EVALUATION OF RESULTS OF CONFORMAL CONCURRENT CHEMORADIOTHERAPY AT THE DOSE OF 50.5 Gy IN THE TREATMENT OF NON-SURGICAL ESOPHAGEAL CANCER AT 103 MILITARY HOSPITAL

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SUMMARY

Objectives: To evaluate the efficacy and adverse effects of conformal concurrent chemoradiotherapy at the dose of 50.4 Gy in non-surgical esophageal cancer patient at 103 Military Hospital. Subjects and methods: A cross-sectional and prospective study was performed in 66 patients who were diagnosed with non-surgical esophageal cancer at 103 Military Hospital from January 2015 to June 2018. Results: The complete response rate was 34.85%, the partial response rate was 45.45%. The overall survival rate after 18 months was 74.24%, the survival rate after 18 months with stages II, III and IV was 100%, 80.43%, 55.56%, respectively; common adverse effects were eosinophilia I (84.85%), uncommon adverse effects were complications of pneumonia (6.06%), esophageal fistula (4.54%). Conclusion: Conformal concurrent chemoradiotherapy at the dose of 50.4 Gy and PF therapy significantly improves clinical symptoms, prolongs survival time, reduce complications and adverse effects.

** Keywords: Esophageal cancer; Concurrent chemoradiotherapy; 3D conformal radiation therapy.*

INTRODUCTION

According to Globocan 2012, esophageal cancer is the eighth most common cancer in the world and ranks third in gastrointestinal cancers after stomach cancer and colon cancer [3].

For non-surgical esophageal cancer, concurrent chemoradiotherapy is highly effective in significantly improving the clinical symptoms and prolonging the patient's life time. In Vietnam, there are several studies about chemoradiotherapy in the treatment of esophageal cancer, such as the study of Han Thanh Binh in 2004, Nguyen Duc Loi in 2015, but these studies were limited to 2D radiotherapy and 60 Gy high dose radiation therapy [1, 2].

Minsky's RTOG 94-05 in 2002 showed no difference in median survival (median survival 13 months vs. 18 months), overall survival (OS) after 2 years (31% vs. 40%) between the 65 Gy high dose radiotherapy group and the 50.4 Gy radiotherapy group while the adverse effects in the 65 Gy radiation group were significantly higher than the 50.4 Gy group (10% vs. 2%) [4].

Additionally, the introduction of 3D dimensional conformal radiation therapy (3D CRT) with the use of multileaf collimator MLC allows the creation of radiographic fields according to the shape of the tumor;

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this helps to focus high doses at the tumor and minimize the harm to the surrounding health tissues.

This is a modern technique being deployed in some radiotherapy centers in the country. Based on these issues, we propose the implementation of the project with the objects*: Evaluating the efficacy and adverse effects of conformal concurrent chemoradiotherapy at the dose of 50.4 Gy in treatment of non-surgical esophageal cancer.*

SUBJECTS AND METHODS

1. Subjects.

A cross-sectional and prospective study was performed on 66 patients who were diagnosed with non-surgical esophageal cancer at 103 Military Hospital from January 2015 to June 2018.

** Inclusion criteria:*

- Patients diagnosed with stage II, III and IV esophageal cancer, according to AJCC7 classification, have no indication of surgery.
- Patient refused surgery

** Exclusion criteria:*

- Patients with a performance status (PS) > 3.
- Patients with severe combined diseases.
- Patient refused to participate in the study.

