Rational Approach to Cancer in the Elderly

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Take Home Pearls

- Colorectal cancer is a frequent and potentially curable disease (when localized) in the elderly.
- Decision making in the elderly is complex due to the underlying health status that can interfere with the management from diagnosis to treatment.
- Preserving the quality of life and autonomy are more important to consider in this population rather than increased survival alone. However, physicians tend to underestimate life expectancy that will lead to suboptimal management.
- Some form of geriatric assessment done at the time of diagnosis may help the physician in their decision making.

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4.1   Introduction

The incidence and mortality of cancer increase with age (Yancik and Ries 2000). Over 60% of cancers and more than 70% of cancer deaths occur in people over 65. The risk of cancer in this age group is 11 times higher than in people under 65. Thus, two-thirds of tumors of the colon, rectum, stomach, pancreas, prostate, and urinary tract affect patients older than 65. Colorectal cancer is the second cause of death among people over 65 (Aouba et al. 2007). Due to the aging population and the increased cancer incidence due to age, clinicians should expect that they will have to care for an ever growing number of elderly cancer patients.

4.2   Specific to Colorectal Cancer in the Elderly

4.2.1   Epidemiological Data

The number of new cancer cases (all types) almost doubled between 1980 and 2005 (170,000–320,000), and over 45% of these cancers were diagnosed in the population of patients aged 70 and over. Colorectal cancer is a disease of the elderly. The average age at diagnosis is 70 for men and 73 for women. Colorectal cancers are the third cause in terms of incidence and the second cause in terms of mortality in people aged over 65. Over 75% of deaths from colorectal cancers involve patients over 70.

4.2.2   Why Treat Elderly Patients with Colorectal Cancer?

Data from the National Institute of Statistics and Economic Studies (INSEE) show that overall life expectancy has increased. According to estimates in France, in 2020, life expectancy at birth will be 78.1 years for men and 86.4 years for women (http://www.iinsee.fr). In 2050, it will be 82.2 years for men and 90.4 years for women. In 2050, one out of every three will have lived 60 or more years. In 1991, life expectancy was 73 years for men and 81.1 years for women. Between 1981 and 1991, life expectancy without disability increased by 3 years for men and by 2.6 years for women. All these data indicate the need for concerted and optimal management of cancer in the elderly (Aparicio et al. 2005). Yet it is often the idea of a shortened life expectancy that leads doctors and family not to propose optimal management. Montaigne said, "Age imprints more wrinkles in the mind than it does on the face." Are we really "too old" at age 70? A person who has reached that age still has an additional life expectancy estimated overall to 14.2 years. An 80-year life expectancy has an additional 7.7 years; an 85-year expectancy, an additional 5.4 years. Beyond these theoretical figures, it should be noted that three-quarters of the population over the age of 85 lives independently at home, without any major physiological or psychological impairment.

The main question is whether newly diagnosed elderly cancer patients will suffer from the cancer, in particular those who have slow-growing cancers such as prostate, breast, and kidney. The treatment decision is based more on the state of the patient's underlying health than on the cancer itself. We should not treat slowly evolving tumors that will never become symptomatic in patients whose life expectancy is already limited by comorbidities or impaired functional status. In the case of colorectal cancer, most patients – except those with a very short life expectancy (less than 6 months) – will suffer from complications that include anemia, obstruction, perforation, metastasis, and others. In most cases, the life expectancy of an elderly patient is often underestimated by the family and the physician. Consequently, too often do patients come to us with advanced stages or even with metastases, even though a potentially curative treatment would have been possible. Treatment options had been rejected a few months or years earlier because the cancer was not considered then to be an immediate threat to the patient's survival. To underestimate the potential impact of cancer and life expectancy can expose an elderly patient to a high risk of loss of autonomy and of deterioration in the quality of life that could have been preserved longer had we decided to control the tumor at diagnosis. Finding the right balance between cancer burden and life expectancy remains the main priority of oncologists and geriatricians who treat cancer in the elderly.

4.2.3   Prognosis of Colorectal Cancer in Elderly Patients

Colorectal cancer provides a relatively prolonged survival: a survival rate of 79% at 1 year and 57% at 5 years. However, several studies have shown that age is an independent prognosis factor, as the survival rates of all cancers decrease with age (Vercelli et al. 2000). The Vercelli study that compared the survival rates of two groups of patients (aged 65 and over 65 years), at 1 year and 5 years, revealed a significant difference – regardless of the type of tumor – with a much lower survival rate at 1 year and 5 years in groups of older patients. The 1-year survival rate for men was 71% (aged 65–69), as opposed to 49% (aged 85 and over); the corresponding rates for women were 72% and 44%.

