


Impact of self-decision to stop cancer treatment on advanced genitourinary cancer patients

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Abstract

Decision-making to stop cancer treatment in patients with advanced cancer is stressful, and it significantly influences subsequent end-of-life palliative treatment. However, little is known about the extent to which the patient's self-decisions influenced the prognostic period. This study focused on the patient's self-decision and investigated the impact of the self-decision to stop cancer treatment on their post-cancer treatment survival period and place of death.

We retrospectively analyzed 167 cases of advanced genitourinary cancer patients (kidney cancer: 42; bladder cancer: 68; prostate cancer: 57) treated at the University of Fukui Hospital (UFH), who later died because of cancer. Of these, 100 patients decided to stop cancer treatment by themselves (self-decision group), while the families of the remaining 67 patients (family's decision group) decided to stop treatment on their behalf because the patient's decision-making ability was already impaired. Differences in the post-cancer-treatment survival period and place of death between the 2 groups were examined. The association between place of death and survival period was also analyzed.

The median survival period after terminating cancer treatment was approximately 6 times longer in the self-decision group (145.5 days in self-decision group vs 23.0 days in family's decision group, $P < .001$). Proportions for places of death were as follows: among the self-decision group, 42.0% of patients died at UFH, 45.0% at other medical institutions, and 13.0% at home; among the family's decision group, 62.7% died at UFH, 32.8% at other medical institutions, and 4.5% at home. The proportion of patients who died at UFH was significantly higher among the family's decision group ($P = .011$). The median survival period was significantly shorter for patients who died at UFH (UFH: 30.0 days; other institutions/home: 161.0 days; $P < .001$).

Significantly longer post-cancer-treatment survival period and higher home death rate were observed among patients whose cancer treatment was terminated based on their self-decision. Our results provide clinical evidence, especially in terms of prognostic period and place of death that support the importance of discussing bad news, such as stopping cancer treatment with patients.

Abbreviations: ACP = advance care planning, CI = confidence interval, PS = performance status, UFH = University of Fukui Hospital.

Keywords: advance care planning, bladder cancer, decision making, kidney cancer, palliative care, place of death, prostate cancer

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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1. Introduction

Systemic pharmacotherapy is the standard cancer treatment for metastatic advanced genitourinary cancer. In recent years, immune checkpoint inhibitors have become available, contributing to the improved prognosis of advanced cancer.^[1] However, in many cases, cancer-related symptoms such as pain or malaise increase with the progression of the disease, which hinders the continuation of cancer treatment. Although there are some case reports of dramatic improvement from severe conditions,^[2,3] many studies have revealed that end-of-life cancer treatment neither contributes to an improved prognosis nor leads to appropriate palliative care.^[4–9]

In contrast, for oncologists, the termination of cancer treatment is a difficult subject to discuss with terminally-ill patients and their families.^[10] Some reports have shown that difficulties in such discussions result in the continuation of cancer treatment or the use of invasive medical procedures until the patient dies.^[11–13] Decreased performance status (PS) and the number of chemotherapy lines has been reported as significant factors that oncologists should consider while stopping cancer treatment.^[5,6,14] However, numerous studies have reported that many cancer patients receive systemic cancer treatment within their last month of life.^[15–18] In an attempt to decrease non-

beneficial medical treatments for terminally-ill patients, there has been increasing recognition regarding decision-making support and patients' wishes about palliative care.^[19] Previous reports have indicated that decision-making support involves more than merely identifying the goal of treatment or a patient's preference for palliative care; it leads to an improved end-of-life palliative environment and consequently the satisfaction of the patient and their family.^[20]

The decision to stop cancer treatment is an important process that significantly influences subsequent end-of-life palliative treatment. However, it is a complicated issue to find an appropriate time to discuss such a delicate topic regarding cancer treatment termination with the patients. In the study of incurable cancer patients receiving palliative chemotherapy, termination of cancer treatment was mentioned to only half of the patients.^[21] In the real clinical setting, the severity of some patients' conditions renders them unable to decide to stop cancer treatments by themselves. For such patients, the responsibility of determining when their treatment should be terminated is on the family. Thus, whether the decision-makers are the patients or their families can be a factor affecting the prognosis. Although previous studies have revealed the factors associated with difficulty and burden of the decision-making process,^[22,23] it has been unclear to what extent the patient's self-decisions influenced the prognostic period. Information about how the survival period and palliative care would be affected by cancer treatment terminated by patients themselves, as compared to treatments terminated by the family, will lead to better decision-making support regarding the termination of cancer treatment. Therefore, this study focused on patients' self-decision in stopping cancer treatment. This study aims to investigate

- 1) the differences of post-cancer treatment survival period and place of death among the patients whose decisions were made by themselves or not, and
- 2) the difference of post-cancer treatment survival period depending on the place of death, and to strengthen the importance of the decision-making support for terminal cancer patients by the aspect of prognostic differences.

