

CURRENT OPTIONS FOR THERAPEUTIC MANAGEMENT OF ESOPHAGEAL
CANCER IN TERTIARY CARE HOSPITALBeulah Mariam Jacob^{1*}, Bobas Jose¹, Axa Mariam Babu¹, Amratha Johnson¹, Rilly Anil Mathew²,
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Article Received on 14/12/2023

Article Revised on 04/01/2024

Article Accepted on 25/01/2024

ABSTRACT

Background and aim: The multistep process of carcinogenesis includes the stages of initiation, promotion, conversion, and progression. Clinical trials are being conducted on combined modality therapies, which include surgery alone, chemotherapy, immunotherapy, and radiation therapy. The aim of the study is to analyze and evaluate the current options for therapeutic management of oesophageal cancer dose, frequency and route of administration using WHO and NIH as reference therapy. **Materials & Methods:** It was a prospective observational study on Oesophageal cancer patients that was carried out in collaboration with the Department of Medical Oncology at KIMS, Hubli, Karnataka. The study was conducted for a period of 6 months from March 2022 to August 2022. A sample size of 100 people was included in the study. The study inclusion criteria selected people with esophageal cancer, people of all age, people of either sex and people with oesophageal cancer with comorbid conditions. **Result:** The study's finding presented that the majority of the treatments given for esophageal patients were chemotherapy. In surgery procedures, feeding jejunostomy was mostly done. Cisplatin is given mostly as monotherapy and carboplatin + paclitaxel was given mostly as combination therapy. **Conclusion:** Chemotherapy emerges as the most effective treatment for esophageal cancer patients in this study. Although treatment outcomes have improved and death rates have decreased in recent years, there is still room for enhancement in the treatment plan. Despite advances in multimodal treatments, the overall prognosis for esophageal cancer remains challenging.

KEYWORDS: Oesophageal cancer, squamous cell carcinoma, adenocarcinoma, cisplatin, carboplatin, oxaliplatin, 5-fluorouracil, paclitaxel.

INTRODUCTION

The development of cancer, including esophageal cancer, is a multistep process involving stages such as initiation, promotion, conversion, and progression. The balance or imbalance of genetic factors, including oncogenes, proto-oncogenes, and tumor suppressor genes, determines the rate of growth for both normal and malignant cells. Carcinogenesis, the process leading to cancer, requires multiple genetic mutations in normal cells. Cancer can manifest as benign or malignant tumors. Malignant tumors have the ability to metastasize, which involves migrating to distant parts of the body and invading neighboring tissues, leading to the formation of new tumors. There are 19 different types of cancer that, in general, can be associated with lifestyle factors. Esophageal cancer ranks as the sixth most frequent cause of cancer-related death globally. Understanding the

genetic and molecular processes underlying cancer development is crucial for developing effective prevention, early detection, and treatment strategies. Lifestyle choices, environmental factors, and genetic predisposition can all contribute to the risk of developing esophageal cancer and other types of malignancies.^[1]

Esophageal cancer is categorized into two main histological subtypes: esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC). EAC originates from the mucus-producing cells in the esophagus. It is often found in the lower part of the esophagus. Adenocarcinomas may also develop in the mid-esophagus. ESCC begins in the flat, slender cells that form the inner lining of the esophagus. This type is associated with the squamous epithelium of the esophagus.^[2] Squamous cell carcinoma and

adenocarcinoma, often associated with Barrett's esophagus, make up over 50% of malignant lesions. The incidence of this histology appears to be on the rise, based on esophageal cancer cellular classification. Barrett's esophagus features glandular epithelium cephalad to the esophagogastric junction. Three distinct forms of glandular epithelium, including metaplastic columnar epithelium, metaplastic parietal cell glandular epithelium in the esophageal wall, and metaplastic intestinal epithelium with goblet cells, can be identified. The intestinal type mucosa is particularly prone to dysplasia.^[3]

The treatment plan will be determined based on the results of blood tests, imaging, and biopsy. Standard treatment options for esophageal cancer include.

- Surgery and endoscopic resection for stage 0.
- For stage I, options include chemo-radiation or surgery.
- Stage II offers varied choices such as chemo-radiation, surgery alone, or preoperative chemotherapy followed by surgery.
- Stage III treatments encompass chemo-radiation, surgery, or definitive chemo-radiation.
- Stage IV A may involve chemo-radiation followed by surgery. Palliative measures for metastatic cases include chemotherapy, endoscopic stents, and radiation.
- Recurrent esophageal cancer may be managed palliatively with standard therapies and supportive care.^[2]

Surgery is employed to remove malignant cells from the body, often through open procedures like thoracotomy and laparotomy. The objective is to achieve a malignancy-free surgical margin with acceptable functional outcomes. Esophagectomy, involving the removal of all or part of the esophagus, is a significant procedure even when performed minimally invasively. The procedure, spanning the abdomen, chest, and neck, typically lasts 4 to 6 hours. Systemic therapies such as chemotherapy, targeted therapy, and immunotherapy act throughout the body. Neo-adjuvant therapy refers to preoperative systemic treatment, while perioperative therapy is administered both before and after surgery. Chemotherapy and radiation may be combined pre- and post-surgery. Chemotherapy drugs, including docetaxel, fluorouracil, irinotecan, and others, are used. Chemo-radiation combines chemotherapy and radiation and serves various purposes in cancer treatment. Targeted therapy focuses on specific cancer cell characteristics, inhibiting the chemicals supporting their growth and survival. Esophageal cancer treatments include preoperative chemotherapy, definitive chemotherapy, adjuvant therapy, immunotherapy, chemo-immunotherapy, postoperative radiation therapy, surgery for Barrett's esophagus, and other modalities. Clinical trials explore combined therapies, including surgery alone, chemotherapy, immunotherapy, and radiation therapy. Palliation options for specific cases include

stents, photodynamic therapy, chemotherapy, and radiation therapy in various combinations.^[2]

