

A novel method to predict nonvisible symptoms using machine learning in cancer palliative care

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Article

Keywords: Cancer palliative care, Cancer supportive care, Symptom assessment, Machine learning, Decision tree analysis

Posted Date: December 16th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1161022/v1>

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Abstract

Patients with cancer at the end of life may find it difficult to express their symptoms if they can no longer communicate verbally because of deteriorating health. In this study, we assessed these symptoms using machine learning. We conducted a clinical survey of 213 cancer patients from August 2015 to August 2016. We divided the reported symptoms into two groups—visible and nonvisible symptoms. Our machine learning model used patient background data and visible symptoms to predict nonvisible symptoms: pain, dyspnea, fatigue, drowsiness, anxiety, delirium, inadequate informed consent, and spiritual issues. The highest and/or lowest values for prediction accuracy, sensitivity, and specificity, respectively, are as follows: 88.0%/55.5%, 84.9%/3.3%, and 96.7%/24.1%. This work will facilitate better assessment and management of symptoms in patients with cancer.

Introduction

Palliative care has developed in Japan primarily because of a policy focus on cancer care.¹ Because of the increased life expectancy of patients with cancer, these individuals are no longer confined to inpatient settings during their illness.² The focus of palliative care for patients with cancer is shifting to general practice by healthcare professionals who do not specialize in this type of care. Although palliative care training is offered to healthcare professionals across Japan,³ short-term training is insufficient.⁴ Previous studies have reported that the availability of palliative care services is associated with general practitioner confidence and improved patient quality of life.⁵

Palliative care often begins with an assessment of symptoms that are known only to the patient and require a certain amount of time to evaluate. However, in general practice, the hectic and broad nature of care implies that there may be insufficient time to perform these detailed evaluations. Additionally, the hectic nature of general practice may result in a lower quality of clinical care, so recent studies have aimed to support medical care through investigations of clinical data using machine learning.⁶ In recent years, machine learning has been used to increase the diagnostic quality of imaging information such as radiological images.^{7,8} The application of machine learning focuses on avoiding diagnostic errors in imaging and improving diagnostic efficiency.^{7,8} Therefore, machine learning could provide improved methods for assessing nonvisible symptoms in patients with cancer, leading to improvements in the overall quality of health care, including palliative care, and better prognoses for these patients.⁹

Patients with cancer at the end of life may have difficulty expressing their symptoms if they can no longer communicate verbally owing to the deterioration of their general condition.¹⁰ When verbal communication with the patient is difficult, experience is required for assessing subjective symptoms known only to the patient.⁵ Additionally, there is often a dearth of palliative care specialists in rural areas.¹¹ Therefore, a supportive tool that can aid symptom assessment and management in cancer palliative care is greatly needed. The study aimed to create a model to predict nonvisible symptoms from visible symptoms and basic patient characteristics using machine learning.

Results

The patient characteristics varied in terms of cancer type, treatment stage, and general condition

The patient characteristics are shown in Table 1. Only adults aged 33 to 98 years were included, and 53.5% of the patients were male. A wide variety of cancer types were included. The total number of cancer center hospitals and university hospitals was 75.6%, which included many patients from hospitals with cancer treatment as their main institutional function. Most of the patients were inpatients. Although 67.1% of the patients had an ECOG-PS of 3 or higher, 32.8% had an ECOG-PS of 2 or lower, 41.8% received anticancer treatment, and 40.3% had a combined outcome of transfer to a palliative care unit and death. It was estimated that 32.8% to 41.8% of the patients were in good general condition.

The prediction performance of the learning model using decision trees for invisible symptoms was highest for drowsiness

The predictive performance of the learning model with decision trees for nonvisible symptoms is shown in Table 2. The symptoms in Table 2 are arranged in order of prediction accuracy. Drowsiness, which had the highest accuracy, also had the highest specificity compared to other symptoms. For fatigue, accuracy was third, while the area under the receiver operating characteristic curve was highest compared to other symptoms. For pain, the accuracy was fifth highest, but the prediction sensitivity was the highest among the nonvisible symptoms.

Visible symptoms were extracted as features of the prediction model for non-visible symptoms

The aggregated results are shown in Table 3, and constipation and sleep disturbance, both considered visible symptoms, were among the top three features for drowsiness that achieved the highest prediction accuracy. In addition, two of the top three features for drowsiness were visible symptoms, whereas only one visible symptom, edema, was included in the top three features for fatigue. As with fatigue, only one visible symptom, edema, was included in the top three features for delirium, dyspnea, and anxiety. There were no visible symptoms in the top three features for spiritual issues, pain, and inadequate informed consent.

