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Abstract: Quality-of-life (QOL) is important for cancer patients with poor prognosis. However, QOL survey is difficult using patients. We created cancer scenarios and investigated QOL utility values among the general public using vignette-based methods. On the other hand, some scenarios may have been difficult for the general public to image and understand. Therefore, we conducted a QOL survey among physicians. This survey was conducted by interviewing physicians administering chemotherapy to patients for recurrent/metastatic pancreatic cancer. Responses were evaluated using Composite Time Trade-Off (cTTO) and Visual Analog Scale (VAS) for 11 pancreatic cancer status scenarios to be evaluated (survey scenarios). Survey scenarios consisted of health state, type and Grade of adverse events. Health status was classified into two categories: Stable disease (SD) and Progressive disease (PD). Twenty responders answered in this survey, however two responses were excluded because of inconsistent responses. The stable disease had the highest QOL value for both assessment method. Whereas progression disease (PD) had the lowest QOL value. The physicians scored higher QOL values on VAS and cTTO than the general public in all survey scenarios. The QOL values obtained by physicians were consistent with the degree of status in any assessment scenarios.

Keywords: quality-of-life; pancreatic cancer; physicians; VAS; cTTO; EQ-5D

1. Introduction

hemotherapy plays a major role in cancer with distant metastasis. In the 21st century, in addition to cell-killing drugs and molecularly targeted drugs, immune checkpoint inhibitors have emerged as anti-cancer drugs, and have greatly contributed to prolonged survival [1]. However, drug costs and medical expenses are increasing yearly, and clinical efficacy and medical economic efficiency are being questioned [2]. In Japan, the medical economic assessment was introduced in 2019 as part of medical technology assessment in the medical insurance system [3]. Quality-Adjusted Life Year (QALY) assessment is useful for medical economic assessment; however, the quality-of-life (QOL) value (utility value) evidence required for calculation is limited [4].

Patient-reported outcome (PRO)/QOL assessment is one of the secondary endpoints in many of the recent phase III trials for various cancers such as lung, esophageal, gastric, and breast cancers [5–

8]. The Food and Drug Administration (FDA) and European Medicines Agency (EMA) issued guidance on the use of PRO/QOL in 2009, and Health-related QOL (HR-QOL) in 2012, respectively, for cancer treatment assessment. In Japan, the PRO/QOL study group was established in January 2011 [9–11]. Advances in chemotherapy are believed to place importance on prolonged survival and treatment selection based on QOL assessment.

Various questionnaires have been developed to assess health-related QOL. However, to calculate QALYs, one of the outcomes of cost-utility analysis, it is necessary to measure utility values using preference-based measures (PBMs) including EuroQol five-dimensions (EQ-5D), Short Form six-dimensions (SF-6D), and health utilities index (HUI) [12–14]. In particular, the EQ-5D questionnaire method of asking specific patients to provide their QOL values is widely and commonly used. In oncology, the QOL utility value measured by EQ-5D is relatively stable for each cancer type, condition, and treatment [15]. This method is recommended by NICE, as evidenced by its valuation using the time trade-off (TTO) method for the general public in the UK [16]. Therefore, QOL is generally measured subjectively by the patient, and the health technology assessment (HTA) organizations in other countries have emphasized economic assessment using the results of QOL assessment questionnaires such as EQ-5D. However, there are many instances of poor disease prognosis or insufficient number of patients. Recently, the Vignette-based method, which investigates QOL utility values using specific disease scenarios, has been widely used for the general public [17]. In addition, Japan's cost-effectiveness assessment guideline (version 3) states that QOL value calculation method using TTO can be used as one of the measurement scales that can be converted to QALY that reflects the value of the general public [18].

Pancreatic cancer, a typical cancer with poor prognosis, is difficult to detect in its early stages and often diagnosed as unresectable due to locally advanced or metastatic cancer. The treatment for unresectable pancreatic cancer is basically chemotherapy. There are several chemotherapy options with different possible adverse events (AE) depending on the treatment choice. Depending on the severity of the side effects, QOL may be reduced. In pancreatic cancer patients with poor prognosis, QOL is important in addition to therapeutic efficacy. However, in cancer patient QOL surveys, lack of data due to deterioration in patient's health can be a problem. In the QOL survey of non-small cell lung cancer in older adults, the quantity of data decreased by 57%, and analysis results based on data only for patients who completed the survey did not reflect the overall QOL results and were biased for patients in good condition [19]. Pancreatic cancer’s prognosis is poorer than lung cancer and more likely to have insufficient data. It is considered challenging based on the feasibility of QOL data collection from clinical trials.

