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Geriatric Oncology

Basic Assessment of the Older Cancer Patient

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Opinion statement

Cancer is a disease of the elderly (median age 67 in the US), and this is a population with a variable health status. Therefore, treating the older half of the cancer population will present the challenge of not only addressing tumor diversity (the side often referred to in "personalized cancer care" discussions), but patient diversity as well as the interaction between these two heterogeneities. In that sense, geriatric oncology is the ultimate personalized cancer care. In this article, we will address the recent updates in the basic assessment of the patient's condition, and their implication for clinical and research use. The main progresses reported in the last couple of years pertain to geriatric screening tests, and to prediction of the tolerance to treatment. Some important data on the impact of comorbidities on cancer behavior have emerged, but the clinical implications of these data are still being sorted out. We recommend a two-step approach to the basic evaluation of the older cancer patient. First a short screening with a tested screening instrument. Then further work-up of the geriatric findings in parallel with the oncology work-up to define an integrated treatment plan.

Introduction: the two-step approach

It is now well established that older cancer patients present a significant prevalence of geriatric problems. Some 20% have an ECOG PS of 2 or higher. An equal proportion has a dependence in basic activities of daily living (ADL). More than half have a dependence in Instrumental activities of daily living (IADL). More than 90% have at least one comorbidity, 30–40% of those comorbidities are severe. Depression is present in 20–40% of patients, and cognitive impairment in 25–35% of patients. Finally, 30–50% of patients are at risk of malnutrition or frankly malnourished [1]. The average number of medications taken by older patients is a half-dozen, with a significant potential for interactions [2]. It has risen since the mid-nineties, when it was four [3], and is likely to keep rising. Therefore, as a population, older patients need to be assessed for more than just their cancer status.

As a general approach to their treatment, we suggest a two-step process in daily oncology practice, illustrated in Fig. 1. Several short screening instruments are available with some validation in geriatric oncology. They are usually simple to use, and although all the details of their use have not yet been worked out, many of them have at least some validation. If one chooses a tool designed to assess who needs a more comprehensive multidisciplinary geri-

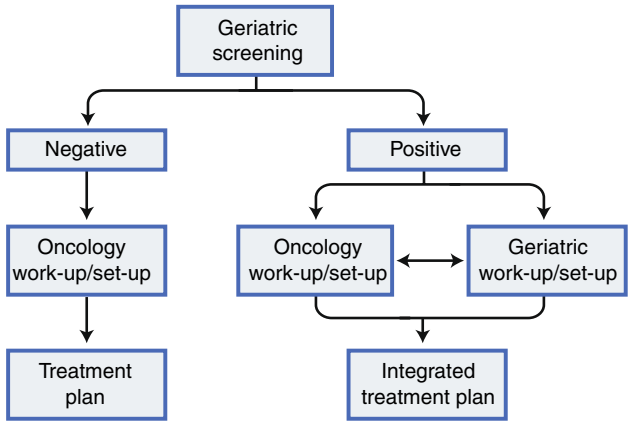

Figure 1. General approach to treatment planning in an older cancer patient.

atric assessment, then the rapid screening can be done on all new patients, and about half of them will need a comprehensive geriatric work-up in parallel with their oncology work-up. Such an approach has been used routinely over the last decade in our clinic with the Senior Adult Oncology Program (SAOP) screening tool.

Short screening tools

These are rapid triage tools taking only a few minutes to answer. This is an area in active development and the list below does not claim to be exhaustive. But here are some instruments that were used and tested in recent articles.

The abbreviated Comprehensive Geriatric Assessment (aCGA) [4, 5]

Overcash et al. isolated 15 items (an abbreviated CGA) that correlated with the findings of a Multidisciplinary Geriatric Assessment (MGA) in a large database of older patients with cancer who underwent a CGA as part of their oncology evaluation. These 15 items include 3 questions about ADLs, 4 questions about IADL, 4 questions from the Mini Mental Status Exam (MMS), and 4 questions from the Geriatric Depression Scale (GDS). If the patient has any impairment in the ADL or IADL items in the abbreviated CGA, then the full ADL and IADL scales should be administered. If 2 depression items are altered, a full GDS should be administered. A score of 6 or less in the cognitive screen triggers a full MMS [5]. The score can be obtained from Overcash's 2005 article [4]. Last year, Kellen et al. compared in older cancer patients the performance of the aCGA with that of the Vulnerable Elder Survey (VES) 13 and the Groeningen Frailty Index (GFI) in predicting impairments in ADL, IADL, MMS, and GDS [6]. The aCGA was more sensitive than the other two other indices for functional impairments, with a sensitivity of 97% for

ADL and 92% for IADL, but less performing for depression (69%) and cognitive impairment (23%).

