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Chemotherapy for Head and Neck Cancer

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Abstract

Head and Neck Cancer (HNC) is the 6th ranked cancer in the World the incidence of HNCs is increasing every 5 years. There are about seven hundred thousand new patients in which four hundred thousand people died. The majority of HNC cancer patients who come to the hospital are at locally advanced stage. Incidence of stage III reaches 24%-25% and stage IV 44%-54%.

Keywords: Head and neck; Cancer; Rhizomucor; Hypothesis; Nasopharynx

Introduction

Progression Free Survival (PFS) is a substitute for Overall Survival (OS) in evaluating the survival of HNC patients. The advantage of PFS over OS is that it can be used to evaluate survival, it can also be used for treatment evaluation. PFS is defined as the time from when a cancer is treated until the patient experiences progression or death from any cause [1].

Several studies have shown that various factors can affect 2-years PFS, however, there is no such study in Indonesia. This study aims to determine the 2-years mortality of HNC patients, to find out the proportion of 2 years PFS, and assess the factors that affect 2-years PFS in HNC patients [2].

Case Presentation

Study with a retrospective cohort design was conducted to examine the factors that affect 2-years PFS including consumption of salted ish, age>60 years, ECOG, smoking with Brinkman index>250, comorbid, LFG ≤ 60 g/min, hemoglobin <12 g/dl, BMI<18.5 kg/m^2, albumin <3.5 g/dl, neutrophil lymphocyte ratio>2, lymphocyte platelet ratio>100, HNC keratinous squamous cell, and therapeutic response [3] .

Sample calculation to ind the relationship between dependent and independent variables using the hypothesis test formula for 2 independent proportions with a minimum sample size of 188. Sampling was done consecutively with inclusion criteria was patients with locally advanced head and neck cancer undergoing chemoradiation at RSUPN. Cipto Mangunkusumo from January 2015 to December 2017 and aged ≥ 18 years. Criteria for exclusion of patients include patients who have chemotherapy or chemoradiation in hospitals other than RSUPN DR. Cipto Mangunkusumo, undergoing full-dose chemotherapy or Neo-Adjuvant Chemotherapy (NAC), the status was not found/burned/retained, and the patient could not be contacted. Locally advanced HNC patients who do not complete chemoradiation are categorized as drop outs. Bivariate analysis uses the *Chi square* test or Fisher's exact test if the *Chi square* test requirements are not met and the multivariate analysis uses logistic regression.

Results

There were 281 HNC patients undergoing chemoradiation at the RSUPN DR. Cipto Mangunkusumo, but there were 30 patients who underwent NAC chemotherapy, 10 patients were not found and 35 patients met the drop out criteria from January 2015 to December 2017. So as to get 216 eligible patients. The majority of HNC patients are 56-65 years old (27.31) with a mean age of 50 years and a standard deviation of 13.06. The youngest age range is 18 years and the oldest age is 77 years. Proportion of male and female patients 3:1. Most of the HNC patients come from the Javanese, Sundanese, Batak and Betawi tribes with the most education graduating from high school. The characteristics of HNC patients can be seen in Table 1 [4].

Characteristic	n=216
Age, year n (%)	
18-25	14 (6.48)
26-35	13 (6.02)
36-45	51 (23.61)
46-55	57 (26.39)

56-65	59 (27.31)
above 65	22 (10.19)
Mean±SD	50 ± 13.06
Gender, n (%)	
Male	165 (76.39)
Female	51 (23.61)
Occupation n (%)	
Enterpreneur	53 (24.54)
Private employee	52 (24.07)
Housewife	35 (16.20)
Goverment employee	23 (10,65)
Other	51 (23.61)
Education level, n (%)	
Senior high school	102 (47.22)
S1	38 (17.59)
Junior high school	35 (16,20)
Elementary school	25 (11.57)
Other	41 (18.98)
Tribes, n (%)	
Javanese	64 (29.63)
Sundanese	39 (18.06)
Batak	27 (12.50)
Betawi	20 (9.26)
Other	66 (30.56)
Cancer location, n (%)	
Larynx	38 (17.59)
Oropharynx	12 (5.56)
Nasopharynx	155 (71.76)
Sinonasal	12 (5.56)
PFS, n (%)	
>2 years	108 (50)
≤ 2 years	108 (50)