4.2.4   Under Inclusion of Elderly Patients in Clinical Trials

A literature review indicated a lack of data from clinical trials (Aapro et al. 2005). There is a clear underrepresentation of elderly patients in randomized trials of cancer (Hutchins et al. 1999). Hutchins et al. compared the percentage of patients over 65 included in the trials of the South West Oncology Group (SWOG) to that of the general population. Regardless of cancer site (with the exception of lymphomas), the percentage of patients over 65 was consistently below the proportion of people in the general population. The barriers to the inclusion of patients in the studies are

numerous: the doctors' attitudes (most exclude patients based on age criteria alone), the eligibility criteria of the studies themselves that set an age limit or exclude some frequent comorbidities in the elderly, and the patients themselves and their families (Benson et al. 1991; Freyer et al. 1999; Townsley et al. 2003; Tyldesley et al. 2000). This lack of data from the literature prevents clinicians from basing optimal thera-peutic management of elderly patients on research findings or recommendations (guidelines) (Fentiman et al. 1990). Groups of experts in geriatric oncology are cur-rently working on developing recommendations for the management of colorectal cancer in the elderly (Aparicio et al. 2010).

4.2.5 Delay of Care for Elderly Patients

Whether at the screening, diagnosis, or treatment stage, there is suboptimal treatment of cancer in the elderly. Cancer is diagnosed at a more advanced stage than in younger subjects, thus worsening the prognosis (Diab et al. 2000; Tan et al. 2007). The delay of care is often multifactorial. Elderly patients usually consult several months after the onset of symptoms. Some symptoms, such as fatigue, weight loss, dyspnea, pain, constipation, and rectal bleeding, are often incorrectly attributed to advancing age. As a result, all diagnostic examinations are delayed. The presentation of the disease can be misleading (confusion, depression, impaired general condition, body pain). Further investigations are sometimes more difficult to perform in elderly patients (lack of prepa-ration for colonoscopy, cardiovascular and respiratory complications related to anesthe-sia, colonic perforations) and often less frequent than in the young (Turner et al. 1999).

4.2.6 Suboptimal Treatment of Elderly Cancer Patients

Several studies have also shown that older patients are more at risk of inadequate treatment (over- or undertreatment) (Goodwin et al. 1993, 1996). Poor access to health care contributes to suboptimal treatment. Elderly patients are referred to a specialist practitioner less often because of their "potential vulnerability" that could complicate surgical management and/or oncology (Papamichael et al. 2009). A retro-spective study of the French registry of digestive cancers showed that the treatment of stage III colorectal cancer varied according to age. In this study, treatment (surgery, adjuvant chemotherapy, radiotherapy) offered to patients over 75 did not include comorbidities, a clear indication of age discrimination in contrast to younger subjects (Quipourt et al. 2011). These results are confirmed by the study of Aparicio et al., where half (48%) the patients received suboptimal treatment of colorectal cancer that included metastatic tumors (Aparicio et al. 2009). Some factors related to surgical management directly influence the prognosis. The surgeries are more often done in an emergency context rather than a scheduled one (12% for patients over 80 vs. 5% for those under 65 in the case of rectal cancer; 17% for those over 80 years vs. 12%

for those under 65 in the case of colon cancer). Postoperative mortality is significantly higher in the elderly. In patients over 80, 6% of deaths occurred during hospitalization and 29% within 1 year of the intervention. In this study, predictors of poor outcome were the high number of comorbidities and the stage of cancer (Kunitake et al. 2010). Therefore, the later diagnosis of cancer in the elderly and inadequate cancer treatment in relation to the actual health status of the patient often render the management of cancer in the elderly suboptimal.

4.3   Special Features of the Care for Elderly Cancer Patients

4.3.1   Heterogeneity of the Cancer Population

One of the difficulties in managing elderly cancer patients is the heterogeneity of this population. All individuals do not age in the same way or at the same speed. Some patients suffer from multiple comorbidities; others have none. Some patients are completely dependent, while others retain complete autonomy, even in old age.