Therefore, we created pancreatic cancer scenarios and conducted a QOL survey among the general public [20]. We believe that we could evaluate the impact of pancreatic cancer on QOL from the perspective of the general public. On the other hand, creating disease scenarios for pancreatic cancer whose various symptoms occur in a complex and severe manner, has led to the suggestion that some disease scenarios are difficult to imagine and understand by the general public who have not experienced such and that a proper assessment of the impact on QOL is limited. Therefore, by conducting a QOL survey using a recurrent or metastatic pancreatic cancer disease scenario and targeting physicians with a deeper understanding of the disease, we believe that it would be possible to examine the limitations of surveys targeting the general public. However, there are limitations in the assessment of QOL values based on disease scenarios for medical professionals, including physicians, due to reported discrepancies in the assessments of physicians and patients. For example, in the assessment of prostate cancer symptoms, peripheral neuropathy due to taxane preparations in breast cancer, and symptoms and side effects of anticancer drugs in the palliative area, physicians tend to evaluate QOL higher than do the patients, suggesting a discrepancy in patient assessments [21–24]. It is assumed that the differences between the physician and patient are largely due to their characteristics. Therefore, it is assumed that physicians have a breaking point in a direction different from that of the general public. As such, we believe that comparing QOL survey results between physicians and the general public will help in the calculation of an appropriate QOL value for recurrent/metastatic pancreatic cancer.

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Therefore, we conducted a QOL survey of recurrent/distant metastatic pancreatic cancer scenarios for physicians and compared the results obtained with a previously conducted QOL survey results for the general public.

2. Materials and Methods

Survey

This survey was conducted by interviewing (face-to-face interview) physicians (respondents) administering chemotherapy to patients for recurrent/metastatic pancreatic cancer. This method is similar to the QOL survey conducted among the general public.

For the survey, we requested the cooperation of physicians who belong to the department of medical oncology or the department of gastroenterology at three hospitals in Japan and that administer chemotherapy for recurrent/metastatic pancreatic cancer. The participants of the survey were physicians working at three hospitals as of February 2022. In the questionnaire, we examined the age, employment category, educational background, and marital status of the survey respondents.

Responses were evaluated using Composite Time Trade-Off (cTTO) and Visual Analog Scale (VAS) for 11 pancreatic cancer status scenarios to be evaluated (survey scenarios). In addition, we conducted a survey using EuroQol 5 Dimensions 5-Level (EQ-5D-5L) as reference values.

The cTTO compares two health statuses ("Full health", and "Suboptimal health state") while changing the years of survival. It is a method of calculating the QOL value from the content of the responses when the two health statuses have the same value. The question was formatted such that the patients were asked to select their preferred prognosis case, including the Worse than death (WTD) and answers are highly reproducible, and the visual effects have a small impact. In addition, the QOL value can be calculated directly, which facilitates result interpretation. However, this format has limitations, a few of which are as follows: (1) It has several questions that require time to answer and trade-offs become difficult especially when there are many items to compare; (2) the framing effect affects the evaluability of very serious diseases.

The EQ-5D is a method used to rate a specific health condition based on a 5-point scale for five items: degree of mobility, self-care, normal life, pain or discomfort, and anxiety or depression [25]. This method has only a few items that are easy to answer and require less time. It has a high comparability because it is used in various disease areas. However, due to its 5-item 5-point assessment, its responsiveness to detailed changes and symptoms without items is low. Since the minimum value of the conversion table for the Japanese population is -0.019, it does not correspond to lower values. In addition, EQ-5D is a questionnaire created to evaluate the patient's disease status. As such, the conversion table to the QOL value is the assessment result of the Japanese general public. Therefore, the conversion of the assessment results by physicians has not always been validated. VAS is a method used to determine a specific health condition on a scale of 0–100 and calculate the QOL value [26].It is easy to visualize and answer, and it requires a short completion time. However, this method uses a scale; therefore, respondents tend to avoid choosing extremely positive or negative values, indicating that it is impossible to score worse health conditions, such as death.

The survey scenario was expressed with five items: "overview," "physical symptoms (appetite, fatigue, and body pain)," "daily life at home and outside," "mental state," and " adverse events (AE) " (Table 1). This scenario was created and used during the survey among the members of the general public. AE grades were defined by The Common Terminology Criteria for Adverse Events (CTCAE) versions 4 and 5 [26,27].

