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Kemoterapiye Bağlı Ayak Derisi Mikrobiyotasında Gözlenen Değişiklikler ve Klinik Yansımaları
Chemotherapy-Associated Alterations In Foot Skin Microbiota And Their Clinical Implications

Ayşegül Sarpkaya[1*]

[*1] Harran Üniversitesi, Sağlık Hizmetleri MYO, Podoloji Programı, Şanlıurfa/TÜRKİYE
aysegulsarpkaya@harran.edu.tr, ORCID: 0000-0002-8479-0235

ÖZET

Kemoterapiye bağlı immünsüpresyon, yalnızca sistemik savunma mekanizmalarını değil, aynı zamanda deri mikrobiyotasının dengesini de olumsuz etkileyerek onkoloji hastalarında cilt komplikasyonlarının gelişimini kolaylaştırmaktadır. Bu derleme, özellikle ayak derisi mikrobiyotasında gözlenen değişikliklerin nedenlerini, fırsatçı patojen kolonizasyonlarıyla ilişkili dermatolojik komplikasyonları ve bunların klinik yansımalarını incelemektedir. Tinea pedis, onikomikoz, intertrigo ve el-ayak sendromu gibi komplikasyonların, mikrobiyota bozulmalarıyla yakından ilişkili olduğu vurgulanmaktadır. Ayrıca, klasik antimikrobiyal tedavilere ek olarak mikrobiyota dostu topikal ajanlar, fotodinamik terapi ve antiseptik banyolar gibi yeni nesil yaklaşımların etkileri ele alınmıştır. Ayak derisi için multidisipliner bakım algoritmalarının geliştirilmesi gerektiği ve deri bariyerinin korunmasının enfeksiyon kontrolü, yara iyileşmesi ve yaşam kalitesi üzerindeki stratejik önemi vurgulanmaktadır. Makale, ayak mikrobiyotasına özel farkındalığın artırılması ve bu alanda moleküler düzeyde araştırmaların teşvik edilmesi gerektiği sonucuna varmaktadır.

Anahtar Kelimeler: Ayak derisi, Dermatolojik Komplikasyonlar, Immünsüpresyon, Kemoterapi, Mikrobiyota.

ABSTRACT

Chemotherapy-induced immunosuppression adversely affects not only systemic defense mechanisms but also disrupts the balance of skin microbiota, thereby facilitating the development of cutaneous complications in oncology patients. This review focuses on the alterations observed in the foot skin microbiota, the associated opportunistic pathogen colonization, and their clinical implications. Conditions such as tinea pedis, onychomycosis, intertrigo, and hand-foot syndrome are highlighted as being closely linked to microbiota imbalances. In addition to conventional antimicrobial therapies, the effectiveness of novel approaches such as microbiota-friendly topical agents, photodynamic therapy, and antiseptic foot baths is discussed. The article underscores the need to develop multidisciplinary foot care algorithms and highlights the strategic importance of maintaining skin barrier integrity for infection control, wound healing, and quality of life. It concludes by emphasizing the necessity to increase awareness and encourage molecular-level research focused specifically on foot microbiota in oncology care.

Keywords: Chemotherapy, Dermatological Complications, Foot Skin, Immunosuppression, Microbiota.

Sorumlu Yazar/Corresponding Author: Ayşegül Sarpkaya, Harran Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Podoloji Programı, Şanlıurfa, Türkiye, 0000-0002-8479-0235

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INRODUCTION

Chemotherapeutic agents, while targeting cancer cells, also affect rapidly proliferating healthy cells, leading to immunosuppression. This suppression, particularly when resulting in neutropenia, renders patients more susceptible to infections. Neutropenia is a commonly encountered condition during chemotherapy and increases the risk of infections across various barrier systems, including the skin (1).

The weakening of the immune system disrupts the balance between the host and its symbiotic microorganisms. When microbial homeostasis (microbiota) is disturbed in barrier organs such as the skin, opportunistic pathogens can overgrow, leading to cutaneous toxicities and infections. A decrease in skin microbiota diversity facilitates the colonization of pathogens, particularly *Staphylococcus aureus*. This alteration has been associated with the development of treatment-related skin complications such as acute radiation dermatitis and hand-foot syndrome (2–4).

