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Determining desire to live among patients with advanced hepatobiliary-pancreatic cancer for whom curative treatment is not indicated

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Abstract: This study aimed to evaluate the desire to live among patients with advanced hepatobiliary-pancreatic cancer who were excluded from radical treatment and to examine the ideal nursing support for them. We recruited 18 patients in a department specializing in the treatment of hepatobiliary-pancreatic cancer at a university hospital in the metropolitan area of Japan. We included those with advanced hepatobiliary-pancreatic cancer who received a treatment other than definitive treatment. We conducted semi-structured interviews, and the responses were analyzed qualitatively and descriptively. Events experienced by patients with advanced hepatobiliary-pancreatic cancer and out of indication for radical treatment were divided into five major phases, while desire to live was divided into 11 categories. Two of these categories were represented by the word "death". The desire to live was present in all phases, and the expressions of these desires were diverse. Patients suppressed expressing their desire to live because they understood that their situation was challenging. In addition, there was a tendency to avoid expressing their desire to live to medical staff and their families. We found that nurses need to establish a medical relationship in which patients can express their desire to live and become connected to nursing support.

***Keywords*:** advanced cancer, well-being, nursing support, chemotherapy, intractable cancer

Introduction

Hepatobiliary and pancreatic cancer are subjected to poor prognosis because the number of morbidities and deaths are almost equal. In Japan, the five-year relative survival rate for regional lymph node metastases and invasion of adjacent organs is 3.5% for liver cancer, 1.9% for biliary tract cancer, and 1.3% for pancreatic cancer (*1*), which is extremely low when compared to other forms of cancer. One of the many factors attributed to these percentages is an extremely high recurrence rate even after radical surgical resection (*2-4*). In addition, biliary-pancreatic cancer and non-viral liver cancer are difficult to detect at an early stage. Hepatitis-derived hepatocellular carcinoma may be associated with cirrhosis and markedly impaired liver function, making some patients ineligible for surgical resection and making radical cure difficult (*5-7*). Chemotherapy, which is administered when surgical resection or effective local therapy (*i.e.*, radiofrequency ablation [RFA] or transcatheter arterial chemoembolization [TACE]) is unavailable, has very few drug options and a poor response rate (*2,8,9-11*). Advanced hepatobiliary-pancreatic cancer is generally treated as an intractable form of cancer.

Since hepatobiliary-pancreatic cancer progresses asymptomatically, most patients are diagnosed with an advanced stage of cancer. Consequently, patients are deeply shocked by the sudden diagnosis (*12*) and experience a high proportion of psychological distress during treatment (*13-15*). In addition, patients with hepatobiliary-pancreatic cancer show more depressive symptoms (*16,17*) and experience a lower quality of life than healthy people and patients diagnosed with other forms of cancer (*18,19*). When advanced hepatobiliary-pancreatic cancer is beyond the scope of curative treatment, not only are treatment options limited, but there is also uncertainty about the continuity of treatment. Therefore, it is commonly presumed that patients will experience an immense psychosocial burden.

In Japan, a previous study (*20*) reported the various implications regarding the feelings of patients with advanced cancer who wish to continue treatment knowing that they cannot be cured. It was found that these patients have a strong desire to live and hold positive expectations for treatment. Some qualitative studies have reported the experiences of patients under treatment for an advanced stage of cancer, in which patients expressed "I want to stay alive" (*21,22*). For patients with intractable cancer, receiving treatment is the only hope (*23*). Moreover, they are more eager to survive in the face of the side effects of treatment and endure them (*24*). It is presumed that patients with advanced hepatobiliary-pancreatic cancer, who are excluded from curative treatment, want to stay alive with standard treatment, despite knowing they are incurable. However, few studies have focused on the implications of these patients' desire to live.

In this study, we clarify how patients with advanced hepatobiliary-pancreatic cancer who are not indicated for curative treatment continue to feel the desire to live, based on the events they experience during the treatment process. By doing so, we will deepen the understanding of patients and consider the role of nursing support.

Methods

Study design

Qualitative research has been used by psychologists and sociologists since the early 20th century. The life events that humans experience are interdependent and form complex fabrics (*25*). A narrative refers to the making of meaning through personal experience by way of reflection, in which storytelling is a key element, and metaphors and folk knowledge take what place (*26*).