MATERIALS AND METHODS

ETHICAL CONSIDERATION / INFORMED CONSENT FORM

The institutional ethics committee gave its clearance before the study could be carried out. After receiving informed consent from the study's participants, data were gathered. The collecting of samples was done in accordance with moral guidelines.

MATERIALS

From March 2022 to August 2022, a six-month descriptive prospective observational study was carried out at the Medical Oncology department of the Karnataka Institute of Medical Sciences, a tertiary care teaching hospital. The study comprised 100 populations in total. Patient case papers and patient interviews were used to gather the data.

METHODS

The oncology department's patient interview and the patient's medical records are used to gather all the information required for the study, including demographic information, social habits, BMI status, diagnosis, co-morbidities, risk factors, cancer stages, tumor size, chemotherapy cycles, route of administration, drug name, dose, indication, frequency, disease information and a detailed history of clinical symptoms and treatment plan. The study included every patient who matched the inclusion and exclusion requirements.

INCLUSION CRITERIA

Patients with esophageal cancer, patients of all ages, patients of either sex and patients with esophageal cancer and concomitant disease were included in the study.

EXCLUSION CRITERIA

Patients with other linked cancers and patients who were unwilling to participate were excluded from the trial.

RESULT

1. Distribution based on age

Figure 1 depicts the age distribution of patients, highlighting a predominant representation in the 40-59 years age group (52%). Following closely, 44% of patients belong to the old adult category (>60 yrs). Notably, the age group of 13-39 years constitutes the smallest proportion, with only 4% of the total patients.

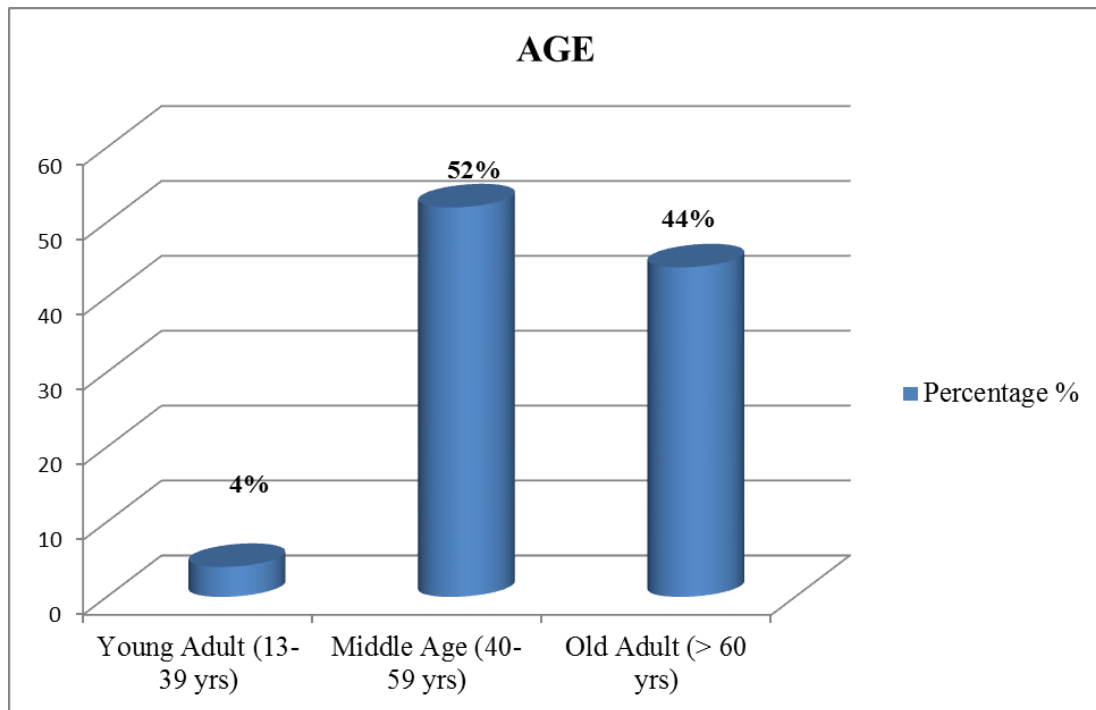


Figure 1: Distribution based on age.

2. Distribution based on gender

In Figure 2, the gender distribution is presented, revealing that 67% of the patients are male, while 33% are female, all diagnosed with esophageal cancer.

