



Is the 1-day surprise question a useful screening tool for predicting prognosis in patients with advanced cancer? – a multicenter prospective observational study

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Background: For cancer patients nearing death, the prediction of their prognosis by physicians is crucial. This study examined the usefulness of the 1-Day Surprise Question (1DSQ).

Methods: This study was conducted as part of a multicenter prospective observational study. The physicians answered the 1DSQ “Would I be surprised if this patient died in the next 1 day?” when patients have palliative performance scale (PPS) ≤ 20 . We calculated the sensitivity and specificity of the 1DSQ. Moreover, using multivariate analysis, we evaluated the characteristics of patients who died among those whose physicians answered the 1DSQ as “not surprised”.

Results: Overall, 1,896 patients were enrolled, and 1,411 (74.4%) were analyzed between January and December 2017. Among these, 847 (60.0%) patients were placed in the “not surprised” group. The sensitivity, specificity, and positive and negative predictive values of the 1DSQ were 82.0% [95% confidence interval (CI): 77.5–85.8%], 45.5% (95% CI: 44.4–46.4%), 27.4% (95% CI: 25.9–28.7%), and 91.0% (95% CI: 88.9–92.9%), respectively. Multivariate analysis revealed that urine output over last 12 hours <100 mL, decreased response to visual stimuli, respiration with mandibular movement, pulselessness of radial artery, and saturation of percutaneous oxygen $<90\%$ were characteristics of patients who died as predicted by the physicians.

Conclusions: The 1DSQ is a helpful screening tool for identifying cancer patients with impending death.

Keywords: Surprise question; screening tool; impending death; cancer patient; palliative care unit (PCU)

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Introduction

Accurate survival prediction of cancer patients is critical (1). It is essential for determining the goals of care among physicians, patients, and their families because many important decisions, such as those determining care plans and advance care planning depend on expected survival time (2,3). Therefore, if the responsible physicians' prognosis is inaccurate or wrong, patients may receive unwanted and harmful treatments (4). It is even more important to predict the prognosis of cancer patients with impending death because their conditions change rapidly, and individualized care that incorporates predicting prognosis is key for providing better care to patients and their families (5). Several prognostic tools such as prognosis in palliative care study predictor models (PiPS), palliative prognostic index (PPI), and palliative prognosis (PaP) Score have been utilized to predict the prognosis of cancer patients on a weekly or monthly basis (6-10). However, these tools have not been validated as tools for predicting prognosis on daily basis.

The surprise question (SQ), "Would I be surprised if this patient died in the next 12 months?" is widely known as a practicable, simple, and helpful tool for identifying cancer patients who are at increased risk of one year mortality and would respond well to hospice and palliative care (11,12). Previous studies have shown that the 7-day SQ (7DSQ), "Would I be surprised if this patient died in the next 7 days?" is a highly sensitive and feasible way to predict the prognosis (13). Our study group had previously reported that the 3-Day SQ (3DSQ), "Would I be surprised if this patient died in the next 3 days?" was also highly sensitive in cancer patients with impending death (14).

There are few screening tools to identify cancer patients who die within one day, and we examined the possibility that the 1-Day Surprise Question (1DSQ), "Would I be surprised if this patient died in the next 1 day?" may be as helpful as the 3DSQ to predict the prognosis of cancer patients with impending death. It has been previously reported that family members were most stressed during the unpredictable death of the patient (15). If the sensitivity of the 1DSQ was as high as that of the 3DSQ, physicians and family members would be able to better prepare for rapidly changing conditions at the time of ending, and allow patients and their family members to be together at the time of death.

Therefore, our aims were to elucidate the usefulness of the 1DSQ in cancer patients with impending death, and to identify the characteristics of patients who ultimately died

among those whose physicians answered "not surprised" to the 1DSQ.

We present the following article in accordance with the STROBE reporting checklist (available at <https://dx.doi.org/10.21037/apm-21-1718>).

Methods

Participants

The current study was a sub-analysis using Japanese domestic data as a part of the East-Asian collaborative cross-cultural Study to Elucidate the Dying process (EASED) data. The EASED was a multicenter, prospective, observational study conducted to better understand the process of death and terminal care in patients with advanced cancer admitted to palliative care units (PCUs) in Japan, Korea, and Taiwan.

