Distribution of oral carcinoma case requiring radiotherapy in the Oral and Maxillofacial Surgery Clinics

Dinda Tegar Jelita*, Lucky Riawan*, Herman Hambali**

***Department of Oral and Maxilloacial Surgery Faculty Of Dentistry Universitas Padjadjaran, Indonesia**

****Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital, Indonesia**

ABSTRACT

Introduction: Carcinoma is a highly malignant tumour of epithelium that occurred in the oral cavity. One of the most common therapies given is radiotherapy, with healing, adjuvant, and palliative intentions. This research was aimed to discover the distribution of oral carcinoma requiring radiotherapy. **Methods:** This study was a retrospective, descriptive method. Samples were taken from the medical record of patients with oral cavity carcinoma requiring radiotherapy at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital, Bandung, of January 2006–December 2010. **Results:** This study indicated that as many as 23 (20.9%) cases of oral carcinoma requiring radiotherapy from a total of 110 oral carcinoma cases in that period. Type of radiotherapy most frequently found was adjuvant radiotherapy, by 14 (60.8%) cases. The most frequent type of oral carcinoma case requiring radiotherapy was squamous cell carcinoma, by 12 (52.1%) cases. Tongue become the most common area of oral carcinoma requiring radiotherapy, by 7 (30.4%) cases. Oral carcinoma case requiring radiotherapy was most frequently found in men by 14 (60.8%) cases. The age group of 41-50 was become the majority by 7 (30.4%) cases from all of the oral carcinoma case requiring radiotherapy. **Conclusion:** Distribution of oral carcinoma case requiring radiotherapy in the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital is found in as many as 23 (20.9%) cases. Most frequent radiotherapy given is adjuvant radiotherapy (14 (60.8%) cases). The most frequent type of oral carcinoma case requiring radiotherapy is squamous cell carcinoma (12 (52.1%) cases). The most common area of oral carcinoma requiring radiotherapy is tongue (7 (30.4%) cases). Oral carcinoma case requiring radiotherapy was most frequently found in men (14 (60.8%) cases). The age group of 41-50 is the majority age suffered from disease (7 (30.4%) cases).

Keywords: Oral carcinoma, radiotherapy, oral maxillofacial surgery.

INTRODUCTION

Oral cavity carcinoma is a possible risk caused by deviation of human life activity. Unhealthy lifestyle changes such as smoking, alcoholic drinks, sexual behaviour aberrations, and foods containing preservatives.[1,2] Carcinoma cannot be directly proven because of its complex malignancy and multifactorial likelihood factor.[3] Carcinoma is commonly found in the oral cavity. The data stated that every year in the UK, there are 2000 cases of intraoral carcinoma and lips at the age of 30-50 years. While in India and Sri Lanka, there is found 40% cancer in the oral

Corresponding author: Lucky Riawan, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry Universitas Padjadjaran, Indonesia. Jalan Sekeloa Selatan I, Bandung, West Java, Indonesia, 40132; Phone: +6222-2504985/2532805

cavity of all cancer. About 90% of oral cancers are squamous cell carcinomas derived from the epithelium mucosa.[3]

Carcinoma of the oral cavity is a severe malignancy because patients are often late to realize there are abnormalities when it has spread further and is in an advanced stage.[4] Carcinoma treatment is surgery, radiotherapy, chemotherapy, and combination.[5] Selection of treatment depends on cell type and tumour differentiation (tumour type), TMN (primary tumour size, metastasis, node), bone involvement, location of primary lesion, and the general state of the patient.[6]

Radiotherapy may be given to a radiosensitive type of tumour, such as squamous cell carcinoma at stage I and II, moderately differentiated tumour cells due to the more poorly differentiated radiosensitive, and ulcers that have not infiltrated the tissues too profound.[6] Approximately 60-70% of patients have received radiotherapy tumours. Therapeutic effectiveness is increasingly becoming increasingly becoming a major technique in tumour therapy.[2]

Based on the above description, the authors are interested in researching the prevalence of carcinoma in the oral cavity, which requiring radiotherapy treatment. Complete information and data on this case are expected to be a reference for people who experience cases like this. This research was aimed to discover the distribution of oral carcinoma requiring radiotherapy.

