Age-related Differences in Recall of Information and Handling of Chemotherapy-related Side Effects in Cancer Patients: The ReCap Study

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Abstract

Background: To prevent severe toxicity and hospital admissions, adequate management and recall of information about side effects are crucial and health literacy plays an important role. If age-related factors impact recall of given information and handling of side effects, revised ways to give information are required.

Patients and Methods: We undertook a questionnaire-based survey among 188 newly diagnosed patients with pancreatic cancer or colorectal cancer and chemo-naïve patients with prostate cancer treated with adjuvant or first-line palliative chemotherapy comprising satisfaction with given information, recall of potential side effects, and handling of hypothetical side effect scenarios. We evaluated the association between baseline characteristics, ie, age, frailty (G8 score), comorbidity (Charlson Comorbidity Index), cognitive function (Mini-Cog), satisfaction, recall of information, and handling of side effects.

Results: Reduced ability to recall information about several side effects (eg, chest pain) was associated with older age (odds ratio adjusted for cancer [aOR] 0.94 [95% CI, 0.89-0.98]) and poor cognitive screening (aOR 0.56 [95% CI, 0.33-0.91]). Insufficient or dangerous handling of side effects was associated with older age (aOR 0.96 [95% CI, 0.92-0.99]) and cognitive impairment (aOR 0.70 [95% CI, 0.50-0.95]).

Conclusion: Older age and poor cognitive screening may impact patients’ ability to understand and adequately handle chemotherapy-related side effects. Cognitive screening and focus on individual ways to give information including assessment of recall and handling are needed.

Key words: age; chemotherapy; side effects; information; recall.

Implications for Practice

To reduce the risk of severe side effects and hospitalizations during chemotherapy, patients’ recall and understanding of information and awareness of clinical symptoms are crucial for adequate handling of side effects at home. The Recap study found older age and poor cognitive screening to be negatively associated with the recall of information about side effects as well as insufficient or dangerous handling of potential side effects at home. Our findings call for an increased focus on needs for individual information methods including following up on recalled information by hospital staff among older patients.

Introduction

Health literacy and a patient’s ability to be aware of side effects and morbidity are crucial in the trajectory of cancer treatment.1 For adequate handling of side effects, patients need sufficient information about treatment and symptoms, along with a comprehensive understanding of potential risks and how to act if side effects occur.

Advanced age is the leading risk factor for the development of cancer,2 and although the number of older patients with cancer is expected to rise,3,6 research is limited regarding the management of comorbidities, geriatric syndromes, and optimal doses and regimens of chemotherapy in older cancer patients.7,8 Aging is a highly individual process and involves a continuum of changes in biological and psychological functions. Older patients with cancer comprise a highly heterogeneous group, ranging from fit to frail, with varying comorbidities including cognitive impairments.9 Older patients, and especially frail patients,10 have an increased risk...
of severe toxicity. Many older patients present with various geriatric impairments,\textsuperscript{11} which must be considered to provide optimal treatment and care. Chemotherapy agents cause several distressing side effects such as fatigue, anorexia, nausea, diarrhea, mucositis, infections, nerve, and skin problems.\textsuperscript{12,13} Chemotherapy-induced side effects can have a considerable impact on patients’ daily activities and are associated with impaired quality of life (QoL) and increased psychological distress.\textsuperscript{14-16} Side effects from chemotherapy can frequently be prevented or managed with appropriate medical interventions. To mitigate chemotherapy-induced side effects and to prevent the development of severe toxicity including hospital admissions and life-threatening conditions, it is important that patients are provided with adequate information about possible side effects and that patients understand and recall the given information.

Reasons for developing severe toxicity in older age might not be due to comorbidity and physical impairment alone. Hearing impairments, cognitive function, and attention seem crucial to enable patients to understand and adequately handle toxicity at home. However, as there is a research gap with only a single study has investigated recall of toxicity information among older patients with cancer, and it did not include cognitive screening or frailty indicators.\textsuperscript{17}

In the present study, we investigated the impact of age and age-related variables and educational level on recall of and satisfaction with information and the ability of patients with newly diagnosed pancreatic cancer (PC), colorectal cancer (CRC), or prostate cancer (PRC) to adequately handle treatment-related side effects.

Methods and Materials

Study Population

Patients diagnosed with PC, CRC, or PRC and assessed for chemotherapy at the Department of Oncology, Copenhagen University Hospital were eligible for the study.