The skin of the foot harbors one of the most complex and unique microbial ecosystems of the human body. Moist and enclosed environments make this region a favorable habitat for bacteria, fungi, and viruses. Especially between the toes and on the plantar surface, bacterial densities can reach up to 10^7 CFU/cm² (5–6). This microbiota plays a critical role in maintaining skin health by competing with pathogens, producing antimicrobial substances, and modulating the immune system (7–8).

The surface pH of the foot typically ranges between 4.5 and 5.5. This acidic environment supports the survival of host-specific microorganisms while limiting the growth of potential pathogens. This pH range is also essential for the optimal function of epidermal enzymes (9–10).

Protecting the foot skin microbiota in immunosuppressed individuals not only reduces the risk of local infections but also supports the integrity of the skin barrier, thereby contributing to overall quality of life (11). Despite this, much of the existing literature focuses on the upper extremities such as the hands and face, while the foot microbiota and its clinical implications remain largely neglected. This creates a significant knowledge gap, particularly in understanding foot-related complications in oncology patients.

The Impact of Chemotherapy-Induced Immunosuppression on the Microbiota

Neutropenia and Microbial Dysbiosis

One of the most prominent consequences of chemotherapy-induced immunosuppression is neutropenia, which leads to a significant weakening of systemic immune defenses. This condition not only increases susceptibility to internal infections but also disrupts the balance of symbiotic microorganisms residing on barrier organs such as the skin. Neutrophil deficiency eliminates the competitive advantage that commensal bacteria provide against pathogenic organisms, thereby facilitating the colonization of opportunistic microbes (1). Studies have shown that in immunosuppressed individuals, the diversity of the epidermal microbiota decreases, while the abundance of potential pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* increases (9). This microbial imbalance poses a particularly high risk of infection in warm, moist, and enclosed areas such as the feet. Therefore, in patients with neutropenia, not only systemic infections but also localized microbial dysbiosis should be closely monitored.

Colonization by Opportunistic Microorganisms

Chemotherapy-induced immunosuppression significantly increases the risk of opportunistic pathogen colonization, particularly on cutaneous and mucosal surfaces. This risk is especially pronounced in moist and occluded environments such as the foot. In immunosuppressed individuals, opportunistic microorganisms such as *Candida* spp., *Fusarium* spp., and *Pseudomonas* spp. can readily colonize epidermal surfaces that are normally protected by the microbial barrier (3). These pathogens may lead not only to superficial infections but also to chronic ulcerations, cellulitis, and, in rare cases, systemic invasive infections. *Candida albicans* is well-documented in association with clinical presentations such as onychomycosis and intertrigo. *Fusarium* species have the potential to cause not only nail and skin infections but also disseminated infections in immunocompromised individuals (8). Furthermore, *Pseudomonas aeruginosa* colonization of the foot region can rapidly progress to invasive infection, particularly in the presence of plantar fissures or radiation-induced disruptions in skin integrity. Therefore, the early identification of opportunistic species within the foot microbiota and implementation of localized prophylactic strategies are of critical importance in reducing complication development in cancer patients.

Dermatological Complications Observed in the Foot Skin and Their Relationship With the Microbiota

The foot skin represents a critical area of vulnerability to infections in immunosuppressed individuals. Several dermatological complications commonly observed during oncological treatment are closely associated with alterations in the foot microbiota.

Common Skin Conditions

Tinea Pedis (Athlete's Foot): Tinea pedis is a superficial fungal infection usually caused by dermatophytes such as *Trichophyton rubrum*. It typically affects areas like the interdigital spaces, plantar surface, and lateral edges of the foot. In cancer patients, chemotherapy-induced neutropenia, disruption of the skin barrier, and compromised hygiene increase susceptibility to tinea pedis infections. Clinically, it presents with erythema, pruritus, desquamation, and macular lesions. In immunosuppressed individuals, the infection tends to be more extensive and persistent, predisposing to secondary bacterial superinfections. In a study involving 1,292 cancer patients receiving checkpoint inhibitors, the incidence of dermatologic infections was reported as 17.5%, with 34.5% of these being fungal infections, predominantly classified as tinea pedis and similar dermatophytoses (12).