2. Methods.

Patients who met the study criteria will receive concurrent chemoradiotherapy. Chemotherapy of PF regimen (cisplatin 75 mg/m^2 body area, intravenous infusion on the first day; 750 mg^5 FU/m^2 body area, intravenous on 1st - 4th day), cycle of 28 days x 04 cycles, of which 2 cycles of concurrent chemoradiotherapy followed by 2 cycles of chemotherapy alone. 3D conformal radiation therapy with a total dose of 50.4 Gy in tumors and lymph nodes, 1.8 Gy/day, 5 days/week. Patients were then evaluated for clinical response, according to RECIST, evaluating the overall survival rate after 6 months, 12 months, and 18 months; stage-dependent survival rate and adverse effects. The data was processed by SPSS software version 20.0

RESULTS AND DISCUSSION

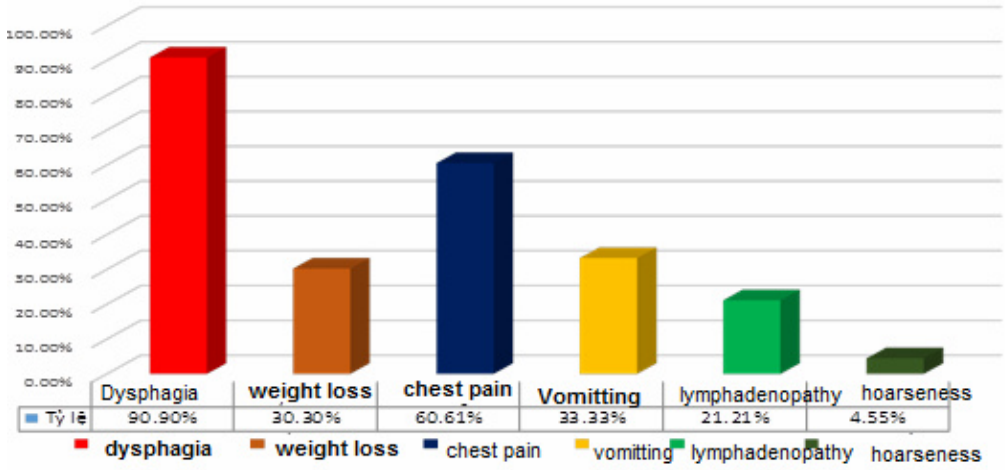

Diagram 1: Clinical symptoms before treatment.

Dysphagia was the most common symptom with a percentage of 90.9%, chest pain 60.61%, weight loss 30.3%, vomiting 33.33%, lymphadenopathy 21.21%, hoarseness 4.55%. The incidence of dysphagia was similar to that in the study of some authors in Vietnam and other countries. According to the study by Han Thanh Binh in 2004, the percentage of dysphagia was 99.2% [1]; in the study by Nguyen Duc Loi in 2015, this figure was 87.9% [2]; and Theodore's in 2000, it was 96% [5].