**Inclusion criteria**

Received adjuvant, neoadjuvant, or first-line palliative chemotherapy, ability to speak and read Danish and provide a signed informed consent.

**Exclusion criteria**

Prior chemotherapy, severe dementia, psychotic disorders, or other cognitive diseases that hindered informed consent.

Design

At the first visit to the clinic, an oncologist assessed patients diagnosed with PC, CRC, or PRC and determined the chemotherapy regimen. All patients received oral and written information about possible side effects of the planned chemotherapy according to hospital guidelines.

At the second visit, ie, first treatment cycle, an oncological nurse again gave patients oral and written information about possible side effects of the scheduled chemotherapy. Furthermore, all patients were informed about the current study and given written patient information and time to consider participation in the study.

At the third visit, ie, second treatment cycle, patients who accepted participation in the study signed a written consent form and participated in the survey.

Data Collection

**Clinical and demographic baseline data**

Included age, sex, treatment regimen, performance status (PS),\textsuperscript{18} comorbidities (assessed by age-adjusted Charlson Comorbidity Index [CCI]),\textsuperscript{19} number of medications, civil status, and educational level divided into no further education versus further or higher education.

The Survey

**Recall of information**

Assessed by using a list of 13 frequently experienced side effects. Participants were asked to note which side effects they could recall being informed about. According to departmental guidelines, all patients treated with 5-fluorouracil (5-FU) or capectabine should be informed about possible diarrhea, fever, chest pain, mucositis, and palmar-plantar erythrodysesthesia. All patients treated with oxaliplatin or docetaxel/nab-paclitaxel should be informed about diarrhea, fever, and neuropathy. Analyses of recalled information were performed only in participants likely to have been informed about the above-mentioned side effects.

**Handling of side effects**

Participants were asked to describe how they would handle three hypothetical scenarios. One scenario was about fever, a potentially serious treatment-related side effect, and two of the scenarios were about diarrhea of various intensity and potential severity (Supplementary Material). The participants were asked to describe their likely actions, which could include the use of prescribed medications, whether they would stay at home and observe further development, or if they would contact the Department of Oncology or a general practitioner. The author team created a predefined scoring manual, and one of the authors (HMM) performed the scoring. Uncertain answers were assessed within the author group. Patients received 2 points for a “Correct” answer (eg, when to contact the department or the general practitioner, what to observe at home, and how to use prescribed medications [non-chemotherapy]). An answer was considered “Insufficient” and patients were given 1 point if the answer was not according to the written patient information, but there was no increased risk of severe toxicity (eg, contacting a general practitioner and not the Department if high fever occurred or not taking drugs as prescribed). Zero points were given for a “Dangerous” answer, where there was an increased risk of aggravation of toxicity or morbidity (eg, getting into bed with long-lasting high fever or severe diarrhea without contacting anyone). “Insufficient” or “Dangerous” handling was considered as “Incorrect” handling of side effects.

**Patients’ evaluation of received information**

Evaluated by the validated European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ-Info 25).\textsuperscript{20} The questionnaire (25 items) evaluates the level of received information regarding disease, prognosis, treatment, side effects, and patients’ satisfaction with the provided information. The study focused on the question regarding satisfaction with information and the global total score.
Frailty

The survey also included a few complementary questions including self-rated health to allow the authors to complete a full G8 frailty screening. The G8 is specifically developed and validated for use in the oncological setting to identify frail or vulnerable patients. The questionnaire consists of eight items concerning nutritional status, weight loss, body mass index (BMI), motor skills, psychological status, number of prescribed medications, self-perception of general health, and the patient’s age. For a G8 score ≤ 14, a full geriatric assessment is recommended. A recent Danish study has suggested a cut-off of ≤ 11 as a more suitable cut-off for older Danish patients with cancer.

Cognitive impairment

Screening for cognitive impairment was done by an oncological nurse using the Mini-Cog. The Mini-Cog is validated for use in community-based populations and has demonstrated high sensitivity and specificity for the detection of cognitive impairment. The Mini-Cog consists of a three-word recall test and a clock drawing test. The test score is graded on a 5-point scale, where 3-5 indicate a lower risk of dementia, but a score of <3 does not rule out some degree of cognitive impairment.