METHODS

This research used a retrospective descriptive method. This research was conducted by collecting medical records of oral cavity carcinoma patients. The population in this study was medical records of patients diagnosed with oral carcinoma at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital, Bandung, of January 2006–December 2010.

The sample in this research was medical records of patients diagnosed with oral carcinoma given radiotherapy and had data completeness in the form of radiotherapy type, carcinoma type, location, sex, and age group. Data from the medical records of patients diagnosed with oral carcinoma and given radiotherapy at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital, Bandung, of January 2006–December 2010 recorded frequency of oral carcinoma requiring radiotherapy and the type of radiotherapy, type of carcinoma, location, sex, and age group.

The research was conducted through various stages: data collection; the grouping of patient status based on diagnosis, therapy, and radiotherapy type; resulting; presentation of data (in tables and graphs); conclusion withdrawal; and suggestions. The research instrument used in this research was the medical record cards of Hasan Sadikin Hospital. Data was processed by frequency. The presentation of data was arranged and presented in the form of tables and graphs of frequency distribution, and calculation was presented in the form of a percentage.

RESULTS

Based on the results of research from secondary data in the form of medical records of patients diagnosed with oral carcinoma at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital, Bandung, of January 2006–December 2010, regarding the number of patients with oral

Table 1. Percentage of oral carcinoma cases at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital Bandung, of January 2006 - December 2010

Year	Total of patients	Total of carcinoma patients	%
2006	9517	13	0.1
2007	8792	42	0.4
2008	7561	13	0.1
2009	7863	25	0.3
2010	7104	17	0.2
Total	40837	110	0.27

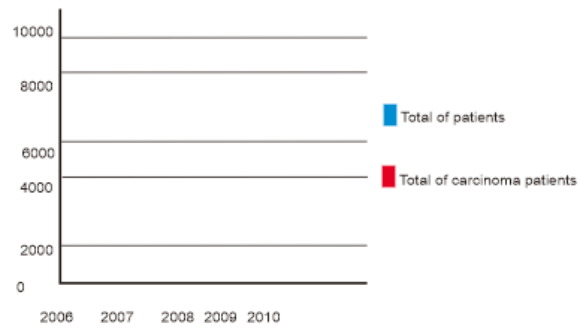

Figure 1. Graph of cases of oral carcinoma at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital Bandung, of January 2006 - December 2010

cavity carcinoma, the number of oral carcinoma given radiotherapy treatment, and distribution of cases based on the type of carcinoma by location, sex, and age group.

Patients who came as much as 40,837 while the number of carcinoma of the oral cavity among them only 110 patients (0.27%). Most cases of oral cavity carcinoma in 2007 were 42 cases (38%), 25 cases (22,7%) in 2009, 17 cases (15,5%) in year 2010, 13 cases in 2008 11.8%), in 2006 as many as 13 cases (11.8%).

Data shows that surgical therapy was given to 11 cases (10%). A total of 23 cases of carcinoma (20.9%) performed radiotherapy,

Table 2. Percentage of oral carcinoma cases at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital Bandung, of January 2006 - December 2010 based on type of treatment

Year	Total of carcinoma patients	Surgery		Radiotherapy		Chemotherapy	
		Total	(%)	Total	(%)	Total	(%)
2006	13	2	15.3	2	13	1	6.6
2007	42	1	2.3	5	11.9	-	-
2008	13	3	23	5	33.3	-	-
2009	25	3	12	10	40	-	-
2010	17	2	11.7	1	5.8	-	-
Total	110	11	10	23	20.9	1	0.9

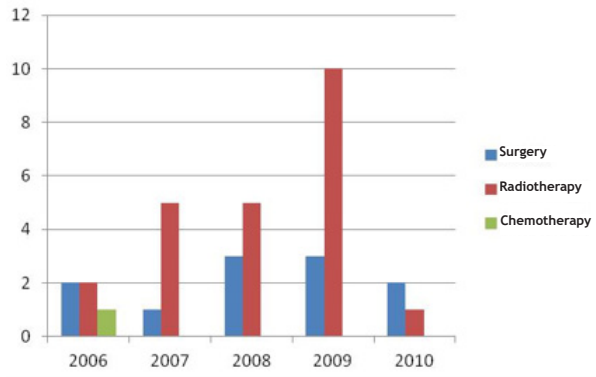

Figure 2. Graph of cases of oral carcinoma based on type of treatment

Table 3. Percentage of oral carcinoma cases at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital Bandung, of January 2006 - December 2010 based on type of radiotherapy treatment

