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Income and Employment of Patients at the Start and in the Follow-up of Palliative Radiotherapy for Bone Metastasis

Palliative Radiotherapy and Employment

Hiroki Shirato, MD[1], Hideyuki Harada, MD[2], Yukako Iwasaki, MS[1], Akifumi Notsu, PhD[3], Kazunari Yamada, MD[4], Haruka Uezono, MD[5], Yutaro Koide, MD[6], Hitoshi Wada, MD[7], Hikaru Kubota, MD[8], Naoto Shikama, MD[9], Takuya Yamazaki, MD[10], Kei Ito, MD[11], Joichi Heianna, MD[12], Yukinori Okada, MD[13], Ayako Tonari,MD[14], Shigeo Takahashi, MD[15], Takashi Kosugi, MD[16], Yasuo Ejima, MD[17], Norio Katoh, MD[18], Kayo Yoshida, MD[19], Takafumi Komiyama, MD[20], Nobue Uchida, MD[21], Misako Miwa, MD[22], Miho Watanabe, MD[23], Hisayasu Nagakura,MD[24], Tetsuo Saito, MD[25], Hiroko Ikeda, MD[26], Isao Asakawa, MD[27], Tateishi Seiichiro, MD[28], Takeo Takahashi, MD[29], Naoyuki Shigematsu, MD[19].

1. Global Center for Biomedical Science and Engineering, Faculty of Medicine, Hokkaido University, Hokkaido Prefecture, Japan
2. Division of Radiation Therapy, Shizuoka Cancer Center, Shizuoka Prefecture, Japan
3. Clinical Research Center, Shizuoka Cancer Center, Shizuoka Prefecture, Japan
4. Department of Radiation Oncology, Seirei Mikatahara General Hospital, Shizuoka, Japan
5. Department of Radiation Oncology, Hyogo Cancer Center, Akashi, Japan
6. Department of Radiation Oncology, Aichi Cancer Center, Nagoya, Japan
7. Department of Radiation Oncology, Southern Tohoku General Hospital, Kōriyama, Japan
8. Department of Radiation Oncology, Kobe Unicersity, Kobe, Japan
9. Department of Radiation Oncology, Juntendo University, Tokyo, Japan
10. Department of Radiological Science, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan

11. Division of Radiation Oncology, Department of Radiology, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan
12. Department of Radiology, Graduate School of Medical Science, University of the Ryukyus, Nishihara, Okinawa, Japan.
13. Department of Radiation Oncology, St. Marianna University School of Medicine, Kanagawa, Japan.
14. Department of Radiation Oncology, Kyorin University Hospital, Tokyo, Japan.
15. Department of Radiation Oncology, Kagawa University Hospital, Kagawa, Japan
16. Department of Radiology, Fujieda Heisei Memorial Hospital, Fujieda, Shizuoka, Japan.
17. Department of Radiology, Saitama Medical Center, Dokkyo Medical University, Saitama, Japan.
18. Department of Radiation Oncology, Faculty of Medicine, Hokkaido University
19. Department of Radiology (Radiation Oncology), School of Medicine, Keio University, Tokyo, Japan
20. Department of Radiology, University of Yamanashi, Yamanashi, Japan
21. Department of Radiation Oncology, Tokyo Saiseikai Central Hospital, Tokyo, Japan
22. Department of Radiology, Sendai Kousei Hospital, Sendai, Japan
23. Department of Radiology, Chiba University Hospital, Chiba City, Japan
24. Department of Radiology, KKR Sapporo Medical Center, Sapporo, Japan.
25. Department of Radiation Oncology, Arao Municipal Hospital, Kumamoto, Japan.
26. Department of Radiation Oncology, Osaka City General Hospital, Osaka, Japan
27. Department of Radiation Oncology, Nara Medical University, Nara, Japan
28. Department of Disaster Occupational Health Center, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan.
29. Department of Radiation Oncology, Saitama Medical Center, Saitama Medical University, Saitama Prefecture, Japan

Corresponding Author:
Hiroki Shirato, MD, PhD
shirato@med.hokudai.ac.jp

Statistical Analysis:
Yukako Iwasaki, iyukako@pop.med.hokudai.ac.jp
Akifumi Notsu, a.notsu@scchr.jp

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Abstract

Purpose: To understand the income and employment status of patients at the start and in the follow-up of palliative radiotherapy for bone metastasis.