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Table 1. Definitions of health status scenario.

No	health status scenarios	Definition overview [*1]
1	SD (Reference)	State in which symptoms are SD with chemotherapy. A state of no occurrence of adverse events associated with chemotherapy.
2	SD + Neutropenia G1/2	State of SD with grade 1–2 neutropenia.
3	SD + Neutropenia G3/4	SD with grade 3–4 neutropenia.
4	SD + FN	SD with grade 3–4 FN.
5	SD + Diarrhea G1/2	SD with grade 1–2 diarrhea.
6	SD + Diarrhea G3/4	SD with grade 3–4 diarrhea.
7	SD + Nausea/Vomiting G1/2	SD with grade 1–2 nausea and vomiting.
8	SD + Nausea/Vomiting G3/4	SD with grade 3–4 nausea and vomiting.
9	SD +Neuropathy G1/2	SD with grade 1–2 peripheral neuropathy.
10	SD +Neuropathy G3/4	SD with grade 3–4 peripheral neuropathy.
11	PD	The patient's condition is deteriorating despite chemotherapy treatment. Chemotherapy has already been stopped. Therefore, no adverse events are assumed Grade 3–4.)

SD: stable disease; FN: febrile neutropenia; PD: progressive disease; G: grade (adverse events)
[*1] These differ from the scenario used directly in the study.

The cTTO was answered in the same format as the computer-based response system used in QOL surveys of members of the general public (Supplemental Figure S1). EQ-5D-5L and VAS were performed using the survey forms provided by EuroQOL [28,29].

As for the actual survey procedure, after interviewing the respondents about their backgrounds, instructions on how to answer the questionnaires were explained in the following order: EQ-5D-5L, VAS, and cTTO. Subsequently, respondents performed three cTTO exercises (evaluating "suboptimal health state" as wheelchair status, better than wheelchair status, and WTD status,), and then answered 11 survey scenario questions with cTTO. The scenarios were presented randomly. After completing the cTTO, all the 11 survey scenarios were presented again, rearranged starting from the scenario with the best health condition as considered by the respondent, and answered the EQ-5D-5L and VAS in the new order.

This study was approved by the Institutional review board of Kanagawa Cancer Center (2021-Epidemiology-99), the Ethics Committee of St. Marianna University School of Medicine, and the Ethical Review Committee of Yamagata University Faculty of Medicine.

Statistical Analysis

The primary and secondary endpoints were cTTO and QOL values, respectively and they were derived from EQ-5D-5L and VAS scale. QOL values were calculated from the cTTO, EQ-5D-5L, and VAS answers of each physician, and summary statistics were calculated for each survey scenario.

Welch t-test was used to compare the cTTO and VAS-derived survey results of the general public to the current survey results of the physicians. Based on existing studies, the equivalence margin of 0.1 for Minimally Important Difference was used for the analysis.

As this survey was targeted at members of the general public, the aggregated results based on the anonymized data were used as control and were compared to the results of the survey among physicians.

Furthermore, to eliminate the impact of respondents who may not have a correct understanding of the cTTO concept and how to answer it, respondents with inconsistencies, such as inconsistent answers to cTTO practice questions or identical answers to all questions in the actual answers, were excluded. Specifically, those that corresponded to any of the following were excluded. (1) Those who

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gave contradictory answers to cTTO exercises 1 and 2 (when the QOL value calculated in exercise 2 was higher than the QOL value calculated in exercise 1) or (2) those who answered all questions with QOL value = -1, 0, or 1. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R software version 4.0.4. [30].

3. Results

A questionnaire was sent to a total of 20 people. Responses were obtained from the 20 people for cTTO calculation; however, only 18 responses were included in the analysis. The remaining two respondents were excluded because of inconsistent responses. EQ-5D-5L or VAS responses were obtained from 16 respondents, all of whom were included in the analysis. (Figure 1) The backgrounds of the physicians included in the analysis of the questionnaire survey are summarized in Table 2. Most respondents were male physicians in their 30s(range: 26-62), and approximately 80% of them were married, with similar educational background such as university and graduate school graduates.