4.3.2   Impact of Comorbidities

The underlying health status of elderly patients interacts with the diagnostic and therapeutic decisions, thus preventing at times standard treatment. Age is not the only determinant. Several studies have shown the impact of comorbidities in the treatment of colon cancer. In the study by Janssen-Heijnen et al., the patients treated for colorectal cancer had surgery, regardless of their age and comorbidities (Janssen-Heijnen et al. 2007). Patients operated on in emergency; patients with comorbid conditions, such as cardiovascular, thromboembolic events, diabetes, and/or chronic bronchitis, had more postoperative complications and a higher mortality. In the case of colon surgery, patients over 80 suffered more pulmonary complications and a higher mortality (13%) than those under 80 (2%). In the case of rectal surgery, patients over 80 suffered significantly more bleeding complications, cardiovascular, renal failure, and death. In multivariate analysis, the risk of death increased with age and comorbidities. Assessing comorbidities and risk of decompensation is a major step in the management of elderly patients, with special attention being paid to the very elderly.

4.3.3   Specific Attention for Cognitive Impairment

Among all geriatric diseases, the special case of dementia is the most complex. In the study by Raji et al., the diagnosis of dementia was associated with a delayed diagnosis of cancer (including colorectal cancer) occurring at a later stage and with increased mortality from all causes (cancer-related or not). Survival also decreased when the

diagnosis of dementia was made before the cancer (Raji et al. 2008). Dementia is a major cause of undertreatment in elderly cancer patients.

With the expansion of surgical indications in the elderly, one of the major postoperative complications is delirium. Because of previous unfortunate experiences involving a high prevalence of delirium during cancer treatments – whatever their intensity – health-care teams are reluctant to propose any cancer treatment whatsoever. Delirium and dementia are related: two-thirds of delirium syndromes occur in patients with dementia. Delirium has major implications in terms of loss of autonomy, morbidity, and mortality. A study of postoperative delirium was conducted among subjects over 75 who were to benefit from serious abdominal surgery. One-quarter of the operated patients presented postoperative delirium. The average length of stay was significantly higher for these patients (19 ± 11 days vs. 14 ± 8 days); postoperative mortality was significantly higher after delirium (14% vs. 9%). An ASA score greater than 3, impaired mobility (defined as a timed up and go test >20 s), and postoperative administration of tramadol were major risk factors for delirium, justifying a preoperative geriatric assessment (Brouquet et al. 2010).

Literature review shows that a history of cognitive impairment, advanced age, the preoperative use of psychotropic drugs, and a high number of comorbidities are also high-risk factors for postoperative delirium (Dasgupta and Dumbrell 2006). The prevalence of delirium also raises the issue of cost, due to the increase in length of stay, bedridden complications, decompensation of underlying diseases, risk of dependency, and workload (Sieber 2009). Postoperative delirium is a major problem in the surgical management of cancers, notably cancer of the colon. A delirium risk assessment must be offered to all patients to whom abdominal surgery is proposed, during the anesthesia and/or surgery consultation. Preventive measures can be proposed at that time (Inouye 2006; Inouye et al. 1999; Retornaz et al. 2010).

4.3.4 How to Assess the Underlying Conditions of Elderly Cancer Patients

In oncology, antineoplastic treatment is usually standardized: each type of cancer requires a particular combination of treatments, protocol, and order. In the case of colon cancer, treatment consists mainly of surgery, chemotherapy based on 5-fluorouracil, and targeted therapies. This relative standardization does not always apply to elderly patients. Comorbidities, disability, cognitive impairment, depression, mobility impairment, malnutrition, polypharmacy, and social context may interfere with the management of the cancer. Some nonspecific diseases can directly impact the treatment decision. For example, parameters such as malnutrition and renal failure may interfere directly with the pharmacokinetic of the chemotherapy and require an adaptation to reduce the risk of toxicities. The presence of severe neuropathy can indicate that a platinum-based chemotherapy should be avoided. The question of adjuvant chemotherapy is even more complex. Given after the tumor is removed to reduce the risk of recurrence or distant metastases, this chemotherapy can cause immediate toxicities that will aggravate the health of the patient without providing the potential benefit.