Materials and Methods: From December 2020 to March 2021, a prospective multi-institutional observation study was conducted to investigate income and employment of patients at the start of administration of radiotherapy for bone metastasis and 2 and 6 months after the treatment. In 333 patients referred to radiotherapy of bone metastasis, 101 were not registered mainly because of their poor general condition and another 8 were excluded from the following analysis due to ineligibility.

Results: In 224 patients analyzed, 108 had retired for reasons unrelated to the cancer, 43 had retired for reasons related to the cancer, 31 were taking leave, and 2 lost their jobs at the registration. The number of patients who were in the working group was 40 (30 with no change in income and 10 with decreased income) at the registration, 35 at 2-months, and 24 at 6-months respectively. Younger patients (p=0.000), better performance status (p=0.000), patients who were ambulatory (p=0.008), and patients with lower numerical rating scale of pain (p=0.000) were significantly more likely to be in the working group at the registration. There were 9 patients who experienced improvements in their working status or income at least once in the follow-up after the radiotherapy.

Conclusions: The majority of patients with bone metastasis were not working at the start of and after the radiotherapy but the number of patients who were working was not negligible. Radiation oncologists should be aware of the working condition of the patients and provide appropriate support for each patient. The benefit of radiotherapy to support patients continuing their work and return-to-work should be investigated further in prospective studies.

Introduction

Survival of patients with bone metastasis is now improved considerably by new anti-cancer drugs, such as tyrosine kinase inhibitors and immune checkpoint inhibitors.[1] With the wide usage of the new anti-cancer drugs, the medical costs for patients at advanced stages of the cancer have risen recently.[2] As this population lives longer, and radiotherapy may be used for anything from simple palliation to near curative-intent treatment, understanding the financial toxicity (FT)[3] in patients who receive radiation for bone metastasis and impact on work will become progressively more relevant.

Japanese medical services are based on the free-access policy with a public medical insurance system pursuing universal health coverage by establishment of employee-based and community-based social health insurance.[4] The national pension system for all residents and employer pension systems for employees are available for older

persons (62 - 65 years or older) and the average annual gross income per household of the older persons was ¥3,126,000 at 2019. There is a unique system of a ceiling amount of high-cost medical expenses.[5] For example, when the total medical expenses is ¥1,000,000 (US$ 8,000) per month, the maximum amount any patient has to pay in personal reimbursement ranges from approximately ¥8,000 to ¥300,000 per month (US$ 64 to US$ 2,400) depending on the patient age and income. During leave of absence, patients can receive two thirds of the original income for up to one and a half year in general. When retired, unemployment insurance covers 45 – 80% of the original income for 90 – 360 days depending on the age, income, and years insured. Despite such systems, more than 60% of patients with cancer in Japan use alternative strategies, such as cutting spending on food, clothing, or leisure to cope with FT in cancer care.[5] Financial toxicity is now recognized as a serious issue for patients with cancer even in countries which have national health insurance systems such as Japan and Italy.[6] The FT in such cancer patients and their families is composed of three factors: 1. expenditures such as drug costs, other direct medical costs, and related treatment costs; 2. loss or decrease of wealth including income, savings, and assets; and 3. anxiety and discomfort.[7] Recently, active support is recommended for all oncologists to reduce the FT as well as the physical toxicity of the cancer treatment.[7-10] Adding to the medical

costs, low income and unemployment are known to be strongly associated with FT.[11,12] The Japanese government has started full-scale efforts to support working people who suffer from cancer. Several university hospitals and cancer centers started to support the balance of work and treatment for cancer patients not to lose income and employment as far as possible.[13] However, few oncologists have time, interest, knowledge, or skills to mitigate the FT of the patients by interviews about these financial issues as is the case in other countries.[7,10,14,15]