Sample Size and Statistical Analyses

The power calculation was based on the results from the international validation study of the EORTC QLQ-INFO25 questionnaire. The minimal clinically important difference in the EORTC QLQ-INFO25 has not been established but was estimated to be a 10% difference between two groups (eg, patients below versus above 70 years of age) in the total test score. With 100 patients included, such a difference would be detected with a probability (power) of 90% at a 5% significance level. To account for differences in cancer diagnoses, we included 60 patients from each cancer group to ensure a broad spectrum of cancer diagnoses, 180 in all.

Categorical variables were analyzed using a chi-square test where appropriate; otherwise, Fischer’s exact test was used. Binary outcomes were analyzed by logistic regression and presented as odds ratios (ORs) and 95% CIs. Analyses were made as crude analyses and adjusted for cancer diagnosis. Info 25 QLQ data were presented as means and SDs, and differences between the groups were analyzed using the Wilcoxon test or Kruskal-Wallis test where appropriate.

Outcomes

Recall of given information

Nausea, diarrhea, fever, fatigue, and loss of hair were side effects most frequently remembered being informed about (Table 3). Although all patients should have been informed about diarrhea and fever, in sub-group analyses based on received chemotherapy (Table 3), 86%-88% of patients recalled information about diarrhea and 81%-84% of patients recalled being informed about fever. Furthermore, only 69% of patients receiving capecitabine or 5-FU remembered being informed about chest pain.
After adjustments for cancer disease, older age was associated with poorer odds of recalling information about diarrhea (adjusted OR [aOR] 0.94 [95% CI, 0.91-1.00]) (Table 4), fever (aOR 0.96 [95% CI, 0.91-1.00]), neuropathy (aOR 0.94 [95% CI, 0.89-0.99]), and chest pain (aOR 0.94 [95%, CI 0.88-0.98]). Cognitive impairment was associated with reduced odds of recalling information about chest pain (aOR 0.56 [95% CI, 0.33-0.91]), Further or higher education was associated with higher odds of recalling information about diarrhea (aOR 1.91 [95% CI, 1.14-12.39]).

Handling of side effects
Fourteen patients (7.4%) were handled dangerously in at least one scenario, and 48 patients (26%) were handled insufficiently in at least one scenario. Only 64% of patients managed to handle all scenarios adequately. Three patients with dangerous handling of the fever scenario did not recall being informed about fever as a common side effect.

Nine percent of patients ≥70 years handled dangerously in at least one scenario compared with 6.5% of younger patients (P = .67). After adjusting for all other factors, cognitive impairments were found to be associated with incorrect handling of side effects (aOR 0.70 [95% CI, 0.50-0.95]), but frailty or comorbidity was not.

Satisfaction with given information
For scores of the Info 25 questionnaire, see Supplementary Table S1. Patients with PC reported having received less information about the disease, medical tests, and treatment than patients with CRC and PRC. Furthermore, the mean satisfaction with information was lower for patients with PC compared with the other groups (78.7 versus 87.1, P = .029) (Table 2) as was the global score (65.1 versus 70.9, P = .010).
Patients with PRC had a higher global score compared with the other two groups (72.0 versus 67.3, \( P = 0.037 \)). There was no difference in satisfaction of given information or global score among older patients compared with younger patients or for patients with possible cognitive impairments (Mini-Cog < 3), compared with patients with normal screening (Mini-Cog ≥ 3) (Table 2). For frail patients (G8 ≤ 14 points) compared with fit patients, the satisfaction of given information was comparable; however, frail patients had a lower global score than fit patients \( (P = .023) \). Using the cut-off of G8 ≤ 11, frail patients were less satisfied with given information \( (P = .006) \). No differences were seen for patients with and without comorbidities and for patients with further or higher education compared with patients without further education.

In an analysis of baseline characteristics and satisfaction with given information, fitness (G8 >14) was found to be positively associated with higher satisfaction \( (P < .001) \), as was normal cognitive function \( (P = .049) \).

### Discussion

In this cross-sectional survey investigating satisfaction with and recall of information and ability to handle side effects, we found age and age-related factors negatively associated with the recall of information of some side effects and management of potential adverse events. Furthermore, we found significant differences between patients with PC, PRC, and CRC in median age, PS, comorbidity, and frailty, all of which were expected to have a possible impact on outcomes. Therefore, analyses were performed with and without adjustments for cancer diagnosis. Patients with PRC were older, had higher comorbidity, all were treated with palliative chemotherapy, their cognitive screening scores were slightly better, and they were more satisfied and had a more positive evaluation of given information than the other patients.