Adult patients over 18 years old who were diagnosed with metastatic or locally extensive cancer and were newly admitted to PCUs were included. Patients who refused to be enrolled in this study or were scheduled to be discharged within 1 week were excluded. Consecutive patients were registered if they had been referred to the participating PCUs during the study duration.

The observations were conducted in daily clinical practice. The responsible physicians prospectively reported data on a data-collecting sheet created for this study, which was piloted prior to study initiation.

Data collection

We collected data regarding the characteristics of the patients and medical care received during the PCUs admission. The characteristics of the patients were sex, primary cancer site, metastasis, and past medical treatment as examples. The medical care received during the PCUs admission were oxygen and opioid administration, corticosteroid medication, infusion therapy, sedative therapy, administration of benzodiazepines, and administration of airway secretion inhibitors. Furthermore, we also collected data on patients' vital signs, physical signs, and clinical symptoms on the first day, when the patient had palliative performance scale (PPS) ≤ 20 . The vital signs were respiratory rate, oxygen saturation of peripheral artery, urine output, and body temperature. The physical signs were modified Richmond Agitation Sedation Scale score (modified RASS), pulse of radial artery,

peripheral cyanosis, bronchial secretions, respiration with mandibular movement, Eastern Cooperative Oncology Group Performance Status, dysphagia of liquids, response to visual stimuli, hyperextension of neck, response to verbal stimuli, grunting of vocal cords, inability to close eyelids, apnea periods, and Cheyne–Stokes breathing. The modified RASS has been validated as a tool for assessing the severity of agitation and sedation levels in cancer patients (16). The clinical symptoms were dyspnea, pain, fatigue, delirium, and edema. The clinical symptoms were assessed using the integrated palliative care outcome scale (IPOS). The IPOS of Japanese version has been demonstrated to be valid for assessing the physical and psychological status of patients with cancer (17).

All factors were chosen as representative factors, which we considered to be prognostic in daily clinical practice.

Measurements

We defined “day 0” as the first day on which each patient had PPS ≤ 20 ; physicians’ answers to the 1DSQ, “Would I be surprised if this patient died in the next 1 day?” were collected on this day. The same responsible physician, who collected the patient information, including physical signs and clinical symptoms, answered the 1DSQ. The response was categorized as “surprised” or “not surprised”. We followed up the patients until death, and defined “died in the next 1 day” as death having occurred between day 0 and day 1.

Data analysis and statistics

First, to summarize the patients’ baseline characteristics, we performed descriptive analyses.

Second, the patients were placed in the “surprised” and “not surprised” groups according to the 1DSQ answers of responsible physicians. We also added the patients’ state: alive or dead, on day 1 and created a 2×2 contingency table based on these results. We used simple statistical analysis to compute the sensitivity, specificity, positive predictive value and negative predictive value based on this table.

Third, to clarify factors of patients who died within the next 1 day as those whom the physicians answered “not surprised” to the 1DSQ, we categorized the patients into two groups. Patients whose physicians answered “not surprised” and died within the next 1 day were categorized group A and defined as the “predictable death group”. Patients whose physicians answered “not surprised” but did not die within the next 1 day were categorized as group B.

Fourth, we performed a Fisher’s exact test for categorical variables and a Cochran–Armitage trend test for ordinal variables to clarify patients’ factors related to the “Predictable death group”.

Fifth, we put variables with $P < 0.05$ derived from univariate analyses into a multivariate logistic regression analysis to identify the patients’ factors related to the “predictable death group”.

We performed statistical analyses using JMP Pro version 14 (SAS, Cary, NC, USA).

Ethical statement

The present study was conducted in accordance with the ethical standards of the Declaration of Helsinki (as revised in 2013) and the ethical guidelines for medical and health research involving human subjects presented by the Ministry of Health, Labour, and Welfare in Japan, and was approved by the local institutional review boards of all participating institutions. All procedures were in accordance with the ethical standards of the independent ethics committee of Tohoku University School of Medicine (approval No. 2016-1-689). Japanese law does not require individual informed consent from participants in a non-invasive observational trial, such as in the present study. Therefore, we used an opt-out method rather than acquiring written or oral informed consent.

Results

A total of 1,896 patients were enrolled from 22 PCUs in Japan between January and December 2017. Among these, 485 patients were excluded: 245 patients were discharged from the hospital alive and 240 patients had missing data on day 0. The remaining 1,411 patients were analyzed (*Figure 1*).

