Preoperative Visitation Effect on Quality of Life of Patients Undergoing Transarterial Chemoembolization for Hepatocellular Carcinoma

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Abstract

Background/Aim: While transcatheter arterial chemoembolization (TACE) is a treatment option for patients with Barcelona Clinic Liver Cancer stage B hepatocellular carcinoma, it is associated with physical and psychological pain, with concerns regarding its effect on quality of life (QOL). In December 2020, we introduced radiology nurse-led preoperative visits to patients undergoing TACE. This study aimed to examine QOL improvement following a preoperative visit.

Patients and Methods: Among patients scheduled to undergo TACE for hepatocellular carcinoma, 48 received a preoperative visit and 22 did not (control group). We compared QOL variables between the groups using the Short-Form 36 (SF-36) at hospital admission and discharge.

Results: No significant between-group differences in clinical backgrounds were observed. In the control group, SF-36 scores at admission/discharge were as follows: physical function (PF), 42.87±14.46/34.71±19.70 and mental health (MH), 51.32±8.67/45.26±11.35, respectively. In the subgroup analysis, the PF/MH item results were PF 40.89±14.55/31.46±19.25 and MH 51.10±9.07/44.79±12.04 for older adult patients in the control group. In the preoperative visit group, PF (admission, 42.31±14.23; discharge, 41.54±14.12; *p*=0.989) and MH (admission, 48.45±10.97; discharge, 49.59±10.05; *p*=0.399) were maintained.

Conclusion: PF/MH items at admission and discharge were maintained or improved in the preoperative visit group, whereas those in the control group showed a significant decrease. Preoperative visits contributed to maintaining patient QOL.

Keywords: Hepatocellular carcinoma, preoperative visits, quality of life, transcatheter arterial chemoembolization.

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Introduction

Treatment for hepatocellular carcinoma (HCC) is selected according to an algorithm, and transcatheter arterial chemoembolization (TACE) is one treatment option, particularly for patients with intermediate Barcelona Clinic Liver Cancer stage B HCC (1), in whom it is considered a standard treatment. However, TACE is also associated with physical and psychological pain and may be associated with decreased hepatic reserve. Currently, team-based medicine is useful in various types of treatment, and the usefulness of preoperative visits has been reported even for surgeries performed in operating rooms (2-4).

Patients undergoing TACE, a minimally invasive interventional radiology (IVR) procedure generally performed under conscious conditions, may experience pain, discomfort, and anxiety (5), and the effectiveness of preoperative visits prior to TACE performed in an abdominal angiography room remains unclear. In this study, we aimed to determine whether preoperative visits by radiology nurses to patients scheduled to undergo TACE could contribute to improved patient quality of life (QOL).

Patients and Methods

The study comprised 70 patients who were scheduled to undergo TACE for HCC [preoperative visit group, n=48; control group (no preoperative visits), n=22]. Scores derived from the Medical Outcomes Study Questionnaire Short Form 36 Health Survey (SF-36) (6) were used for QOL assessment at admission and discharge.

The inclusion criteria comprised: 1) patients scheduled to undergo TACE; 2) patients who had no diseases requiring hospitalization other than HCC; and 3) patients with Eastern Cooperative Oncology Group performance status scores between 0 and 2.

The exclusion criteria comprised: 1) patients with other cancer complications, and 2) those with incomplete SF-36 questionnaires.

QOL evaluation. The SF-36, administered at admission to patients undergoing TACE and then at discharge, was used to assess QOL. The SF-36 includes four items assessing physical QOL, namely, physical function (PF), role-physical (RP), bodily pain (BP), and general health perception (GH); and four items assessing mental health QOL, namely, vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH) (6).

Between-group comparison of SF-36 score fluctuation values at admission and discharge. Between-group differences in SF-36 score fluctuations at admission and discharge according to factors in the SF-36 were compared.

Ethics approval and informed consent. The study protocols were approved by the Institutional Review Board of Saiseikai Niigata Hospital and conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013). Prior to participation in this study, written informed consent was obtained from all patients.

Data analysis. Categorical variables are expressed as numbers and percentages, and continuous variables are expressed as medians and interquartile ranges. Differences in the percentages between the groups were analyzed using a chi-square test. Differences in quantitative values were analyzed using a Mann–Whitney *U*-test. All data analyses were performed using EZR (Saitama Medical Centre, Jichi Medical University, Shimotsuke, Japan), a graphical user interface for R version 3.2.2 software (The R Foundation for Statistical Computing, Vienna, Austria) (7). All *p*-values were derived from two-tailed tests, with statistical significance set at $p<0.05$.