This study evaluates patients diagnosed with advanced hepatobiliary-pancreatic cancer, a rare form of intractable cancer, not identified for curative treatment. To investigate such rare phenomenon, it can be challenging to secure a sample large enough to achieve the representativeness and generalization required for survey research. Additionally, to understand the complexity of the patient's experience, it is necessary to be in their proximity to gain insight. Therefore, it was appropriate to use qualitative research for this study.

Definition of terms

"*Desire to live*": With reference to research by Morishita *et al.* (*20*), we defined desire to live as the desire of patients with advanced hepatobiliary-pancreatic cancer to continue receiving standard treatment despite their poor prognosis and absence of a curative treatment. There are individual differences in their expression of the desire to live such as "want to stay in the world" or "do not want to die".

"*Standard treatment for advanced hepatobiliary-pancreatic cancer that has been excluded from curative treatment*": Standard treatment is a method specified in the treatment algorithm of clinical practice guidelines created by the Japanese Society of Hepatology, Japan Pancreas Society, and the Society of Hepatobiliary and Pancreatic Surgery, most of which have adopted chemotherapy and radiation therapy. Recently, a large study in Japan has shown that survival rate of RFA is equivalent to that of surgical resection (*27*). In addition, TACE has been reported to improve prognosis (*3*), so we decided to exclude RFA and TACE for liver cancer.

Recruitment of the participants

The participants of this study consisted of patients visiting the oncology department of a university hospital in the Tokyo metropolitan area. The selection criteria were as follows: a formal diagnosis of advanced hepatobiliary-pancreatic cancer, receiving chemotherapy or radiation therapy beyond the indication of a curative treatment, aged between 20 and 80 years, and having a performance status of 0 to 2. Moreover, we excluded those who had difficulty communicating, a mental illness or cognitive problems, and serious complications such as cancer or heart conditions.

Data collection and procedure

The data were collected from March 2017 to August 2018. We asked the doctors who cooperated in this study to select eligible patients and provide them with an overview of the research during outpatient treatment. We offered a more detailed explanation to patients interested in the study.

To collect the data, we developed a semi-structured interview guide to include processes ranging from detecting cancer to ongoing treatment, changes in physical and psychological conditions, and relationships with healthcare providers (Table 1).

The interview time was limited to 40 minutes. However, where additional data were required, interviews were conducted multiple times with patients' approval. In addition, as complementary data for the interview, we observed patients' appearance during outpatient visits and hospitalization.

Data analysis

The data were analyzed qualitatively (*25*). First, we read the recorded data thoroughly and carefully, focusing on the statements that expressed patients' desire to live, and coded each statement. Second, we combined similar codes to generate subcategories. By considering the differences and similarities in the subcategories, we weighed the time course of the events experienced by the participants, finally integrating them into the categories. We then created a structural diagram with categories arranged to visualize the transition of patients' desire to live.

To ensure reliability, we conducted participant observations for nearly 20 months and continuously compared the data directly obtained from the participants. We also had regular discussions with nurses and researchers involved in cancer treatment (*26*). This entire process was supervised by a qualitative research expert who confirmed the validity of the analyses.

Table 1. Semi-structured interview guide

Outline	Interview question
Process from detection of cancer to treatment	Please tell us about your work and daily life before your diagnosis. What did the doctor tell you? How did you feel about the diagnosis and treatment? Why did you decide to have treatment?
Changes in physical condition	How have you changed physically since you started treatment? How do your symptoms affect your daily life? How do your symptoms affect your feelings? What do you do about your symptoms?
Changes in psychological condition	How has your psychology changed since diagnosis and the start of treatment? Do you have any concerns? When do you feel positive/negative? How do you cope with difficult times?
Relationships with healthcare providers	What do you discuss with your healthcare provider? What has been your most memorable experience of working with healthcare professionals? What are your requirements for medical care and staff?