We summarized the baseline characteristics of 1,411 patients in *Table 1*. The mean (standard deviation) age was 72.6 (12.2) years, and the most common primary cancer site was the lungs (17.1%).

We indicate a 2×2 contingency table (*Table 2*). The responsible physicians answered “not surprised” for 847 (60.0%) patients. This prediction showed a sensitivity of 82.0% [95% confidence interval (CI): 77.5–85.8%] and specificity of 45.5% (95% CI: 44.4–46.4%). The positive predictive value was 27.4% (95% CI: 25.9–28.7%), and the negative predictive value was 91.0% (95% CI: 88.7–92.9%).

Table S1 showed the results of all variables for which univariate analysis was performed to clarify factors related

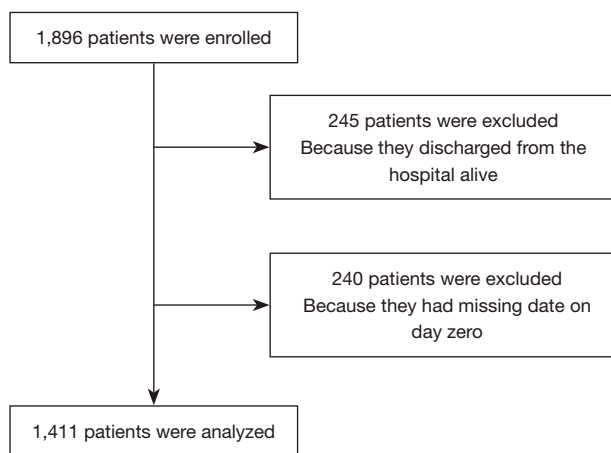


Figure 1 Patient selection for this study.

to the “predictable death group”, and *Table 3* summarizes 17 variables with $P < 0.05$. The 17 variables were urine output over last 12 h < 100 mL ($P < 0.01$), decreased response to verbal stimuli ($P < 0.01$), oxygen administration ($P < 0.01$), decreased response to visual stimuli ($P < 0.01$), radial artery ($P < 0.01$), dysphagia of liquids ($P < 0.01$), peripheral cyanosis ($P < 0.01$), respiration with mandibular movement ($P < 0.01$), saturation of percutaneous oxygen (SpO_2) ($P < 0.01$), hyperextension of neck ($P = 0.02$), grunting of vocal cords ($P = 0.02$), dyspnea ($P = 0.02$), infusion therapy ($P = 0.02$), age ($P = 0.03$), sex ($P = 0.04$), inability to close eyelids ($P = 0.04$), and opioid administration ($P = 0.04$).

Table 4 lists the results of the multivariate analysis. We found that five factors associated with the “predictable death group”. The five factors were urine output over the last 12 hours [< 100 vs. ≥ 100 mL; odds ratio (OR) 2.11; 95% CI: 1.41–3.12; $P < 0.01$], decreased response to visual stimuli (present vs. absent; OR 1.71; 95% CI: 1.03–2.82; $P = 0.04$), respiration with mandibular movement (present vs. absent; OR 2.69; 95% CI: 1.28–5.63; $P = 0.01$), radial artery (pulselessness vs. palpable; OR 2.32; 95% CI: 1.21–4.46; $P = 0.01$), and SpO_2 ($< 89\%$ vs. $\geq 90\%$; OR 3.20; 95% CI: 1.95–5.26; $P < 0.01$).

Discussion

This is the first study to verify the usefulness of the 1DSQ as a tool for estimating the prognosis of cancer patients with impending death using a large group.

Our analyses revealed that the 1DSQ has a high sensitivity in predicting death in cancer patients within