Recently, there are increases in the number of reports about FT related to radiotherapy with curative intent.[16-19] However, a survey for this paper found that there are no reports on the FT of patients, worldwide, receiving palliative radiotherapy except one study which analyzed patients treated in 1992-1993 and which reported 22 disability days on average that prevented performance of usual daily duties.[21] There can be a large gap between the general belief held by physicians about FT and actual FT of the current patients. Patients with metastatic bone disease are often treated with palliative radiotherapy but little is known about their incomes or employment at the start of the radiotherapy. The changes in income and employment status after radiotherapy are also worthwhile to be made known.

From these considerations, we have conducted a prospective multi-institutional

observation study about the income and employment status of patients with bone metastasis at the start of and after radiotherapy. The relationship between the employment status, patient characteristics and radiotherapy methods were also reported. These basic data from observational study will be useful to find solutions in the next prospective studies.

Materials and Methods

From December 2020 to March 2021, patients with bone metastasis and planned to be treated by external beam radiotherapy were eligible for inclusion after informed consent. Patients who the attending physician evaluated as unsuited for study participation and follow-up for 6 months were not eligible. Patients were registered with basic information including age, gender, and performance status (PS(ECOG)) before radiotherapy. Detailed information was registered at the end of the radiotherapy. Each institution was asked to use the techniques, target volume, dose, fractionation, and treatment periods in the radiotherapy and combination/supportive care which was usually used in the clinic. Since the purpose of this study was to understand the real-world practice and patient outcomes in the same time period throughout Japan, the study was not designed to be powered to a number to achieve any specific threshold for significance. The maximum number of patients per institution was limited to 10 to

gather data not only from large cancer centers but also from regular sized cancer centers. A detailed study about pain relief, bone related events, adverse effects, and quality of life after the external radiotherapy has been published elsewhere.[21]

Age, gender, PS (ECOG), primary cancer site, the region treated with radiotherapy, numerical rating scale (NRS) of the pain at the region treated with radiotherapy, ambulatory status (fully ambulatory, ambulatory only indoors, or not ambulatory), planning/irradiation technique (two dimensional, three dimensional, SBRT/IMRT), and fractionation number of the radiotherapy (1, 2-9, 10, 11, or more) were used for the analysis in the present study. The NRS is an 11-point left-right scale anchored at 0 and 10: "no pain" was printed at the left under the 0 and under the 10 "pain, which could not be more severe" at the right. Patients were asked to select the number which is closest to the worst pain which they had felt. Narcotic doses were converted to oral morphine doses.

For the income and employment status the patients were asked using the preset items and phrases listed as follows:

At the registration, patients were asked to select one from the following items regarding their present situation. The word in the parenthesis is used to represent the item in this paper.

(1) There was no decrease in income of 10% or more (No change).

(2) Income decreased by 10% or more including relocation and job change (Income decreased).

(3) I took leave of absence (Taking leave).

(4) I lost my job including early retirement (Lost my job).

(5) At the start of bone treatment, I was no longer working for reasons related to the cancer (Retired_cancer).

(6) At the start of bone treatment, I was not working for reasons other than the cancer including unemployment and illness diagnosed post-retirement (Retired_non-cancer).

Answers were collected at the end of the first radiotherapy and these data are used as the registration (base values) in this study.

The follow-up examinations were performed at 2 and 6 months after the registration either with face-to-face interviews or on-line. Patients were asked to select one from the list of items (1) to (6) or the following (7) and (8) regarding their present situation at 2 and 6 months.

(7) I was on leave or lost my job, but I was able to return to work (Return to work).

(8) My income decreased by more than 10%, but it has now returned to my previous income (Income returned).

At 2 and 6 months after the registration, if the patients were unable to be interviewed, the last follow-up status was investigated through the referring physician as far as it was possible.

