Survival Rates of Concurrent Chemo-Radiation versus Radiation Alone in Locally Advanced, Unresectable Head and Neck Cancers: A Retrospective Cohort Study

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Objective: *To compare survival rates of concurrent chemo-radiation (CRT) and radiation (RT) alone in locally, advanced unresectable head and neck cancers and to assess factors associated with survival.*

Material and Method: *A retrospective cohort study was conducted of 165 patients treated for locally advanced unresectable head and neck cancers (Stage III, IV) at the Department of Radiation Oncology, Rajavithi Hospital, from 1 January 2011 to 31 December 2013. Patients were divided into two groups: in the first group, 68 patients received CRT, and in the second, 97 patients received RT alone. The Cox proportional hazards model was used to assess the factors which had an impact on survival while controlling for known prognostic factors. The ethics committee of Rajavithi Hospital reviewed and approved this study.*

Results: *There was an overall survival (OS) rate of 1 year (1 year OS) in 27% of cases, and 2 years (2 years OS) in 15.4% of cases with a median overall survival rate of 7.63 months (7.63 OS) (95% CI 6.99-8.27). The mean follow-up time was 7.34 months with maximal follow-up time of 41.77 months and minimal follow-up time of 0.2 months (6 days). Patients who received chemotherapy had better overall survival rates than those who had no chemotherapy with 1 year OS of 52% vs. 9.5%, 2 years OS of 36.7% vs. 1.5%, and median OS of 13.17 vs. 5.4 months, p<0.001. However, no significant difference for median survival was observed among three different chemotherapy regimens with median OS of 11-13 months but chemotherapy group had significant difference from no chemotherapy group with median OS of 5.40 months (4.59-6.21).*

Conclusion: *Concurrent chemo-radiation (CRT) should be used as the standard treatment in patients who are medically fit. A Cisplatin or Carboplatin weekly regimen can be used as an alternative to a Cisplatin three-weekly regimen. Site of primary tumor, N-stage, recurrent tumor, low RT dose (below 70 Gy), and co-morbidity (with impaired renal or liver function) are significant predictors of overall survival.*

Keywords: *Chemoradiation, Radiation oncology, Survival rate, Head and Neck cancer*

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Squamous cell carcinoma of the head and neck affects 550,000 new patients worldwide annually and is considered to be the sixth most common cancer in the world. The majority of head and neck cancer patients (60-70%) present at the locally advanced stage (stage III, IV)[1], and these patients have a poor prognosis. About 50-60% of newly diagnosed patients develop recurrent tumors within 2 years and 20% of patients develop distant metastasis with a median survival time of less than 1 year[1]. Treatment for early stage (stage I, II) is single modality treatment, either surgery or radiation (RT) alone. Treatment for locally advanced (stage III, IV) is multimodality treatment such as surgery plus RT for resectable cancers. RT alone is insufficient for locally advanced cases; therefore, concurrent chemo-radiation (CRT) plays an important role in treatment of unresectable cancer. Concurrent chemo-radiation (CRT) is now accepted as the standard treatment for locally advanced head and neck cancer if the patient is medically fit[2]. Wedsley and Bentzen[3,4] have concluded that a 10% increase in 2-year local control rates equates to a 6.7% increase in overall survival.

The Meta-Analysis of Chemotherapy on Head and Neck Cancer (MACH-NC) showed that adding chemotherapy to RT in both definitive and adjuvant postoperative settings resulted in a 12% reduction in the risk of death from squamous cell carcinoma of the head and neck (SCCHN), corresponding to an absolute improvement of 4% in 5-year survival compared with

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RT alone[5,6].

A systemic review by Browman et al[7] pooled analysis of 18 RCTs and detected a reduction in mortality where CRT was used compared with RT alone. The survival benefit associated with adding chemotherapy to RT was 8% at 5 years, mainly due to an improvement in the loco-regional control, and had only a marginal effect on distant metastasis. A study by Adelstein et al[8] of 295 patients with locally advanced unresectable SCCHN showed a survival benefit in the CRT arm with 3 year OS of 37% compared with 23% in the RT alone arm. In the GORTEC 94-01 study of 226 patients with advanced oropharyngeal cancers (stage III and IV), CRT patients were found to have three-year survival compared with those treated with RT (51 vs. 31%). Patients with CRT had a disease-free survival rate of 42%, compared with 20% for RT. Loco-regional control in CRT patients was higher than in those with RT alone (66 vs. 42%); however, CRT had more grade 3 and 4 mucositis and hematologic toxicity[9,10].