Discussion

To our knowledge, this study is the first to predict nonvisible symptoms using decision tree analysis in cancer palliative care. We developed a simple method to predict nonvisible symptoms from the patient's background and visible symptoms that are easy to assess objectively using decision tree analysis, a machine learning algorithm. Recently, research on clinical applications of machine learning has grown at a remarkable rate.¹² However, most of that research is retrospective and theoretical, and only a small number of studies are of sufficient quality to justify costly clinical trials and ongoing quality control as medical devices.¹² Overcoming translational barriers such as real-time access to clinical data, data security, release of black-box results, and performance evaluation are considered necessary for the clinical application of machine learning-based predictions.¹³ However, we predicted symptoms that are difficult to assess objectively from symptoms that are easy to assess, rather than making a diagnosis and prognosis prediction from images and laboratory data. Our model has the potential to advance clinical applications with a simpler system than traditional machine learning studies that use images and molecular biology markers. In this study, clinical data were collected retrospectively. In addition to the ethical aspects of clinical data collection, such as the potential harm to patients, the safety of the data is ensured by the fact that the data used by machine learning as the correct answer have been confirmed by experts in palliative care. SF-PCTA1.0 describes the process of support as part of the medicine team that includes consultation with members of the palliative care team assigned to each facility, so in effect the accumulated results of multidisciplinary medical care was used as data for machine learning.

Furthermore, the use of SF-PCTA1.0 allowed us to avoid natural language processing problems, even though the study was conducted with linguistic information on symptoms. Research on the automatic extraction of useful patient information from medical records using natural language processing is still in its infancy and has not yet been applied in actual clinical practice.¹⁴ There are few studies that aim to assess symptoms that are not found in medical records to help with medical treatment, as in this study. Both in Japan and abroad, symptom assessment tools for cancer patients are mainly in the form of questionnaires completed by the patients themselves or their healthcare professionals.¹⁵ The application of machine learning in this study has high potential for widespread use in clinical practice because it uses items as input that can be assessed by non-specialists in palliative care.

Moreover, the features extracted by the decision tree analysis can provide clues to the pathophysiology of cancer. Traditionally, in situations where palliative care is more important than anticancer treatment, it has been difficult to conduct clinical trials because of ethical considerations and the difficulty of adjusting patient backgrounds.¹⁶ Thus, exploratory basic research on the pathogenesis of the various symptoms to serve as a basis for drug development has not been adequately conducted. In Table 3, the visible symptoms can also be considered as dysfunctions in which the sympathetic nervous system becomes unilaterally overactive, resulting in abnormalities in human body functions such as digestion, absorption, rest, and peripheral circulation. By contrast, nonvisible symptoms can be considered disorders within the central nervous system, with the addition of higher brain dysfunction, unlike visible symptoms. It is well known that various distressing symptoms accumulate during the clinical course of patients with cancer, and methods for predicting prognosis based on various symptoms are being investigated.¹⁷⁻²⁰ The fact that visible symptoms were extracted as features in the prediction of nonvisible symptoms in this study suggests the possibility of predicting central nervous system disorders from autonomic nervous system disorders. Further research is needed to determine whether there is a causal relationship between autonomic nervous system disorders and central nervous system disorders and what mechanisms of these disorders underlie various distressing symptoms in cancer patients.

Strength of this study is that applications based on our results may be able to assess symptoms to the same extent as healthcare professionals. To determine how much accuracy should be ensured in symptom prediction in the decision tree analysis, we searched for previous studies of symptom assessment by healthcare professionals in cancer palliative care but found no suitable precedents. Although there are several studies that examined the frequency of symptoms in cancer patients,^{17,21} no previous studies have examined indicators that can be used as a reference for how much prediction accuracy by machine learning can withstand clinical application, such as the rate of correct responses to symptom assessment by healthcare professionals. Therefore, we examined the accuracy of symptom prediction by physicians and nurses who are the referring individuals from the database used in this study (Supplementary Data 3). Because false positives (FP) results in symptom prediction cannot be accurately confirmed by the referring person, sensitivity and negative predictive value (NPV), which are measures of prediction accuracy and do not include FP, are presented in Supplementary Data 4. For the physical symptoms, drowsiness, fatigue, pain, and dyspnea and the psychiatric symptoms, delirium and inadequate informed consent, both sensitivity and NPV are better for prediction by healthcare professionals than for prediction by decision tree analysis, as can be seen in Table 4 and Supplementary Data 4. In another study predicting patient internalization by objective measures, the primary goal of machine learning was to achieve the same level of accuracy as the assessment by healthcare professionals.²² In addition, the sensitivity of the decision tree analysis was better than that of the referring person's ratings for anxiety and spiritual issues. This means that our application may perform better than healthcare professionals in terms of anxiety and spiritual issues. We expected it to be useful in screening symptoms, especially because of its high sensitivity.²³ Although anxiety has a high prevalence among patients with cancer,

this may be overlooked because it rarely occurs in isolation but is combined with physical symptoms such as dyspnea and fatigue and the psychological symptom of sleep disturbance.²⁴ Spiritual issues have not been adequately evaluated even with conventional questionnaire methods^{25,26} and are also easily overlooked. Therefore, our application may surpass the skills of general healthcare professionals in terms predicting anxiety and spiritual issues. In the future, empirical research should be conducted to evaluate the performance of the results of this study when applied in clinical practice.

