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ESOPHAGEAL CANCER: FROM DIAGNOSIS TO TREATMENT, A LITERATURE REVIEW

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ABSTRACT

Esophageal cancer is an aggressive malignant disease, with high incidence and mortality rates, being the eighth most common type in the world and the sixth cause of cancer death globally. The disease has a higher prevalence among men and in developing countries, with a peak incidence after the age of 55, especially in individuals over 65 years of age. Risk factors include smoking, excessive alcohol consumption, and very hot foods. The diagnosis is confirmed by upper GI endoscopy with biopsy, supplemented by imaging tests. Reviewing the literature on esophageal cancer is critical to updating knowledge, identifying advances in diagnosis and treatments, and providing a basis for future research and improvements in clinical management. **OBJECTIVE:** to compile and critically analyze the research already carried out, to offer a comprehensive view of the advances in the diagnosis, clinical and surgical management and prognosis of esophageal cancer. **METHODS:** This is a literature review on esophageal cancer adenoma. The research used the Virtual Health Library (VHL) as a data source and applied specific terms such as "esophageal cancer", "esophageal tumors", "diagnosis" and "treatment", with language filters (Portuguese, English and Spanish) and publication period (2019-2024). A total of 18 studies were selected after applying the inclusion and exclusion criteria. Although it does not require ethical approval, the review follows good scientific practices. **DISCUSSIONS:** Esophageal cancer is an aggressive neoplasm with a high rate of morbidity and mortality, often diagnosed in advanced stages due to the late onset of symptoms, such as progressive dysphagia. Treatment depends on the stage and location of the tumor, and involves surgery, chemotherapy, radiation therapy, and endoscopic therapies. New approaches, such as immunotherapy and targeted therapies, have shown promising results, especially in advanced cases. The combination of traditional and modern treatments has improved survival, but early diagnosis and personalization of therapies

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remain important challenges to optimize long-term outcomes. **CONCLUSION:** Esophageal carcinoma is an aggressive disease, usually diagnosed in advanced stages. Treatment includes surgery, chemotherapy, radiation therapy, and emerging therapies such as immunotherapy and targeted therapies, with a focus on personalization to improve outcomes. Early diagnosis remains a major challenge.

Keywords: Esophageal cancer. Esophageal neoplasm. Diagnosis and treatment.

INTRODUCTION

Esophageal cancer is a malignant disease with gradual development and marked by high aggressiveness, in addition to having high incidence and mortality rates. This neoplasm is the eighth most frequent type in the world. In terms of mortality, it is the sixth leading cause of cancer death globally (FERLAY, J. et al., 2021).

Esophageal neoplasia has a higher incidence among men, with an approximate ratio of 3:1 when compared to women. The prevalence is significantly higher in developing countries, where esophageal cancer is among the ten most common, being the sixth most frequent among men and the fifteenth among women (SHEA, M. et al., 2021).

The age group most affected by this neoplasm is generally over 55 years of age, with a significant predominance in individuals over 65 years of age. The increase in incidence in this age group is a reflection of the aging population and risk factors, such as smoking and excessive alcohol consumption, which contribute to the development of esophageal cancer. The disease tends to be more aggressive in men, with diagnoses usually made in more advanced stages, which negatively impacts treatment outcomes. In addition, it is important to highlight that mortality related to esophageal cancer is also higher in this age group, due to the late detection of the disease, associated with the scarcity of effective screening tests for this type of cancer (AGUIAR, D. L. et al., 2024).

The classification of esophageal neoplasia is according to its histological composition, with squamous cell carcinoma (SCC) being the predominant type, responsible for approximately 96% of the diagnoses. On the other hand, adenocarcinoma (AC), despite being less common, has shown a considerable increase in recent years. This growth has been related to the increase in cases of obesity and the higher prevalence of gastroesophageal reflux disease. Among the main risk factors for esophageal cancer, the use of tobacco and alcohol stand out, especially when consumed in combination, in addition to the intake of very hot foods and drinks (HULL et al., 2020).

