Older Patients, Cognitive Impairment, and Cancer: An Increasingly Frequent Triad

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Abstract
The incidence of both cancer and cognitive impairments from various origins increases with age. Oncologists are increasingly being confronted with cancers occurring in patients with cognitive impairment, yet very few studies have addressed the problem. Cognitive impairment affects a patients’ survival to an extent similar to an average cancer, and this can be an important thing to consider, especially in the adjuvant setting. Cognitive impairment also predisposes patients to delirium in the surgery setting or during hospitalization. Because effective preventive measures exist, careful attention should be paid to identifying patients at risk. Cognitive impairment does not automatically mean inability to consent, but particular precautions should be taken. For outpatient treatments such as chemotherapy, a comprehensive multidisciplinary approach is key for a good outcome. Proper caregiver support should be ensured upfront, and aggressive supportive care should be used. In the setting of an experienced geriatric oncology team, patients with cognitive impairment appear more likely to receive standard oncologic therapies. Cancer patients with cognitive impairment are at high risk of concomitant depression. (JNCCN 2005;3:593–596)

Key Words
Carcinoma, aged, cognitive impairment, dementia, decision making, cancer treatment, delirium, dementia screening, informed consent

Half of all cancers occur in patients 70 and older. This population has, on average, three comorbidities in addition to cancer, and a frequently seen comorbidity is cognitive impairment. For example, in a tertiary cancer center such as Moffitt Cancer Center, 18% of patients screened positive on the Mini Mental Status exam (MMSE). However, the MMSE is not very sensitive to minor impairments, and the true prevalence of cognitive problems in older patients is probably higher. How should these impairments impact our approach to cancer treatment?

General Evaluation
Dementia shortens survival in geriatric patients, which is a significant effect. For example, in a recent study, the presence of moderate to severe cognitive impairment (MMSE ≤17) was associated with an increase in 5-year mortality equivalent to the diagnosis of cancer (hazard ratio [HR], 2.41 [95% confidence interval or CI, 1.74–3.34] vs. 2.60 [1.96–3.44]). Mild impairment (MMSE 18–23) was also associated with an increased mortality (HR, 1.56; CI, 1.28–1.92). More-specific data are available in older cancer patients. Patients aged 70 and older who showed positive screening results for cognitive impairment (MMSE ≤24) had about half the survival of patients whose screening results were negative for it: 41.8 versus 93.5 months.

Cognitive impairment also appears to significantly impact functional status, even when measured with a low sensitivity tool such as the Eastern Cooperative Oncology Group Performance Status (ECOG PS). It is also associated with a higher prevalence of depression (49% vs 12%) and more severe comorbidities.

These points should be considered in treatment planning, especially for patients with limited stage cancer. A major modifier in our ability to offer treatment will be the presence, involvement, and resources of a caregiver (or better, several). Therefore, the social resources of the patient need to be assessed carefully, ideally with the help of a social worker, and if necessary reinforced before treatment.

How can we recognize dementia and cognitive impairment in oncology patients? The usual physician visit is far from obtaining perfect results. In a general study,
physicians recognized 81% of the dementia in their patients and 44% of their cognitively impaired patients. However, the odds ratio of recognition for patients with cancer was 0.49 (95% CI, 0.18–0.90). Similar results have been found in many other studies.

A first step is to be aware of the definition of dementia. Although many nuances exist, a practical definition based on the Diagnostic and Statistical Manual (DSM-IV) criteria reads, “Dementia is an acquired decline in memory and in at least one other cognitive function (e.g., language, visual-spatial, executive) sufficient to affect daily life in an alert person.”

Several short screening instruments have been published. The most frequently used and widely taught is Folstein’s MMS. The MMS is moderately sensitive to mild cognitive impairment, but quite specific. It is sensitive to age and education, and best performance is obtained with adapted scores. For clinical use, an easy rule is to have a threshold at 24 of 30 for a positive screen. However, some sensitivity or specificity is lost. MMS compares well with more sophisticated cognitive instruments, such as the Mattis Dementia Rating Scale or the Information-Memory-Concentration test. It takes 5 to 10 minutes to complete, and a rater must be present. Abbreviated versions of the MMS and shorter screening tests are available to screen for dementia in general clinical practice. Discussed subsequently are some examples of tests with a good clinical performance.