This study also had several limitations. First, this study only included adult patients with cancer. Previous reports show that adults and children show differences in reporting symptoms, so our results may not be valid in children. Second, the number of outpatients included in this study was small, so additional studies should focus on the validity of our model for these patients. Third, our model may not accurately predict future events, so further work should investigate this question.

We created a learning model to predict non-visible symptoms from patient background and visible symptoms, which can be useful as a supportive tool in cancer palliative care. Although the proposed application is unlikely to be an absolute replacement for palliative care specialists, it is expected to at least help improve the quality of palliative care provided by healthcare professionals. Our results will help to better assess and manage symptoms in patients with cancer.

Methods

Data collection

We collected patient data from three institutes located in Fukui Prefecture, Japan: University of Fukui Hospital, Fukui Prefectural Hospital, and Sugita Genpaku Memorial Obama Municipal Hospital (Supplementary Data 1). A total of 213 patients with cancer were included. Among the patients treated by the palliative care teams of the three institutions, only those cases in which the first author was also involved were included in the analysis. Both outpatients and inpatients were included in the study. There were no exclusion criteria based on patient background or disease. We collected patient characteristics via an initial assessment at the time of palliative care team intervention, including symptoms and details of the palliative care team's intervention. Patients were recruited for a period of 1 year, and patients who were included at the end of the recruitment period were observed for 28 days as follows.

To assess palliative team activities consistently across multiple institutions, appropriate formatting of palliative team activity records is necessary. Therefore, we used the previously published Standard Format for Palliative Care Team Activities 1.0 (SF-PCTA 1.0) to collect and standardize activity records.²⁷ The contents of SF-PCTA 1.0 were divided into: Section I. Cover sheet, Section II. Reasons for referral and initial assessment, and Section III. Activities. The method for completing each item of the SF-PCTA 1.0 is presented in Supplementary Data 2. The first author recorded the cover sheet, reasons for referral, and activities, referring to the original publication.²⁷ Two differences in the use of the SF-PCTA1.0 in this study compared to the original work were (1) that it was used in supporting activities at multiple sites and (2) that the observation period and site name were added to the cover sheet.

Patients were enrolled over a 12-month period and data were collected over a 13-month period beginning in August 2015, including the observation period of the last patient enrolled. In the study by Sasahara et al., to create SF-PCTA1.0, the interventions of the palliative care team were described daily, but the observation period was over a monthly basis. In the present study, the observation period was also on a daily basis. Consistent with the

original publication on SF-PCTA1.0, the maximum observation period for a patient was 28 days.²⁷ Additionally, as per the original paper, the participants were patients who had been referred to the palliative care team for treatment, and the data was a simple aggregation of routine medical care.²⁷ Because the first author is a consultant on palliative care in workplaces, he reviewed the records of all items of the SF-PCTA1.0. to avoid duplicate recommendations and implementations for the same item.

Our goal was to create a machine learning-based model to predict symptoms that were difficult to assess by general observation from patient characteristics and symptoms that were easy to assess. General observation was based on visual information, such as quantity and degree. Section I of SF-PTCA1.0 was used as the source of patient characteristics data and section II as the source of symptom data (Figure 1). We assigned variables X1–X26 to patient characteristics as input data (Table 4). Variables X1–X26 included the place of medical treatment, age, sex, cancer site within the body, status of anticancer treatment, ECOG performance status, and referring person. We assigned variables X27–X32 as visible symptoms, including decrease in food intake, nausea, abdominal distension, constipation, edema, and sleep disturbances. We assigned Y variables, the nonvisible symptoms, as output data. The Y variables included pain, dyspnea, fatigue, drowsiness, anxiety, delirium, inadequate informed consent, and spiritual issues. The distinction between visible and nonvisible symptoms did not correspond to a medical definition, such as their subjective or objective symptoms, but was based on a simple assessment from a clinical perspective by healthcare professionals, patients, and their families.

Ethics

This study was conducted in accordance with the Ethical Guidelines for Medical Research Involving Human Subjects issued by the Ministry of Education, Culture, Sports, Science, and Technology and the Ministry of Health, Labor, and Welfare (issued February 9, 2015 and revised March 31, 2015). We did not obtain informed consent for the data collection because the data were anonymized and we used existing materials and information. We followed the Declaration of Helsinki in collecting patient data, and the study was ethically reviewed and accepted by the three participating institutions.

Data preprocessing

The overview of data preprocessing is shown in Figure 1. We obtained patient characteristics from section I of the SF-PCTA1.0. We excluded data from the cover sheet as input data because the information would be used for a time frame that was after the time of symptom assessment. The University of Fukui Hospital and Fukui Prefectural Hospital are specialized in cancer care. Sugita Genpaku Memorial Obama Municipal Hospital is engaged not only in cancer care but also in various other medical services as a central public hospital in the region. Institutional information about the presence or absence of specialized cancer care was not associated with the frequency of “reason for referral” and “problem identified by the first author” in symptom assessment (Supplementary Data 3). Therefore, we excluded institutional information from the input data. For patients in whom the cancer site was “other,” only “0” was assigned without specifying the cancer type.