The follow-up period was 6 months after the registration of the last patients. Analysis was started 12 months after the last follow-up of the last patient. No data was recorded regarding the actual amount of income and retirement income.

The basic statistical analysis was made using EXCEL functions (Microsoft, USA). The Mann-Whitney U test with independent samples was used for the comparison between two groups. Pearson's chi-square test was used for testing the independence between two qualitative variables.

Results

There were 333 patients with bone metastasis referred to radiotherapy during the study period in the 26 institutions (Figure 1, supplemental Table 1). One hundred-one patients were not registered since registration was rejected in 11 patients, the attending physician determined that the performance status was not good enough for 6 months follow-up in 68, the performance status was good but not fit for the follow-up in 13, and the treatment needed to start before explanation about this study in 9. Two hundred and thirty-two patients were registered, and 224 patients were analyzed, after excluding 5

ineligible patients, 1 patient who withdrew the consent, and 2 patients who did not receive protocol treatment. Mean ± standard deviation (SD) of the age was 68 ± 11 years, 38% were female, 61% were PS 1-2, 63% were ambulatory, and the mean ± SD of NRS of the pain was 5.3 ± 3.0 (Table 1). Primary sites were lungs in 36%, breasts in 15%, prostate in 7%, and others in 42% of the patients (Table 1). The summery of irradiated sites, biological equivalent dose (BED) assuming $\alpha/\beta = 10$, and treatment periods are listed in Supplemental Table 2. The income and employment status at the registration, 2 months, and 6 months are shown in Figure 2.

At the registration, there was 30 patients with no change in income, and 10 with decreased incomes: corresponding to 13% and 5% of 224 patients analyzed and 9% and 3% of 333 patients referred to radiotherapy. Thirty-one patients were taking leave, 2 patients lost their jobs, 43 had retired for reasons related to the cancer, and 108 patients had retired for reasons unrelated to the cancer (Figure 2).

At 2-months, 26 were dead, 12 were lost to the follow-up, and the remaining 186 patients completed the follow-up (Figure 1). At 2 months after the registration, 23 patients reported no change in income, 8 were working with decreased income, and 4 patients who had been taking leave or lost their jobs at the time of registration were able to return to work. Twenty-eight patients were taking leave at 2 months, and 1 lost their

job. The number of patients who had retired for reasons related to the cancer and that unrelated to the cancer was decreased to 25 and 97 respectively (Figure 2).

At 6-months, an additional 35 were dead, 20 were lost to the follow-up, and the remaining 131 patients completed the follow-up (Figure 1). At 6 months after the registration, 18 patients reported no change in income, 6 were working with decreased income, 4 patients returned to work, and 2 who had been working with a decreased income had been able to return to earn the original income. Eight patients were taking leave and 7 lost their jobs. The number of patients who had retired for reasons related to the cancer and that was unrelated to the cancer was decreased to 19 and 64, respectively (Figure 2).

When the patients selected answers (1), (2), (7), or (8), we classified them into the working group. Others were classified into the non-working group. Since the patient can earn only two thirds of the original income when they take leave of absence, the patients selecting answer (3) were classified into the non-working group in this study. The percentage of patients in the working group was 18% (40), 16% (35), and 11% (24) at the registration, 2-months, and 6-months respectively of 224 patients analyzed and 12%, 11%, 7% of 333 patients referred to radiotherapy.

At the registration, the age distribution was significantly younger for the 40 patients in the working group (mean ±1SD, 62.8±9.8 years old) than in the 184 patients in the non-working group (69.0±10.4 years old) (Z=15.15, p=0.000). The PS(ECOG) was significantly better in working group (0.73±0.72) than in the non-working group (1.5±1.1) (Z=17.13, p=0.000). The distribution of gender and primary sites in each group are shown in Table 2. There was no difference in gender and primary cancer sites between the two groups (Table 2).