Table 4.1 Areas and main assessment tools used in standardized geriatric assessment in oncology

Areas assessed	Main tools
Functional status	ECOG-PS
	ADL (version Katz)
	IADL (version Lawton)
	IADL (version OARS à 14, 21, 29 items)
Comorbidities	CIRG-S, Charlson index, Satariano index
Drugs	Number, drug interactions
Cognition	MMSE, BOMC, clock-drawing test
Depression	GDS (4, 5, 15 items), HADS
Nutrition	BMI, MNA, weight loss
Mobility	TUG, Tinetti test, falls

ECOG PS Eastern Cooperative Oncology Group performance status, *ADL* basic activities of daily living, *IADL* instrumental activities of daily living, *CIRS-G* cumulative illness rating scale for geriatrics, *MMSE* Mini Mental Status Examination, *BOMC* Blessed Orientation-Memory-Concentration, *GDS* Geriatric Depression Scale, *HADS* Hospital Anxiety and Depression Scale, *BMI* body mass index, *MNA* Mini Nutritional Assessment, *TUG* Timed Up and Go test

4.3.5 Comprehensive Geriatric Assessment

The American National Comprehensive Cancer Network (NCCN) (Carreca et al. 2005) and the International Society of Geriatric Oncology (SIOG) (Extermann et al. 2005) both very involved in geriatric oncology research, and numerous literature reviews (Balducci and Beghe 2000; Bernabei et al. 2000; Chen et al. 2004; Misra et al. 2004; Repetto et al. 2003) propose the use of a comprehensive geriatric assessment (CGA) to determine optimal oncologic care, on the basis of the patient's health status rather than empirically. The CGA is a multidisciplinary evaluation in which potential problems of an older person are identified, listed, and explained, if possible; the economic and physical resources of the patient are identified; and a coordinated plan is proposed to target interventions in the issues identified in this patient (Solomon et al. 2003). Several randomized studies have shown that the CGA followed by interventions improves patients' functional status, prevents disability, reduces the risk of falls, reduces hospital readmissions and institutionalization, and reduces the incidence of mortality and costs (Cohen et al. 2002; Stuck et al. 1993). The main tools for CGA used in oncology are detailed in Table 4.1. The CGA is recommended for cancer patients so as to detect the vulnerability of these patients, estimate their tolerance to cancer treatment, define the optimal treatment, and determine the plans for those patients having multiple health problems related or unrelated to their underlying cancer.

4.3.6 Limitations of CGA

Several recent literature reviews, however, have questioned the real value of the CGA in geriatric oncology (Ferrucci et al. 2003; Maas et al. 2007). The limitations of the CGA are probably related to the target population. Indeed, the CGA was

designed and validated for a population of older persons with disabilities and multiple diseases, who are hospitalized in geriatric wards, and/or require multiple interventions at home. It has not proven of interest in older adults without disabilities who live at home with a single medical condition, albeit it severe, i.e., in patients having relatively good underlying health (Ferrucci et al. 2003). According to the literature data, 70–80% of patients referred to oncology are independent for ADL (domestic activities of daily living), 50% are independent for IADL, half have no comorbidity, and 60% have a normal cognitive status. The older cancer patients represent a population that differs from the traditional geriatric patients: they have fewer comorbidities and good functional and underlying health status at the time of diagnosis. On the other hand, these patients have a higher prevalence of certain frailty markers such as malnutrition and impaired mobility. It is to be hoped that, in the future, a specific oncologic geriatric assessment "SOGA" will be developed, specifically tailored to older cancer patients, and adjustable according to the type of cancer and proposed treatment, with varying implications in terms of management.

4.3.7   When Should a CGA Be Proposed?

In oncology, many factors can interfere with the results of the CGA. Currently, patients are often sent to the geriatrician after surgery or after initiation of chemotherapy. These treatments, however, can affect the results of the CGA. The patient should ideally be evaluated right after the diagnosis of cancer and before any treatment.

It is also important to consider the impact of the cancer on the health of the patient at the time of CGA. For example, the classification of a patient suffering rapid weight loss, marked fatigue, and loss of autonomy related to aggressive or advanced cancer, as a "fragile subject," can conceivably change with optimal cancer treatment. The patient should, therefore, not be refused an aggressive cancer treatment. In the case of a patient who suffers progressive loss of weight and autonomy during the year preceding the cancer, the results of CGA will reflect the alteration of the reserves prior to the onset of the illness. This patient is considered vulnerable before the diagnosis of cancer, and there are risks of major toxicity, probably due to the underlying fragility (Fig. 4.1).