All sub-items in the nine domains of section II of SF-PCTA 1.0 were categorized with “reason for referral” and “problem identified by first author” as 1 and “not applicable” as 0. Section II of SF-PCTA 1.0 included nine domains: (1) physical/pharmacological issues, (2) psychiatric/emotional/spiritual issues, (3) diagnosis/anticancer treatment issues, (4) social issues, (5) family issues, (6) place of care, (7) ethical issues, (8) bereaved family issues, and (9) discussion of referral options (Supplementary Data 2). We focused on (1) physical/pharmaceutical issues, (2) psychological/spiritual issues, and (3) issues related to the diagnosis and

treatment of cancer that were directly related to the patient's symptoms in section II of the SF-PCTA1.0. We divided the symptoms into two groups.

We excluded Section III of the SF-PCTA1.0 as input data for the machine learning model because these were used later than the time of symptom assessment. The Section III of SF-PCTA 1.0 included thirteen domains: (1) comprehensive assessment, (2) care for patient's physical symptoms, (3) care for psychiatric symptoms/emotional support for patients, (4) support for patient's decision making, (5) support for decision making about place of care, (6) support for patient at home, (7) family support, (8) support for ethical issues, (9) referral to specialist, (10) medical procedure/investigation, (11) staff support, (12) coordination within palliative care team, and (13) pharmacological treatment. The activity items were collected throughout the observation period for each case (Supplementary Data 2).

Statistical software and analysis flow

We used both Microsoft Excel for Microsoft 365 (Redmond, WA, USA) to prepare the data and RapidMiner software v.9.8.001 (RapidMiner, Dortmund, North Rhine-Westphalia, Germany) to create a decision tree. RapidMiner is a flexible Java environment for knowledge discovery in databases, machine learning, and text data mining.

The analysis procedure with RapidMiner is shown in figures 2 and 3. We performed prediction using the test data in the learning model with a cross-validation method, as shown in Figure 2. In steps (i)–(ii) of Figure 2, we divided the data of 213 patients into non-overlapping groups A and B,²⁸ and created 10 sets of combinations of the data. Following the general method of k-split cross-validation, we set $k = 10$ since the total number of patients was in units of 100. The dataset was also divided according to the order of the dataset. We used the group B datasets as the test data in each iteration. Next, we created a learning model from each group A dataset in steps (iii) to (iv) of Figure 2. After prediction on the 10 sets of test data, as shown in Figure 3, we used the average of the prediction results of 10 iterations as the final result. Moreover, RapidMiner combines tools called operators to program machine learning, and in this study, we used the decision tree operator (Figure 3). The gain ratio was used in the decision tree operator and the random generation of training and validation datasets was specified in the cross-validation operator, but the other operators and the basic settings of RapidMiner were left at their default values. In this study, we predicted the eight nonvisible symptoms individually rather than simultaneously. We also performed feature extraction to identify the top three features that appeared frequently in the 10 tests from the root node to the leaf node up to and including branch 3 of the decision tree. The frequency of occurrence was set to $\geq 20\%$, and if there was no corresponding feature, the features were examined on branch 3 or higher.

Although in the collection of patient data, a statistical analysis method was not specified to analyze data from the SF-PCTA1.0 database, the goal of our study was to create a baseline database to validate various methods to obtain useful results in clinical practice. Therefore, we used these patient data to create a model using machine learning and as test data to test the machine learning-based model.

Each statistical index was calculated as follows. Sensitivity was defined as true positives (TP)/(TP + false negatives (FN)). Specificity was defined as true negatives (TN)/(TN + FP). Accuracy was determined using the following calculation: $(TP + TN)/(TP + FP + TN + FN)$. Finally, we calculated the positive predictive value as $TP/(TP + FP)$ and the NPV as $TN/(FN + TN)$.

Data availability

The individual-level data reported in this study are not publicly available. Individuals wishing to access disaggregated data, including the specific data reported in this study, should submit a request for access to KS (mobile_pcu@kuhp.kyoto-u.ac.jp). Deidentified data (including, as applicable, participant data and relevant data dictionaries) will be shared upon approval of analysis proposals with signed data access agreements in place.

Declarations

Acknowledgments

All authors have not received any financial support from any organization for this study. KS was affiliated with an endowed chair at the University of Fukui established by Fukui Prefecture at the time of data collection for this study, but this study has not received any financial support from Fukui Prefecture. We would like to thank the palliative care teams at University of Fukui Hospital, Fukui Prefectural Hospital, and Sugita Genpaku Memorial Obama Municipal Hospital for their cooperation in collecting data for this study. KS confirms that he had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Author Contribution: KS conceived and designed the analysis, data collection, contributed data/analysis tools. KS and S T performed the analysis and wrote the paper

Conflict of interest disclosure statement: This study is not directly related to financial and personal relationships with other people or organizations.

Financial support: There are no study sponsors.

