The importance of geriatric and surgical co-management of elderly in muscoloskeletal oncology: A literature review

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Abstract

People over 65 years old are the fastest-growing part of the population and also the most common population in oncological practice. The geriatric co-assessment when involved in the management of orthopedic elderly patients could improve the survival and clinical outcomes of the patients. The aim of this review is to understand the importance of comprehensive geriatric assessment in elderly cancer orthopaedic patients affected by bone and soft tissue sarcoma in order to apply it and identify the mean surgical prognostic factors of this population.

Introduction

People over 65 years old are the fastest-growing part of the population, thus the National Institute of Aging describe our society ageing as a "silver tsunami". By 2030, 20% of the world population will be older than 65. Ageing is a highly individualized process. Older adults are heterogeneous and have varying degrees of comorbidities, functional impairments, geriatric syndromes and social support systems. Due to the increasingly complex nature of the ageing patients, frailty has become a high-priority theme.[1] Population ageing emerged on a worldwide scale for the first time in history within the last century.

Ageing is characterized by a decrease in fitness occurring with advancing chronological age. It is a developmental phase beyond the normal life trajectory exhibiting characteristics that are discontinuous and less desirable compared with earlier life periods; it's a time of increased risk of physical and psychological disability testing the limits of resilience. However, chronological age is increasingly seen as no longer sufficient to describe the processes of ageing, which is why the concept of "biological age" has been introduced.[2,3] Biological age can be defined by the individual's functional reserve, the specific risk linked to his/her personal characteristics and his/her current physical performance. A challenge for non-geriatric specialists is to determine the optimum treatment for aged people, so a geriatric co-management has become a necessity in all specialist fields today. The benefits of a comprehensive geriatric assessment (CGA) performed in older people admitted to the hospital have been demonstrated. A metanalysis in 2011 defined the CGA effective at reducing mortality and institutionalization.[4] Several systematic reviews showed that multicomponent interventions, a proportion of which included CGA, are effective to identify and to minimize risks and complications connected to frailty in many fields: orthopaedics, oncology, cardiology, etc.[5-7]

Assessment of frailty is useful to define estimates of risk and guide patients toward personalized treatment plans that will maximize their likelihood of a positive outcome. A geriatric co-management in orthopaedics has been already established, in particular about hip fracture.[5,8-10]

Early orthogeriatric management, based on joint postoperative care among orthopaedic surgeons and geriatricians appeared to demonstrate a shorter length of inpatient stay and better outcomes.[11,12]

The use of standardized geriatric screening tools can identify the coexisting geriatric syndromes and hidden comorbidities. In addition, inquiring about caregiver stress, home support and the management of the pharmacologic regimen is part of the geriatric assessment.

Bone cancer in elderly patients

A geriatric co-management in oncology has already been established. Cancer incidence is 11-fold-higher in the over 65 years old people than in the younger ones. More than 60% of patients who are newly diagnosed with cancer are aged 65 years or older, which makes this the most common population seen in oncology practice. As more and more cancers occur in elderly people, oncologists have to deal, increasingly, with the necessity of integrating geriatric parameters in the treatment of their patients.

70% of all cancers and almost all the cancer-related deaths occur in patients older than 65. Moreover, nearly half of all soft tissue sarcomas occur in patients 65 or older.[13] With the increasing age of people around the world and with the increasing incidence of elderly cancers, a much deep knowledge of the clinicopathologic and treatment differences in this population is something to aim at.[14]

Generally, three are the most frequent bone and soft tissue cancers in the elderly patients: chondrosacoma, myxofibrosarcoma and bone metastasis.[15]

Chondrosarcoma (CS) is a malignant mesenchymal neoplasia that produces chondroid matrix. There is a wide spectrum of varieties as regards localization (central and peripheral), cellular composition (mixoid, clear cells, mesenchymal) and histological grading which provides for a 3-stage classification that identify increasing

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levels of atypia and cellular activity and the resulting malignancy.[15]

Central CS is the most frequent variety among the elderly and represents the second most diagnosed primitive malignant bone tumor in this population. Pelvis, scapula, proximal epiphysis of humerus, tibia and femur and distal epiphysis of femur are mostly involved. Beside this, dedifferentiated CS is more typical among elderly patients: it is a high grade malignant cartilaginous neoplasia which derives from a central or peripheral CS or even from a benign cartilaginous neoplasia. CS is radio- and chemoresistant, so its treatment is almost always surgical, and it is planned according grade, radiographic features and localization. The prognosis of the CS is related to the histological grade, the anatomical site and the size of the lesion, as well as the age of the patient at the diagnosis and his general conditions. Adequate clinical and radiological follow-up in the medium and long term is of crucial importance.[15,16]