Year	Type of radiotherapy			
	Curative	Adjuvant	Palliative	Total
2006	1	1	-	2
2007	2	2	1	5
2008	1	2	2	5
2009	2	8	-	10
2010	-	1	-	1
Total	6	14	3	23

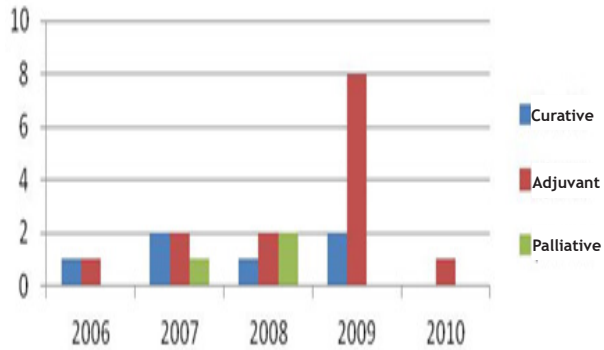

Figure 3. Graph of cases of oral carcinoma based on type of radiotherapy treatment

Table 4. Percentage of frequency distribution of oral carcinoma cases requiring radiotherapy by location

Location	Type of radiotherapy				
	Curative	Adjuvant	Palliative	Total	Percentage
Salivary gland	-	1	-	1	4.3
Gingiva	-	1	-	1	4.3
Buccal	1	2	-	3	13
Palatum	1	5	-	6	26
Tongue	3	3	1	7	30.4
Mandibular	-	1	1	2	8.6
Mandibular	-	1	-	1	4.3
Sinus maxillaries	1	-	-	1	4.3
Parotid	-	-	1	1	4.5
Total	6	14	3	23	100

while chemotherapy was given to as much as 1 case or 0.9%. The year 2009 showed the highest percentage of oral cavity carcinoma treated with radiotherapy, which was found in 10 cases from 25 cases of carcinoma (40%), 2008 in 5 cases from 13 carcinoma cases (38,4%), in 2006 2 cases from 13 carcinoma cases (15.3%), followed in 2007 by 5 cases from 42 cases of carcinoma (11.9%), and found least in 2010, which was 1 case out of 17 carcinoma cases (5.8%).

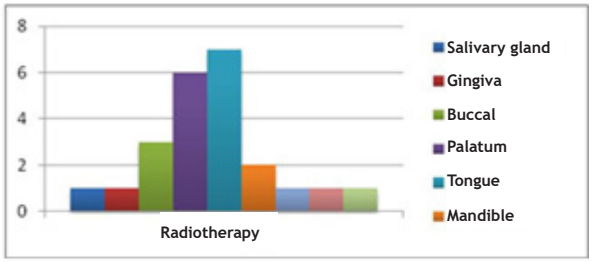

Figure 4. Frequency distribution of oral carcinoma cases requiring radiotherapy based on location

The authors found oral carcinoma that required curative radiotherapy treatment in as many as 6 cases, adjuvant radiotherapy treatment in 14 cases, and palliative radiotherapy treatment in 3 cases. Table 3 shows that most commonly performed radiotherapy was adjuvant radiotherapy, which was found in 14 cases or 80.6%, curative radiotherapy in 6 cases or 26% and palliative radiotherapy in 3 cases or 13%.

Table 5. Percentage of frequency distribution of oral carcinoma cases requiring radiotherapy based on sex

Sex	Type of radiotherapy				
	Curative	Adjuvant	Palliative	Total	Percentage(%)
Male	2	9	3	14	60.8
Female	4	5	-	9	39.1
Total	6	14	3	23	100

Table 6. Percentage of frequency distribution of oral carcinoma cases requiring radiotherapy based on age group