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Tables

Table 1. Background of cancer patients (n = 213)

Clinical Factors		N (%)
Age (Range: 33–98, Average \pm SD: 68.2 \pm 13.1)	<69 years old	102 (47.9)
	\geq 69 years old	111 (52.1)
Gender	Male	114 (53.5)
	Female	99 (46.5)
ECOG ^a performance status	1	15 (7.0)
	2	55 (25.8)
	3	81 (38.0)
	4	62 (29.1)
Types of hospitals	Regional core hospital	52(24.4)
	Cancer hospital	115 (54.0)
	University hospital	46 (21.6)
Referring person	Doctor	75 (35.2)
	Nurse	138 (64.8)
Place of medical treatment	Outpatient	15 (7.0)
	Hospitalization	198 (93.0)
Cancer site	Lung	35 (16.4)
	Pancreas	22 (10.3)
	Colon/rectum	20 (9.4)
	Lymph node/hematology	20 (9.4)
	Stomach	18 (8.5)
	Breast	14 (6.6)
	Uterus/ovary	14 (6.6)
	Head and neck	14 (6.6)
	Kidney/bladder	13 (6.1)

	Biliary tract	8 (3.8)	
	Other ^b	8 (3.8)	
	Liver	7 (3.3)	
	Unknown	7 (3.3)	
	Prostate	6 (2.8)	
	Under investigation	6 (2.8)	
	Esophagus	1 (0.5)	
Status of anticancer treatment	No further anticancer treatment	113 (53.1)	
	Under anticancer treatment	89 (41.8)	
	Before anticancer treatment	11 (5.2)	
Patient outcome when observation ends	Observation period ended	67 (31.5)	
	Died	71 (33.3)	
	Discharge or transfer to	Home	50 (23.5)
		Other	5 (2.3)
		Inpatient hospice/palliative care unit (PCU)	15 (7.0)
	Problem resolved	5 (2.3)	
Observation period (Range: 1–28, Average \pm SD: 17.5 \pm 9.6)	<18 days	103 (48.4)	
	\geq 18 days	110 (51.6)	

^aECOG: Eastern Cooperative Oncology Group.

^bOther: skin cancer, pudenda cancer, retroperitoneal tumor, liposarcoma, cardiac tumor.

Table 2. Predictive performance of learning models created by decision trees on nonvisible symptoms

Nonvisible symptoms	Frequency of patients labeled as symptom positive (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Area under receiver operating characteristic curve (AUROC)	Positive predictive value (PPV) (%)	Negative predictive value (NPV) (%)
Drowsiness	9.5 ± 7.2	3.3 ± 10.5	96.7 ± 3.9	88.0 ± 8.2	0.450 ± 0.207	10.0 ± 31.6	90.6 ± 7.2
Spiritual issues	21.5 ± 9.4	21.7 ± 35.2	90.8 ± 8.4	74.0 ± 10.7	0.558 ± 0.235	25.0 ± 35.4	79.7 ± 10.9
Fatigue	25.5 ± 9.3	34.5 ± 30.8	88.0 ± 12.0	73.5 ± 6.3	0.706 ± 0.146	48.0 ± 38.9	80.4 ± 9.7
Delirium	19.0 ± 3.2	29.8 ± 20.9	85.7 ± 11.2	71.0 ± 10.2	0.654 ± 0.147	40.2 ± 27.4	78.6 ± 10.7
Pain	70.5 ± 16.4	84.9 ± 7.1	24.1 ± 19.6	68.5 ± 14.2	0.582 ± 0.151	72.9 ± 16.4	37.7 ± 27.4
Dyspnea	27 ± 13.0	27.9 ± 28.1	70.6 ± 13.8	59.5 ± 11.4	0.482 ± 0.175	19.6 ± 20.3	72.3 ± 15.7
Anxiety	52.5 ± 15.1	67.3 ± 12.5	41.8 ± 21.6	56.0 ± 8.1	0.533 ± 0.162	56.8 ± 15.8	51.0 ± 24.7
Inadequate informed consent	38.0 ± 18.9	28.0 ± 16.2	71.2 ± 10.0	55.5 ± 14.6	0.460 ± 0.134	36.6 ± 17.8	62.3 ± 20.5

TP: true positive, TPR: true positive rate, TN: true negative, FN: false negative, FP: false positive, FPR: false positive rate, ROC: receiver operating characteristic curve

$$\text{Sensitivity} = TP / (TP + FN)$$

$$\text{Specificity} = TN / (TN + FP)$$

$$\text{Accuracy} = (TP + TN) / (TP + FP + TN + FN)$$

$$\text{Area under ROC (AUROC)} = \int_{x=0}^1 TPR(FPR^{-1}(x)) dx$$

$$\text{Positive predictive value (PPV)} = TP / (TP + FP)$$

$$\text{Negative predictive value (NPV)} = TN / (FN + TN)$$

Table 3. The top three features for predicting nonvisible symptoms extracted by decision trees