Onychomycosis (Fungal Nail Infection): Onychomycosis is a fungal infection affecting the nail bed and plate. The most commonly identified pathogens include *Candida* spp., *Trichophyton* spp., and *Fusarium* spp. Immunosuppression due to chemotherapy, peripheral circulatory impairment, and structural weakening of the nails increase vulnerability to onychomycosis in oncology patients. A cross-sectional study conducted in Iran in 2025 reported a 37.6% prevalence of onychomycosis in 165 cancer patients receiving chemotherapy. The most frequently isolated organisms were *Candida albicans* (21%), *Candida glabrata* (11.3%), and *Fusarium solani* (6.4%). Clinical findings commonly include onycholysis, dystrophic changes, and discoloration, leading to both aesthetic and functional impairment, thereby negatively affecting quality of life (13).

Intertrigo: Intertrigo is an inflammatory dermatological condition that develops in skin folds due to friction, moisture, and heat accumulation. In cancer patients, increased perspiration, limited mobility, and immunosuppression facilitate the onset of intertrigo. Disruption of epidermal integrity in these regions allows for colonization by opportunistic microorganisms such as *Candida* spp., *Staphylococcus aureus*, and *Corynebacterium*. In immunocompromised individuals, intertrigo often presents with a more severe course and prolonged response to

antifungal or topical antibacterial treatments. Increased microbial load can aggravate local inflammation and precipitate secondary infections (11).

Hyperkeratosis and Fissures: Hyperkeratosis refers to thickening of the stratum corneum and is commonly observed on the soles of the feet. Certain chemotherapeutic and targeted therapies used in cancer treatment promote epidermal proliferation, leading to thick, hardened, and painful lesions in the plantar area. Fissures developing in these hyperkeratotic zones compromise skin integrity and provide entry points for pathogens, particularly in immunosuppressed individuals. Deep cracks are often painful, impair ambulation, and serve as portals for bacteria such as *Pseudomonas aeruginosa*, which thrive in moist environments. Disruptions in microbiota balance further increase infection rates in these lesions (9). Conditions such as tinea pedis, onychomycosis, intertrigo, hyperkeratosis, and fissures are more frequent and persistent in immunocompromised patients.

Treatment-Related Skin Disorders

Dermatological toxicities resulting from oncological treatments disrupt the integrity of the skin barrier and predispose patients to secondary microbial colonization. These complications not only pose a risk for local infections but also negatively impact patients' quality of life and adherence to treatment. Among these, radiation dermatitis and hand-foot syndrome (palmar-plantar erythrodysesthesia) are particularly noteworthy.

Radiation Dermatitis and Secondary Infections: Radiation dermatitis, observed in patients receiving radiotherapy, manifests as erythema, edema, desquamation, and epithelial loss. Damage to the epidermal barrier facilitates microbial colonization, with opportunistic bacteria such as *Staphylococcus aureus* being frequently implicated. Recent studies have shown that *S. aureus* colonization can exacerbate the severity of radiation dermatitis and prolong the healing process (14). Furthermore, radiotherapy equipment such as thermoplastic masks and storage trays have been reported to be contaminated with pathogenic microorganisms, including *Pseudomonas aeruginosa*, *Enterobacter cloacae*, and *Candida albicans*, increasing the risk of secondary infections in damaged skin areas (15).

Hand-Foot Syndrome and Microbial Complications: Hand-foot syndrome is a common side effect of chemotherapeutic agents such as capecitabine, 5-fluorouracil, and pegylated liposomal doxorubicin. Clinically, it presents with erythema, edema, pain, and desquamation on the palms and soles. Pressure-exposed areas develop microcracks and ulcerations,

compromising the skin barrier and facilitating colonization by opportunistic pathogens like *Staphylococcus aureus* and *Candida* spp. Case reports in the literature have documented that these infections exacerbate symptoms and hinder the continuity of treatment (16–18).

Prevention and Management Strategies: The management of treatment-induced skin disorders focuses on preserving the skin barrier and reducing infection risk. In cases of radiation dermatitis, topical antibacterial and antifungal agents can mitigate infection risks. Regular disinfection of radiotherapy equipment also helps reduce contamination. For managing hand-foot syndrome, adjusting chemotherapy dosage may alleviate symptom severity. Supportive treatments such as moisturizers and cold compresses contribute to skin barrier maintenance (16,19).

In summary, radiation dermatitis and hand-foot syndrome increase the risk of secondary microbial colonization, thereby adversely affecting the patient's quality of life. Therefore, preserving skin integrity, minimizing infection risk, and implementing appropriate management strategies are essential in the care of oncology patients.