Adelstein (2003)[8] reported that in the CRT group, the addition of high-dose, single-agent Cisplatin to conventional single-daily fractionated RT significantly improved survival; however, it also increased toxicity, so patient selection for CRT is crucial, as is adequate supportive care. Co-morbidity, which caused impaired renal function or liver function, played an important role in determination of treatment[11].

This retrospective cohort study attempted to analyze the survival benefits of CRT and to select the proper treatment for patients with locally advanced, unresectable head and neck cancers.

Objective

To compare survival rates of treatment by CRT and RT alone in locally, advanced unresectable head and neck cancers, and to assess factors associated with survival.

Material and Method

A retrospective cohort study was conducted of 165 patients treated for locally advanced head and neck cancers (Stage III, IV) at the Department of Radiation Oncology, Rajavithi Hospital from 1 January 2011 to 31 December 2013. Inclusion criteria were squamous cell carcinoma at oral cavity, oropharynx, larynx, or hypopharynx stage III, IV, with complete treatment as planned. Exclusion criteria were patients who: had received previous surgery or chemotherapy; had had incomplete treatment; had more than one primary cancer; or had distant metastasis. Patients were divided into two groups: 68 received CRT and 97 patients received RT alone. Medical records from RT charts were reviewed, together with corrected data including age, sex, site of primary tumor, TNM staging, performance status, comorbidity (such as DM, HT, renal disease, liver disease), radiation technique and dose, chemotherapy regimen, and results of treatment. All baseline characteristics were analyzed using the log-rank test, and stepwise analysis was performed to identify prognostic factors. This study was approved by the ethics committee of Rajavithi Hospital.

Statistical analysis

All analyses were performed with the statistical program SPSS version 17.0. Data were presented as mean, standard deviation (SD), minimum, and maximum for continuous variables, and number (%) for categorical variables. The Kaplan-Meier method was used to generate survival curves and calculate 1- and 2-year overall survival rates, and the log-rank test was used to test for survival differences. Multivariate analysis was performed using the Cox proportional hazards model to assess the factors, which had an impact on survival while controlling for known prognostic factors. A *p*-value of less than 0.05 was set for statistical significance for all tests.

Results

Patient characteristics

The 165 patients were divided into a CRT group of 68 patients and a RT alone group of 97 patients. All baseline characteristics are shown in Table 1. All patients were treated with conventional one daily fraction using a linear accelerator (LINAC) with 6mV photon and electron beam.

Overall survival rates

The total of 165 patients had 1-year overall survival rate (1yr OS) of 27%, 2 yr OS of 15.4%, and median OS of 7.63 months (95% CI, 6.99-8.27 months). The minimal follow-up time was 0.2 months (6 days), the maximal follow-up time was 41.77 months, and the mean follow-up time was 7.34 months. Gender had no significant effect on overall survival. Site of primary tumor had a significant impact on overall survival, and CA Oropharynx had the best prognosis with median OS 8.93 months (95% CI, 7.47-10.39 months). TNM staging had a significant effect on overall survival: T1 had the best prognosis with 1 year OS 77.8%, 2 year OS 64.8%, median OS 34.67 months (95% CI, 9.54-59.73

