



PROGNOSTIC FACTORS OF RADIATION-INDUCED BRAIN NECROSIS AFTER RADIOTHERAPY IN NASOPHARYNGEAL CARCINOMA

P805

Henry WC Leung* ¹, Shyh-Yau Wang ²

¹Radiation Oncology, ² Radiation , An Nan Hospital, China Medical University, Tainan, Taiwan.

INTRODUCTION

Radiation-induced brain necrosis (RIBN) is a late life-threatening complication appeared after treatment in patients with nasopharyngeal carcinoma (NPC). Although its incidence has decreased with the widespread use of intensity-modulated radiation therapy (IMRT), early detection of RIBN in patients before any serious and irreversible damage occurs is essential and prolongs their survival. However, research reports in this area are limited.

AIM

We aim to examine the incidence of RIBN and explore the major prognostic factors and preventive strategies in order to provide radiation oncologist with an evidence to ensure treatment quality.

METHOD

First, we identified a cohort of HNC patients from the catastrophic illness patient dataset of Taiwan National Health Insurance Research Database (NHIRD) using ICD-9 or ICD-10 to investigate the incidences of radiotherapy induced brain necrosis and its risk factors among NPC patients between January 2005 and December 2018. The incidence and hazard ratios were quantified using Cox proportional hazards models. Second, we identified published literature from PubMed using MeSH terms of RIBN and prognostic factors of RIBN from 2015 to 2022.

RESULTS

We identified 435 and 359 patients who had received radiotherapy and who did not receive radiotherapy. Among them, patients who received radiotherapy had a significantly increased risk of brain necrosis compared with patients who did not receive radiotherapy (HR=1.29; 95% CI: 1.11-1.50, p< 0.001). Multivariate logistic regression models showed that male patients aged 20-59 years, with grade 1 and 2 tumors, or with a follow-up period of more than 6 years, were associated with a significantly increased risk of RIBN (Table 1). During the 6-year follow-up period, there was no significant difference in the cumulative incidence of RIBN between the two groups (Fig 1A). Patients who received radiotherapy had a significantly lower overall mortality rate than those who did not (Fig 1B).

Three published literatures were identified as appropriated literatures after searching and appraisal. From the literatures, we believe that brain magnetic resonance imaging (MRI) is the best technique used to detect human white matter abnormalities in NPC patients. In addition, our study showed that hyperlipidemia, hypertension, and higher cumulative incidence of RIBN were significantly associated with radiotherapy in patients who received radiotherapy after 5 years of follow-up. This result is consistent with recently published findings that hyperlipidemia and hypertension, as well as the interval between radiotherapy and RIBN, are significant prognostic factors of RIBN.