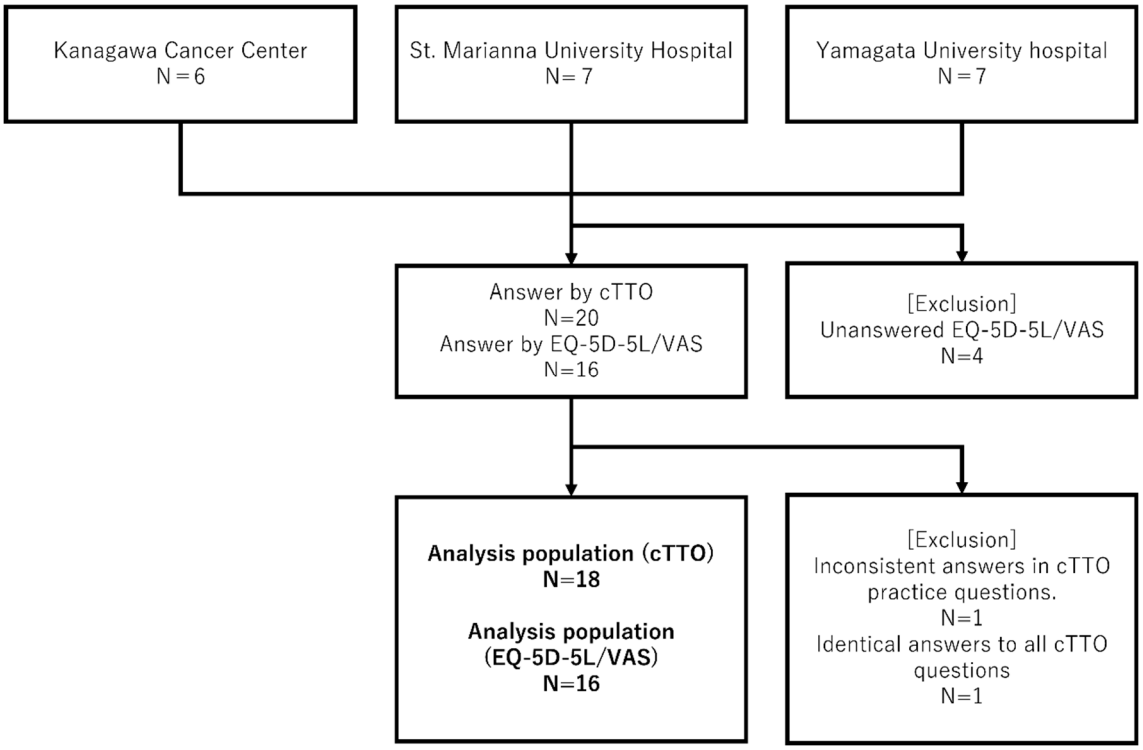

Figure 1. Participants' flow diagram.

Figure 2 shows the QOL values for cTTO, EQ-5D, and VAS survey results of the physicians for each scenario. Stable disease (SD) had the highest QOL value for both assessment methods (cTTO: 0.78, EQ-5D-5L: 0.57, VAS: 0.52), whereas progressive disease (PD) had the lowest QOL value (cTTO: 0.15, EQ-5D-5L: 0.08, VAS: 0.06). In each scenario, the values were in the order of cTTO>EQ-5D-5L>VAS.

