

Current Status of Palliative and Terminal Care for Patients with Primary Malignant Brain Tumors in Japan

Tomokazu AOKI,¹ Yoshitaka NARITA,² Kazuhiko MISHIMA,³ and Masao MATSUTANI⁴

¹Department of Neurosurgery, Kyoto Medical Center, Kyoto, Kyoto, Japan

²Department of Neurosurgery and Neuro-Oncology, National Cancer Center Hospital, Tokyo, Japan

³Department of Neurosurgery and Neuro-Oncology, Saitama Medical University, International Medical Center, Hidaka, Saitama, Japan

⁴Gotanda Rehabilitation Hospital, Tokyo, Japan

Abstract

Palliative care and advance care planning (ACP) from the first diagnosis of glioblastoma are important. This questionnaire survey was conducted to understand the current status of palliative care for brain tumors in Japan. Representative characteristics of Japan in comparison with Western countries ($P < 0.01$) are described below: (1) Gender ratio of male in physicians who treat brain tumors in Europe and the United States/Canada are about 70%, but 94% in Japan. (2) The specialty is predominantly neurosurgeon (93%) in Japan. The ratio of neurologists is predominantly 40% in Europe. In the United States/Canada, neurologist (27%) and neurosurgeon (29%) are main parts. (3) Years of medical experience over 15 in physicians is 73% in Japan. Proportions of those with over 15 years are 45% in Europe and 30% in the United States/Canada. (4) In practicing setting, the rate of academic medical centers is about 80% in Europe and the United States/Canada, and ~60% in Japan. Representative differences compared with past domestic data (2007) ($P < 0.01$): (1) In glioblastoma, the rate of explaining about median survival time increases from 39% (2007) to 80% (2018). Explanation about medical conditions to the patient himself with his family increases from 20% (2007) to 39% (2018). (2) Place of death: The rate at hospital is decreasing from 96% (2007) to 79% (2018) and at home is increasing from 3% (2007) to 10% (2018) (3) The rate of ventilator in adult has decreased from 74% (2007) to 54% (2018), but nasal tube feeding has remained unchanged from 62% (2007) to 60% (2018). These results will be shared with physicians to make better care systems for patients with brain tumors.

Keywords: palliative care, terminal care, advance care planning, malignant brain tumor, glioblastoma, glioma

Introduction

Glioblastoma is one of the representative malignant brain tumors. The median survival time of glioblastoma is 14–16 months, and the 5-year survival rate is extremely low^{1,2)} and the 5-year survival rate of Japan is 16%.³⁾ The median survival time of elderly glioblastoma is less than 12 months.⁴⁾ From the viewpoint of other cancer types, the prognosis of glioblastoma at the time of initial diagnosis is equivalent to those at stage 4 of other cancers

including pancreatic or lung cancer, and it is recommended to consider the end-of-life care including advanced care planning (ACP) at an early stage of glioblastoma.⁵⁾ Other cancer types have comparatively long time with stable quality of life (QOL) and sharp decline in the last 3 months,⁶⁾ but glioblastoma is often accompanied with cognitive dysfunction, paralysis, and language disorders from the initial diagnosis and the half of glioblastoma patients are disabled at initial presentation with a KPS (performance status) 70 or less.³⁾ The period which needs cares and supports for patients with glioblastoma starts earlier than other cancers.⁷⁾ In 2011, the monumental study was reported that QOL and life prognosis were improved when palliative care teams intervened early in patients with advanced lung cancer.⁸⁾ The same benefit may be expected for

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patients with other cancer types including brain tumors. The demand of pain management for patients with brain tumors is relatively lower than other cancers, but early interventions of general palliative care are expected to make some significant contributions to improving QOL patients with cognitive dysfunction and motor paresis in patients with brain tumors.⁹⁾ Early ACP is also important, which enhances satisfaction with patients and their family and reduces anxiety.¹⁰⁾ Due to the differences in cultures and medical systems in each country, the percentage of patients who die at home is very low in Japan compared with Europe and the United States.¹¹⁾ In treatments, the main primary endpoint in clinical trials is prolonged survival, and the improving and maintaining QOL is main purpose in palliative or end-of-life care. There are several reports of palliative care for patients with malignant brain tumors in overseas, there are few reports in Japan. In 2017, European Brain Tumor Society (European Association of Neuro Oncology [EANO]) reported a guideline of palliative care guidelines for adult glioma.¹²⁾ In Japan as well, it seems to be important to consider the current status and issues regarding end-of-life care for patients with malignant brain tumors and their families. Therefore, we have performed this questionnaire survey for the members of the Japan Society for Neuro-Oncology (JSNO) and compared these results with those of EANO, Society for Neuro-Oncology (SNO), and past results of JSNO.^{13,14)}

Methods

The instrument used for this study was an ad hoc survey questionnaire to assess the utilization patterns of palliative care and hospice in the neuro-oncology community in Japan. The questionnaire was designed by the investigators after extensive discussions and comprehensive literature reviews of supportive care needs^{13,15,16)} and end-of-life symptom management¹⁶⁾ for patients with brain tumors.

Statistical Analysis

In July 2018, the questionnaire of 36 items was sent by e-mail to 767 members of JSNO, and in August replies were received from 154 members (20%). The same 17-item questionnaire in 2012–2013 was compared internationally with a report¹³⁾ by SNO and the EANO. In addition, we compared parts of them domestically with a 19-item questionnaire¹⁴⁾ in 2007. Demographic differences in responses to those questions were assessed using chi-square and nonparametric methods including Mann–Whitney's U test, the Wilcoxon two-sample and Kruskal–Wallis tests. SAS, version 9.2, was used for all statistical

analyses. If the test for overall differences in responses across practice regions in the world and different ages in Japan was significant ($P \leq .05$), pairwise comparisons were used to compare the responses of each pair of regions at a more stringent level ($P \leq .016$) to correct for multiple testing bias.