### Recall of Information and Handling of Side Effects

In the present study, hypothetic scenarios were created to evaluate the most important questions: can we as health care professionals deliver information enabling patients to recall information and manage potential side effects at home (or after discharge)? And can we identify patients for whom the current type of information (oral and written) should be improved?

More than a third of all patients failed to handle scenarios with potential side effects adequately. Older patients and patients with poor cognitive function were more likely to handle potential side effects incorrectly than younger patients and patients with higher cognitive scores.

In agreement with prior studies, poor recall of information about some of the side effects was found to be associated with higher age. Jansen et al\(^{27,28}\) investigated recall of information among newly referred cancer patients compared with actual communication from audio-recordings and found that recall of information decreased with age and information load. Their findings suggest an adverse effect of cognitive overload among older patients with cancer, which is also in line with the results of Lehmann et al who found that patients who prefer limited information recall even less if provided with extensive information.\(^{29}\)
The age-dependent differences in the handling of side effects could be due to reduced recall, but also because some older patients do not want to be a burden to caregivers or the health care system. Further research should focus on interviews illuminating causes and reasons for patterns of action among older patients. In the CARG score by Hurria et al., hearing impairment in older patients is associated with a higher risk of toxicity, and may, therefore impact perception, recall, and handling of side effects.

The age-dependent differences seen could also be due to the poor health literacy and reduced health-related knowledge seen among older patients. Thus, improved knowledge contributes to better health literacy and can compensate for small cognitive impairments like processing capacity.

In the present study, cognitive impairment was associated with the reduced recall of chest pain as a potential side effect and thus incorrect handling of it. Cognitive impairments were not identified in the oncological assessment prior to chemotherapy, and cognitive screening should be considered before chemotherapy is given to older adults with cancer.

The distress of being diagnosed with cancer can itself cause slow cognitive processing speed and reduced verbal memory and have a negative influence on medical information recall. Patients with cancer perform worse in cognitive tests including tasks

| Table 4. Association between age-related factors and recall of side effect information. |
|-----------------------------------------|----------------|----------------|----------------|
|                                        | Crude OR 95% CI| Adjusted for cancer diagnosis aOR 95%CI |
|-----------------------------------------|----------------|----------------|----------------|
| Diarrhea                                |                |                |
| Older age                               | 0.96 0.91-1.00 | 0.94 0.91-1.00 |
| Low G8 score                            | 0.96 0.82-1.12 | 0.96 0.82-1.12 |
| Low Mini-Cog score                      | 0.82 0.59-1.19 | 0.82 0.54-1.19 |
| High comorbidity                        | 1.01 0.68-1.56 | 1.03 0.63-1.74 |
| Further or higher education             | 1.92 1.14-12.45| 1.91 1.14-12.39|
| Fever                                   |                |                |
| Older age                               | 0.97 0.93-1.01 | 0.96 0.91-1.00 |
| Low G8 score                            | 0.95 0.82-1.10 | 0.94 0.81-1.09 |
| Low Mini-Cog score                      | 0.78 0.57-1.10 | 0.77 0.55-1.08 |
| High comorbidity                        | 0.93 0.64-1.40 | 0.92 0.63-1.38 |
| Further or higher education             | 1.39 0.96-6.20 | 1.37 0.99-6.08 |
| Mucositis**                             |                |                |
| Older age                               | 0.99 0.95-1.03 | 0.99 0.95-1.03 |
| Low G8 score                            | 0.91 0.75-1.09 | 0.91 0.73-1.11 |
| Low Mini-Cog score                      | 0.93 0.57-1.55 | 0.95 0.58-1.60 |
| High comorbidity                        | 1.15 0.72-1.97 | 1.16 0.72-2.01 |
| Further or higher education             | 0.99 0.96-1.03 | 0.99 0.96-1.02 |
| Neuropathy**                            |                |                |
| Older age                               | 0.96 0.91-1.01 | 0.95 0.89-0.99 |
| Low G8 score                            | 1.00 0.84-1.17 | 0.98 0.83-1.16 |
| Low Mini-Cog score                      | 0.75 0.53-1.09 | 0.73 0.51-1.06 |
| High comorbidity                        | 0.74 0.49-1.13 | 0.72 0.47-1.11 |
| Further or higher education             | 0.99 0.97-1.02 | 0.99 0.97-1.02 |
| Chest pain**                            |                |                |
| Older age                               | 0.94 0.87-0.98 | 0.94 0.88-0.98 |
| Low G8 score                            | 0.94 0.78-1.13 | 0.97 0.78-1.20 |
| Low Mini-Cog score                      | 0.54 0.32-0.88 | 0.56 0.33-0.91 |
| High comorbidity                        | 0.81 0.51-1.30 | 0.83 0.52-1.33 |
| Further or higher education             | 0.99 0.96-1.03 | 0.99 0.96-1.02 |
| PPE**                                   |                |                |
| Older age                               | 0.97 0.92-1.02 | 0.97 0.92-1.02 |
| Low G8 score                            | 0.93 0.75-1.14 | 0.96 0.75-1.22 |
| Low Mini-Cog score                      | 0.66 0.40-1.11 | 0.61 0.35-1.05 |
| High comorbidity                        | 0.81 0.41-1.41 | 0.83 0.41-2.50 |
| Further or higher education             | 2.02 1.02-39.06| 1.95 0.99-38.01|