Table 1 Patient’s characteristics of the analyzed 1,411 patients at hospitalize

Characteristics (n=1,411)	No. (%)
Age (years), mean (SD) [range]	72.6 (12.2) [25–100]
Sex (male)	716 (50.7)
Primary cancer site	
Lung	242 (17.1)
Stomach/esophagus	207 (14.7)
Colon/rectum	186 (13.1)
Pancreas	146 (10.3)
Liver/biliary system	121 (8.5)
Prostate/bladder/kidney/testis	102 (7.2)
Ovary/uterus	82 (5.8)
Others	325 (23.0)
Metastatic site	
Liver	565 (40.0)
Lung	530 (37.5)
Bone	380 (26.9)
Cancer treatment	
Chemotherapy	866 (61.3)
Surgery	594 (42.0)
Hormonal therapy	14 (0.9)
Radiation therapy	11 (0.7)
Eastern cooperative oncology group performance status	
0–1	8 (0.6)
2	79 (5.6)
3	549 (38.9)
4	775 (54.9)
Palliative performance scale	
20 or less	326 (23.1)
30	296 (21.0)
40	410 (29.0)
50	281 (20.0)
60 and above	98 (6.9)
Median survival time (days), mean (SD) [range]	16.0 (29.9) [0–375]

Based on (14). SD, standard deviation.

Table 2 2×2 contingency table

Group	Death within 1 day	Not death within 1 day	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Not surprised	232 (group A)	615 (group B)	82.0% (95% CI: 77.5–85.8%)	45.5% (95% CI: 44.4–46.4%)	27.4% (95% CI: 25.9–28.7%)	91.0% (95% CI: 88.7–92.9%)
Surprised	51	513				

Group A: patients whose physicians answered “not surprised” and actually died in the next 1 day. We defined group A as “predictable death group”; group B: patients whose physicians answered “not surprised” and did not actually die in the next 1 day. CI, confidence interval.

Table 3 The results of univariate analysis which associated with the factors related to the “predictable death group”

Variables	Subgroup	Total (n=847), n	Predictable death group (group A)		Group B		P value
			n	%	n	%	
Age	20–69 year	328	104	31.7	224	68.3	0.03
	70 and above year	519	128	24.7	391	75.3	
Sex	Male	429	104	24.2	325	75.8	0.04
	Female	418	128	30.6	290	69.4	
Decreased response to verbal stimuli	No	648	150	23.1	498	76.9	<0.01
	Yes	186	69	37.1	117	62.9	
Decreased response to visual stimuli	No	549	116	21.1	433	78.9	<0.01
	Yes	285	103	36.1	182	63.9	
Dysphagia of liquid	Absent	444	169	38.1	275	61.9	<0.01
	Present	952	446	46.9	506	53.1	
Peripheral cyanosis	Absent	638	142	22.3	496	77.7	<0.01
	Present	196	77	39.3	119	60.7	
Pulselessness of radial artery	Absent	769	184	23.9	585	76.0	<0.01
	Present	65	35	53.9	30	46.1	
Respiration with mandibular movement	Absent	784	186	23.7	598	76.3	<0.01
	Present	50	33	66.0	17	34.0	
Hyperextension of neck	Absent	789	200	25.4	589	74.6	0.02
	Present	45	19	42.2	26	57.8	
Inability to close eyelids	Absent	773	196	25.4	577	74.6	0.04
	Present	61	23	37.7	38	62.3	
Grunting of vocal cords	Absent	793	201	25.4	592	74.6	0.02
	Present	41	18	43.9	23	56.1	
Urine output over last 12 hour	200 mL and above	630	132	21.0	498	79.0	<0.01
	200 mL or less	204	87	42.7	117	57.3	
Dyspnea (IPOS)	0–1	493	115	23.3	378	76.7	0.02
	2–4	341	104	30.5	237	69.5	

Table 3 (continued)

Table 3 (continued)

Variables	Subgroup	Total (n=847), n	Predictable death group (group A)		Group B		P value
			n	%	n	%	
SpO ₂	90% and above	92	48	52.2	44	47.8	<0.01
	89% or less	707	158	22.4	549	77.6	
Oxygen administration	Absent	327	63	19.3	264	80.7	<0.01
	Present	507	156	30.8	351	69.2	
Opioid administration	Absent	188	38	20.2	150	79.8	0.04
	Present	646	181	28.0	465	72.0	
Infusion therapy	Absent	331	102	30.8	229	69.2	0.02
	Present	503	117	23.3	386	76.7	

Group A: patients whose physicians answered “not surprised” and actually died in the next 1 day. We defined group A as “predictable death group”; group B: patients whose physicians answered “not surprised” and did not actually die in the next 1 day. IPOS, integrated palliative care outcome scale; SpO₂, saturation of percutaneous oxygen.

