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A Comprehensive Analysis of Treatment Approaches for Cancerous Lesions or Wounds

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Abstract

Background: The occurrence of malignant wounds is around 5% in late cancer stages, and the predicted life expectancy is no more than 6 to 12 months. Without an interdisciplinary and personalised treatment plan, symptoms worsen and have a negative impact on quality of life.

Methods: Based on radiological data, the authors summarised surgical, oncological, radiation oncological, nursing, and palliative care components of various treatment algorithms for malignant wounds published by a wide range of medical experts.

Results: An interdisciplinary strategy combined with ongoing consultation amongst different professionals can resolve or ameliorate conditions that appear hopeless.

Conclusion: To reduce the severe symptoms of this agonising illness, a complete treatment plan is required. Without appropriate treatment, non-healing fungal wounds place a heavy socioeconomic burden on all parties involved, including patients, carers, and healthcare providers. The authors of this research gathered suggestions for further guidelines that will be crucial in the near future.

Keywords: Malignant; Wounds; Lesions; Cancerous; Fungating; Treatment; Quality of life; Tumours; Hemostasis; Palliative care; Chemotherapy

Introduction

Cancerous wounds are described as complex, chronic, painful wounds that do not heal and produce a significant amount of foul-smelling discharge due to increasing necrosis and infection [1]. Malignant fungating wounds may develop up to 5% in late cancer stages, although this number is likely underestimated because there is no population-based cancer registry that tracks the occurrence of this disorder. About 6 to 12 months are thought to be the average lifespan [2-4]. This illness is difficult and causes a wide range of uncomfortable symptoms. In the majority of cases, discharge from a non-healing wound that is foul-smelling, bleeding, and inflamed around it, together with intense pain and social isolation, creates a scenario where there are few alternatives for therapy and a very bad prognosis.

Usually from breast, lung, head and neck, and genital cancers, cancerous wounds develop from original skin tumours or from metastatic lesions of primary tumours [5]. In order to develop fundamental guidelines for medical practise, the authors of this article gathered recommendations from numerous medical specialties, examined how they overlapped, and came to some key findings.

Methods

The National Centre for Biotechnology Information (NCBI) PubMed database was used by the authors to do a systematic review to find pertinent papers relating to treatment options for malignant fungating wounds up to 2021. Following a title/abstract evaluation of each search, the full text of all relevant articles was identified and obtained. The following essential phrases were used: "malignant", "wounds", "fungating", "cancerous", "palliative care", "radiotherapy", "surgery", and their conceivable reasonable combinations. Original research papers, clinical trials, meta-analyses, randomised controlled trials, reviews, and systematic reviews were listed as the inclusion criteria for the search. All of the peer-reviewed studies were published in an academic medical journal and were in the English language. The gathered information presented the oncological clinical outcome in adult patients (over 18 years). From the perspective of recommendations for clinical practise, paediatric cases and non-human experimental outcomes were omitted.

Results

181 articles met the eligibility requirements, however only 31 of them were released in the previous five years. In order to gain a contemporary, interdisciplinary perspective on the treatment of malignant wounds, we chose to utilise these publications as the foundation of our review and finished it (Figure 1).

We can evaluate and quantify the impact of a particular symptom with the use of measurement or grading methods. The most helpful grading methods for malignant fungating wounds that have been verified and are perfectly repeatable are listed below. The most recent version of the Common terminology criteria for adverse events (CTCAE) grading system from the National Cancer Institute is helpful for comparing various adverse events [6,7]. The following symptoms and their most severe grade are associated with malignant fungating wounds and are included in the chapter on skin and subcutaneous disorders: Body odour, bullous dermatitis, dry skin, eczema, erythroderma, pain, pruritus, skin atrophy, skin induration, skin ulceration, Stevens-Johnson