4.3.8   How to Identify Patients Who Need a CGA?

Currently, no recommendations from prospective randomized studies regarding the place of the CGA in cancer treatment are available, even though the various societies favor its use. Several teams are working on the validation of "screening" tools to identify patients requiring a CGA, for it cannot be offered to all patients, given the available resources and costs. In France, the objective of the "Oncodage" trial is to validate a questionnaire entitled "G8" that determines whether a CGA is necessary before the introduction of treatment, particularly chemotherapy. The G8 considers seven items of the MNA (Mini Nutritional Assessment), together with chronological age and perceived health status. The results should be available in 2012. Other teams
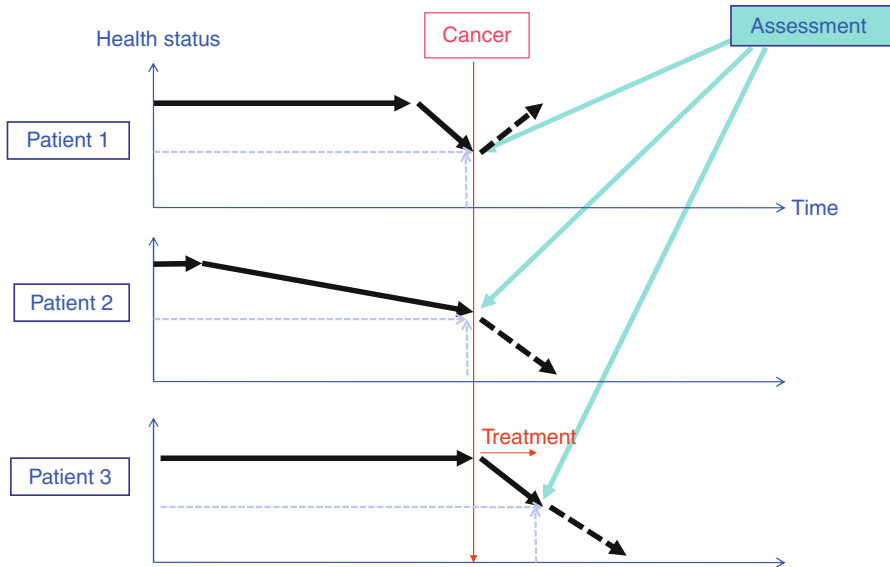
Fig. 4.1 Impact of cancer burden on the result of the assessment. *Explanation*: It is very important to consider the impact of the cancer on the health of the patient at the time of assessment. All three patients have similar health status at the time of assessment. Patient 1 suffers rapid weight loss, marked fatigue, and loss of mobility related to aggressive or advanced cancer. His classification as a "frail patient" can dramatically change with optimal cancer treatment. This patient should, therefore, not be refused an aggressive cancer treatment. Patient 2 suffers progressive loss of weight and mobility during the year preceding the cancer. The results of assessment will reflect the alteration of the reserves prior to the onset of the cancer. This patient is considered vulnerable before the diagnosis of cancer, and there are risks of major toxicities with aggressive therapies. For Patient 3, the assessment is done only after the start of cancer treatment. The result of your assessment may reflect the impact of the treatment rather than the underlying patient heath status. Continuing these treatment will probably lead to toxicities

use the VES-13 as a screening tool or the a-CGA, although both have not been validated in various cancer types and in many patients (Luciani et al. 2010; Overcash et al. 2010). The use of frailty markers as a tool for screening patients (Retornaz et al. 2008) or as a predictor of toxicity is potentially a new way of research in oncologic (Puts et al. 2011) or surgery settings (Makary et al. 2010; Tan et al. 2011).

4.4 Specific Issues Concerning Chemotherapy in Elderly Patients

4.4.1 Can the Patient Tolerate Chemotherapy?

Choosing the optimal treatment regimen for an elderly patient, in terms of schema and dose, is challenging because one must take into account not only the physiological changes associated with aging but also the pathological changes which are added