Age group	Type of Radiotherapy						Total	(%)
	Curative		Ajuvan		Palliative			
	Total	(%)	Total	(%)	Total	(%)		
0-10	-	-	-	-	-	-	-	-
11-20	-	-	1	7.1	-	-	1	4.3
21-30	-	-	1	7.1	1	33.3	2	8.6
31-40	1	16.6	1	7.1	-	-	2	8.6
41-50	2	33.3	5	35.7	-	-	7	30.4
51-60	1	16.6	4	28.5	1	33.3	6	26-
61-70	1	16.6	1	7.1	1	33.3	3	13
71-80	1	16.6	1	7.1	-	-	2	8.6
81-90	-	-	-	-	-	-		-
Total	**6**	**100**	**14**	**100**	**3**	**100**	**23**	**100**

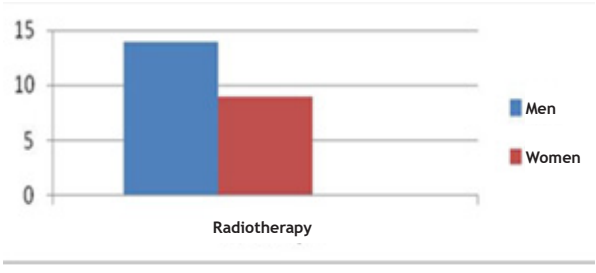

Figure 5. Frequency distribution of oral carcinoma cases requiring radiotherapy based on sex

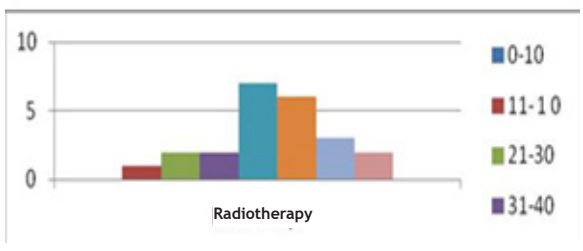

Figure 6. Frequency distribution of oral carcinoma cases requiring radiotherapy based on age group

The frequency distribution of oral carcinoma cases requiring radiotherapy based on the type of carcinoma showed that the most common type of carcinoma performed was squamous cell carcinoma of 12 (52.1%) cases, most with adjuvant radiotherapy of 6 cases, 5 cases given curative radiotherapy, and palliative radiotherapy was given to 1 case. The second most type of carcinoma of the oral cavity treated with radiotherapy was mucoepidermoid carcinoma (5 (21,7%)) cases, followed by 3 cases given with adjuvant radiotherapy and 2 cases with palliative radiotherapy. This study found no type of carcinoma of acinic cells, anaplastic carcinoma, and mixed malignant carcinoma.

Frequency distribution of oral carcinoma patients requiring radiotherapy based on sex, cases of oral carcinoma requiring radiotherapy was found more commonly in men than women, consisted of 14 (60.8%) cases in men and 9 (39.1%) cases in women. Men were mostly treated with 9 adjuvant radiotherapy cases and 3 palliative radiotherapy cases, and at least two curative radiotherapy was done.

Frequency distribution of oral cavity carcinoma cases requiring radiotherapy by age group was more commonly found in the age group of 41-50 years of 7 cases (30.4%) of all oral carcinomas requiring radiotherapy. Age group 41-50 years mostly treated with adjuvant radiotherapy, which was found in 5 cases, followed by curative radiotherapy found in 2 cases. The second most common age group was 51-60 years, with 6 (26%) cases, mostly treated with adjuvant radiotherapy in 4 cases, followed by the same amount of curative radiotherapy and palliative radiotherapy, each was found in 1 case.

DISCUSSION

From January 2006 through December 2010, the number of patients who came to the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital, Bandung, were as many as 40,837 people and amongst 110 of them suffer from oral carcinoma. Comparison of the number of cases of oral carcinoma with the number of patients who came to the clinics in 2006 - 2010 found somewhat less.

This condition was influenced by several factors, such as the majority of patients with oral cavity carcinoma was referred to a specialist for tumour handling, which is the oncology section. As we know, there are some parts for handling tumours in the oral cavity in Hasan Sadikin Hospital, such as Oncology Clinics, Ear-Nose-Throat Clinics, and General Surgery Clinics. Patients with oral cavity carcinoma who went to the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital, Bandung, came from initial diagnosis, referrals, or with own's will. The second reason was that medical record in 2006 some have been destroyed and scattered.