Table 2. Participants' characteristics

ID	Gender	Age	Diagnosis	surgical history	Month of chemotherapy	Employment status
A	Female	50	Recurrence of pancreatic cancer	surgical resection	1	Employed
B	Male	50	Pancreatic cancer with hepatic artery infiltration	none	16	Employed
C	Male	50	Pancreatic cancer with liver metastasis	none	3	Employed
D	Male	50	Pancreatic cancer with liver metastasis	none	17	Medical leave
E	Female	50	Bile duct cancer Lymph node metastasis	none	3	Unemployed
F	Female	50	Bile duct cancer with liver metastasis	none	3	Employed
G	Female	60	Pancreatic cancer with liver metastasis, peritoneal dissemination	none	12	Unemployed
H	Female	70	Pancreatic cancer and lung cancer (double cancer)	none	28	Unemployed
I	Female	70	Recurrence of pancreatic cancer	surgical resection	17	Unemployed
J	Male	70	Pancreatic cancer with hepatic artery infiltration	none	15	Retired
K	Female	70	Recurrence of hepatocellular carcinoma	surgical resection	2	Unemployed
L	Male	70	Recurrence of hepatocellular carcinoma	surgical resection	2	Retired
M	Male	70	Recurrence of hepatocellular carcinoma	surgical resection	24	Retired
N	Female	70	Pancreatic cancer with hepatic artery infiltration	none	1	Unemployed
O	Male	70	Pancreatic cancer with hepatic artery infiltration	none	4	Employed
P	Female	70	Pancreatic cancer with lymph node metastasis	none	1	Unemployed
Q	Female	70	Pancreatic cancer	none	5	Unemployed
R	Female	80	Gallbladder cancer with lymph node metastasis	none	5	Unemployed

Ethical considerations

We used the research explanation document to inform participants about the purpose and methods of this study, their free will to participate and withdraw from the research, protection of their personal information, and disclosure of research results. Subsequently, participants gave their consent in writing.

We surveyed in a private room where participants could maintain confidentiality and confirm the stability of their physical condition and side effects before and after the interview. This study was conducted in accordance with the Declaration of Helsinki principles and approved by the Ethics Review Committee of the National Center for Global Health and Medicine (approval number: NCGM-G-002109-00), the Ethical Review Committee of the Faculty of Medicine, and the Faculty of Health Sciences attached to the institution where the research was carried out (approval number H28-166 and 902).

Results

Participants' characteristics

During the survey period, 18 patients, 7 males (38.9%) and 11 females (61.1%), received a referral from a doctor and provided their consent to participate (Table 2). The average age of participants was 67.2 (± 10.2) years. Regarding the types of carcinomas detected, 3 (16.7%) participants had liver cancer, 12 (66.6%) had pancreatic cancer, and 3 (16.7%) had gallbladder and bile duct cancer; most of them had distant metastases. Either RFA or TACE was performed previously on 13 (72.2%) participants who had already opted out of radical treatment at first onset and 5 (27.8%) who relapsed after surgical resection. All participants were receiving chemotherapy for an average duration of 8.8 (± 8.6) months. Interviews were conducted one to three times per person. In total, there were 27 interviews, which took 1,242 minutes.

Patients with advanced hepatobiliary-pancreatic cancer who were no longer eligible for radical treatment and wanted to live

The analyses led to identifying 11 categories, of which 2 were represented by the word "death", a thought-provoking word meant to cause reflection on the termination of life. We observed that such paradoxical expressions of life underlie the desire to live. Events experienced by patients with advanced hepatobiliary-pancreatic cancer who were out of indication for radical treatment were classified into five major phases: "Cancer detection", "Receipt of diagnosis/notification", "Seeking a place to receive treatment", "Receipt of treatment", and "Uneven therapeutic effect".