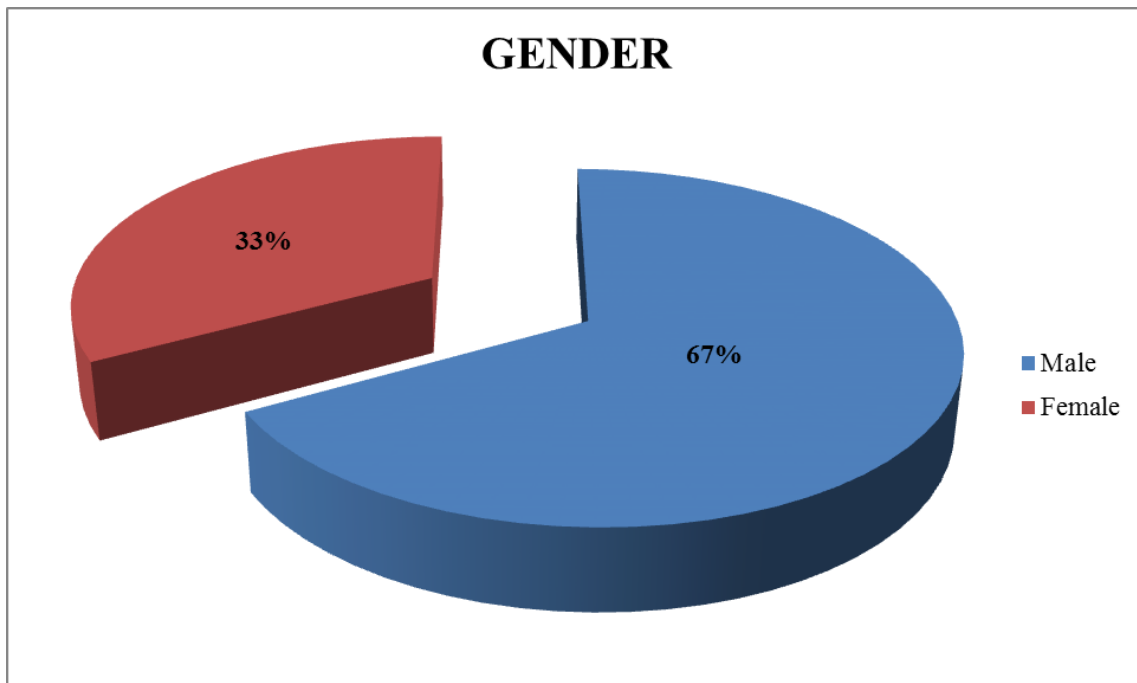


Figure 2: Distribution based on gender.

3. Distribution based on stages of esophageal cancer

Figure 3 illustrates the distribution according to the stages of esophageal cancer. Notably, no patients are categorized under stage 0, 18% are diagnosed with stage 1, 11% with stage 2, 23% with stage 3, and the majority, comprising 48%, are identified with stage 4 cancer.

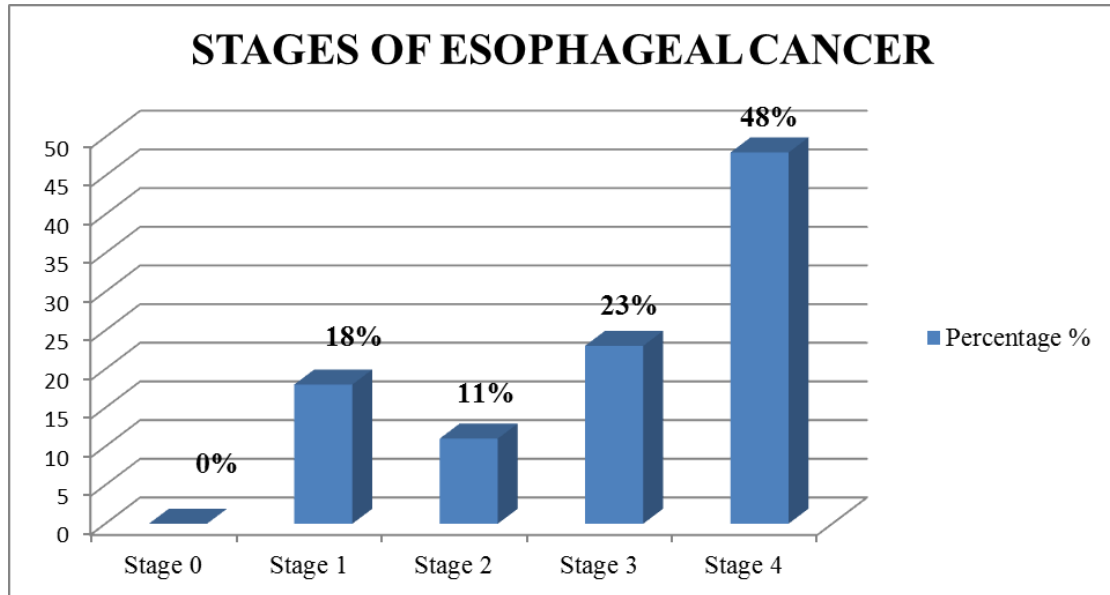


Figure 3: Distribution Based on Stages of Esophageal Cancer.

4. Distribution based on types of esophageal cancer

In Figure 4, the distribution based on types of esophageal cancer is depicted. Among the 100 patients examined,

adenocarcinoma represents the minority at 3%, while the predominant histological type is squamous cell carcinoma, accounting for 97% of cases.