Patients were fully ambulatory, ambulatory only indoors, or not ambulatory in 55, 12, and 4 patients in the working group and 86, 45, and 22 patients in the non-working group, respectively at the registration (Figure 3). A statistically significant relationship was found between the ambulatory status and the ratio of the number of patients in the working group and that in the non-working group; patients who were ambulatory were more likely to be in the working group at the registration (Pearson's chi-square test, χ= 9.659, p=0.008).

The mean and SD of NRS of the pain were 4.0 ± 3.0 (median 3.5, range 0 – 10) and 5.5 ± 3.0 (5, 0 – 10) for working group and non-working group respectively at the registration (Figure 4). The NRS of pain was significantly smaller in working group compared to that in the non-working group at the registration (Z=24.92, p=0.000).

No significant statistical relationship was found between either treatment planning/irradiation techniques or fractionation number and the ratio of the number of patients in these two groups (working and non-working).

There were 9 patients who experienced improvements in their working status or income at least once in the follow-up (Table 3). Five were taking leave of absence and 2 were not working for reasons unrelated to cancer at the registration. Seven of the 9 patients had been ambulatory throughout and 2 other patients had been ambulatory only indoors at the registration. All patients were fully ambulatory when they returned to work or experienced improvement in income.

Discussion

Since palliative radiotherapy for bone metastasis is commonly using single or hypofractionation schedules without meticulous treatment planning, the risk of FT due to the radiotherapy-related cost should not be serious. However, if the patients are not working, the risk of FT can be high. The present study showed that as many as 82 % of the patients who registered in this study were not working at the registration. Since this study analyzed only those who had been evaluated as eligible for the 6-months follow-up and agreed to be registered, the actual percentage of patients who were not working must have been higher than this value. If we use the number of all patients with bone

metastasis referred to radiotherapy during the study period as the denominator, the percentage of patients who were not-working was 88%.

The low percentage of the patients who were working may be different in different countries due to the differences in healthcare systems. However, the distributions of age, gender, PS (ECOG), and primary site in this study are not particularly different from the studies of palliative radiotherapy for bone metastasis from other countries.[20-24] It is notable that the ambulatory status and NRS of pain were associated with working status at the registration in addition to the age and PS. It is suggested that patients who are fully ambulatory or ambulatory only indoors and patients who have low NRS have a higher possibility to be working at the registration. Oncologists should be aware of the findings in this study when they see patients with bone metastasis. They should try to help these patients not become exposed to FT by starting palliative radiotherapy.

It is well-known that single fraction palliative radiotherapy is as effective as a hypofractionation schedule in pain relief and quality of life.[24-26] Single fraction radiotherapy can be more beneficial than multiple fractions because of reducing the risk of loss or decrease in income for patients with bone metastasis especially for those who are working. The benefit of single fraction radiotherapy in terms of reducing the risk of FT should be investigated in a prospective study.

Although the percentage of the working group is low, considering the large total number of patients with bone metastasis, the actual number of working patients is not negligible. The number of patients who maintained status in the working group were 35 and 24 at 2 and 6-months after the radiotherapy. The number in the working group increased 4 and 4 at 2 and 6 months respectively by the increase in patients who returned to work after taking leave of absence or were not employed at the registration. In addition, there were 2 patients whose income had fully returned after the radiotherapy. Oncologists should be aware of the low but definite possibility of the return to work or to regain full income after radiotherapy in patients who are taking leave of absence or are not employed at the start of the radiotherapy.

Having said that, the possibility of a return-to-work in the follow-up period was quite low in patients who had retired before the registration. For these patients, it is more important for the physicians to pay attention to their FT not by persuading them to return to work but in other ways. Also, mental support is highly recommended since FT is associated with lower health-related quality of life in older adults with advanced cancer.[27]

Shih et al. have shown that more than half of cancer patients were willing to discuss costs with physicians but less than one-third of patients actually discussed costs with

their physicians.[10] Similar results were shown in research in Japan.[14] Medical oncologists are recommended to discuss FT with their patients.[8,9] Our results in this study and other previous studies suggest that discussion about FT is also recommended for radiation oncologists who are recommending treatment with radiotherapy irrespective of radical or palliative intent.[16-19]