The diagnosis of this pathology involves a combination of clinical evaluations, imaging tests, and endoscopic procedures. Initially, medical history and evaluation of symptoms such as dysphagia and weight loss may raise suspicion of the disease. Upper GI endoscopy with biopsy is the gold standard for definitive diagnosis, allowing direct visualization of the lesion and collection of samples for histopathological analysis. In addition, imaging tests such as computed tomography (CT) and magnetic resonance imaging (MRI) are used to assess the extent of the tumor and possible metastases (ALMEIDA et al., 2021). These approaches, combined with immunohistochemistry and

molecular techniques, are essential for an accurate definition of the diagnosis and staging of the disease.

The present study is extremely important, since this disease has high rates of morbidity and mortality worldwide. By addressing this theme, the review allows a critical and comprehensive analysis of existing research, identifying trends, advances in diagnosis, treatments, and epidemiological aspects of the disease. In this way, it not only expands knowledge about esophageal cancer, but also serves as a basis for future research and improvements in clinical management, offering valuable perspectives for health professionals and researchers.

METHODOLOGY

This study is a literature review on esophageal cancer, with the objective of exploring and synthesizing information on the best diagnostic practices, which may include clinical exams, imaging and biopsies, in addition to the most effective therapeutic options, such as clinical treatment, surgical techniques and postoperative management. To achieve this objective, rigorous research procedures and selection of relevant scientific articles were followed, using the Virtual Health Library (VHL) as the main source of data.

The search strategy involved the use of specific terms and appropriate filters to ensure the relevance and quality of the selected studies. The keywords used in the search were "esophageal cancer", "esophageal tumors", "diagnosis" and "treatment" and their equivalents in English. These terms were combined in order to optimize the results and applied with specific filters.

Initially, the "full text available" filter was applied to ensure that all selected articles were accessible in their entirety, enabling a detailed analysis and complete extraction of relevant information. Next, the language filter was used, covering publications in Portuguese, English and Spanish, ensuring a broad review of the available literature. In addition, filters were activated so that the main theme of the articles was "esophageal cancer" and that the selected studies included prognostic, risk factor, diagnostic and systematic review research. Finally, the publication interval was restricted to the years 2014 to 2024, in order to incorporate the most recent and significant findings on the subject.

Inclusion criteria for the selection of studies included those published in English, Portuguese, and Spanish; indexed in the period from 2014 to 2024; with free and complete publication; and that address the aforementioned descriptors in the abstract or title. On the other hand, the exclusion criteria were: articles that were not in English, Portuguese or

Spanish; published before 2014; that did not have free or complete disclosure; and that did not address the descriptors in the title or abstract.

The study selection process resulted in the initial collection of articles. After applying the inclusion and exclusion criteria, 18 articles were selected. These studies were analyzed and their findings were synthesized in order to provide an analysis of esophageal cancer.

As this is a literature review, there is no need for approval by an ethics committee, however, the review respects the principles of good scientific practice, such as the correct citation of sources and non-plagiarism.

In this way, the article allows a comprehensive understanding of esophageal cancer, providing a solid foundation for future research and clinical advances.

DISCUSSION

DIAGNOSIS

Esophageal carcinoma is a malignant neoplasm that affects the esophagus and has a high rate of morbidity and mortality. Symptoms usually appear in advanced stages, which makes early diagnosis difficult. The most characteristic symptom is progressive dysphagia, present in about 90% of cases, starting with difficulty ingesting solid foods and evolving to liquids as the disease progresses (FERREIRA et al., 2021). Weight loss is also frequent, being caused by difficulty in food intake and increased metabolic expenditure associated with cancer (SILVA; OLIVEIRA, 2020).