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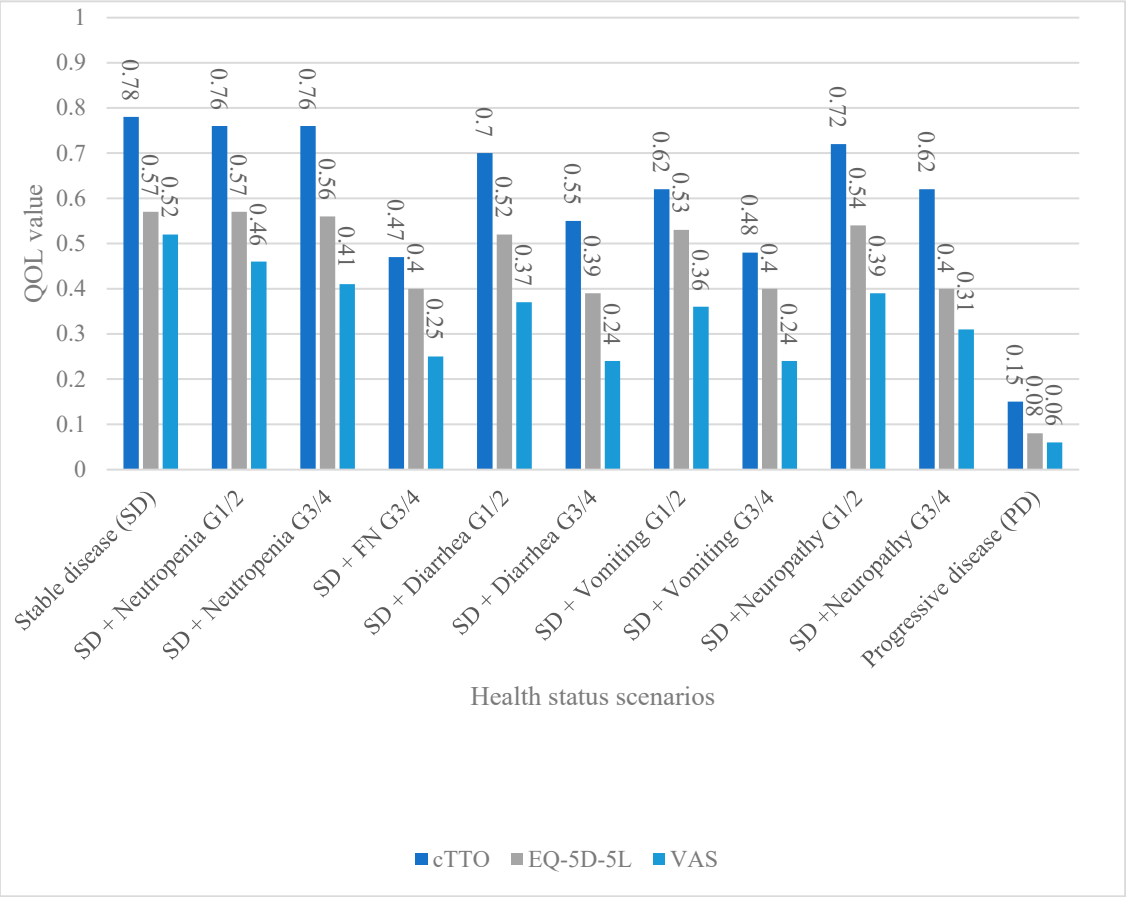

Figure 2. Comparison of the physician assessment results. FN: febrile neutropenia; G: grade (adverse events).

Regarding cTTO, compared with the members of the general population in each study scenario, the physicians scored higher QOL values than the general population in all survey scenarios. (Table 3) Regarding the order of QOL values in the survey scenarios, although there were not much differences between the respondents, the physicians ranked febrile neutropenia (FN) grade 3–4 (G3/4) lower than diarrhea G3/4 and nausea/vomiting G3/4 (physicians: 10th, general public: 8th). The ranking of G3/4 neutropenia and grade 1–2 (G1/2) peripheral neuropathy was reversed between physicians and the general public.

Table 3. Comparison of cTTO-derived QOL values in physician and general populations.

Health status scenarios	Physician				General population				P value
	N	Mean	Std	Ranking	N	Mean	Std	Ranking	
SD (Reference)	18	0.78	0.21	1	201	0.63	0.02	2	0.013
SD + Neutropenia G1/2	18	0.76	0.21	2	201	0.65	0.03	1	0.058
SD + Neutropenia G3/4	18	0.76	0.19	3	105	0.51	0.04	4	0.000
SD + FN	18	0.47	0.41	10	201	0.32	0.04	8	0.163
SD + Diarrhea G1/2	18	0.70	0.27	5	105	0.50	0.04	5	0.012
SD + Diarrhea G3/4	18	0.55	0.29	8	201	0.31	0.04	9	0.005
SD + Nausea/Vomiting G1/2	18	0.62	0.25	6	201	0.42	0.04	6	0.006
SD + Nausea/Vomiting G3/4	18	0.48	0.25	9	105	0.24	0.06	10	0.005
SD +Neuropathy G1/2	18	0.72	0.21	4	105	0.54	0.04	3	0.008

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SD +Neuropathy G3/4	18	0.62	0.28	6	201	0.37	0.04	7	0.002
PD	18	0.15	0.52	11	201	-0.12	0.04	11	0.052

SD: stable disease; FN: febrile neutropenia; PD: progressive disease; G: grade (adverse events)

By comparing the relative values of cTTO using SD as a control, there was no difference in the degree of decline in QOL values for FNG3/4 between the physicians and the general public (Supplementary Table S1). Only neutropenia G1/2 scored higher in the general public. There was almost no inter-group difference in diarrhea and peripheral neuropathy in G1/2; however, in G3/4, respondents from the general public gave values smaller than the physicians by approximately -0.1. The respondents from the general public scored neutropenia G3/4, nausea/vomiting G1/2, and G3/4 as low as approximately -0.05.