The Senior Adult Oncology Program (SAOP) 2 screening tool

This empirical tool was developed by the multidisciplinary clinical team of the SAOP at Moffitt to determine when a multidisciplinary team consultation was required in new patients. In addition to function, depression, and cognitive screening, the screen includes questions regarding quality of life, self-rated health, falls, nutrition, sleep, polymedication, and social questions (drug payment and caregiver availability). After more than 8 years of clinical use in its second version, this screen has demonstrated face validity, finding that 63% of senior cancer patients needed psychosocial counseling, 40% dietary intervention, and 14% medication counseling and assistance (the latter probably underestimated) [7]. Its performance was validated against an multidimensional geriatric assessment [8]. It is a sensitive tool, but there is low internal specificity, meaning that if a question is positive in one domain of the questionnaire, it might reflect a problem in another domain, reflecting the importance of a multidisciplinary team approach. The first page is answered directly by the patient, and the second page is administered by the clinic staff. If one item is positive, the respective specialist is called in with possible secondary referral to other members of the team. If several items are impaired, the multisiciplinary team is called in or a geriatric referral is made for a CGA. The tool has been translated in Spanish and in French, and Italian and Chinese translations are in progress.

The Triage Risk Screening Tool (TRST)

This tool was developed for geriatric screening in the emergency room setting [9]. Patients screening positive then underwent a half-hour evaluation by a geriatric nurse practitioner. Its performance was compared to a full CGA in oncology patients [10]. It proved sensitive, provided the threshold was lowered from 2 to 1 point. Therefore any positive item would warrant geriatric evaluation in cancer patients. It was compared to the G8 and the GFI in its ability to detect a "geriatric profile" as defined by a multidisciplinary geriatric oncology team [11]. With a cut-off value of 1, its sensitivity was 92%, vs 64% with a cut-off of 2 (the original cut-off), 80% for the G8, and 57% for the GFI.

The Vulnerable Elders Survey (VES) 13

Mohile et al. analyzed the performance of the VES13 [12], developed in a large geriatric survey cohort, in older prostate cancer patients [13]. Fifty percent of patients were identified as impaired on the VES 13 (score ≥3). That cutoff had a sensitivity of 72.7% and a specificity of 85.7% for impairment in 2 or more dimensions on an MGA. The score can be obtained from e.g. http://www.usafp.org/Word_PDF_Files/Best-Practices/Vulnerable%20Elders%20Survey.doc. It was compared to the aCGA in the study mentioned above but was not as sensitive to impairments in ADL (76%) and IADL (67%) [6]. Lucianni et al. found a high sensitivity of the VES13 for geriatric problems in their study: 87% compared to a CGA, and 90% compared to ADL/IADLs [14]. However, they "adapted"

the tests for patients above age 85. Although they do not specify the adaptation, the understanding of this author is that they might have counted all patients 85 and above as frail. On the other hand Falci et al. found 30% of elderly patients with favorable VES-13 scores to be vulnerable or frail at full CGA, and 40% of patients with unfavorable VES-13 scores to be fit [15].

The Groeningen Frailty Index [16]

This index is a list of 15 screening questions addressing various geriatric domains. A score of 4 or higher indicates frailty. In a screening role in older cancer patients, it underperformed the aCGA and VES13 in detecting impairments in ADL and IADL (47% and 39% respectively). It did not either fare as well as the TRST and the G8 in detecting a geriatric profile in the study by Kenis et al. [11]. Therefore it might be more valuable to use it as a frailty defining tool than as a screening instrument in older cancer patients.

The G8

This index was developed by the Institut Bergonié team in France [17]. It consists of 8 items with a score ranging from 0 to 18. It was compared to the TRST and the GFI by Kenis et al., and its sensitivity was intermediate between the TRST and the GFI, at 80%. It is presently being compared to the VES 13 in a large French randomized multicenter trial.