2 years mortality, n (%)	
No	113 (52.31)
Yes	103 (47.69)
Age, year, n (%)	
≤ 60	166 (76.85)
>60	50 (23.15)
HN-CCI	
0	156 (72.2)
1	39 (18.06)
2	16 (7.41)
3	4 (1.85)
4	1 (0.46)
Hemoglobin, n (%)	
>12 g/dl	139 (64.35)
≤ 12 g dl	77 (35.65)
Albumin, n (%)	
>3.5 g/dl	92 (81.42)
≤ 3.5 g/dl	21 (18.58)
Albumin, g/dL, Mean SD4.	01 0.51
BMI, n (%)	
>18.5kg/m^2	176 (81.48)
≤ 18.5kg/m^2	40 (18.52)
ECOG	
0	24 (11.11)
1	156 (72.22)
2	36 (16.67)
NLR, n(%)	
≤ 2	43 (19.91)
>2	173 (80.09)
PLR, n(%)	
≤ 100	21 (9,72)
>100	195 (90.28)

eGFR, n(%)	
>60 ml/min/1,73m^2	205 (94,91)
≤ 60 ml/min/1,73m^2	11 (5.09)
Delta Hb	
<10%	80 (37.04)
≥ 10%	136 (62.96)
Delta BMI,	
<10%	72 (33.33)
≥ 10%	144 (66.67)
Smoking, n (%)	
Brinkmann index ≤ 250	100 (46.30)
Brinkmann index>250	116 (53.70)
Comsumption of Salted fish, n (%)	
≤ 5 times during lifetime	62 (28,70)
>5 times during lifetime	154 (71.30)
Duration of salted fish consumption, n(%)	
≤ 10 years	72 (33.33)
>10 years	144 (66.67)
Stadium	
III	47 (21.76)
IVA	142 (65.74)
IVB	27 (12.50)
Keratinized squamous cell	
No	176 (81.48)
Yes	40 (18.52)
Therapeutics response	
Response	195 (90.28)
Unresponse	21 (9.72)
Radiotherapy plane	
IMRT	115 (53.24)
2D/3D	101 (46.76)
Evaluation accuracy, n (%)	
Yes	6 (2.78)
No	210 (97.22)

Table 1: The characteristics of HNC patients.

As many as 47.69% of local HNC patients died within 2 years, while there were around 50% with 2-years PFS. In bivariate analysis, factors that significantly influence hemoglobin level ≤ 12 g/dl (p=0.0157), ECOG 1-2 (p=0.0004), albumin level ≤ 3.5 g/dl (p=0.0023), the Brinkman index>250 (p=0.05), and the[5]. therapeutic response (p=0.0004). Some other variables that are eligible for multivariate with the condition p<0.25 include NLR> 2 (p=0.233), LFG ≤ 60 ml/min 1.73 m^2 (p=0.1072), and the stage of cancer (p=0.1017). The complete bivariate analysis results can be seen in Table 2.

Variable	**PFS**		**p**
	≤ 2 years	**>2 years**	
Age, year n (%)			
≤ 60	85	81	0.519
>60	23	27	
Comorbid			
No commorbidities	79	77	0.761
With commorbidities	29	79	
Hemoglobin			
>12 g/dl	61	78	0.0157
≤ 12 g/dl	47	30	
Albumin			
>3,5 g/dl	41	51	0.0023
≤ 3,5 g/dl	17	4	
BMI			
>18,5 kg/m^2	85	91	0.29
≤ 18,5 kg/m^2	23	17	
ECOG			
0	4	20	0.0004
1-2	104	88	
NLR			