Mixofibrosarcoma (MFS) represents 1% of all soft tissue sarcomas and has a higher incidence in males over 65 years of age: despite its low total incidence, MFS represents a typical musculoskeletal oncological pathology of the third age. MFS involves more often lower limbs, upper limbs and rarely pelvis and retroperitoneal. In literature they report two different varieties according histological grade: a low-grade, with a low number of cells immersed in a stroma with characteristic vessels, and a high-grade, with numerous spinous or pleomorphic cells, with a high rate of atypical mitosis. To date, the most effective treatment of MFS is a surgical wide resection, even if, given the frequent deepening of the lesion beyond the fascia, a radical resection with negative margins is rare. So, local recurrence is a frequent complication. The patient's advanced age and tumor size at diagnosis have proven to be the most important negative prognostic factors for patient survival after surgical resection.[15] Among the patients aged 65 or more, compared to younger ones, it's more than double the risk of developing a bone metastasis. The tumors that most frequently (about 60%) cause secondary lesions in the bone are breast, prostate and lung cancer; metastases from kidney cancer and multiple myeloma are less frequent (about 7%).[15,17] The most frequent bony localizations are the femur, humerus, tibia and spine.

The metastatic elderly patient is a frail patient. Frailty is given by the complex association of the underlying disease and its systemic spread, together with patient's general condition and comorbidities.[18-20]

The purpose of the treatment of secondary lesions is to ensure the resolution of painful symptoms, prevent or treat any pathological fractures and improve the patient's quality of life.

Surgical treatment of bone cancer in elderly

The evaluation of the main prognostic factors is mandatory in order to identify the most suitable treatment for any single patient, whether it is surgical or simply palliative. Generally, we can state that a comprehensive geriatric assessment has to be considered in the choice of treatment in a metastatic elderly patient. Radical resection and implant of megaprosthesis, in association with adjuvant or neoadjuvant radio- or chemotherapy, is advisable in patients with a good prognosis; otherwise in patients with poor prognosis, the treatment should be palliative and not invasive.[21,21-23] As literature reports, surgical resection of bone tumors and soft tissue sarcomas in the elderly, especially in those with good prognosis, can be performed as safely as in the younger population.[14] Nevertheless, studies have shown that decisions on curative treatment, palliative chemotherapy and surgery can be affected by the patient's chronological age. In daily clinical practice elderly patients tend to be undertreated compared to young or middle-aged patients and this behavior affects their prognosis, with worse outcomes and higher tumor-related mortality.[13]

The reasons for undertreatment of elderly patients are several. First of all, surgeons are not inclined to treat elderly patients as aggressively as younger ones because of their comorbidities: often, an intralesional resection is the best option, even if this treatment is suboptimal or inappropriate. There are significant differences in survival between young and elderly patients with bone or soft tissue tumors, mainly in stage II and III: suboptimal treatment in the elderly, contribute to worse survival rates in stage II and III patients.[13] Actually, according to literature, even if elderly patients may suffer from a higher 90-day mortality after surgery principally related to comorbidities, it is acclaimed that surgery remains a key factor in the improvement of long-term outcomes especially in patients with a good prognosis.[14] Lahat *et al*. report that properly selected 75-aged or older patients can safely undergo radical resections: in their group more than half survived 5 years or more when treated with aggressive surgery.[24] Buchner *et al*. also support extensive surgery in bone and soft tissue sarcoma patients aged >70. However, general condition and comorbidity should be taken in consideration.[25] Moreover, neoadjuvant or adjuvant RT or CT are less administered in the elderly group compared to younger groups: better expected long-term outcomes are counterfeit to the misbelief of poor tolerance of these treatments by the elderly and to, not less important, logistical problems and patients availability to undergo these treatments.[13] Furthermore, bone and soft tissue tumors in elderly often come to diagnosis late due to a lack of public awareness of the symptoms, coupled with limited experience among healthcare professionals.[26] In the elderly, bone and soft tissue tumors often present at diagnosis as an advanced disease, larger and at a higher grade or stage than younger patients. These features, in addition to the frailty at this age, play a role in the decision to undergo the elderly to less aggressive treatment with lower survival rates compared to younger patients. At last, as suggested by Tsuchie *et al*, elderly patients, especially older than 80 (the oldest old patients), refused more frequently surgical treatment for bone and soft tissue sarcoma.[27]. By using a geriatric evaluation, characterizing functional status (physical, cognitive, psychosocial) and comorbidities, and taking into account the patient's wishes, a more meaningful and proactive approach can be used to manage cancer.

