

Q1. As authors mentioned in this article, there were a variety of HER2 gene and protein laboratory assays to determine HER2 status of patients. Based on these respective methods, there were also many reports about the ratio of HER2 positive status. Considering previous reports, the only IHC analysis, which FISH was not performed, was also widely accepted method, however, I'm afraid that the positive ratio of HER2 expression in this cohort was a little too high. Authors should explain its reason.

A1. In this manuscript, we reported a positive rate of Her2 being 35.08%. Previous studies reported the prevalence of HER2 amplification is highly heterogeneous in GC with an estimated rates ranged from 4% to 53% owing to the different techniques, methodologies, and scoring systems applied in the studies. Besides, selection bias for patients with GC undergoing R0 resection should take into consideration.

Q2. To discuss the relationships between HER2 status and clinicopathological factors in gastric cancer patients, authors should use Lauren classification to compare with past reports about higher positive HER2 ratio. Furthermore, the adeno-carcinoma of gastroesophageal junction has tended to be treated as a distinct subtype and known as higher positive HER2 ration than the other type, authors should discuss the tumor location by EGJ and the other type.

A2. Owing to the lack of data related to Lauren classification, we had to ignore this important information. Therefore, we list this important information as one limitation in the discussion part – “Thirdly, Lauren classification was also reported to be an important pathological features of gastric cancer patients combined with HER2 status, which indicated a better prognostic factor, while we failed to test the Lauren classification.” Besides, we analyzed the tumor location, which including Non-Cardia and Cardia in this manuscript and found that gastric body had more positive status of HER2 than Cardia with P value being 0.001. However, no associations between tumor location and DFS/OS were observed in this study. We also described this information in discussion section.

Q3. There were many similar studies and the results were not identical. From viewpoints of novelty, authors should advocate what kind of points are different from other studies.

A3. We did this study with a prior - Whether the positive status of HER2 can be regarded as an effective prognostic factor for patients with gastric cancer undergoing R0 resection among Chinese population, and found that the positive status of HER2 based on IHC was not related to the survival in patients with gastric cancer among the Chinese population. The findings in this manuscript are credible. However, it is acceptable to the highly heterogeneous of associations between HER2 and GC, owing to the different techniques, methodologies, study population, scoring systems applied in the studies. Hence, it should be prudent when apply these results.

Q4. The manuscript is very interesting and well written, considering that the results were retrospectively analyzed the authors should use the score matched analyses in her2 positive Patients to better explore the prognostic significance of her2 status in Chinese population.

A4. We re-analyzed the data with COMMENTS — using propensity score matched analyses under the instruction of biostatistician, and the results are as follows. **Figure 1.** shows the distribution of propensity of scores which is the conditional probability of each patient with positive status of Her2 based on potential confounders, including categorical age, gender sex, minority, tumor location, TNM stage, tumor embolus, neural invasion, adjuvant chemotherapy and adjuvant radiotherapy. Significant difference ($t = 7.72, P < 0.0001$) of propensity scores was observed between group with positive status of Her2 and these of negative. Then, 1:1 ratio match using the GREEDY method with the maximum of propensity score being 0.01. 533 pairs of observations were obtained. **Figure 2.** shows the distribution of propensity of scores after matching. There was no significant association between two groups ($t = 0.00, P = 0.9997$). Finally, matched analyses was also used to calculate the HR and 95% CIs. **Table 1.** and **Table 2.** show the baseline characteristics according to status of Her2 after matching and results of matched analyses, respectively. No significant association between positive status of Her2 and disease free survival (HR = 1.06, 95% CI: 0.92 – 1.21) or OS (HR = 1.07, 95% CI: 0.92 – 1.24) of gastric cancer undergoing R0 resection were observed. These results were comparable with results (DFS: HR = 0.19, 95% CI: 0.96 – 1.46; OS: HR = 1.19, 95% CI: 0.96 – 1.48) in the manuscript. Besides, several disadvantages of using propensity score match method should also

take into consideration. Firstly, a total of 506 patients with lower or higher propensity scores were loss to matched (**Figure 3.**). Secondly, family history of cancer was removed from the analysis owing to missing value. Therefore, it is essential to be prudent in making conclusions about the results of propensity score analyses.