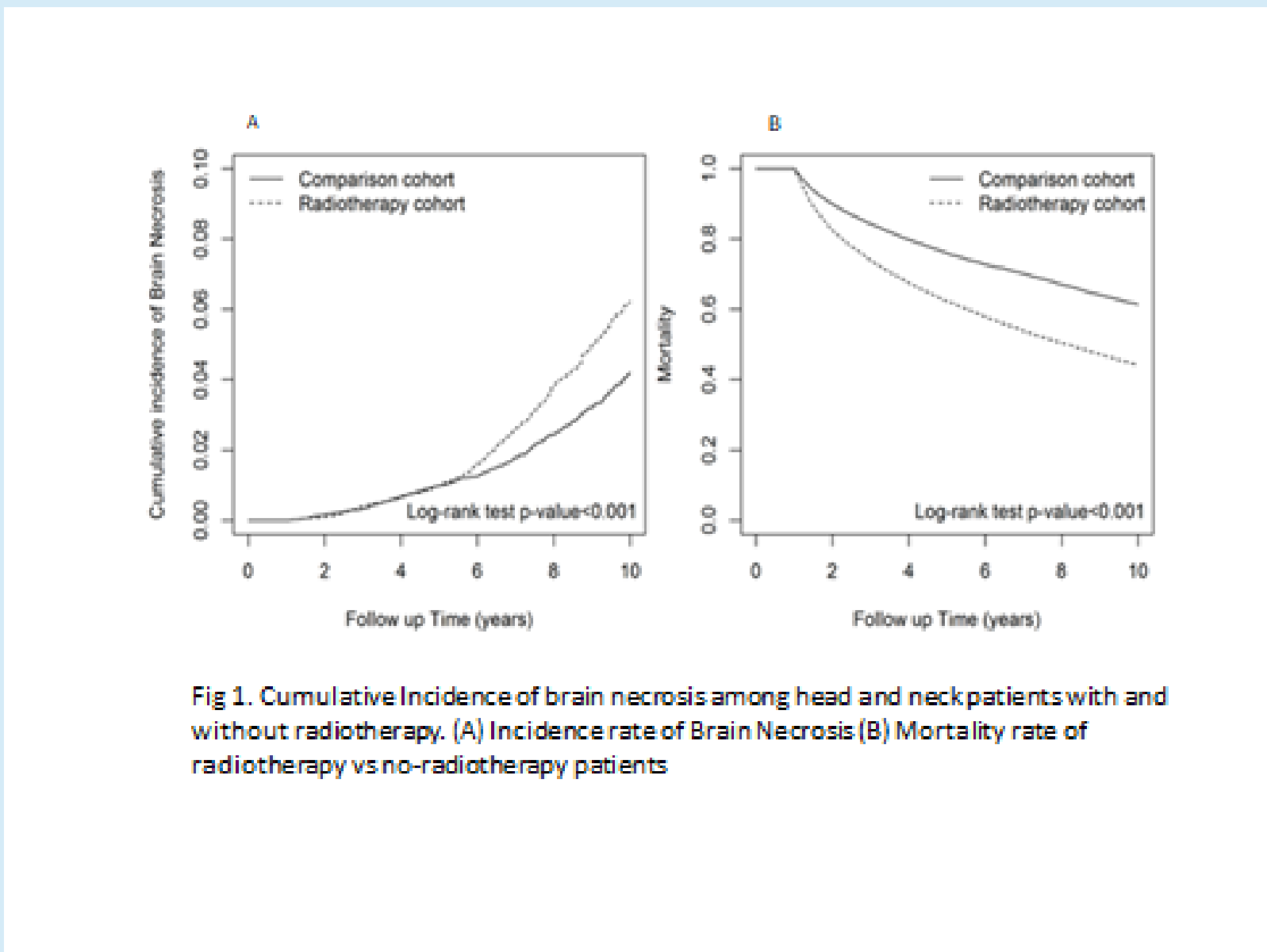


Table 1. Comparison of RIBN risks in radiotherapy and non-radiotherapy groups associated with all covariates