Results

International comparison

We compared our questionnaires in Japan with those in Europe and the United States/Canada (Table 1).

Demographics (Q1–Q7)

Q1: Regarding “gender ratio,” ratios of male in Europe and the United States/Canada are around 70%, but its ratio in Japan is 94%, which is very high.

Q2: Regarding “specialty,” the ratio of neurologists in Europe is 40%, which is main part, and rates among other specialists are almost the same. In the United States/Canada, neurologist (27%) and neurosurgeon (29%) are main parts, medical oncologist (18%) and radiation oncologist (13%) are next. The ratio of neurosurgery in Japan is 93%, which is extremely prominent.

These (Q1, Q2) can be explained by that most patients with brain tumors are treated by male neurosurgeons in Japan.

Q3: Regarding “training system of neuro-oncology,” each percentage of formal training among Japan, Europe, and the United States/Canada is not so different statistically.

Q4: About 80% of physicians who answered those questionnaires in Japan participate in Palliative care Emphasis program on symptom management and Assessment for Continuous medical Education (PEACE) workshop, which is comparable to CME lectures in the United States.

Q5: The number of patients which are examined per week in Japan is not so high comparing to those of Europe and the United States/Canada. Each rate of various groups from “under 1” to “over 15” gradually increase. The rate of group of “over 15” is main part. Each rate among various groups is roughly even balanced in Europe and the United States/Canada.

Q6: Regarding “years of medical experience,” rates of those with over 15 years are 45% in Europe and 30% in the United States/Canada, but 73% in Japan.

Q7: Regarding “practicing setting,” about 80% of it are academic medical centers in Europe and the United States/Canada, and about 60% in Japan. The system of Japan may be not so centralized.

Palliative care (Q8–Q17)

Q8: Regarding “timing of referral to palliative care,” the timing of “at the end of life” (31%) in Japan is higher than Europe (20%) and the United

Table 1 Comparison of international patterns of palliative care in neuro-oncology

Questionnaire	Variable	Response	Japan (n = 154) (%)	Europe (n = 75) (%)	United States/ Canada (n=164) (%)	P value J/E : Japan/ Europe J/USA: Japan/ United States/Canada
1	Sex	Male Female	141 (94) 9 (6)	53 (71) 22 (29)	117 (71) 47 (29)	J/E 0.000118 J/USA 0.00011
2	Specialty	Neurology Medical oncology Neurosurgery Radiation oncology Others	6 (4) 2 (1) 143 (93) 2 (1) 1 (1)	30 (40) 14 (19) 16 (21) 14 (19) 1 (1)	44 (27) 30 (18) 48 (29) 22 (13) 20 (12)	J/E 0.0001 J/USA 0.00015
3	Formal training in neuro-oncology	No formal special training Attendance at courses, CME, lectures, and conference Formal rotation during residency/fellowship	5 (3) 72 (47) 77 (50)	5 (7) 41 (55) 29 (39)	16 (10) 40 (24) 108 (66)	J/E 0.0982 J/USA 0.03255
4	Training for palliative care	No formal special training Attendance at courses, CME lectures, and conferences Formal rotation, training during residency, fellowship	18 (12) 125 (81) 11 (7)	31 (41) 34 (45) 10 (13)	62 (38) 62 (38) 40 (24)	J/E 0.144 J/USA 0.06255
5	Patients with brain tumors seen per week	<1 1-5 5-15 >15	17 (11) 29 (19) 49 (32) 59 (38)	0 (0) 15 (20) 36 (48) 24 (32)	7 (4) 49 (30) 53 (32) 55 (34)	J/E 0.553195 J/USA 0.830402
6	Practicing independently	<1 years 1-5 years 5-15 years >15 years	2 (1) 14 (9) 26 (17) 112 (73)	9 (12) 10 (13) 22 (29) 34 (45)	68 (41) 24 (15) 22 (13) 50 (30)	J/E 0.000362 J/USA 0.000282
7	Practicing setting	Academic Private/group/solo	91 (59) 63 (41)	63 (84) 12 (16)	131 (80) 33 (20)	J/E 0.000169 J/USA 0.001357
8	I prefer patients to palliative care/symptom management at the moment of:	Diagnosis Recurrent disease Onset of symptoms requiring palliation End of life Other	15 (10) 21 (14) 68 (44) 48 (31) 2 (1)	7 (9) 2 (3) 43 (57) 15 (20) 5 (7)	5 (3) 16 (10) 90 (55) 28 (17) 17 (10)	J/E 0.13073 J/USA 0.034923
9	What percentage of all of your patients are referred to hospice for end-of-life care?	0% 1-25% 26-50% 51-75% 76-100%	15 (10) 89 (58) 23 (15) 19 (12) 7 (5)	6 (8) 42 (58) 11 (15) 9 (13) 4 (6)	5 (3) 31 (20) 21 (14) 30 (19) 68 (44)	J/E 0.922304 J/USA 0.0