Other symptoms include chest or retrosternal pain, often described as a burning sensation or pressure, hoarseness, which may indicate recurrent laryngeal nerve involvement in more advanced stages, and regurgitation or vomiting, due to the accumulation of undigested food by esophageal obstruction. In addition, hematemesis and melena can occur in cases of tumor bleeding, while fatigue is associated with weight loss and disease progression. The clinical presentation of esophageal carcinoma can vary according to the location and stage of the tumor, highlighting the importance of an early diagnosis to improve the prognosis (MOREIRA et al., 2019).

The diagnosis of esophageal cancer is a multifactorial process that involves a clinical approach and the performance of complementary tests to confirm the presence of the tumor and assess its extent. Initially, clinical suspicion is raised based on the symptoms presented by the patient, with progressive dysphagia being the most characteristic sign (SILVA et al., 2020).

The main test for diagnosis is upper digestive endoscopy (UDE), which allows direct visualization of the lesion, collection of material for biopsy and histopathological

confirmation. Biopsy is essential because it provides definitive evidence of the presence of malignant cells in the esophageal tissue (MARTINS; OLIVEIRA, 2021). In addition, UGI is efficient in identifying the location of the tumor and its macroscopic characteristics.

According to the World Health Organization, malignant tumors that affect the esophagus are classified into two main types, the first is squamous cell (or epidermoid) carcinoma, which is more prevalent in various regions of the world, especially in developing countries. This type of cancer is often associated with alcohol consumption, smoking, and eating foods that are too hot or high in carcinogens. The second type is adenocarcinoma, which has become more common in developed countries, particularly among people with a history of gastroesophageal reflux disease (GERD). This type of cancer is often related to the process of esophageal metaplasia, known as Barrett's esophagus, which can serve as a precursor to the development of esophageal cancer (WHO, 2019).

Therefore, esophagoscopy, complemented by biopsy and cytology, is considered the most efficient method for diagnosing esophageal cancer. During endoscopic evaluation, the neoplasm may present different morphological patterns, such as vegetative, ulcerated, or infiltrating appearance. Early-stage tumors, known as superficial tumors, often appear as small, flat, erosive, or raised lesions. Any alteration in the esophageal mucosa, whether in relation to coloration, brightness or relief, should be considered suspicious and investigated appropriately. These characteristics make esophagoscopy essential to identify lesions in early stages and guide early diagnosis, improving the chances of treatment and prognosis (FERREIRA et al., 2019).

After histopathological confirmation, other imaging tests are performed to stage the disease. Computed tomography (CT) of the chest and abdomen is used to assess the local extent of the tumor, the invasion of adjacent structures, and the presence of distant metastases. In some cases, endoscopic ultrasound (EUS) can be employed to determine the depth of tumor invasion in the esophageal wall and evaluate regional lymph nodes (FERREIRA et al., 2019). Positron emission tomography (PET-CT) may be recommended in selected cases to identify metastases not detected by other methods.

The spread of esophageal carcinoma can occur through different routes, such as contiguity, lymphatic, hematogenous, and intramural. A clinical sign frequently associated with metastatic dissemination is the appearance of hardened and palpable lymph nodes, such as the Troisier-Virchow nodule, located in the supraclavicular fossa, and the Ireland nodule, identified in the axilla. Lymphatic drainage from the esophagus is related to the location of the tumor: tumors located in the upper or middle third drain into deep cervical, paraesophageal, posterior mediastinal, and tracheobronchial lymph nodes, while those

located in the distal third drain into paraesophageal, celiac, and hilum lymph nodes As for distant metastases, the most frequently affected organs are the liver and lungs, representing the main sites of disease progression (SOUZA et al., 2018).

TREATMENT

The treatment of esophageal cancer depends on the stage of the disease, the location of the tumor, and the overall condition of the patient. The main types of treatment include surgery, radiotherapy, chemotherapy, and endoscopic therapies, which can be combined to optimize outcomes (SOUZA et al., 2022).