over time. The various types of chemotherapy do not all have the same toxicity profile. Myelosuppression is the main toxic effect of most chemotherapy agents, predisposing the patient for infections. Fever requires prompt treatment. The administration of leukocyte growth factors can limit the effects of myelosuppression; these agents are recommended by the SIOG in chemotherapy having high myelosuppressive effects. Nausea and vomiting are not more frequent in elderly patients, but their consequences are more severe (dehydration, malnutrition). On the other hand, elderly patients are at increased risk of gastrointestinal toxicity, such as mucosal damage (mucositis) and diarrhea, due to a decrease in the turnover time of the digestive epithelium. If possible, these side effects should be prevented (mouthwashes, antidiarrheals) and actively treated (intravenous or subcutaneous infusion). Other toxicities such as neurotoxicity are often overlooked in oncology, even though they have a major impact on elderly patients. Some drugs (e.g., platinum salts) lead to neuropathies responsible for disabling pain, gait disturbance leading to increased risk of falling, loss of autonomy, etc. The fatigue caused by chemotherapy can also cause a loss of autonomy. Even without training in oncology, the geriatrician should ideally know, when assessing the patient, the proposed chemotherapy regimen and potential toxicities or the assistance of the oncologist as to the potential toxicity of the proposed processing.

Most types of chemotherapy are administered with drugs that limit the side effects of the treatment. However, these drugs have their own side effects that can be just as deleterious in the elderly. For instance, antiemetic drugs may lead to constipation that must be prevented. Steroids are also often administered as a bolus before the infusion of chemotherapy and are a source of glycemic decompensation or delirium. Again, a good knowledge of the entire proposed treatment is the key to preventing side effects.

Adjuvant chemotherapy requires special attention when a patient is assessed by a geriatrician. In fact, this chemotherapy is delivered after curative treatment (usually surgery) to reduce the risk of recurrence or metastasis by destroying islet cell cancer that could escape from the tumor before surgery and nest in different organs. The chemotherapy can, however, cause toxicities that can aggravate the condition of the patient without providing the potential benefit. Statistically speaking, patients are more likely to survive with adjuvant chemotherapy than without, but, for any given patient, the complications of chemotherapy can destroy the expected positive effects. Administering chemotherapy (of which the expected theoretical benefit is the reduction of the risk of recurrence or metastases within 5 years) to vulnerable patients exposes them to a high risk of complications and a risk of early death; any benefit from the treatment is lost (e.g., decompensation cascade evolving from a loss of autonomy). The geriatrician should try to determine whether the overall life expectancy of the patient is greater than the risk of relapse and whether any underlying factors may increase the risk of toxicity. To calculate the overall life expectancy, the geriatrician can use predictive tools of mortality such as the Walter score (score at 1 year) or the Lee score (score at 4 years) (Lee et al. 2006; Walter et al. 2001).
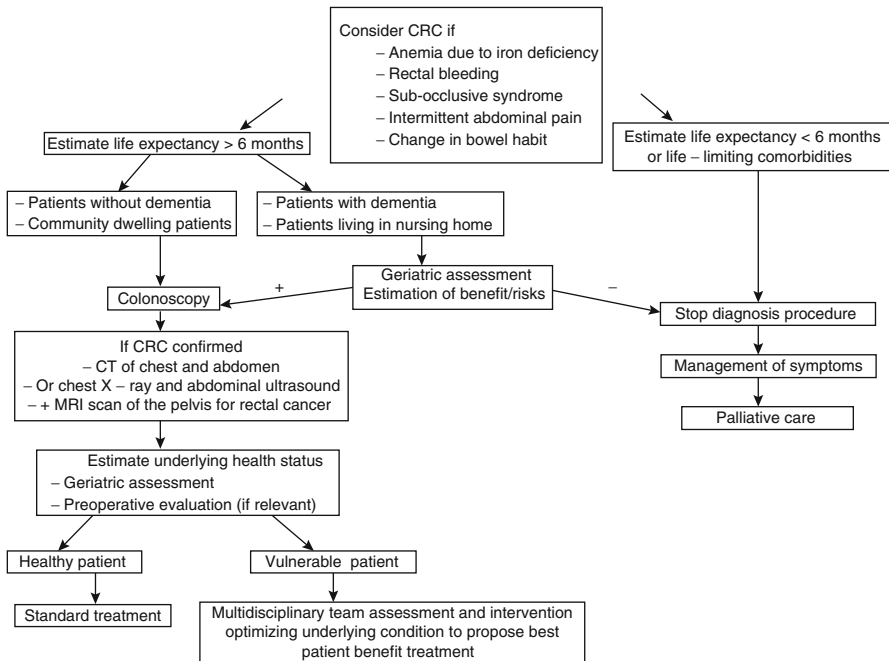
Fig. 4.2 Decision making algorithm from diagnosis to treatment decision. *CRC* Colorectal cancer

Two recent studies have provided predictive tools for toxicity from chemotherapy in the elderly (Extermann et al. 2011; Hurria et al. 2011). However, these are too complex for everyday use.