Results

The mean age in the preoperative visit group (37 men, 11 women) was 69.75±8.88 years, and that in the control group (14 men, 8 women) was 72.45±9.40 years (p=0.612).

The Child-Pugh (A/B-C) classification was 27/21 in the preoperative visit group and 15/7 in the control group

Table I. *Comparison of baseline data between the two groups.*

Categories	Preoperative visit group (n=48)	Control group (n=22)	*p*-Value
HBV/HCV/NASH/ALC/PBC·AIH	9/7/10/18/4	3/10/3/5/1	0.547
Age (years)	69.75±8.88	72.45±9.40	0.612
Age <65 : Age ≥65	9:39	3:19	0.741
Sex (male: female)	37:11	14: 8	0.260
Child-Pugh A/B/C classification	27/18/3	15/7/0	0.118
Initial/recurrence	18/30	7/15	0.790

ALC: Alcohol-associated liver disease; HBV: hepatitis B virus; HCV: hepatitis C virus; NASH: nonalcoholic steatohepatitis; PBC·AIH: primary biliary cholangitis/autoimmune hepatitis.

Table II. *Comparison of SF-36 score at admission and discharge between the preoperative visit and control groups.*

	Preoperative visit group			Control group		
	At admission	At discharge	*p*-Value	At admission	At discharge	*p*-Value
PF	42.31±14.23	41.54±14.12	0.989	42.87±14.46	34.71±19.70	0.023
RP	38.00±14.95	39.55±14.95	0.694	40.35±14.77	38.00±13.15	0.304
BP	51.41±12.06	50.67±10.11	0.555	52.71±11.24	52.66±9.89	0.802
GH	42.15±9.82	42.05±8.62	0.615	42.00±8.49	40.59±8.26	0.456
VT	49.43±10.19	49.88±9.51	0.805	51.35±7.74	47.35±8.23	0.083
SF	46.28±14.08	44.13±14.43	0.217	49.28±9.98	45.30±11.00	0.170
RE	43.49±13.10	42.28±13.99	0.537	41.79±13.31	40.74±12.94	0.556
MH	48.45±10.97	49.59±10.05	0.399	51.32±6.67	45.26±11.35	0.035

BP: Bodily pain; GH: general health perception; MH: mental health; PH: physical function; RE: role-emotional; RP: role-physical; SF: social functioning; VT: vitality.

(*p*=0.118). In the preoperative visit and control groups, background liver disease-related factors were hepatitis B virus (HBV, n=9 and n=3, respectively), hepatitis C virus (HCV, n=7 and n=10, respectively), nonalcoholic steatohepatitis (NASH, n=10 and n=3, respectively), alcohol-associated liver disease (ALC, n=18 and n=5, respectively), and primary biliary cholangitis/autoimmune hepatitis (PBC/AIH, n=4 and n=1, respectively) (*p*=0.547). No significant differences in first HCC occurrence or HCC recurrence were observed between the groups with (18/30) and without (7/15) preoperative visits, respectively (*p*=0.790) (Table I).

Overall, the control group had lower SF-36 scores at admission and discharge, with significant decreases in PF (admission, 42.87±14.46; discharge, 34.71±19.70; *p*=0.023) and MH (admission, 51.32±6.67; discharge, 45.26±11.35; *p*=0.035). In the preoperative visit group, PF (admission, 42.31±14.23; discharge, 41.54±14.12; *p*=0.989) and MH (admission, 48.45±10.97; discharge, 49.59±10.05; *p*=0.399) were maintained and improved (Table II).

In the subgroup analysis, a significant decrease was observed in PF in older patients in the control group (admission 40.89±14.55; discharge, 31.46±19.25; *p*=0.027) and in MH in patients with recurrent HCC in the control group (admission, 53.79±6.99; discharge, 46.59±9.64; *p*=0.019) (Table III).

