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### THE RELATIONSHIP OF RISK FACTORS ON QUALITY OF LIFE OF LARYNGEAL CARCINOMA PATIENTS AFTER CHEMORADIATION AT KARIADI GENERAL HOSPITAL

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### ABSTRACT

**Background:** Laryngeal carcinoma is a carcinoma that forms in the tissue of the larynx. The cause of laryngeal carcinoma is unknown, but many risk factors can cause laryngeal carcinomas, such as a history of smoking, alcohol consumption, gender, age, and exposure environment. The quality of life of patients with laryngeal carcinoma after chemoradiation can be influenced by several things, including several risk factors for laryngeal carcinoma. **Objective:** The purpose of this study was to assess the association of risk factors with the quality of life of laryngeal carcinoma patients after chemoradiation at Kariadi General Hospital. **Methods:** This study is a cross-sectional study with samples of laryngeal carcinoma patients who have received chemoradiation therapy at Kariadi General Hospital. Sampling was carried out using a consecutive sampling technique using a Univesity of Washington Quality of Life (UW-QoL) questionnaire which was translated into Bahasa. The data from the sampling was then processed using the IBM SPSS Statistics 25.0 application. **Results:** Overall, the quality of life of laryngeal carcinoma patients after chemoradiation was categorized as "good" quality of life with a mean score of 62. There was no significant relationship (p<0.05) between the quality of life scores and each risk factor for laryngeal carcinoma. **Conclusion:** There is no significant relationship between risk factors on the quality of life of laryngeal carcinoma at Kariadi General Hospital.

Keywords: chemoradiation, laryngeal carcinoma, quality of life, risk factors

### **INTRODUCTION**

Laryngeal carcinoma is the third most common malignancy of the head and neck in the United States.<sup>1</sup> While in Indonesia, laryngeal carcinoma holds the 14<sup>th</sup> position as the most common cancer in 2018.<sup>2</sup> A study conducted at Kariadi General Hospital in Semarang from 2001 to 2005 identified 19 cases of laryngeal carcinoma out of 448 cases of head and neck carcinoma (4%).<sup>3</sup>

The exact cause of laryngeal carcinoma is not known, but several risk factors can contribute to its development, including a history of smoking, excessive alcohol consumption, gender, age, and occupational environmental exposure. Smoking and excessive alcohol consumption are the primary risk factors for laryngeal carcinoma as they can adversely affect the cells in the larynx.<sup>4</sup>

Laryngeal carcinoma patients commonly present with complaints of persistent and worsening hoarseness, painful swallowing, shortness of breath, and cough.<sup>5</sup> On physical examination, laryngoscopy is performed to determine the location and size of the tumor.<sup>6</sup> The diagnosis is confirmed through radiological and anatomical pathology examinations.<sup>5</sup> Treatment for laryngeal carcinoma may involve laryngectomy and chemoradiation.

The quality of life of patients with laryngeal carcinoma after chemoradiation can be influenced by various factors, including smoking, alcohol consumption, gender, age, and exposure to the work environment. Additionally, the classification of TNM stage, comorbidities, and socioeconomic conditions has shown an association with the quality of life of laryngeal carcinoma patients after chemoradiation.<sup>7</sup> This study was conducted to assess the association of risk factors with the quality of life of laryngeal carcinoma patients after chemoradiation at Kariadi General Hospital.

### **METHODS**

The research is a cross-sectional study conducted in Semarang from October to November 2021. The sample in this study was laryngeal carcinoma patients at Kariadi General Hospital who met the inclusion criteria and did not have exclusion criteria. The inclusion criteria for this study are laryngeal carcinoma patients who have undergone chemoradiation therapy. Meanwhile, the exclusion



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criteria for this study are laryngeal carcinoma patients who are unwilling to fill out the questionnaire, cannot be further contacted for questionnaire completion, or provide incomplete questionnaires. Patients with reading or writing limitations will be assisted by the researcher in filling out the questionnaire.

Sampling was carried out using a consecutive sampling technique with the University of Washington Quality of Life (UW-QOL) questionnaire, translated from English to Bahasa and modified.

The smoking history is divided into 4 categories based on the Brinkman index score: nonsmoker (0), light smoker (<200), moderate smoker (200-599), and heavy smoker ( $\geq$ 600). The Brinkman index score is obtained by multiplying the average number of cigarettes smoked per day by the years of smoking.

The alcohol consumption history is divided into 4 groups: non-alcohol consumer, light (drinking less than once a week), moderate (drinking one to three times a week), and heavy (drinking more than three times a week). One instance of drinking is defined as the patient consuming 1200 ml of beer (alcohol content 4-6%), 800 ml of wine (alcohol content 9-16%), or 150 ml of a beverage with alcohol content exceeding 20%.