Nonvisible symptoms	Rank	Branch number ^a	Frequency (%) ^b	Features used to predict nonvisible symptoms	
				Clinical factors	Attributes
Drowsiness	1	1	80	Constipation	Visible symptoms
	2	2	70	Age	Background of cancer patients
	3	2	60	Sleep disturbance	Visible symptoms
Spiritual issues	1	1	80	Age	Background of cancer patients
	2	4	20	Biliary tract cancer	Background of cancer patients
	2	4	20	Prostate cancer	Background of cancer patients
Fatigue	1	1	60	Edema	Visible symptoms
	2	1	20	Cancer of unknown origin	Background of cancer patients
	3	2	70	Age	Background of cancer patients
Delirium	1	1	80	Age	Background of cancer patients
	2	2	80	ECOG performance status ^c	Background of cancer patients
	3	3	20	Edema	Visible symptoms
Pain	1	1	80	Age	Background of cancer patients
	2	4	40	Male	Background of cancer patients
	2	4	40	Biliary tract cancer	Background of cancer patients
Dyspnea	1	1	70	Age	Background of cancer patients
	2	2	40	Breast cancer	Background of cancer patients
	3	3	30	Edema	Visible symptoms
Anxiety	1	1	100	Age	Background of cancer patients
	2	5	20	Edema	Visible symptoms
	3	8	40	Lymphatic/hematological cancer	Background of cancer patients
Inadequate informed consent	1	1	50	Outpatient	Background of cancer patients

2	1	20	Under investigation of cancer	Background of cancer patients
3	2	60	Breast cancer	Background of cancer patients

^aThe branch number represents the number of branches from the root node of the tree.

^bFrequency indicates how often the feature appears in predictions of learning models created by decision trees for test data.

^cECOG: Eastern Cooperative Oncology Group.

Table 4. Contents of the variables

Background of patients		Variables
Place of medical treatment	Hospitalization	X1
	Outpatient	X2
Age		X3
Gender	Male	X4
	Female	X5
Cancer site	Pancreas	X6
	Unknown	X7
	Lung	X8
	Breast	X9
	Head and neck	X10
	Biliary tract	X11
	Colon/Rectum	X12
	Prostate	X13
	Under investigation	X14
	Kidney/Bladder	X15
	Esophagus	X16
	Uterus/Ovary	X17
	Liver	X18
	Stomach	X19
Lymph node/Hematology	X20	
Status of anticancer treatment	No further anticancer treatment	X21
	Before anticancer treatment	X22
	Under anticancer treatment	X23
ECOG performance status		X24
Referring person	Doctor	X25
	Nurse	X26
Visible symptoms		Variables
Decrease in food intake		X27
Nausea		X28
Abdominal distension		X29
Constipation		X30

Edema	X31
Sleep disturbance	X32
Nonvisible symptoms	Variables
Pain	Y
Dyspnea	
Fatigue	
Drowsiness	
Anxiety	
Delirium	
Spiritual issues	
Inadequate informed consent	