In the preoperative visit group, a decrease in SF was observed in patients with Child-Pugh A classification (admission, 52.96±7.40; discharge, 48.91±11.24; *p*=0.040)

Table III. *Comparison of factor-specific SF-36 score at admission and discharge in the control group.*

	At admission	At discharge	p-Value	At admission	At discharge	p-Value	At admission	At discharge	p-Value	At admission	At discharge	p-Value
	Male			Female			Older adults (aged ≥65 years)			Adults aged <65 years		
PF	48.24±11.78	40.80±18.89	0.086	33.48±14.54	24.05±17.26	0.195	40.89±14.55	31.46±19.25	0.027	55.44±4.17	55.30±2.21	1.000
RP	41.37±15.84	40.21±14.96	0.533	38.55±13.54	34.12±8.70	0.441	40.19±15.31	36.60±13.00	0.155	41.32±13.43	46.86±12.58	0.371
BP	56.81±8.72	54.34±10.01	0.353	45.53±12.04	49.71±9.59	0.446	52.18±11.60	51.23±9.92	0.485	56.06±9.80	61.71±0.00	1.000
GH	42.51±10.12	41.75±8.90	0.875	41.12±4.96	38.56±7.10	0.310	42.47±8.65	41.34±8.52	0.679	39.03±8.28	35.84±4.95	0.500
VT	52.44±8.19	47.54±8.67	0.070	49.43±6.96	47.02±7.95	0.787	52.09±7.59	47.47±8.62	0.077	46.62±8.50	46.62±6.42	1.000
SF	49.00±10.64	47.35±10.03	0.574	49.77±9.39	41.72±12.39	0.171	50.09±9.63	44.13±11.16	0.073	44.13±12.88	52.72±7.44	0.371
RE	44.05±11.28	44.18±11.98	0.919	37.86±16.34	34.73±13.06	0.461	41.29±13.66	40.51±13.08	0.756	44.97±12.72	42.19±14.62	0.371
MH	52.57±9.08	45.69±13.08	0.117	49.14±7.99	44.53±8.22	0.232	51.10±9.07	44.79±12.04	0.053	52.72±6.75	48.24±5.59	1.000
	First HCC occurrence			HCC recurrence			Child-Pugh A classification			Child-Pugh B/C classification		
PF	47.92±10.89	41.40±14.94	0.293	40.52±15.63	31.59±21.30	0.056	40.04±16.23	30.20±18.48	0.038	48.95±7.38	44.38±20.04	0.787
RP	47.44±9.37	39.11±15.35	0.297	37.04±15.90	37.48±12.55	0.695	41.15±13.40	35.12±13.88	0.208	38.63±18.45	44.17±9.48	0.834
BP	51.84±8.07	52.65±10.25	0.834	53.11±12.69	52.66±10.09	0.726	51.33±11.14	51.41±11.22	1.000	55.65±11.74	55.33±6.07	0.855
GH	44.78±11.25	40.84±6.35	0.418	40.70±6.94	40.47±9.23	0.925	43.15±8.68	41.26±9.55	0.510	39.54±8.13	39.16±4.76	0.892
VT	50.46±6.89	46.62±5.24	0.498	51.76±8.30	47.69±9.45	0.115	52.05±7.27	47.90±9.46	0.142	49.83±9.08	46.16±5.05	0.344
SF	48.34±9.29	42.29±12.17	0.529	49.72±10.58	46.71±10.56	0.307	51.25±8.29	44.13±11.68	0.061	45.05±12.57	47.81±9.74	0.787
RE	46.89±9.48	38.23±17.45	0.106	39.42±14.42	41.92±10.77	0.807	44.57±10.12	37.48±12.87	0.064	35.85±17.90	47.75±10.75	0.178
MH	46.03±10.06	42.43±14.84	0.938	53.79±6.99	46.59±9.64	0.019	50.91±9.54	45.07±12.75	0.182	52.21±7.00	45.69±8.45	0.106

BP: Bodily pain; GH: general health perception; MH: mental health; PH: physical function; RE: role-emotional; RP: role-physical; SF: social functioning; VT: vitality.

and in patients who had first HCC occurrence (admission, 46.64±11.72; discharge, 39.12±15.55; p=0.050) (Table IV). In a comparative study of SF-36 score changes at admission and discharge, MH was maintained in the preoperative visit group (1.13±9.66) but was significantly decreased in the control group (−6.06±11.90 p=0.026) (Table V). Factor analysis showed a significant decrease in MH with HCC recurrence (admission, 1.34±9.71; discharge, −7.20±9.05; p=0.006) and among older adults (admission, 0.97±6.21; discharge, −4.47±10.16; p=0.041) when comparing the preoperative visit group to the control group (Table VI).

