Original Article

Characteristics of patients reporting symptoms by open-ended questions in specialist palliative care

Leslye Rojas-Concha[1], Morten Aagaard Petersen[1] & Mogens Groenvold[1, 2]

1) Palliative Care Research Unit, Department of Geriatrics and Palliative Medicine, Copenhagen University Hospital – Bispebjerg and Frederiksberg Hospital, 2) Department of Public Health, University of Copenhagen, Denmark

ABSTRACT

INTRODUCTION Comprehensive symptom assessment may be achieved by combining patient-reported outcome instruments with open-ended questions. The open-ended "Write In three Symptoms/Problems" (WISP) instrument allows patients to report symptoms and problems (S/Ps) not covered by the EORTC QLQ-C15-PAL. This study investigated whether sociodemographic or clinical variables were associated with the reporting of additional S/Ps on WISP.

METHODS Data from the Danish Palliative Care Database included all patients admitted to specialist palliative care in Denmark in 2016 who completed the EORTC QLQ-C15-PAL. The associations between patient characteristics and the reporting of a) any additional symptom/problem and b) each of the ten most prevalent additional S/Ps (oedema, dizziness, cough, sweats, diarrhoea, dry mouth, incontinence, sore mouth, vomiting and dysphagia) were investigated using multiple logistic regression.

RESULTS In total, 1,295 patients reported additional S/Ps on WISP. Reporting any additional symptom/problem was associated with having younger children and living with someone. The reporting of the most prevalent additional S/Ps was associated with cancer diagnosis, having younger children, living with someone and being an outpatient.

CONCLUSIONS This study gives new insights into the characteristics of patients reporting S/Ps that are not assessed by standard measures. The results may assist clinicians in improving palliative care.

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TRIAL REGISTRATION not relevant.

Patients with advanced cancer experience a variety of symptoms that intensify when they approach death [1]. These symptoms and quality of life (QOL) can be systematically assessed by validated patient-reported outcome (PRO) instruments commonly used in palliative care, such as the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care (EORTC QLQ-C15-PAL), the Edmonton Symptom Assessment Scale (ESAS) and the Memorial Symptom Assessment Scale (MSAS) [2].

Systematic assessment of symptoms has been highly recommended to identify symptoms not reported voluntarily by patients [3, 4] and to prevent clinicians from underestimating patient symptomatology [5]; however, no instruments can measure all symptoms experienced by patients in palliative care [4]. Thus, comprehensive symptom assessment may be achieved by combining PRO instruments with open-ended

questions.

To increase the recognition of symptoms in patients who are admitted to specialist palliative care (SPC) in Denmark, a brief instrument named Write In three Symptoms/Problems" (WISP) was developed to supplement the EORTC QLQ-C15-PAL, which is the standard questionnaire for symptom assessment of patients undergoing SPC [6, 7]. WISP is an open-ended question permitting patients to report 1–3 symptoms and problems (S/Ps) not covered by the EORTC QLQ-C15-PAL, and to rate their severity. This combined instrument became a national standard in SPC when its use was introduced as a quality indicator in the Danish Palliative Care Database (DPD) in 2010. The first study reporting results from the WISP showed that 2,796 S/Ps were listed on WISP by 1,788 patients admitted to SPC, and 63.6% of the S/Ps were not covered by the EORTC QLQ-C15-PAL. The ten most prevalent additional S/Ps were oedema, dizziness, cough, sweats, diarrhoea, dry mouth, incontinence, sore mouth, vomiting and dysphagia (ranging 1-3%) [6].

Several studies suggest that sex, age, cancer diagnosis, cohabitation and inpatient/outpatient status are associated with symptoms systematically assessed by PRO instruments [8-10]. In contrast, the evidence needed to determine whether patient characteristics are associated with S/Ps assessed via open-ended questions is minimal. Therefore, this study aimed to investigate whether sociodemographic variables, diagnosis (cancer site) or type of first contact (in/outpatient) were associated with S/Ps reported using the WISP instrument at admittance to SPC in Denmark.

METHODS

Patients

This study was based on register data collected from the DPD, which comprises clinical and demographic information on all patients referred to the 43 SPC services in Denmark, 26 hospital-based palliative care teams and 17 hospices.

Included were data from patients admitted in 2016 who were at least 18 years of age, diagnosed with advanced cancer and had completed the EORTC QLQ-C15-PAL at the day of admittance or up to three days before. Information on sex, age, children, cohabitation status, diagnosis, type of first contact and S/Ps reported on WISP were collected from the DPD.

