

# Symptom Management in Geriatric Hematologic Malignancy Patients: Traditional Review

## Geriatrik Hematolojik Maligniteli Hastalarda Semptom Yönetimi: Geleneksel Derleme

 Nurhan DOĞAN<sup>a</sup>

<sup>a</sup>Amasya University Faculty of Health Sciences, Department of Medical Nursing, Amasya, Türkiye

**ABSTRACT** The proportion of the older adult population is increasing all over the world. One of the conditions frequently encountered with aging is hematological malignancies. In hematological malignancies, there are many symptoms related to cancer and its treatment, and when the decrease in physical functions in old age is added to this situation, symptom management becomes difficult. Symptoms are frequently seen in individuals, pain, anxiety, nausea and vomiting, and dyspnea. However, geriatric syndromes such as malnutrition, delirium, frailty and falls are also seen. In geriatric individuals, complex symptoms such as dermatologic problems, peripheral neuropathy, fatigue, loss of muscle tone and financial toxicity, which have been taken into consideration more in recent years, are known to negatively affect quality of life and are difficult to manage. In individuals with geriatric hematological malignancies, a geriatric evaluation with a holistic and multidisciplinary approach will be more effective in terms of symptom management. In symptom management of geriatric individuals, it is important to provide a holistic approach in team collaboration with individualized care and treatment methods. The issue of incorporating evidence-based practices into care and treatment is another issue that needs to be addressed. As a result of the literature review, it was determined that more studies are needed on symptom management of geriatric individuals in order to reveal the importance of the subject. This review aims to improve care by providing information about common symptoms and management of these symptoms in geriatric individuals with hematological malignancies. The article was compiled by examining current literature.

**Keywords:** Hematologic cancer; nursing care; symptom management; older adult

**ÖZET** Tüm dünyada yaşlı nüfusun oranı giderek artmaktadır. Yaşlanmayla birlikte sıklıkla karşılaşılan durumlardan biri de hematolojik malignitelerdir. Hematolojik malignitelerde kansere ve tedavisine bağlı pek çok semptom vardır ve bu duruma yaşlılıkta fiziksel fonksiyonlardaki azalma da eklenince semptom yönetimi zorlaşmaktadır. Bireylerde sıklıkla görülen semptomlar; ağrı, anksiyete, bulantı, kusma ve dispnedir. Bununla birlikte malnütrasyon, deliryum, kırılabilirlik ve düşmeler gibi geriatrik sendromlar da görülmektedir. Geriatrik bireylerde, dermatolojik problemler, periferik nöropati, yorgunluk, kas tonusu kaybı ve son yıllarda daha çok dikkate alınmaya başlanan finansal toksisite gibi kompleks semptomların yaşam kalitesini olumsuz etkilediği ve yönetiminin zor olduğu bilinmektedir. Geriatrik hematolojik malignitesi olan bireylerde öncelikle bütüncül ve multidisipliner bir yaklaşımla geriatrik değerlendirmenin yapılması, semptom yönetimi açısından daha etkili olacaktır. Geriatrik bireylerin semptom yönetiminde ise bireyselleştirilmiş bakım ve tedavi yöntemleri ile ekip iş birliğinde bütüncül yaklaşımın sağlanması önemlidir. Kanıta dayalı uygulamaların bakım ve tedaviye katılması konusu ise ele alınması gereken bir başka konudur. Yapılan literatür incelemesi sonucunda konunun önemini ortaya koymak için geriatrik bireylerin semptom yönetimi konusunda daha fazla çalışmaya ihtiyaç duyulduğu saptanmıştır. Bu derleme, hematolojik maligniteli geriatrik bireylerde sık görülen semptomlar ve bu semptomların yönetimi hakkında bilgi vererek bakımın iyileştirilmesini amaçlamaktadır. Makale güncel literatür incelenerek derlenmiştir.

**Anahtar Kelimeler:** Hematolojik kanser; hemşirelik bakımı; semptom yönetimi; yaşlı birey

**TO CITE THIS ARTICLE:**

Doğan N. Symptom management in geriatric hematologic malignancy patients: Traditional review. Turkiye Klinikleri Journal of Gerontology. 2023;2(2):69-80.

**Correspondence:** Nurhan DOĞAN

Amasya University Faculty of Health Sciences, Department of Medical Nursing, Amasya, Türkiye

**E-mail:** nurhan\_dogan38@hotmail.com

Peer review under responsibility of Türkiye Klinikleri Journal of Gerontology.

**Received:** 16 Feb 2024

**Received in revised form:** 16 Oct 2024

**Accepted:** 11 Nov 2024

**Available online:** 07 Jan 2025

2822-5627 / Copyright © 2023 by Türkiye Klinikleri. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



Individuals over 65 years old are the most frequently diagnosed group for cancer and face a range of complex physical and psychosocial issues that necessitate multidisciplinary support. However, they remain underrepresented in research. Optimal strategies to facilitate the participation of older adults in research have yet to be developed, but researchers should be encouraged to do so.<sup>1,2</sup> When studies on geriatric individuals are not conducted, gaps in continuity of care and unmet needs of older individuals cannot be identified, which hinders access to guidelines that can be developed for cancer and its treatment and their related impacts.<sup>3,4</sup> In symptom management and treatment decisions; Beyond clinical trial efficacy and safety, additional considerations such as treatment feasibility (frequency of clinic/hospital attendance), tolerability, effects on quality of life, and impact of comorbidities should also be considered. And also; There are many important factors to consider, including disease symptoms, treatment burden and toxicities, ability to participate in daily activities, financial burden, access to treatment and treatment centers, and appropriateness of treatment. All these factors are drivers of quality of life and treatment satisfaction/compliance.<sup>5</sup>

#### THE IMPORTANCE OF COMPREHENSIVE GERIATRIC ASSESSMENT/ GERIATRIC ASSESSMENT IN SYMPTOM MANAGEMENT OF OLDER ADULTS WITH CANCER