Questionnaire	Variable	Response	Japan (n=154) (%)	Europe (n=75) (%)	United States/ Canada (n=164) (%)	P value J/E : Japan/ Europe J/USA: Japan/ United States/Canada
10	I feel comfortable dealing with end-of-life issues on my own without the need for a formal palliative care support service	Strongly agree Agree Neutral Disagree Strongly disagree	2 (1) 14 (9) 52 (34) 63 (41) 23 (15)	12 (17) 16 (22) 11 (15) 23 (32) 10 (14)	30 (19) 54 (35) 27 (17) 36 (23) 9 (6)	J/E0.0099 J/USA0.03255
11	Our unit assesses symptom burden and quality of life on a routine basis	Strongly disagree Agree Neutral Disagree Strongly disagree	54 (35) 83 (54) 14 (9) 1 (1) 1 (1)	14 (19) 32 (44) 10 (14) 13 (18) 3 (4)	47 (30) 71 (46) 15 (10) 17 (11) 5 (3)	J/E0.000018 J/USA0.018203
12	Our unit routinely utilizes palliative medicine professionals at the time of first diagnosis for our high-grade primary brain tumor patients (WHO grade III and IV)	Strongly agree Agree Neutral Disagree Strongly disagree	9 (6) 46 (30) 54 (35) 40 (26) 5 (3)	7 (10) 10 (14) 9 (13) 31 (43) 15 (21)	9 (6) 19 (12) 25 (16) 68 (44) 32 (21)	J/E0.000011J/ USA0.000000018
13	My patients have easy referral access to outpatient palliative care services	Strongly agree Agree Neutral Disagree Strongly disagree	40 (26) 86 (56) 23 (15) 3 (2) 2 (1)	12 (17) 31 (43) 17 (24) 8 (11) 4 (6)	43 (28) 61 (39) 24 (15) 19 (12) 8 (5)	J/E0.000000029J/ USA0.0061
14	My patients have easy referral access to in-patient palliative care services	Strongly agree Agree Neutral Disagree Strongly disagree	36 (23) 83 (54) 20 (13) 12 (8) 3 (2)	18 (25) 27 (38) 13 (18) 10 (14) 3 (4)	56 (36) 51 (33) 16 (10) 22 (14) 10 (6)	J/E0.272 J/USA0.729
15	My patients have easy access to hospice services	Strongly agree Agree Neutral Disagree Strongly disagree	23 (15) 71 (46) 35 (23) 19 (12) 6 (4)	11 (15) 31 (44) 15 (21) 9 (13) 5 (7)	60 (39) 59 (38) 12 (8) 18 (12) 5 (3)	J/E0.98 J/USA0.000267
16	Patient' expectations for ongoing therapies hinder my ability to offer palliative medicine referral	Strongly agree Agree Neutral Disagree Strongly disagree	12 (8) 60 (39) 43 (28) 36 (23) 3 (2)	1 (1) 17 (24) 17 (24) 30 (43) 5 (7)	6 (4) 39 (25) 47 (31) 44 (29) 17 (11)	J/E0.000058 J/USA0.000262
17	As a brain tumor specialist, I would prefer a service called supportive care rather than palliative care	Strongly agree Agree Neutral Disagree Strongly disagree	12 (8) 46 (30) 71 (46) 23 (15) 2 (1)	20 (28) 21 (30) 20 (28) 7 (10) 3 (4)	29 (19) 64 (41) 30 (19) 28 (18) 5 (3)	J/E0.00291 J/USA0.00373

States/Canada (17%). The timing of “at onset of symptoms” in Europe and the United States/Canada is 55%–57%, which is the most major part. Physicians in Japan tend to refer late.

Q9: Regarding “referral rate to hospice at the end of life,” each rate among Japan and Europe is almost same, there is 58%–60% of physicians with its referral rate (1%–25%), which is the largest part. In the United States/Canada, there is 44% of physicians with its referral rate (76–100%), which is the largest. In the United States/Canada, the rate of referrals to hospice at the end of life is higher than other areas.

Q10: Regarding “dealing with end-of-life issues without palliative care support services,” compared to Europe and the United States, most physicians in Japan seems to feel uncomfortable.

Q11: Regarding “assessing patients on a routine basis,” the rate (35+54%) of “strongly agree” and “agree” in Japan is higher than Europe (19+44%) or the United States/Canada (30+46%).

Q12: Regarding “timing at explanation about palliative care for patients with high grade gliomas,” the rate of “strongly agree” and “agree” at first diagnosis in Japan is 6+30%, its rate in Europe is (10+14%) and in the United States/Canada is (6+12%). This timing in Japan may be a little earlier.

Q13: Regarding “easy referral access to outpatient palliative care services,” the rate of “strongly agree” or “agree” in Japan is 26+56%, it seems to be easier to refer outpatients to palliative care services than Europe (17+43%) or the United States/Canada (28+39%). But, this result in Japan may be inconsistent with that of Q10 (hospice at end of life).

Q14: Regarding “easy referral access to inpatient palliative care services,” the rate of “strongly agree” or “agree” in Japan is 23+54%, which may not be so different from those in Europe (25+38%) and the United States/Canada (36+33%).

Q15: Regarding “easy access to hospice service,” the rate of “strongly agree” or “agree” in Japan is 15+16%, which is low, comparing to 15+44% in Europe, but 39+38% of hospice service in the United States is higher than those in Japan or Europe. In the United States, hospice services may be easily available.

Q16: Regarding “patient’s expectations for ongoing therapies hindered referral to palliative care,” the rate of “strongly agree” or “agree” in Japan is 8+39%, which is higher, comparing to 1+24% in Europe and 4+25% in the United States/Canada.