This study found that based on the type of therapy, as many as 10% performed surgery because it was the primary choice of treatment with the maximum success rate for epidermal carcinoma treatment at stage 1. As mentioned by Desen[2], the success rate of operation in stage I reached 90%. This success is because surgical therapy can achieve maximum treatment efficacy of stage I carcinoma, a non-radiosensitive carcinoma type, a location where surgical action is possible. Desen[2] also mentioned that surgery could obtain maximum results if the pathological spread of tumours can be known for sure.

Further action radiotherapy in this study showed there were 23 patients with oral carcinoma requiring radiotherapy or equal to 20.9%. As Halperin et al.[7] argued that modern radiotherapy is now supported by advanced technology. As stated by Susworo[8], the use of radiation as one of the treatment modalities of cancer has grown rapidly with the advancing technology, especially in the field of biomolecular.

Chemotherapy treatment in this study only found in 1 (0.9%) cases because it is intended for tumours that have metastasized far (to other organs) while patients who come at the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital Bandung, most likely diagnosed with oral cavity carcinoma in stage 1. Desen[2] said that chemotherapy is a systemic therapy method against systemic cancer (e.g. leukemia, myeloma, lymphoma), cancer with clinical or subclinical metastasis, and advanced-stage cancer (stage IV). Pindborg[9] also mentioned that majority chemotherapy serves as sterilization of

the possibility of micrometastasis that also helps to achieve palliative goals after surgery and/or radiotherapy. The rest treatment was 67%, only performed a biopsy and referred to other clinics.

Oral carcinoma treatment mostly performed was adjuvant radiotherapy found in 14 (60,8%) cases, curative radiotherapy in 6 (26%) case, followed by palliative radiotherapy in 3 (13%) case. Robertson[10] researched in the U.K. involving 350 cases of T2-4 N0-2 carcinoma of the oral cavity as a sample comparing the treatment of radiotherapy alone with radiotherapy and surgery. After 23 months, the combined results of radiotherapy and surgical treatment showed significant treatment success.

Adjuvant radiotherapy was found more in this study to achieve maximum success. Radiotherapy performed before surgery in the case of a large carcinoma where radiotherapy will reduce the size to facilitate surgery, whereas, after surgery, in the size of T3-T4, cases of carcinoma can not be excised radically because of the limit is doubtful by cancer cells.[6]

Adjuvant radiotherapy is mostly performed to support surgical treatment as mentioned in the literature that the majority of oral carcinomas was treated with surgery with a combination of radiotherapy.[3] Adjuvant radiotherapy is a therapy that supports surgical treatment which is mostly performed because it can increase the effectiveness of treatment to achieve treatment success. This statement supported by the theory in the literature that surgery, radiotherapy, chemotherapy have advantages and limitations of each, then to improve the effectiveness better performed in combination.[2]

Squamous cell carcinoma is the highest case found in this study. The authors found that squamous cell carcinoma was the most common type of oral carcinoma requiring radiotherapy during January 2006 - December 2010, with 12 (52.1%) cases. The highest therapy was performed with adjuvant radiotherapy, which was 6 cases, then curative radiotherapy in 5 cases, and the least was palliative radiotherapy in 1 case. The cause of oral squamous cell carcinoma is a medical indication in radiotherapy treatment because most oral cavities are coated by layered epithelium. Local, multiple and systemic factors may affect the oral epithelium and alter normal clinical or microscopic sighting.[11]

The investigators found that the number of cases close to curative radiotherapy (5 cases) and adjuvant radiotherapy (6 cases) due to squamous cell carcinoma has an intermediate level of radiation sensitivity then proper treatment to achieve the effectiveness of succession done by adjuvant radiotherapy or curative therapy. Wetter[12] classifies tumour radiosensitivity based on histologic type, Peterson divided into 3 different types of tumours: radiosensitive, intermediate, and radioresistant. The first category such as tumour germ cells, reticuloid; the latter such as squamous cell and adenocarcinoma; and a third such as soft tissue, bone sarcoma, and melanoma. Therefore radiotherapy in squamous cell carcinoma has a high percentage of success in the early phase, especially in the mucosa.[7]

The second most prevalent case in this study was mucoepidermoid carcinoma, which was found in 5 (21.7%) cases, with 3 cases treated with adjuvant radiotherapy and 2 cases with palliative radiotherapy. This considerable amount is due to the treatment of mucoepidermoid carcinoma is a wide excision, but the treatment alone is not enough because the majority will reappear, hence the combination of the adjuvant or palliative radiotherapy.[3]