Table 4 The results of multivariate analysis which associated with the factors related to the “predictable death group”

Variables	Subgroup	OR (95% CI)	P value
Decreased response to visual stimuli	Yes	1.710 (1.03–2.82)	0.04
	No	Ref	
Radial artery	Pulselessness	2.325 (1.21–4.46)	0.01
	Palpable	Ref	
Respiration with mandibular movement	Present	2.695 (1.28–5.63)	0.01
	Absent	Ref	
Urine output over last 12 hour	200 mL or less	2.107 (1.41–3.12)	<0.01
	200 mL and above	Ref	
SpO ₂	89% or less	3.204 (1.95–5.26)	<0.01
	90% and above	Ref	

OR, odds ratio; CI, confidence interval; SpO₂, saturation of percutaneous oxygen.

1 day and may be useful as a screening tool in this context. White *et al.* reported the mean sensitivity of SQs to predict the prognosis cancer patients within 12 months was 77.1% (18). In comparison, the 1DSQ has a higher sensitivity (82.0%). This may be attributed to the standardization of the question when a patient had PPS ≤20. Most of palliative physicians recognize that patients with PPS ≤20 have a poorer prognosis, which may have

caused a physician to respond with “not surprised”. When physicians answered “not surprised” to the 1DSQ, the physicians should carefully explain to the family member the possibility of the patient dying within 1 day. We believe that using the 1DSQ to carefully explain the prognosis to the patient’s family will significantly improve psychological care for those affected.

However, compared to other studies that used SQs for short-term prognosis, the 1DSQ had a slightly lower sensitivity; Hamano *et al.* reported that the sensitivity and specificity of the 30-day surprise question were 95.6% and 37.0%, respectively, and 7-day surprise question were 84.7% and 68.0%, respectively (13). In addition, our previous findings revealed a sensitivity and specificity of 94.3% and 26.3% for the 3DSQ, respectively (14). One possible explanation for the discrepancy in sensitivity may be that physicians could not confidently answer “not surprised” to cancer patients who died within 1 day. It is known that physicians refer to the physical signs and clinical symptoms of cancer patients with impending death when predicting their prognosis (5). Hui *et al.* reported on 16 clinical signs that often occur between 1.5 and 5.5 days prior to death in cancer patients (19). Among them, the clinical sign that occurred most often within 1 day before death was only “pulselessness of radial artery (19-21)”. The lack of clarity in the physical signs and clinical symptoms of cancer patients who die within 1 day may cause physicians to hesitate in making their decisions. However, we believe that the 1DSQ is a valuable screening tools to identify cancer patients who

die within one day, as it has a high sensitivity while there are few accurate physical signs and clinical symptoms that can predict death within one day. In addition, the 1DSQ can be conveniently performed at a patient's bedside. The usefulness of the 1DSQ may be further enhanced as more research is conducted on the clinical signs and symptoms that often occur immediately before death.

We identified five variables associated with the factors of patients who were likely to die within 1 day, as the physicians predicted. These were urine output over last 12 hours <100 mL, decreased response to visual stimuli, respiration with mandibular movement, pulselessness of radial artery, and SpO₂ <90%. These signs have been previously reported to occur in cancer patients 3 days before death (5,19-22). In particular, urine output over last 12 hours <100 mL, respiration with mandibular movement, and pulselessness of radial artery have been shown to be the signs that most likely occur 1-1.5 days before death (20). If physicians answer the 1DSQ with "not surprised" and notice these clinical signs, the patients' condition should be observed more carefully.

In our previous study investigating the 3DSQ, adjunctive medical treatment, such as opioid administration and continuous deep sedation, was identified as a factor to assist in predicting prognosis (14). However, this study only presented the patients' physical signs. The result of this study suggests that the physical signs may be more important for predicting which patients will die within 1 day.

