

Original Article

Addressing geriatric oncology in Danish cancer guidelines to meet future challenges

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ABSTRACT

INTRODUCTION. The risk of cancer increases with age. Furthermore, frailty and age-related impairments significantly impact treatment outcomes. With an aging population, it is crucial to ensure a tailored, evidence-based cancer care approach. This study evaluated the extent to which frailty and age-related considerations are incorporated into current Danish national cancer guidelines across six frequent cancer types.

METHODS. We systematically reviewed all guidelines from the Danish Multidisciplinary Cancer Groups on lung, breast, colorectal, ovarian, bladder and prostate cancer. Guidelines were screened to identify how they address age, frailty, performance status (PS), comorbidity, functional status, general health status and individualised assessment. Identified comments were graded based on their level of specificity and clinical applicability.

RESULTS. All cancer guidelines addressed age and comorbidity. Frailty was explicitly mentioned in four out of six, of which only one guideline provided specific recommendations. PS was frequently included (5/6), and individualised assessments were encouraged in four of six guidelines, but lacked clarity regarding implementation.

CONCLUSIONS. Danish national cancer guidelines acknowledge age, PS and comorbidity, but lack specific recommendations for frailty assessment and management. By addressing these gaps, we encourage future guidelines to include recommendations on frailty assessment to help clinical decision-making and improve treatment outcomes for older people with cancer.

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Cancer incidence increases significantly with advancing age. In 2020, 37% of people diagnosed with cancer in Denmark were aged 75 years or older [1]. With an aging population, the proportion of older people undergoing cancer diagnostics and therapy is expected to increase [2]. Furthermore, more patients live with coexisting health issues such as functional and cognitive decline, multimorbidity, social support needs and frailty; factors that must be addressed in cancer treatment planning [3].

Frailty, a decline in physiological reserves and resilience, reduces stress tolerance and increases vulnerability to

adverse outcomes [4]. It is associated with higher rates of post-operative complications, treatment-related toxicity, prolonged hospital stay, mortality and compromised functional recovery [5, 6]. Guidelines from the European Society of Medical Oncology (ESMO), the International Society of Geriatric Oncology (SIOG) and the American Society of Clinical Oncology (ASCO) recommend frailty screening for all patients ≥ 65 years to identify individuals in need of geriatric assessment in the cancer care trajectory [7].

Age-related challenges and the need for interdisciplinary collaboration are increasing, yet older patients with frailty remain underrepresented in clinical cancer trials and guidelines [8]. In cancer treatment, evidence-based guidelines are essential for daily clinical practice. Since 2004, the Danish Multidisciplinary Cancer Groups (DMCG) have developed and updated interdisciplinary guidelines to ensure high-quality cancer care and support continuous improvements in cancer treatment.

The Danish Society of Geriatric Oncology (DSGO) was recently established to strengthen research and treatment for older patients with cancer in Denmark. To map current gaps and set the stage for future initiatives, we aimed to examine whether Danish national guidelines address geriatric oncology and provide guidance on how to assess and treat patients with frailty and age-related impairments in the cancer treatment trajectory.

Methods

Material

The study evaluated DMCG guidelines for six major cancer diagnoses (lung, breast, colorectal, ovarian, bladder and prostate), all with an overall median age at diagnosis above 65 years. The diagnostic process, treatment and management of solid tumours involve close collaboration of surgical and oncological departments.