Salivary gland carcinoma slowly responds to radiation, so it is considered radioresistant but denied through some research using modern radiotherapy with reasonable local control, then observed at least a local recurrence rate.[6] As seen in this study, the third most found oral carcinoma in this study was adenoid cystic carcinoma, which was found in 4 (17.3%) cases, treated with curative radiotherapy in 1 case, and 3 cases treated with adjuvant radiotherapy. No acinic cells were found in this study because the acinic cells originated from the parotid glands where the parotid gland is the major salivary gland. As in the literature stated that histologically, the salivary glands differentiate with the tend to have mitosis rarely, hence the salivary gland cells more directed to radioresistant, but can also be treated with radiation therapy that includes the major salivary glands are often followed by a decrease in the output of saliva secretion. Neville[14] stated that

treatment of carcinoma of functional acinic cells is lobectomy or when parotidectomy is needed.

The tongue is the most found location of oral carcinoma requiring radiotherapy in this research (7 (30,4%) cases). Both curative radiotherapy and adjuvant radiotherapy was found equally as the treatment of each 3 cases, while other 1 case of palliative radiotherapy. The most frequent amount of radiotherapy on the tongue is due to radiotherapy is a treatment option to minimize disability when surgery, especially the base of the tongue. As mentioned by Wang6, on the size of T1-T2 primary tumour posterior part of the tongue of surgery will cause speech disorders, swallowing disorders and aesthetic complaints so that radiotherapy is done.[6]

According to Ackerman[15], the most effective therapy for carcinoma of the tongue is interstitial radiation using other radium or radioactive needles. Another reason why radiotherapy is the majority of choice as mentioned in the literature that the tongue is a muscle organ covered by layered epithelium that has little keratinase and more susceptible to carcinogenic substances then the tongue is the location most often exposed to oral carcinoma.[5,6,16]

According to gender-based groupings, cases of oral carcinoma requiring radiotherapy were more common in men than women, consisted of 14 (60.8) cases in men and 9 (39.1%) of cases in women. The most common men were treated with adjuvant radiotherapy (9 cases), 3 cases were treated with palliative radiotherapy, and another 2 cases were treated with curative radiotherapy.

Research showed that the number of cases performed more radiotherapy in men than women because the majority of patients affected by oral carcinoma is male. As stated in the literature, the frequency ratio of cancer of the male oral cavity is higher than that of women due to the high smoking habit that becomes carcinogen causing the possible risk of carcinoma of the oral cavity in men that occurs almost all over the world.[3] Tobacco may stimulate normal, non-keratinous squamous epithelium to be thick keratinous that may allow leukoplakia where it is one of the forerunners that can develop into squamous cell carcinoma.

Data of frequency distribution of carcinoma of the oral cavity that require radiotherapy based on age group was more suffered in the age range of 41-50 years in as many as 7 cases (30.4%) from the whole carcinoma of the oral cavity that requiring radiotherapy. Age group 41-50 years mostly treated with adjuvant radiotherapy (5 cases), followed by curative radiotherapy in as many as 2 cases. The second most common age group was 51-60 with 6 (26%) cases. Mostly treated with adjuvant radiotherapy (4 cases), followed by the same cases treated with curative radiotherapy and palliative radiotherapy (1 case each).

These results correspond to the literature stated that 95% of oral carcinoma occurs at the age of more than 40 years, with the average onset of the disease occurs in the sixth decade. The condition may be due to the declining tissue resistance resulting in the initiation and promotion of genes that lead to malignant circumstances. Radiotherapy treatment, curative, adjuvant, and palliative, have better results at age under 40 years.[6,17,18] Surgical therapy is riskier because in the decade the tissue has been a decrease in cell regeneration, then the choice of treatment is radiotherapy to achieve maximum results.

The number of cases with a diagnosis of oral cavity carcinoma in the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital Bandung in the period January 2006 - December 2010 were found in as much as 0.27% from the total number of patients. 20.9% of all cases or 23 cases of 110 cases of oral cavity carcinoma was treated by radiotherapy, and type of radiotherapy treatment in oral carcinoma most often done was the adjuvant radiotherapy, in as many as 14 patients (60.8%).

