

# Prognostic Value of C-Reactive Protein-to-Albumin Ratio in Head and Neck Cancer: A Meta-Analysis

Chih-Wei Luan, Hsin-Yi Yang, Yao-Te Tsai, Meng-Chiao Hsieh, Hsin-Hsu Chou and Kuo-Su Chen

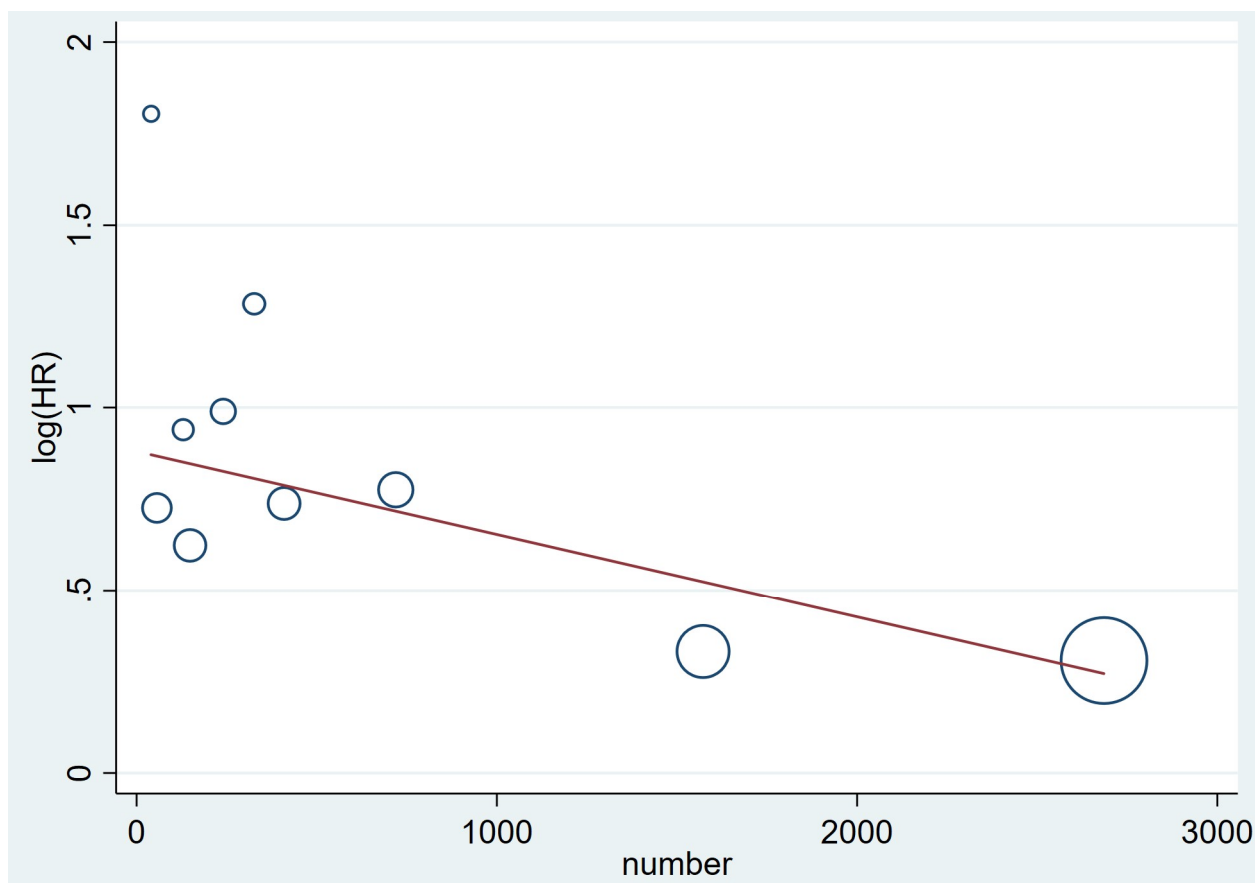
Table S1. The Newcastle–Ottawa Scale score of included studies.