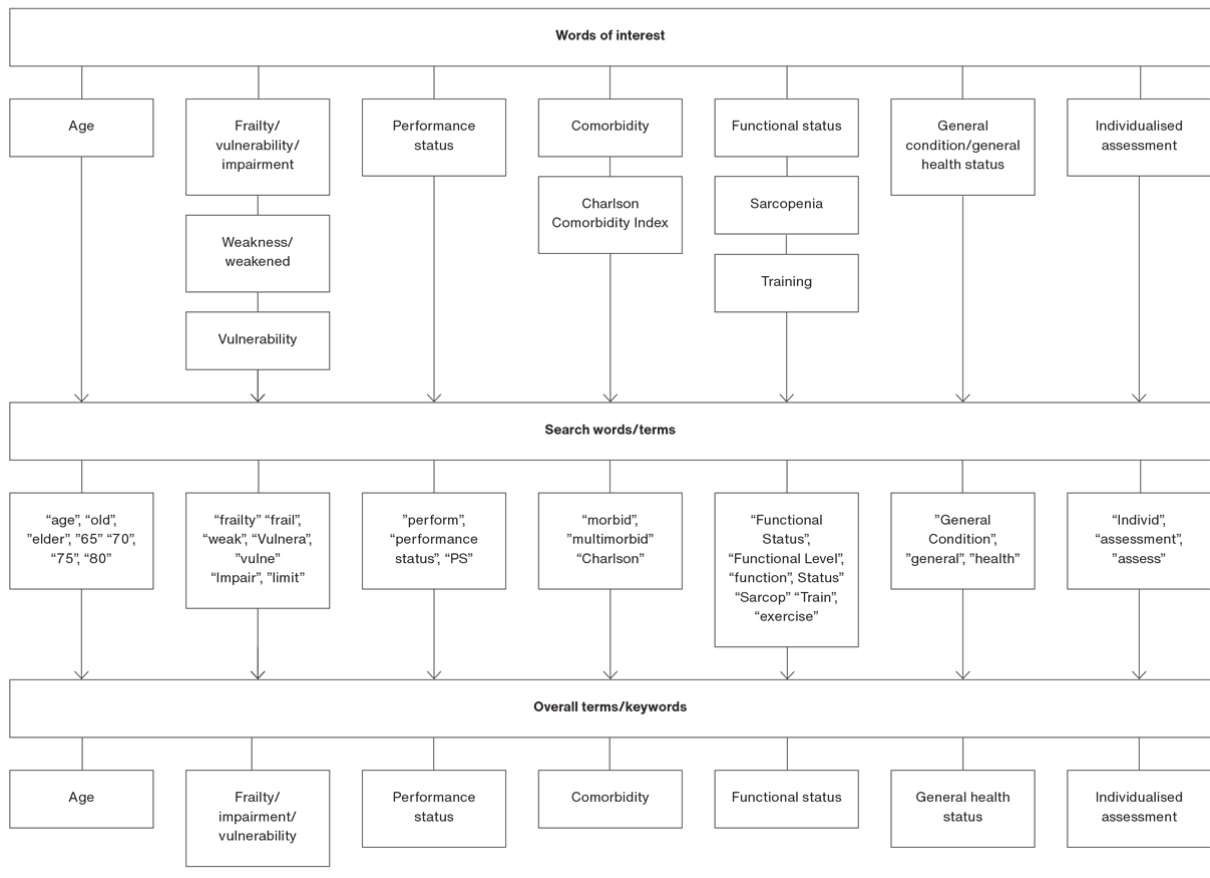
An assessment of all available guidelines focusing on surgical and oncological treatment for the six cancer diagnoses was conducted in late 2023. The most recently approved guidelines incorporated in this study were Lung 2022; Breast 2020-2022; Colorectal 2018-2023; Ovarian 2020-2023; Bladder 2023 and Prostate 2022-2023.

Guidelines within pathology and radiology were excluded as they focus on methodological domains and do not provide treatment recommendations.

Data collection

To assess the extent to which guidelines addressed the unique needs of older patients, a systematic approach was adopted. Initially, a gross list of relevant keywords and abbreviations was compiled for a systematic search (Figure 1). The list was then reviewed and approved by an expert panel comprising clinicians from relevant specialities (geriatric, oncology and surgical specialities). Final refinement and validation of the search list was conducted by two clinicians independently, who evaluated selected cancer guidelines using the developed search list. Specific keywords or search terms were then modified, deleted or added to ensure comprehensive coverage of the following domains before use: age, frailty, performance status, comorbidity, functional status, general health status and individual assessment.

FIGURE 1 Flow chart illustrating the process of identifying relevant topics, search terms, and final keywords on age-related factors in cancer treatment.