**Clock Drawing Test**

The Clock Drawing Test consists of having patients draw a circle, place the numbers, and set up the hands of the clock at a specific time (e.g., 8:20). The test is considered correct if all the numbers are in sequence and in the right position, and if the hands readable display the requested time. Its advantage is that it tests several cognitive functions together (e.g., long-term memory, visual-spatial function). Its sensitivity has been reported in the range of 48% to 94% and specificity from 42% to 97%. Therefore, despite its simplicity, it is often associated with a 3-items recall in the following test.

**Mini-Cog**

The Mini-Cog combines the 3-item recall from the MMS with the clock drawing test. The immediate recall is done first, the clock-drawing test is used as a distracting task, and then the 1-minute recall is performed. Patients who recall all 3 items are unlikely to have dementia; those who score 0 are very likely to have it. Those who recall 1 or 2 items are likely to be nondemented if the clock drawing test is normal and demented otherwise. This test had a higher sensitivity (99%) and correct classification (96%) than the MMS and the Cognitive Abilities Screening Instrument (CASI) in one study. It takes about 3 minutes to complete.

**Semantic Fluency Test**

The Semantic Fluency Test is very simple: patients are asked to name as many animals as possible in 1 minute. A score of less than 15 separates patients with dementia from normal controls with a sensitivity of 88% and a specificity of 96% when compared with standard neurologic diagnostic criteria.

More instruments exist, and a very informative review was written by Lorentz et al. All of these screening instruments are not diagnostic. A positive screening test should always be followed with a more detailed neuropsychologic evaluation.

**Informed Consent**

Cognitive impairment can interfere with consent processes. However, if patients are known to have or show positive screening results for cognitive impairment, this is not an automatic indication of consent incapacity. Often mildly impaired patients retain sufficient understanding to consent validly. However, more caution should be exerted in assessing patient understanding (e.g., obtaining formal verbalized feedback from the patient as to what is planned, double checking with the caregiver the level of understanding, having the caregiver present in any decision-making situation).

**Impact of Cognitive Disorders on Survival and Treatment Tolerance**

**Ability to Deliver Treatment**

A key concern is the ability of cognitively impaired patients to tolerate treatment, notably chemotherapy. This can lead to withholding of this treatment. In a review of colon cancer patients 67 years and older in the Medicare/Surveillance Epidermiology and End Results (SEER) database, dementia patients were significantly less likely to have undergone a histologic diagnosis (OR, 0.50). If they had stage I to III disease, they were less likely to be offered surgical resection.
(OR, 0.48). If they had stage III colon cancer, their OR of receiving adjuvant chemotherapy was 0.22. Interestingly, in a specialized geriatric oncology program, a significant proportion of cognitively impaired patients underwent chemotherapy (34%, compared with 35% of non-impaired patients).³

Although a referral bias is possible, it might also indicate that these patients would benefit from a multidisciplinary approach by a specialized team. Whether to use chemotherapy in a patient with cognitive impairment is a multifactorial issue. In a palliative setting, the benefits and risks are both immediate and can be directly balanced. From a safety point of view, the immediate support of a caregiver should be available. Oral chemotherapies should be avoided. The risk of delirium complicating events such as diarrhea, dehydration, or febrile episodes is higher than in other individuals, and these problems should be addressed immediately. Symptom recognition by the patient may be impaired and delayed. Therefore, we usually insist that a cognitively impaired patient live with a caregiver or in an institutional setting for the duration of the chemotherapy.