Multidimensional Geriatric Assessment (MGA) packages

These are sets of a half dozen questionnaires or tests aimed at either providing an overall geriatric evaluation in the study setting, a second step in patients screening positive on short screens, a preoperative evaluation, or a first evaluation in an obviously frail patient. They usually screen for functional and cognitive impairments, depression, malnutrition, and comorbidity, using validated geriatric instruments. A couple of study-specific questionnaires can easily be added for an overall evaluation time of about 20 min. Some examples are:

- Katz ADL [18], Lawton's 9-item IADL [19], ECOG PS, GDS (15 items) [20], Folstein's MMS [21], MNA [22], Cumulative Illness Rating Scale-Geriatric (CIRS-G) [23]. This set was used for example in several Moffitt & RTOG studies [24, 25•, 26–28].
- ADL (MOS physical health) [29], IADL (OARS subscale) [30], Timed get-up and go [31], comorbidity (OARS subscale) [29], Blessed Orientation Memory-Concentration test [32], Hospital Anxiety-Depression Scale (HADS) [33], MOS social functioning and support subscales [34], BMI and weight loss. Used for example in CALGB studies [35].
- Katz ADL, Lawton's IADL, ECOG PS, MMS, GDS, comorbidity (CIRS-G or Satariano [36]), ± EORTC-QLQ30/social support [37]. Used for example in EORTC or GIOGER studies.
- Katz ADL, Lawton's IADL, ECOG PS, GDS, MMS, Brief Fatigue Inventory [38], comorbidity (Satariano), ASA score. Used for example by the SIOG (International Society of Geriatric Oncology) Surgical Task Force [39].

The component instruments are available in several languages through online sources.

Using multidimensional geriatric information in practice

Physiologic information

Instruments should not make us forget basic physiologic parameters. A low albumin or an anemia will mean more free chemotherapy drug in the patient's system [40]. A normal creatinine does NOT equal a normal renal function. In fact, the majority of patients aged 75 and older will have a creatinine clearance below 60 ml/min with a normal serum creatinine [41]. The Cockroft-Gault formula and the MDRD both give reliable results in the elderly, with the former underestimating slightly the clearance, and the later overestimating it [42••].

Drug interactions

Many physicians are aware of the importance of p450 genetic variation in the metabolism of drugs. However, in the elderly, this is often compounded or blurred by the use of an average of 6 medications, at least 2 of which will interfere with p450 enzymatic function [2]. This can significantly interact with chemotherapy toxicity: major interactions double the risk of severe toxicity, and if these interaction involve the chemotherapy drug directly, the risk is tripled [43].

Risk prediction models

The prediction of treatment outcome in a situation where multidimensional variables occur as with the older patient is difficult. Trained oncologists have difficulty integrating in their treatment plan more than three variables at one time [44]. Our interpretation of the patient's desires might be biased by cultural expectations [26, 45], and our reading of the literature is selective due to time constraints. Therefore good quality decision models based on systematic reviews of available data are very precious.

A geriatric evaluation has so far mostly been used as a detection tool to address problems that might interfere with cancer treatment and have them addressed by the multidisciplinary team or the respective specialists. However, 2010 brought to the scene harbingers of the next generation of tools in geriatric oncology: tools that use the information gathered by the geriatric assessment to guide oncologic choices. Two oral presentations at ASCO presented instruments to predict the risk of severe side effects from chemotherapy. Abstract 9000, by our group, reported the results of the Chemotherapy Risk Assessment Scale for High-age patients: the CRASH score [25•]. This score identified four risk categories for grade 4 hematologic, grade 3–4 hematologic, or combined severe toxicity. Of interest, this study, that assessed both geriatric instruments and classic oncologic predictors, retained 3 geriatric instruments in its final model: the IADLs, MNA, and MMS. This study included both a derivation and a validation cohort, and therefore provided a validated instrument. In the future, it might be possible to identify a subset of the most discriminative questions within the geriatric instruments. Abstract 9001, by the Cancer and Aging Research Group, presented another predictive score, this time for the occurrence of grade 3–4 hematologic and

non-hematologic toxicity [46•]. They derived a 3-level score which again included several geriatric instruments, and extracted a subset of discriminative questions. This came at the cost of running a validation cohort, and Hurria et al. are now working on a validation study.