Study	Selection				Comparability		Outcome		Non Response Rate	Score
	Is the Case Definition Adequate?	Representa- tiveness of the Cases	Selection of Controls	Definition of Controls	Main Factor	Additional Factor	Ascertainment of Exposure	Same Method for Cases and Controls		
Li et al. [1]	v	v	v	x	v	x	v	v	v	7
He et al. [2]	v	v	v	x	v	x	v	v	v	7
Zhang et al. [3]	v	v	v	x	v	v	v	v	v	8
Wang et al. [4]	v	v	v	x	v	v	v	v	v	8
Tao et al. [5]	v	v	v	x	v	x	v	v	v	7
Sun et al. [6]	v	v	v	x	v	v	v	v	v	8
Kuboki et al. [7]	v	v	x	v	v	v	v	v	v	8
Yu et al. [8]	v	v	x	x	v	v	v	v	v	7
Wang et al. [9]	v	v	v	x	v	v	v	v	v	8
Park et al. [10]	v	v	x	v	v	x	v	v	v	7
Fang et al. [11]	v	v	x	x	v	v	v	v	v	7

**Table S2.** The detail for included studies.

<i>p</i> Value	Clinical Staging with CAR	T Staging with CAR	N Staging with CAR	Independent Risk Factor	Analysis	Survival	CAR Unit	CAR Mean/Median	CAR Range	Study Period
Li et al. [1]	NA	NA	NA	Yes	Multivariate analysis	5 years OS	CRP: mg/L albumin: g/L	NR	NR	Jan 2009 to Jan 2010
He et al. [2]	<0.001	<0.001	<0.001	Yes	Multivariate analysis	5 years OS, DMFS	CRP: mg/L albumin: g/L	NR	NR	Mar 2000 to Oct 2013
Zhang et al. [3]	NA	NA	NA	Yes	Multivariate analysis	3 years OS	CRP: mg/L albumin: g/L	0.093/0.036	0.002–4.594	Nov 2009 to Feb 2012
Wang et al. [4]	NA	<0.001	=0.005	Yes	Multivariate analysis	5 years DMFS	CRP: mg/L albumin: g/L	NR/0.032	NR	Dec 2009 to May 2011
Tao et al. [5]	=0.024	<0.001	=0.842	Yes	Multivariate analysis	5 years OS	CRP: mg/L albumin: g/L	NR/0.138	0.010–1.932	Jan 2007 to Dec 2012
Sun et al. [6]	NA	NA	NA	Yes	Multivariate analysis	5 years OS	CRP: mg/L albumin: g/L	NR/0.164	NR	Jan 2008 to Oct 2011
Kuboki et al. [7]	=0.008	=0.1	=0.1	Yes	Multivariate analysis	5 years OS, DFS	CRP: mg/L albumin: g/L	NR	NR	Feb 2003 to April 2012
Yu et al. [8]	<0.05	NA	<0.01	Yes	Multivariate analysis	5 years OS	CRP: mg/L albumin: g/L	NR/0.374	0.006–2.020	May 2006 to Oct 2011
Wang et al. [9]	<0.001	<0.001	<0.001	Yes	Multivariate analysis	5 years OS, DFS	CRP: mg/L albumin: g/L	NR	NR	Jan 2005 to Mar 2018
Park et al. [10]	=0.002	=0.002	=0.006	Yes	Multivariate analysis	5 years OS, DFS	CRP: mg/L albumin: g/L	0.137/NR	0.005–1.124	May 2004 to Dec 2011
Fang et al. [11]	<0.001	<0.001	NA	Yes	Multivariate analysis	5 years OS, DFS	CRP: mg/L albumin: g/L	NR/0.08	0.01–5.48	Jan 2008 to Dec 2017