Shortcomings of this study are the following. At first, there is a selection bias for patients. There were patients who were evaluated by the attending physicians as not eligible to enter this study mainly because of their poor general condition and each institution could only contribute 10 patients. As stated above, the percentage of patients in each category should be interpreted cautiously considering this selection bias. Second, we did not ask about the status of actual incomes, full or part time employment, retirement, and assets. These are important data but difficult to be obtained without detailed explanations to the patients about the purpose of the study. The patients who had taken leave of absence were classified into the non-working group in this study even though in general such patients may earn two thirds of the original income when they take leave of absence in Japan. Third, we have not examined treatment-related costs in this study, one of the important factors of FT. Palliative radiotherapy does not cost much generally but the patients may have received expensive anti-cancer

medications simultaneously or traveled large distances to the radiotherapy administering facility. These can have increased the risk of FT significantly. Fourth, we have not used validated measures of FT such as the Comprehensive Score for financial Toxicity (COST) which is known to be an internationally comparable scale for FT.[11] Honda et al. have shown that the mean COST in Japan is the same as in the United State in patients with various cancers who were receiving anti-cancer drugs.[5] It is also important to investigate the FT in palliative radiotherapy using validated measures. Lastly, this study does not answer to the questions as to whether the radiation they received made a difference in their employment. A prospective study is required to answer to this question.

In conclusion, the majority of patients with bone metastasis for palliative radiotherapy were subject to decreased incomes or not working. However, at the same time, not negligible numbers of patients were working at the start of the radiotherapy. Oncologists should be aware of the low but definite possibility of a return-to-work or regaining-full-income after radiotherapy in patients who were taking leave of absence or have lost their job at the start of the radiotherapy. For patients who were no longer working for reasons related to the cancer or who were not working for reasons unrelated to the cancer at the start of the radiotherapy, it is better not to persuade a return-to-work

and provide other ways to take care of the FT. Mental support is highly recommended for all patients not to suffer from FT. The benefit of radiotherapy to support patients continuing their work and return-to-work should be investigated further in prospective studies.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Figure legends

Figure 1. Flow diagram of this study.

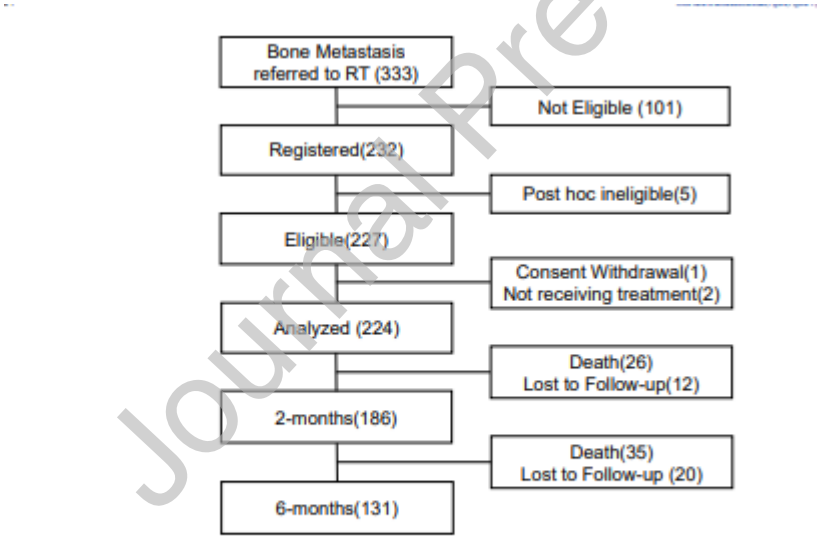

Figure 1

Figure 2. The income and employment status at the registration (start of radiotherapy), 2-months, and 6-months after radiotherapy. The number of patients who selected each item at the registration(blue), 2-months(orange), and 6-months (gray) is listed from left to right respectively.