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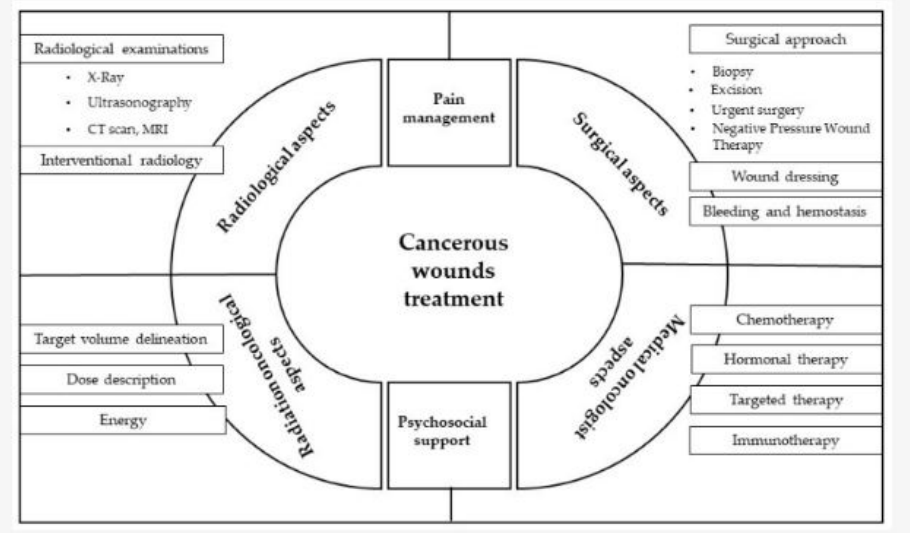

Figure 1: Multidisciplinary view of cancerous wounds treatment.

syndrome, toxic epidermal necrolysis are some of the conditions that are present. A deadly consequence is indicated by a CTCAE grade of 5, therefore malignant wounds may result in death. To accurately assess and manage symptoms, patient reported outcomes (PROs) must be included into doctors' regular practises. PROs and CTCAE have a specific relationship that has been well researched in the literature, and these scoring systems exhibit metric agreement. Prognosis, Advance Care Planning, Living Situation, Comprehensive History, Assessment, Recommendation, and Education are all evaluated using the PALCARE method. A conventional initial state record requires photo evidence taken using the same tool, such a cell phone. It must be repeated in the same condition every two weeks throughout a certain time period. The backdrop colour "medical green" is recommended since it offers the best colour contrast. To determine the wound's maximum perpendicular diameters, always use a millimetre ruler. We suggest that 20% of dimensional change implies advancement or regression based on the RECIST system evaluation. To get the 3D parameter of the wound, it is necessary to determine the depth of the wound in the case of ulcerating wounds or the maximum height in the case of exophytic wounds. It is required to complete a medical written administration, which may be done with extra standardised images. The frequency with which wound dressings are changed each day and the size of the wound dressing are both quantifiable variables that may be compared. The TELER system, which stands for Treatment Evaluation by A Le Roux's Method, can quantify odour numerically. It has a scale of 0 to 5.

Malignant fungating wounds typically develop during end-of-life care, thus the likelihood of developing cancer must also be determined. The modified Glasgow Prognostic Score (mGPS), which considers the C-reactive protein level (less or more than 10 mg/L) and the albumin level (less or over 35 g/L), is highly helpful for this assessment. mGPS 0 denotes a favourable prognosis, while mGPS 2 denotes a less favourable result [3].

Radiological aspects

If a fistula or perforation is suspected in a malignant incision, an X-ray may be instructive. In this situation, free air may be seen on an X-ray. A diagnostic X-ray is also necessary to assess bone involvement and subsequent osteomyelitis. Ultrasonography is effective for finding free fluid and air. It can be used to designate the drainage point. Radically complex techniques include CT and MRI scans. Use them only if the outcome alters the therapeutic choice and lengthens a meaningful life when providing end-of-life care. In the event of severe bleeding, interventional radiology may be beneficial. Endovascular embolisation is an option if the radiologist can see and access the feeding artery.

Surgical considerations

Since surgery has a limited role in managing cancerous wounds, it is not often the first option for treating malignant fungating wounds. Inflammatory cytokines found in tumour microenvironments have a detrimental effect on how quickly wounds heal. Therefore, surgically removing malignant wounds affects the success of wound healing. Unnecessary surgical excision might accelerate tumour growth [8]. Additionally, pruritus and wounds to the skin brought on by wetness impair wound healing. According to Chrisman et al., it's crucial to understand that effective surgical operations are onerous or even unreasonable expectations for the improvement of malignant wounds [9].

A biopsy must be performed if the histology is unclear or if progression occurs while receiving systemic therapy and the new biopsy results potentially alter the therapeutic strategy, i.e., a novel mutation with therapeutical implications. Excision of a malignant wound is uncommon. In addition to requiring systemic therapy when such lesions manifest and penetrate the skin, R0 resection is exceedingly improbable. In exceptional circumstances, a complete excision of the tumour may be possible. In exceptional circumstances, immediate surgery might be required. Bleeding, ileus (requiring palliative deviation), septic state (requiring even amputation) [10], myelon compression, etc. are examples of acute surgical indications. A significant mortality rate exists. Negative pressure wound therapy (pressure between 100 and 125 mmHg continuously for 24 hours) is not often recommended for malignant fungating wounds because it affects lymphatic drainage and might introduce tumour cells into the circulation. On the other hand, it may be a pain-relieving technique that lessens symptoms and enhances quality of life in the latter stages of the disease, making it suitable for use in palliative care in some circumstances [5,11,12].