Recently, the usefulness of geriatric assessment conducted by multiple staff with different medical backgrounds has been reported; however, there is not yet a consensus on the effectiveness of geriatric assessment. Treatment-induced side effects have been significantly reduced by geriatric assessment interventions. Health-related quality of life improves with geriatric assessment interventions.<sup>3,6</sup> Geriatric assessment reduces the risk of under-treatment of healthy patients and over-treatment of frail/unfit patients. Geriatric assessment is a global health assessment for older adults that goes beyond a disease-focused assessment to develop appropriate

interventions and identify unidentified problems that can prevent future geriatric problems.<sup>6,7</sup> Geriatric assessment has been used to predict treatment-related toxicity and survival using domains of comorbidities, functioning, cognitive status, polypharmacy, social support, depression and/or psychological distress.<sup>3,7</sup> Geriatric assessment requires time and resources but is beneficial for patients. For geriatric assessment to be more widely used in the clinic, the number of health care providers needs to be increased, and geriatric assessment skills need to be improved.<sup>3,6</sup> Geriatric assessment provides insights into changing movement disorders and serious comorbidities. However, geriatric assessment has also been reported to be important for therapeutic treatment decision-making and is important to provide personalized treatment and to evaluate its predictive effect on survival and treatment toxicity.<sup>3,4,8</sup> Although “chronological age” is an important consideration when making treatment decisions for hematologic malignancies, it has been reported that “functional status” is more important in treatment outcomes and that “variables beyond age”, including functional and physical performance and comorbidities, should be taken into account in the treatment and care of older individuals.<sup>7</sup>

#### ASSESSMENT AND MANAGEMENT OF SYMPTOMS

Geriatric individuals have different physical symptoms compared to younger patients, and the frequency of their symptoms varies. Cognitive, motor, visual and auditory losses in the older adult may cause difficulties in detecting the presence and severity of symptoms and lead to poor management of symptoms. Pain, anxiety and nausea are the most common symptoms in the older adult group.<sup>9</sup> Geriatric individuals are also reported to experience dyspnea, feeding problems, delirium, incontinence and respiratory distress and these symptoms are reported to be inadequately managed. It is also seen that a comprehensive geriatric evaluation, especially when consulting geriatric patients, is important in terms of adequate symptom control and monitoring of functions.<sup>9,10</sup> The degree to which geriatric individuals re-

ceive and understand information about potential symptoms and symptom management affects their ability to cope with side effects related to cancer and its treatment.<sup>11,12</sup>

## PAIN AND ITS MANAGEMENT

Pain can severely affect the physical activity levels, social interactions, sexuality, emotional and psychological states of geriatric individuals. Patients in remission may also have phantom pain, pain from irradiated areas, and neuropathic pain due to chemotherapy or surgery.<sup>13</sup> Inadequate pain control is provided in geriatric individuals. Because pain in the older adult is not seen as a symptom that needs to be managed, but as a normal part of aging. Failure to manage pain in the older adult leads to depression, decreased socialization, sleep disorders, immobility, and increased health care needs.<sup>9,13</sup> In addition to the underlying disease and treatments received, taking a comprehensive anamnesis including the effect of pain on quality of life will be important in pain management.<sup>13</sup> In older adults, it is recommended that painkillers should not be given on demand and pain should be objectively evaluated every two hours.<sup>9,13</sup>

In the pharmacologic management of pain, acetaminophen (paracetamol) should be the first choice in the presence of mild pain, and the use of non-steroidal anti-inflammatory drugs should be avoided in older adults (gastrointestinal side effects, kidney damage, risk of increasing heart failure). It is recommended to use the WHO three-step analgesia ladder for pain management.<sup>9,13</sup> In the 1st step of the pain ladder developed by WHO in 1986, for mild pain with visual analog scale (VAS) grades 1-3, analgesics containing acetaminophen and non-steroidal drugs are used. Here, anti-inflammatory drugs are preferred. If the pain continues or if there is moderate pain (Grade 4-6 on the VAS), weak opioids are used on step 2 of the ladder to treat the pain. For severe pain (rating 7-10 on the VAS), treatment with stronger opioids at step 3 of the ladder is recommended.<sup>14</sup> Opioids can be used for moderate to severe pain. The opioid dose should be increased by carefully monitoring the patient.<sup>9,13</sup> If the older adult

has heart failure, opioids should be used with caution due to their fatal effects, morphine and codeine should be avoided in case of renal and liver failure, and meperidine should be avoided due to side effects such as delirium.<sup>13,15,16</sup> In geriatric individuals, the best choice of analgesic and dose adjustment is important. In addition, cognitive impairment, multiple comorbidities and malnutrition may increase inappropriate drug consumption by making pain management difficult. However, reports indicate that pain perception and severity do not diminish in individuals with dementia and Alzheimer's disease, underscoring the importance of assessing pain in these individuals. It was found that numerical rating scales used for pain could be used in 75% of geriatric individuals with mild cognitive impairment, only 57% of those with moderate impairment, and none of those with severe cognitive impairment could use these tools.<sup>13</sup>

Unmanaged pain in older adults has been shown to exacerbate frailty, impair performance status, and significantly reduce quality of life. The cooperation of physicians and nurses is important in the evaluation of pain. Visual scales should be used in the diagnosis of pain for the older adult with communication disorders, and non-pharmacological methods should be integrated into care for pain control (massage, acupuncture, cognitive and behavioral techniques, psychotherapies and nerve blocks, etc.). It has been reported that pain control in geriatric individuals requires a complementary approach and multidisciplinary treatment, and that randomized clinical trials are insufficient in the management of cancer-related pain in older adults.<sup>9,13</sup>

## ANXIETY AND ITS MANAGEMENT

Anxiety is a cognitive, emotional, physiological and behavioral response to unexpected, unpredictable and threatening events or situations. Anxiety may also be associated with impaired social interaction, cognitive and emotional functioning, malnutrition and comorbidities. In older adults diagnosed with cancer, anxiety is seen between 12-21% and negatively affects survival. Psychiatric evaluation should be performed for anxiety. Pharmacologic anxiolytics may be bene-

ficial in its treatment.<sup>9,17,18</sup> In addition, music therapy has been reported to reduce the anxiety level of older adults with hematologic cancer.<sup>19,20</sup> Studies on the anxiety status of geriatric individuals are limited in literature and there is a need for further studies in this field.