CONCLUSION

Distribution of oral carcinoma case requiring radiotherapy in the Oral and Maxillofacial Surgery Clinics of Hasan Sadikin Hospital is found in as many as 23 (20.9%) cases. Most frequent radiotherapy given is adjuvant radiotherapy (14 (60.8%) cases). The most frequent type of oral carcinoma case requiring radiotherapy is squamous cell carcinoma (12 (52.1%) cases). The most common area of oral carcinoma requiring radiotherapy is tongue (7 (30.4%) cases). Oral carcinoma case requiring radiotherapy was most frequently found in men (14 (60.8%) cases). The age group of 41-50 is the

majority age suffered from disease (7 (30.4%) cases).

REFERENCES

1. Rajendran R, Sivapathasundharam B. Shafer's textbook of oral pathology. 6th ed. New Delhi: Elsevier.2009. p. 141-69.
2. Desen W, Japaries W. Buku ajar onkologi klinis edisi 2. Jakarta: Balai Penerbit Fakultas Kedokteran Universitas Indonesia. 2008. p. 54,162-75,195-6.
3. Cawson RA, Odell EL. Cawson's essential of oral pathology and oral medicine 8th ed. London: Churcill Livingstone. 2010. p. 277-90,283284,300-8.
4. Laronde DM, Poh CF, Williams PM, Hislop TG, Zhang L, MacAulay C et al. A magic wand for the community dental office? observations from the British Columbia oral cancer prevention program. J Can Dent Assoc. 2007 Sep;73(7):607-9. Available from: http://. cdaadc.ca/jcda. [Cited 14 Februari 2012].
5. Sapp JP, Eversole LR, Wysocki GP. Contemporary oral and maxillofacial pathology 2nd ed. Missouri: Mosby. 2004. p. 164206.
6. Wang CC. Radiation Therapy For Head And Neck Neoplasms 2nd ed. London: Year Book Medical Publishers. 1990. p. 5,28-33,95-147,320-4,405.
7. Halperin EC, Perez CA, Brady LW. Perez and brady's principles and practice of radiation oncology 5th ed. Lippincott Williams & Wilkins. 2008. p. 16-7.
8. Susworo R. Radioterapi dasar-dasar radioterapi dan tata laksana radioterapi penyakit kanker. Jakarta: Penerbit Universitas Indonesia (UI Press). 2007. p. 1,12-19,82.
9. Pindborg JJ. Kanker dan prekanker dalam rongga mulut. Jakarta: Penerbit Buku Kedokteran EGC.1990. p. 165-74
10. Robertson AG, Soutar DS, Paul J, Webster M, Leonard AG, Moore KP, et al. Early closure of a randomized trial: surgery and postoperative radiotherapy versus radiotherapy in the management of intra-oral tumours. Clin Oncol (R Coll Radiol). 1998;10(3):155-60. DOI: 10.1016/s0936-6555(98)80055-1
11. Sapp JP, Eversole LR, Wysocki GP. Contemporary oral and maxillofacial pathology 2nd ed. Missouri: Mosby. 2004. p. 164206.
12. Zevallos JP, Mallen MJ, Lam CY, Karam-Hage M, Blalock J, Wetter DW, et al. Complications of radiotherapy in laryngopharyngeal cancer. Cancer. 2009;115(19):4636–44.
13. Epperly MW, Melendez JA, Zhang X, Nie S, Pearce L, Peterson J, et al. Mitochondrial Targeting of a Catalase Transgene Product by Plasmid Liposomes Increases Radioresistance In Vitro and In Vivo. Radiation Res. 2009;171(5):588–95.
14. Neville B, Damm DD, Allen C. Bouquot J. Oral and maxillofacial pathology. 2nd ed. Philadelphia: Saunder. 2002. p. 356-70,420-30.
15. Ackerman LV, Regato JA. Cancer Diagnosis Treatment and Prognosis, 4th ed. St Louis: Mosby.1970. p. 31.
16. Little JW, Miller CS, Rhodus NL. Dental management of the medically compromised patient 6th ed. Missouri: Mosby. 2002. p. 387-9.
17. Greenberg MS, M.Glick. Burket's Oral Medicine 10th ed. Hamilton: B.C. Decker. 2003. p. 40.
18. Silverman S, Eversole R, Truelove EL. Essentials of oral medicine. London: B.C. Decker. 2001. p. 13.