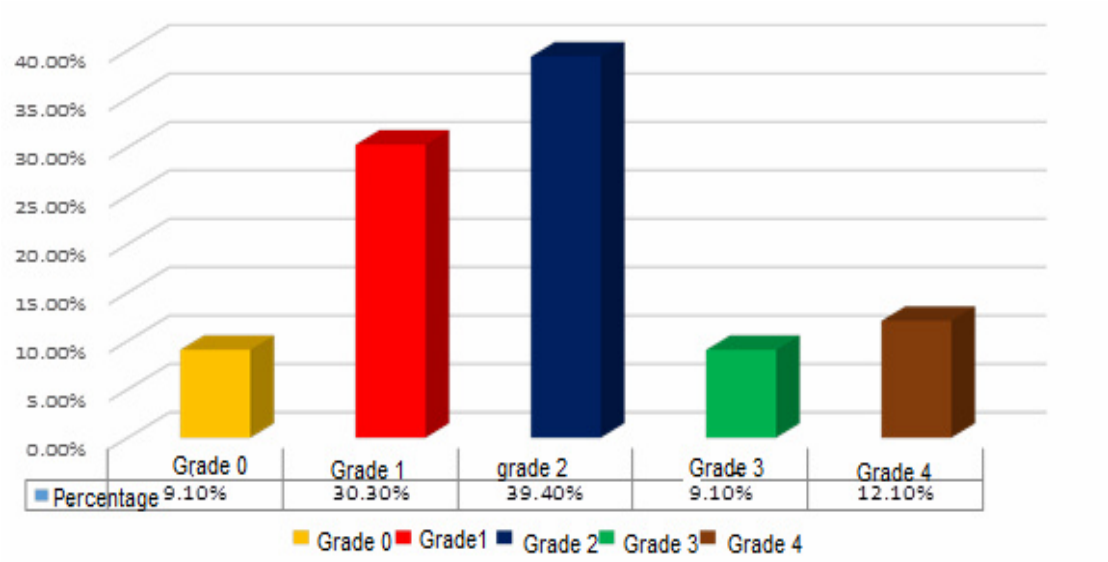

Diagram 2: Classification of dysphagia before treatment.

The classification of dysphagia was mainly grade 2 (39.4%), which means dysphagia to semi-solid food, ability to eat porridge, milk; and grade 1 (dysphagia to solid food) accounted for 30.3%; for grade 3 (dysphagia to liquid food), the rate was 9.1%; as for grade 4 (complete dysphagia), it was 12.1%. Patients in our study mainly came from rural areas with low education and the examination time was not early so the percentage of grade 3 and 4 of dysphagia was higher than that in Nguyen Duc Loi's study (2015) by 8.3% and 0%, respectively [2].

** AJCC 7 classification for the stage of injury:*

Patients in our study were mainly in stages III and IV, which was the period of no longer indicative of surgery; of which, 69.69% of patients were in stage III, mainly in stage IIIC with 48.48% (32 patients); stage IIIA accounts for 21.21% (14 patients); 27.28% of patients (18 patients) were in stage IV. In the study by Deren (1989), the percentage of patients with stage III was 73.9% [6], in the study by Nguyen Duc Loi (2015), it was 86.4% [2]. Particularly in this study, we had 2 patients in stage IIB, accounting for 3.03% who had indication of surgery but they refused and had a desire to undergo chemoradiotherapy.

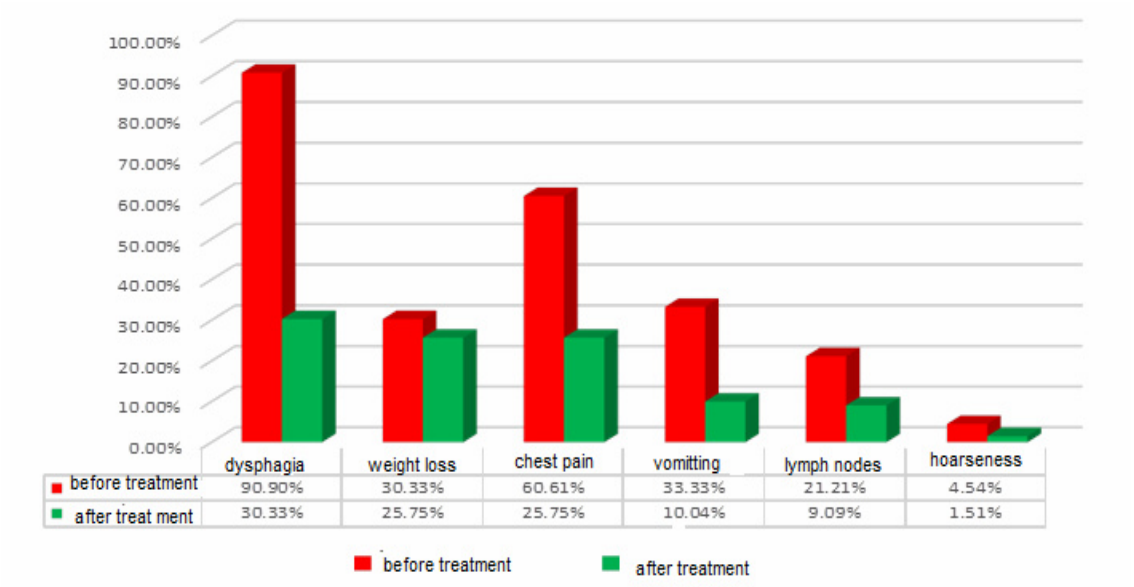

Diagram 3: Changes in clinical symptoms before and after treatment.