Material and Methods

A literature review using Pubmed/Medline and Cochrane database was performed in order to identify scientific publications relevant to evaluate the impact of age, comprehensive geriatric assessment and treatment on the survival and functional outcomes of elderly patients affected by malignant bone and soft tissue tumors. "Bone tumors", "soft tissue sarcoma", "elderly", "surgery", "outcome", "score", "prognostic factors", "comprehensive geriatric assessment" were used in our search in order to retrieve the relevant publications.

Discussion

Multidimensional assessment

Older people have coexisting medical conditions that can adversely affect surgical care and surgical outcomes, and these must be taken into consideration. Improving the quality of geriatric surgical care will require careful preoperative evaluation, risk factors

and comorbidities assessment, anesthesiological management, optimal surgical technique and post-operative care.

Since the comorbidities and the functional status of the patients have a significant impact on prognosis and on treatment choice, it is necessary to carefully consider the health status of the elderly patients in an integrated way.[28] For these reasons, all international guidelines today insist on the need to set treatment based on the patient's clinical condition and functionality, rather than age.[29,30]

The explanation of these age-related differences in the approach to treatment is, in any case, complex and also involves other factors besides the doctor and the patient: relatives and / or caregivers, psychosocial problems, costs and, in some cases, even the proximity to a specialized oncology and radiotherapy center.[31,32]

Considering that, the multidimensional and interdisciplinary approach with the collaboration of a geriatrician specialized in the oncology field is fundamental.

The CGA represents the "standard of care", as recommended by the SIOG (International Society of Oncological Geriatrics) 4 and recently by the ASCO (American Society of Clinical Oncology), to identify and define the fragility of the patient and his functional reserve. In the Italian context, the AIOM (Italian Association of Medical Oncology) has repeatedly reiterated the need to integrate CGA in the path of treatment of the elderly patient with cancer.[33]

CGA permits the assessment of frailty, predicting the risk of toxicity associated with treatments and mortality risk.

Performing a CGA is considered essential to identify problems that are not immediately evident, as geriatric syndromes.[34] Numerous studies have in fact demonstrated the ability of CGA to identify otherwise unknown conditions of vulnerability, to support the decision-making process of the specialist, whether he/she is an oncologist, radiotherapist or surgeon, to estimate the risk of toxicity, to prevent it and to preserve the functional performance of patients.[34-36]

In a systematic review about the impact of geriatric assessment on treatment decisions, it was observed that after a CGA, the 39% of previously decided treatments were modified based on the geriatric indications received.[37]

Unfortunately, this doesn't always happen either because of a lack of interdisciplinary collaboration or because of management limits linked to the distance between the cancer center and a geriatrician.

A complete assessment, as recommended by the SIOG, must include at least a functional state, cognitive performance and mood assessment; conditions such as nutritional status, polypharmacy, comorbidities, social support, add further data and make this evaluation even more complete for elderly patients with cancer.[38] No articles were found concerning CGA use in bone cancer management.

Prognostic factors

There are numerous papers that are focused on prognostic factors in elderly patients undergoing surgery for bone and soft tissue sarcomas.

In his study Tsuda *et al*, analyzed the impact of geriatric factors in elderly patients with soft-tissue sarcoma; a complete and proper resection is associated with a better sarcoma-specific survival and event-free survival, while a lower body mass index, below 16 points, is a risk factor for post-operative events.[39] Miwa *et al*, focused in their paper about the surgical site infection and specify that a prolonged operative time is associated with this complication, in elderly as much as younger.[40]

According to Iwai *et al*, another risk factor associated with a poorer prognosis in these patients are the ASA-PS score (in particular higher than 2) and a more aggressive histological type of sarcomas.[41]

Regarding the prognostic factors and outcomes in the myxofibrosarcoma patients, Hong *et al* demonstrated that increased age and tumor size are negatively correlated with overall survival and that positive margin status predicted worsened local recurrence.[42] Contrariwise either Iwai *et al* or Tsuda *et al* assert that the age is not a prognostic factor, considering that there is no statistical difference between the group of people aged 75 years or more and the younger ones.