Dressing the wound

The choice of the proper wound dressing is crucial for malignant

wound care since it may be influenced by a variety of factors. Due to the concomitant infection, the antimicrobial impact of the dressing is beneficial. According to studies [13,14], the antimicrobial characteristics of silver dressings are particularly efficient at reducing malignant fungating wound discharge and odour. However, it should be noted that radiotherapy is incompatible with silver-containing bandages since the latter affects ionising radiation, mostly amplifying undesirable side effects. In randomised tests, several antimicrobial bandages were evaluated to identify the most efficient ones. The effects of a silver-containing bandage and a honey-coated foam treatment are identical [14,15]. However, because honey cannot be a standardised therapy agent, authors do not advise using it. Hydrocolloid foam bandages' moisturising function helps the potential healing process while simultaneously absorbing significant exudate. A compress made of calcium alginate helps reduce bleeding [16].

Time to get dressed

The patient's daily routine should include changing the wound dressing at the appropriate time, along with bathing or other sanitary practises. In the event of a severe ailment, pain management is required. Depending on the condition of the wound, it is advised to reduce how often you change your dressing. Antibiotics and topical hemostasis agents work well to reduce discharge and odour:

- A very effective antibacterial action is provided by topical metronidazole (0.8%) [5,17].
- The effects of metronidazole and polyhexamethylene biguanide (PHMB, 0.2%) are same. By day eight, both drastically lessen wound odour [17].
- Malignant wounds respond less well to 6% miltefostine solution. With the intention of delaying progression, it was used on breast cancer patients [18].
- A simple and affordable substance for topical application is arsenic trioxide with hemostyptic action [19].
- As a crucial component of traditional phytotherapy, green tea extract has antibacterial effects and also reduces odour [19,20].
- Alpha adrenoreceptor agonist oxymetazoline exhibits decongestant and vasoconstrictor sympathomimetic effects [21].
- Etamsylate is a sulfonic acid derivative with hemostatic and vascular protecting effects that may be administered directly to the site.
- Malodor is blocked by charcoal as an absorbent.

Hemostasis

It's crucial to consider all potential causes of bleeding in order to avoid serious problems. Direct vessel invasion, bioburden during dressing removal due to friable tissues, paraneoplastic or chemotherapy-induced thrombocytopenia, aplastic condition caused by bone marrow infiltration or radiation, coagulopathy associated with liver involvement, disseminated intravascular coagulation due to any reason, improper anticoagulation therapy, etc. are the most common causes. Proper hemostasis is difficult to achieve; local approaches include radiation and specific dressings, while systemic therapies include etamsylate, which raises capillary endothelial resistance and encourages platelet adhesion. Nevertheless, it is dangerous to provide tranexamic acid, a synthetic lysine amino acid derivative with antifibrinolytic effects, to cancer patients who have thrombogenic paraneoplastic syndrome. In order to avoid further discomfort, it is also crucial to protect the nearby skin region.

Radiation oncological aspects

The obvious macroscopic tumour mass plus any nearby tissues that appear to be implicated on topometric CT make up the gross tumour volume (GTV). The radiopaque agent (wire, gel) must be used to designate the edematous and hyperemic periwound tissues. Clinical target volume (CTV) refers to the probable microscopically involved region in this case. Depending on the patient's overall health (taking into consideration the possibility of deep vein thrombosis, an extremely big volume proportional to the entire body surface), the CTV does not always cover the locoregional lymph nodes in palliative instances. Due to possible daily setup margin discrepancies as well as inter- and intrafractional variances, planning target volume (PTV) accounts have a comparatively greater safety margin.