Instruments

The EORTC QLQ-C15-PAL questionnaire contains 15 items assessing the severity of ten symptoms/functions: physical function, emotional function, pain, fatigue, nausea, dyspnoea, sleeping difficulties, appetite loss, constipation and overall QOL. Symptoms are scored as 1 (not at all), 2 (a little), 3 (quite a bit) or 4 (very much) [7].

WISP is a brief instrument supplementing the EORTC QLQ-C15-PAL. It allows patients to report up to three additional S/Ps (via open-ended responses) and to rate their severity using the response categories (see above) from 1 (not at all) to 4 (very much) [6]. Both instruments are presented in **Supplementary Material 1 (https://ugeskriftet.dk/files/a12200916_-_supplementary.pdf)**.

Statistical analyses

Sociodemographic and clinical patient characteristics were summarised as proportions.

We computed the dichotomous outcome "any additional symptom/problem" dividing patients into those who reported at least one additional S/P on WISP, i.e., S/Ps not covered by the EORTC QLQ-C15-PAL, and those who had reported no additional S/Ps on WISP. For each of the ten most prevalent S/Ps reported on WISP (see also [6]), patients were divided into those who had reported the symptom/problem (a score of at least "a little") and those

who had not.

We performed multiple logistic regression to investigate associations between patient characteristics and the eleven computed dichotomous outcomes, "any additional symptom/problem" and "each of the ten most prevalent additional S/Ps". A stepwise procedure was used until the model only contained covariates significantly associated with the outcome. The covariates tested were sex, age, having children, cohabitation status, diagnosis and type of first contact. The results from the logistic regressions are reported as odds ratios with 95% confidence intervals.
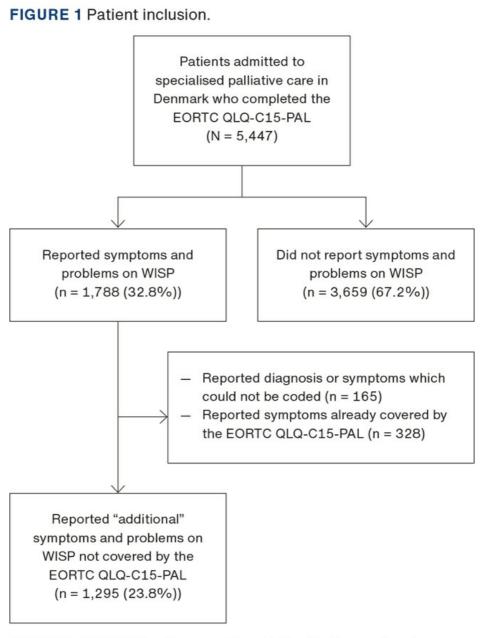
Finally, for each of the ten most prevalent S/Ps reported on WISP, we converted scores into 0–100-scales following the EORTC Scoring Manual [11], where 0 corresponds to "not at all" and 100 to "very much". The mean scores of the S/Ps were calculated according to patient characteristics. Differences in the distribution of S/P scores across patient characteristics were tested using the Mann-Whitney U test and Kruskal-Wallis test. A p-value < 0.05 was considered statistically significant. The analyses were conducted using Statistical Package for the Social Sciences version 23.

Trial registration: not relevant.

RESULTS

Study population

In 2016, 5,447 patients with advanced cancer were admitted to SPC and completed the EORTC QLQ-C15-PAL of whom 1,788 patients reported at least one symptom/problem using the WISP instrument [6]. Among these, 1,295 patients reported additional S/Ps not covered by the EORTC QLQ-C15-PAL (**Figure 1**).

FIGURE 1 Patient inclusion.


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                    ┌─────────────────────────┐
                    │   Patients admitted to   │
                    │ specialised palliative   │
                    │   care in Denmark who    │
                    │      completed the       │
                    │     EORTC QLQ-C15-PAL    │
                    │       (N = 5,447)        │
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Patients admitted to specialised palliative care in Denmark who completed the EORTC QLQ-C15-PAL (N = 5,447)

Reported symptoms and problems on WISP (n = 1,788 (32.8%))

Did not report symptoms and problems on WISP (n = 3,659 (67.2%))

— Reported diagnosis or symptoms which could not be coded (n = 165)
— Reported symptoms already covered by the EORTC QLQ-C15-PAL (n = 328)

Reported "additional" symptoms and problems on WISP not covered by the EORTC QLQ-C15-PAL (n = 1,295 (23.8%))

EORTC QLQ-C15-PAL = European Organisation for Research and Treatment of Cancer, Quality of Life Questionnaire Core 15 Palliative Care; WISP = *Write In three Symptoms/Problems intrument*.