2. Methods

2.1. Study design

We conducted a retrospective chart review of patients who received cancer treatment for advanced genitourinary cancer (kidney, bladder, and prostate cancer) at the University of Fukui Hospital (UFH) and died with disease progression from October 2006 to March 2019. Patient information was extracted using the hospital cancer registry database.

The main points of this study were as follows:

- 1) differences in the post-cancer-treatment survival period based on whether the cancer treatment was terminated by the patient's or family's decision, and
- 2) the association between self-decision and place of death.

The clinical charts of 219 patients who died with advanced genitourinary cancer (kidney cancer: 48 cases; bladder cancer: 89 cases; prostate cancer: 82 cases) were reviewed, and the description of the informed consent about the termination of cancer treatment was examined. A total of 167 patients (kidney

cancer: 42; bladder cancer: 68; prostate cancer: 57) were finally enrolled in this study after excluding 52 patients who met the exclusion criteria. To reduce selection bias, 219 patients who enrolled received cancer treatment for advanced genitourinary cancer at the UFH and died with disease progression from October 2006 to March 2019. However, patients who received cancer treatment but whose cause of death was not related to genitourinary cancer were excluded before the initial enrollment.

2.2. Indications for stopping cancer therapy

Indications for stopping cancer treatment in this study were defined as follows:

- 1) When the patient wishes to stop cancer treatment for whatever reason.
- 2) When the cancer progression was detected under standard cancer therapy.
- 3) When the continuation of cancer treatment was considered difficult due to severe side effects or deterioration of the physical condition, including cachexia.

When these situations were found, doctors provided the medical information to patients and their families and discussed whether patients could finally stop cancer treatments or not.

2.3. Exclusion criteria

Cases that met the following criteria were excluded.

- 1) Cases whose cancer treatments were terminated because of dropout
- 2) reasons or discussions for stopping cancer treatment were uncertain in the clinical charts, and
- 3) cases whose main cancer treatments were conducted in other medical institutions.

Cases were divided into 2 groups depending on whether the decision to stop cancer treatment was made by the patients themselves (self-decision group) or by their families (family's decision group) due to the severe cancer state of the patients.

This study defined cancer treatment as surgical treatment, curative radiation therapy, and chemotherapy, including hormonal therapy for prostate cancer. Treatment for symptom palliation, such as radiation therapy for bone metastasis, was not included in cancer treatment. Cancer treatments were counted at all stages, not limited to the advanced stage. Reasons for stopping cancer treatment were categorized into the following three groups, cancer progression, adverse events, and others. The post-cancer-treatment survival period was defined as the number of days between the day when the decision to stop cancer treatment was confirmed and the date of death. Figure 1 shows a flowchart of this study.

The UFH has 600 inpatients beds, and the urology division has an average of 25 beds. All beds are for patients who receive acute-phase urological treatment, such as surgical treatment, chemotherapy, or infectious disease therapy. The UFH does not have a palliative care unit and a department providing home-visit medical care. Thus, patients who wish to receive supportive care at home, in a palliative care unit, or in a long-term care facility are referred to other medical institutions. The date and the place of death of patients who did not die at the UFH were confirmed by medical institutions or clinics that provided end-of-life palliative care.