The traditional 10 times daily, 3 Gy fractionation plan throughout the workweek is the most suitable dosage in palliative situations. In unique circumstances, a dosage of 5 4 Gy or even 20 2 Gy can be given. It is usually required to factor in prior in-field radiation when calculating the dosage. According to the predicted model of Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) data, the three-dimensional dosage volume limitations for organ at risk (OAR) are acceptable [22]. These constraints were derived using just reasonable short-term Normal Tissue Complication Probability (NTCP). It should be remembered that these restrictions apply to traditionally fractionated metric models. Hypofractionated doses are frequently used in palliative care and are set at larger daily fraction doses to achieve an early radiobiological impact because of the short life expectancy time restriction and the severe suffering patients endure. In order to provide patients with malignant fungating wounds with high-quality care, optimisation system requires the incorporation of cutting-edge methods into palliative radiation oncology. In general, teletherapy combined with a linear accelerator is advised. The appropriate energy is impacted by the height or depth of the wound. While 6-10 MeV electrons can be utilised with boluses for extremely shallow wounds, 6-10 MV photons are needed for deeper penetration. 3D conformal radiation is the recommended method in straightforward conditions. Instances when delicate organs in the affected region are at risk should be treated with intensity-modulated radiation. Dosimetrists and medical physicists must be consulted often.

A medical oncologist's view on systemic therapy

Chemotherapy: The less when there is a metastatic setting and poor physical state, the better. To lessen the possibility of unpleasant and upsetting side effects, select a single medication. Pick a chemotherapy treatment that doesn't affect bone marrow.

Hormonal therapy: Comparatively speaking to other cytostatic drugs, hormone treatment is less burdensome and rather safe. They're simple to serve and perfect for outpatient care. Remember that they raise the possibility of cardiac adverse effects and deep vein thrombosis.

Targeted treatment: In cases of low performance status, targeted therapy should be the best option if it is available. The best targetable medicine may be offered by employing artificial intelligence algorithms and multigene panels, which display the many targets. Avoid using tyrosine kinase inhibitors, particularly epidermal growth factor receptor blockers, in cases of malignant fungal wounds since they increase the risk of skin ulcerations and fistula development with vascular endothelial growth factor inhibitors.

Immunotherapy: Immunotherapies are becoming more and more readily available for clinical use nowadays. As an example, CTLA-4 and PD-1 blockers were employed in the treatment of metastatic melanoma [23]. PDL1 blockers appear to be an effective therapy for squamous cell skin cancer.

Aspects of pain management: Only a small number of controlled research examining the causes and treatment methods of pain have been published, despite the great relevance of pain management in malignant wounds. Between 50 and 75 percent of breast cancer patients who have malignant wounds experience excruciating pain [24,25,26].

Mechanism of pain

Different patho mechanisms are in charge of different pain levels in malignant wounds. The best analgesic strategy must be chosen based on a fuller knowledge of these pathomechanisms. The inflammatory component is evident and frequently linked to tissue hypoxia, particularly in tumours that resemble cauliflowers. These two elements increase the risk of peripheral sensitization. The skin around the wound is frequently affected by inflammation-related discomfort, which is frequently correlated with the presence of polyamines (putrescin, cadaverine), granulation tissue, exudate, and wound edge deterioration. With peripheral nerve damage, neuropathic pain is frequent and typically severe. Large tumour masses, particularly those in the breast, may exert a tensile tension on the nearby soft tissues as a result of their gravitational influence, which may account for traditional nociceptive discomfort. The existence of tension-induced myofascial components may be anticipated in specific muscle groups, most frequently in the neck and shoulder, and is partially connected with this and partially with abnormal posture for other reasons. The so-called breakthrough cancer pain [27] that negatively impacts the patient's quality of life is addressed in clinical settings as a different entity from short-term incidental pain. This unique excruciating accidental discomfort mostly happens when changing clothes.

In order to alleviate the pain of persistent non-malignant wounds, Price and colleagues created a sound proposal in 2007 known as the "Wound Pain Management Model" that is still relevant today [26]. Although local recommendations may exist, as far as we are aware, there is no comparable, generally acknowledged guidance for malignant wounds. It's important and challenging to determine the relative importance of each component in complicated aches. Since there may be additional causes for the patient's pain, a customized pain management plan is also necessary. Preventing and reducing discomfort brought on by wound dressings is crucial. Debridement, mechanical, enzymatic, or osmotic cleansing, removal of necrotic tissue, and, if necessary, local or systemic antibiotic therapy can all assist to lessen pain by reducing peripheral sensitivity. However, cleaning itself can be uncomfortable, so it's important to carefully weigh the predicted advantages and hazards. For pain alleviation, selecting the proper bandage is also crucial [28].

