Can accelerated hypofractionated radiotherapy (AHRT) be an acceptable treatment option in inoperable non-small cell lung cancer Myanmar patients?

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BACKGROUND AND OBJECTIVE

The prognosis of lung cancer is poor even if patients can undergo curative treatments such as radical surgery or standard radical radiotherapy treatment (60 Gy in 30 fractions over six weeks with or without concurrent chemotherapy). Most lung cancer patients are diagnosed as advanced inoperable stage and majorities are old age, with comorbid diseases or with poor lung/ cardiac function. Therefore, for those patients, shorter course radiation regime such as accelerated or hypofractionated regime should be considered. This study was conducted to assess the outcomes of accelerated hypofractionated radiotherapy (AHRT) (45 Gy in 15 fractions over three weeks by using 3D conformal planning) in inoperable non-small cell lung cancer (NSCLC) patients who were ineligible for surgery or standard concurrent chemo radiotherapy (CCRT).

METHODS

A hospital based prospective study done in Radiotherapy Department, Yangon General Hospital, Myanmar (2018 January- 2019 June). A total of 65 patients with unresectable or medically inoperable non-small cell lung cancer, who were unfit for chemotherapy due to some comorbidities (E.g., poor cardiac, liver or renal function, etc., or old age) were enrolled. Patients with poor PS (ECOG PS >2), patients with distant metastasis or patients previously treated with thoracic radiotherapy or chemotherapy were excluded. They were treated with the regime of 45 Gy in 15 fractions over 3 weeks by using 3D conformal RT technique. Locoregional response was assessed by chest CT before and six weeks after RT. Revised RECIST (Response Evaluation Criteria in Solid Tumours) guideline version 1.1 was used to detect locoregional response [1]. Relief of symptoms such as cough, dyspnoea and chest pain was evaluated before RT, during RT and six weeks after RT. Treatment related acute toxicities such as dysphagia and radiation dermatitis were observed during and six weeks after RT. Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 was used to study these symptoms and toxicities [2].

RESULTS

Sixty-five patients with inoperable NSCLC (7 patients with stage II and 58 patients with stage III) were participated in this study. The most common age group was 71-80 years (36.92%) and most commonly found cell type was squamous cell carcinoma (73.9 %). The majorities were male (69.2%), smokers (67.7%), with PS1 (44.6%). Among them, two patients were lost to follow-up at 12 weeks after RT due to non cancer related death. Assessment of locoregional response six weeks after RT showed that partial response (PR) was seen in 69.23% of patients and stable disease (SD) was seen in 30.77% while there was neither complete response (CR)

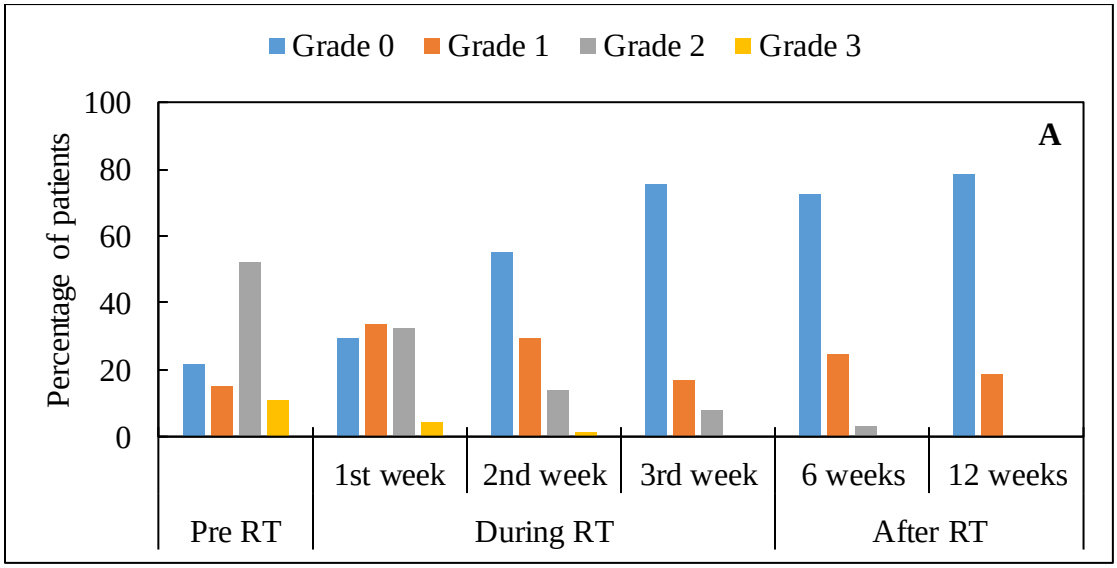
nor progressive disease (PD). Associations between baseline characteristics and tumour response were also observed. Statistically significant associations were only found between pre-treatment tumour size vs tumour response and performance status of the patients vs tumour response (Table 1).