Surgery is often indicated for patients with localized esophageal cancer. When the tumor is restricted to one part of the esophagus, esophagectomy (partial or total removal of the esophagus) is the treatment of choice. However, surgery is most effective in the early stages of the disease, and is less applicable when the cancer has spread to other parts of the body (WONG et al., 2016).

Chemotherapy is widely used for both advanced esophageal cancers and localized neoplasms, especially when associated with radiotherapy. Chemotherapy treatment may be given before surgery (neoadjuvant chemotherapy) to shrink the tumor or after surgery (adjuvant chemotherapy) to eliminate remaining tumor cells. Regimens with drugs such as cisplatin, fluorouracil, and docetaxel are often used (SMYTH et al., 2018).

Radiation therapy can be applied as a primary treatment in patients who are not candidates for surgery or as an add-on treatment in cases of advanced cancer. It is also used to relieve symptoms, such as difficulty swallowing. External radiotherapy and brachytherapy, which involves inserting radioactive sources directly into the tumor, are also viable options (SMYTH et al., 2018).

In addition, endoscopic therapies such as radiofrequency ablation and endoscopic dilation have been explored as less invasive alternatives for early cases or patients with comorbidities (WHO, 2020).

Recently, more modern approaches have been evaluated, including immunotherapy and targeted therapy, which aim to block specific proteins involved in the growth of cancer cells. The use of immune checkpoint inhibitors, such as nivolumab and pembrolizumab, in patients with esophageal cancer work by blocking proteins, such as PD-1, that normally inhibit the body's immune response. By blocking these proteins, immunotherapy allows immune cells to recognize and attack cancer cells more effectively (LANGER et al., 2021).

In addition to immunotherapy, targeted therapies are becoming an increasingly relevant option. Drugs that specifically target cancer cells or cell growth mechanisms, such

as trastuzumab, have been used in specific subtypes of esophageal cancer. Trastuzumab is a monoclonal antibody that blocks the HER2 protein, which is often overexpressed in some types of esophageal adenocarcinoma. The use of targeted therapies in combination with chemotherapy has been shown to improve treatment response and increase survival in patients with HER2-positive esophagus (GARRIDO et al., 2020).

Combining traditional chemotherapy with more modern therapies, such as immunotherapy and targeted therapies, has been an effective approach in several clinical trials. The FLOT regimen (fluorouracil, leucovorin, oxaliplatin, and docetaxel) has been shown to be effective in neoadjuvant (before surgery) and adjuvant (after surgery) treatment for patients with resectable esophageal cancer. In addition, new combinations of chemotherapy drugs and PD-1 inhibitors are being evaluated to try to maximize efficacy and reduce side effects (LANGER et al., 2021).

CONCLUSION

In conclusion, the diagnosis and treatment of esophageal cancer have evolved significantly in recent decades, with notable advances in both diagnostic techniques and therapeutic options. Early diagnosis, although challenging, is crucial for the success of treatment, and the combination of methods such as endoscopy, biopsy, and imaging has allowed for more accurate detection and adequate staging of the disease. Therapeutic options have also expanded, with chemotherapy, radiotherapy and surgery still being pillars of treatment, especially in the early stages. However, the emergence of more innovative therapies, such as immunotherapy and targeted therapies, has offered new treatment perspectives, especially for advanced or metastatic cases, providing improvements in survival rates and quality of life for patients.

Although treatment options have diversified, esophageal cancer remains a challenging condition with high mortality rates, especially due to the often late diagnosis. The combination of therapeutic approaches, including conventional and emerging treatments, represents a promising advance, but more clinical studies and improvements in treatment access are still needed to maximize long-term benefits for patients. Multidisciplinary treatment, which involves surgery, chemotherapy, radiotherapy, and advanced therapies, along with a personalized approach based on the molecular and clinical characteristics of the tumor, seems to be the most promising path to effectively cope with this type of cancer.

Thus, advances in molecular understanding and in the development of new therapies reflect a more promising future for patients with esophageal cancer, although the challenge

remains great, requiring continuous efforts in research and improvement of therapeutic strategies.

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