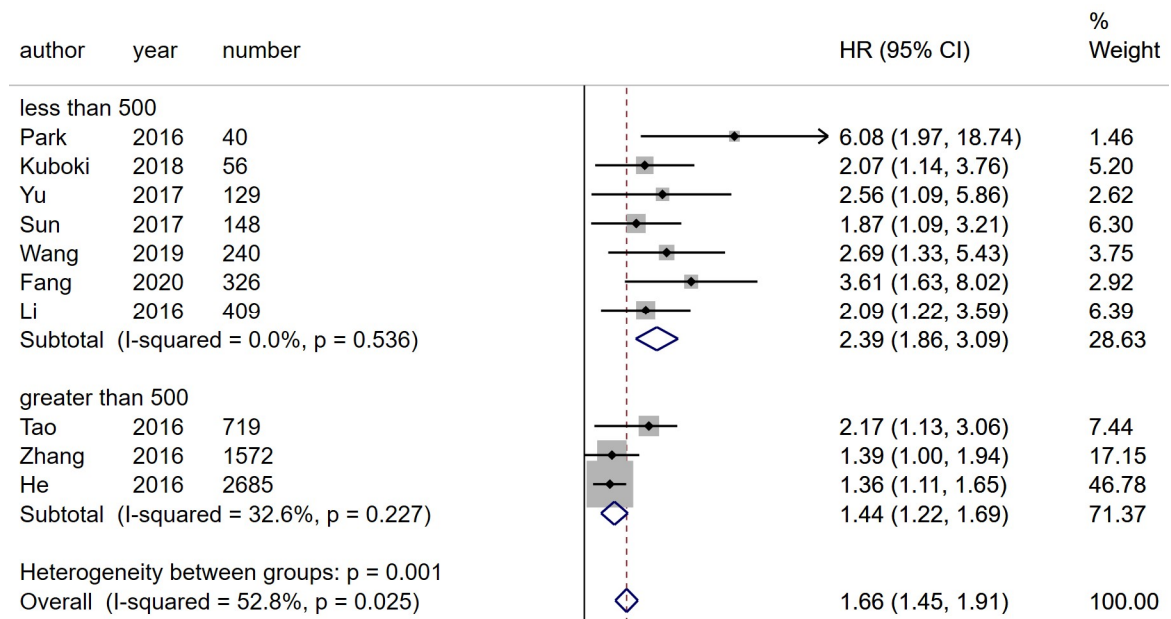
NA, not available; OS, overall survival; DFS, disease free survival; CAR, C-reactive protein to albumin ratio.



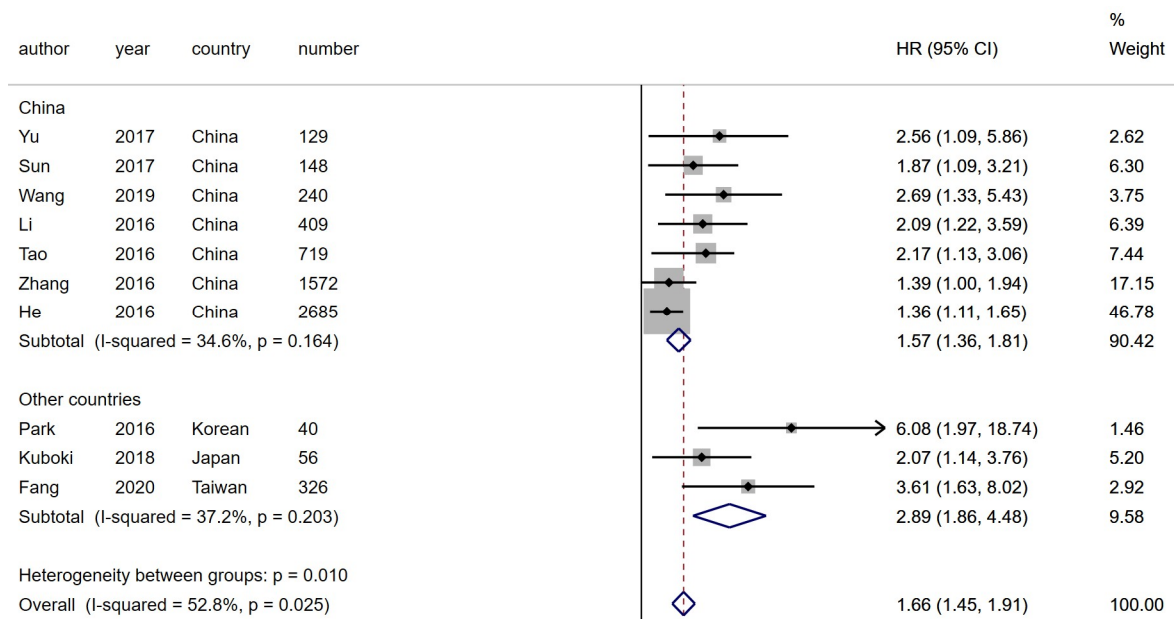
**Figure S1.** Meta-regression of sample size and overall survival. HR, hazard ratio.

author	year	number	HR (95% CI)	
Park	2016	40		6.08 (1.97, 18.74)
Kuboki	2018	56		3.18 (1.13, 8.93)
Yu	2017	129		2.73 (1.58, 4.73)
Sun	2017	148		2.33 (1.58, 3.44)
Wang	2019	240		2.35 (1.72, 3.20)
Fang	2020	326		2.49 (1.86, 3.32)
Li	2016	409		2.39 (1.86, 3.09)
Tao	2016	719		2.35 (1.87, 2.94)
Zhang	2016	1572		2.13 (1.68, 2.71)
He	2016	2685		1.99 (1.57, 2.53)