In a curative setting (e.g., large cell non-Hodgkin’s lymphoma), our default attitude is that every effort should be made to enable the patient to receive standard chemotherapy. A multidisciplinary approach is crucial to identify and prevent potential sources of complications. In an adjuvant setting, considerations of life expectancy become a major issue. As mentioned previously, cognitively impaired patients have about half the survival of nonimpaired patients.³ Nevertheless, the median projected survival of cognitively impaired patients with early stage cancers was 69.7 months. Therefore, adjuvant systemic treatment should not automatically be ruled out. On one hand, one may consider the risk of complications from adjuvant treatment. On the other hand, one may consider that, should the patient relapse, the oncologic management of the relapse may be complicated by the progression of the cognitive impairment over time. Presently, no data are available as to how severe the impact of chemotherapy is in older patients with baseline cognitive impairment.

**Delirium**

Another important issue is that cognitive impairment is a risk factor for delirium. This can be prompted by an acute stress such as surgery or a hospitalization, or by complications from chemotherapy, such as infection or dehydration. Marcantonio et al.¹³ designed a predictive score for postoperative delirium that can be helpful in treatment planning around surgery (Table 1). A similar predictive score exists for hospitalized medical patients.¹⁴ In that population, visual impairment, severe illness, cognitive impairment, and high BUN/creatinine ratio were risk factors.

### Table 1 Marcantonio Predictive Score for Risk of Postoperative Delirium

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Points</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Age ≥ 70 years</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>TICS score &lt; 30</td>
<td>1</td>
<td>Telephone interview for cognitive status (= MMSE &lt; 24)</td>
</tr>
<tr>
<td>SAS class IV</td>
<td>1</td>
<td>Specific Activity Scale. (e.g., unable to walk 4 km/h for 1 block, make their bed, or dress themselves without stopping)</td>
</tr>
<tr>
<td>Very abnormal sodium, potassium, or glucose</td>
<td>1</td>
<td>Sodium &lt;130 or &gt; 150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potassium &lt; 3.0 or &gt; 6.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose &lt; 3.3 or &gt; 16.7 mmol/L (&lt;60 or &gt;300 mg/dL)</td>
</tr>
<tr>
<td>Aortic aneurysm surgery</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Noncardiac thoracic surgery</td>
<td>1</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Total points</th>
<th>Risk of Delirium</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>2%</td>
</tr>
<tr>
<td>1 or 2</td>
<td>11%</td>
</tr>
<tr>
<td>≥ 3</td>
<td>50%</td>
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Adapted from Marcantonio et al.¹³; used with permission.
A high risk of delirium is not necessarily a contraindication to surgery but should certainly prompt delirium-prevention measures. For example, in a randomized trial, hospitalized patients experienced less delirium with a multicomponent intervention proposed by Inouye et al. The intervention comprised elements such as reorientation strategies, sleep enhancement strategies, early mobilization protocols, visual aids, hearing devices, and early identification of dehydration. The incidence of delirium was 9.9% in the intervention group versus 15% in the control group (OR, 0.60).

Also, as with for all elderly patients, elective surgery is markedly preferred to emergency surgery. In a study from the Mount Sinai hospital, morbidity and mortality rates in patients 70 and older were 6.8% and 1.9%, respectively, in elective surgery; these numbers jumped to 31% and 20% in emergency surgery. This illustrates the fact that functional reserve is decreased in the elderly.

This is even more true for cognitively impaired patients. Therefore, every effort should be made to either prevent the need for emergency surgery by proactive elective surgery, or reduce if possible the emergency situation (e.g., with a stent for colonic obstruction) to allow surgery to be performed in better conditions.

In general, aggressive supportive care should be undertaken. Other examples of effective measures are upfront growth factors in patients at high risk of neutropenia to reduce febrile neutropenia. The development of anemia is a risk factor for delirium and increased toxicity from chemotherapy, and should also be prevented. Early rehydration should be pursued in cases of diarrhea, because this is one of the key causes of delirium. Close monitoring by home health care services should be implemented if deficiencies in caregiving support are identified.

In conclusion, the need to treat cognitively impaired elderly patients with cancer is an increasingly frequent situation. This article delineates strategies that should help address the problems of these patients. However, specific research is still needed in several areas.

References