



It is time to take action to prevent cardiovascular disease in postirradiation head and neck cancer patients

Yu Chun Yeh¹ · Kai Min Fang² · Wan-Lun Hsu³ · Li-Jen Liao^{2,4,5}

Received: 25 May 2019 / Accepted: 29 May 2019 / Published online: 10 June 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Keywords Head and neck cancer · Irradiation · Cardiovascular disease · Statistical issues

Dear Editor,

Regarding our recent publication about the role of ultrasound measurement of carotid intima-media thickness in head and neck cancer survivors [1], we thank the readers for reminding us of the possibility of estimation bias and sparse data bias and suggesting some methods of avoiding these types of bias. As suggested, we performed bootstrapping analysis of our original data, and we showed the results of 1000-sample bootstrapping for the β -coefficients of multivariate linear regression in Table 1. The coefficient is 0.129 (95% CI 0.054–0.204) for irradiation related to mean carotid intima-media thickness (CIMT), with the theory of regression to

the mean. After repeated bootstrapping analysis, we believe the results further support our hypothesis.

Due to the limitations of a small sample size, we found large odds ratios (ORs). We further used Firth penalization to recheck the odds ratios for significant variables identified in multivariate logistic regression analysis; the original published regression analysis results were compared to the new results after Firth penalization in Table 2. We found that the OR for developing cardiovascular disease (CVD) after irradiation in patients with an abnormal mean CIMT (≥ 1.0 mm, which indicates a risk of developing CVD) is slightly different from the original published value; the new OR is 7.53 (95% CI 1.36–41.81); however, the positive OR still supports our hypothesis that irradiation to the neck is an independent risk factor for CVD.

As mentioned in our publication, some previous studies reported that irradiation for HNC wound-induced extracranial carotid stenosis was associated with an increased CVD risk [2–5].

Overall, our results and related published studies support that irradiation to the neck is positively related to CIMT and

This comment refers to the article available at <https://doi.org/10.1007/s00405-019-05302-1>.

✉ Li-Jen Liao
liao1j@ntu.edu.tw; deniro@mail2000.com.tw

Yu Chun Yeh
rambleurban@gmail.com

Kai Min Fang
u701048@gmail.com

Wan-Lun Hsu
lun0112@ms26.hinet.net

¹ Department of Family Medicine, Far Eastern Memorial Hospital, New Taipei, Taiwan

² Department of Otolaryngology Head and Neck Surgery, Far Eastern Memorial Hospital, No. 21, Sec. 2, Nanya S. Rd., Banqiao Dist., New Taipei 220, Taiwan ROC

³ Genomics Research Center, Academia Sinica, Taipei, Taiwan

⁴ Department of Electrical Engineering, Yuan Ze University, Taoyüan, Taiwan

⁵ Biomedical Engineering Office, Far Eastern Memorial Hospital, New Taipei, Taiwan

Table 1 Results of 1000-sample bootstrapping for the β -coefficients of multivariate linear regression

Risk factors	β -Coef. (95% CI)	P value
Age	0.006 (0.004 to 0.008)	0.001
BW	0.003 (0.001 to 0.005)	0.011
HTN	0.107 (0.024 to 0.179)	0.017
DM	– 0.079 (– 0.215 to 0.079)	0.237
Hyperlipidemia	– 0.012 (– 0.145 to 0.131)	0.845
Smoking	– 0.023 (– 0.127 to 0.107)	0.688
Irradiation	0.129 (0.054 to 0.204)	0.001

β -coef. β coefficient, 95% CI 95% confidence interval, BMI body mass index, HTN hypertension, DM diabetes mellitus

Table 2 Results of original published regression analysis (left two columns) compared to the results after Firth penalization

	Univariate		Multivariate		Multivariate (Firth penalization)	
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Age	1.06 (1.01–1.12)	0.019	1.07 (0.99–1.16)	0.077	1.06 (1.00–1.14)	0.071
Weight	1.07 (1.01–1.13)	0.016	1.09 (1.01–1.18)	0.027	1.07 (1.01–1.14)	0.03
Smoking	1.36 (0.16–11.93)	0.779	0.22 (0.02–2.93)	0.252	0.30 (0.03–2.79)	0.287
Irradiation	24.75 (2.98–205.52)	0.003	13.50 (1.48–122.81)	0.021	7.53 (1.36–41.81)	0.021

95% CI 95% confidence interval

could be a risk factor for CVD. We suggest that head and neck surgeons and oncologists should address this problem and take action to prevent CVD in postirradiation head and neck cancer patients.

Acknowledgements This work was supported by Grants from the Far Eastern Memorial Hospital Research Program (FEMH—2017-C-012).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

References

1. Yeh Y-C, Fang K-M, Hsu W-L et al (2019) The effectiveness of high-resolution ultrasound in the assessment of the carotid intima-media thickness for postirradiated neck. *Eur Arch Otorhinolaryngol* 276(4):1167–1173
2. Cheng SW, Wu LL, Ting AC et al (1999) Irradiation-induced extracranial carotid stenosis in patients with head and neck malignancies. *Am J Surg* 178(4):323–328
3. Smith GL, Smith BD, Buchholz TA et al (2008) Cerebrovascular disease risk in older head and neck cancer patients after radiotherapy. *J Clin Oncol* 26(31):5119–5125
4. Dorth JA, Patel PR, Broadwater G et al (2014) Incidence and risk factors of significant carotid artery stenosis in asymptomatic survivors of head and neck cancer after radiotherapy. *Head Neck* 36(2):215–219
5. Xu J, Cao Y (2014) Radiation-induced carotid artery stenosis: a comprehensive review of the literature. *Interv Neurol* 2(4):183–192

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.