Discussion

To the best of our knowledge, this is the first study to investigate the effect of preoperative nurse visits on the QOL of patients with HCC scheduled to undergo TACE. We specifically investigated the significance of preoperative visits for BCLC B (intermediate) stage HCC on QOL. Notably, the significance of QOL has been reported in the treatment of various types of cancers (8-14).

A BCLC algorithm has been proposed for the treatment of HCC (1). TACE, the standard treatment in the BCLC B (intermediate) stage, is a part of IVR. Compared with surgical treatment, IVR is noninvasive while providing the same or better therapeutic effects. As such, IVR plays a significant role in improving patient QOL, particularly in those with advanced cancer.

However, with advances in systemic therapy, some patients eligible for TACE are instead administered systemic therapy, which is a more invasive form of therapy. This study was conducted to investigate the effect of invasive TACE procedures on QOL.

In this study, an overall decrease in each SF-36 score was observed pre- and post-treatment in the control

Table IV. *Comparison of factor-specific variations in SF-36 scores at admission and discharge in the preoperative visit group.*

	At admission	At discharge	*p*-Value	At admission	At discharge	*p*-Value	At admission	At discharge	*p*-Value	At admission	At discharge	*p*-Value
	Male			Female			Older adults (aged ≥65 years)			Adults aged <65 years		
PF	45.38±12.18	45.20±11.30	0.812	31.96±16.29	29.22±16.18	0.575	41.38±14.97	39.38±14.63	0.532	46.31±10.15	50.93±5.78	0.104
RP	39.64±15.36	40.76±14.28	0.809	32.46±12.52	35.48±15.83	0.834	38.17±14.40	38.37±13.56	0.658	37.26±18.06	44.64±18.72	0.100
BP	52.66±12.03	50.88±10.37	0.530	47.22±11.75	49.98±9.62	0.906	51.49±11.23	50.67±9.59	0.648	51.09±15.98	50.70±12.77	0.752
GH	43.49±10.22	43.58±8.35	0.742	37.65±5.40	36.87±7.75	0.594	42.66±8.90	41.85±8.91	0.379	39.98±12.68	42.88±7.61	0.551
VT	52.09±8.25	52.32±7.72	0.952	40.49±11.35	41.66±10.69	0.790	49.83±10.55	49.64±10.25	0.426	47.69±8.79	50.90±5.56	0.397
SF	48.66±11.25	45.87±13.55	0.114	38.28±19.64	38.28±16.41	1.000	45.62±14.74	43.64±13.89	0.227	49.14±11.05	46.28±17.35	0.590
RE	44.82±12.37	44.71±13.66	0.951	39.04±15.06	34.12±12.36	0.343	41.77±13.43	41.23±13.30	0.741	50.98±8.53	46.82±16.75	0.462
MH	51.37±8.83	51.82±8.49	0.866	38.65±12.15	42.06±11.59	0.248	48.52±11.87	49.69±10.93	0.468	48.17±6.14	49.14±5.02	0.553
	First HCC occurrence			HCC Recurrence			Child-Pugh A classification			Child-Pugh B/C classification		
PF	43.62±13.85	41.60±12.64	0.679	41.52±14.63	41.51±15.15	0.773	45.02±12.34	43.57±12.74	0.640	38.81±15.98	38.93±15.65	0.763
RP	38.18±17.43	39.29±16.18	0.925	37.89±13.56	39.70±13.94	0.627	42.92±12.79	43.58±12.14	1.000	31.67±15.41	34.36±16.20	0.513
BP	52.88±11.74	50.57±10.13	0.456	50.53±12.36	50.73±10.27	0.945	55.43±9.48	53.75±9.79	0.438	46.25±13.24	46.72±9.29	1.000
GH	44.81±8.24	42.91±11.38	0.276	40.56±10.15	41.53±6.61	0.709	45.57±9.89	43.52±9.45	0.112	37.77±7.37	40.15±7.20	0.124
VT	50.55±8.92	51.08±9.80	0.950	48.76±10.97	49.15±9.43	0.709	54.35±7.62	52.21±9.94	0.069	43.10±9.68	46.88±8.21	0.276
SF	46.64±11.72	39.12±15.55	0.050	46.07±15.52	47.14±13.07	0.720	52.96±7.40	48.91±11.24	0.040	37.69±16.04	38.00±15.97	0.824
RE	42.89±14.99	41.50±16.24	0.900	43.86±12.07	42.75±12.72	0.586	45.89±11.16	47.44±10.39	0.831	40.41±14.95	35.65±15.41	0.293
MH	48.36±11.08	49.14±10.97	0.897	48.51±11.09	49.85±9.64	0.314	51.40±9.56	52.32±9.21	0.519	44.66±11.71	46.07±10.19	0.619