Conclusion

Till today, older colorectal cancer patients have delayed diagnosis and receive suboptimal treatment. Elderly patients should be exposed to more aggressive management more similar to their counterparts.

Due to the heterogeneity of the elderly patient population, patients over 65 years of age need to undergo preoperative evaluation, which should include a cancer-specific assessment as well as a whole patient evaluation for the most common physiological effects of aging, physical and mental ability, and social support (Fig. 4.2). A geriatric team should be involved in patient management in the case of a patient with comorbidities or poor health status.

Age alone should not be a barrier to treatment. Patients should receive the most intensive and appropriate treatment thought to be safe and effective according to their underlying health status and comorbidities.

References

Aapro MS, Kohne CH, Cohen HJ et al (2005) Never too old? Age should not be a barrier to enrolment in cancer clinical trials. Oncologist 10:198–204

Aouba A, Péquignot F, Le Toullec A, et al (2007) Les causes médicales de décès en France en 2004 et leur évolution 1980–2004. Bulletin Epidémiologique Hebdomadaire 35–36:308–14. http://www.insee.fr

Aparicio T, Mitry E, Sa Cunha A et al (2005) Management of colorectal cancer of elderly patients. Gastroenterol Clin Biol 29:1014–1023

Aparicio T, Navazesh A, Boutron I et al (2009) Half of elderly patients routinely treated for colorectal cancer receive a sub-standard treatment. Crit Rev Oncol Hematol 71:249–257

Aparicio T, Bouché O, Carola E et al (2010) Recommandations du GEPOG (Groupe d' Echanges et de Pratique en Onco-Geriatrie) pour le traitement des cancers colorectaux métastatiques des patients âgés. Journal d'Onco-Gériatrie 3(4):157–163

Balducci L, Beghe C (2000) The application of the principles of geriatrics to the management of the older person with cancer. Crit Rev Oncol Hematol 35:147–154

Benson AB III, Pregler JP, Bean JA et al (1991) Oncologists' reluctance to accrue patients onto clinical trials: an Illinois Cancer Center study. J Clin Oncol 9:2067–2075

Bernabei R, Venturiero V, Tarsitani P et al (2000) The comprehensive geriatric assessment: when, where, how. Crit Rev Oncol Hematol 33:45–56

Brouquet A, Cudennec T, Benoist S et al (2010) Impaired mobility, ASA status and administration of tramadol are risk factors for postoperative delirium in patients aged 75 years or more after major abdominal surgery. Ann Surg 251:759–765

Carreca I, Balducci L, Extermann M (2005) Cancer in the older person. Cancer Treat Rev 31:380–402

Chen CC, Kenefick AL, Tang ST et al (2004) Utilization of comprehensive geriatric assessment in cancer patients. Crit Rev Oncol Hematol 49:53–67

Dasgupta M, Dumbrell AC (2006) Preoperative risk assessment for delirium after noncardiac surgery: a systematic review. J Am Geriatr Soc 54:1578–1589

Diab SG, Elledge RM, Clark GM (2000) Tumor characteristics and clinical outcome of elderly women with breast cancer. J Natl Cancer Inst 92:550–556

Extermann M, Aapro M, Bernabei R, Task Force on CGA of the International Society of Geriatric Oncology et al (2005) Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol 55:241–252

Extermann M, Boler I, Reich RR et al (2011) Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. Cancer. doi:10.1002/cncr.26646

Fentiman IS, Tirelli U, Monfardini S et al (1990) Cancer in the elderly: why so badly treated? Lancet 335:1020–1022

Ferrucci L, Guralnik JM, Cavazzini C et al (2003) The frailty syndrome: a critical issue in geriatric oncology. Crit Rev Oncol Hematol 46:127–137

Goodwin JS, Hunt WC, Samet JM (1993) Determinants of cancer therapy in elderly patients. Cancer 72:594–601

Goodwin JS, Samet JM, Hunt WC (1996) Determinants of survival in older cancer patients. J Natl Cancer Inst 88:1031–38. http://www.iinsee.fr

Hurria A, Togawa K, Mohile SG et al (2011) Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol 29:3457–3465

Hutchins LF, Unger JM, Crowley JJ et al (1999) Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med 341:2061–2067