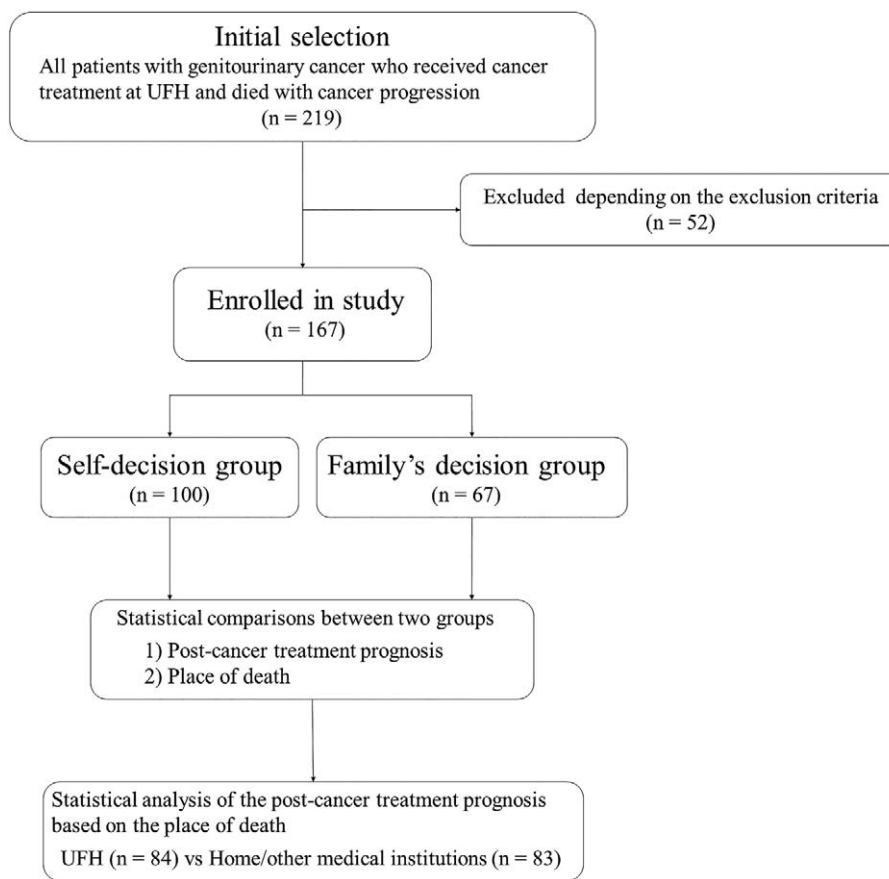


Figure 1. A flowchart of this study. UFH=University of Fukui Hospital.

2.4. Statistical analysis

All statistical analyses were performed using EZR (Easy R) software version 1.40 (Available at: <http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmed.html>).^[24] For the statistical comparison of each patient's characteristics between Self-decision and Family's decision group, the Mann-Whitney U test was used to evaluate the median age of death, and the chi-square test was used to compare the ratio of gender, primary organ, performed cancer treatment, and reasons for stopping cancer treatment. The statistical comparison of the survival period after the termination of cancer treatment was performed using the Kaplan-Meier curve and log-rank test. The association between self-decision and place of death was analyzed using the chi-square test. A *P*-value <.05 was considered statistically significant.

2.5. Ethical Statement

This study was approved by the Research Ethics Committee of University of Fukui (No. 20190174).

3. Results

The agreement to stop cancer treatment was obtained from patients themselves in 100 cases (self-decision group) and from the patient's family in 67 cases (family's decision group). Table 1 shows the characteristics of the patients in each group. The median age was 78.0 years in the self-decision group and 77.0 years in the family's decision group. The ratio of male patients

Table 1
Patients' characteristics and comparison between Self-decision and Family's decision group.

Group	Self-decision N=100 n (%)	Family's decision N=67 n (%)	<i>P</i> value
Age (years)			
<59	11 (11.0)	6 (9.0)	
60-69	12 (12.0)	14 (20.9)	
70-79	33 (33.0)	24 (35.8)	
>80	44 (44.0)	23 (34.3)	
Median age (years)	78.0	77.0	0.50
Gender			
Male	83 (83.0)	55 (82.1)	1.00
Female	17 (17.0)	12 (17.9)	
Primary organ			
Kidney	23 (23.0)	19 (28.4)	0.42
Bladder	39 (39.0)	29 (43.2)	
Prostate	38 (38.0)	19 (28.4)	
Cancer treatment*			
Surgery	31 (31.0)	24 (35.8)	0.63
Pharmacotherapy	74 (74.0)	50 (74.6)	1.00
Radiation therapy**	17 (17.0)	14 (20.9)	0.67
Reasons for end of cancer treatment			
Cancer progression	58 (58.0)	48 (71.6)	0.18
Adverse event	13 (13.0)	7 (10.4)	
Others	29 (29.0)	12 (18.0)	

* Cancer treatments were counted at all stages, not limited to the advanced stage.