Compared to the general public, physicians tended to score higher QOL values on VAS than the general public, similar to cTTO. (Table 4). The survey scenarios ranking showed no significant difference between the respondents.

Table 4. Comparison of VAS-derived QOL values in physician and general populations.

Health status scenarios	Physician				General population			
	N	Mean	Std	Ranking	N	Mean	Std	Ranking
SD (Reference)	16	0.52	0.20	1	105	0.47	0.019	1
SD + Neutropenia G1/2	16	0.46	0.20	2	105	0.44	0.019	2
SD + Neutropenia G3/4	16	0.41	0.19	3	105	0.35	0.019	3
SD + FN	16	0.25	0.16	8	105	0.20	0.017	8
SD + Diarrhea G1/2	16	0.37	0.20	5	105	0.30	0.018	6
SD + Diarrhea G3/4	16	0.24	0.17	9	105	0.19	0.017	10
SD + Nausea/Vomiting G1/2	16	0.36	0.18	6	105	0.30	0.018	5
SD + Nausea/Vomiting G3/4	16	0.24	0.15	9	105	0.19	0.016	9
SD +Neuropathy G1/2	16	0.39	0.18	4	105	0.33	0.019	4
SD +Neuropathy G3/4	16	0.31	0.17	7	105	0.25	0.018	7
PD	16	0.06	0.22	11	105	0.11	0.020	11

SD: stable disease; FN: febrile neutropenia; PD: progressive disease; G: grade (adverse events)

Regarding the relative values of VAS using SD as control, there was not much difference in the degree of decline in QOL between the physicians and the general public in any scenario except for PD. (Supplementary Table S2). The respondents from the general public gave neutropenia G1/2 and PD higher scores.

Relative to the SD+no adverse events (AE) control, the study scenario with the least variation in QOL values was neutropenia G1/2, followed by neutropenia G3/4. The study scenarios with the greatest variation in QOL values from SD, excluding PD, were febrile neutropenia G3/4 (-0.31) for cTTO, diarrhea G3/4 (-0.18) for EQ-5D, and nausea and vomiting G3/4 (-0.27) in addition to the two aforementioned scenarios for VAS. Disutility due to adverse events was greater with cTTO and VAS than with EQ-5D. (Supplementary Figure S2).

4. Discussion

In this study, we analyzed the QOL values given by physicians on recurrent or distant metastatic pancreatic cancer. First, the QOL values obtained were consistent with the degree of status in the assessment scenarios, regardless of whether the assessment method was cTTO or EQ-5D-5L. Based on the results of the physician responses, the QOL value of SD, which was the best status, was the highest, and the QOL value of PD was the lowest in all assessments. Adverse events were ranked between SD and PD in terms of QOL, and disutility increased according to grade. In addition, only two respondents with low engagement gave inconsistent answers to the exercises or answered all questions with the same QOL value. Based on these findings, the respondents of this study were able to appropriately evaluate the situation of the scenarios and their impact on QOL; therefore, the obtained responses were considered consistent.

A comparison of the relative QOL values derived from cTTO and VAS calculated using SD + no AE as control showed that neutropenia had a smaller degree of disutility than other adverse reactions, regardless of the severity (Supplementary Figure S2). The results suggested that the effects of neutropenia are limited to laboratory values, and that its effects on the physical functions of the patients are thought to be small. There was a difference of ≥0.1 for other Grade 3/4 AEs regardless of the assessment. In general, the clinically meaningful change in the QOL value of EQ-5D in cancer is considered approximately 0.07–0.12 [31]. Therefore, Grade 3/4 AEs are considered to have a large clinical impact. Neutropenia, even at Grade 3/4, is an adverse event that is assessed through blood sampling and generally does not appear as a subjective symptom in patients. Febrile neutropenia presents with at least subjective symptoms of fever. In addition, other adverse events such as nausea and diarrhea are perceived by patients as symptoms. Based on their daily clinical experience, physicians are aware that adverse events perceived by patients are side effects that cause physical pain; therefore, we believe that they considered these events to have a significant effect on patient QOL. Furthermore, a retrospective study on the relationship between the side effects and QOL of patients with advanced pancreatic cancer reported that anorexia, pain, and peripheral neuropathy were significantly associated with decreased QOL [32]. Based on this study, it can be inferred that side effects perceived by patients as subjective symptoms have a significant impact on QOL.