Belief that the disease was curable

Participants were made aware of their physical condition through medical examinations and subjective symptoms. Those who presented no history of drinking, smoking, or problems in their medical examination six months prior did not consider the abnormalities significant. They reported that in the few days before their definitive diagnosis, living was "matter-of-fact". Therefore, participants strongly believed that they could be discharged or return to their healthy selves when the symptoms subsided. One such participant stated, "When I was admitted to the hospital because of jaundice, I thought I would have to cure only that. I didn't think it was a rainy day". (ID: M)

Everything is overshadowed by death

During cancer treatment, participants received three notifications. The first informed them of their refractory and progressive disease, the second was that Stage IV was already unresectable, and finally that the treatment was limited. In addition, some doctors affirmed life expectancy. Some participants who had suffered from another type of cancer and overcame it perceived this multiple announcement method to be different from their past experiences. Both new and recurrent patients were unwilling to accept the information and reported that it did not feel real. In particular, new patients said they had no hope of living or were about to give up on living. In fact, one of them reported, "Until the treatment started, I felt like I was dead. On my way to work, the people I passed by looked so energetic that it was very painful. I am still very lonely". (ID: A)

Cannot die yet

Despite being aware that they would most likely die, participants sought treatment because of the importance they gave to their parents, children, and spouses; they prioritized their families over themselves. Some participants stated that they could not afford to die because they had children with illnesses or disabilities, while others in their 70s and older, caring for their parents and grandchildren, reported the same feeling. One of them stated, "Old mother is still alive. So, I thought I couldn't go away first". (ID: E)

Unfulfilled wishes

After the cancer diagnosis, some participants requested a second opinion. They hoped to somehow receive effective treatment and survive cancer. However, those doctors expressed harsh opinions, such as "It is too late to treat". The participants were disappointed because they felt that people with medical conditions like theirs might not be allowed to express that they want to live: "At the time of the announcement, the doctor told me that the survival rate of pancreatic cancer was about five years even for Stage I people. I was in Stage IV, so I thought it would be impossible to survive". (ID: H)

"Maybe I can live"

A doctor at a research facility specializing in the treatment of advanced hepatobiliary-pancreatic cancer stated that participants were relieved when doctors presented a new regimen or announced that treatment would begin immediately. For instance, one of the participants stated the doctor denied the use of the term "terminal cancer". "The doctor said, 'Who said? I only use the term terminal cancer when there is not one thing I can do'. I was very happy, because he said, 'Let's do our best because there is still something I can do'." (ID: E)

Continuing treatment and living as long as possible

Participants recognized that the only way to stay alive was to receive treatment. Those who experienced side effects such as peripheral neuropathy were concerned that worsening of symptoms would prevent their visit to the hospital; hence, their desire for receiving an effective drug was stronger than their fear of treatment. One of them reported, "I'm just hoping that this treatment will go well now. I have the goal of staying alive for as long as possible". (ID: C)

Want to continue planning the future even with illness

Participants said they were jealous of the elderly after being notified of the cancer because they could not imagine themselves living for 10 more years and thought they had no choice but to suffer from intractable cancer. These participants were unambitious and set realistic goals to remain calm in the days ahead. One of them stated, "I have a daughter in the third year of college. I wish I could see her as a bride and the face of a grandchild. I used to think that I would live long until I was 80 years old, but now I wish I could live for 5 years... 10 years". (ID: F)

Constantly anticipating death

Despite feeling hopeful during the treatment, participants always felt profound anxiety. One of them reported feeling a lack of time and, in urgency, told their family to prepare for death. However, there were instances where participants reported avoiding discussions with family and friends about cancer-related anxiety and dying due to the seriousness and privacy of the matter. In fact, one participant stated, "I don't want to be distracted by telling my friends so many negative things, so I won't tell them. You have to be prepared... But... I'm worried about the death in front of me... Even though I am prepared...". (ID: I)

Willingness to do anything to stay alive

Participants did their best to survive during treatment. They remained self-motivated by believing that there might be a cure one day. Consequently, they collected a wide range of information on advanced and alternative medicine on the Internet. Some even expressed their willingness to participate in new clinical trials. In fact, one of them reported, "I'd like to talk to my doctor about combining treatments that are not covered by insurance. I don't have the evidence. It depends on how your doctor decides...". (ID: O)

Death may be difficult to overcome this time

When the therapeutic effect of the treatment started to wear off, one of the participants lost physical strength and motivation to fight due to weakness and difficulty in commuting. In addition, those who hoped to survive through the third line of treatment were disappointed when their doctor recommended hospice care rather than the third line of treatment. One of them reported, "When I went to visit a hospice, the doctor there told me, 'I think hospice is better than living on third rate drugs'... At this point, it seems that treatment or no treatment will make no difference". (ID: B)