#### NAUSEA-VOMITING AND ITS MANAGEMENT

Nausea is a symptom that significantly affects quality of life and adherence to treatment. Symptoms such as pain, anorexia, depression and anxiety accompanying nausea should be questioned. The severity of nausea should be assessed with numerical or analog scales and attention should be paid to oral and general body hygiene.<sup>3,9,21</sup> It is important to determine whether nausea and vomiting are treatment-related (chemotherapy, radiotherapy, other pharmacologic treatments) or independent of cancer treatment.<sup>22</sup> In opioid-induced nausea, dose reduction or opioid rotation may be considered. If constipation is present, it should be treated. Olanzapine is often used to control nausea and vomiting after chemotherapy or surgery. It is generally preferred in patients at high risk, especially when other antiemetic drugs are ineffective or inadequate.<sup>23</sup> Olanzapine 5 mg per day is reported to control nausea and vomiting.<sup>3,9,21,23</sup> In a study, it was emphasized that the antiemetic efficacy of olanzapine 2.5 mg was not lower than 10.0 mg and that lower doses resulted in less daytime sleepiness in patients receiving chemotherapy and should be considered as a new standard of care.<sup>23</sup> It is emphasized that the choice of antiemetic should be individualized in geriatric individuals.<sup>3,9,21,23</sup>

#### MALNUTRITION AND ITS MANAGEMENT

Malnutrition is a challenging health problem in geriatric individuals. Malnutrition in geriatric individuals is associated not only with increased mortality and morbidity, but also activities of daily living and quality of life. Malnutrition is common in geriatric individuals and may contribute to the development of geriatric syndromes.<sup>24</sup> Both acute and chronic diseases have the potential to cause or worsen malnutrition. Because the risk of developing chronic disease increases with age, older adults are at the highest risk of malnutrition.<sup>24</sup> According to the re-

sults of three different screening tests related to malnutrition in geriatric individuals, 55.7% of geriatric individuals were found to have malnutrition and/or malnutrition risk according to the Mini Nutritional Assessment, 56.9% according to the Nutritional Risk Screening-2002, and 50.4% according to the Malnutrition General Screening Test.<sup>10</sup> Malnutrition screening tests should be used in combination and repeated at regular intervals, and nutritional interventions that the individual needs should be started early with a multidisciplinary approach and a program that includes dietitians in the team. It is important to identify malnutrition in the early process and to make the necessary interventions in order to increase the effectiveness of the treatment applied, to increase the quality of life, to shorten the length of hospital stay and to reduce costs.<sup>10</sup> In older adults, high nutrient density in the diet is required and targeted supplementation of micronutrients may be beneficial.<sup>25</sup>

#### DYSPNEA AND ITS MANAGEMENT

More than half of the patients seeking medical attention for shortness of breath are 65 years of age or older. The older adult's perception of the intensity of dyspnea may also be affected by psychological factors such as anxiety and depression. It is important to recognize and treat sarcopenia in older adults with dyspnea.<sup>9,26</sup> Sarcopenia is a geriatric disease characterized by progressive loss of skeletal muscle mass and loss of muscle function. It is a health problem that is increasingly common among older individuals and is often undiagnosed. Its frequency varies between 5% and 50% depending on gender, age, pathological conditions and diagnostic criteria.<sup>27</sup> This loss in muscle mass and strength caused by sarcopenia also affects respiratory muscle strength, causing low respiratory function. This condition, also called respiratory sarcopenia. It can be caused by various factors such as aging, decreased activity, malnutrition, disease, cachexia and iatrogenic causes.<sup>28</sup> Physical activity (resistance training, aerobic exercise, high-intensity interval training, multimodal exercise and whole-body vibration therapy) and nutrition (diet and supplementation) can be effective in preventing sarcopenia.<sup>27</sup> The main aim of dyspnea management

is to reduce the distress caused by dyspnea. Non-pharmacological methods (relaxation techniques, breathing techniques, use of fans blowing cold air into the face, chest wall vibration, pulmonary rehabilitation, mechanical air blowing devices, oxygen therapy and non-invasive mechanical ventilation) and pharmacological methods (short-acting opioids, long-acting bronchodilators) are important in dyspnea management.<sup>9,26</sup>

## DELIRIUM AND ITS MANAGEMENT

Delirium is a common acute cognitive dysfunction in geriatric individuals. Delirium is a life-threatening, costly condition that often goes undiagnosed in the clinic.<sup>29</sup> Delirium may be caused by urinary retention (catheter obstruction or globe development), pain, drug side effects or constipation. It limits the decision-making process regarding the care of the geriatric individual. It is a major concern for both the family and the healthcare team. Patients and their relatives should be informed about the clinical features of the first signs of delirium (focusing problems, distraction and indifference to surrounding events) and patient safety should be ensured.<sup>9,29</sup> It is observed that the patient has difficulty in focusing, maintaining and shifting attention. He/she has difficulty in following what is said and in conversation and usually perseveres by giving the answer to the previously asked question. Cognitive evaluation reveals impairment in simple word repetition and in following commands. The patient cannot count days or months backwards. Tools that can be used to assess delirium; Tools to Assess Pre-Delirium Alertness, Tools to Screen for Delirium, Tools to Diagnose Delirium, Delirium Assessment Tools and Assessment Tools for Cognitive Symptoms of Delirium.<sup>30</sup>

Non-pharmacologic approach should be prioritized in treatment. It is important to ensure day-night adaptation, to prevent the perception of the environment as unfamiliar, and to provide a quiet environment at night.<sup>9,29</sup>

In the prevention of delirium, cognitive interventions include verbal-visual stimuli and reorientation such as addressing the patient by name, giving information about the name of the hospital,

service, disease prognosis, reducing noise and light levels at night, providing bedside clocks and newspapers. Environmental arrangements include lighting, sound regulation, having a calendar and clock, introducing the tools and equipment (pictures, decoration tools, alarm, call systems, etc.) that should be present in the patient environment and explaining the reason for their existence. Providing physiological support includes ensuring the patient's fluid-electrolyte balance, nutrition, body temperature, natural excretion, oxygenation and blood sugar control, regulating blood pressure and controlling infection. Ensuring early mobilization includes the implementation of movement programs starting from in-bed passive Joint Range of Motion and Stretching Exercises according to the tolerance level of the patients and extending to independent walking in the ward.<sup>31</sup>