Both local and systemic pharmacological therapy is possible. In order to remove the dressing, it may also be essential to provide local anaesthetics, ideally in the form of a cream, gel, or hydrogel that is administered for about 20 minutes before to dressing. A Cochrane systematic review found sufficient evidence to support the use of a cream containing a combination of lidocaine and prilocaine (Eutectic Mixture of Local Anaesthetics, or EMLA) for treating pain, despite the fact that the polarity of the lidocaine molecule changes in an inflammatory (acidic) environment and cell membrane penetration is more challenging [29]. Ibuprofen foam and diclofenac gel, which are non-steroidal anti-inflammatory medicines used topically, have also been proven to be successful. However, in both cases, the statistical effectiveness was lower than anticipated, with an NNT (number required to treat) of 6. Topical ketamine, amitriptyline, morphine, methadone, buprenorphine, aspirin, capsaicin (0.025 to 0.075%), clonidine 0.1%, and menthol have all been described as effective painkillers, however there is insufficient or insufficient data to support their safety and effectiveness. The use of non-steroidal anti-inflammatory drugs is reasonable in the treatment of systemic pain since there is an inflammatory pathomechanism present, albeit it may slightly increase bleeding. Opioids have a weak effect on the myofascial and inflammatory components of pain. In the latter situation, applying a local anaesthetic to the afflicted muscles and engaging in light massage and gymnastics might be beneficial. Simple drug tests can predict the opiate response in the event of a neuropathic pathomechanism, although adjuvant analgesics are almost certainly necessary. It is preferable to choose the first adjuvant so that it may be paired with other treatments because the statistical efficacy of each drug in neuropathic pain is modest [30]. When choosing these agents, the patient's age, comorbidities, and prescriptions should be taken into consideration. Although it is outside the purview of this research, some particular facets of the problem ought to be discussed. Although several additional medicines have been studied, the evidence for their effectiveness is occasionally in doubt. Strongly serotonergic medications like clomipramine and SNRIs may modestly increase bleeding. It is generally known that gabapentinoids have an edematous side effect based on vasodilation. It is not yet known if this may play a negative function in increasing the quantity of wound exudate. A powerful inductor of the CYP system, tramadol, fentanyl, oxycodone, and methadone are just a few of the medications that interact strongly with carbamazepine. It may also cause more bleeding. Most NSAIDs' metabolism is inhibited by valproate, which may also slightly worsen bleeding. Over the past ten years, systemic lidocaine and ketamine have been used regularly in palliative care to treat neuropathic pain, although the method of administration and quantities utilised have not been agreed upon. Data on effectiveness are also contradictory. Fast-acting opioids (parenteral or transmucosal fentanyl, sublingual methadone), parenteral or nasal ketamine, and nitrous gas may be helpful in preventing dressing discomfort.

Relaxation, aromatherapy, music therapy, meditation, and other complementary practises might assist lessen anticipation of anxiety and pain, which in turn inhibits central pain processes. Interventional therapy: In a limited number of patients who are refractory to conventional therapies, intrathecal medication delivery (opioids, local anaesthetics, ziconotide, baclofen, clonidin) may be required. In circumstances when other treatments have failed, a neuroablative therapy (chemical or thermal) may possibly be an option. The use of a simple intercostal neurolytic blockade should be taken into consideration in cases of thoracic or abdominal wall invasion. Sacral neurolytic inhibition may be quite helpful in cases of perineal tumours if the patient has a catheter, stool deviation, or both. Both experimental and clinical studies on wound pruritus in the context of neurobiological processes have mostly concentrated on non-malignant diseases (such as trauma, burns, leg ulcers, epidermolysis bullosa, atopic dermatitis, etc.). Itching was ranked as the sixth most frequent symptom with a frequency of 6% by Maida, who discovered malignant wounds in 67 of 472 cancer patients receiving palliative treatment.

In terms of how the itching sensation develops and spreads, the prevailing theory over the past ten years is that a small portion of nonmyelinated C fibers roughly 5% are specifically trained to perceive

and transmit pruritogenic stimuli through a variety of peripheral nerve ending mediators, including histamine, B-alanine, somatostatin, IL-31, serotonin, proteases, substance-P, and nerve growth factor. The considerable disparities in the incidence of pruritus associated with malignant and non-malignant wounds may be due in large part to the non-healing characteristics of malignant wounds. It may be helpful to describe the itchy-related sensations (tickling, stinging, stabbing, pinching, burning, etc.) together with the localization, severity, frequency, and duration of the itching during a complete investigation of the condition. Reducing those causes, if they can be recognised (dressing type, quantity and quality of wound exudate, local heat under occlusive dressing, stress), may help lessen the itching.