Several studies focused on geriatric assessment: Watt *et al* observed that, in an older population undergoing an elective surgery, the presence of frailty and cognitive impairment is associated with the development of post-operative complications.[43] Moreover, in the same paper the authors suggest other potentially modifiable prognostic factor: depressive syndrome and smoking.[43] In his paper, Fahimnia *et al* reported the prevalence and association of geriatric syndromes and disability in older patients with cancer.[44] Another aspect that could play a key role in the prognostic evaluation is the history and number of falls. These studies underline the intrinsic necessity of mixing the geriatric assessment with surgical parameters to achieve a comprehensive evaluation of the elderly patients affected by bone and soft tissue sarcomas.

Last but not least, treatment in an Academic/Research center is more likely associated with a surgical resection with negative margins: treatment in specialized centers positively affects outcomes in terms of survival and functional level, particularly when attempting to save critical structures and avoiding worse oncologic outcome.

Surgical score

On the basis of the CGA, risk assessment scales have been developed such as the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score proposed by Extermann M *et al*. and as the Cancer and Aging Research Group (CARG) Toxicity tool proposed by Hurria A. *et al*. to predict the risk of toxicity related to chemotherapy treatments.[45,46]

About surgery, the America College of Surgeon (ACS) has developed a surgical risk calculator as part of its National Surgical Quality Improvement Program (NSQIP).[47] The ACS-NSQIP tool quickly and easily estimates patient-specific postoperative complication risks for almost all operations.

Although this score is available to any surgical specialty, the calculator was developed and validated by data obtained from colorectal procedures and its use in orthopedic surgery is limited.

Currently, there are no studies about CGA use in the orthopedic oncology field and there is also very little data on the use of NSQIP in orthopaedic.

The use of scores for predicting post-operative morbidity after orthopaedic surgery is not commonly employed yet, although it is developed in other surgical fields such as gastrointestinal and pulmonary surgery.[48] The Estimation of Physiologic Ability and Surgical Stress (E-PASS) is a score developed in the aforementioned surgical fields. E-PASS score is composed of a preoperative risk score (PRS) that considers patients' comorbidities and performance status, like CGA; a Surgical Stress Score (SSS) that includes intraoperative factors as blood loss, surgical times and other. Both these scores create a Comprehensive Risk Score (CRS). This score has been recently used to evaluate orthopaedic population after total hip arthroplasty, spine surgery and tumor surgery.[49]

In their review Nagata *et al* included 1183 patients, 436 of which affected by bone or soft tissue tumors, and applied E-PASS score to all of them.[50]

They showed how PRS, SSS and CRS were all significantly higher in the group with complications than in those without complications. The E-PASS score is surely a powerful instrument to predict post-operative morbidity in orthopaedic patient

but is not age- nor tumor-specific, so the knowledges in the use of this kind of score have to be deepened.

Preoperative assessment of cancer in elderly (PACE) has been developed to assess the functional life of an oncogeriatric patient and predict the individualized risk for cancer surgery.[51] It is a multiparametric score, that considers mini mental state examination (MMSE), activities of daily living (ADLs), ASA score and other parameters. The surgical outcome is defined by 30-day mortality and morbidity, but neither this score is specific for orthopaedic oncologic patients.

Conclusions

The elderly patient with musculoskeletal oncological disease represents a challenge in terms of treatment and prognosis for the orthopedic surgeon. We have schematized which are the most frequent pathologies in this population and the main surgical treatment options available.

Despite the growing scientific attention on clinical and management peculiarities of this group of patients, at the moment scientific research on this topic is poor.

Considering the demographic and social changes taking place, it is necessary to review the common vision that generally justifies less invasive, and/or less radical, treatments in elderly cancer patients. For bone and soft tissue sarcomas, surgical therapy and adjuvant therapy can often be safely performed regardless of age. Age should be no longer considered as a contraindication to attempting curative surgical procedures. Finally, it is necessary to underline how new research is needed for the future, aimed at confirming the real limits of oncological surgery in this patient, providing surgeons with more systematic and rigorous research data, and any pre-operative risk assessment scores that are currently in short supply.

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