Abbreviations: OR Odds ratio; aOR adjusted Odds ratio; PPE Palmar Plantar Erythrodysesthesia.
*Only for patients receiving 5-fluorouracil (5-FU) or capecitabine.
**Only for patients receiving oxaliplatin, docetaxel, or nab-paclitaxel.
Correct handling of scenarios and baseline characteristics may explain the poorer prognosis and thus higher level of distress, which can affect cognitive functioning including memory. Younger median age. The differences seen might be due to the poorer prognosis and thus higher level of distress, which can affect cognitive functioning including memory and is also in accordance with a cross-sectional study where patients with a poorer prognosis were found to consistently remember less information from medical consultations than patients with a better prognosis. Thus, the poor cognitive screening with Mini-Cog in the present study might also be explained by distress due to of being diagnosed with cancer.

In the present study, a further or higher level of education was only associated with better recall of information about side effects. Unsurprisingly, we found an association between poor cognitive screening scores and reduced recall of information and handling of side effects in older patients. But there was a tendency toward poorer cognitive screening scores in patients with PC compared with the other two groups, despite their younger median age. The differences seen might be due to the poorer prognosis and thus higher level of distress, which can affect cognitive functioning including memory and is also in accordance with a cross-sectional study where patients with a poorer prognosis were found to consistently remember less information from medical consultations than patients with a better prognosis. Thus, the poor cognitive screening with Mini-Cog in the present study might also be explained by distress due to of being diagnosed with cancer.

In conclusion, we found older age and poor cognitive screening associated with decreased recall of information and incorrect management of side effects. Cognitive impairments requiring attention compared with healthy controls, especially older patients and those with low educational level.

Unsurprisingly, we found an association between poor cognitive screening scores and reduced recall of information and handling of side effects in older patients. But there was a tendency toward poorer cognitive screening scores in patients with PC compared with the other two groups, despite their younger median age. The differences seen might be due to the poorer prognosis and thus higher level of distress, which can affect cognitive functioning including memory and is also in accordance with a cross-sectional study where patients with a poorer prognosis were found to consistently remember less information from medical consultations than patients with a better prognosis. Thus, the poor cognitive screening with Mini-Cog in the present study might also be explained by distress due to of being diagnosed with cancer.
were not acknowledged at oncological assessment, and cognitive screening should be considered prior to chemotherapy. For older patients and patients with poor cognitive screening scores, current written and oral treatment-related information may be insufficient, and future focus on individualized information, including assessment of information recall and handling, is crucial.

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Conflict of Interest
The authors indicated no financial relationships.

Author Contributions
Conception/design: C.M.L., D.L.N., M.K.M., H.M., and L.S. Provision of study material or patients: H.M., M.K., and C.M.L. Collection and/or assembly of data: H.M., S.T., and M.K.M. Data analysis and interpretation: C.M.L., M.S., S.T., M.K.M., D.L.N., and L.S. Manuscript writing: All authors. Final approval of manuscript: All authors.

Data Availability
The data underlying this article will be shared on reasonable request to the corresponding author.

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