For all final search terms, an individual search through the entire text document was performed across all cancer guidelines. Each guideline was assessed by two clinicians, who independently registered and assessed sentences with identified words according to the grading system below. The presence of a keyword alone was not sufficient to increase the score; the context and clinical relevance of the statement were evaluated before categorisation.

Graduation and assessment

A grading system was developed to assess the incorporation of frailty and age-related considerations within the guidelines. Each identified search term was allocated into one of three categories based on clinical relevance and guideline recommendations. The scores ranged from zero to two, with two representing the highest score:

0: Absence or no relevance of the search term.

1: Identification of the search term as risk factors but without specific recommendations or intervention proposals.

2: The search term was included in the recommendations for clinical practice.

For each cancer diagnosis, guidelines were screened and evaluated by two clinicians with expertise in geriatric oncology and the specific cancer domain. Any discrepancies in grading were resolved through consensus within the project group, ensuring uniformity and agreement in the assessment across guidelines.

Trial registration: not relevant.

Results

A total of 59 different guidelines across the six different cancer diagnoses were identified. The number of guidelines per cancer diagnosis varied. Colorectal cancer was covered by 22 specific sub-guidelines addressing different disease stages and treatment modalities, whereas other cancers were represented by fewer, broader guidelines. All available sub-guidelines relevant to treatment were included.

The results regarding search terms in the individual guidelines are presented in **Table 1**. While all guidelines across the six cancer diagnoses included recommendations addressing age and comorbidity, frailty/vulnerability were less consistently integrated. Three guidelines (ovarian, bladder and colorectal cancer) mentioned frailty as risk factors in cancer treatment, whereas only the breast cancer guidelines explicitly provided a recommendation related to frailty. Two guidelines did not mention frailty at all.

TABLE 1 Presence of identified keywords in individual Danish cancer treatment guidelines across six different frequent cancer types. The numbers (0-1-2)^a indicate the highest score identified for each factor addressed, with the number 2 representing the highest score in the grading system and identified guidelines with a specific recommendation for older cancer patients.

Guideline	Age	Frailty/impairment/ vulnerability	Performance status	Comorbidity	Functional status	General health status	Individualised assessment
Lung cancer	2	0	2	2	0	2	2
Breast cancer	2	2	0	2	0	0	0
Prostate cancer	2	0	2	2	2	2	2
Bladder cancer	2	1	2	2	0	2	2
Ovarian cancer	2	1	2	2	0	2	1
Colorectal cancer	2	1	2	2	1	2	2

a) 0: absence or no relevance of search words; 1: identification of search words as risk factors, but without strong recommendations or specific intervention proposals; 2: inclusion of specific interventions for older patients with cancer in guideline recommendations.

Performance status (PS) and general health status were included with recommendations in the guidelines across five of the six cancer diagnoses, whereas functional status was explicitly addressed in one guideline within prostate cancer. Individual assessment was mentioned in the guidelines for five cancer diagnoses, with specific recommendations made in four of the five cases.

The guideline recommendations varied in their level of unambiguity, straightforwardness or specificity. **Table 2** includes examples of both very clear and less explicit recommendations for all search domains.

TABLE 2 Examples of recommendations from different Danish cancer treatment guidelines, stratified according to clear and unclear formulation.