Descriptive analysis is conducted to determine the general characteristics of the quality of life data in laryngeal carcinoma patients who have undergone chemoradiation therapy. The Shapiro-Wilk normality test is performed to assess the distribution of research data. Data is considered normally distributed if the p-value > 0.05. The Mann-Whitney test is used to assess the relationship between 2 variables, while the Kruskal-Wallis test is employed to evaluate the relationship between more than 2 variables. Result are deemed significant if the p-value < 0.05 for both the Mann-Whitney and Kruskal-Wallis tests.

### RESULTS

### Subject Characteristics of the Study

This study was conducted from October to November 2021. The study subjects were 24 laryngeal carcinoma patients at the Ear, Nose, and Throat (THT-KL) Clinic of the Merpati Installation and the Oncology THT-KL Clinic of the Kasuari Installation at Kariadi General Hospital, Semarang. In this study, it was found that 95.8% of the subjects were male, 87.5% were above 50 years old, 91.7% had a history of smoking, with the majority falling into the moderate smoking category (37.5%), 33.3% had a history of alcohol consumption, with the majority falling into the light alcohol consumption category (33.3%), and 41.7% had a history of occupational exposure, with the most common occupation being construction labor. The average age of the study subjects was 63 years with an age range of 30 to 82 years. (Table 1)

Variable	Results (n[%])	
Gender	Male	23 (95,8)
	Female	1 (4,2)
Age Group		
	$\leq 50$ years	3 (12,5)
	old	21 (87,5)
	> 50 years	
	old	
Smoking History		
	Yes	22 (91,7)
	No	2 (8,3)
	Light	5 (20,8)
	Moderate	9 (37,5)
	Heavy	8 (33,3)
History of Alcohol	•	
Consumption	Yes	8 (33,3)
-	No	16 (66,7)
	Light	7 (33,3)
	Moderate	1 (4,2)
	Heavy	0 (0)
Occupational Exposure	•	
History	Yes	10 (41,3)
	No	14 (58,3)
Age (years old)		63 (30-82)

Table 2.	Occupation	of research	subjects

Occupation	Amount	Percentage (%)
Civil Service Unit	1	4,2
Security	2	8,3
Employee	2	8,3
Driver	3	12,5
Fisherman	1	4,2
Farmer	2	8,3
Breeder	1	4,2
Merchant	2	8,3
Construction Workers	6	25
Miners	4	16,7

### **Results of UW-QoL Questionnaire Completion**

An overview of the quality of life of laryngeal carcinoma patients after chemoradiation at Kariadi General Hospital obtained an average score of 62, categorized as a "good" quality of life with a score range of 13 to 95. Based on the data collected, 25%



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had a "very good" quality of life score, 41.7% with a "good" score, 12.5% with a "fair" score, 12.5% with a "poor" score, and 8.3% with a "very poor" score.

The "Speech" domain had the lowest average score and the highest percentage of poor scores

among the 12 domains, with a score of 41 and 66.7%, respectively. This was followed by the "Anxiety" domain with a score of 52 and a percentage of poor scores at 45.8%. (Table 3)

Table 3. Results	of the	e UW-0	QoL	Questionnaire	per Domain
	-				

UW-QoL	n		Questionnaire Score				% Worst Score	Mean		
		0	25	30	50	70	75	100	_	
Pain	24	1	1		7		4	11	8,3	74
Appearance	24	0	6		4		9	5	25	64
Activity	24	7	0		2		7	8	29,2	59
Recreation	24	0	10		0		4	10	41,7	65
Swallowing	24	5		4		4		11	37,5	63
Chewing	24	6			6			12	25,0	63
Speech	24	5		11		5		3	66,7	41
Shoulder	24	1		4		9		10	20,8	73
Taste	24	6		3		5		10	37,5	60
Saliva	24	0		7		7		10	29,2	71
Mood	24	1		7		10		6	33,3	63
Anxiety	24	3		8		10		3	45,8	52

#### Description:

%Worst score is the percentage of the number of participants filling in the lowest 2 scores with all participants (except for the "Chewing" component, calculated only in the lowest 1 score)

# Differential Test of Risk Factors with Quality of Life Scores

The Shapiro-Wilk normality test indicates that the distribution of quality of life score data is not normal (p<0.05). Therefore, the results of the average quality of life scores are presented in the form of median (minimum-maximum) values. Based on the median values, the average quality of life scores have a higher median in the age group under 50, the female group, the non-smoker group, the alcohol consumer group, and the group not exposed to environmental pollutants at work.