Do not want to die

When an undulation of the therapeutic effect appeared, participants became increasingly motivated to continue their current treatment and extend their lives. However, one of the patients refrained from communicating with family and medical staff to avoid confusion or sadness. Talking to a medical practitioner about home care and hospice distressed another patient, as this gave the impression of accepting death. The patient stated, "We asked Mr. A from the Cancer Counseling Support Office to introduce us to the people at the Regional Comprehensive Center. I decided to ask about home-visit nursing. But I don't really want to die... I want to live a little longer for my son and my husband". (ID: H)

Structural diagram of desire to live in patients with advanced hepatobiliary-pancreatic cancer for whom curative treatment is not indicated

Figure 1 is a structured representation of the changes in desire to live during the five phases. In investigating the characteristics of each category, "positivity toward life" was shown as a white ellipse, "negativity toward life" was shaded, and "related to death" was black.

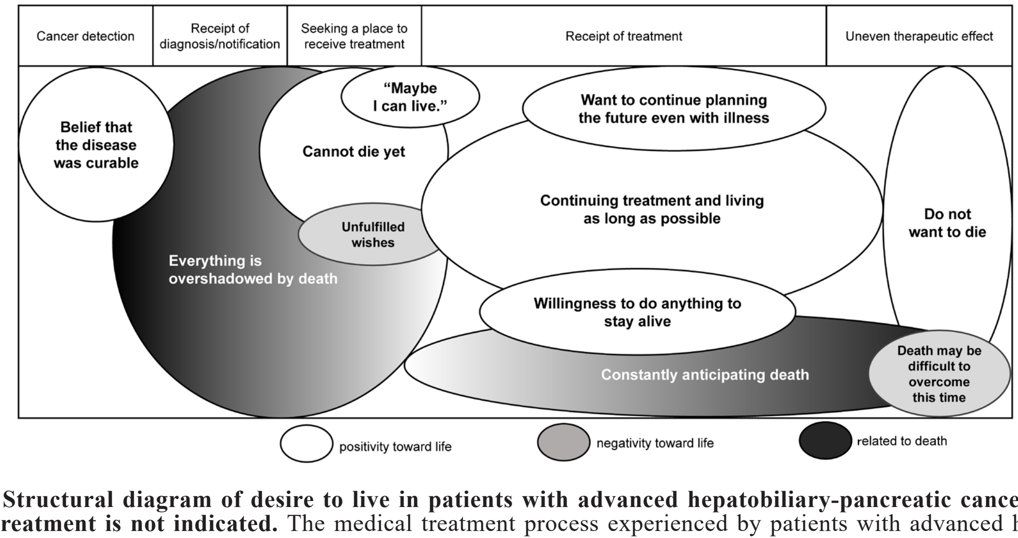

Figure 1. Structural diagram of desire to live in patients with advanced hepatobiliary-pancreatic cancer for whom curative treatment is not indicated. The medical treatment process experienced by patients with advanced hepatobiliary pancreatic cancer who are not indicated for curative treatment is shown in five stages, and the category of desire to live is placed there. Patients continued to express their desire to live in various ways, such as positive or negative, and using the word death.

An overview of Figure 1 shows that patients experienced changes in their desire to live and have an uninterrupted involvement in all the phases of treatment. Their expressions were diverse and associated with life-threatening events. Patients revealed feeling positive as well as negative toward dying, even though the treatment made them hopeful. The illustration of the desire to live provides an overview of the extracted categories and the observations of patients trying to stay alive.