## FALLS AND ITS MANAGEMENT

Falls are significantly associated with inappropriate drug use, thrombocytopenia and delirium. In 527 individuals aged 60 years and older, delirium was observed in 21% up to day 100 after bone marrow transplantation and falls in 7% after day 100. In those older than 70 years, age and impairment in activities of daily living are significantly associated with falls. Falls are associated with decreased survival, and delirium and falls are associated with increased mortality and decreased survival.<sup>32</sup> Approximately one-third of individuals aged 65 years and older have been found to fall and half of hospitalized individuals are at risk of falling.<sup>33</sup> Falls can negatively affect the independence of the individual by bringing consequences such as injury, decrease in physical capacity, dependence in performing activities of daily living, decrease in quality of life and the need for nursing home placement. Serious injuries caused by falls lead to prolonged care, hospitalization, increased treatment needs, and consequently increased costs and deaths. Falls also have psychological consequences on older adults such as anxiety, fear, and decreased self-confidence.<sup>33</sup>

Exercise is an important factor to prevent falls. Progressive muscle strengthening, balance training



and gait planning programs reduce the incidence of falls. Exercise improves muscle strength and balancing ability of the lower limbs to prevent falls in older adults. Recent evidence has shown that exercise can reduce the rate of falls in older adult by 24%, significantly reducing the risk of fractures, head injuries, soft tissue injuries and all other injuries requiring hospitalizations.<sup>34</sup> In the 2019 Cochrane Review to update WHO guidelines on physical activity and inactivity, it was reported that the risk of falls was reduced by 24% in geriatric individuals performing balance and functional exercise (high-certainty evidence), the risk of falls was reduced by 28% when resistance exercises were added to programs that included more than one type of exercise (usually balance and functional exercises) (moderate-certainty evidence), and a total of three hours of balance and functional exercise per week resulted in a 42% reduction in the rate of falls.<sup>35</sup>

While it has been reported that exercise training administered by health professionals is not superior to programs led by exercise instructors, it remains evident that exercise under the guidance of health professionals is safer and more effective for high-risk individuals. No difference was found in the effect of group or individual exercise on falls. Exercise programs including balance and functional exercises reduce falls. Tai Chi and programs that include multiple exercise programs (typically balance and functional exercises plus resistance exercises) may reduce falls. The effect of resistance exercises (without balance and functional exercises), dancing and walking on fall rate remains unclear. It is important to pay attention to both the type and dose of exercise. There is an urgent need for research to improve the incorporation of exercise-based interventions for falls prevention into the routine care of older adults by health professionals and community organizations. There is also a need to develop objective tools for self-reporting, reliable fall detection. Studies with large sample groups are needed to determine the effect of interventions implemented to prevent falls on fall-related fractures and conditions requiring medical intervention.<sup>35</sup>

## FRAILITY AND ITS MANAGEMENT

Frailty is a clinical syndrome defined as the presence of at least three of the following characteristics: weakness, decreased physical resistance, involuntary weight loss, slow gait and low physical capacity. Frailty has been reported to constitute a risk factor for treatment tolerance and is also associated with an increased risk of death at 5, 7 and 10 years in both frail and pre-frail patients.<sup>36</sup> Understanding the heterogeneity of outcomes for hematologic malignancies, treatment challenges, and management of frailty and comorbidities in older individuals may help to better address the burden of hematologic cancer and mortality in the aging population.<sup>37</sup> Fragmentation of care in cancer care for geriatric individuals, especially when comorbid conditions are present, is a concern in terms of frailty. There is considerable evidence of the positive effects of early detection and comprehensive geriatric assessment on frailty. It is recommended to plan and implement individualized care to maintain functionality and well-being in frail older adults with or without cancer and comorbid conditions.<sup>11,38,39</sup> In the management of frailty, vitamin D supplementation, a diet rich in protein and calories, fall risk evaluation and planning interventions for improvement by determining the risk factors, informing about the environment and medications (such as benzodiazepines, antidepressants, antipsychotics, antihistamines, hypnotics, antihypertensives, insulin, hypoglycemic agents, antiarrhythmics) and regular exercise may reduce the risk of falling.<sup>33,38</sup>

Complex symptoms that are challenging to manage in older adults and significantly impact their quality of life include dermatological issues, peripheral neuropathy, fatigue, and a decline in strength and muscle tone.<sup>11</sup>

## DERMATOLOGICAL PROBLEMS AND ITS MANAGEMENT

The most common dermatologic problems in geriatric patients are fungal infections, eczematous dermatitis and pruritus.<sup>40</sup> Topical moisturizers, corticosteroids, antibiotics, antihistamines and anti-acne medications can be used for dermatologic problems

in geriatric individuals. It is important to inform the patient and family about drug-specific dermatologic side effects and their management. Non-pharmacologic applications such as sunscreen, showering with warm water, using neutral soap, regular use of moisturizers (alcohol and perfume-free) may be preferred. Topical gels containing vitamin E and lidocaine can be used to relieve itching.<sup>41,42</sup>

## PERIPHERAL NEUROPATHY AND ITS MANAGEMENT

The incidence of peripheral neuropathy between 60-74 years of age is 7% when diabetes and carbohydrate tolerance are excluded. Paraneoplastic agents are one of the most common causes, just after diabetes. Over 65 years of age, decreased sensory and motor nerve conduction and sensory perception, and loss of the ankle reflex increase the risk. After the age of 80, symptoms tend to increase. Although it is said not to affect quality of life, it affects morbidity due to the frequency of falls, pain, deformity of the feet, amputation and skin ulcerations.<sup>43</sup> "Rat" nerve growth factor combined with vitamin B is a safe and effective method for the treatment of peripheral neuropathy. Vitamin E, Glutathione, Glutamine, Melatonin can be used in the treatment, and among non-pharmacological applications; methods such as massage, exercise, reflexology and acupuncture can be applied. Treatment options are very limited and there is no single effective treatment method.<sup>44,45</sup>

## FATIGUE AND ITS MANAGEMENT

Fatigue can be defined as impaired physical performance capacity, lack of energy, helplessness and depressed mood. Fatigue is frequently seen in older adults with hematological malignancies, is a negative prognostic factor, has a strong impact on clinical performance, gives positive results to individualized care and treatment algorithms, early detection of fatigue and timely intervention are effective. The association of fatigue with impaired performance, nutritional status and inflammation may suggest a common solution.<sup>46</sup> Data on the effect of fatigue on the clinical picture and outcomes in older adults with hematologic malignancy are limited. In addition to fatigue,

serum ferritin has been reported to be an independent prognostic parameter.<sup>46</sup>