Clear formulation (rated 2)	Unclear formulation
<p><i>Age</i></p> <p>"For patients aged ≥ 80 years or with concerning comorbidities, sublobar resection is recommended as the primary surgical approach" (lung cancer)</p> <p>"Patients over the age of 80 are generally not offered adjuvant chemotherapy and for combination therapy for tumours > 10 cm the age limit is 70 years" (colorectal cancer)</p>	<p>"For patients in good general health: PS 0-1, < 75 yrs in biological age, concomitant chemotherapy should be considered" (bladder cancer)</p>
<p><i>Frailty/impairment/vulnerability</i></p> <p>"For frail and/or comorbid patients, who according to the guidelines are recommended dose-dense chemotherapy, six cycles of a taxane, e.g. docetaxel, and cyclophosphamide: TC, are recommended, possibly corresponding to dose level -1, alternatively three cycles of paclitaxel followed by three cycles of E90C600, possibly at a reduced dose considering current and expected quality of life" (breast cancer)</p>	<p>"It is essential to carefully screen patients to identify the group of patients who are expected to profit from the treatment and to schedule individual treatment plans for the older patients who are most frail" (ovarian cancer)</p>
<p><i>Performance status</i></p> <p>"Preoperative neoadjuvant chemotherapy should be offered to eligible patients: age < 75 years, PS 0-1, normal kidney function, $<$ grade 2 hearing loss, $<$ grade 2 peripheral neuropathy, $<$ NYHA-class III" (bladder cancer)</p>	<p>"For patients with poor performance status, the dose can be adjusted to 20 Gy in 4-5 fractions, or palliative radiotherapy may be omitted" (lung cancer)</p>
<p><i>Comorbidity</i></p> <p>"To assess expected survival on a patient without cancer, look at local life expectancy tables, biological age and comorbidity calculated from the Charlson Comorbidity Index" (prostate cancer)</p>	<p>"Treatment can be offered, taking into account disease stage and patient-related factors such as frailty and comorbidity" (colorectal cancer)</p> <p>"Treatment can be administered considering comorbidity, organ function, and PS" (colorectal cancer)</p>
<p><i>Functional status</i></p> <p>-</p>	<p>"Older patients should be assessed based on comorbidity and functional status rather than chronological age in relation to radical treatment" (bladder cancer)</p>
<p><i>General health status</i></p> <p>"The patient may preoperatively also be investigated with a screening of health status in accordance with the G8 screening tool, nutritional status, cognitive functions: mini-COG, and assessment of physical ability: ECOG performance status" (prostate cancer)</p>	<p>"When considering the indication for adjuvant treatment in patients with NSCLC, general health condition and comorbidity should be taken into account, ensuring that adjuvant treatment is only administered to patients expected to tolerate the therapy" (lung cancer)</p>
<p><i>Individualized assessment</i></p> <p>"Based on the described standard follow-up program, an individual follow-up plan must be tailored for each patient after completion of the initial treatment" (prostate cancer)</p>	<p>"Following surgery for LCNEC, guidelines for SCLC are followed, and adjuvant chemotherapy may be considered based on individual assessment" (lung cancer)</p>

ECOG = Eastern Cooperative Oncology Group; LCNEC = large-cell neuroendocrine carcinoma; NYHA = New York Heart Association; PS = performance status; SCLC = Small-Cell Lung Cancer; TC = taxotere and cyclophosphamide.

Discussion

In this assessment of current evidence-based Danish national cancer treatment guidelines, we found several guidelines addressing age- and frailty-related issues. However, very few guidelines provided specific guidance on assessing or treating older patients with comorbidity and/or frailty. Despite previous studies indicating frailty status as a significant predictor of risk of complications to treatment and poor recovery, only one guideline contained a specific recommendation regarding frailty.

The gold standard for frailty assessment is a comprehensive geriatric assessment (CGA), which evaluates, e.g.,

medication use, comorbidity, physical function, nutrition and social support. CGA-guided interventions can reduce toxicity [9], functional decline and post-operative complications [10], while improving treatment completion and patient-centred outcomes [11-13]. Mapping of geriatric impairments could also be done with a simpler geriatric assessment (GA), which, unlike the CGA, does not include any interventions.

Structural screening for frailty and impairments to uncover the need for geriatric interventions is recommended by international societies. However, no such screening is implemented in Denmark or included in the Danish cancer guidelines. A newly published SIOG review highlights the limited representation of geriatric oncology also in other European cancer guidelines [14]. A Danish consensus on screening tools is needed to describe the consequences of identified frailty and detail recommended handling. A CGA might not be available at all cancer centres and would require a much larger number of geriatricians. Instead, GA-identified impairments could also be handled by the patients' general practitioner or cancer-treating departments. A challenge remains in defining actionable cut-offs and determining the consequences of identified vulnerabilities. CGA does not provide clear-cut thresholds for treatment modification, but could be a tool to facilitate individualised optimisation and guide shared decision-making.