PH: Physical function; RP: role-physical; BP: bodily pain; GH: general health perception; VT: vitality; SF: social functioning; RE: role-emotional; MH: mental health.

group, particularly in relation to PF and MH (*p*<0.05). Moreover, the control group exhibited a significant decrease in PF among the older adult group and MH in the HCC recurrence group (*p*<0.05), as well as a decrease in PF/VT in men, VT/SF in the older adult group, and PF in the HCC recurrence group; however, these differences were not significant. The preoperative nursing visit group exhibited a decrease in SF scores only in the first HCC occurrence/Child-Pugh A classification group pre- and post-treatment.

In the control group, QOL scores decreased overall, and there was a significant decrease in PF and MH scores (*p*<0.05). This finding was more pronounced in the older adults and those with HCC recurrence. Furthermore, the difference in scores between the groups was significantly lower in the MH group than in the PF/MH group, and this tendency was more pronounced in the older adult/HCC recurrence group.

Table V. *Comparison of the difference in SF-36 score changes at admission and discharge between the preoperative visit group and the control group.*

	Preoperative visit group	Control group	*p*-Value
PF	−0.77±13.19	−8.16±15.21	0.061
RP	1.55±13.80	−2.35±18.35	0.368
BP	−0.74±13.20	−0.05±12.70	0.959
GH	−0.11±9.49	−1.41±7.33	0.795
VT	0.45±10.71	−4.00±8.58	0.372
SF	−2.15±12.20	−3.97±15.26	0.920
RE	−1.21±13.95	−1.05±17.07	0.903
MH	1.13±9.66	−6.06±11.90	0.026

BP: Bodily pain; GH: general health perception; MH: mental health; PH: physical function; RE: role-emotional; RP: role-physical; SF: social functioning; VT: vitality.

A preoperative visit for the purpose of preoperative orientation provides an opportunity to obtain an overview of the patient and information necessary for nursing care in the IVR room. A preoperative visit has an important role

Table VI. *Comparison of differences in SF-36 score changes at admission and discharge between the preoperative visit group and the control group.*

	Preoperative visit group	Control group	*p*-Value	Preoperative visit group	Control group	*p*-Value	Preoperative visit group	Control group	*p*-Value	Preoperative visit group	Control group	*p*-Value
	Male			Female			Older adults (aged ≥65 years)			Adults aged <65 years		
PF	−0.18±11.89	−7.44±14.49	0.189	−2.73±17.39	−9.43±17.36	0.385	4.61±7.72	10.13±3.14	0.112	−2.01±13.93	−9.43±16.00	0.386
RP	1.11±13.28	−1.66±21.22	0.661	3.02±16.04	−4.43±12.86	0.361	7.38±10.08	5.54±6.92	0.364	0.20±14.29	−3.59±19.37	0.921
BP	−1.78±12.68	−2.46±12.89	0.396	2.76±14.90	4.19±11.95	0.709	−0.40±18.78	5.66±9.80	0.860	−0.82±11.88	−0.95±13.08	0.565
GH	0.09±10.39	−0.76±8.38	0.966	−0.78±5.83	−2.56±5.32	0.590	2.90±8.87	−3.20±5.41	0.835	−0.80±9.60	−1.13±7.67	0.263
VT	0.23±8.66	−4.90±8.60	0.205	1.17±16.39	−2.41±8.88	0.901	3.21±10.53	0.00±5.56	0.447	−0.19±10.79	−4.63±8.91	0.780
SF	−2.79±10.02	−1.64±15.50	0.543	0.00±18.22	−8.05±14.91	0.445	−2.86±10.74	8.59±7.44	0.478	−1.98±12.64	−5.96±15.33	0.122
RE	−0.11±13.86	0.13±15.24	0.626	−4.92±14.28	−3.12±20.85	0.678	−4.16±19.64	−2.78±2.40	0.967	−0.53±12.53	−0.78±18.40	0.774
MH	0.45±7.98	−6.88±12.94	0.108	3.42±14.21	−4.01±10.48	0.105	0.97±6.21	−4.47±10.16	0.041	1.17±10.35	−6.31±12.38	0.394
	First HCC occurrence			HCC Recurrence			Child-Pugh A classification			Child B/C classification		
PF	−2.02±14.76	−6.52±14.10	0.562	−0.01±12.35	−8.93±16.11	0.071	−1.46±12.76	−9.84±15.88	0.065	0.12±13.98	−4.57±14.11	0.395
RP	1.11±14.91	−8.33±17.38	0.287	1.82±13.35	0.44±18.69	0.687	0.66±14.32	−6.03±16.11	0.412	2.69±13.36	5.54±21.59	0.872
BP	−2.31±15.00	0.81±14.34	0.783	0.20±12.16	−0.45±12.38	0.961	−1.68±12.45	0.08±12.15	0.466	0.47±14.32	−0.32±14.83	0.470
GH	−1.89±10.93	−3.95±7.82	0.952	0.96±8.53	−0.23±7.05	0.762	−2.05±10.96	−1.90±8.01	0.608	2.39±6.63	−0.38±6.04	0.370
VT	0.54±8.76	−3.84±10.06	0.783	0.39±11.87	−4.07±8.18	0.452	−2.14±7.01	−4.15±9.20	0.979	3.77±13.60	−3.67±7.74	0.229
SF	−7.52±14.53	−6.04±16.84	0.499	1.07±9.43	−3.01±14.98	0.368	−4.06±9.65	−7.12±13.43	0.707	0.31±14.76	2.76±17.78	0.618
RE	−1.39±19.53	−8.66±11.64	0.427	−1.11±9.59	2.50±18.34	0.556	1.54±10.14	−7.09±13.84	0.079	−4.76±17.33	1.90±6.90	0.652
MH	0.78±9.84	−3.60±17.15	1.000	1.34±9.71	−7.20±9.05	0.006	0.92±9.29	−5.84±13.74	0.160	1.41±12.74	−6.52±7.41	0.061