The Mann-Whitney test was conducted to determine the relationship between 2 risk factor variables and the quality of life of laryngeal carcinoma patients after chemoradiation. Statistically, no significant difference (p<0.05) was found between the average quality of life scores and risk factors such as age, gender, smoking history, alcohol consumption history, and exposure to workplace pollutants. (Table 4)

The Kruskal-Wallis test was conducted on the risk factors of smoking history and alcohol consumption history in relation to the quality of life scores to assess the relationship between more than 2 variables. The obtained p-values >0.05 indicate no significant relationship between the history of smoking and alcohol consumption and the quality of life scores of laryngeal carcinoma patients after chemoradiation. (Table 5)

Risk Factor	Quality of Life Score	p*
≤ 50 years old	77,5 (74,2 - 85,0)	0,176
> 50 years old	67,1 (13,3 – 95,4)	
Male	67,1 (13,3-95,4)	0,718
Female	74,2	
Smoke	67,1 (13,3 - 95,4)	0,174
Do not smoke	81,3 (77,5 - 85)	
		0,976
Consume Alcohol	70,6 (19,2 - 95,4)	
Not Consume Alcohol	67,3 (13,3 - 90,8)	
		0,703
Exposure to	64,6 (19,2-95,4)	
Occupational		
Pollutants		
Not Exposed to	72,5 (13,3 - 90,8)	
Occupational		
Pollutants		

\* Mann-Whitney test (p < 0.05)

Table 5. Kruskal-Wallis Test of Smoking History on Quality of Life

Smoking History	Quality of Life Score	p*	
No	81,3 (77,5 - 85)		
Light	79,6 (67,1 -83,3)	0 1 2 2	
Moderate	63,3 (13,3 - 90,1)	0,132	
Heavy	57,7 (28,3 - 95,4)		

\*Kruskal-Wallis test (p > 0.05)



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Table 6. Kruskal-Wallis Test of Alcohol Consumption History on					
Quality	Quality of Life Score				
Alcohol Consumption	Quality of Life	<b>p</b> *			
History	Score	h.			
No	67,3 (13,3 - 90,8)				
Light	74,2 (19,2 – 95,4)	0.361			
Moderate	28,3	0,501			
Heavy	-				
* Krukal-Wallis test ( $p > 0.05$ )					

### DISCUSSION

The results of respondent characteristics based on gender in this study revealed that the majority of respondents were male, accounting for 23 individuals (95.8%). This finding is consistent with Williamson et al.'s study, which explored the quality of life of laryngeal carcinoma patients post-therapy and found 32 male respondents (78%).<sup>7</sup> Additionally, a study in the Netherlands on the quality of life of early-stage laryngeal carcinoma patients who had undergone radiotherapy also showed a higher number of male respondents (89%) compared to females.<sup>8</sup> Regarding age, most respondents in this study belonged to the age group above 50 years (87.5%), with a mean age of 63 years and an age range of 30 to 82 years. This result is almost similar to a study conducted by Al-Mamgani et al. in the Netherlands, with a median respondent age of 66 years and an age range of 30 to 92 years.8

The general overview of the quality of life of laryngeal carcinoma patients after chemoradiation at Kariadi General Hospital indicates different results from the quality of life of laryngeal carcinoma patients post-therapy in England, which reported an average quality of life as "very good" with an average score of 81. The range of quality of life scores in that study was 52 to 90.7 Based on the assessment domains of quality of life, the "Speech" domain was the one with the lowest average score (41) and the highest percentage of poor scores (66.7%) among the 12 domains. This was followed by the "Anxiety" domain with an average score of 52 and a percentage of poor scores at 45.8%. These results are similar to a study in 2018 on the quality of life of laryngeal cancer patients in Poland, where the "Speech" domain had the lowest average score (57).9

Chemoradiation therapy for laryngeal carcinoma patients can lead to neuromuscular weakness of the vocal cords, fibrosis or atrophy of the vocal cords, and inflammation in the laryngeal tissue, all of which can reduce the speaking quality of

patients post-therapy.<sup>10</sup> This is a crucial factor contributing to the low score in the "Speech" domain of the quality of life for laryngeal carcinoma patients after chemoradiation. This study was conducted during the Covid-19 pandemic, while the aforementioned studies were conducted before the pandemic. According to Marie Claire et al., the quality of life of patients with acute or chronic diseases has decreased during the Covid-19 pandemic. The emotional domain is particularly affected, followed by the functional condition of the body.<sup>11</sup> This is one of the factors influencing the "Anxiety" domain in this study.

