BACKGROUND
Between seventy¹ and ninety percent² of all patients with cancer experience pain. The incidence and prevalence of cancer increase with age, with greater than half of all cancer patients being over age sixty.³ In addition, the percentage of older adults in the U.S. population is increasing dramatically as a result of improved medical care and the graying of the baby boomer generation. By 2030, individuals aged 65 and older will comprise 20% of the population compared to today’s 13%⁴—allready the highest percentage in history. Understanding the nature of cancer pain in older patients and improving our ability to adequately assess and treat pain is of ever increasing importance. Unfortunately, comfort measures, pain control, and palliative care are often delayed, and “[e]lderly patients, like minority populations, are less likely than younger adults to receive proper pain management.”¹(p.414)

Many factors contribute to elderly patients receiving inadequate pain treatment. Psychosocial patient factors include an unwillingness to complain,³ age-related stoicism,⁵ the fact that older patients “may have lower expectations for pain control”⁶(p.120) or assume that their physician knows best. Because of other comorbidities such as extreme frailty or cognitive difficulties, older patients may simply be less capable of reporting their pain than younger patients.³ Cognitively intact older patients may have more negative connotations toward opioid therapy than younger patients.⁶(p.130)

Are there differences in how and to what extent elderly patients experience pain caused by cancer when compared with younger patients?

Most of the authors in this review discuss the possibility that older patients may, in fact have a lower sensitivity, or increased threshold for pain. There is, in fact, a term “presbyalgos,” which, Hall et al. note, “refers to a decreased sensitivity of elderly patients to painful stimuli, but could reflect diminished cognitive capacity to report or quantify pain.”⁶(p.131)

The question of decreased pain sensitivity in the elderly is usually approached indirectly in the literature. An answer is sought by comparing the amount of opioid required to alleviate pain in different populations. Amount of opioid or rate of increase are set up as dependent variables and compared with different independent variables among which are age, gender, primary tumor site, or type of pain (e.g. neuropathic vs. non-neuropathic).

Among the articles reviewed here, only Viganò et al.² directly address the question of whether the elderly in fact experience less pain. In their retrospective study of 197 advanced cancer patients, they found no statistically significant difference in mean daily pain intensity (MDPI) over a 7-day admission to a Canadian Palliative Care Unit when patients aged less than 65, those aged 65-75 and those aged 75 and older were compared with each other.²

Delgado-Guay and Bruera⁷ mention that some of the laboratory studies which indicated a higher threshold of pain with age relied on [painful]stimuli that were too mild to truly allow the generation of meaningful conclusions—and also failed to take into account confounding factors. They do note, however, that phenomena such as silent Ms and absent abdominal pain in peritonitis may indeed be signs of a reduced experience of pain, especially visceral pain, among older adults.⁷

In general, the question of whether or not the primary experience of cancer pain differs in the older vs. younger individuals remains unresolved because it is so often confounded by psychosocial issues; co-morbidities; polypharmacy including use of adjuvant medications; site of primary tumor; presence and location of metastases; and history of therapies such as chemo and radiation therapies. Chemo and radiation therapy, as one example can both cause complicated pain syndromes such as neuropathies. Older patients are more susceptible to developing painful neuropathies than younger patients though less likely to receive chemo and radiation therapy in the first place.

Are there differences in how elderly patients respond to pain medications and pain-management protocols?

Most authors do agree that opioids are the “mainstay of cancer pain management,”¹ and that the elderly are more likely to suffer both acute and chronic toxicities from their use. The physiological causes of increased toxicity also account for the fact that older adults tend to need lower total doses of opiates for pain control reached after a slower, gentler titration than for younger patients. These physiological factors include

1. “Pharmacokinetic”
   a. Changes in body composition such as diminished volume of distribution which can be further complicated by an increased susceptibility to dehydration.
   b. Diminished function of drug eliminating organs as evidenced, for example, by the decreased renal clearance associated with age.²,⁵

2. “Pharmacodynamic”
   c. Heightened CNS sensitivity to opioids and opioid metabolites.² Older patients are therefore more likely to experience neurotoxicity “characterized by cognitive impairment, severe sedation, hallucinosis, delirium, myoclonus, seizures, aloldynia, and hyperalgesia.”⁸

Additionally there are anatomic factors. Delgado and Guay, for example, point out that opioid neurotoxicity may be aggravated by the “reduction in brain volume (approximately 20%), which occurs between ages 20 and 80, and consequent alteration in the ration of mu and delta receptors.”⁹
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There is also the drug-specific characteristic of morphine, namely, that it has a significant first-pass metabolism, resulting in plasma metabolite concentrations of active morphine-6-glucuronide (M6G) and inactive morphine-3-glucuronide (M3G). M6G is believed to be 4–200 times more potent than morphine itself, while M3G has not demonstrated any analgesic effects. M3G has been associated with hyperactive motor behavior, hyperalgesia, and allodynia in experimental studies.6,7

These drug-specific factors are essentially compounded by patient-specific pharmacokinetic, pharmacodynamic and anatomic changes of aging. Taken together, these factors help shed light on why the elderly as a whole require less morphine and are more susceptible to morphine toxicity.