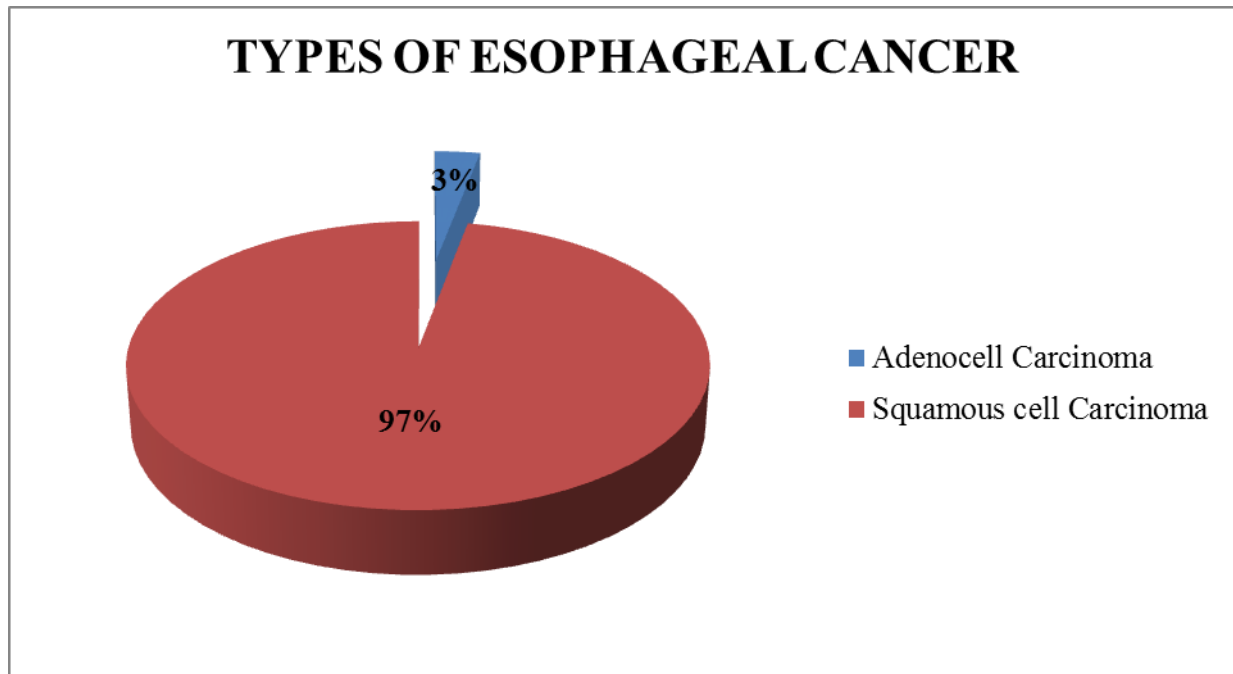


Figure 4: Distribution based on types of esophageal cancer.

5. Distribution based on location of esophageal cancer

In Figure 5, the distribution based on the location of esophageal cancer is presented. Among the 100 patients examined, the upper esophagus is the most commonly affected site, accounting for 38% of cases. This is followed by 35% of patients with middle esophageal cancer and 27% of patients with lower esophageal cancer.

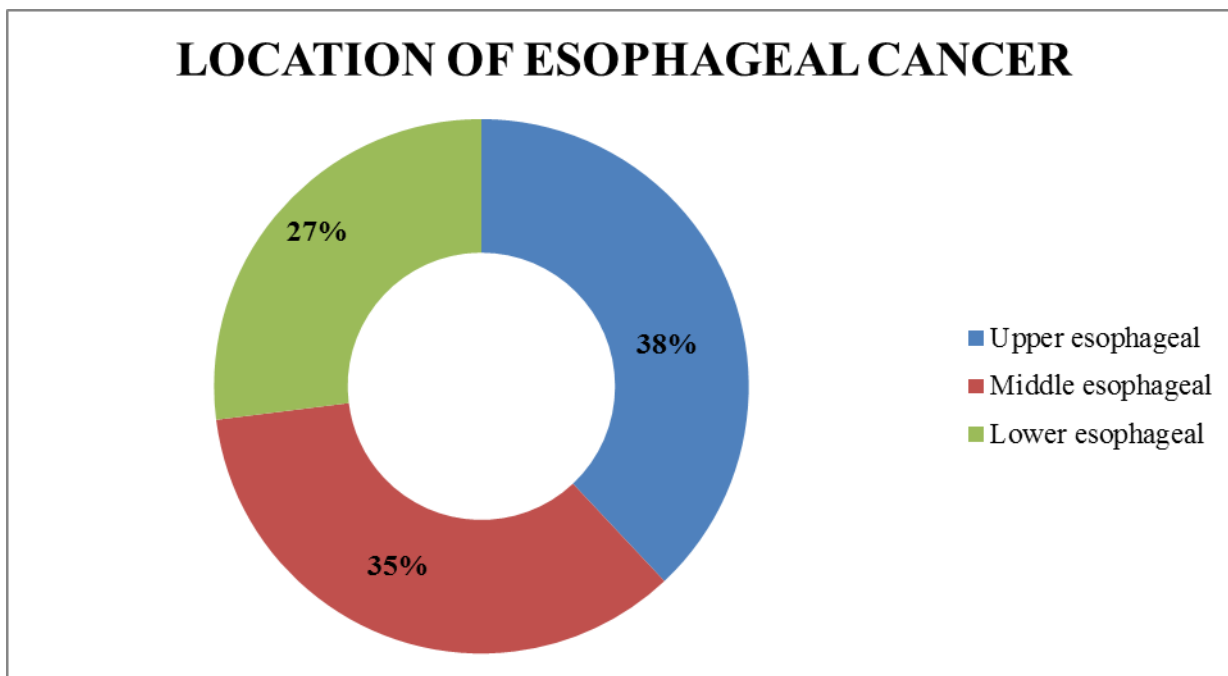


Figure 5: Distribution based on location of esophageal cancer.