Q17: Regarding “preference to supportive care than palliative care,” the rate of “strongly agree” or “agree” in Japan is 8+30%, which is lower, comparing to 28+30% in Europe and 19+41% in the United States/Canada.

Comparison with the past in Japan

Next, we compared our results with past survey in Japan which were conducted in 2007 (Table 2).¹³⁾

Cancer notification (Q18–21, Q23, 24)

Q18: Regarding “confirmation of patient’s death per year by yourself,” 47% of physicians in Japan have 1–3 patient’s deaths per year and 30% have 4–9 in 2018. This cannot be compared to past data because there are no data about this question in 2007. Physicians in JSCO confirm several patient’s deaths per year.

Q19: Regarding “how to explain about to adult patients with gliomas,” the rate of “tell pathology and grade” increased from 9% (2007) to 34% (2018). There is a tendency to explain about details including pathology and grade, regardless of age, comparing to the past.

Q20: Regarding “explanation about gliomas to the patient and his family,” there is an explanation that the context is the same to both the patient and his or her family. The rate increases almost two-fold from 20% (2007) to 39% (2018). And the rate of detailed explanations only for family members decreased from 68% (2007) to 57% (2018). It has changed into an era that physicians explains about in detail to the patient himself or herself.

Q21: Regarding “how to explain about the prognosis of glioblastoma,” the rate of explaining about median survival time increases from 39% (2007) to 80% (2018), and the rate of not explaining about in detail decreases from 41% (2007) to 13% (2018). Currently, there is a growing tendency to explain about the prognosis in detail.

Q23: Regarding “cancer notification without exception,” the rate has increased from 8% (2007) to 24% (2018).

Q24: Regarding “whom do you explain to?,” the rate of both the patient and his or her family has increased from 75% (2007) to 90% (2018), the rate of family only has decreased from 22% (2007) to 6% (2018). There is a tendency to explain about not only to the family but also to the patient, comparing to the past.

Psychiatric support (Q22,26)

Q22: Regarding “patient with depression,” the rate between treating by yourself and consulting with a psychiatrist has changed little over the last 11 years.

Q26: Regarding “treatments of restless,” about a half of physicians in Japan consulted psychiatrists about patients with restless. The rate of consulting psychiatrists may have increased from 47% (2007) to 56% (2018).

Table 2 Comparison of awareness of palliative care in neuro-oncology in Japan between 2018 and 2007.

Questionnaire		2018 (n = 154)	2007 (n = 132)	P value	
18	How many people do you confirm patient's death by yourself in a year?	0 1-3 4-9 8-10 ≥11	11 (7) 72 (47) 46 (30) 9 (6) 16 (10)		
19	How to explain about to adult patients with gliomas	1. Regardless of age, if consciousness is clear, tell pathology/grade 2. Inform pathology name/grade in consideration of age, consciousness state, and neurological symptoms 3.If the consciousness is clear and it is other than glioblastoma, regardless of age, tell the pathological diagnosis name/grade 4. If it is other than glioblastoma, tell pathology/grade in consideration of age, consciousness state, neurological symptoms 5. Inform diagnosis of glioma and prognosis 6.Inform malignant brain tumor and the approximate prognosis 7. Inform brain tumor and the approximate prognosis 8.Others	52 (34) 69 (45) 8 (5) 13 (10) 8 (5) 9 (6) 3 (2) 6 (5) 0 (0) 3 (2) 5 (3) 16 (12)	48 (36) 21 (16) 13 (10) 13 (10) 12 (9) 6 (5) 3 (2) 16 (12)	0.000001
20	How to explain to the patient himself and his/her family	1. The explanation to the patient himself and the family is the same 2. Do not give a very strict explanation to the patient himself, tell the family in detail 3. Do not announce the disease name to the patient himself, tell the family in detail 4. Others	60 (39) 88 (57) 1 (1) 5 (39)	26 (20) 90 (68) 3 (2) 13 (10)	0.000774
21	When glioblastoma, how to explain about the prognosis? Multiple answers allowed	1. Median survival time 2. Progression-free survival 3. 5-year survival rate 4. Late complication (cognitive function) 5. No explanation about details 6. Others	123 (80) 62 (40) 82 (53) 62 (40) 20 (13) 5 (3)	51 (39) 34 (26) 30 (23) 26 (20) 54 (41) 25 (19)	0.0000163
22	Treatment when depressed: Multiple answers allowed	1. Treat by yourself 2. with psychiatrist 3. No treat	65 (42) 126 (82) 5 (3)	63 (48) 104 (79) 8 (6)	0.725
23	When glioblastoma, do you announce?	1. Cancer notification without exception 2. Cancer notification in consideration of age and symptom 3. Others	37 (24) 116 (75) 1 (1)	11 (8) 92 (70) 29 (29)	0.0000001
24	To whom do you explain?	1. Patient only 2. Patient with family 3. Family only	6 (4) 139 (90) 9 (6)	4 (3) 99 (75) 29 (22)	0.000132
25	Until when chemotherapy?	1. As far as possible 2. Until patients cannot go home 3. Patient cannot judge 4. Family wish 5. Others	58 (32) 46 (30) 25 (16) 14 (9) 11 (7)	46 (35) 17 (13) 21 (16) 33 (25) 15 (11)	0.0281