** Radiation therapy for symptom palliation is not included.

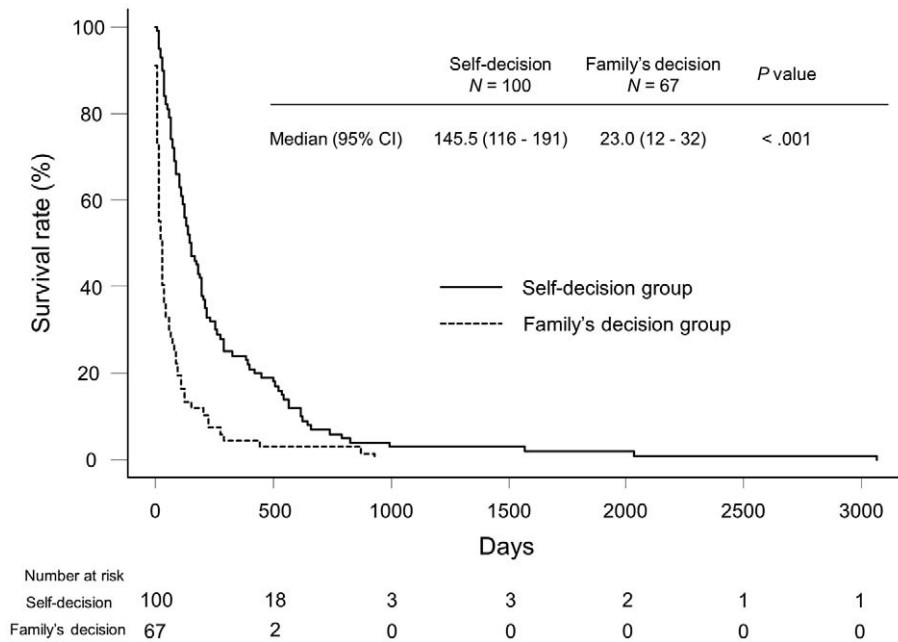


Figure 2. Kaplan-Meier curve of post-cancer-treatment survival period for self-decision and family's decision groups. The Kaplan-Meier curve and log-rank tests were used to statistically compare the survival period between the two groups. CI = confidence interval.

was high because patients with prostate cancer were included. In both groups, surgical treatments and systemic pharmacotherapy were provided to approximately 30% and 70% of patients, respectively, and no significant differences were found in cancer treatments between the 2 groups. The pharmacotherapy length could not be evaluated because drug therapy, in many cases, was initiated at other institutions before visiting our hospital. The reasons for stopping cancer treatment in the self-decision group and the family's decision group were cancer progression: 58.0% and 71.6%, adverse events: 13% and 10.5%, and others: 29.0% and 17.9%, respectively. No statistical difference was observed in the ratio for each reason between the two groups. PS could not be evaluated because the information about PS was not written adequately in many cases in the clinical charts.

Figure 2 shows the Kaplan-Meier curve of the post-cancer-treatment survival period for the self-decision and family's decision groups. The median survival period was significantly longer in the self-decision group (145.5 days in the self-decision group and 23.0 days in the family's decision group, $P < .001$). Ten

of 100 patients (10.0%) in the self-decision group and 40 of 67 patients (59.7%) in the family's decision group received cancer treatment within their last month of life.

Regarding the effect of self-decision to stop cancer treatment on the place of death, in the self-decision group, 42.0% of patients died at UFH, 45.0% at other medical institutions, and 13.0% at home; in the family's decision group, 62.7% died at UFH, 32.8% at other medical institutions, and 4.5% at home (Table 2). The ratio of patients who died at UFH was significantly higher in the family's decision group than that in the self-decision group ($P = .011$).

Regarding the association between place of death and survival period after cancer treatment termination, Figure 3 shows the survival curve for patients who died at UFH and other institutions/home. The median survival period of patients who died at UFH (30.0 days) was significantly shorter than that of patients who died at other institutions/home (161.0 days) ($P < .001$).

4. Discussion

This study focused on the patient's self-decision and examined the relationship between self-decision to stop cancer treatment and post-cancer-treatment survival period, as well as the effect of self-decision to stop cancer treatment on the place of death among advanced genitourinary cancer patients. A substantial difference was observed in the survival period after termination of cancer treatment between the groups, with a median survival period of 145.5 days in the self-decision group and 23.0 days in the family's decision group. The survival period in the self-decision group was therefore approximately six times longer. Additionally, the ratio of patients who died at UFH was significantly higher in the family's decision group. In a study of patients with hematological malignancy conducted in the United Kingdom, it was found that

Group	Self-decision	Family's decision
	N=100 n (%)	N=67 n (%)
Place of death		
UFH	42 (42.0)*	42 (62.7)*
Other	58 (58.0)*	25 (37.3)*
Medical institutions	45 (45.0)	22 (32.8)
Home	13 (13.0)	3 (4.5)

A chi-square test was used to determine the statistically significant difference between UFH and other medical institutions/home.