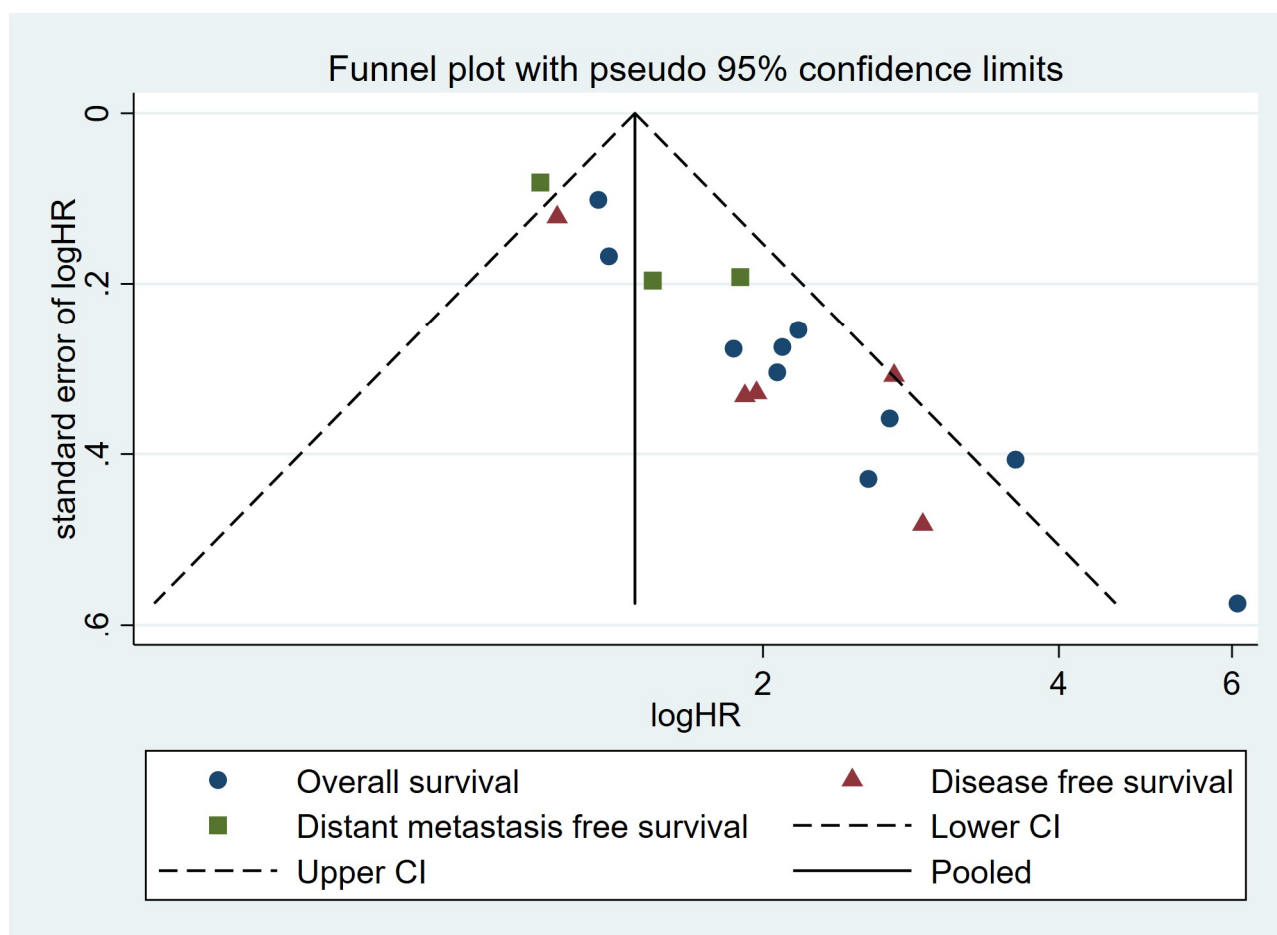
**Figure S2.** Cumulative meta-analysis by sample size.



**Figure S3.** Forest plots for the subgroup analysis by sample size. OS, overall survival. CAR, C-reactive protein-to-albumin ratio. HNC, head and neck cancer.