Questionnaire		2018 (n = 154)	2007 (n = 132)	P value	
26	Treatment for restless patients	1. Treat on your own 2. consult with psychiatrist 3. No treat	66 (43) 86 (56) 2 (1)	67 (51) 62 (47) 3 (2)	0.227
27	Hospice for malignant brain tumor	1. Any patients 2. Mild symptoms 3. None	66 (43) 54 (35) 34 (22)	26 (20) 36 (27) 70 (53)	0.0000001
28	If a patient cannot be discharged to home?	1. Our hospital 2. Hospital with neurosurgeon 3. Hospital without neurosurgeon 4. Nursing home 5. Home care	36 (23) 29 (19) 35 (23) 23 (15) 31 (20)	58 (44) 40 (30) 24 (18) 4 (3) 6 (5)	0.0042
29	Utilization of Nursing home at the end of stage	1. Active use 2. I want to use 3. No use	36 (23) 89 (58) 29 (19)	16 (12) 73 (55) 43 (33)	0.00132
30	The timing of explaining about DNR	1. In good condition 2. No chance of recovery 3. Not explain	15 (10) 134 (87) 5 (3)	8 (6) 123 (93) 1 (1)	0.848
31	Use of ventilator at end of stage in adult patients with gliomas	1. All cases 2. More than half 3. Sometimes 4. No cases	0 (0) 1 (1) 39 (25) 114 (74)	0 (0) 3 (2) 58 (44) 71 (54)	0.000351
32	Use of ventilator at the end of stage for child patients with gliomas	1. All cases 2. More than half 3. Sometimes 4. No cases	5 (3) 14 (10) 78 (51) 55 (36)	3 (2) 20 (15) 69 (52) 38 (29)	0.127
33	When patients with gliomas at the end of stage cannot eat.	1. Nasal tube feeding 2. Gastrostomy 3. Central venous port 4. peripheral drip infusion	92 (60) 11 (7) 21 (14) 30 (19)	82 (62) 17 (13) 18 (14) 15 (11)	0.336
34	Palliative care at home	1. Strong recommendation 2. Possible recommendation 3. No recommendation	38 (25) 88 (57) 28 (18)	30 (23) 69 (52) 33 (25)	0.204
35	Place of death	1. Our hospital 2. A hospital with neurosurgeon 3. A hospital without neurosurgeon 4. Nursing home 5. Home	50 (32) 30 (20) 42 (27) 17 (11) 15 (10)	61 (46) 49 (37) 17 (13) 1 (1) 4 (3)	0.0000106
36	Opioids for brain tumor	1. Analgesia 2. Analgesia 3. Respiratory comfort 4. Others 5. No usage	59 (38) 14 (9) 25 (16) 2 (1) 35 (23)		

End of life care (Q25, 30–33)

Q25: Regarding “until when is chemotherapy continued?,” the rate of “family’s wish” has declined from 25% (2007) to 9% (2018), and the rate of “patients cannot go home” has increased from 13% (2007) to 30% (2018). Physicians in Japan become to perform more aggressive chemotherapy than before.

Q30: Regarding “The timing of explaining about DNAR (Do Not Attempt to Resuscitation),” the rate of “no prospect of recovery” has little changed from 93% (2007) to 87% (2018) over 11 years, which is a major part.

Q31: Regarding “ventilators at the end of stage for patients with malignant brain tumors,” during the last 11 years, the rate of no ventilator has decreased from 74% (2007) to 54% (2018).

Q32: Regarding “ventilators at the end of stage for child with gliomas,” “no cases” has increased from 29% (2007) to 36% (2018), “sometimes” has little changed from 52% (2007) to 51% (2018). In general, there has been no significant change for 11 years. Compared to adults, the rate of ventilator attachment for child is rather high rate.

Q33: When oral intake becomes difficult at the end of life, the rate of nasal tube feeding has remained unchanged from 62% (2007) to 60% (2018), which is very high in Japan. Nasal tube feeding is little performed in the West.

Place of death (Q27–29, 34, 35)

Q27: Regarding “hospices for malignant brain tumors,” the rate of “any patient is acceptable” has increased from 20% (2007) to 43% (2018). The number of hospices that can accept patients with malignant brain tumors has increased significantly over last 11 years.

Q28: Regarding “if patient could not go home,” the rate of “care at home” has increased from 5% (2007) to 20% (2018) and that of “nursing home” have also increased from 3% (2007) to 15% (2018). The rate of hospitals (our hospital, hospital with or without neurosurgeons) has decreased from 92% (44 + 30 + 18) (2007) to 65% (23 + 19 + 23) (2018).

Q29: Regarding, “utilization of nursing homes at the end of stage,” the rate of “active use” has increased from 12% (2007) to 23% (2018), while that of non-use has decreased from 33% (2007) to 19% (2018). The rate of nursing homes at the end of stage has been increasing over last 11 years.

Q34: Regarding “palliative care at home,” the rate of “strong or possible recommendation,” is the majority, and it has little changed from 23+52% (2007) to 25+57% (2018), over 11 years.

Q35: Regarding “place of death,” the rate at hospitals (our hospitals and hospitals with or without neurosurgeons) has decreased from 96% (46 + 37 + 13) (2007) to 79% (32 + 20 + 27) (2018), and the rate of home and nursing home has increased from 4% (1 + 3) (2007) to 21% (11 + 10) (2018).

Others (Q36)

Q36: Regarding “opioids,” there were not the question about opioids in 2007. Therefore, we cannot compare it to past data. Twenty-three percent of physicians in Japan did not use opioids for patients with brain tumors. In patients with brain tumors, the usage of opioids is thought to be less frequent, because they have less pains than other cancers.