Overhydration and skin maceration brought on by copious discharge and infections are the main causes of moisture-related skin damage. Additionally, the periwound region is disturbed, and the accompanying lympho-vascular damage may cause edoema and an increased hypoxic layer, exacerbating the effects of irritation. Inflammation, edoema, and pruritus are the outcomes, and these might cause discomfort. Aspirin and other non-steroidal anti-inflammatory medicines can be helpful in cases of pruritus. Although some pruritoceptive components are anticipated to be caused by complicated pathomechanism, wound-associated pruritus is often thought to be histamine insensitive. The best non-oncological systemic therapy should take into account the patient's other symptoms (sleep disturbance, neuropathic pain components, depression, possibly nausea, co-morbidities, and underlying medications) since there is very little evidence that treatments for neuropathic pain have antipruritogenic effects. It is recommended to use some antidepressants, such as doxepin, amitriptyline, mirtazapine, and paroxetine, as well as anticonvulsants, such as gabapentinoids, sodium channel blockers, and valproate. Mu receptor antagonists and kappa agonists have been successfully used to treat chronic itch of unrelated aetiology, but their usage is not yet advised for neuropathic or wound-associated itch. An evidence-based advice to reduce the pruritus of tumour wounds is currently lacking due to a lack of data, and more study is required. Even with aromatherapy, relaxation can be beneficial for symptom relief. Along with moisturisers, mild soaps, and natural chemicals, topical therapies are known to reduce persistent itching. Andrade recently reviewed the formulations (clobetasol, mometasone, menthol, camphor, tacrolimus) that have been examined thus far in clinical trials. For pruritoceptive pruritus, the majority of them have been examined. Most often, periwound application is taken into consideration in tumour wound cases. Palliative practise frequently employs local anaesthetics on the wound site while treating ulcerative tumours.

Psychosocial dimension

A screening by an oncopsychologist is required for all cancer patients and their carers to determine whether adjuvant mental assistance is required. Isolation and sadness are the two primary psychosocial issues affecting individuals with malignant wounds. Increasing quality of sleep is also essential. Due to its potential to boost the activation of descending analgesic pathways, psychological support is also crucial for analgesia. All of the aforementioned pain mechanisms have a psychosocial component that makes them worse. In anticipation of upcoming pain, anxiety can increase pain severity and decrease pain tolerance.

Discussion

Malignant fungating wounds have a devastating effect that cannot be overstated [2,3,9]. For medical practitioners, a detailed overview of the combined symptoms and severity of the suffering is required. Always address the most upsetting symptom first, and then address other issues. Since they have varied origins, comparing various malignant wounds is exceedingly challenging. Systems for scoring and grading help to make each topic similar to itself [2].

To track the trend of wound growth and do temporal follow-up, photo recording with measuring instruments is useful. Artificial intelligence will probably assist photo photographers in making decisions in the near future. Applications for mobile devices are still in the development stage and need academic approval, but they will be used in palliative care. To help doctors, there is a lack of unanimity. Due to poor methodology, incomparable instances, and a lack of multidisciplinary interaction, scientific proof of data published in connection with malignant wound is at a very low level. Therefore, a proper meta-analysis is still lacking, but there is compelling evidence that patients with smaller wounds can achieve longer life times [15]. Hydrocolloid foam dressings containing silver are used in contemporary wound dressings to control moisture. Topical medications may be helpful, but mixing them might result in inefficiency or undesirable side effects owing to the interaction of their components. Treatment with systemic antibiotics is still debatable. Palliative radiation oncology must include cutting-edge radio therapeutic methods as well to offer patients with malignant wounds the best possible therapy. The authors of this publication compiled guidelines and reviews on palliative treatment for malignant wounds and emphasised the key points in an organised manner for medical professionals and carers. This collection could serve as the foundation for a basic methodology and a legally required therapeutic standard for treating malignant wounds. In the future, inter- and interdisciplinary coordination will be required to support personalised medicine, an extremely difficult and complex effort.

Conclusion

Patients with malignant wounds require extensive, holistic treatment plans that include surgeons, radiation oncologists, and medical oncologists in addition to palliative care providers. Complex interdisciplinary collaboration is necessary to address the main problem for the benefit of effective or cost-effective therapy. The advice provided in this article can be a good compass as all medical providers need to be able to relieve this distressing illness.

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Conflict of Interest

Author declares no conflict of interest.

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