Table 1. Baseline characteristics

Characteristics	Number	Percent
Sex		
Male	142	86.1
Female	23	13.9
Age (years)		
Mean ± SD	58.20±10.42 (range 36-91)	
Diagnosis		
CA oral	21	12.7
CA oropharynx	80	48.5
CA larynx	27	16.4
CA hypopharynx	37	22.4
Stage T		
1	9	5.5
2	37	22.4
3	42	25.5
4	77	46.7
Stage N		
1	52	31.5
2	78	47.3
3	35	21.2
Stage		
3	29	17.6
4	136	82.4
Comorbidity	118	71.5
RT planning		
Low dose	69	41.8
300cGy*10F	41	24.8
400cGy*5F	22	13.3
200cGy*25F	6	3.6
High dose (200cGy*35F)	96	58.2
Chemotherapy		
No chemotherapy	97	58.8
Chemotherapy	68	41.2
Carboplatin 150 mg	24	14.5
Cisplatin 40 mg/m^2	19	11.5
Cisplatin 100 mg/m^2	25	15.2
Cycles of chemotherapy (n = 68)		
Chemotherapy <5 cycles	35	51.5
Chemotherapy ≥5 cycles	33	48.5
Response RT group		
Complete response	38	23.0
Partial response	127	77.0
Recurrent tumor		
No	33	20.0
Yes	132	80.0
Local	76	57.6
Distant metastasis	56	42.4

months), and N1 had the best prognosis with 1 year OS 41.1%, 2 year OS 24.9%, and median OS 10.27 months (95% CI, 8.79-11.74 months). M0 had 1 year OS 28.1%, 2 year OS 16.5%, median OS 7.67 months (95% CI, 7.00-8.33 months). Stage IV had 1 year OS 20.5%, 2 year OS 11.6%, and median OS 6.97 months (95% CI, 6.02-7.92 months). Patients with co-morbidity had lower overall survival rates than those without it, with 1 year OS 21.9 vs. 40.1%, 2 year OS 8.0 vs. 33.9%, median OS 7.10 months (95% CI, 5.80-8.39 months) vs. 10.50 months (95% CI, 8.68-12.32 months). Patients who received a high RT dose had better overall survival rates than those with low RT doses, with 1 year OS 43.7 vs. 4.3%, 2 year OS 26.3 vs. 0%, median OS 10.73 vs. 4.30 months, p<0.001. Advanced techniques such as 3D and IMRT had better overall survival rates than 2D treatment (median OS 13.57 vs. 5.83 months, p<0.001).

Patients who received chemotherapy had

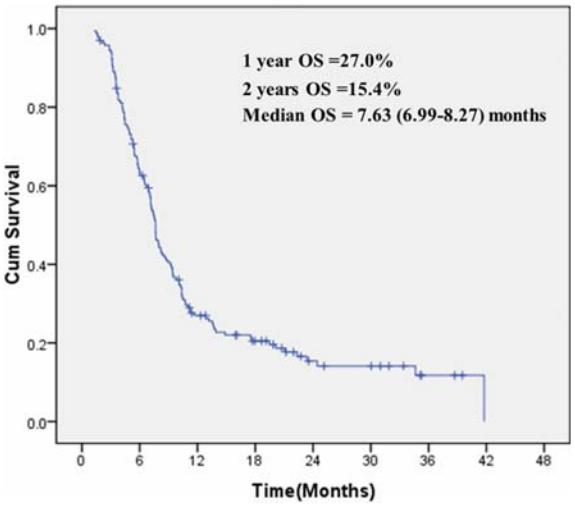

Fig. 1 Kaplan-Meier overall survival curve.

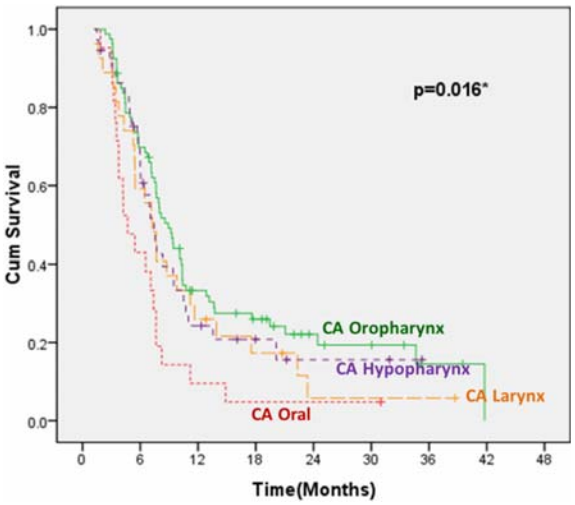

Fig. 2 Kaplan-Meier overall survival curves for sites of primary tumor.