Based on the statistical analysis in this study, no significant relationship was found between the quality of life scores and the smoking history of laryngeal carcinoma patients after chemoradiation. Aarstad et al.'s study also showed no significant relationship between smoking history and the quality of life of head and neck carcinoma patients.<sup>12</sup> Additionally, Al-Mamgani et al.'s study found no significant relationship between smoking history before therapy and the quality of life of laryngeal carcinoma patients post-therapy.<sup>8</sup> The long and varying time intervals between smoking history before therapy and the sampling time for assessing the quality of life of laryngeal carcinoma patients posttherapy were considered factors influencing this relationship. In this study, the median quality of life scores for laryngeal carcinoma patients after chemoradiation without a smoking history was higher than for subjects with a smoking history.

Regarding the statistical analysis in this study, no significant relationship was found between alcohol consumption history and the quality of life of laryngeal carcinoma patients after chemoradiation. Similar results were found in Aarstad et al.'s study, which assessed the quality of life of head and neck carcinoma patients.<sup>12</sup> However, other studies have shown a significant decrease in the quality of life for laryngeal carcinoma patients who continue the habit of alcohol consumption post-therapy.<sup>13,14</sup> It is essential to monitor the alcohol consumption habits of laryngeal carcinoma patients post-therapy to prevent a decline in their quality of life.

Statistically, in this study, no significant relationship was found between gender and the quality of life of laryngeal carcinoma patients after chemoradiation. Similar results were found in other



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studies, including those conducted by Aarstad et al. and Al-Mamgani et al., where both studies showed no significant relationship between gender and the quality of life of head and neck carcinoma patients post-therapy.<sup>8,12</sup> However, according to studies conducted by Tan et al. and Lee et al., a significant relationship was found between gender and the quality of life of laryngeal carcinoma patients. Female patients had lower quality of life scores than male patients, attributed to emotional conditions and social support.<sup>15,16</sup> Based on the number of study subjects, a more balanced distribution was found in Lee et al.'s study (51% female subjects), while in other studies, more than 85% of the subjects were male.<sup>8,12,15</sup> In this study, the distribution of gender among the study subjects was uneven, with only 4.2% of the study subjects being female. Therefore, the researchers believe that further research is necessary to explore the relationship between gender and laryngeal carcinoma patients after chemoradiation.

This study categorizes patients into two age groups: those aged 50 years and below, and those aged over 50 years. Based on this classification, it was found that the median quality of life score for laryngeal carcinoma patients after chemoradiation in the age group of 50 years and below was higher compared to the quality of life scores for laryngeal carcinoma patients in the age group above 50 years. However, statistically, the relationship between age and the quality of life of laryngeal carcinoma patients after chemoradiation was not significant. Similar results were found in other studies assessing overall quality of life scores against the age of laryngeal patients.<sup>7,17</sup> However. carcinoma significant associations were found in several domains related to functional decline in elderly patients.<sup>17</sup>

Statistically, there was no significant relationship between exposure to the work environment and the quality of life of laryngeal carcinoma patients after chemoradiation. No study that directly assesses the relationship between exposure to the work environment and the quality of life of patients with laryngeal carcinoma. Meanwhile, another study found a significant relationship between exposure to the work environment and the incidence of laryngeal carcinoma.<sup>18,19</sup>

several unexplored This study has limitations. The limited number of research subjects, coupled with a relatively high absolute precision value, is one of the constraints that results in an of uneven distribution research variables. Additionally, certain aspects were not assessed in this study, such as the potential exposure to environmental dust (including asbestos dust, coal dust, and textile dust) around the subjects' residences, the post-therapy habits of research subjects related to risk factors, and confounding factors (such as comorbidity, TNM stage, and socioeconomic conditions) that may influence the quality of life. Some responses from research subjects were also conveyed by the subjects' families due to the limited speaking ability of the research subjects, potentially introducing bias into the research questionnaire.

### CONCLUSION

Based on the results and discussions above, it can be concluded that there is no relationship between risk factors and the quality of life of laryngeal carcinoma patients after chemoradiation at Kariadi General Hospital.

### ETHICAL APPROVAL

Ethical clearance was obtained with the approval and consideration of the Health Research Ethics Commission, Faculty of Medicine, Diponegoro University with ethical clearance No. 379/EC/KEPK/FK-UNDIP/X/2021.

### **CONFLICT OF INTEREST**

There is no conflict of interest in this research.