Although we identified recommendations related to selected keywords, many were vague and open for interpretation, e.g., “*Treatment can be offered taking into account disease stage and patient-related factors such as frailty and comorbidity*” (colorectal cancer). This recommendation does not provide the clinician with specific guidance, making it difficult to translate into practical use in everyday clinical work. A list of more detailed considerations would be useful.

Age and comorbidity were the most frequently mentioned terms with associated recommendations. Some guidelines applied explicit age cut-offs, recommending against treatment above a certain chronological age. This contrasts with international consensus, which advocates decisions based on biological rather than chronological age, incorporating assessments of frailty and comorbidity [7]. However, these recommendations are based on available evidence from subgroup analyses on older patients who were fit enough to participate in larger RCTs, but provide no answers for more frail patients.

Comorbidity is an important domain that can influence cancer care by directly affecting non-cancer mortality and treatment decisions. However, only a few guidelines provided specific criteria regarding the type or severity of comorbid conditions that should influence treatment decisions.

Most guidelines included PS as a central concept in treatment decisions, and probably as a surrogate for the two less mentioned search terms: functional level and general health. PS has historically been the gold standard for physical and functional performance assessment and a strong predictor for prognosis, complications, treatment toxicity and adherence [15]. The simplicity of PS has led to its outstanding position in oncology. However, PS cannot differentiate impairments due to musculoskeletal issues from organ dysfunction and lacks evaluation of the psycho-cognitive dimension, which are crucial to treatment decision-making capacity and adherence [15]. Several guidelines recommend using PS in combination with age and comorbidity; thus, it is recognised that PS must be supplemented [16].

The clinical guidelines are based on evidence graded A-D by the Oxford 2009 Levels of Evidence. Most guidelines that included recommendations or notes on frailty were based on studies with an evidence grade of C-D. The growing awareness of age-related challenges is reflected in ongoing high-quality clinical trials assessing treatment strategies in older or frail patients with cancer (e.g. the DPCG-01, N9 [17, 18]). These trials evaluate the initial dose reduction of combination therapy. To further provide knowledge on cancer care for older patients, broader clinical trials including real-world populations and the use of real-world data are needed to guide evidence-based treatment decisions.

While this study may be limited by potential guideline updates being developed during the screening process and the possible omission of relevant search terms, its strengths include coverage of the most common cancer types, ensuring broad representation across multiple oncological settings, a systematically developed and multidisciplinary-reviewed search strategy, a comprehensive guideline search and meticulous full-text review to ensure contextual accuracy. Our grading system was self-constructed and not formally validated. All assessments were followed by consensus discussions to reduce subjectivity; however, we did not calculate an interrater reliability measure such as a kappa score. A potential bias is that terminology might have influenced the score even without concrete recommendations, as search terms can appear in background text as well as in explicit guidance. Although we only scored terms in clinically relevant contexts, some degree of interpretation remains unavoidable.

The absence of definitive guidance on cancer treatment and the assessment of older patients may be attributed to the limited availability of robust evidence on age-related considerations when the guidelines were developed. However, our review indicates that some DMCGs include dedicated sections focused on the treatment of older patients, particularly concerning oncological therapy.

For patients with colorectal cancer, the DMCG has compiled a guideline regarding prehabilitation for all age groups, including the older population, to enhance physical and functional status before surgery. The Danish National Cancer Program, which has secured fast-track diagnosis and enhanced treatment trajectories [19, 20], has historically left few possibilities for individual assessment and optimisation before treatment. The strict timelines of the cancer pathways may be counterproductive in a geriatric context where a one-size-fits-all approach is rarely suitable. In line with the Danish Cancer Initiative V, which emphasises individualised treatment, future guidelines should balance rapid care with tailored preparation and prehabilitation.

Conclusions

Our assessment of Danish national cancer guidelines found that, although age and frailty are acknowledged, specific guidance on frailty screening and management is lacking. A dedicated geriatric oncology guideline to support specific DMCG recommendations across cancer types is warranted. Further research, including dose-guiding clinical trials and real-world data, is needed to inform Danish cancer guidelines and improve future care for older patients.

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