VOLUME 32 · NUMBER 28 · OCTOBER 1 2014

JOURNAL OF CLINICAL ONCOLOGY

CORRESPONDENCE

Reply to M. Honda et al

We would like to thank Honda et al[1] for their comments on our recent study, entitled "Long-Term Results of Laparoscopic Gastrectomy for Gastric Cancer: A Large-Scale Case-Control and Case-Matched Korean Multicenter Study."[2]

Honda et al [1] were concerned about whether our variable selections in the propensity score analysis were appropriate. They suggested that, for an ideal statistical approach, propensity score matching should be performed using all preoperative factors related to the selection of laparoscopy or open surgery. We had the same concern, so we agree with their criticism to a certain extent. However, we believe that potential confounding variables, which probably influenced survival, should be included, and even perioperative factors as well.

Propensity score matching was developed to select sets of patients with similar values, as derived from a propensity score model in a retrospective study; it was intended to mimic a randomized controlled trial. Although there have been some controversies related to choosing variables for a propensity score model, it has been suggested that potential confounding variables that are unrelated to the exposure but related to the outcome should be included in a propensity score model, and that this will decrease the variance of an estimated exposure effect without increasing bias.[3]

In our study,[2] the most important limitation was selection bias, which was caused by the retrospective nature of the study. The clinicopathologic characteristics of patients in the laparoscopic group showed statistically significant differences compared with those of patients in the open group with respect to age, sex, body mass index (BMI), the type of procedure, lymph node dissection, and TNM stage. For instance, young female patients tended to more frequently undergo laparoscopic gastrectomy for early-stage gastric cancer than other patients. To overcome the selection bias resulting from these different distributions between the two groups, we performed both a multivariable analysis and a propensity score analysis. In the multivariable analysis, using a Cox proportional hazard model, we identified that the operative approach (open or laparoscopy) was not an independent factor associated with survival (hazard ratio, 1.19; 95% CI, 0.91 to 1.55; $P = .214$). In the propensity score analysis, we first considered only preoperative variables such as age, sex, BMI, and operator. However, these preoperative variables could not reflect the exact survival, which was the primary aim of the study. Therefore, we added postoperative variables that intimately influenced survival, including the resection type (subtotal or total), extent of lymphadenectomy, and cancer stage.

On the basis of the recommendation made by Honda et al,[1] we used a more comprehensive propensity score model with plausible confounding variables that could be intraoperative or postoperative (unless those were modified by the surgery method) but which were strongly related to survival.[4] These included age, sex, BMI, tumor location, tumor size, histologic type, operator, operative procedure, extent of lymphadenectomy, tumor depth, nodal metastasis, and stage of cancer. We confirmed that the inclusion of such variables improved the balance between the treatment groups.

Using the available variables that were definitely unrelated to selection of the operative approach but were related to survival, such as operative methods, extent of lymphadenectomy, and stage of cancer, the residual systematic differences between the open and the laparoscopic surgery groups were smaller in the propensity score–matched data (Appendix Table A1, online only). In both propensity score analyses, overall survival was not associated with group (open or laparoscopy group) at any cancer stage (Appendix Fig A1, online only).

We wish to express our thanks again to Honda et al[1] for their excellent comments on this retrospective study. We will report the final results of the randomized controlled trial showing survival rates of patients who underwent laparoscopic surgery versus open procedures next year.[5]

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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DOI: 10.1200/JCO.2014.56.7271; published online ahead of print at www.jco.org on August 11, 2014

Appendix

Table 1. Patient Characteristics After Propensity Scoring Matching by Age, Sex, BMI, Tumor Location, Tumor Size, Histologic Type, Operator, Operative Procedure, Extent of Lymphadenectomy, Tumor Depth, Nodal Metastasis, and Stage of Cancer