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### REFERENCES

- 1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin*. 2016;66(1):7-30. doi:10.3322/caac.21332.
- 2. Kemenkes RI. Profil Kesehatan Indonesia 2018 Kemenkes RI.; 2019.
- Wiliayanto O. Insidensi Kanker Kepala Leher Berdasarkan Diagnosis Patologi Anatomi di RS Kariadi Semarang Periode 1 Januari 2001 - 31 Desember 2005. Fak Kedokt Univ Diponegoro. Published online 2006.
- Bosetti C, Gallus S, Franceschi S, et al. *Cancer* of the larynx in non-smoking alcohol drinkers and in non-drinking tobacco smokers. *Br J Cancer*. Published online 2002. doi:10.1038/sj.bjc.6600469.
- 5. Steuer CE, El-Deiry M, Parks JR, Higgins KA, Saba NF. An update on larynx cancer. *CA Cancer J Clin*. Published online 2017. doi:10.3322/caac.21386.
- Rahman S, Budiman BJ, Swanda D. Diagnosis dan Penatalaksanaan Karsinoma Sel Skuamosa Glotis Stadium Dini. J Kesehat Andalas. Published online 2016.
- Williamson JS, Ingrams D, Jones H. Quality of life after treatment of laryngeal carcinoma: A single centre cross-sectional study. *Ann R Coll Surg Engl.* 2011;93(8):591-595. doi:10.1308/147870811X13137608455253.
- Al-Mamgani A, van Rooij PH, Woutersen DP, et al. Radiotherapy for T1-2N0 glottic cancer: A multivariate analysis of predictive factors for the long-term outcome in 1050 patients and a prospective assessment of quality of life and voice handicap index in a subset of 233 patients. *Clin Otolaryngol.* 2013;38(4):306-312. doi:10.1111/coa.12139.
- Kolator M, Mikuła B, Maciejczyk A, Zatoński T. Polish validation of the University of Washington "quality of life" questionnaire in patients with cancer of the larynx. *Br J Oral Maxillofac Surg.* 2019;57(3):226-231. doi:10.1016/j.bjoms.2018.12.013.
- Meleca RJ, Dworkin JP, Kewson DT, Stachler RJ, Hill SL. Functional outcomes following nonsurgical treatment for advanced-stage laryngeal carcinoma. *Laryngoscope*. 2003;113(4):720-728. doi:10.1097/00005537-200304000-00025.

- Odwyer MC, Meixner K, Albiac LC, et al. Health-related quality of life for people with acute and chronic illnesses during the covid-19 pandemic. *J Am Board Fam Med.* 2021;34(3):509-521. doi:10.3122/JABFM.2021.03.200593.
- Aarstad HJ, Østhus AA, Aarstad HH, Lybak S, Aarstad AKH. EORTC Quality of Life Questionnaire Head and Neck (H&N)-35 scores from H&N squamous cell carcinoma patients obtained at diagnosis and at 6, 9 and 12 months following diagnosis predict 10-year overall survival. *Eur Arch Oto-Rhino-Laryngology*. Published online 2019. doi:10.1007/s00405-019-05630-2.
- Duffy SA, Terrell JE, Valenstein M, Ronis DL, Copeland LA, Connors M. Effect of smoking, alcohol, and depression on the quality of life of head and neck cancer patients. *Gen Hosp Psychiatry*. 2002;24(3):140-147. doi:10.1016/S0163-8343(02)00180-9.
- 14. Danker H, Keszte J, Singer S, et al. Alcohol consumption after laryngectomy. *Clin Otolaryngol.* 2011;36(4):336-344. doi:10.1111/j.1749-4486.2011.02355.x.
- Tan S, Duong Dinh TA, Westhofen M. Evaluation of gender-specific aspects in qualityof-life in patients with larynx carcinoma. *Acta Otolaryngol.* Published online 2016. doi:10.1080/00016489.2016.1211319.
- Lee MT, Gibson S, Hilari K. Gender differences in health-related quality of life following total laryngectomy. *Int J Lang Commun Disord*. 2010;45(3):287-294. doi:10.3109/13682820902994218.
- 17. Leoncini E, Ricciardi W, Cadoni G, et al. Adult height and head and neck cancer: A pooled analysis within the INHANCE Consortium. *Head Neck*. 2014;36(10):1391. doi:10.1002/HED.
- Bouvard V, Baan R, Straif K, et al. A review of human carcinogens--Part B: biological agents. *Lancet Oncol.* Published online 2009. doi:10.1016/s1470-2045(09)70096-8.
- Peng W-J, Mi J, Jiang Y-H. Asbestos exposure and laryngeal cancer mortality. Laryngoscope. 2016;126(5):1169-1174. doi:10.1002/lary.25693.