Discussion

Aspects of patients with advanced hepatobiliary-pancreatic cancer for whom curative treatment is not indicated

This study assessed the desire to live, based on the events they experienced during the treatment and recuperation process, in patients with advanced hepatobiliary-pancreatic cancer who had been excluded from curative treatment. By dividing their experience into five phases and structuring the categories, it became clear that the patients' desire to live undergoes changes depending on their situations and that multiple thoughts can occur in conflicting times. These patients were found to have an uninterrupted – sometimes complex – expression of the desire to live. The desire to live in patients with advanced hepatobiliary-pancreatic cancer who had been excluded from curative treatment began with their belief that their disease was curable. However, after the diagnosis of refractory cancer and receiving a series of discouraging news, their feelings of positivity toward life diminished and they surrendered to death. Nevertheless, some participants insisted that they could not die yet because of their loved ones and fought to live through self-help. In the likelihood of being unable to regain their will to live, they might have abandoned the opportunity to survive, resulting in abandonment of information gathering and treatment. It is important to help patients with intractable or difficult-to-cure cancers find a place to receive treatment as soon as possible.

During the treatment period, the participants remained positive, yet also realistic and unassuming, while thoughts of death existed in them. The words and actions of patients with advanced cancer anticipating death have various meanings, including "an expression of the will to live" and "a desperate cry describing the misery of the present" (*28*). The narratives of death by patients who have incurable cancer should not be isolated from their desire to live. We need to be mindful of the fact that patients' narratives may paradoxically express a desire to live. In addition, the fact that there are many ways of expressing the desire to live suggests that patients are in control of their desire to live. The participants in this study were aware that their disease was incurable and the future was uncertain; thus, they did not have a strong desire to live. The more advanced the cancer is, the greater the focus of healthcare professionals may be on the treatment, and the lesser they may be able to recognize a patient's desire to live. Therefore, it is important for medical professionals to understand that such patients continue to desire living and offer an environment in which they can express it.

The results of this study verbalize the sensitive and sincere feelings of patients and will be an important resource for understanding not only advanced hepatobiliary-pancreatic cancer but also intractable cancer in Stage IV patients. We believe that this study will contribute to nursing support for patients with intractable and advanced cancers.

The importance of patients expressing their desire to live

This study found that patients were careful not to bring up serious topics in conversation with family and friends during treatment. It is also possible that they did not consult any medical professional during their treatment, nor did they think of doing so. Perception of refractory and Stage IV cancer may be one of the reasons for participants being unable to express their feelings to others. In Japanese media and on the Internet, there is an increasing amount of negative published content about intractable cancers such as advanced hepatobiliary-pancreatic cancer. Furthermore, some healthcare providers have classified patients with Stage IV intractable cancers as being near the terminal stage, that is, as "dying people". Such prejudice makes patients even more distressed (*15*). The more negatively people and healthcare providers perceive the course of a patient's life as incurable, the more difficult it will be for the patient to express that he or she wants to live.

Fortunately, with the accelerating development of new drugs, the number of patients with Stage IV refractory cancer who can maintain their health by continuing treatment is increasing. The survival rates for liver and pancreatic cancer in Japan are generally improving (*1*). The development of advanced medicine, new treatments, and measures to reduce side effects will enable patients with intractable cancers to extend their lifespan. Thus, it is necessary for medical practitioners to change the existing value system with the progress in medicine and medical care and dispel their perception of Stage IV intractable cancer.

Recently, the importance of Narrative Based Medicine in considering patient-centered medicine has been increasing (*29,30*). However, it is not easy to draw a story from the patients who keep their thoughts to themselves. Nurses can largely contribute to deciphering the messages behind the patients' words and work to understand the patients' desire to live. Furthermore, the ability to carefully interpret the patients' symptoms and feelings and to read their silence is also essential. Creating a medical treatment environment in which patients can express their desire to live will not only help patients to process complicated information but also come to terms and have a better understanding of their suppressed feelings. A previous study reported that sometimes, speaking can create healing effects for patients themselves (*31*). When patients communicate their desire to live, healthcare providers need to be receptive and exercise patient-centered medical care. Ultimately, even if the treatment is interrupted, healthcare providers should consider the patients' desire to live as realistic and willingly seek ways to empathize with the patients.

Limitations

In this study, theoretical sampling was performed at medical institutions that specialize in the treatment of hepatobiliary-pancreatic cancer. Although there were patients from all over the country, the number of cancer types was biased due to the scarcity of patients with biliary tract cancer and the exclusion of several candidates for liver cancer.

In future studies, it would be useful to expand the number of facilities to verify the results of this study and examine specific nursing support measures that reinforce patients' desire to live.

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