Also recently published is a simple tool that might help identify patients at very low risk of severe neutropenia and febrile neutropenia after their first cycle of treatment [47] . In such patients, weekly blood counts beyond the first cycle might be avoidable. In a different domain, Audisio et al. explored the potential of geriatric instruments to predict complications of surgery with the PACE score [39, 48]. IADL dependence and the number of geriatric domains altered correlates with the risk of complication within 30 days after surgery. These studies do represent the future of the use of geriatric instruments in geriatric oncology. We need to harness the now well established correlation of geriatric instruments with various oncology outcomes to transform them into decision helps to guide our integrated onco-geriatric approach.

Other very helpful models are general models that exist for example for the adjuvant treatment of breast, colon, and lung cancer (www.adjuvantonline.com) or for initial treatment of prostate cancer [49]. These allow an objective quantification of benefits that can be weighed against potential harms in the individual discussion with the patient. As there will never be therapeutic studies focused only on –say- older women with lung cancer, diabetes, and coronary artery disease, there is a clear need for more such models in geriatric oncology.

Treatment of frail patients

A challenge in oncology is to treat frail patients. These patients are rarely included into clinical trials, and few data are available as to their definition and treatment. The definition of frailty is a very active area in the field of Geriatrics. The last two years have shown the testing of several instruments. Beside the classic definition by Fried et al. [50], recent articles demonstrated a comparable performance of the Study of Osteoporotic Fractures Frailty Index, which might be easier to apply in clinic [51–53]. The allostatic index [54] analysis several biological and physiological variables. The Rockwood index considers frailty as an accumulation of altered parameters [55, 56]. Other indexes are created and tested at a rapid pace. However, these indexes remain yet to be formally tested for their usefulness among cancer patients.

The EORTC is to be congratulated for the recent publication of the results of EORTC 20992, which studied the use of CVP in frail patients with lymphoma [57]. Overall, the prognosis of this group of patients was much poorer than healthier patients treated with CHOP, as expected. But a subset (37.2%) benefitted from the treatment and was still progression-free a year later. The important lesson from this study is that if these patients had a severe toxicity, it had an important risk of fatality. Therefore these patients should be monitored closely, and proactive supportive care needs to be aggressive. These patients should be referred to specialized multidisciplinary geriatric oncology clinics for treatment. Another study addressing frail patients with lymphoma reached similar conclusions [58].

The impact of comorbidity

Another aspect of geriatric oncology that has seen a lot of results published in the last year is the impact of comorbidity on cancer prognosis. The prevalence of comorbidity increases with age. Diseases such as diabetes and obesity influence the behavior of the cancer. This is a very active area of recent publications and clear conclusions are hard to draw at this point. Inflammatory disease might have an impact as well. A review of recent articles on these diseases is beyond the scope of the present article. Interestingly, a treatment such as metformin might also have antitumoral properties as well. In one study, whereas diabetic patients had higher relapse rates from their breast cancer than normal controls, those treated with metformin actually had the lowest relapse rate of any group [59]. Interestingly enough, hyperglycemia during treatment might also worsen the side effects of chemotherapy in the elderly [24]. The risk of hospital death from febrile neutropenia and documented infections increases markedly with the number of comorbidities as well [60]. Cognitive impairment can reduce by half the overall survival of older cancer patients [61]. Interestingly, the impact is visible in an equal proportion for patients with early and advanced stage cancer. Although one might think this might be due to less intensive treatment, the treatment pattern of those patients were in fact very similar, with an equal rate of use of chemotherapy (35%). This treatment pattern is at odds with epidemiologic findings [62] and might suggest a beneficial effect of being treated in a dedicated geriatric oncology program.

Conclusions

There is no doubt that a comprehensive approach is becoming widespread in treating older cancer patients. As convenient screening tools are being developed, attention to geriatric problems can be improved in oncology clinics. A geriatric work-up can be run in parallel with an oncology work-up for the half of patients who need it, and some tools have now emerged that use the information from the geriatric assessment to guide oncologic therapeutic decisions.

Disclosure

No potential conflicts of interest relevant to this article were reported.

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