Figures

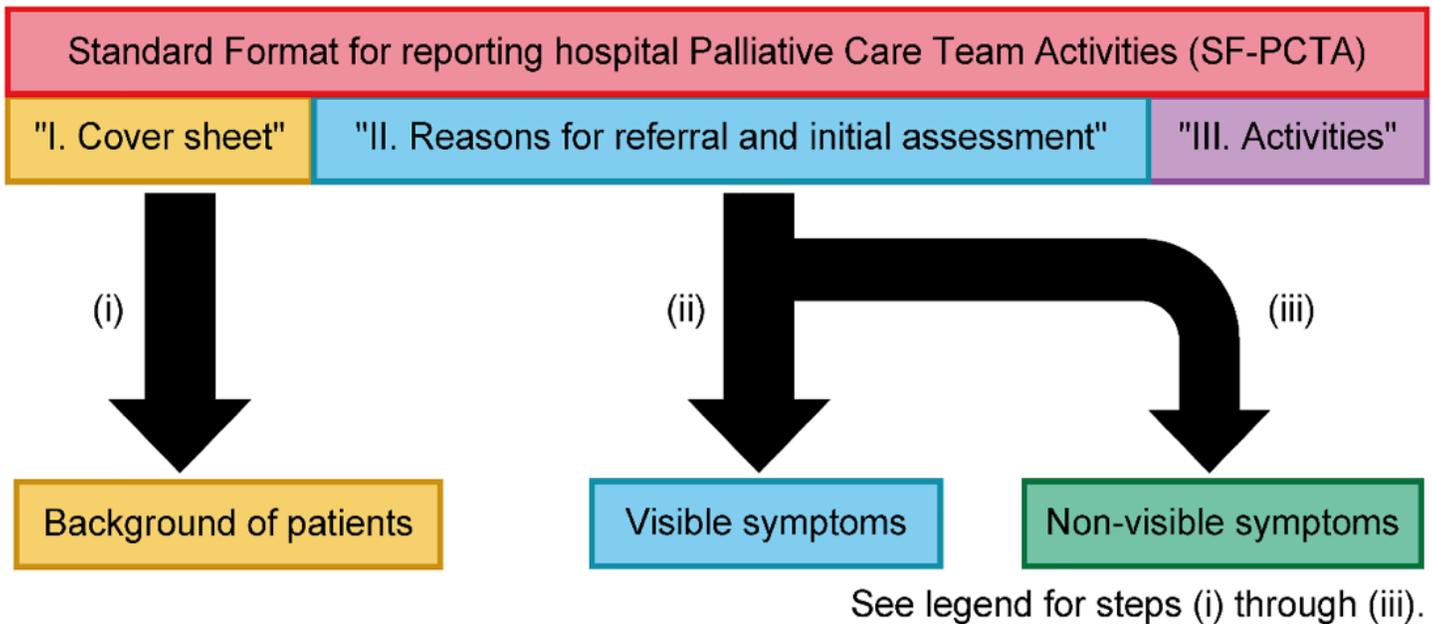


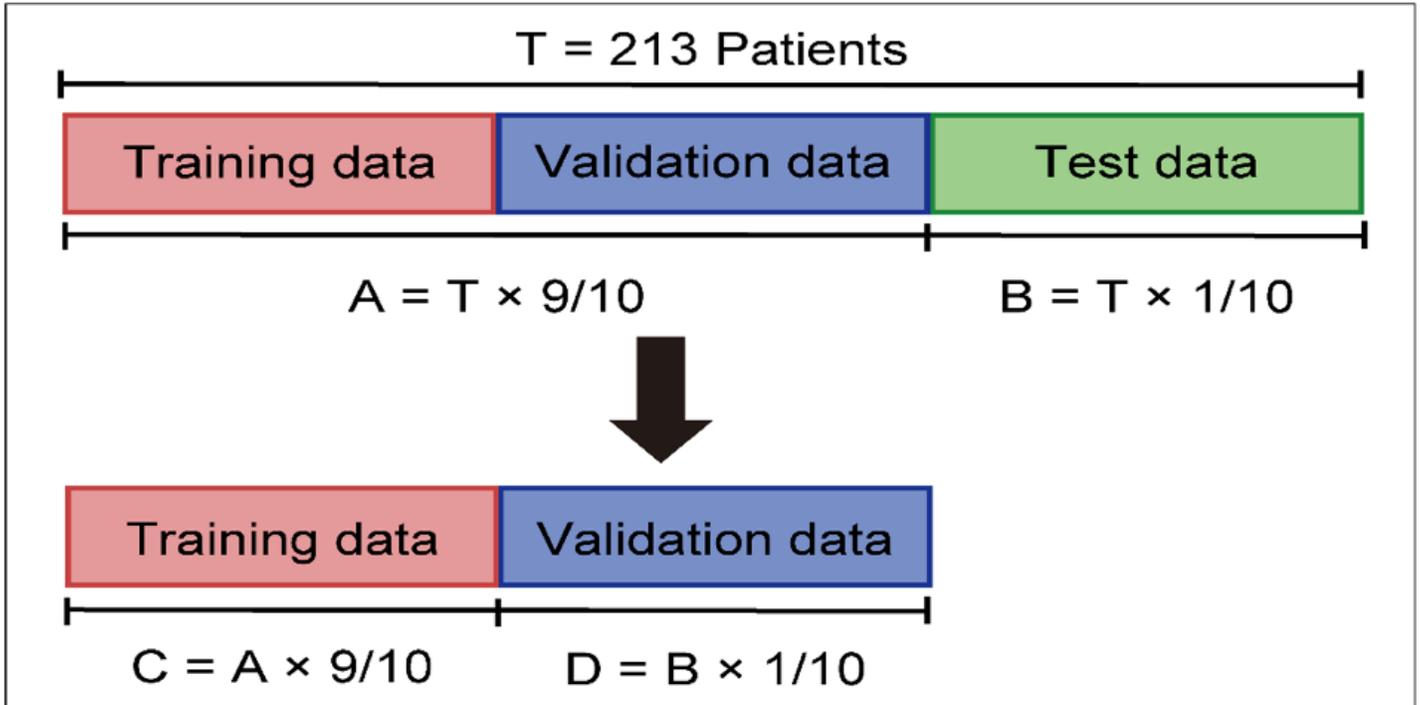
Figure 1

Data preprocessing. (X) In the process of changing from "I. Cover sheet" in SF-PCTA 1.0 to "Background of cancer patients," the following processes were followed. X1 to X26 variables were assigned for categories under place of medical treatment, age, gender, cancer site, status of anticancer treatment, Eastern Cooperative Oncology Group Performance Status (ECOG-PS), and referring a person. Cancer sites included in "other" were excluded. Real numbers were used for the variable representing age. Other variables were categorized as 1 for presence and 0 for absence. Patient outcomes, observation periods, and types of hospitals were excluded from the input data for this

study.

(X) Among the items included in “II. Reason for referral and initial assessment” in the SF-PCTA 1.0, “Visible symptoms” was defined as symptoms that could be easily assessed in our observation. The categorization was done 1 if the patient was presumed to have symptoms and 0 if the patient was presumed not to have symptoms.

(X) On the other hand, symptoms that are difficult to evaluate by general observation were designated as nonvisible symptoms. The categorization was 1 if the patient was presumed to have symptoms and 0 if the patient was presumed not to have symptoms.