better overall survival than those who had no chemotherapy with 1 year OS 52 vs. 9.5%, 2 year OS 36.7 vs. 1.5% and median OS 13.17 months (95% CI, 7.30-19.03 months) vs. 5.4 months (95% CI, 4.59-6.21 months). There was no statistical significance between 3 different chemotherapy regimens with median OS between 11-13 months; however, a significant difference was found between OS of patients who received chemotherapy and those who did not. Patients who received chemotherapy of less than 5 cycles had the highest median OS of 11.63 months compared to those who received more than 5 cycles (7.36 months) and no chemotherapy (5.40 months).

With regard to response to treatment, there was a significant difference in survival rates between patients with complete response and those with partial response, with median OS more than 41.77 months vs. 6.5 months. Patients with local recurrence had lower overall survival rates than those with no recurrent tumor, with 1 year OS 17.8%, 2 year OS 4.7%, median OS 7.63 months (95% CI, 7.10-8.20 months). Patients with distant metastasis had the worst prognosis with 1 year OS 7.1%, 2 year OS 0%, median OS 5.77 months (95% CI, 4.83-6.70 months). Patients without tumor recurrence had the best prognosis with 1 year OS 89.8%, 2 year OS 81.2%, and median OS of more than 39.5 months.

Multivariate analysis of overall survival rates

Univariate analysis showed that factors associated with overall survival with *p*-value <0.05 were

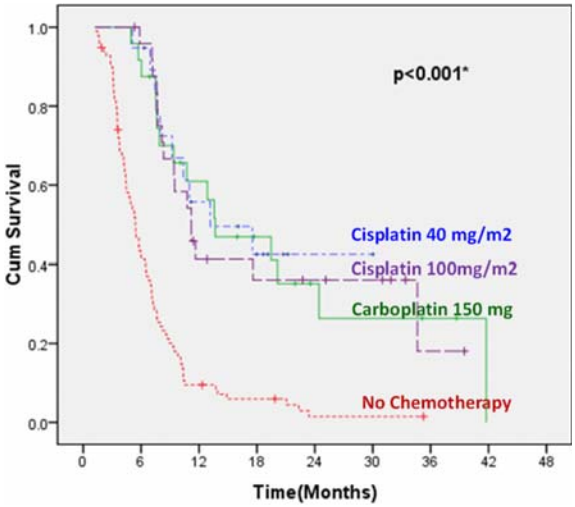

Fig. 3 Kaplan-Meier overall survival curves of chemotherapy regimens.

Table 2. Multivariate analysis of overall survival

Factors	Crude HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value
Diagnosis				
CA oropharynx	1		1	
CA oral	2.25 (1.35-3.74)	0.002	2.38 (1.36-4.15)	0.002
CA larynx	1.34 (0.83-2.15)	0.227	0.52 (0.30-0.91)	0.022
CA hypopharynx	1.22 (0.78-1.91)	0.390	0.85 (0.52-1.38)	0.512
Stage tumor				
T1 + T2	1		1	
T3	1.85 (1.13-3.04)	0.015	1.24 (0.73-2.12)	0.422
T4	3.23 (2.07-5.05)	<0.001	1.38 (0.82-2.33)	0.230
Stage node				
N1	1		1	
N2	2.00 (1.32-3.02)	0.001	1.62 (1.02-2.56)	0.039
N3	2.32 (1.42-3.80)	0.001	1.63 (0.94-2.81)	0.079
Recurrence				
No recurrence	1		1	
Local	13.69 (5.49-34.17)	<0.001	17.16 (6.50-45.28)	<0.001
Metastasis	22.37 (8.75-57.19)	<0.001	18.48 (6.77-50.47)	<0.001
RT low dose	6.48 (4.44-9.47)	<0.001	4.75 (2.65-8.51)	<0.001
No chemotherapy	6.49 (4.44-9.47)	<0.001	1.35 (0.79-2.31)	0.271
Comorbidity	4.09 (2.80-5.99)	<0.001	2.19 (1.39-3.44)	0.001

Significant at *p*-value <0.005

site of primary tumor (CA oral cavity), T-stage (T3, T4), N-stage (N2, N3), recurrent tumor, low RT dose, no chemotherapy, and comorbidity. Stepwise multivariate analysis of prognostic factors showed that factors with *p*-value <0.05 were site of primary tumor, N-stage, recurrent tumor, low RT dose, and comorbidity.