UFH = University of Fukui Hospital

* $P = .011$.

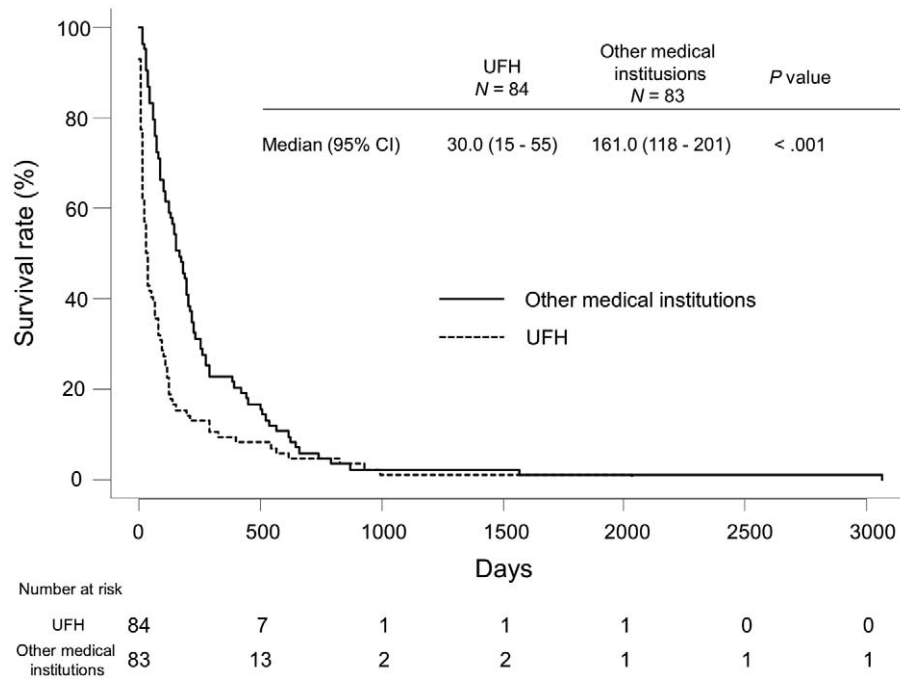


Figure 3. Survival curve for patients who died at UFH and other medical institutions/home. The Kaplan-Meier curve and log-rank tests were used to statistically compare the survival period between the two groups. CI = confidence interval; UFH = University of Fukui Hospital.

patients who did not discuss their preferred place of death were more likely to die in hospital, and 90% of those who died in hospital received cancer treatment within their last month of life.^[25] In our study, the median survival period after the termination of cancer treatment was only 23 days in the family’s decision group. Although the patient’s preference of the place of death was not analyzed, many patients whose cancer treatment continued until they could no longer make decisions were at risk of not receiving their preferred palliative care before the end of their life because the remaining prognostic period was short.

Many reports have described the negative impact of chemotherapy on terminally ill cancer patients. Palliative chemotherapy often does not contribute to prolonged prognosis; moreover, its adverse effects can negatively impact the palliative treatment.^[4–9] However, 50 of 167 patients (29.9%) in this study received anti-cancer treatment within the last month of their life. Similar situations in which systemic cancer treatments are provided just before death are common.^[15–18] One of the factors leading to the continuation of cancer treatment until the end of life is the lack of clear criteria for deciding the termination of cancer treatment. A retrospective study with non-small cell lung cancer patients reported that systemic chemotherapy for PS 3 and 4 patients did not contribute to prolonged prognosis.^[14] The American Society of Clinical Oncology has also advocated against providing aggressive cancer treatment for patients with poor PS.^[5] PS is an essential factor for determining the indication of systemic cancer treatment. Whether a patient can visit a clinic on foot without any help or not was reported as a simplified rule for providing chemotherapy.^[26] Lack of response to the last regimen or the development of new metastases were reported as other factors used to predict a low chance of response to subsequent cancer treatment.^[27] As stated previously, there have been numerous reports that offer evidence for stopping cancer

treatment; however, the decision to stop cancer treatment finally depends on the oncologist’s ability to confirm the patient’s will.