See the legend for the steps of the cross-validation method.

Figure 2

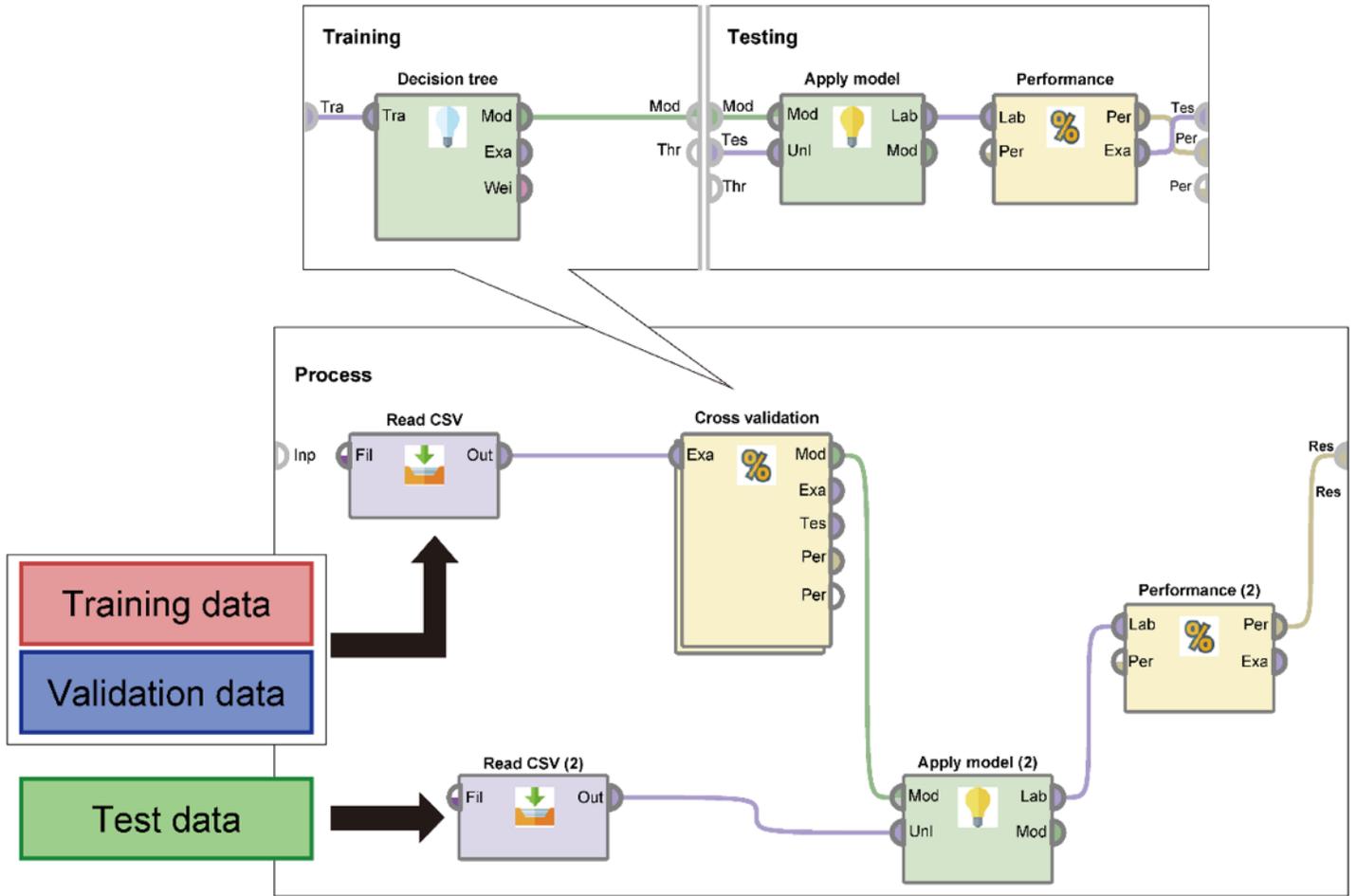
Cross-validation method for learning model creation

(X) 213 patients (= T) were divided into 10 groups that did not overlap with each other, and 10 groups were created by combining 9/10 (= A) and 1/10 (= B).

(X) B in (i) is the test data, and there is no overlap among the 10 groups. Ten sets of A and B were created from the data of 213 patients.

(X) The A of each group created in (i) was further divided into 10 parts, one for training (= C) and one for validation (= D).

(X) A cross-validation method to randomly generate 10 sets of C and D and a learning model was created on RapidMiner.



See the legend for definitions of abbreviations in the figure.

Figure 3

<p>Prediction process for test data</p><p>Tra: Training</p><p>Mod: Model</p><p>Exa: Example</p><p>Wei: Weight</p><p>Thr: Threshold</p><p>Tes: Testing</p><p>Unl: Unlabel</p><p>Lab: Label</p><p>Per: Performance</p><p>Inp: Input</p><p>Fil: File</p><p>Out: Output</p><p>Res: Result</p>

Supplementary Files

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