PH: Physical function; RP: role-physical; BP: bodily pain; GH: general health perception; VT: vitality; SF: social functioning; RE: role-emotional; MH: mental health.

in IVR nursing, such as providing patient information (15). This type of visit was introduced to alleviate preoperative anxiety in patients undergoing IVR and to share information in relation to medical care. The preoperative visit's purpose was intended to reduce patient anxiety and relieve tension through addressing as many related factors as possible, and to check for physical and mental risk factors involved during treatment so that the TACE procedure could be performed safely and with patient peace of mind. Meanwhile, the evaluation of TACE treatment efficacy and the development of more effective TACE methods have recently advanced (16, 17). The preoperative visit was also used to identify various anxieties that the patients may have had in relation to the IVR treatment, help them visualize the preoperative-to-postoperative process, and promote mental and physical preparation for IVR treatment.

Study limitations. The sample size was relatively small, and the study was retrospective in design. Further multicenter, prospective studies focusing on QOL are needed. Furthermore, there were several issues in relation to the preoperative visits, namely, time constraints given the clinical load on medical staff, who may not have had sufficient time to comprehensively undertake these preoperative visits. This may have led to inadequate responses to patient questions and concerns. Furthermore, a one-size-fits-all approach may lack individualization based on each patient's background and specific needs.

Conclusion

TACE is an effective treatment for HCC, but its effect on QOL varies between patients. Treatment and side-effects

must be appropriately managed, and patients should receive support in maintaining and improving their QOL. Appropriately timed preoperative visits, regular follow-up, and support systems are likely to contribute to improved patient QOL.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

Conceptualization: Toru Ishikawa; Data Curation: Toru Ishikawa, Atsuko Suzuki, Hiromi Yamamoto, Nao Kobayashi, Eriko Nakagawa; Formal Analysis: Toru Ishikawa; Investigation: Toru Ishikawa, Atsuko Suzuki, Hiromi Yamamoto, Narumi Arita, Yusuke Matsuhashi, Nao Kobayashi, Eriko Nakagawa, Nanako Terai, Asami Hoshii, Terasu Honma; Methodology: Toru Ishikawa; Project Administration: Toru Ishikawa; Resources: Toru Ishikawa; Software: Toru Ishikawa; Visualization: Toru Ishikawa; Writing – Original Draft: Toru Ishikawa; Writing – Review & Editing: Toru Ishikawa, Atsuko Suzuki, Hiromi Yamamoto, Narumi Arita, Yusuke Matsuhashi, Nao Kobayashi, Eriko Nakagawa, Nanako Terai, Asami Hoshii, Terasu Honma.

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