Discussing the prognosis with terminal cancer patients is a challenging medical skill for oncologists. Keating et al^[10] indicated that even if the expected prognosis was 6 months or less, oncologists found it difficult to discuss end-of-life palliative care with patients when their condition was good. Other studies have also reported that discussions about unoptimistic prognosis may disrupt the patient-oncologist relationship.^[28,29] However, Fenton et al^[30] prospectively examined the impact of discussions about prognosis on the patient-oncologist relationship and found no significant negative effects when patients were correctly informed about their prognosis by oncologists.^[30]

Meanwhile, it has been reported that the preferred place of death often differs between patients and their families.^[31] In our study, the ratio of patients who died at UFH was significantly lower among patients who decided to stop cancer treatment themselves compared to those whose families made the decision. This result indicates that the patient’s self-decision to stop cancer treatment had a significant impact not only on the survival period but also on the place of death. Therefore, oncologists should take into consideration the patient’s preferred type of palliative care, and bring up the termination of cancer treatment as one of the possible options before the patient’s ability to make an informed decision is affected.

In recent years, much emphasis has been placed on advance care planning (ACP) as a process to provide end-of-life palliative care that better reflects patients’ will, and it has been gradually adopted in Japan. Importantly, it is a process that allows the patient, family, and healthcare professionals to work together to make plans to meet the patient’s wishes, especially against future occurrences when the patient may not be able to communicate their preferred healthcare options.^[32] Therefore, ACP in terminal

cancer patients might be an effective procedure to discuss the end of cancer treatment with patients and their families. Regarding the problem with ACP, Toguri et al evaluated the oncologist's views on ACP and reported that many oncologists found difficulty in determining an appropriate time of initiating ACP.^[33] It has also been reported that if ACP was initiated too early, the decisions would be ambiguous, and if it were too late, it would be difficult to perform ACP itself.^[34] Although the presence or absence of ACP could not be evaluated in this study, there was a 6-fold difference in post-cancer treatment prognosis between the self-decision group and the family's decision group. Particularly, the prognostic period in the family's decision group was only three weeks, which was when the patient's death was imminent. End of cancer treatment is a major issue in ACP of terminal cancer patients. Our results suggest that at least one month is required for a prognosis to provide decision-making support that respects the patient's will. Conversely, this study indicates that the prognostic period would be several weeks if the cancer treatment continued until the patients could not express their exact wishes. Our results found that the patient's self-decision had a significant impact on the post-cancer treatment survival period and place of death, which will provide new evidence to support the importance of discussing stopping cancer treatment with the patients.

5. Limitations

Our study has some limitations. First, it was performed at a single university hospital in Japan, and all data were analyzed retrospectively. Therefore, our results may not be generalizable to other institutions or countries. Second, our sample comprised patients with genitourinary cancer and has a higher proportion of elderly and male patients. Thus, the results may be different for younger or female patients, such as female patients with breast cancer. Moreover, all participants in this study were Japanese. Individuals' views regarding life and death can vary depending on factors such as region, religion, and traditions. The results of similar studies conducted elsewhere, therefore, may be different. Our study could not evaluate the patient's PS, cognitive function, social status, financial status, family structure, and religion because they were not sufficient in the clinical charts. These factors may have affected the patient's decision-making process as confounders.

6. Conclusion

Our study highlighted the significant impact of patients' self-decision to stop cancer treatment on their post-cancer-treatment survival period and place of death among patients with advanced genitourinary cancer. In patients who could decide to stop cancer treatment (the self-decision group), the median survival period after terminating cancer treatment was approximately 6 times longer, and the ratio of patients who died at a university hospital was significantly lower than those who could not decide to stop treatment themselves (the family's decision group). Notably, the median post-cancer treatment survival period in the family's decision group was only about 3 weeks. Our results provide new clinical evidence, especially in terms of prognostic period and place of death that support the importance of discussing the termination of cancer treatment with patients. Furthermore, these results provide beneficial prognostic information for oncologists when considering their patients' termination of cancer treatment.

Meanwhile, this study could not investigate the background factors that influenced the self-decision to stop cancer treatment. Decision-making is a multi-factorial and complicated process; therefore, in the future, prospective studies considering the influences of multiple background factors should be designed to examine the significance of self-decision more accurately.

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