Microbiota Disruption and Ulceration: The skin microbiota is a microbial community that supports the physiological integrity of the skin barrier and plays a critical role in host defense. This microbial ecosystem is regulated by factors such as pH level, moisture, lipid composition, immune response, and the structural integrity of the barrier. However, immunosuppressive interventions like chemotherapy and radiotherapy disrupt this balance and promote pathogen colonization (20). Disruption of microbial homeostasis is particularly problematic in regions such as the feet, which are prone to mechanical trauma, perspiration, and remain covered for extended periods. Dominance of pathogens like *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* can lead to chronic inflammation and delayed epithelialization, resulting in non-healing ulcers resembling diabetic foot ulcers (9). Moreover, chronic microbial imbalance facilitates biofilm formation, reducing the efficacy of topical and systemic therapies. A decrease in microbiota diversity and pathogen overgrowth not only impairs wound healing but also increases the risk of secondary bacterial or fungal superinfections (21). Therefore, maintaining the integrity of foot skin microbiota is critical—not only for preventing infections but also for supporting wound healing and preventing ulcer formation. For cancer patients, microbiota-targeted screening, application of microbiota-supportive topical products, and multidisciplinary wound care strategies are strongly recommended.

Such complications are frequently observed in immunosuppressed oncology patients and may become persistent if the microbial balance is not restored. *(Table 1 summarizes the major foot dermatologic complications encountered in oncology patients, along with their microbiota associations, predisposing factors, and clinical features.)*

Table 1. Major Dermatologic Complications of the Foot in Oncology Patients and Their Microbiota Associations

Condition	Common Pathogens	Predisposing Factors	Clinical Manifestations
Tinea pedis	*Trichophyton rubrum*, *Epidermophyton spp.*	Moist environment, neutropenia, skin barrier damage	Erythema, desquamation, itching
Onychomycosis	*Candida spp.*, *Fusarium spp.*, *Trichophyton spp.*	Chemotherapy-induced nail fragility, vascular compromise	Nail discoloration, dystrophy, onycholysis
Intertrigo	*Candida albicans*, *Staphylococcus aureus*	Friction, humidity, immunosuppression	Erythema in skin folds, maceration, burning
Hand-foot syndrome	*Staphylococcus aureus*, *Candida spp.*	Chemotherapeutic agents (e.g., capecitabine, 5-FU)	Erythema, pain, peeling in palms and soles
Radiodermatitis	*Staphylococcus aureus*, *Pseudomonas spp.*	Radiation exposure, barrier breakdown	Dry or moist desquamation, ulceration, infection

Topical Interventions and Next-Generation Approaches

In individuals undergoing cancer treatment, disruption of the skin barrier facilitates pathogen colonization and increases the frequency of dermatological complications. In this context, topical interventions applied to infection-prone areas such as the foot play a critical role in both symptom management and infection prevention. These interventions range from conventional antimicrobial agents to next-generation microbiota-supportive strategies.

Conventional Antifungal and Antibacterial Agents

The first-line approach in topical treatments typically involves conventional antifungal and antibacterial agents. Antifungal medications such as nystatin, terbinafine, and clotrimazole are effective against superficial candidiasis and dermatophyte infections. For bacterial colonization, agents like mupirocin and fusidic acid are commonly used. Additionally, povidone-iodine-based antiseptics possess broad-spectrum antimicrobial activity. However, prolonged or widespread use of these agents may lead to adverse effects such as skin irritation, dryness, and the development of microbial resistance (11). Therefore, while conventional treatments can provide symptomatic relief, they are best employed in conjunction with barrier-supportive and adjunctive approaches to optimize skin integrity.

Emerging Approaches: Microbiota-Friendly Products

With the growing understanding of the role of microbiota in dermatological health, interest in topical agents that support the skin microbiome has increased. Topical probiotics—particularly creams containing *Lactobacillus* species—have been shown to promote the production of antimicrobial peptides on the skin surface, offering protective effects against pathogenic organisms. Moreover, by preserving microbial diversity, these agents help suppress cutaneous inflammation (9). Moisturizers containing ceramides, urea, glycerin, and linoleic acid support the integrity of the stratum corneum's lipid layer and reduce transepidermal water loss. This not only limits microbial entry points but also helps maintain skin pH, fostering colonization by commensal microorganisms (22).