Hematopoietic, antidepressants, psychostimulants, steroids and so on are used in the management of fatigue.<sup>47-49</sup> Erythropoietin administration in hematologic toxicity-induced fatigue has been associated with an increased risk of thromboembolic events, as well as an increased risk of hypertension and headache. Those over 75 years of age and with a Charlson Comorbidity Index greater than 0 were also reported to be more likely to be hospitalized for thromboembolism.<sup>3</sup> Acupressure has been reported to significantly reduce the severity and level of fatigue, and low- and high-intensity Tai Chi and resistance exercise have been reported to significantly increase muscle strength, reduce cancer-related fatigue and improve quality of life in middle-aged and older adults' cancer patients.<sup>47-49</sup>

## LOSS OF STRENGTH/MUSCLE TONUS AND ITS MANAGEMENT

Physical inactivity during active treatment, catabolic effects of cytotoxic and immunosuppressive therapies, metabolic changes due to long-term glucocorticoid use and unfavorable changes in body composition due to myopathy result in high muscle dysfunction. When muscle dysfunction develops, physical therapy, moderate or high intensity aerobic and resistance exercises, high frequency low intensity exercise therapy, neuromuscular electrical stimulation and whole body electromyostimulation may be recommended. Moderate or high intensity exercises are difficult to implement in older adults due to side effects.<sup>50,51</sup> In a study comparing older adults (aged 55-79 years) who were sedentary and master athletes (men who could cycle 100 km in 6.5 hours or women who could cycle 60 km in 5.5 hours), it was found that immune aging was less in athletic older adults, the immune component of T cells in athletic older adults was similar to that of young healthy individuals (aged 20-36 years), and even a single exercise session showed an increase in the cytotoxic activity of T cells against tumor antigens.<sup>52-54</sup> Natural Killer (NK) cells are highly sensitive to exercise training in healthy individuals and cancer survivors, have a high potential to kill tumor cells during and

after exercise, and have been reported that exercise improves, NK cell function and antitumor properties. Another positive effect is that older individuals (>60 years) who walk at least 10,000 steps per day show better neutrophil response than those who walk only 5,000 steps per day.<sup>54</sup>

### FINANCIAL TOXICITY AND ITS MANAGEMENT

Direct medical costs, measured by insurance payments and out-of-pocket co-payments and prepayments by the patient, and direct non-medical costs, including payments for transportation, accommodation, childcare, housework, and so on due to illness and its treatment, are called financial toxicity. When combined with emotional stress, it becomes difficult to cope effectively with physical symptoms and treatment, monetary losses associated with inability to participate in work or other daily activities (morbidity costs) and monetary losses associated with productivity losses due to death (mortality costs).<sup>55</sup>

Risk factors associated with financial toxicity include socio-demographic characteristics of the patient and family (age, socioeconomic status, household size, etc.), financial and employment-related characteristics (employment status, insurance status, out-of-pocket expenses, financial aid, etc.), environmental and logistical characteristics (relocation status during treatment, distance from the hospital, rural/urban residence, etc.), and cancer-related characteristics (stage of disease, whether actively receiving chemotherapy, financial concerns about the physician, etc.), environmental and logistical characteristics (relocation status during treatment, distance to the hospital, living in rural/urban areas, etc.), and cancer-related characteristics (stage of the disease, whether actively receiving chemotherapy, discussing financial concerns with the physician, etc.).<sup>55,56</sup>

Management of Financial Toxicity: Informing patients about treatments, supporting individual healthcare preferences, assisting in the planning and implementation of social support services, establishing fair, yet sustainable healthcare policies, measuring financial toxicity (which helps identify gaps in

the healthcare system), and universally screening for financial toxicity before, during and after treatment should be a standard of care.<sup>55,57</sup>

### PSYCHOLOGICAL IMPACTS ASSOCIATED WITH CANCER AND ITS MANAGEMENT

Adverse psychological effects in cancer patients can arise from fluctuations in health status, uncertainties regarding future treatments, geographical barriers, and cultural factors. Support from friends and family, professional assistance, access to benefits, and having a reliable point of contact, along with referrals to other services during the transition from active treatment to observation, can be very helpful. Additionally, technology offers valuable opportunities to fill care gaps through phone support, virtual consultations, and online information systems. While close friends can be a vital source of support, they may sometimes provide well-meaning but unhelpful assistance if they don't fully understand the individual's needs. Stigmatization is another problem experienced by older adults, and both themselves and family members try to cope with this situation by distancing themselves from their friends in order to cope with treatment due to stigmatization.<sup>11</sup>

Individualized care and treatment offer an opportunity to further improve clinical outcomes, particularly in older individuals with hematological malignancies. Individualized care requires careful consideration of disease- and patient-specific characteristics throughout the survival process. Geriatric assessment guides treatment selection and contributes to supportive care to optimize functionality and quality of life.<sup>4,58,59</sup>

### DIGITAL INTERVENTION IN SYMPTOM MANAGEMENT

Older adults represent a diverse group, and when creating digital interventions, it's essential to take into account the variations in digital literacy, technology preferences, and the factors that influence their access to technology.<sup>11,60,61</sup> Recent technological advancements in Virtual Reality (VR) have led to the development and implementation of innova-



tive, non-invasive methods for managing cancer-related symptoms in healthcare. VR utilizes a computer that generates real-time animations, controlled through various sensory input devices, a location tracker, and a head-mounted display for visual output. There is increasing interest in employing VR-based therapies as part of a multidisciplinary approach to address issues such as pain relief, cancer-related fatigue, anxiety, depression, and cognitive dysfunction.<sup>62,63</sup> VR-based intervention improves the emotional, cognitive and physical well-being of cancer patients. VR-based interventions appear to provide significant improvement in cancer-related fatigue symptoms. In contrast to conventional symptom management strategies in cancer care, VR-based interventions-particularly VR cognitive training-facilitate easier learning for cancer patients, provide instant feedback on their performance, and adjust the difficulty level according to individual patient needs.<sup>64-66</sup> There are also symptoms associated with VR such as motion sickness effect, VR is not without complications.<sup>67</sup> A review of VR-based interventions for managing symptoms related to cancer treatment found that these interventions positively impacted symptoms like anxiety, depression, and pain, and enhanced cognitive functions, including verbal memory and processing speed. However, the only statistically significant difference noted was for fatigue. It is reported that more research is needed to

evaluate the effectiveness of VR-based interventions in cancer rehabilitation.<sup>66</sup>

## CONCLUSION

In conclusion, it can be recommended that more studies on geriatric hematology patients should be included, gerontologists should be included in the team, geriatric evaluation should be performed and made a protocol, individualized treatment and care should be applied with a multidisciplinary approach, and a holistic approach should be considered in symptom management of geriatric individuals.