Site of primary tumor was the most significant prognostic factor (*p*-value = 0.002), and CA oral cavity had the worst overall survival rate (HR = 2.38, 95% CI 1.36-4.15) when compared with CA Oropharynx. CA Larynx cases had a shorter overall survival than CA Oropharynx (HR = 0.52, 95% CI 0.30-0.91, *p*-value = 0.022). N-stage was also a prognostic factor (*p*-value = 0.039), and N2 had lower survival rates than N1 (HR = 1.62, 95% CI 1.02-2.56). Another prognostic factor was a recurrent tumor (*p*-value <0.001), and patients with distant metastasis had a higher risk of death than those with no recurrent tumor (HR = 18.48, 95% CI 6.77-50.47). Patients with local recurrence had significantly lower survival rates than those with no recurrent tumor (HR = 17.16, 95% CI 6.50-45.28), and patients with low RT dose had worse survival rates than those who received high RT dose (200cGy x35F), *p*-value <0.001 with HR = 4.75, 95% CI 2.65-8.51). Cases of co-morbidity had significantly shorter survival rates than ones with no co-morbidity (HR = 2.19, 95% CI 1.39-3.44).

Discussion

A total of 165 patients were treated for locally advanced head and neck cancers (Stage III, IV): 68 received CRT and 97 had RT alone. The most common primary tumor was CA Oropharynx. As found in the American study of Das LC et al, the increasing incidence of CA Oropharynx is associated with the Human papilloma virus (HPV) infection. The US cancer registry revealed an elevation in the incidence of HPV-positive Oropharynx SCCA, from 16.3% (in years 1984-1989) to 71.7% (in years 2000-2004); however, the prevalence of non-oropharyngeal cancer has not risen; in fact, it is showing a downward trend, possibly secondary to the fall in tobacco use. HPV positivity is a positive prognostic factor for improved overall survival, progression-free survival and responsiveness to CRT[12]. The present study showed that CA Oropharynx had the best overall survival rate when compared with CA Larynx and CA Hypopharynx, while CA Oral cavity had the shortest overall length of survival. Most of our patients were in stage IV of the disease (T4 and N2 were the most common stages); consequently, the results of treatment were poor with median OS of less than 1 year. Univariate analysis showed that T4 had HR 3.23 compared with T1, but in multivariate analysis, T-stage was not significant, and N-stage had more effect on overall survival. N-stage was a prognostic factor (*p*-value = 0.039), and N2 had lower survival rates than N1 (HR = 1.62, 95% CI 1.02-2.56). The author found that these results were compatible with a study by Brockstein and Vokes (2011)[13,14]. The prognostic factors, which affected survival in locally, advanced head and neck cancers treated with CRT, were T-stage and N-stage. T4 is associated with loco-regional recurrence and N3 is associated with distant metastasis, resulting in poor prognosis. An Indian study by Gupta et al (2009)[15], found that site of primary tumor, TNM staging, and choice of treatment were prognostic factors which had an impact on loco-regional control and disease-free survival. Recurrent tumors had a negative effect on survival: patients with metastasis had HR 18.48 and those with local recurrence had HR 17.16 compared with patients who had no recurrent tumor. Aldelstein et al[16] showed that failure of treatment is due to local recurrence and metastasis, resulting in poor overall survival. Adding chemotherapy to RT can prolong survival. Patients with low RT doses (below 70Gy) had shorter overall survival than those who received high RT doses, with HR 4.75, and a high RT dose of 70Gy (200cGy in 35 fractions) resulted in the best survival rates. The most widely used dose is 70Gy with 3D conformal RT or the Intensity Modulated Radiotherapy (IMRT) technique. IMRT should be used to reduce the exposure of normal tissue to radiation while preserving excellent dose coverage to the target volume; thereby, the rate of late toxicity, especially of xerostomia, is minimized.