Table 1. Association between tumour response and baseline patients' characteristics

	Partial response **Mean ± SD/ No. (%)** **(n = 46)**	**Stable disease** **Mean ± SD/ No. (%)** **(n = 19)**	***p***
Age (years)	70.46 ± 10.21	68.26 ± 7.60	0.403#
Sex			
Male	31 (67.4)	14 (73.7)	0.617^
Female	15 (32.6)	5 (26.3)	
Stages			
IIB	6 (13)	1 (5.3)	0.329$
IIIA	18 (39.1)	4 (21.1)	
IIIB	17 (37)	11 (57.9)	
IIIC	5 (10.9)	3 (15.8)	
Size of tumour (cm)	5.65 ± 1.62	7.73 ± 1.50	0.00001# ***
Performance status			
0	8 (17.4)	2 (10.5)	0.010^ *
1	25 (54.3)	4 (21.1)	
2	13 (28.3)	13 (68.4)	

* - $p < 0.05$, *** - $p < 0.001$, # - Independent samples t test. ^ - Chi-square test, $ - Fisher's exact test

Good relief of symptoms such as cough, dyspnoea and chest pain was found after RT, but no severe acute toxicities such as dysphagia and radiation dermatitis (more than grade 3) were resulted at the end of the study (Figure 1 and Table 2).



