to identify the predictors of pain palliation after RT [7]. The data of these 302 patients were used in this secondary study to investigate the effect of the presence of a neuropathic component on the change in pain interference scores after RT. This secondary study was approved by the participating centers' institutional review boards; written informed consent was obtained from all participants for the primary study.

Evaluation

We previously reported how the patients were assessed at baseline and follow-up evaluations [7]. In brief, immediately prior to RT, the treating radiation oncologist identified the pain caused by the irradiated tumor using physical examination and diagnostic imaging; this pain was recorded as the index pain for the study. The treating radiation oncologist recorded whether the index pain had a neuropathic component according to the definition provided by the International Association for the Study of Pain – Neuropathic Pain Special Interest Group [9]. Patients with definite and probable neuropathic pain were recorded as having a neuropathic component. The Brief Pain Inventory (BPI) short form (Japanese version) was used to evaluate the intensity of pain and its interference in the patient's life using an 11-point scale (0 to 10); higher scores indicate greater pain intensity and interference [10]. Patients assessed their worst pain (in terms of the index pain) experienced in the previous 3 days. Pain interference was assessed using seven subscales: general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life. The BPI data and analgesic data were collected at baseline, and 1, 2, and 3 months (± 7 days) after initiation of RT.

Statistical analysis

The patients' characteristics, analgesic use, and baseline pain interference scores were analyzed using the Mann–Whitney U test for continuous variables; the Fisher exact test was used for categorical variables. Univariable and multivariable linear regression analyses were performed to investigate the effects of the presence of a neuropathic component of the index pain on the change in pain interference scores. The outcome variables were the changes in the functional interference scores from baseline (i.e., follow-up minus baseline). In the multivariable analysis, we used 10 covariates as potential confounders: age, sex, Eastern Cooperative Oncology

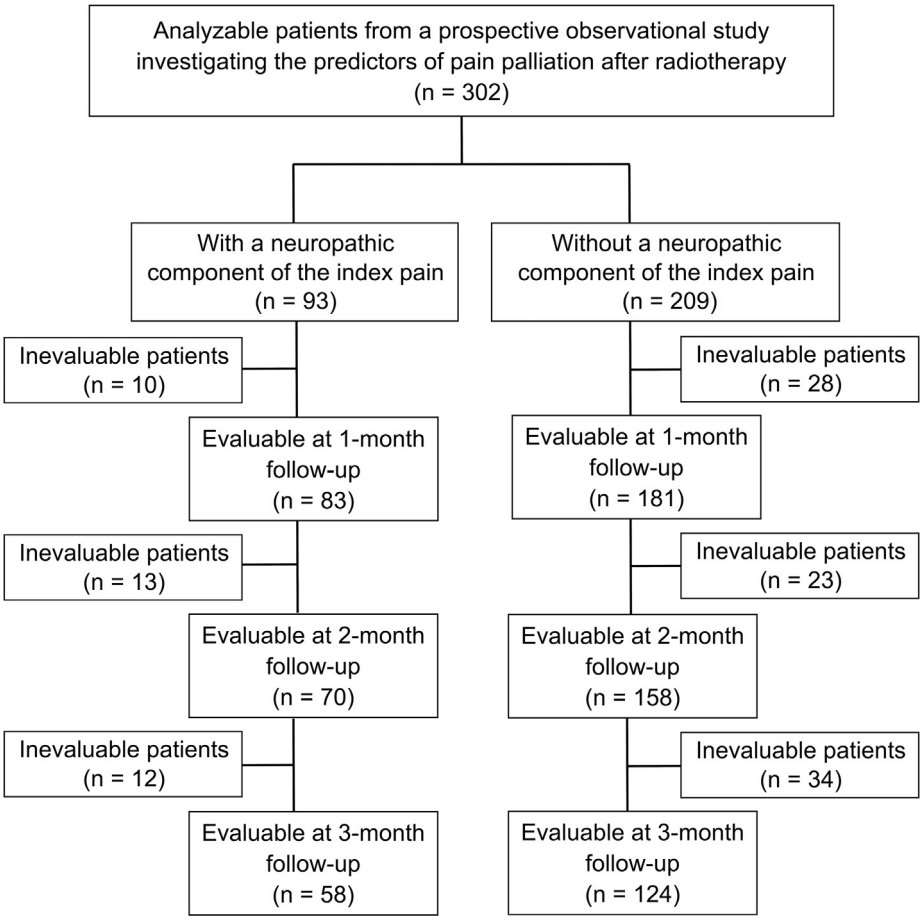

Fig. 1. Flow diagram of the study cohort. The index pain is the pain caused by the irradiated tumor.