**Figure S4.** Forest plots for the subgroup analysis by country of origin.



**Figure S5.** Funnel plots providing a graphic estimate of bias for all three outcomes. Each point represents a separate study. The two sloping lines represent the 95% confidence interval.

## Reference

1. Li, J.P.; Chen, S.L.; Liu, X.M.; He, X.; Xing, S.; Liu, Y.-J.; Lin, Y.-H.; Liu, W.-L. A Novel Inflammation-Based Stage (I Stage) Predicts Overall Survival of Patients with Nasopharyngeal Carcinoma. *Int. J. Mol. Sci.* **2016**, *17*, 1900.
2. He, S.; Wang, Y.; Chen, H.; Yang, L.; Liang, S.; Lu, L.; Chen, Y. C-Reactive Protein/Albumin Ratio (CAR) as a Prognostic Factor in Patients with Non-Metastatic Nasopharyngeal Carcinoma. *J. Cancer* **2016**, *7*, 2360–2366.
3. Zhang, Y.; Zhou, G.Q.; Liu, X.; Chen, L.; Li, W.-F.; Tang, L.-L.; Liu, Q.; Sun, Y.; Ma, J. Exploration and Validation of C-Reactive Protein/Albumin Ratio as a Novel Inflammation-Based Prognostic Marker in Nasopharyngeal Carcinoma. *J. Cancer* **2016**, *7*, 1406–1412.
4. Wang, Y.; Yang, L.; Xia, L.; Chen, Y. High C-reactive protein/albumin ratio predicts unfavorable distant metastasis-free survival in nasopharyngeal carcinoma: A propensity score-matched analysis. *Cancer Manag. Res.* **2018**, *10*, 371–381.
5. Tao, C.J.; Chen, Y.Y.; Jiang, F.; Feng, X.-L.; Jin, Q.-F.; Jin, T.; Piao, Y.-F.; Chen, X.-Z. The C-reactive Protein/Albumin Ratio Is an independent Prognostic Factor for Overall Survival in Patients with Nasopharyngeal Carcinoma Receiving Intensity-Modulated Radiotherapy. *J. Cancer* **2016**, *7*, 2005–2011.
6. Sun, P.; Chen, C.; Xia, Y.; Bi, X.; Liu, P.; Zhang, F.; Yang, H.; An, X.; Jiang, W.; Wang, F. The Ratio of C-Reactive Protein/Albumin is a Novel Inflammatory Predictor of Overall Survival in Cisplatin-Based Treated Patients with Metastatic Nasopharyngeal Carcinoma. *Dis. Markers* **2017**, *2017*, 6570808.
7. Kuboki, A.; Kanaya, H.; Nakayama, T.; Konno, W.; Goto, K.; Nakajima, I.; Kashiwagi, T.; Hirabayashi, H.; Haruna, S.I. Prognostic value of C-reactive protein/albumin ratio for patients with hypopharyngeal and laryngeal cancer undergoing invasive surgery involving laryngectomy. *Head Neck* **2019**, *41*, 1342–1350.
8. Yu, S.T.; Zhou, Z.; Cai, Q.; Liang, F.; Han, P.; Chen, R.; Huang, X.-M. Prognostic value of the C-reactive protein/albumin ratio in patients with laryngeal squamous cell carcinoma. *OncoTargets Ther.* **2017**, *10*, 879–884.
9. Wang, Q.; Song, X.; Zhao, Y.; He, Q.; Shi, M.; Xu, P.; Ni, S.; Chen, Y.; Lin, J.; Zhang, L. Preoperative high c-reactive protein/albumin ratio is a poor prognostic factor of oral squamous cell carcinoma. *Future Oncol.* **2019**, *15*, 2277–2286.

10. Park, H.C.; Kim, M.Y.; Kim, C.H. C-reactive protein/albumin ratio as prognostic score in oral squamous cell carcinoma. *J. Korean Assoc. Oral Maxillofac. Surg.* **2016**, *42*, 243–250.
11. Fang, K.H.; Lai, C.H.; Hsu, C.M.; Huang, E.; Tsai, M.-S.; Chang, G.-H.; Lee, Y.-C.; Tsai, Y.-T. A retrospective study on the prognostic value of preoperative C-reactive protein to albumin ratio in patients with oral cavity squamous cell carcinoma. *PeerJ* **2020**, *8*, e9361.