Discussion

The response rate of JSNO members to this questionnaire in 2018 was 20%. The response rate in 2007 was 51%. The questionnaire survey in 2007 was conducted only for 259 participants at 25th annual meeting of JSNO. This time, all 767 active members of JSNO in 2018 were surveyed. The difference may affect the response rate. Those rates of SNO and EANO in 2012 were 5% and 6%. Although there are differences among those response

rates, we think those results of questionnaires might be considered to reflect and be consistent largely with general whole opinions of each society.

International comparison of demographics

In sex, man accounts for 94% and male neurosurgeons engage mainly in treating patients with brain tumors including chemotherapy and palliative therapy as well as surgery in Japan and there are few neuro-oncologist. In Europe and the United States/Canada, man accounts for about 70% (Figs. 1A and 1B). In specialty, neurosurgery accounts for 93% in Japan. However, in Europe, neurology accounts for 40%, and medical-oncology, neurosurgery, and radiation oncology account for about 20% each. In the United States/Canada, neurosurgery and neurology are lined up at about 30%, giving the impression that specialists in the United States/Canada and Europe are providing treatments in a well-balanced proportion. Treatment of patients with brain tumors involves surgery combined with radiation and chemotherapy, and in Japan both surgery and chemotherapy are performed by neurosurgeons. In Europe and the United States/Canada, surgery is by neurosurgeons, and chemotherapy is by medical-oncologists. The participation of specialists from other fields like Europe and the United States/Canada would be necessary to treat patients with various brain tumors properly.

Regarding years of experience of physicians, in Japan, 73% of physicians have more than 15 years of medical experience (Fig. 1C). In Europe, the rate of more than 15 years is up to about 45%. In the United States/Canada, young physicians with less than 5 years of experience accounted for 41% of the total. In Japan, it is only 1% and there seems to be small number of young physicians in the field of neuro-oncology. In Japan, it is an urgent issue to consider various ways and means to increase the number of young physicians which are interested in treatments for patients with brain tumors.

In Europe and the United States/Canada, patients with brain tumors are treated at mostly academic hospitals (80–84%) (Fig. 1D). In Japan, the rate of private hospitals is 41%. It may be necessary to organize many various local hospitals into several highly specialized cancer-based centers in Japan.

Cancer notification

We compare this result with past result of questionnaire survey of 132 members of JSNO in 2007, contexts of explanation about information of gliomas have become more detailed, and types of persons receiving explanations shifted from family only to the patient with his or her family (Figs. 2A and

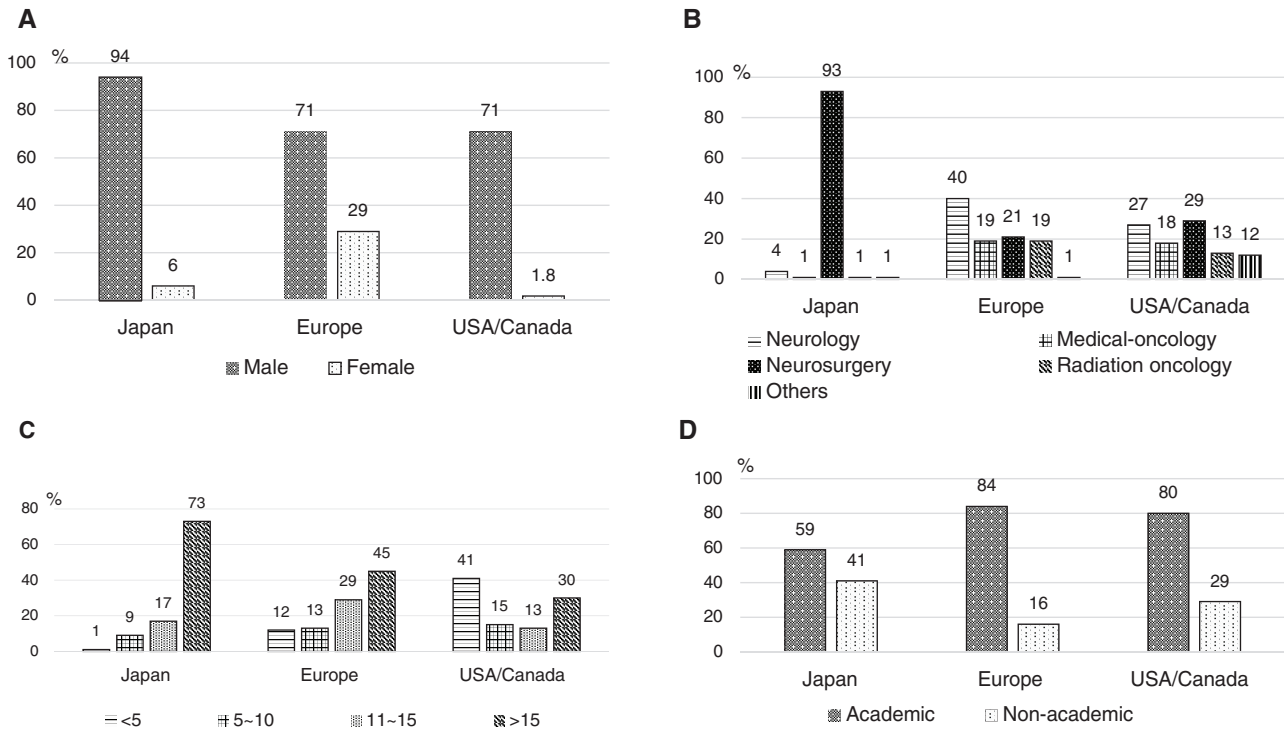


Fig. 1 Representative questionnaires: Part 1. Data of Japan from this study. Data of Europe and the United States/Canada from Ref. 14. (A) Sex of physicians in Neuro-oncology (Q1). (B) Speciality of physician in Japan, Europe, and the United States/Canada (Q2). (C) Practicing independently (years of medical practice) (Q6). (D) Practice setting (Q7).