6. Distribution based on treatment of esophageal cancer

In Figure 6, the distribution based on the treatment of esophageal cancer is presented. Among a group of 100 patients undergoing treatment, 3% received surgery, chemotherapy, and radiation therapy combined.

Additionally, 8% received radiation therapy, 8% underwent surgery and chemotherapy, 18% received chemotherapy and radiotherapy, 23% underwent surgery alone, and the majority, comprising 40%, received chemotherapy as part of their treatment.

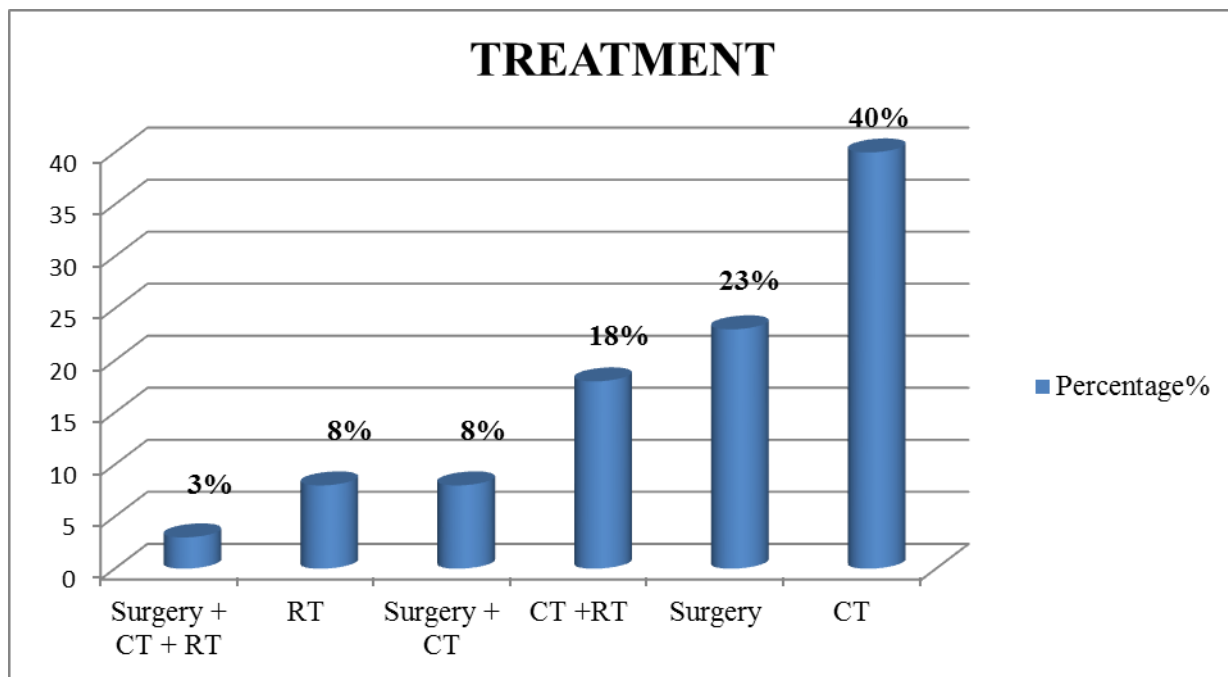


Figure 6: Distribution based on treatment of esophageal cancer.

7. Distribution based on surgery

Figure 7 illustrates the distribution based on surgical procedures among the 100 patients in the study. Out of the total, 34 patients underwent surgical procedures, with 2.94% having gastrostomy, 2.94% undergoing Ryle's

tube insertion, 5.88% having tracheostomy, 11.76% undergoing esophagectomy, and the majority, comprising 76.47%, undergoing feeding jejunostomy.