This study has some limitations. First, physical signs and clinical symptoms of patients might influence the physician's answer to the 1DSQ. However, as the SQ is a tool that relies on the physician's intuition, we believe that it is unavoidable in this study and in clinical practice. We consider that the 1DSQ is not a screening tool to be used alone, but rather should be used in conjunction with physical signs and symptoms. Among these, we revealed the five signs that may be more helpful when combined in this study. Second, the 1DSQ was answered by palliative care physicians; non-palliative care physicians may have provided different answers and thus yielded different results. Further studies involving non-palliative care physicians should be conducted to clarify this possibility. Third, the physicians may have been influenced by other prognostic tools such as PiPS models, PPI, or PaP score when answering the 1DSQ. However, we considered this effect to be unclear as these tools have not been optimized for predicting the prognosis of cancer patients with impending death (6-8). Fourth, the medical care provided in PCUs may differ from that provided in a

general ward. However, the medical care provided to patients with PPS ≤ 20 was expected to be almost identical, and thus, it might not be a determining factor for this study. Fifth, we lack information regarding the attending physicians, such as age, gender, and years of experience, which might have influenced our results.

Conclusions

Based on our findings, the 1DSQ has proven to be a helpful screening tool for identifying cancer patients with impending death.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The present study was conducted in accordance with the ethical standards of the Declaration of Helsinki (as revised in 2013) and the ethical guidelines for medical and health research involving human subjects presented by the Ministry of Health, Labour, and Welfare in Japan, and was approved by the local institutional review boards of all participating institutions. All procedures were in accordance with the ethical standards of the independent ethics committee of Tohoku University School of Medicine (approval No. 2016-1-689). Japanese law does not require individual informed consent from participants in a non-invasive observational trial, such as in the present study. Therefore, we used an opt-out method rather than acquiring written or oral informed consent.

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References

1. White N, Reid F, Vickerstaff V, et al. Specialist palliative medicine physicians and nurses accuracy at predicting imminent death (within 72 hours): a short report. *BMJ Support Palliat Care* 2020;10:209-12.
2. Hui D, Nooruddin Z, Didwaniya N, et al. Concepts and definitions for "actively dying," "end of life," "terminally ill," "terminal care," and "transition of care": a systematic review. *J Pain Symptom Manage* 2014;47:77-89.
3. Hwang IC, Ahn HY, Park SM, et al. Clinical changes in terminally ill cancer patients and death within 48 h: when

- should we refer patients to a separate room? Support Care Cancer 2013;21:835-40.
4. Ellershaw J, Ward C. Care of the dying patient: the last hours or days of life. *BMJ* 2003;326:30-4.
 5. Domeisen Benedetti F, Ostgathe C, Clark J, et al. International palliative care experts' view on phenomena indicating the last hours and days of life. *Support Care Cancer* 2013;21:1509-17.
 6. Maltoni M, Nanni O, Pirovano M, et al. Successful validation of the palliative prognostic score in terminally ill cancer patients. Italian Multicenter Study Group on Palliative Care. *J Pain Symptom Manage* 1999;17:240-7.
 7. Morita T, Tsunoda J, Inoue S, et al. The Palliative Prognostic Index: a scoring system for survival prediction of terminally ill cancer patients. *Support Care Cancer* 1999;7:128-33.
 8. Gwilliam B, Keeley V, Todd C, et al. Development of prognosis in palliative care study (PiPS) predictor models to improve prognostication in advanced cancer: prospective cohort study. *BMJ* 2011;343:d4920.
 9. Billings JA, Bernacki R. Strategic targeting of advance care planning interventions: the Goldilocks phenomenon. *JAMA Intern Med* 2014;174:620-4.
 10. Baba M, Maeda I, Morita T, et al. Survival prediction for advanced cancer patients in the real world: A comparison of the Palliative Prognostic Score, Delirium-Palliative Prognostic Score, Palliative Prognostic Index and modified Prognosis in Palliative Care Study predictor model. *Eur J Cancer* 2015;51:1618-29.
 11. Moss AH, Lunney JR, Culp S, et al. Prognostic significance of the "surprise" question in cancer patients. *J Palliat Med* 2010;13:837-40.
 12. Moroni M, Zocchi D, Bolognesi D, et al. The 'surprise' question in advanced cancer patients: A prospective study among general practitioners. *Palliat Med* 2014;28:959-64.
 13. Hamano J, Morita T, Inoue S, et al. Surprise Questions for Survival Prediction in Patients With Advanced Cancer: A Multicenter Prospective Cohort Study. *Oncologist* 2015;20:839-44.
 14. Ikari T, Hiratsuka Y, Yamaguchi T, et al. "3-Day Surprise Question" to predict prognosis of advanced cancer patients with impending death: Multicenter prospective observational study. *Cancer Med* 2021;10:1018-26.
 15. Barry LC, Kasl SV, Prigerson HG. Psychiatric disorders among bereaved persons: the role of perceived circumstances of death and preparedness for death. *Am J Geriatr Psychiatry* 2002;10:447-57.
 16. Benítez-Rosario MA, Castillo-Adrós M, Garrido-Bernet B, et al. Appropriateness and reliability testing of the modified Richmond Agitation-Sedation Scale in Spanish patients with advanced cancer. *J Pain Symptom Manage* 2013;45:1112-9.
 17. Sakurai H, Miyashita M, Imai K, et al. Validation of the Integrated Palliative care Outcome Scale (IPOS) - Japanese Version. *Jpn J Clin Oncol* 2019;49:257-62.
 18. White N, Kupeli N, Vickerstaff V, et al. How accurate is the 'Surprise Question' at identifying patients at the end of life? A systematic review and meta-analysis. *BMC Med* 2017;15:139.
 19. Hui D, Hess K, dos Santos R, et al. A diagnostic model for impending death in cancer patients: Preliminary report. *Cancer* 2015;121:3914-21.
 20. Hui D, dos Santos R, Chisholm G, et al. Clinical signs of impending death in cancer patients. *Oncologist* 2014;19:681-7.
 21. Hui D, Dos Santos R, Chisholm G, et al. Bedside clinical signs associated with impending death in patients with advanced cancer: preliminary findings of a prospective, longitudinal cohort study. *Cancer* 2015;121:960-7.
 22. Bruera S, Chisholm G, Dos Santos R, et al. Variations in vital signs in the last days of life in patients with advanced cancer. *J Pain Symptom Manage* 2014;48:510-7.