Patient characteristics are presented in **Table 1**. Patients reporting additional S/Ps on WISP were slightly younger than those who did not. Slightly higher proportions of these patients had younger children and lived with someone.

TABLE 1 Characteristics of patients who reported or did not report additional symptoms and problems using the *Write In three Symptoms/Problems* instrument. The values are n (%).

Patient characteristics	Did report (N = 1,295)	Did not report (N = 4,152)
Sex		
Women	618 (22.8)	2,088 (77.2)
Men	677 (24.7)	2,064 (75.3)
Age		
18-59 yrs	269 (27.1)	723 (72.9)
60-69 yrs	349 (24.1)	1,099 (75.9)
≥ 70 yrs	677 (22.5)	2,330 (77.5)
Having children?		
No	155 (26.8)	424 (73.2)
At least 1 younger than 18 yrs	106 (29.4)	255 (70.6)
All at least 18 yrs	1,008 (23.2)	3,339 (76.8)
Unknown	26 (16.3)	134 (83.8)
Cohabitation status		
Living alone	386 (20.8)	1,472 (79.2)
Living with someone	854 (25.8)	2,454 (74.2)
Unknown	55 (19.6)	226 (80.4)
Diagnosis: cancer site, ICD-10		
Digestive system: C15-17 & C22+25	235 (24.2)	737 (75.8)
Colorectal: C18-C20	149 (22.9)	503 (77.1)
Lung: C33-C34	299 (21.5)	1,089 (78.5)
Breast: C50	111 (24.9)	335 (75.1)
Female genital organs: C53-55 & C56, C570-C574	90 (26.2)	254 (73.8)
Prostate: C61	99 (24.4)	307 (75.6)
Other cancers: all other C codes	282 (25.2)	836 (74.8)
Unknown primary cancer: C76-C80	30 (24.8)	91 (75.2)
Type of 1st contact		
Inpatient	331 (24.0)	1,050 (76.0)
Outpatient	964 (23.7)	3,102 (76.3)

ICD-10 = International Statistical Classification of Diseases and Related Health Problems, 10th rev.

Logistic regression analyses showed that the highest probability of reporting any additional symptom/problem was seen for patients with younger children compared with patients with older children, and for patients living with someone compared with those living alone, whereas no association was seen for age, sex, diagnosis or type of contact (**Table 2**).

TABLE 2 Associations between patient characteristics and additional symptoms and problems reported on the *Write In three Symptoms/Problems* instrument using stepwise multiple logistic regression[a]. The values are stated as OR[b] (95% CI).

Patient characteristics	Any additional symptom/problem (N_tot = 1,295[c])	Oedema (N_o = 183[c])	Cough (N_c = 85[c])	Sweats (N_s = 80[c])	Dry mouth (N_dm = 73[c])	Incontinence (N_i = 72[c, d])	Sore mouth (N_sm = 69[c])	Vomiting (N_v = 66[c])
Having children?								
No	1.26 (1.02-1.54)	1.77 (1.18-2.66)					1.20 (0.57-2.55)	
At least 1 younger than 18 yrs	1.34 (1.06-1.71)	2.00 (1.24-3.22)					2.45 (1.23-4.87)	
All at least 18 yrs	1.00 (ref.)	1.00 (ref.)					1.00 (ref.)	
Cohabitation								
Living alone	0.76 (0.66-0.86)		0.47 (0.28-0.80)	0.54 (0.31-0.99)				
Living with someone	1.00 (ref.)		1.00 (ref.)	1.00 (ref.)				
Diagnosis: cancer site								
Digestive system				1.28 (0.62-2.68)		0.95 (0.39-2.34)		6.90 (2.34-20.3)
Colorectal				0.83 (0.32-2.16)		3.07 (1.46-6.47)		6.49 (2.08-20.1)
Lung				1.00 (ref.)		1.00 (ref.)		1.00 (ref.)
Breast				1.07 (0.39-3.00)		1.56 (0.58-4.19)		3.92 (1.05-14.7)
Female genital organs				0.54 (0.12-2.34)		2.04 (0.76-5.46)		14.7 (4.80-44.8)
Prostate				4.10 (2.05-8.25)		2.60 (1.09-6.21)		4.31 (1.15-16.1)
Other cancers				1.48 (0.74-2.94)		1.24 (0.56-2.78)		2.18 (0.64-7.45)
Type of 1st contact								
Inpatient					0.61 (0.38-0.99)			
Outpatient					1.00 (ref.)			