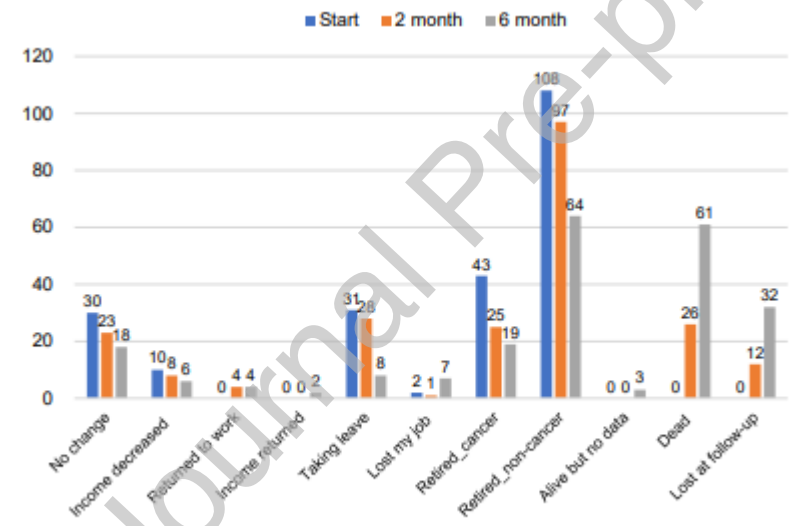

Figure 2

Figure 3. The number of patients who were fully ambulatory, ambulatory only indoors, or not ambulatory at the registration in the working group (blue, left) and non-working group (orange, right) respectively.

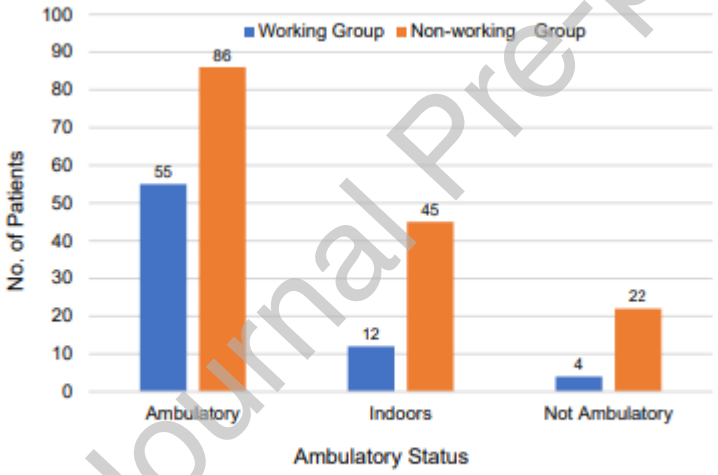

Figure 3

Figure 4. The number of patients with each NRS of pain (0 -10) at the registration in the working group (blue, left) and non-working group (orange, right) respectively.