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Table S1 The results of all variables for which univariate analysis was performed to identify the factors related to the “predictable death group”

Variables	Subgroup	Total (n=847)	Group A (n=232)		Group B (n=615)		P value
		n	n	%	n	%	
Age	20–69 year	328	104	31.7	224	68.3	0.03
	70 and above year	519	128	24.7	391	75.3	
Sex	Male	429	104	24.2	325	75.8	0.04
	Female	418	128	30.6	290	69.4	
Primary cancer site	Lung	146	41	28.1	105	71.9	0.84
	Stomach/esophagus	125	28	22.4	97	77.6	0.19
	Colon/rectum	186	29	30.5	66	69.5	0.47
	Liver/biliary system	70	21	30.0	49	70.0	0.68
	Pancreas	92	22	23.9	70	76.1	0.46
	Ovary/uterus	46	18	39.1	28	60.9	0.09
	Prostate/bladder/kidney/testis	67	15	22.4	52	77.6	0.39
Liver metastasis	Absent	503	128	25.5	375	74.6	0.14
	Present	344	104	30.2	240	69.8	
Bone metastasis	Absent	614	170	27.7	444	72.3	0.80
	Present	380	62	26.6	171	73.4	
Lung metastasis	Absent	515	128	24.9	387	75.2	0.05
	Present	331	104	31.4	227	68.6	
Cardiovascular comorbidity	Absent	796	219	27.5	577	72.5	0.87
	Present	51	13	25.5	38	74.5	
Cerebrovascular comorbidity	Absent	780	216	27.7	564	72.3	0.57
	Present	67	16	23.9	51	76.1	
Kidney comorbidity	Absent	832	229	27.5	603	72.5	0.77
	Present	15	3	20.0	12	80.0	
Diabetes comorbidity	Absent	735	201	27.4	534	72.7	1.00
	Present	112	31	27.7	81	72.3	
Dementia comorbidity	Absent	775	217	28.0	558	72.0	0.22
	Present	72	15	20.8	57	79.2	
Surgery	Not performed	482	129	26.8	353	73.2	0.64
	Performed	365	103	28.2	262	71.8	
Chemotherapy	Not receive	312	78	25.0	234	75.0	0.12
	Receive (not within 1 month)	461	139	30.2	322	69.9	
	Receive (within 1 month)	73	15	20.6	58	79.5	
Radiation therapy	Not receive	842	231	27.4	611	72.6	1.00
	Receive	5	1	20.0	4	80.0	

Table S1 (continued)

Table S1 (continued)