### *Source of Finance*

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### *Conflict of Interest*

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### *Authorship Contributions*

*This study is entirely author's own work and no other author contribution.*

## REFERENCES

1. Bumanlag IM, Jaoude JA, Rooney MK, Taniguchi CM, Ludmir EB. Exclusion of older adults from cancer clinical trials: review of the literature and future recommendations. *Semin Radiat Oncol.* 2022;32(2):125-34. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
2. Mishkin GE, Denicoff AM, Best AF, Little RF. Update on enrollment of older adults onto national cancer institute national clinical trials network trials. *J Natl Cancer Inst Monogr.* 2022;2022(60):111-6. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
3. Feliu J, Heredia-Soto V, Gironés R, Jiménez-Munarriz B, Saldaña J, Guillén-Ponce C, et al. Management of the toxicity of chemotherapy and targeted therapies in elderly cancer patients. *Clin Transl Oncol.* 2020;22(4):457-67. [[Crossref](#)] [[PubMed](#)]
4. Rosko AE, Cordoba R, Abel G, Artz A, Loh KP, Klepin HD. Advances in management for older adults with hematologic malignancies. *J Clin Oncol.* 2021;39(19):2102-14. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
5. Terpos E, Mikhael J, Hajek R, Chari A, Zweegman S, Lee HC, et al. Management of patients with multiple myeloma beyond the clinical-trial setting: understanding the balance between efficacy, safety and tolerability, and quality of life. *Blood Cancer J.* 2021;11(2):40. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
6. Ninomiya K, Inoue D, Sugimoto K, Tanaka C, Murofushi K, Okuyama T, et al. Significance of the comprehensive geriatric assessment in the administration of chemotherapy to older adults with cancer: Recommendations by the Japanese Geriatric Oncology Guideline Committee. *J Geriatr Oncol.* 2023;14(5):101485. [[Crossref](#)] [[PubMed](#)]
7. Nathwani N, Kurtin SE, Lipe B, Mohile SG, Catamero DD, Wujcik D, et al. Integrating touchscreen-based geriatric assessment and frailty screening for adults with multiple myeloma to drive personalized treatment decisions. *JCO Oncol Pract.* 2020;16(1):e92-e99. [[Crossref](#)] [[PubMed](#)]
8. Briand M, Gerard S, Gauthier M, Garric M, Steinmeyer Z, Balardy L. Impact of therapeutic management and geriatric evaluation on patient of eighty years and older with diffuse large B-cell lymphoma on survival: a systematic review. *Eur J Haematol.* 2022;108(1):3-17. [[Crossref](#)] [[PubMed](#)]
9. Uğur Ö. Geriatrik palyatif bakım ve hemşirelik yaklaşımı [Geriatric palliative care and nursing approach]. *Abant Tıp Dergisi.* 2022;11(1):112-22. [[Link](#)]
10. Özel V, Alphan E. Yetişkin hematolojik kanserli hastaların malnütrisyon düzeylerinin farklı tarama araçları ile değerlendirilmesi [Evaluation of malnutrition levels of patients with adult hematological cancer with different screening tools]. *Sağlık ve Yaşam Bilimleri Dergisi.* 2019;1(1):21-9. [[Crossref](#)]
11. Drury A, O'Brien A, O'Connell L, Cosgrave S, Hannan M, Smyth C, et al. Setting a patient-driven agenda for cancer research priorities in geriatric oncology: a qualitative study. *Semin Oncol Nurs.* 2023;39(4):151463. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
12. Neter E, Brainin E. Association between health literacy, ehealth literacy, and health outcomes among patients with long-term conditions. *European Psychologist.* 2019;24(1):68-81. [[Crossref](#)]
13. Hachem GE, Rocha FO, Pepersack T, Jounblat Y, Drowart A, Lago LD. Advances in pain management for older patients with cancer. *Ecancermedicalscience.* 2019;13:980. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
14. World Health Organization. WHO Guidelines for the Pharmacological and Radiotherapeutic Management of Cancer Pain in Adults and Adolescents. Geneva: World Health Organization; 2018. [[Link](#)]
15. Miró Ò, Gil V, Martín-Sánchez FJ, Herrero-Puente P, Jacob J, Mebazaa A, et al; ICA-SEMES Research Group(\*). Morphine use in the ED and outcomes of patients with acute heart failure: a propensity score-matching analysis based on the EAHFE registry. *Chest.* 2017;152(4):821-32. [[PubMed](#)]
16. Agewall S. Morphine in acute heart failure. *J Thorac Dis.* 2017;9(7):1851-4. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
17. Ding T, Wang X, Fu A, Xu L, Lin J. Anxiety and depression predict unfavorable survival in acute myeloid leukemia patients. *Medicine (Baltimore).* 2019;98(43):e17314. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
18. Meier C, Taubenheim S, Lordick F, Mehnert-Theuerkauf A, Götze H. Depression and anxiety in older patients with hematological cancer (70+) - Geriatric, social, cancer- and treatment-related associations. *J Geriatr Oncol.* 2020;11(5):828-35. [[Crossref](#)] [[PubMed](#)]
19. Gökalp K, Ekinçi M. Effect of music therapy on anxiety and sleep quality of geriatric haematological oncology patients. *Turkish Journal of Geriatrics.* 2020;23(4):546-54. [[Crossref](#)]
20. Lu G, Jia R, Liang D, Yu J, Wu Z, Chen C. Effects of music therapy on anxiety: a meta-analysis of randomized controlled trials. *Psychiatry Res.* 2021;304:114137. [[Crossref](#)] [[PubMed](#)]
21. Navari RM, Pywell CM, Le-Rademacher JG, White P, Dodge AB, Albany C, et al. Olanzapine for the treatment of advanced cancer-related chronic nausea and/or vomiting: a randomized pilot trial. *JAMA Oncol.* 2020;6(6):895-9. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
22. Navari RM. Managing Nausea and Vomiting in Patients With Cancer: What Works. *Oncology (Williston Park).* 2018;32(3):121-5, 131, 136. [[PubMed](#)]
23. Bajpai J, Kapu V, Rath S, Kumar S, Sekar A, Patil P, et al. Low-dose versus standard-dose olanzapine with triple antiemetic therapy for prevention of highly emetogenic chemotherapy-induced nausea and vomiting in patients with solid tumours: a single-centre, open-label, non-inferiority, randomised, controlled, phase 3 trial. *Lancet Oncol.* 2024;25(2):246-54. [[Crossref](#)] [[PubMed](#)]
24. Norman K, Haß U, Pirlich M. Malnutrition in older adults-recent advances and remaining challenges. *Nutrients.* 2021;13(8):2764. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
25. Correa-Pérez A, Abraha I, Cherubini A, Collinson A, Dardevet D, de Groot LCPGM, et al. Efficacy of non-pharmacological interventions to treat malnutrition in older persons: A systematic review and meta-analysis. The SENATOR project ONTOP series and MaNuEL knowledge hub project. *Ageing Res Rev.* 2019;49:27-48. [[Crossref](#)] [[PubMed](#)]
26. Zemel RA. Pharmacologic and non-pharmacologic dyspnea management in advanced cancer patients. *Am J Hosp Palliat Care.* 2022;39(7):847-55. [[Crossref](#)] [[PubMed](#)]
27. Papadopoulou SK. Sarcopenia: a contemporary health problem among older adult populations. *Nutrients.* 2020;12(5):1293. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
28. Nagano A, Wakabayashi H, Maeda K, Kokura Y, Miyazaki S, Mori T, et al. Respiratory sarcopenia and sarcopenic respiratory disability: concepts, diagnosis, and treatment. *J Nutr Health Aging.* 2021;25(4):507-15. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
29. Iglseider B, Frühwald T, Jagsch C. Delirium in geriatric patients. *Wien Med Wochenschr.* 2022;172(5-6):114-21. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]