2B). Neurosurgeons in Japan tend to explain about patient's medical information in more detail for last 10 years. Forty-one percent of physicians in 2007 said they did not explain about detailed numerical prognostic indicators, compared to 13% in 2018. In 2018, 80% of physicians explained about median survival time (MST) and 53% of physicians explained about 5-year survival time. Forty-one percent of physicians also explain about progression-free survival (PFS) and late complications. The number of physicians who explain about to the patient himself or herself was 20% in 2007, and doubled to 39% in 2018. In the last decade, more and more physicians have explained about their numerical prognostic indicators properly in Japan.

End of life care

The rate of ventilatory support at the end of life has been decreasing (Fig. 2C). In 2018, 74% did not use ventilator for patients at the end of life. 25% of physicians still use it occasionally, compared to that of 2007, though the rate has decreased. The rate of ventilator for other types of cancer seems to be almost zero in Japan. It is my interpretation

that neurosurgeons in Japan would use it under the same way of stroke treatment.

According to the question about how to provide nutrition for patients with brain tumors who became unable to eat by mouth at the end of life in Japan, about 60% of physicians in 2007 applied nasal tube feeding (Fig. 2D). The rate in 2018 is also about 60%. Like a ventilator, many neurosurgeons in Japan will apply nasal tube feeding under the manner of stroke treatment. Nasal tube feeding may be a major contributor to the survival time of glioblastoma in Japan, which is better than the West, although the PFS in Japan is almost same.^{1,17)}

Place of death

In Japan, about 80% of patients with cancers including brain tumors die in hospitals in 2018.¹⁰⁾ It is still very high. On the other hand, 10% die in nursing homes. About 80% died at home about 40–50 years ago, which is down to about 10% in the 1990s. The rate of hospital care has been declining a little in the last decade. Home care remains stable, and nursing homes has been gradually increasing. These may be affected by the Japanese insurance system or hospice system.

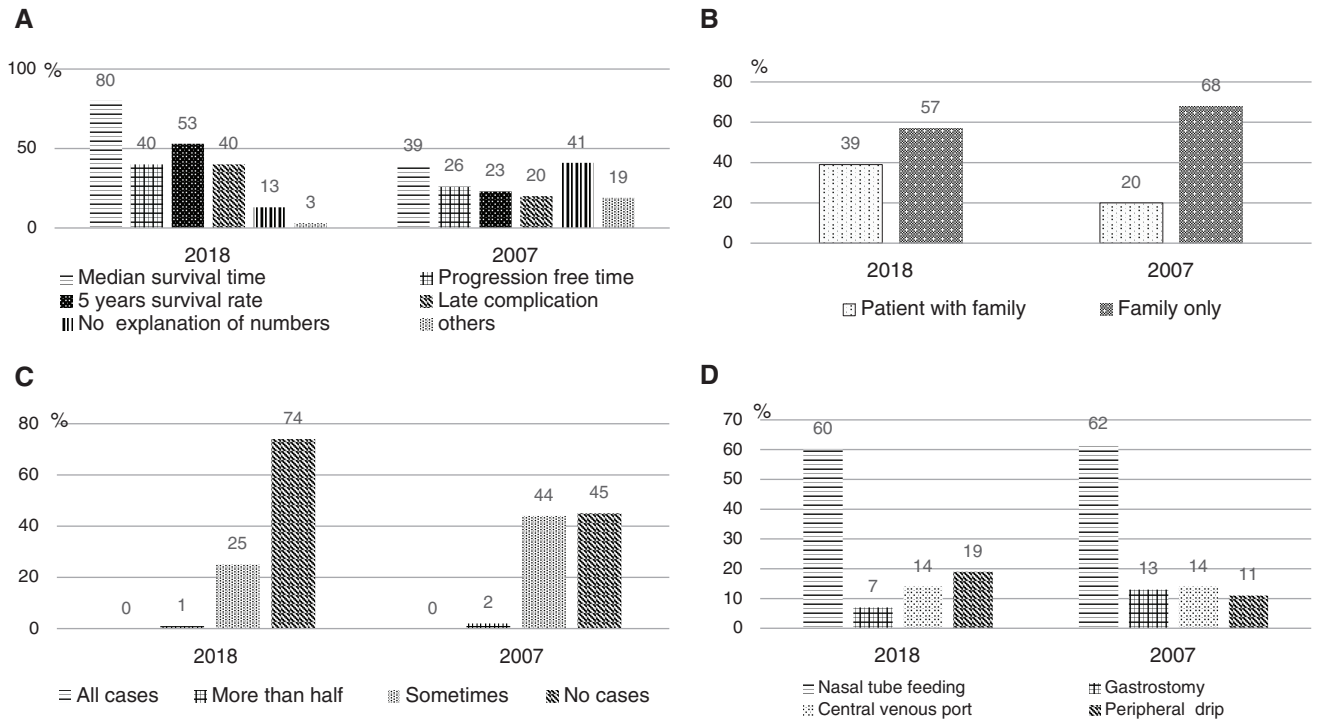


Fig. 2 Representative questionnaires: Part 2. Data of Japan from this study. Data of Europe and the United States/Canada from Ref. 14. (A) How to explain about prognosis? (Q21). (B) To whom do you explain? (Q24). (C) A ventilator at the end of stage of adult malignant brain tumors (Q31). (D) When oral intake becomes difficult at the end of stage (Q33).