Moreover, between the three assessment methods, cTTO had a higher QOL value than EQ-5D and VAS (Figure 2). As cTTO, which directly measures utility, is time-consuming and difficult to measure with actual patients, many studies targeting cancer patients have used EQ-5D. EQ-5D can convert the value measured by the patient into the value measured by cTTO, and a conversion table (tariff) for Japan is available. As it is challenging to measure TTO in cancer, it is also challenging to compare whether other cancer types show similar trends. The QOL value was higher in cTTO than in EQ-5D because EQ-5D is a method that directly evaluates physical function (degree of mobility, personal care, daily life), pain, and anxiety. Therefore, even if the status was SD, EQ-5D may have reflected the disease state of metastatic pancreatic cancer, which is more severe than in the normal state. Regarding why cTTO>VAS, the VAS ceiling effect skews the score toward the higher side in good conditions, and the floor effect skews the score toward the lower side in poor conditions. The disease characteristics of metastatic pancreatic cancer are believed to have had a stronger effect. The cTTO>EQ-5D in the comparison of relative values may be due to the evaluation of EQ-5D-5L on a 5-point scale; therefore, the effect of AE aggravation on the value was small. In cTTO, disutility in AE G3/4 was 0.16–0.31, which was considerably higher than the Minimal Clinical Important Difference (MCID) (0.07 – 0.12) (Supplementary Figure S2). The cTTO can be used to directly calculate the QOL value; however, it is necessary to carefully judge whether the QOL value of AE G3/4 based on the cTTO in this survey, where disutility deviates from MCID, is appropriate as a utility value.

By comparing cTTO and VAS assessments between the physicians and general public, we observed that the general public and physicians have different perceptions of pancreatic cancer pathology. In both assessments, physicians tended to give higher QOL than the general public. Previous studies have confirmed that the general public tends to give low QOL values. A previous study that investigated the impact of low back pain on QOL values in patients and the general public showed that the QOL value of acute low back pain was lower by 0.098 points (95% CI: 0.082 to 0.015)

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in the general public than in patients with low back pain [33]. Patients with a specific disease have a higher degree of understanding and adaptability to their condition than the general public, suggesting that the two groups do not necessarily have the same QOL values. In this study, metastatic pancreatic cancer had a poor prognosis compared to other types of cancer, and the expected survival time is short. Therefore, we believe that the general public assumes a considerably worse condition than the disease scenario of metastatic pancreatic cancer. On the other hand, the results suggested that physicians who have clinical experience with various pancreatic cancer patients had higher QOL values than the general public, even when physical functions were worsened. In addition, there were differences in the assessment order of QOL values in the survey scenarios. This may be due to the difficulty in imagining adverse events such as neutropenia and FN by the general public while it was easy to manage diarrhea, nausea, and vomiting based on patients' experiences. Therefore, we believe that physicians evaluated neutropenia and FN as having a smaller and greater impact, respectively, on QOL than the general public. In terms of relative values, the general public rated FN as having the same degree of disutility as the physicians; however, diarrhea and nausea/vomiting were rated as having more disutility. From these results, we believe that the ease of imagining adverse events affected the QOL value. Conversely, the general public may evaluate an AE such as FN that is difficult to imagine at the same degree of disutility as an oncologist's assessment; therefore, we believe that the responses of the general public and physicians to the survey scenario were reproducible, and there was no problem with the validity of the survey scenarios themselves. Compared with the general public in terms of relative values of VAS, the differences between groups in each survey scenario are almost negligible. However, we believe that the QOL value was lower than cTTO because the QOL value tends to gather smaller values due to the ceiling effect. This suggests that the difference in severe side effects may have been underestimated. (Supplementary Table S2).

