

ADVANCES IN ONCOLOGY

Current Developments in the Management of Solid Tumor Malignancies

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Colorectal Cancer In Focus

Treatment Considerations in Elderly Colorectal Cancer Patients

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H&O What are the treatment considerations in elderly colorectal cancer (CRC) patients?

NJM There are a few considerations that clinical oncologists need to take into account when deciding whether or not to treat elderly CRC patients. In addition to stage, histology, and presentation of the disease, we also need to consider concurrent medical conditions, other medications that the patient may be taking, physical function at the initiation of therapy, and social support (which also plays a role in terms of resources for care outside of the clinical setting, as most of our therapies are outpatient based). Taking into account life expectancy and estimating a patient's physiologic reserve at the time of presentation of cancer are also necessary when deciding what treatment approach is appropriate.

H&O What are the differences in the current management of elderly and younger CRC patients?

NJM One of the largest differences in the management of older and younger CRC patients is that we are willing to take risks with aggressive therapies in younger patients that we would not necessarily be willing to take in older patients with similar presentations. This may be due to increased risk of adverse effects of treatment or decreased quality of life that can occur in older individuals at risk

of functional decline with aggressive treatment. Presently, age is a useful proxy for life expectancy, but we do not have readily available metrics of functional status that can also impact outcome of treatment. Additionally, we may factor in patient and/or provider preference, as there may be objections to a potential temporary or even permanent decrease in quality of life or an increased potential for toxicity.

H&O What are some challenges in treating elderly patients?

NJM The biggest challenge in treating elderly patients are competing medical conditions that impact physiologic reserve and tolerance of therapy. This baseline functional status needs to be considered when discussing treatment. Existing data support the increased morbidity and mortality associated with the increased number and severity of concurrent medical conditions. Further, poor functional status is an independent predictor of morbidity with treatment.

A second challenge in treating elderly patients is lack of generalizability of existing clinical trial data to the general older patient. It is well established that patients participating in clinical trials are not representative of the general population we treat. Further, older patients are underrepresented in clinical trials, disproportionate to the incidence of colorectal cancer in this age group. Thus, the data available provide poor guidance for treatment decisions for older patients.

H&O What should be done in terms of screening elderly patients to identify disease and monitor those who are receiving chemotherapy?

NJM There have been attempts at setting guidelines as to when screening for colon and rectal cancers should be discontinued in older patients. Generally, it is recommended that screening for colorectal cancer should be discontinued when the risk of the procedure outweighs the potential added benefit to life expectancy, although this is not specific to a particular age. Further, screening is not encouraged in patients who are not thought to be able to receive intended treatment due to competing risk factors. For instance, many patients are not offered screening due to concurrent medical conditions that would preclude medical or surgical treatment.

Close monitoring for tolerance of treatment should be done for all patients, but particularly for older patients at risk of adverse effects, as treatment for CRC often involves aggressive combination chemotherapy. In the outpatient setting, we rely on patients and/or their care provider to report their tolerance of the chemotherapy and to contact their provider rapidly if they notice any adverse effects. Ideally, patients should be evaluated at each treatment session and may require additional evaluation at timely intervals, which could include phone monitoring.

The ideal monitoring would involve a consistently applied tool, such as an abbreviated geriatric assessment, to screen for changes in functional status, concurrent medical conditions, or social functioning that can suggest a need to adjust therapy or to provide additional support. Currently, we do not have such a system in place and are therefore relying on vital signs and clinical assessment, which thus far are not sufficient enough to limit the adverse effects seen in many elderly patients.

H&O Why is underrepresentation of the elderly in clinical trials such a problem, and what can be done to combat this issue?

NJM Within the next 30 years, 1 in 8 of the world's population will be over 65 years, accounting for an increasing proportion of individuals diagnosed with cancer. It is imperative to have strategies in place to appropriately evaluate and treat these older patients. The data on which we base our treatment decisions need to be reflective of the patients we see in practice. Current clinical trial data are largely driven by younger participants. Although half of the population diagnosed with CRC are above the age of 70, only approximately one-fifth of patients in this age group are enrolled in the clinical trials on which we base our treatment decisions.

Strategies to address this dichotomy include less stringent eligibility criteria, allowing closer monitoring for patients who have renal insufficiency, or modification of treatment based on the patient's initial presentation. Researchers have begun designing trials specifically for elderly patients. By designing a trial targeting older patients, we are better able to account and adjust for those factors that have otherwise excluded them.

H&O Have there been any trials or analyses that have evaluated chemotherapy in the elderly?

NJM Prospective studies are currently in development for older patients diagnosed with colorectal cancer. Several retrospective analyses have been conducted in this population. In 2009, Dr. Thierry André and colleagues of the MOSAIC (The Multi-center International Study of Oxaliplatin/5-fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer) study published the updated 6-year survival results of oxaliplatin in combination with infusional fluorouracil (5-FU) and leucovorin (FOLFOX) in the postoperative setting. The researchers noted that the survival benefit observed with FOLFOX in the overall population was not maintained in patients older than 65. Of 1,347 patients, 463 were above the age of 65, and their risk of death from CRC was not altered by the use of FOLFOX, showing a disparity in survival outcomes compared to younger patients (<65 years). Further analyses of this disparity are forthcoming.

At the 2009 American Society of Clinical Oncology meeting, we presented results from a retrospective analysis of pooled individual patient data from the ACCENT (Adjuvant Colon Cancer Endpoints) database. The findings from this analysis confirmed those from the MOSAIC trial and from the National Surgical Adjuvant Breast and Bowel Project C07 protocol (presented at Gastrointestinal Symposium 2010). The analysis evaluated data from 6 phase III adjuvant trials comparing intravenous fluoropyrimidine to combinations with irinotecan or oxaliplatin, or oral fluoropyrimidine in stage II/III colon cancer. The population comprised more than 12,000 patients, with nearly 20% over the age of 70 ($n=2,170$). In the overall population, overall survival, disease-free survival, and time-to-recurrence were significantly improved for those in the experimental versus the control arms among patients younger than 70 years but not in those older than 70 years. To date, the ACCENT database has been the largest collection of data including older patients, specifically raising the question about the efficacy of treatment in different age groups. There have been other studies attempting to refute these data, but none yet providing a mechanism for this observed outcome disparity or a strategy to address it.

H&O What needs to be done to provide elderly patients with the best treatment options?

NJM Firstly, we need to increase clinical trial enrollment because the evidence we obtain from clinical trials forms the basis of treatment decisions. Secondly, we should integrate a reliable geriatric assessment tool, such as that proposed by Hurria and colleagues, to screen for patients who may not tolerate treatment or need additional support to do so. Ideally, this tool will also predict toxicity and outcome, resulting in a risk-adjusted treatment approach. The goal is to have knowledgeable and comprehensive discussions with patients and their caregivers to enable appropriate and informed treatment decisions.

Suggested Readings

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