The difference is highlighted when compared to overseas (Figs. 3A and 3B). Regarding places where patients with glioblastoma gliomas die, more than 80% die at a hospital in Japan (hospital with neurosurgical department: 67%, hospital without neurosurgical department: 13%, hospice: 8%, home: 5%, nursing home: 0.7%, unknown: 8%,³⁾ whereas the rate of homes in Europe (Italy/Netherlands) and hospice in the United States account for nearly 70% each.^{18,19)}

Advance care planning

The advance directive ownership ratio in Japan is extremely low compared to other countries.²⁰⁻²²⁾ It is important that ACP should become popular in Japan near future for patients with brain tumors.

In Japan, patients who are in the final stage of life tend to receive invasive intensive care in hospital until just before death.²⁰⁾ In Europe and the United States, they tend to spend with minimal care at home or hospice.

In Europe and the United States, such as the Netherlands and Germany, people have legal documents called advance directives that state whether they want treatment or care when they lose consciousness.²¹⁾ Do you want to be nourished by nasal tube

or infused by drip? Do you want to be treated as much as possible or not?

In Japan, the importance of ACP has been beginning to be emphasized. ACP is the process of discussing and sharing specific treatment/medical care and overall care goals with medical professionals and family members to receive desired medical treatment or care. In particular, early preparation is necessary for patients with malignant tumors such as glioblastoma.

In general cancers, the QOL maintains for a while and then fall shortly just before death, but that with malignant brain tumors is gradually declining from their onset.²³⁾ In particular, most patients with glioblastoma have moderate or severe dysfunction and paralysis from the early days. They will not be able to become independent in about 6 months or 1 year, and their cognitive function will be deteriorating, and communication will become more difficult.

Patients should ask their physicians about their prognosis, how illness will progress in the future, and how long it will be possible for them to keep self-sustaining. It may be scary, but it is important for the limited life. They should have a courage to ask. Physicians in charge who consider about treatments and cares should be able to answer it

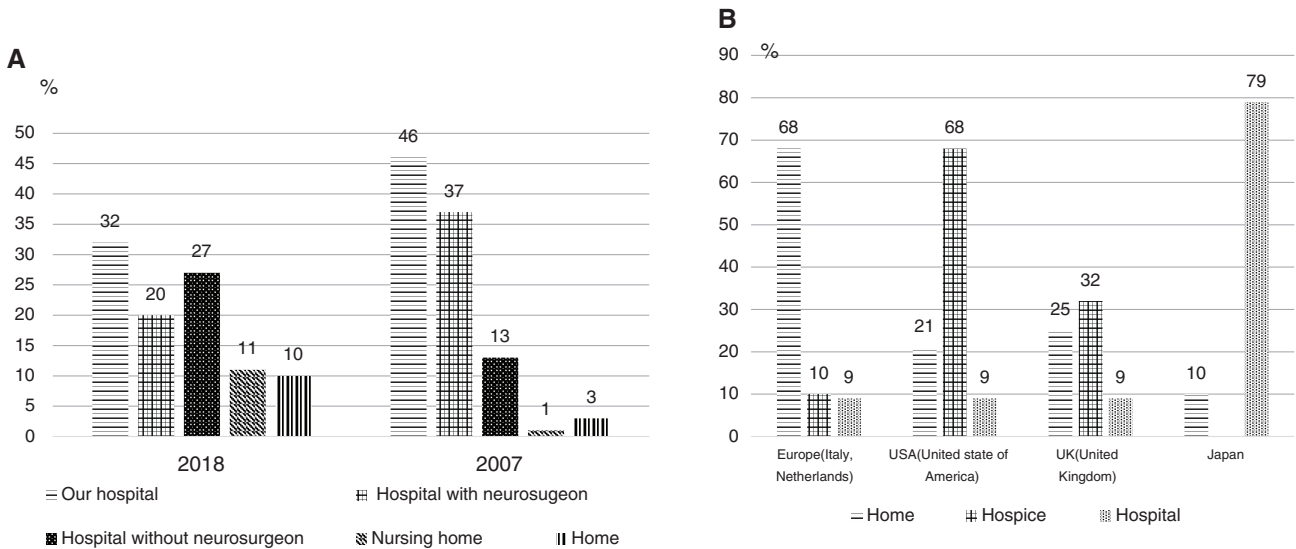


Fig. 3 Representative questionnaires: Part 3. Data of Japan from this study. Data of overseas from Ref. 10. (A) Place of death. (Comparison with the past in Japan) (Q35). (B) Place of death (International comparison).

properly. It is important to share patient's will with their family and physicians.

From this questionnaire, it seems that the situation of treatments and cares for patients with brain tumors has been improving in the last decade in Japan, but various problems have become apparent. We hope that this result will be shared with physicians to make better care systems for patients with brain tumors.

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Conflicts of Interest Disclosure

The authors declare that they have no conflict of interest.

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Corresponding author: Tomokazu Aoki, MD, PhD
Department of Neurosurgery, National Hospital, Organization, Kyoto Medical Center, 1-1 Fukakusamukai-hatacho, Fushimi-ku, Kyoto, Kyoto 612-8555, Japan.
e-mail: totorolangdom@yahoo.co.jp