30. Erbay Ö, Kelebek Girgin N. Deliriumun değerlendirilmesinde sık kullanılan ölçüm araçlarının incelenmesi [Investigation of frequently used measurement tools for evaluation of delirium]. *Uludağ Üniversitesi Tıp Fakültesi Dergisi*. 2020;46(1):113-21. [[Crossref](#)]
31. Karadaş C, Özdemir L. Nursing responsibilities and non-pharmacological approaches in delirium management. *Journal of Psychiatric Nursing*. 2019;10(2). [[Crossref](#)]
32. Lin RJ, Hilden PD, Elko TA, Dahi PB, Shahrokni A, Jakubowski AA, et al. Burden and impact of multifactorial geriatric syndromes in allogeneic hematopoietic cell transplantation for older adults. *Blood Adv*. 2019;3(1):12-20. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
33. Kıymaç Sarı M, Durna Z. Geriatrik sendromlar ve bakım [Geriatric syndromes and care]. *ERÜ Sağlık Bilimleri Fakültesi Dergisi*. 2022;9(1):39-46. [[Link](#)]
34. Zhang Q, Liu Y, Li D, Jia Y, Zhang W, Chen B, et al. Exercise intervention for the risk of falls in older adults: a protocol for systematic review and meta-analysis. *Medicine (Baltimore)*. 2021;100(5):e24548. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
35. Sherrington C, Fairhall N, Kwok W, Wallbank G, Tiedemann A, Michaleff ZA, et al. Evidence on physical activity and falls prevention for people aged 65+ years: systematic review to inform the WHO guidelines on physical activity and sedentary behaviour. *Int J Behav Nutr Phys Act*. 2020;17(1):144. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
36. Feliu J, Heredia-Soto V, Gironés R, Jiménez-Munarriz B, Saldaña J, Guillén-Ponce C, et al. Can we avoid the toxicity of chemotherapy in elderly cancer patients? *Crit Rev Oncol Hematol*. 2018;131:16-23. [[Crossref](#)] [[PubMed](#)]
37. Cordoba R, Eyre TA, Klepin HD, Wildes TM, Goede V. A comprehensive approach to therapy of haematological malignancies in older patients. *Lancet Haematol*. 2021;8(11):e840-e52. [[Crossref](#)] [[PubMed](#)]
38. Antoine-Pepeljoguski C, Braunstein MJ. Management of newly diagnosed elderly multiple myeloma patients. *Curr Oncol Rep*. 2019;21(7):64. [[Crossref](#)] [[PubMed](#)]
39. Choi JY, Kim KI. Assessing frailty using comprehensive geriatric assessment in older patients with hematologic malignancy. *Blood Res*. 2022;57(S1):1-5. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
40. Aksoy Sarac G, Emeksiz MAC, Acar O, Nazlican E, Tanacan E, et al. Retrospective analysis of dermatological diseases in geriatric patients during dermatology outpatient department visits. *Dermatol Pract Concept*. 2022;12(3):e2022145. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
41. Barton-Burke M, Ciccolini K, Mekas M, Burke S. Dermatologic reactions to targeted therapy: a focus on epidermal growth factor receptor inhibitors and nursing care. *Nurs Clin North Am*. 2017;52(1):83-113. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
42. Beech J, Germetaki T, Judge M, Paton N, Collins J, Garbutt A, et al. Management and grading of EGFR inhibitor-induced cutaneous toxicity. *Future Oncol*. 2018;14(24):2531-41. [[Crossref](#)] [[PubMed](#)]
43. Bouche P. Neuropathy of the elderly. *Rev Neurol (Paris)*. 2020;176(9):733-8. [[Crossref](#)] [[PubMed](#)]
44. Yan M, Li Y, Zeng H, Zhao X, Wu H, Qian W, Guo X. The effect of rat nerve growth factor combined with vitamin B on peripheral neuropathy in multiple myeloma patients. *Hematology*. 2020;25(1):264-9. [[Crossref](#)] [[PubMed](#)]
45. Yasuda H, Hoshino Y, Ando J, Miyachi M, Osawa M, Hattori N, et al. Vitamin B6 deficiency polyneuropathy and dermatitis. *Am J Med*. 2023;136(1):e10-e11. [[Crossref](#)] [[PubMed](#)]
46. Hofer F, Koinig KA, Nagl L, Borjan B, Stauber R. Fatigue at baseline is associated with geriatric impairments and represents an adverse prognostic factor in older patients with a hematological malignancy. *Ann Hematol*. 2018;97(11):2235-43. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
47. Cheng D, Wang X, Hu J, Dai LL, Lv Y, Feng H, et al. Effect of tai chi and resistance training on cancer-related fatigue and quality of life in middle-aged and elderly cancer patients. *Chin J Integr Med*. 2021;27(4):265-72. [[Crossref](#)] [[PubMed](#)]
48. Özdemir Ü, Taşçı S. Yorgunluk yaşayan kanserli bireylerde bütünlük sağlığı uygulaması: akupresür [Integrated health implementation in cancer individuals suffering from fatigue: acupressure]. *Journal of Health Sciences*. 2017;26(3):253-6. [[Link](#)]
49. Özdemir Ü, Taşçı S. Acupressure for cancer-related fatigue in elderly cancer patients: a randomized controlled study. *Altern Ther Health Med*. 2023;29(4):57-65. [[PubMed](#)]
50. Ishii S, Hirota K, Nakano J. Muscle mass, cachexia, and health-related quality of life in patients with hematologic malignancies. In: Morishita S, Inoue J, Nakano J, eds. *Physical Therapy and Research in Patients with Cancer*. 1st ed. Singapore: Springer; 2023. p.93-110. [[Crossref](#)]
51. Liu MA, DuMontier C, Murillo A, Hsieh TT, Bean JF, Soiffer RJ, et al. Gait speed, grip strength, and clinical outcomes in older patients with hematologic malignancies. *Blood*. 2019;134(4):374-82. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
52. Duggal NA, Pollock RD, Lazarus NR, Harridge S, Lord JM. Major features of immunosenescence, including reduced thymic output, are ameliorated by high levels of physical activity in adulthood. *Aging Cell*. 2018;17(2):e12750. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
53. LaVoy EC, Bollard CM, Hanley PJ, Blaney JW, O'Connor DP, Bosch JA, et al. A single bout of dynamic exercise enhances the expansion of MAGE-A4 and PRAME-specific cytotoxic T-cells from healthy adults. *Exerc Immunol Rev*. 2015;21:144-53. [[PubMed](#)]
54. Sitlinger A, Brander DM, Bartlett DB. Impact of exercise on the immune system and outcomes in hematologic malignancies. *Blood Adv*. 2020;4(8):1801-11. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
55. Ürek D, Uğurluoğlu Ö. Finansal toksite: kanser bakımında yeni bir yan etki [Financial toxicity: a new side effect in cancer care]. 2021;24(3):651-80. [[Link](#)]
56. McNulty J, Khara N. Financial Hardship—an Unwanted Consequence of Cancer Treatment. *Curr Hematol Malig Rep*. 2015;10(3):205-12. [[Crossref](#)] [[PubMed](#)]
57. Gordon LG, Merollini KM, Lowe A, Chan RJ. Financial toxicity-what it is and how to measure it. *Cancer Forum*. 2017;41(2):30-35. [[Link](#)]
58. Gengenbach L, Reinhardt H, Ihorst G, Ajayi S, Dold SM, Köhler M, et al. Navigating the changing multiple myeloma treatment landscape: clinical practice patterns of MM patients treated in- and outside German DSMM study group trials. *Leuk Lymphoma*. 2018;59(11):2692-9. [[Crossref](#)] [[PubMed](#)]
59. Schumacher M, Hieke S, Ihorst G, Engelhardt M. Dynamic prediction: a challenge for biostatisticians, but greatly needed by patients, physicians and the public. *Biom J*. 2020;62(3):822-35. [[Crossref](#)] [[PubMed](#)]
60. Bian C, Ye B, Hoonakker A, Mihalidis A. Attitudes and perspectives of older adults on technologies for assessing frailty in home settings: a focus group study. *BMC Geriatr*. 2021;21(1):298. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
61. Schreurs K, Quan-Haase A, Martin K. Problematizing the digital literacy paradox in the context of older adults' ICT use: Aging, media discourse, and self-determination. *Canadian Journal of Communication*. 2017;42(2):359-77. [[Crossref](#)]