There was no significant difference in QOL score ranking due to differences in cTTO and VAS assessments. On the other hand, although the QOL value of each assessment scenario deteriorated due to the ceiling effect in the VAS, the difference in the relative value of disutility due to AE against SD was similar between the assessment groups. In the assessment of PD, physicians scored 0 or greater for PD regardless of the assessment method and did not result in worse than death (WTD) as in the general public. It was assumed that the physical condition for PD in metastatic pancreatic cancer is very serious and difficult for ordinary people to imagine. However, based on the assessment results by oncologists, the value fluctuates between 0.06 and 0.15 according to the type of assessment method, suggesting that the situation is not necessarily WTD. When conducting QOL assessment using cTTO in a serious disease scenario, although it is usually assumed that the assessment tends to skew to -1 or 0 (framing effect), in this study, the impact of the framing effect may have been mitigated by the familiarity of respondents (physicians) with the actual situation of pancreatic cancer [34]. From the above, the QOL assessment using target disease scenario is different between the general public and physicians. By evaluating the QOL value of a highly severe disease status such as metastatic pancreatic cancer, it became clear that the QOL value could not always be assessed appropriately in a survey among the general public. In particular, it was suggested that it may be difficult to imagine conditions associated with physical and mental disability such as PD.

Limitations

This study had some limitations. First, the sample size of the targeted physicians is small. The study aimed to conduct an exploratory descriptive research; therefore, the required sample size was not specified. On the other hand, since the physicians who participated in this study are engaged in daily medical care of pancreatic cancer patients, it is easier for them to imagine pancreatic cancer patients who match the details of the health status scenarios provided in the assessment, and we assume that the extent of their impact on QOL will be shared. In addition, respondent engagement was extremely high. Only two of the respondents were excluded in the survey due to engagement issues. The sample size was not large; however, the order of summary statistics of QOL values in each health status scenario resulted in interpretable results.

Second, the survey scenario conditions were assumed to be the clinically worst. The survey scenarios used in this study were created according to the existing creation process frequently used for cTTO. However, in cTTO, questions were asked on the assumption that each disease state will continue for 1 year; therefore, it can be imagined that the worst state of each disease will continue for 1 year. Furthermore, in clinical practice, symptomatic therapy is implemented, and anticancer drugs are reduced or discontinued depending on adverse events and worsening of medical conditions. Therefore, the presented disease state does not necessarily last for a long time. These findings suggest that the QOL value calculated for each disease state may be underestimated compared to that in actual clinical practice.

Thrid, this study analyzed physician-evaluated QOL values for recurrent or metastatic pancreatic cancer. In addition, the discrepancy between the QOL survey results of physicians and the general public suggested that the QOL value of the general public for metastatic pancreatic cancer may not always be evaluated appropriately. In particular, disutility in the cTTO of the general public was greater than the QOL in physicians, and the disutility in severe AE and conditions was significantly greater than the disutility and MCID in existing studies. Therefore, it is necessary to consider the QOL value of cTTO of the general public as the QOL value of distant metastatic pancreatic cancer, which was similar to cTTO among the physicians. From the perspective of disutility due to adverse events, it was suggested that the results of EQ-5D-5L by physicians were the most explainable QOL values. In the results of this study, it is difficult to clarify which of the general public and physicians is closer to the patient's QOL value. From the discrepancy between the general public and physicians, there is a possibility that the QOL values of physicians and patients also differ, that physicians tended to give higher QOL than patients. However, in diseases such as metastatic pancreatic cancer, where various disease states occur in a complex and severe manner, our findings suggested that assessing the results of the survey among physicians and the general public may aid the appropriate assessment of QOL values in pancreatic cancer. In addition, PD showed an exceedingly small QOL value of 0.08, even in EQ-5D-5L, and the difference of 0.15 in cTTO was unclear. In the future, as an effect of extremely low PD QOL value, we believe that there is a need for further investigation to determine whether this reflects disease-specific condition of metastatic pancreatic cancer with a poor prognosis and whether QOL values are valid if this reflects a serious condition.

5. Conclusions

We analyzed the QOL values of recurrent or metastatic pancreatic cancer evaluated by physicians treating pancreatic cancer. In the assessment of disease scenarios that are difficult for the general public to imagine, such as highly severe medical conditions, the results suggested that conducting a survey among physicians may help in the assessment of appropriate QOL values.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. Supplemental Table S1. Comparison of cTTO-derived relative QOL values in physician and general populations (Reference scenario: SD), Supplemental Table S2. Comparison of VAS-derived relative QOL values in physician and general populations (Reference scenario: SD), Supplemental Figure S1. Example of a display screen in a composite time trade-off (English translation), Supplemental Figure S2. Comparison of relative QOL values as physician assessment result (Reference scenario: SD).

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Informed Consent Statement: Informed consent was obtained from all physicians involved in the study. The consent was obtained by completing and returning the questionnaire.

Data Availability Statement: The data used in the present study cannot be made publicly available, because the participants have not given informed consent for public data sharing, The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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