Adjunctive Therapies: Photodynamic Therapy and Antiseptic Baths

Supportive treatments that do not promote microbial resistance and enhance microbial selectivity include photodynamic therapy (PDT) and antiseptic baths. PDT involves the application of a topical photosensitizing agent followed by exposure to low-dose light, inducing targeted damage in microbial cells. This method is considered an effective and safe alternative, particularly in cases where antibiotic resistance is prevalent (23).

Additionally, hypochlorous acid solutions have been reported to exert selective antimicrobial effects by regulating the skin's surface pH while causing minimal disruption to the commensal microbiota. Such antiseptic baths have shown potential in controlling plantar region infections (8).

Topical therapeutic strategies should not only target pathogenic organisms but also aim to preserve the balance of the skin microbiota and support long-term barrier integrity. In oncology patients, especially in vulnerable regions such as the feet, these interventions must be assessed through a multidisciplinary lens.

Preserving the Skin Barrier: An Oncological Support Strategy

The skin is a complex barrier system that serves as the body's first line of defense by providing physical, chemical, and immunological protection. During oncological treatments, the disruption of this barrier increases susceptibility to infections and paves the way for cutaneous toxicities and chronic dermatologic complications. In regions such as the feet—prone to

mechanical trauma and microbial contamination—managing this disruption becomes particularly critical. Therefore, strategies aimed at preserving and supporting the integrity of the skin barrier should be considered a therapeutic priority, especially for immunosuppressed individuals.

The Relationship Between the Stratum Corneum and the Microbiota

The outermost layer of the skin, the stratum corneum, composed of keratinocytes and lipids, serves not only as a physical barrier but also as a vital niche for the skin microbiota. The integrity of the stratum corneum directly influences microbial diversity; when the barrier is compromised, changes in pH, moisture loss, and lipid degradation create favorable conditions for pathogenic colonization (21). In oncology patients, epidermal damage following chemotherapy and radiotherapy disrupts this symbiotic balance and increases susceptibility to opportunistic infections.

Barrier-Supportive Products

One of the most effective ways to support the skin barrier is through the topical application of moisturizers and barrier-repairing agents. Ingredients such as urea, glycerin, ceramides, and linoleic acid help reduce transepidermal water loss, replenish stratum corneum lipids, and maintain the continuity of protective microbial populations. These products are particularly beneficial in preventing dryness, fissures, and desquamation during toxicities such as hand-foot syndrome or radiation dermatitis (22).

The Importance of a Moist Environment

Maintaining skin hydration is critical not only for preserving barrier integrity but also for preventing pathogen colonization. A dry and cracked skin surface provides a favorable environment for opportunistic microorganisms such as *Candida* spp. and *Pseudomonas aeruginosa* to adhere and proliferate. This risk is particularly elevated in areas exposed to high pressure and friction, such as the plantar surface of the foot. In these regions, maintaining a soft and well-hydrated epidermis helps prevent fissure formation and reduces potential microbial entry points (9).

Care Guideline Proposal: A Multidisciplinary Approach to Foot Skin Management

Care algorithms specifically targeting foot skin protection in cancer patients have not yet been systematically integrated into clinical protocols. However, growing evidence indicates that this gap has direct implications for patient comfort, infection control, and treatment adherence. Therefore, it is essential to develop a multidisciplinary guideline dedicated to foot skin care through the collaboration of specialists in dermatology, infectious diseases, oncology, and podology. This guideline should encompass key components such as risk assessment, daily care recommendations, product selection, early identification of infection symptoms, and patient education.

Preserving the integrity of the skin barrier is not only vital for symptom control but also serves as a fundamental component of supportive oncologic care in terms of infection prevention, microbiota balance, and overall quality of life. This approach becomes particularly critical in sensitive areas such as the foot skin. Accordingly, protective interventions aimed at maintaining the skin barrier should be routinely incorporated into standard oncology care protocols.

DISCUSSION

The skin of the foot represents a unique anatomical site in the human body due to its microbial diversity and continuous exposure to environmental factors. Conditions such as perspiration, mechanical friction, and confinement in occlusive footwear make it a favorable niche for microbial colonization. Nevertheless, particularly in cancer patients, dermatological care tailored specifically to this region has not been systematically addressed. While care algorithms have been developed for chemotherapy-associated cutaneous toxicities such as oral mucositis, radiodermatitis, and hand-foot syndrome, the absence of structured clinical guidelines focused on foot skin microbiota highlights a significant gap in the literature (2–3).