Covariate	Brain Necrosis						dHR	(95% CI)	p-value	aHR	(95% CI)	p-value
	No N	Yes PY	IR	No N	Yes PY	IR						
Sex												
female	57	18755.69	3.04	67	17455.39	3.84	1.31	(0.92, 1.86)	0.134	1.10	(0.75, 1.62)	0.615
male	302	95815.41	3.15	568	84685.92	4.35	1.50	(1.29, 1.75)***	<0.001	1.32	(1.13, 1.56)***	<0.001
Age, year												
20-59	210	79025.02	2.66	293	70230.55	4.17	1.69	(1.42, 2.02)***	<0.001	1.47	(1.22, 1.78)***	<0.001
60+	149	35546.08	4.19	142	31910.76	4.45	1.15	(0.91, 1.44)	0.244	1.04	(0.81, 1.32)	0.771
Primary site												
Oropharynx/Larynx/Oesophagus	3	2324.08	1.29	20	4231.31	4.74	3.33	(0.99, 11.21)	0.053	2.87	(0.93, 9.87)	0.095
Nasopharynx	19	4556.60	4.36	92	18057.11	5.09	0.87	(0.53, 1.43)	0.586	0.89	(0.54, 1.47)	0.651
Hypopharynx	3	930.28	3.22	15	3540.12	4.24	1.25	(0.36, 4.30)	0.729	1.24	(0.35, 4.35)	0.742
Other	334	106960.13	3.12	308	76522.78	4.04	1.33	(1.14, 1.56)***	<0.001	1.31	(1.12, 1.53)***	<0.001
Comorbidity												
Hypertension	131	31811.07	4.12	150	28530.72	5.26	1.35	(1.07, 1.71)**	0.011	1.18	(0.91, 1.51)	0.207
Cerebrovascular events	4	981.00	4.08	5	987.25	5.06	1.46	(0.39, 5.48)	0.573	1.00	(0.21, 4.83)	0.996
Hyperlipidemia	190	42853.58	4.43	205	38247.29	5.36	1.29	(1.06, 1.57)**	0.012	1.16	(0.94, 1.43)	0.170
Coronary artery disease	81	17728.01	4.57	75	15864.75	4.73	1.10	(0.80, 1.50)	0.556	0.94	(0.67, 1.31)	0.701
Atrial Fibrillation	13	980.87	13.25	3	1023.80	2.90	0.23	(0.06, 0.79)**	0.020	0.17	(0.04, 0.68)**	0.013
Myocardial infarction	5	1452.45	3.44	5	1183.13	4.23	1.50	(0.43, 5.21)	0.528	0.59	(0.12, 2.99)	0.525
Peripheral artery disease	6	1475.87	4.07	8	1317.60	6.07	1.82	(0.63, 5.27)	0.272	1.58	(0.43, 5.83)	0.491
Smoking	15	4024.76	3.73	17	3516.84	4.83	1.46	(0.73, 2.89)	0.282	1.62	(0.78, 3.39)	0.197
The Charlson comorbidity index, CG												
0-2	245	84411.51	2.94	322	75796.84	4.25	1.56	(1.33, 1.85)***	<0.001	1.37	(1.15, 1.64)***	<0.001
3+	111	30159.59	3.68	113	26344.48	4.29	1.25	(0.96, 1.63)	0.091	1.10	(0.83, 1.45)	0.509
Tumor Grade												
1	31	15579.88	1.99	35	8986.53	3.89	1.83	(1.13, 2.97)**	0.014	1.59	(0.96, 2.63)	0.073
2	54	21076.33	2.56	105	26450.83	3.89	1.50	(1.08, 2.08)**	0.016	1.47	(1.08, 2.06)**	0.022
3	9	3492.18	2.58	21	8749.98	2.40	0.87	(0.40, 1.90)	0.728	0.80	(0.35, 1.82)	0.592
4	17	3125.61	5.39	71	12443.13	5.71	0.77	(0.45, 1.31)	0.336	0.75	(0.43, 1.28)	0.291
9	248	71267.08	3.48	205	45510.84	4.50	1.33	(1.10, 1.60)***	0.003	1.27	(1.05, 1.54)**	0.012
Follow-up interval												
<5 years	165	88261.59	1.87	174	81239.71	2.14	1.20	(0.97, 1.48)	0.098	0.89	(0.71, 1.12)	0.333
5+ years	194	26509.51	7.37	240	20901.60	12.49	1.70	(1.43, 2.01)***	<0.001	1.67	(1.38, 2.03)***	<0.001

Remarks: PY, person-year; IR, Incidence rate, per 1000 persons/years; dHR, Crude Hazard ratio; aHR, Adjusted Hazard Ratio; significant P<0.05*

CONCLUSIONS

RIBN is a late complication with low incidence but still worth of attention. We suggest that early detection with brain MRI and early treatment as well as a short term close imaging follow-up at the beginning of the treatment until the lesion appears, are effective ways to prevent the occurrence of RIBN and improve patient safety.

Acknowledgement

We acknowledge with thanks to An-nan Hospital, China medical University for sponsorship.

REFERENCES

1. Yang X, Ren H, Fu J. Treatment of Radiation-Induced Brain Necrosis. Oxid Med Cell Longev . 2021 Dec 24; 2021:4793517
2. Cai J, Cheng J, Li H, et al. A nomogram for the prediction of cerebrovascular disease among patients with brain necrosis after radiotherapy for nasopharyngeal carcinoma. Radiother Oncol. 2019 Mar;132:34-41.

CONTACT INFORMATION

1. WC Leung. Email: 070506@tool.caaumed.org.tw