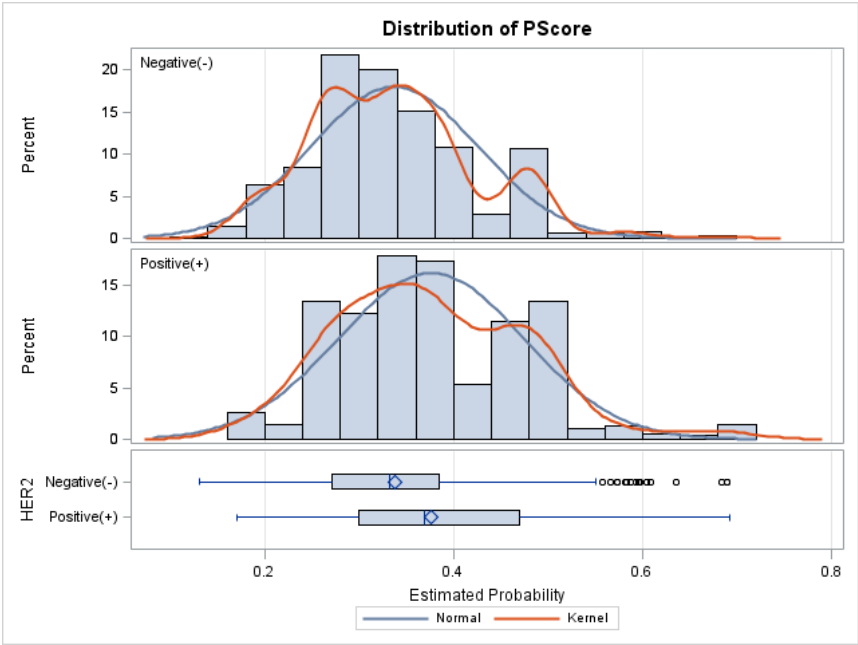


Figure 1. Distribution of propensity scores according to the status of Her2 before matching

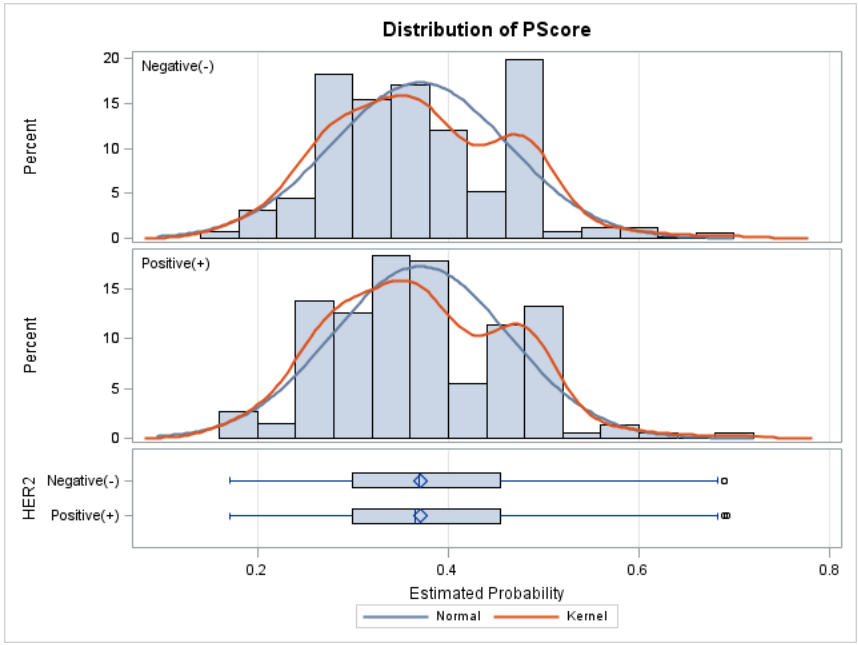


Figure 2. Distribution of propensity scores according to the status of Her2 after matching