Distinct physiological features of the foot skin—such as its moisture level, acidic pH, and direct environmental exposure—have a substantial impact on microbial diversity and can increase the risk of opportunistic pathogen colonization (9). Therefore, dermatological approaches to this area should be revisited within a holistic framework that considers microbiota balance.

To improve the effectiveness of care, it is essential to adopt a multidisciplinary model that integrates dermatology, infectious diseases, and podiatry. Such collaboration not only facilitates early diagnosis and management of dermatological complications but also supports the development of preventive strategies aimed at preserving microbial equilibrium. In

oncology patients, immunosuppression and frequent impairment of the skin barrier suggest that standard foot care practices may be insufficient for this specific patient population (1, 14).

Currently, most of the available data are observational, and molecular-level knowledge about the foot skin microbiota remains limited. Classical culture-based techniques may be inadequate for detecting anaerobic or fastidious species. Therefore, advanced molecular methods such as 16S rRNA gene sequencing, shotgun metagenomics, and metatranscriptomic profiling are necessary to accurately characterize the composition and functional potential of foot microbiota (20, 24). 16S rRNA gene sequencing allows for the taxonomic identification of bacteria based on conserved regions of the ribosomal RNA gene. Shotgun metagenomic sequencing enables a comprehensive analysis of all genetic material in a sample, providing detailed insights into microbial diversity and gene function. Metatranscriptomic profiling further examines actively expressed microbial genes, offering real-time information about metabolic activity and host–microbe interactions. These techniques also enable temporal monitoring of treatment-related microbial shifts, allowing for timely clinical intervention.

In conclusion, preserving and supporting the foot microbiota should be viewed as a strategic priority—not only for the prevention of localized infections but also for reducing systemic complications, promoting wound healing, and enhancing overall quality of life. In this regard, the development of multidisciplinary clinical guidelines and the expansion of molecular-level basic scientific research are of paramount importance.

CONCLUSION

Physiological and microbial alterations in the skin induced by chemotherapy-associated immunosuppression significantly increase the risk of foot-specific dermatological complications in oncology patients, adversely affecting their overall quality of life. Within this context, the microbial health of the foot skin should be considered a critical parameter in terms of treatment adherence, infection control, and patient comfort.

Although the literature provides a wealth of research and clinical guidelines related to the microbiota of the hands, face, and general skin, there remains a notable lack of structured data and clinical protocols specifically addressing the foot microbiota. However, the foot skin possesses unique characteristics—such as distinct humidity levels, pH, pressure exposure, and hygiene challenges—that render it particularly susceptible to infections. Therefore, foot-

specific approaches and evaluations must become an integral component of oncological supportive care.

A preventive triple approach should be implemented, comprising: (1) early identification of microbial shifts, (2) the use of appropriate topical agents aimed at barrier restoration and microbiota balance, and (3) patient education on personal hygiene and skin care. This strategic triad may be highly effective in preventing complications and minimizing the loss in quality of life associated with cancer treatment.

Moreover, follow-up and intervention practices targeting foot skin should be integrated into existing oncological supportive care protocols. This integration must be carried out through a multidisciplinary framework involving collaboration among dermatologists, podiatrists, and infectious disease specialists. Clinically applicable algorithms, patient-centered assessment tools, and recommendation sets for microbiota-friendly products represent essential components of this process.

In conclusion, the foot skin microbiota remains a frequently overlooked yet clinically significant domain in oncological practice. Enhancing awareness, promoting scientific research, and developing practical clinical protocols focused on this area will not only reduce complications but also contribute meaningfully to the quality of life of oncology patients.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Scientific Responsibility Statement

We hereby declare that we (the authors) bear full responsibility for the scientific content of this article, including the study design, data collection, analysis and interpretation, writing of the manuscript, the preparation of some or all of its main framework, the scientific review of its content, and the approval of the final version of the manuscript.

Ethics Approval and Consent

As this study did not involve human participants or experimental procedures, and/or utilized publicly available data, no additional approval by an ethics committee was required.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author Contributions

Ayşegül SARPKAYA: Conceived the idea, conducted the literature review, and prepared the entire draft of the manuscript, including final editing.

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