Patients with co-morbidity (with impaired renal or liver function) had lower rates of overall survival than those without it (HR 2.19) because they had poor performance status and could not tolerate the side effects of combined chemotherapy and radiation.

Patients treated with CRT had better overall survival than those who did not received chemo-therapy, with HR 6.49. MACH-NC concluded that the addition of chemotherapy to RT resulted in 4.5% absolute benefit in survival and reduced the HR by 12% (*p*<0.0001). The author of the present study found that there was no statistically significant difference in overall survival among the three chemotherapy regimens with median OS 11-13 months; however, a significant difference in OS was found between patients who had chemotherapy and those who did not, and patients who received no chemo-

therapy had median OS of only 5.4 months. The author prefers Carboplatin 150 mg IV or Cisplatin 40 mg/m^2 weekly to Cisplatin 100 mg IV every 3 weeks because it results in lower toxicity; furthermore, patients can be treated on an outpatient basis (OPD case), with no need for admission, and this is suitable for limited-resource settings. Meta-analysis reviews have shown that the most widely used standard regimen is Cisplatin 100 mg/m^2 every 3 weeks combined with RT dose of 70 Gy. This regimen, however, causes severe toxic effects (such as nephrotoxicity, ototoxicity, neurotoxicity, nausea and vomiting); therefore, it is suitable only for patients who have normal renal function and a good performance status, so an alternative regimen should normally be used to limit toxic side effects. Gupta et al (2009)[15] concluded that radical radiotherapy with concurrent weekly Cisplatin had moderate efficacy and an acceptable level of acute toxicity with the potential to be an optimal regimen in loco-regionally advanced head and neck cancers, particularly in limited-resource settings. Stage grouping, primary site, and treatment intensity are important determinants of outcome. A study by Calais et al[9], found that the use of CRT with Carboplatin plus 5-FU instead of Cisplatin plus 5-FU decreased the toxicity of treatment. Carboplatin has few nephrotoxic, gastrointestinal toxic, and neurotoxic side effects, but results in some hemato toxicity. A Jeremic study[17] revealed that single-agent Carboplatin-based CRT had a favorable toxicity profile for locally advanced head and neck cancer, and this regimen is usually used in combination with Paclitaxel. The addition of chemotherapy to RT in patients over the age of 70 did not translate into survival benefit. Multi-agent chemotherapy did not provide a significant benefit over single-agent Cisplatin in the concurrent setting.

Concurrent Biotherapy (Cetuximab) and RT is a new alternative standard treatment especially for older people or patients with poor performance status. Further studies should be conducted to compare survival rates of concurrent CRT and bioradiotherapy.

Conclusion

CRT had a greater survival benefit than RT alone in the treatment of locally advanced head and neck cancers; however, it resulted in increased toxicity. CRT should be used as the standard treatment in patients who are medically fit. A weekly regimen of Cisplatin or Carboplatin can be used as an alternative treatment to a Cisplatin three-weekly regimen. Site of primary tumor, N-stage, recurrent tumor, low RT dose (below 70Gy), and comorbidity (with impaired renal or liver function) are significant predictors of overall survival.

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What is already known on this topic ?

Concurrent chemoradiation (CRT) is now considered the standard treatment for locally advanced head and neck cancers. Survival benefit of adding chemotherapy to radiation was mainly due to improvement of loco-regional control and some effect on distant metastasis. No definitive chemotherapy regimen was identified. The most widely used regimen is cisplatin every three weeks but has many toxic effects.

What this study adds ?

Prognostic factors effect overall survival are the site of the primary tumor, N-stage, recurrent tumors, low radiation doses and co-morbidity. A weekly regimen of cisplatin of comboplatin can be used as alternative regimen to a three-weekly cisplatin regimen with comparable survival.