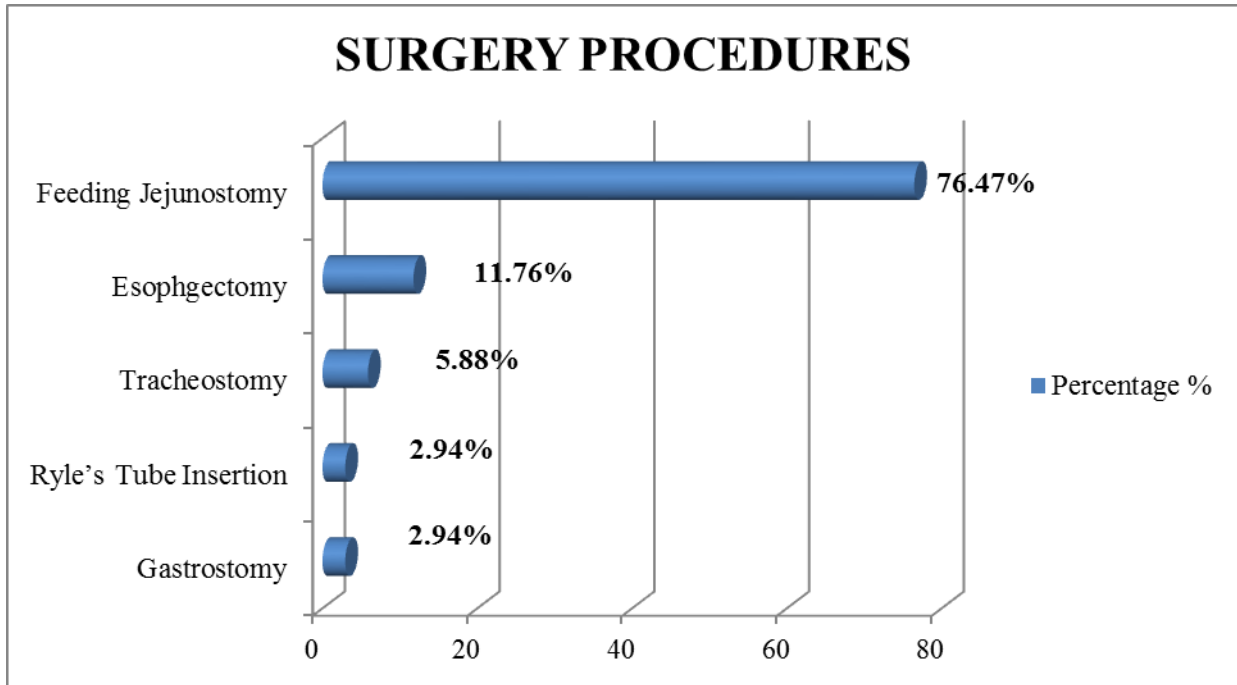


Figure 7: Distribution based on surgery.

8. Distribution based on monotherapy

In Figure 8, the distribution based on monotherapy is presented. Out of the 38 patients who underwent

monotherapy, 7.89% received carboplatin treatment, while the predominant treatment choice for monotherapy was cisplatin, with 92.10%.

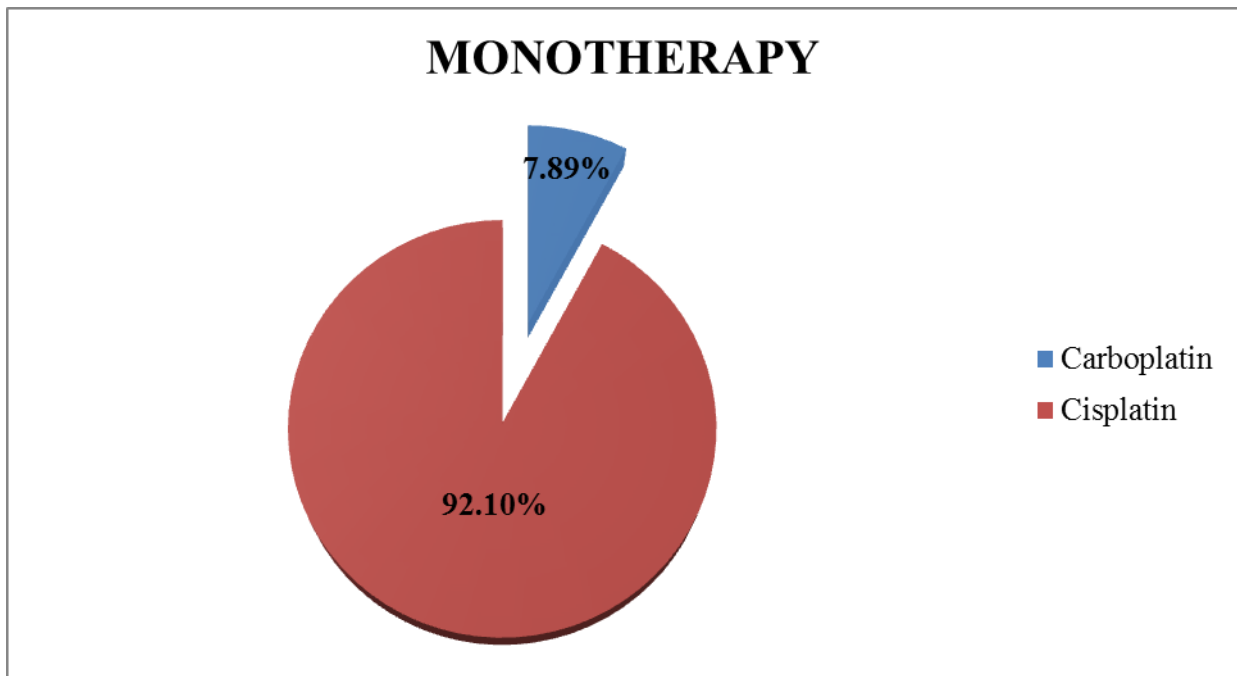


Figure 8: Distribution based on monotherapy.

9. Distribution based on combination therapy

Figure 9 displays the distribution based on combination therapy among the 31 patients. The breakdown includes 3.22% of patients receiving oxaliplatin + 5-fluorouracil, another 3.22% receiving cisplatin + paclitaxel, and an additional 3.22% receiving cisplatin + 5-fluorouracil. Furthermore, 12.90% of patients were treated with cisplatin + carboplatin, 16.12% received oxaliplatin +

capecitabine, and the majority, constituting 61.29%, were given carboplatin + paclitaxel in combination therapy.