The percentage of patients with dysphagia, weight loss, chest pain, nausea, vomiting, lymph nodes, hoarseness before treatment were 90.90%, 30.33%, 60.61%, 33.33%, 21.21%, 4.54% and after treatment were respectively 30.33%, 25.75%, 25.75%, 10.00%, 9.09%, 1.51%. The results showed that concurrent chemoradiotherapy significantly improved clinical symptoms, especially dysphagia (decreased from 90.9% pre-treatment to 30.33%) and chest pain (decreased from 60%, 61% to 25.75%).

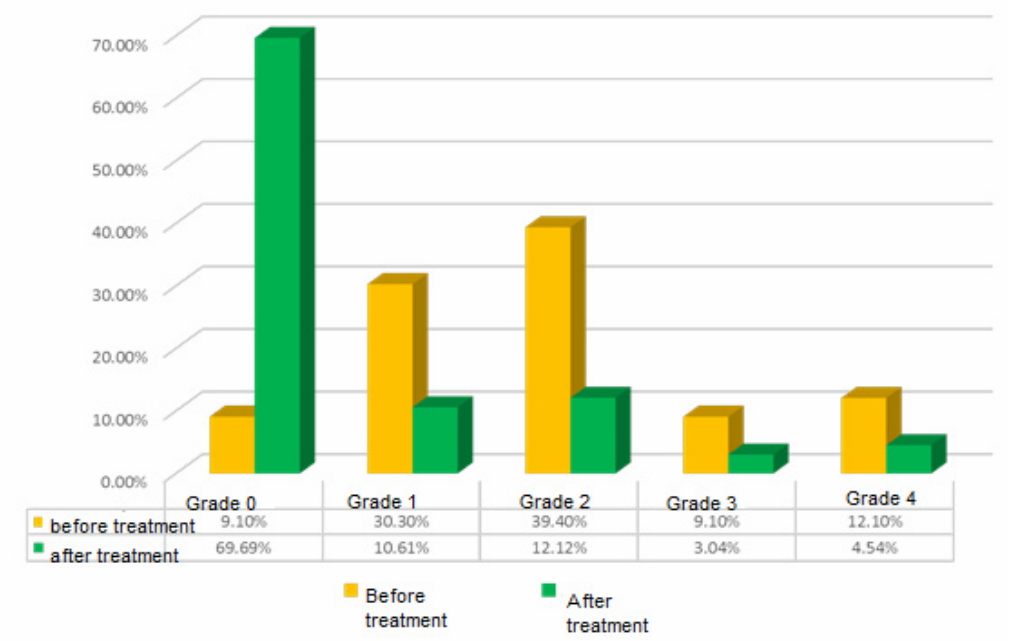

Diagram 4: Changes in pevalence rates of dysphagia before and after treatment.

The most obvious clinical manifestation of the treatment response was a change in dysphagia status, after treatment, the percentage of grade 0 dysphagia increased from 9% to 69.69%, along with that, the percentage of grade 2 and grade 3 dysphagia reduced from 30.3% and 39% before treatment to 10.61% and 12.12% after treatment; grade 3 decreased from 9.10% to 3.04%; grade 4 decreased from 12.10% to 4.54%.