Are elderly cancer patients treated differently than younger cancer patients?

Many providers are wary of prescribing opioids in the elderly because of concerns about their toxicity, augmented by the fact that older patients are more likely than younger patients to be taking multiple medications, this polypharmacy leading to even more potential for toxicity. Additionally, as noted by Mercadante et al., “some side effects, such as confusion, constipation, sedation and urinary retention, that are associated with the use of analgesic drugs are often already evident in aged patients.”3(p.124) Delirium is a classic geriatric syndrome which can obscure the accurate diagnosis of pain. Delirium additionally can be caused/worsened by pain and conversely, pain can cause/worsen delirium. The difficulties inherent in accurately assessing pain and safely prescribing measures for its relief in older patients greatly contribute to physician bias toward undertreatment.

Confounding Factors

Certain types of pain are inherently more refractory to treatment and require significantly higher opiate doses in young and old alike. As noted by Vigano et al., both neuropathic and incidental pain (pain that is “suddenly aggravated as a result of movements, swallowing, defecation or urination,”9(p.1247)) fall into this category.

The fact that patients who have undergone radiation or chemotherapy are more likely to require higher opioid doses is discussed by Mercadante et al.3 and by Hall et al.6 Mercadante et al. noted that as a rule older patients have received less aggressive oncological (i.e., radiation or chemotherapy) treatment and this may itself contribute to their overall lower analgesic requirements. Hall et al. are more specific in proposing that a reason for this is that radiation and chemotherapy themselves cause the more difficult to treat neuropathic pain syndromes. By extension, if the elderly are receiving less radiation and chemotherapy, they are likely to remain among the population subsets requiring lower doses of morphine for adequate pain relief. On the other hand, Delgado-Guay and Bruera point out the fact that cancers tend to be diagnosed at later stages in older adults, both causing a delay in the treatment of pain, and resulting in more advanced symptomatology at the time of presentation.7

Lower morphine requirements among the elderly may also be a result of the effect of primary tumor site on pain, rather than an effect of age. Hall et al.6 for example, discuss the fact that gynecological cancers in general, and cervical cancer in particular, are associated with higher morphine doses. Cervical cancer tends to affect younger patients.6 In other words, patients requiring higher doses because of primary tumor site are likely to be younger—possibly skewing the significance of age analyses.

These authors also bring up the fact that pain as a factor of tumor type is greatly influenced by the widely varying metastatic potential and pattern of different cancers10 which may at the same time have different prevalence rates in different age groups.

It is important to mention that Hall et al. feel that significant limitations of their study were: that they used only sustained release opioids; and that they were unable to incorporate data “regarding the use of adjuvant medication. Although the opioid-sparing effects of adjuvant medications such as nonsteroidal anti-inflammatory agents, anticonvulsants, antidepressants, and corticosteroids remain to be firmly established in the literature, it is possible that adjuvant medication does have a significant impact on opioid dose.”6(p.123)

Conclusion

Treatment of cancer pain in the older adult is an ever-growing concern about which there have been few evidence-based guidelines thus far. As a result, cancer pain in the elderly often remains undertreated. To some extent this is based on what is likely a misconception that the elderly feel less pain. There may be simply too many psychosocial and physiological confounders to be able to prove or disprove this definitively. As a result of age related physiological changes such as diminished volume of distribution, decreased renal clearance and increased CNS sensitivity, however, older patients can definitely be more sensitive to both the therapeutic and toxic effects of morphine. Providers often undertreat cancer pain in older patients for fear of exacerbating opioid toxicities. The potentially confusing clinical picture of these toxicities is further clouded by the fact that the elderly may be demonstrating identical symptoms (such as "confusion, constipation, sedation and urinary retention,"3(p.124)) for age-related reasons which are not necessarily cancer-related. The complex nature of the many factors that interact when older patients have cancer pain, underscores the need for much more research in this area.

In the interim, clinicians should not only be mindful of their own biases as they provide individualized care for their elderly patients with cancer-associated pain, but also consider an interdisciplinary team approach to that care. Professionals from different disciplines and with different perspectives can often elucidate aspects of a patient’s experience that would otherwise go unrecognized by a single provider. “In the interdisciplinary team setting, a group of professionals are joined in a spiritual collective with the mutual goal of relieving patients’ and family members’ suffering.”8

References