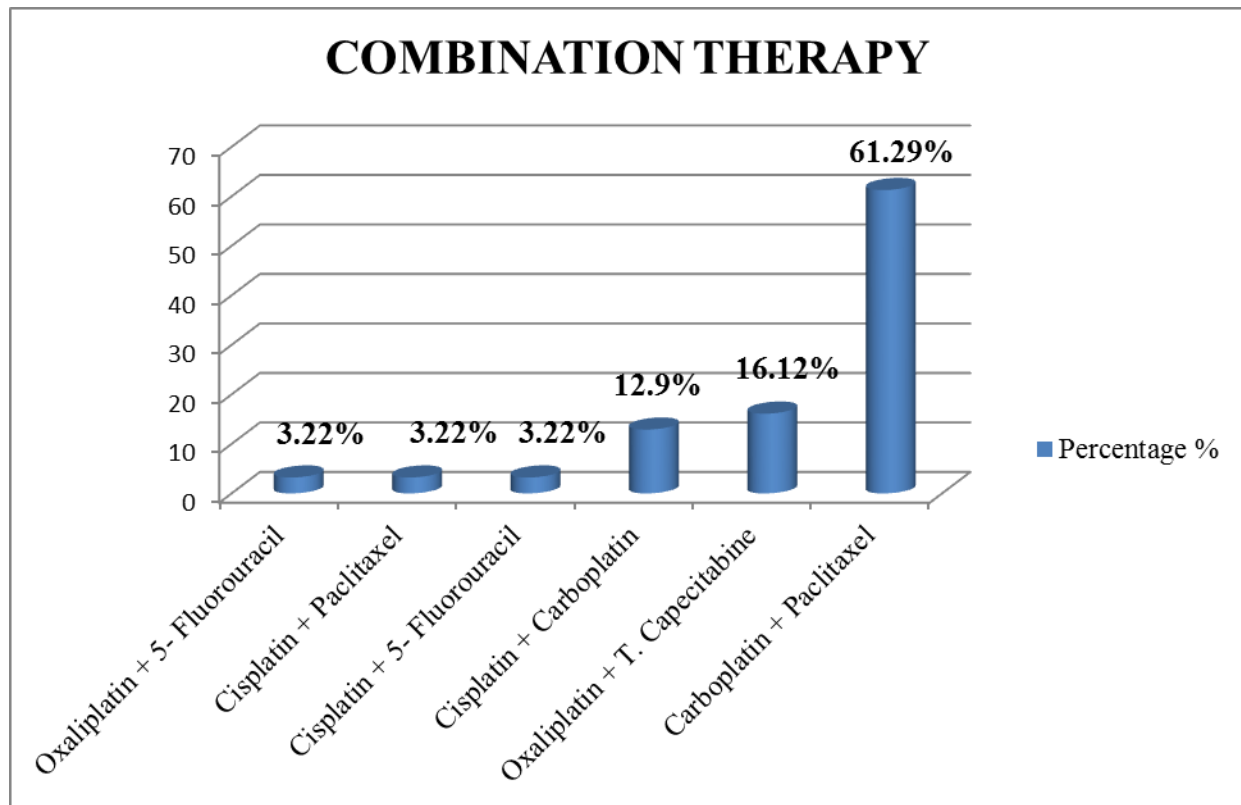


Figure 9: Distribution based on combination therapy.

The findings indicate that chemotherapy was the predominant treatment for esophageal patients. Among surgical procedures, feeding jejunostomy was the most frequently performed. Cisplatin emerged as the primary choice for monotherapy, while the combination therapy of carboplatin + paclitaxel was the most commonly administered.

DISCUSSION

Due to its lower rate of cure, esophageal carcinoma—one of the more frequent malignancies—causes the oncologist great concern. It is the ninth most prevalent disease, accounting for 3.1% of all cancer diagnosis, and the sixth most common cause of death, accounting for 5.5% of all cancer-related deaths globally in 2020.^[4] Most of the 100 patients in our study were between the age of 40 and 59, and the male-to-female ratio was 2.03:1, which is consistent with findings from a study by Ansari F et al. that showed that men were more likely than women to have the condition.^[5] In their study, Yang et al. included 416 esophageal cancer patients, with a median age of 60 and a 4:1 male-to-female ratio.^[6] The study by Swamik Das et al. had a 3:1 male-to-female ratio and a mean age of 50 years.^[7] In a retrospective analysis of 552 patients in a single Indian institute over a 20-year period, Choksi et al. discovered that the average age was 54.78 and that the male-to-female ratio was 1.72.^[8] Most population-based data show that esophageal cancer incidence peaks in the sixth decade worldwide.^[9] In contrast to a study by Ansari F.e. et al., which found a greater incidence in the lower third and GEJ, followed by the mid esophagus, the most common esophageal portion implicated in our study

was the upper esophagus (38%).^[5] Their results were in contrast to the majority of Indian studies, which indicate that the mid-esophagus is the most often affected location.^[10] In our study, squamous cell carcinoma was found in 97% of cases, moderately differentiated in roughly 77.3% of cases, and adenocarcinoma in 3%. This outcome is consistent with prior research from India that demonstrates SCC dominance.^[11-15] With a higher frequency in developing countries, squamous cell carcinoma is the most prevalent histological type of esophageal cancer, whereas in some industrialized countries, such as Australia, Finland, France the United States, and the United Kingdom, adenocarcinoma of the esophagus predominates.^[16] Risk factors, including smoking, using tobacco products, and drinking alcohol, may be the cause of the high prevalence of SCC. Due to its ability to reduce cellular metabolic activity, alcohol can harm cells' DNA, diminish the detoxification process while encouraging oxidation. As a solvent, alcohol specifically of chemicals that are fat-soluble. As a result of dangerous carcinogens the esophageal epithelium is more easily penetrated by substances in smoke. Some of the carcinogens present in tobacco are aromatic amines, nitrosamines, and polycyclic aromatic hydrocarbons, phenols, aldehydes, and hydrocarbons.^[16] Due to the fact that most patients with esophageal cancer present late with an advanced, incurable disease. The disease has a terrible prognosis. This was also observed in our study, where 48% of patients had stage 4 cancer at presentation and 66% had advanced, incurable disease. With the widely used TNM approach created by the American Joint