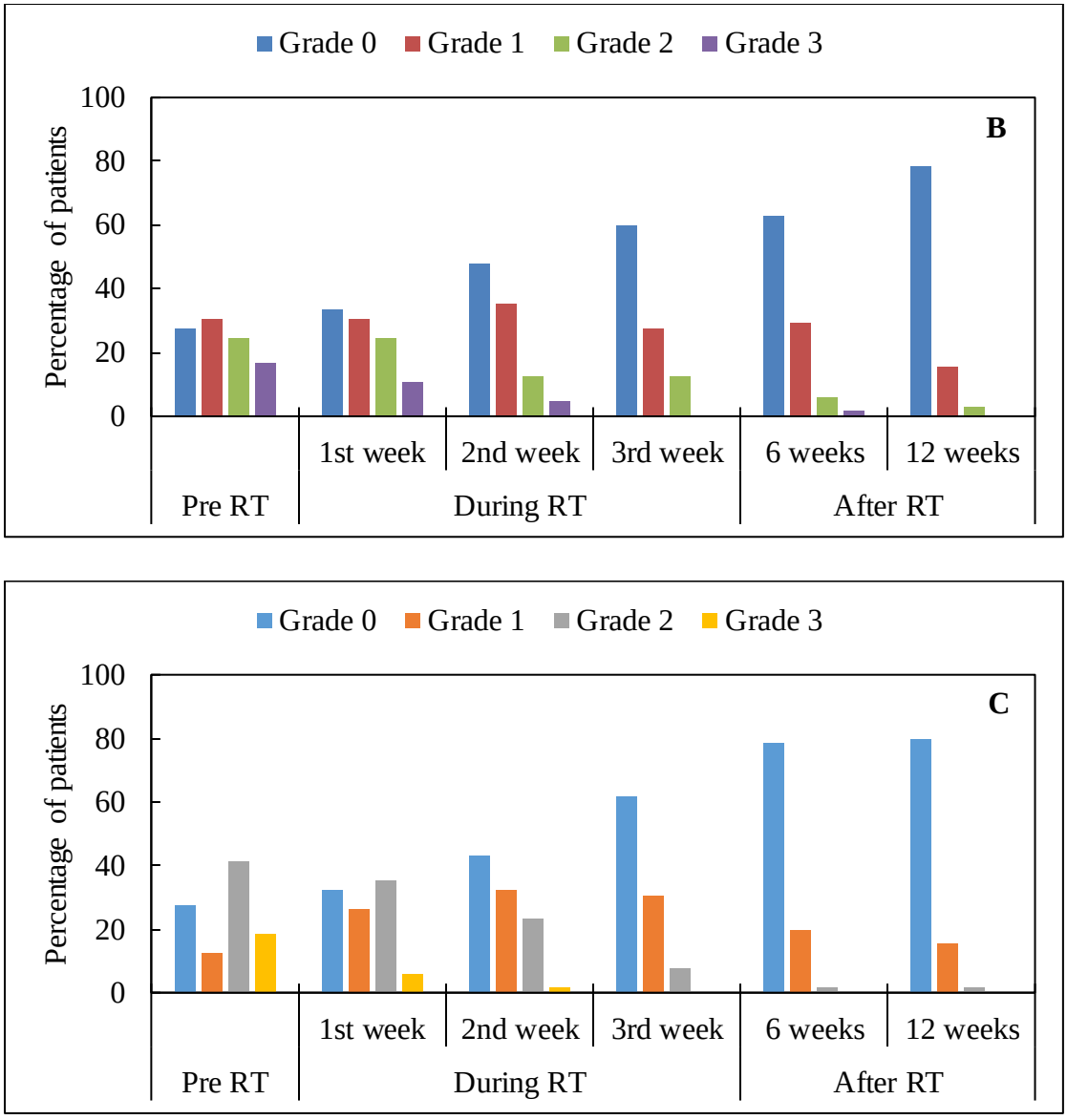


Figure 1. Grading of symptoms at pre-RT, during RT and after RT (n=65). A: cough, B: dyspnea and C: chest pain (2 missing values in 12 weeks after RT)

Table 2. Grading of Acute Toxicities during RT and after RT

Acute toxicities	Grades	During RT No. (%)			6 weeks after RT	12 weeks after RT*
		1st week	2nd week	3rd week	No. (%)	No. (%)
Dysphagia	**Grade 0**	63 (96.92)	60 (92.31)	54 (83.08)	58 (89.23)	60 (92.31)
	Grade 1	2 (3.08)	4 (6.15)	8 (12.30)	5 (7.69)	3 (4.62)

	Grade 2	0 (0.00)	1 (1.54)	3 (4.62)	2 (3.1)	0 (0.00)
Radiation Dermatitis	**Grade 0**	65 (100.00)	65 (100.00)	62 (95.38)	64 (98.46)	63 (96.92)
	Grade 1	0 (0.00)	0 (0.00)	3 (4.62)	1 (1.54)	0 (0.00)

* = 2 missing values in 12 weeks after RT

Due to time limitation and feasibility reason, late toxicities and survival outcome could not be assessed in this study.

CONCLUSIONS

The locoregional and symptomatic response of inoperable non-small cell lung cancer patients to this radiotherapy regime (45 Gy in 15 fractions over three weeks) were good with acceptable acute toxicity results.

As accelerated radiotherapy can decrease treatment time and treatment related costs, this may become an acceptable option for those patients who are unfit for prolonged intensive radical treatment in a resource limiting country like Myanmar.

ACKNOWLEDGMENTS

We wish to thank Prof. Soe Oo Maung, Prof. Win Naing and consultants, seniors, colleagues, physicists and technicians from the Radiotherapy Department, Yangon General Hospital for their kind help and advice.

[1] EISENHAUER, E.A., et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1), European Journal of Cancer **45** (2008) 228-47. https://doi.org/10.1016/j.ejca.2008.10.026

[2] National Cancer Institute (NCI). Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, U.S Department of Health and Human Services, National Institute of health, National Cancer Institute (2009).