62. Chirico A, Lucidi F, De Laurentiis M, Milanese C, Napoli A, Giordano A. Virtual reality in health system: beyond entertainment. A mini-review on the efficacy of VR during cancer treatment. *J Cell Physiol.* 2016;231(2):275-87. [[Crossref](#)] [[PubMed](#)]
63. Glennon C, McElroy SF, Connelly LM, Mische Lawson L, Bretches AM, Gard AR, et al. Use of virtual reality to distract from pain and anxiety. *Oncol Nurs Forum.* 2018;45(4):545-52. [[Crossref](#)] [[PubMed](#)]
64. Gambhir S, Narkeesh A, Arunmozhi R. Role of the virtual reality in cognitive rehabilitation: a review. *International Journal of Therapies and Rehabilitation Research.* 2017;6(2):125. [[Crossref](#)]
65. Indovina P, Barone D, Gallo L, Chirico A, De Pietro G, Giordano A. Virtual reality as a distraction intervention to relieve pain and distress during medical procedures: a comprehensive literature review. *Clin J Pain.* 2018;34(9):858-77. [[Crossref](#)] [[PubMed](#)]
66. Zeng Y, Zhang JE, Cheng ASK, Cheng H, Wefel JS. Meta-analysis of the efficacy of virtual reality-based interventions in cancer-related symptom management. *Integr Cancer Ther.* 2019;18:1534735419871108. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
67. Kocaoğlu Y. Hareket hastalığı ve sanal ortam [Motion sickness and virtual environment]. *Beden Eğitimi ve Spor Bilimleri Dergisi.* 2022;16(1):22-39. [[Link](#)]