** Treatment response on CT according to RECIST 1.1:*

According to RECIST: The complete response percentage was 34.85% (23 patients), the partial response percentage was 45.45% (30 patients). The percentage of stable and progressive disease was 10.61% (7 patients) and 9.09% (6 patients), respectively. This result was similar to some studies in Vietnam and foreign countries. According to the study by Nguyen Duc Loi (2015), using 60 Gy radiation therapy, the complete response percentage was 31.1%, the partial response percentage was 53.8%, the percentage of disease that was stable was 12.9% and progressive was 2.2% [2]. According to Kaosu Ishida (2004), study on concurrent chemoradiotherapy with the regimen of CF + 60 Gy radiation, results showed that the percentage of complete and partial response was 68.2%, stable and progressive disease was 31.8% [7]. This suggests that treatment response at a dose of 50.4 Gy is equivalent to 60 Gy radiation therapy.

** The overall survival rate:*

The overall survival rate after 6 months, 12 months, 18 months was 95.45% (63 patients), 95.45% (63 patients) and 74.24% (49 patients), respectively. According to Nguyen Duc Loi, concurrent chemoradiotherapy using a dose of 60 Gy, the overall survival rate 12 months, 18 months was 92.7%, 67.6%, respectively [2]. According to Han Thanh Binh (2004), use of radiation alone, the overall survival rate of 12 months, 24 months was 20.9% and 9.3% [1]. This indicated that concurrent chemoradiotherapy had a statistically significant overall survival rate of 12 months compared with radiotherapy alone. The overall survival rate after 12 months and 18 months in our study using 50.4 Gy doses was similar to Nguyen Duc Loi's findings with a dose of 60 Gy.

Table 1: Stage-dependent survival rate.

Stage	**Overall survival time**					
	6 months		12 months		18 months	
	n	%	n	%	n	%
II (2 patients)	2	100	2	100	2	100
III (46 patients)	46	100	46	100	37	80.43
IV (18 patients)	15	83.33	15	83.33	10	55.56

According to Nguyen Duc Loi (2015), concurrent chemoradiotherapy with a dose of 60 Gy, survival rate after 12 months and 18 months of phase III was 93.4% and 70.9%; phase IV was 88.9% and 48.1% [2].

Table 2: Adversed effect on hematology.

Leukopenia classification	Number of patient (n = 66)	Percentage (%)
Grade I	56	84.85
Grade II	6	9.09
Grade III	4	6.06
Grade IV	0	0.00

The most common adverse effects in the hematological system were leukopenia, grade 1, grade 2, grade 3, which was 84.85%, 9.09%, 6.06%, respectively, mainly in grade 1 and 2, without affecting the treatment. There were no patients with grade 4 leukopenia. These were low-grade adverted effects and can be controlled in the course of treatment.

** Complications on other organs:*

Pneumonia occured at 6.06% (4 patients) with interstitial pneumonitis. These cases usually recovered after high doses of topical corticosteroids combined with broad spectrum antibiotics. In this study, 3 cases of esophageal fistula during treatment, accounting for 4.54%. Esophageal fistula occurred at the beginning of radiotherapy and we recorded as complications related to the treatment. Ishikura S (2005) studied concurrent chemoradiotherapy with a dose of 50.4 Gy, this figure was 12% [8].

CONCLUSION

For patients with no-longer-prescribed surgery, concurrent chemoradiotherapy, chemotherapy of PF and 3D conformal radiation therapy at the dose of 50.4 Gy significantly improved both subjective and objective symptoms, enhance the quality of life and extend the life span.

The percentage of dysphagia, chest pain, weight loss before treatment were 90.9%, 60.61% and 30.33%, respectively; after treatment, they were 30.33%, 25.75% and 13.63%, respectively. Partial and complete response rates on CT imaging according to RECIST classification was 45.45% and 34.85%; the percentage of disease stability and progression were 10.61% and 9.09%. The overall survival rate after 6 months, 12 months and 18 months were 95.45%, 95.45% and 74.24%, respectively. Stage-dependent survival rate after 18 months with stages III and IV were 80.43%; 55.56%, respectively. Common complication was leukopenia grade I (84.85%), uncommon complications were pneumonia (6.06%) and esophageal fistula (4.54%).

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