Inouye S (2006) Delirium in older persons. N Engl J Med 354:1157–1165

Inouye S, Bogardus S, Charpentier P et al (1999) A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med 340:669–676

Janssen-Heijnen ML, Maas HA, Houterman S et al (2007) Comorbidity in older surgical cancer patients: influence on patient care and outcome. Eur J Cancer 43(15):2179–2193

Kunitake H, Zingmond D, Ryoo J et al (2010) Caring for octogenarian and nonagenarian patients with colorectal cancer: what should our standards and expectations be? Dis Colon Rectum 53:735–743

Lee SJ, Lindquist K, Segal MR et al (2006) Development and validation of a prognostic index for 4-year mortality in older adults. JAMA 295:801–808

Luciani A, Ascione G, Bertuzzi C et al (2010) Detecting disabilities in older patients with cancer: comparison between comprehensive geriatric assessment and vulnerable elders survey-13. J Clin Oncol 28:2046–2050

Maas HA, Janssen-Heijnen ML, Olde Rikkert MG et al (2007) Comprehensive geriatric assessment and its clinical impact in oncology. Eur J Cancer 43:2161–2169

Makary MA, Segev DL, Pronovost PJ et al (2010) Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg 210:901–908

Misra D, Seo PH, Cohen HJ (2004) Aging and cancer. Clin Adv Hematol Oncol 2:457–465

Papamichael D, Audisio R, Horiot J-C et al (2009) Treatment of the elderly colorectal cancer patient: SIOG expert recommendations. Ann Oncol 16:20–25

Puts MT, Monette J, Girre V et al (2011) Are frailty markers useful for predicting treatment toxicity and mortality in older newly diagnosed cancer patients? Results from a prospective pilot study. Crit Rev Oncol Hematol 78:138–149

Quipourt V, Jooste V, Cottet V et al (2011) Comorbidities alone do not explain the undertreatment of colorectal cancer in older adults: a French population-based study. J Am Geriatr Soc 59:694–698

Raji M, Kuo Y-F, Freeman J et al (2008) Effect of a dementia diagnosis on survival of older patients after a diagnosis of breast, colon, or prostate cancer implications for cancer care. Arch Intern Med 168:2033–2040

Repetto L, Venturino A, Fratino L et al (2003) Geriatric oncology: a clinical approach to the older patient with cancer. Eur J Cancer 39:870–880

Retornaz F, Monette J, Batist G et al (2008) Usefulness of frailty markers in the assessment of health and functional status of older cancer patients referred for chemotherapy: a pilot study. J Gerontol A Biol Sci Med Sci 63:518–522

Retornaz F, Potard I, Molines C et al (2010) Quand l'équipe gériatrique restaure la confiance de l'équipe médico-chirurgicale. Journal d'Onco-Gériatrie 1:33–36

Sieber F (2009) Post operative delirium in the elderly surgical patient. Anesthesiol Clin 27:451–464

Stuck AE, Siu AL, Wieland GD et al (1993) Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet 342:1032–1036

Tan E, Tilney H, Thompson M et al (2007) The United Kingdom national bowel cancer project – epidemiology and surgical risk in the elderly. Eur J Cancer 43:2285–2294

Tan KY, Kawamura YJ, Tokomitsu A et al (2011) Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimized. Am J Surg [Epub ahead of print]

Turner N, Haward R, Mulley G et al (1999) Cancer in old age: is it inadequately investigated and treated? BMJ 319:309–312

Townsley CA, Naidoo K, Pond GR et al (2003) Are older cancer patients being referred to oncologists? A mail questionnaire of Ontario primary care practitioners to evaluate their referral patterns. J Clin Oncol 21:4627–4635

Tyldesley S, Zhang-Salomons J, Groome PA et al (2000) Association between age and the utilization of radiotherapy in Ontario. Int J Radiat Oncol Biol Phys 47:469–480

Vercelli M, Capocaccia R, Quaglia A et al (2000) Relative survival in elderly European cancer patients: evidence for health care inequalities. The EUROCARE Working Group. Crit Rev Oncol Hematol 35:161–179

Walter LC, Brand RJ, Counsell SR et al (2001) Development and validation of a prognostic index for 1-year mortality in older adults after hospitalization. JAMA 285(23):2987–2994

Yancik R, Ries LA (2000) Aging and cancer in America. Demographic and epidemiologic perspectives. Hematol Oncol Clin North Am 14:17–23