Table 1. Baseline Characteristics According to Status of Her2 after Matching

Covariates	Her2 Status		P-value*
	Negative(-)	Positive(+)	
	N=533	N=533	
Age			0.668
< 60 years	271 (49.36)	278 (50.64)	
>= 60 years	262 (50.68)	255 (49.32)	
Gender			0.704
Female	106 (48.85)	111 (51.15)	
Male	427 (50.29)	422 (49.71)	
Minority			1.000
Han	512 (50)	512 (50)	
Population			
Others	21 (50)	21 (50)	
Tumor Location			0.792
Non-Cardia	363 (49.73)	367 (50.27)	
Cardia	170 (50.6)	166 (49.4)	
TNM Stage			0.862
I	162 (50.15)	161 (49.85)	
II	105 (48.39)	112 (51.61)	
III	266 (50.57)	260 (49.43)	
Tumor Embolus			0.831
No	403 (50.19)	400 (49.81)	
Yes	130 (49.43)	133 (50.57)	

Covariates	Her2 Status		P-value*
	Negative(-)	Positive(+)	
	N=533	N=533	
Nerve Invasion			0.738
No	450 (50.22)	446 (49.78)	
Yes	83 (48.82)	87 (51.18)	
Adjuvant Chemotherapy			0.668
No	254 (50.7)	247 (49.3)	
Yes	279 (49.38)	286 (50.62)	
Adjuvant Radiotherapy			0.529
No	514 (50.2)	510 (49.8)	
Yes	19 (45.24)	23 (54.76)	

Table 2. Matched Analyses after 1:1 Propensity Score Match

Status of DFS with Her (-)	Status of DFS With Her2 (+)			HR	95% CIs
	Yes	No	Total		
Yes	100 (18.76)	97 (18.20)	197 (36.96)	1.06	0.92 – 1.21
No	108 (20.26)	228 (42.78)	336 (36.96)		
Total	208 (39.02)	325 (60.98)	533 (100.00)		
Status of OSS with Her (-)	Status of OS With Her2 (+)			HR	95% CIs
	Yes	No	Total		
Yes	86 (16.14)	93 (17.45)	179 (33.58)	1.07	0.92 – 1.24
No	105 (19.07)	249 (46.72)	354 (66.42)		
Total	191 (35.83)	342 (64.17)	533 (100.00)		

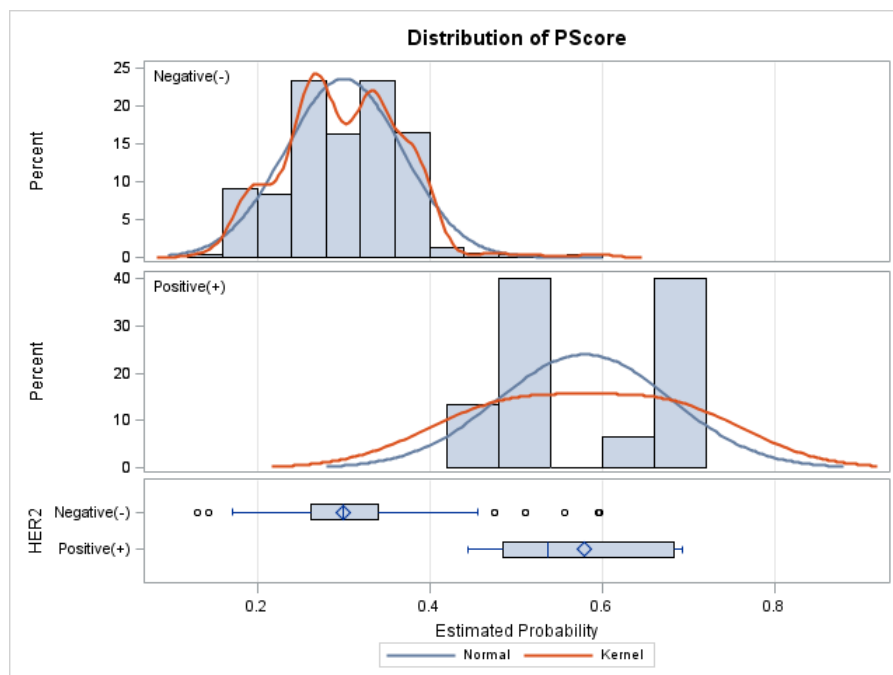


Figure 3. Distribution of propensity scores with those unmatched patients after matching