≤ 2	18	25	0.233
>2	90	83	
PLR			
≤ 100	2	13	0.251
>100	100	95	
eGFR			
>60 ml/min/ 1,73 m^2	105	100	0.1072
≤ 60 ml/min/ 1,73 m^2	3	8	
Delta Hb			
<10%	43	37	0.40
≥ 10%	65	71	
Delta IMT			
<10%	34	38	0.564
≥ 10%	74	70	
Brinkmann Index			
≤ 250	43	57	0.05
>250	65	51	
Comsumption of Salted fish, n (%)			
≤ 5 times during lifetime	31	31	1
>5 times during lifetime	77	77	
Duration of salted fish consumption, n (%)			
≤ 10 years	35	37	0.77
>10 years	73	71	
Stadium			
III	19	29	0.1017
IVA-IVB	89	79	
Keratinized squamous cell			
No	88	88	1
Yes	20	20	
Therapeutics response			
Response	90	105	0.0004
unresponse	18	3	

Table 2: The complete bivariate analysis results.

After multivariate analysis, the factors that influence 2-years PFS are smoking with Brinkmann index>250 (p=0.024), hemoglobin level ≤ 12 g/dl (p=0.008), ECOG (p=0.017), and therapeutic response (p=0.006). Complete multivariate analysis can be seen in Table 3 [6].

Factors	p
Brinkmann Index	0.024
Hemoglobin level below 12 g/dl	0.008
ECOG	0.017
Therapeutic response	0.006

Table 3: Complete multivariate analysis.

Discussion

In this study found 50% of patients who experienced 2-years PFS, with 47.69% died within 2 years. Factors that significantly affect 2-years PFS include smoking with a Brinkman index>250, hemoglobin level<12 g/dl, ECOG, and therapeutic response. Individuals who smoke are generally susceptible to cancer. In this study it turns out smoking can affect cancer progression. This is similar to that found. Who found that smoking affects 2-years PFS.8 The role of cigarettes in tumor progression through hypoxic mechanisms at the tissue level. The hypoxia condition triggers the formation of Hypoxia Inducable Factor 1 (HIF-1). Overexpression of HIF-1 can stimulate VEGF for angiogenesis as well as the aggressiveness of the tumor [7,8].

Hemoglobin level below 12 g/dl is one of the factors that affect 2-years PFS. This is similar to research conducted. Anemia has a role in decreasing intra-tissue oxygenation, reducing levels of free radicals and reducing radiosensitivity. The condition of tissue hypoxia also causes mutations in p53 tumor suppressor genes that trigger the progression and metastasis of a cancer.

Performance status represented by ECOG in this study showed a significant effect on 2-years PFS. This is in line with the results obtained ECOG is a general picture of the patient's overall status. Poor ECOG can affect the progression of cancer. Cancer progression will occur more quickly in patients with poor ECOG, besides ECOG can also describe the readiness of the patient's physical status in receiving chemoradiation.

Therapeutic response affects 2-year PFS in locally advanced HNC patients undergoing chemoradiation. Research on the effect of therapeutic response to 2-year PFS in HNC patients is very rare, but he found that the therapeutic response affected 5-year PFS in non-small cell lung cancer [9].

Strengths and Limitations of Research

This study is the first study to look at 2-year PFS in HNC patients and influencing factors. This research is expected to be the beginning of the next research related to HNCs. This study uses a consecutive sampling technique with a retrospective cohort study design. The limitations of this study are still related to the limitations of data that can be taken as weaknesses of retrospective cohorts in general, but we try to fulfiiled these data by making telephone contact with patients and their families [10,11].

Conclusion

The proportion of deaths within 2 years in RSCM is still quite high (47.69%), with a 2-year PFS reaching 50%. Smoking habits, hemoglobin levels, ECOG and therapeutic response affect 2-years PFS in HNC patients. In this study using [9]. RECIST criteria to evaluate therapeutic responses, by dividing response categories namely complete response and partialresponse and stable disease and progressive disease categories into the non-response criteria.

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