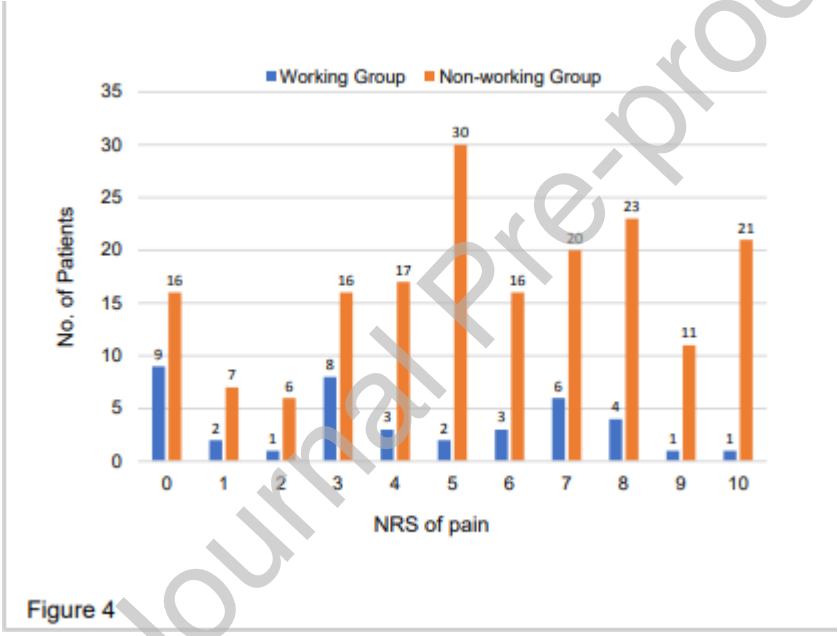

Figure 4

Table 1. Details of patient characteristics

Number of patients	224
Age	
mean(standard deviation)	68(11)
median(range)	70(28-89)
Gender, N(%)	
Female	85(38)
Male	139(62)
PS, N(%)	
0	52(23)
1	86(38)
2	50(22)
3	28(13)
4	8(4)
Primary site	
lung	80(36)
breast	33(15)
hepatobiliary	20(9)
kidney & ureter	19(8)
prostate	15(7)
Rectum	15(7)
Unknown	8(4)
head & neck (excluding thyroid)	6(3)
uterus	3(1)
sarcoma	2(1)
thyroid	1(0)
Walkable status at the registration	
ambulatory	141(63)
ambulatory indoors	57(25)
not ambulatory	26(12)
Numerical rating scale (NRS) of the pain	
mean(standard deviation)	5.3(3.0)
median(range)	5(0-10)

Table 2. The gender and primary site of the cancer according to the working status at the registration

	Working Status		
	Working	Non-working	Total
Gender			
Female	11	74	85
Male	29	110	139
Primary site			
Lung	14	66	80
Breast	7	26	33
Prostate	2	13	15
Kidney	2	12	14
Others	12	63	75
Unknown	3	4	7
Total	40	184	224

Table 3. The list of patients who experienced improved their working status or income at least once in the follow-up

No.	Age	Gender	PS	Primary	Irradiated Site	Opioid	Technique	Daily	Total	Ambulatory status			NRS of the pain			Working status		
			(ECOG)	Site		(mg)		dose(Gy)	dose(Gy)	Start	2 months	6 months	Start	2 months	6 months	Start	2 months	6 months
1	47	F	0	Breast	Thracic spine	0	3DCRT	2.5	37.5	Ambulatory	Ambulatory	Ambulatory	1	0	0	taking leave	taking leave	return to work
2	52	F	1	Breast	Thoracic/pelvis	0	3DCRT	3	30	Indoors	Ambulatory	Ambulatory	5	2	1	taking leave	taking leave	return to work
3	55	F	0	Breast	Thracic spine	0	3DCRT	4	20	Ambulatory	Ambulatory	Ambulatory	0	0	0	taking leave	return to work	return to work
4	79	M	1	Kidney	Pelvis/Rib	0	2D	5	25	Ambulatory	Indoors	unknown	5	6	unknown	no job by cancer	return to work	unknown
5	59	F	2	Lung	Femur	0	3DCRT	3	30	Indoors	Ambulatory	Ambulatory	9	1	0	taking leave	return to work	return to work
6	69	M	1	Lung	Cervical spine	15	3DCRT	4	20	Ambulatory	Ambulatory	Ambulatory	4	3	5	taking leave	return to work	return to work
7	50	M	1	Lung	Lumbar spine	45	3DCRT	3	30	Ambulatory	Ambulatory	Ambulatory	2	0	0	no job by cancer	taking leave	return to work
8	71	M	0	Head &	Lumbar	0	SBRT	12	24	Ambulato	Ambulato	Ambulato	3	1	0	no job by	lost job	return to

				Neck	spine					ry	ry	ry				other		work	
9	68	M	1	Lung	Rib	0	3DCRT	5	25	Ambulatory	Ambulatory	Ambulatory	0	0	0	decreased	decreased	fully employed	