CI = confidence interval; OR = odds ratio; ref. = reference group.
a) Sex and age were not significantly associated with any of the outcomes, and no associations were found between any of the patient characteristics and dizziness, diarrhoea or dysphagia. Therefore, these outcomes are not shown in the table.
b) An OR > 1 reflects higher odds of reporting the symptom.
c) Number of patients reporting the symptom.
d) Including urinary, faecal and unspecified incontinence.

Symptom associations

Multiple logistic regression analyses of the reporting of the ten most prevalent additional S/Ps are shown in Table 2. Patients with younger children had a higher probability of reporting oedema and sore mouth than patients with older children. Patients living with someone had a higher probability of reporting cough and sweats than patients living alone. Diagnosis was significantly associated with the probability of reporting certain S/Ps: patients with prostate cancer had the highest odds of reporting sweats, patients with colorectal and prostate cancer were more likely to report incontinence, and the highest odds of reporting vomiting was seen among patients with cancer in the female genital organs and in the digestive system. Outpatients had higher odds of reporting dry mouth than inpatients. None of the variables were related to the reporting of dizziness, diarrhoea or dysphagia. Sex and age were not significantly associated with any of the outcomes.

Symptom severity

Mean scores for the ten most prevalent additional S/Ps reported on WISP are listed in **Table 3.** Note that the scores are estimated among those reporting the S/P and therefore do not reflect whether the S/P was reported frequently or not. The highest mean scores were reported for dysphagia (mean = 82), diarrhoea (mean = 78), oedema (mean = 77) and incontinence (mean = 77).

TABLE 3 Mean scores for the ten most prevalent additional symptoms and problems reported on *Write In three Symptoms/Problems* instrument by patient characteristics[a].

Patient characteristics	Oedema (N$_o$ = 183[b])	Dizziness (N$_{dz}$ = 169[b])	Cough (N$_c$ = 85[b])	Sweats (N$_s$ = 80[b])	Diarrhoea (N$_{dr}$ = 74[b])	Dry mouth (N$_{dm}$ = 73[b])	Incontinence (N$_i$ = 72[b, c])	Sore mouth (N$_{sm}$ = 69[b])	Vomiting (N$_v$ = 66[b])	Dysphagia (N$_{dy}$ = 65[b])
All	77	64	70	76	78	74	77	72	76	82
Sex										
Women	83*	66	70	78	72*	76	78	78	75	85
Men	72*	62	70	75	85*	72	77	68	77	79
Age										
18-59 yrs	81	69	77	72	63	70	81	82	78	88
60-69 yrs	75	63	63	79	79	76	82	60	72	69
≥ 70 yrs	72	63	70	75	81	74	75	72	77	84
Having children?										
No	78	69	77	73	76	76	85	75	67	83
At least 1 younger than 18 yrs	75	58	78	73	80	60	84	63	83	100
All at least 18 yrs	77	64	68	76	80	74	75	73	77	80
Cohabitation status										
Living alone	81	65	63	77	83	72	76	74	78	83
Living with someone	76	64	72	77	79	74	79	71	76	82
Diagnosis: cancer site ICD-10										
Digestive system	80	61	82*	74	80	73	71	67	77	82
Colorectal	71	63	75*	73	83	74	73	79	75	93
Lung	77	65	58*	80	75	75	78	68	67	78
Breast	90	67	73*	74	73	67	89	93	60	92
Female genital organs	83	71	78*	84	80	76	84	60	83	84
Prostate	73	64	-	72	78	60	78	74	80	72
Other cancers	78	61	79*	80	79	81	75	79	72	81
Type of 1st contact										
Inpatient	83	66	81*	71	86*	81	71	81	87*	92
Outpatient	76	63	67*	77	75*	70	79	69	71*	79

ICD-10 = International Statistical Classification of Diseases and Related Health Problems, 10th rev.
*) p < 0.05.
a) Higher mean scores represent more severe symptoms.
b) Number of patients reporting the symptom.
c) Including urinary, faecal and unspecified incontinence.

The distributions of mean scores differed significantly according to sex, diagnosis and type of first contact. Women presented more severe oedema (p = 0.002) and less severe diarrhoea (p = 0.037) than men. The largest differences between cancer diagnosis groups were seen for cough, where patients with cancer in the digestive system presented more severe cough than patients with other cancer diagnoses (p = 0.043). Inpatients reported more severe cough (p = 0.020), diarrhoea (p = 0.047) and vomiting (p = 0.013) than outpatients.