Variables	Subgroup	Total (n=847)		Group A (n=232)		Group B (n=615)		P value
		n		n	%	n	%	
Oxygen administration	Absent	327		63	19.3	264	80.7	<0.01
	Present	507		156	30.8	351	69.2	
Opioid administration	Absent	188		38	20.2	150	79.8	0.04
	Present	646		181	28.0	465	72.0	
Steroid administration	Absent	568		144	25.4	424	74.7	0.40
	Present	266		75	28.2	191	71.8	
Antipsychotics administration	Absent	476		132	27.7	344	72.3	0.30
	Present	358		87	24.3	271	75.7	
Anxiolytic administration	Absent	599		147	24.5	452	75.5	0.08
	Present	235		72	30.6	163	69.4	
Administration of airway secretion inhibitors	Absent	790		208	26.3	582	73.7	1.00
	Present	44		11	25.0	33	75.0	
Continuous deep sedation	No	802		210	26.2	592	73.8	0.84
	Yes	32		9	28.1	23	71.9	
Infusion therapy	Absent	331		102	30.8	229	69.2	0.02
	Present	503		117	23.3	386	76.7	
Richmond agitation sedation scale score	From -5 to -2	692		187	27.0	505	73.0	0.21
	From -1 to 5	141		31	22.0	110	78.0	
Decreased response to verbal stimuli	No	648		150	23.1	498	76.9	<0.01
	Yes	186		69	37.1	117	62.9	
Decreased response to visual stimuli	No	549		116	21.1	433	78.9	<0.01
	Yes	285		103	36.1	182	63.9	
Peripheral cyanosis	Absent	638		142	22.3	496	77.7	<0.01
	Present	196		77	39.3	119	60.7	
Pulselessness of radial artery	Absent	769		184	23.9	585	76.0	<0.01
	Present	65		35	53.9	30	46.1	
Respiration with mandibular movement	Absent	784		186	23.7	598	76.3	<0.01
	Present	50		33	66.0	17	34.0	
Hyperextension of neck	Absent	789		200	25.4	589	74.6	0.02
	Present	45		19	42.2	26	57.8	
Inability to close eyelids	Absent	773		196	25.4	577	74.6	0.04
	Present	61		23	37.7	38	62.3	
Grunting of vocal cords	Absent	793		201	25.4	592	74.6	0.02
	Present	41		18	43.9	23	56.1	

Table S1 (continued)

Table S1 (continued)

Variables	Subgroup	Total (n=847)	Group A (n=232)		Group B (n=615)		P value
		n	n	%	n	%	
Urine output over last 12 hours	200 mL and above	630	132	21.0	498	79.0	<0.01
	200 mL or less	204	87	42.7	117	57.3	
Apnea	Absent	707	185	26.2	522	73.8	0.91
	Present	127	34	26.8	93	73.2	
Cheyne-Stokes breathing	Absent	781	201	25.7	580	74.3	0.20
	Present	53	18	34.0	35	66.0	
Body temperature	Lower than 37.5 degrees	568	154	27.1	414	72.9	0.08
	Above 37.5 degrees	206	43	20.9	163	79.1	
SpO2	90% and above	92	48	52.2	44	47.8	<0.01
	89% or less	707	158	22.4	549	77.6	
Respiratory rate	24 times or less per minute	689	173	25.1	516	74.9	0.06
	25 times or more per minute	58	21	36.2	37	63.8	
Pain	IPOS (from 0 to 1)	534	129	24.2	405	75.8	0.07
	IPOS (from 2 to 4)	300	90	30.0	210	70.0	
Dyspnea	IPOS (from 0 to 1)	493	115	23.3	378	76.7	0.02
	IPOS (from 2 to 4)	341	104	30.5	237	69.5	
Fatigue	IPOS (from 0 to 1)	434	115	26.5	319	73.5	0.87
	IPOS (from 2 to 4)	400	104	26.0	296	74.0	
Delirium	Absent	398	111	27.9	287	72.1	0.35
	Present	436	108	24.8	328	75.2	
Edema	No	330	78	23.6	252	76.4	0.17
	Yes	504	141	28.0	363	72.0	

Group A: patients whose physicians answered “not surprised” and actually died in the next 1 day. We defined group A as “predictable death group”; group B: patients whose physicians answered “not surprised” and did not actually die in the next 1 day. SpO2, saturation of percutaneous oxygen; IPOS, integrated palliative care outcome scale.