Potential conflict of interest

None

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อัตราการรอดชีพระหว่างกลุ่มที่ได้รับการฉายรังสีร่วมกับเคมีบำบัดกับกลุ่มที่ได้รับการฉายรังสีอย่างเดียวในการรักษาผู้ป่วยมะเร็งศีรษะและลำคอระยะลุกลามเฉพาะที่ไม่สามารถผ่าตัดได้ในโรงพยาบาลราชวิถี

สิริมา เอื้อศรีธนากร

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบอัตราการรอดชีพของผู้ป่วยกลุ่มที่ได้รับการรักษาด้วยการฉายรังสีร่วมกับเคมีบำบัดกับผู้ป่วยกลุ่มที่ได้รับการฉายรังสีอย่างเดียวในมะเร็งศีรษะและคอระยะลุกลามเฉพาะที่ ซึ่งไม่สามารถผ่าตัดได้และศึกษาปัจจัยซึ่งมีผลต่ออัตราการรอดชีพ*

วัสดุและวิธีการ: *เป็นการศึกษาแบบย้อนหลัง Retrospective cohort analysis ในผู้ป่วยโรคมะเร็งศีรษะและคอระยะลุกลามเฉพาะที่ (ระยะที่ 3, 4) ซึ่งไม่สามารถผ่าตัดได้ที่มารักษาด้วยการฉายรังสีที่แผนกรังสีรักษาโรงพยาบาลราชวิถี ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2554 ถึง 31 ธันวาคม พ.ศ. 2556 จำนวนทั้งหมด 165 คน โดยแบ่งเป็นกลุ่มที่ได้รับการฉายรังสีร่วมกับเคมีบำบัด 68 คน และกลุ่มที่ได้รับการฉายรังสีอย่างเดียว 97 คน สถิติเชิงวิเคราะห์ใช้ Cox's proportion Hazards Model เพื่อหาค่า hazard ratio (HR) และปัจจัยที่สัมพันธ์กับการรอดชีพ งานวิจัยนี้ผ่านการพิจารณาจากคณะกรรมการวิจัยและจริยธรรมการวิจัย โรงพยาบาลราชวิถี*

ผลการศึกษา: *ผู้ป่วยทั้งหมด 165 คน มีอัตราการรอดชีพที่ 1 และ 2 ปี เท่ากับ 27% และ 15.4% และค่ามัธยฐานการรอดชีพของผู้ป่วยคือ 7.63 เดือน (95% CI 6.99-8.27) โดยมีระยะเวลามาตรวจรักษาเฉลี่ย 7.34 เดือน (มากที่สุด 41.77 เดือน, น้อยที่สุด 6 วัน) กลุ่มที่ได้รับเคมีบำบัดร่วมกับการฉายรังสีมีการรอดชีวิตดีกว่าไม่ได้เคมีบำบัดโดยมีอัตราการรอดชีพที่ 1 ปี 52 vs. 9.5%, อัตราการรอดชีพที่ 2 ปี 36.7 vs. 1.5%, ค่ามัธยฐานการรอดชีพคือ 13.17 เดือน (7.30-19.03) vs. 5.4 เดือน (4.59-6.21) สูตรยาเคมีบำบัดทั้ง 3 สูตร มีค่ามัธยฐานการรอดชีพไม่แตกต่างกันคือประมาณ 11-13 เดือน แต่มีการรอดชีพต่างจากกลุ่มที่ไม่ได้เคมีบำบัดอย่างมีนัยสำคัญ ซึ่งมีค่ามัธยฐานการรอดชีพ 5.40 เดือน (4.59-6.21)*

สรุป: *การให้เคมีบำบัดร่วมกับการฉายรังสีถือเป็นการรักษาที่เป็นมาตรฐานและควรเลือกใช้ในผู้ป่วยที่มีสภาพร่างกายดีพอ ที่จะรับผลข้างเคียงจากการรักษาที่มากขึ้น การให้ยาเคมีบำบัดสูตร Cisplatin หรือ Carboplatin ฉีดทุกสัปดาห์สามารถใช้เป็นทางเลือกแทนยาเคมีสูตร Cisplatin ทุกสามสัปดาห์ ปัจจัยที่มีผลกับการรอดชีพ ได้แก่ ตำแหน่งมะเร็ง, Stage Node, การกลับเป็นซ้ำของโรคมะเร็ง, ปริมาณรังสีที่ได้รับ (น้อยกว่า 70Gy) และการมีโรคร่วม (ที่มีผลการทำงานของไตหรือตับบกพร่อง)*