DISCUSSION

In this study, 1,295 (23.8%) of the 5,447 patients who completed the EORTC QLQ-C15-PAL reported additional S/Ps not covered by this questionnaire, which confirms the relevance of the use of an open-ended question for an exhaustive symptom assessment. We found that the probability of reporting any additional symptom/problem on WISP was significantly associated with having younger children and living with someone. Patients with younger children may be in a more vulnerable situation, which may increase the risk of distressing symptoms [12]. The higher odds of reporting any additional symptom/problem seen in patients living with someone compared with patients living alone may reflect that the patient's spouse or relatives assist patients in remembering their symptoms.

It is remarkable that despite the relatively large sample size, we found no association between sex, age and the reporting of any additional symptom/problem or each of the ten most prevalent S/Ps although previous studies indicate that being younger or female were significantly associated with symptoms frequently reported in palliative care [1, 8, 9]. Overall, the similarities across age and sex indicate that the EORTC QLQ-C15-PAL has similar coverage of relevant problems across the subgroups.

In relation to diagnosis, patients with prostate cancer had the highest odds of reporting incontinence and sweats, and patients with colorectal cancer had the highest odds of reporting incontinence. These associations could be explained by the curative treatment that prostate cancer patients receive, since several studies have shown that radiotherapy and prostatectomy increase the risk of faecal and urinary incontinence [13]. The same applies to the high risk of sweats, where patients with prostate cancer frequently experience hot flushes and/or night sweats due to castration/endocrine treatment [14]. In patients with colorectal cancer, both faecal and urinary incontinence have been associated with their curative treatment and tumour progression [15]. Furthermore, patients with cancer in the female genital organs and the digestive system had the highest odds of vomiting, which may be related to intestinal obstruction [16]. Our findings were similar to those of another Danish study, where nausea/vomiting was most frequent in patients with gynaecological and stomach cancer [17].

Finally, outpatients had a higher probability of reporting worse dry mouth than inpatients. Dry mouth in patients with advanced cancer has been associated with recent chemotherapy and haematological cancers, which is different from our findings [18]. We found no association between dizziness, diarrhoea, dysphagia and patient characteristics, contrary to a previous study indicating that gynaecological and gastrointestinal cancer diagnoses were associated with more diarrhoea [10].

When interpreting the severity of the ten most prevalent additional S/Ps reported on WISP, we must take into consideration that a symptom gets a high "severity score" if all patients report a moderate severity. In our study, dysphagia, diarrhoea, oedema, and incontinence had the highest overall mean scores. Two previous studies using an open-ended question to identify S/Ps found that diarrhoea [4], oedema and incontinence [3] were also reported with moderate to high severity by advanced cancer patients, similarly to our findings.

A strength of this study is that it included a large data set of 5,447 patients of whom 1,295 reported S/Ps on WISP, coming from all SPC services across Denmark. Additionally, the study provides new knowledge about the profile of cancer patients reporting S/Ps not covered by the EORTC QLQ-C15-PAL. This information should be considered in clinical practice, especially for symptom assessment of subgroups experiencing particular symptoms, e.g., incontinence should be included in routine symptom assessment for patients with prostate cancer and patients with colorectal cancer. Also, in future research, it would be relevant to compare our profile of patients with cancer reporting S/Ps on WISP with patients without cancer in palliative care or from other settings for a better understanding of those who report S/Ps not covered by standard questionnaires.

However, whereas the present study confirms the value of open-ended questions, it is not possible to estimate the frequency of S/Ps from open-ended questions; the frequencies are lower than in systematic assessments [4]. This also means that the power to define subgroups of patients and to detect differences between them is limited. Other PRO instruments such as the ESAS [19], MSAS and its short form, MSAS-SF, have also included open-ended questions [20]. However, the way in which the information is collected varies between the instruments, e.g., how many additional symptoms they allow patients to report and how severity is rated, which means that their results are not comparable to each other or to WISP.

CONCLUSIONS

This large, national study investigated how patients with cancer admitted to SPC report symptoms using the open-ended WISP instrument. The probability of reporting any additional symptom/problem was associated with having younger children and living with someone. Otherwise, remarkably, no differences were found across sex, age, cancer diagnosis and type of first contact. Seven of the ten most prevalent additional S/Ps were associated with having children, cohabitation, cancer diagnosis and type of first contact. A better understanding of the profile of patients reporting various symptoms not always assessed by standard measures may allow

clinicians to improve palliative care interventions.

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