Committee on Cancer (AJCC), esophageal cancer's clinical stage is evaluated. The role of staging is crucial, directing stage-specific treatment strategies and significantly affects overall survival.^[16] In line with the research done by Ansari F. et al., the majority of the patients in our study had advanced illness (stage 4) and severe dysphagia when they were admitted to the hospital.^[5] Surgery, radiation, and chemotherapy are some of the current multimodality therapy's core treatment choices.^[16] Esophageal cancer is managed using a multidisciplinary approach, and the curative course of treatment is still surgery with or without chemo-radiation therapy. Esophagectomy is the mainstay of treatment for resectable locally advanced lesions; the surgeon will decide whether to perform it transthoracic or transhiatal.^[17] In contrast to Ansari F. et al.'s study, jejunostomy (76.47%) was the most popular surgical technique in our analysis, followed by esophagectomy.^[5] Chemo-radiation is the standard of care for locally advanced cases that are unresectable, and it may be followed by radical surgery if it is feasible, which is consistent with our data.^[18] Different combinations of taxanes (paclitaxel and docetaxel), fluoropyrimidines (fluorouracil), and platinum compounds (cisplatin, carboplatin, and oxaliplatin). The literature has examined the use of irinotecan, capecitabine, methotrexate, ifosfamide (with Mesna coverage), and cyclophosphamide to enhance tumor control and raise survival rates,^[19] except for mesna coverage agents and cyclophosphamide which is consistent with our study. Neoadjuvant chemoradiation (NACR) and platinum-based neoadjuvant chemotherapy (NAC) are the primary treatments for locally advanced and resectable ESCC in the United States and Japan, respectively. Recent clinical trials have found that NAC and NACR have comparable therapeutic effects.^[20-22] The usual recommended protocol for definitive CRT consists of four cycles of capecitabine or cisplatin -5-FU coupled with RT at a dosage of 50.4 Gy over 28 fractions (or 50Gy over 25 fractions).^[23] The BC Cancer Agency's recommendations were followed in our hospital's provision of care. Contrary to recommendations, the majority of patients (92.0%) had six rounds of Cisplatin monotherapy, Carboplatin monotherapy came in second (7.89%), according to the doctor, who noted that it has shown much proven efficacy for esophageal cancer in previous years of treatment. It is known that certain chemotherapy drugs, including paclitaxel, cisplatin, gemcitabine, and carboplatin, regulate and alter anti-tumor immune responses.^[24-27] In our study, 61.29% of patients received carboplatin and paclitaxel combination therapy. The preclinical pharmacological synergy between paclitaxel and platinum compounds serves as the justification for the combination.^[28]

CONCLUSION

On the basis of this study, the management of esophageal cancer should be redefined. Recent developments in multimodal therapy hold promise for raising survival

rates and lowering morbidity. According to certain research, it is preferable to evaluate each patient with localized esophageal cancer and discuss their treatment options in order to achieve a good outcome in terms of both the immediate and long-term outcomes. Two kinds of esophageal cancer may have quite varied treatment modalities and prognoses. Chemotherapy has proven to be the most effective treatment for esophageal cancer patients in this study. For those who have esophageal cancer, early detection and diagnosis are crucial. The treatment plan can yet be improved, despite the fact that treatment outcomes have improved and death rates decreased over the past few years. The prognosis for esophageal cancer is still poor despite all efforts in the field of multimodal treatments.

ACKNOWLEDGEMENT

We extend our sincere appreciation to Dr. H. V. Dambal, President, for generously providing the necessary infrastructure and facilities essential for the successful completion of our work. Our profound gratitude goes to our esteemed principal, Dr. V.H. Kulkarni, for offering unwavering support and providing us with the necessary resources for the successful fulfillment of our tasks. Additionally, we would like to convey our heartfelt thanks to the director of KIMS, Hubballi, as this study would not have been possible without their invaluable assistance.

ABBREVIATIONS

EAC –Esophageal Adenocarcinoma
 ESCC- Esophageal Squamous Cell Carcinoma
 GI -Gastrointestinal
 CT -Computed Tomography
 IV - Intravenous
 FDG-PET – Fluorodeoxyglucose -Position Emission Tomography.
 CBC-Complete Blood Count
 ER -Endoscopic Resection
 TNM- Tumor, Node, Metastasis.
 GEJ – Gastroesophageal Junction
 MSI – Microsatellite Instability
 MMR-Measles, Mumps, rubella
 SCC-Squamous cell carcinoma
 AJCC- American Joint Committee on Cancer.
 NACR –Neoadjuvant Chemoradiation
 NAC –Neoadjuvant Chemotherapy

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