	Before Matching					After Matching				
	OG		LG			OG		LG		
Characteristic	No.	%	No	%	*P*	No	%	No	%	*P*
No. of patients	1,358		1,459			493		493		
Age, years					.04617					.2996
Mean	58.5		57.59			58.13		57.33		
SD	12.01		12.09			11.89		12.23		
Sex					< .001					.8386
Male	938	66.8	913	62.5		334	67.7	330	66.9	
Female	420	33.2	546	37.5		159	32.3	163	33.1	
BMI, kg/m^2					.02075					.4052
Mean	23.07		23.34			23.49		23.34		
SD	3.19		2.98			3.06		2.94		
Tumor location										.8718
Upper third	262	19.5	98	6.7		60	12.2	59	12.0	
Middle third	339	25.2	454	31.1		143	29.0	155	31.4	
Lower third	722	53.7	904	61.9		288	58.4	277	56.2	
Whole body	20	1.6	3	0.3		2	0.4	2	0.4	
Tumor size, cm					< .001					.4366
Mean	5.24		2.74			3.33		3.42		
SD	3.23		1.69			1.78		2.06		
Histologic type					< .001					.8632
Papillary	9	0.7	1	0.1		1	0.2	1	0.2	
Tubular, well differentiated	166	12.4	373	25.7		86	17.7	88	18.0	
Tubular, moderately differentiated	384	28.7	394	27.1		147	30.2	144	29.5	
Tubular, poorly differentiated	564	42.2	415	28.6		178	36.6	169	34.6	
Mucinous	42	3.1	19	1.3		9	1.8	11	2.3	
Signet ring cell	172	12.9	250	17.2		66	13.5	75	15.4	
Operator No.					< .001					.1689
1	343		201			99		81		
2	53		87			23		25		
3	266		379			103		106		
4	0		50			0		0		
5	14		51			8		10		
6	0		55			0		8		
7	103		75			29		22		
8	194		108			73		71		
9	191		215			79		83		
10	194		238			79		87		
Type of operative procedure					< .001					.9451
Distal gastrectomy	948	69.8	1,305	89.5		418	84.8	415	84.2	
Total gastrectomy	395	29.1	124	8.5		65	13.2	69	14.0	
Proximal gastrectomy	10	0.7	24	1.6		8	1.6	69	1.2	
Other	5	0.4	6	0.4		2	0.4	3	0.6	
Extent of lymphadenectomy					< .001					.4232
< D2	207	15.2	639	43.8		132	26.8	144	29.2	
≥ D2	1,151	84.8	820	56.2		361	73.2	349	70.8	
Tumor depth					< .001					.997
Mucosa	174	12.8	753	51.6		144	29.2	146	29.6	
Submucosa	238	17.5	474	32.5		158	32.0	162	32.9	
Muscularis propria	225	16.7	128	8.8		96	19.6	90	18.3	
Subserosa	257	18.9	59	4.0		45	9.1	52	10.5	
Penetrate serosa	464	34.1	45	3.1		50	10.1	43	8.7	

(continued on following page)

Table 1. Patient Characteristics After Propensity Scoring Matching by Age, Sex, BMI, Tumor Location, Tumor Size, Histologic Type, Operator, Operative Procedure, Extent of Lymphadenectomy, Tumor Depth, Nodal Metastasis, and Stage of Cancer (continued)

	Before Matching					After Matching				
	OG		LG			OG		LG		
Characteristic	No.	%	No	%	*P*	No	%	No	%	*P*
Nodal metastasis					< .001					.9207
N0	604	44.4	1,248	85.6		348	70.6	347	70.4	
N1	206	15.2	121	8.3		69	14.0	76	15.4	
N2	214	15.8	59	4.0		42	8.5	42	8.5	
N3a	187	13.8	25	1.7		27	5.5	22	4.5	
N3b	147	10.8	6	0.4		7	1.4	6	1.2	
Stage					< .001					.9142
IA	339	25.0	1,122	76.9		261	53.0	264	53.7	
IB	155	11.4	158	10.9		82	16.7	80	16.2	
IIA	144	10.6	76	5.3		52	10.5	52	10.5	
IIB	177	13.0	50	3.4		42	8.5	45	9.1	
IIIA	152	11.2	21	1.4		16	3.2	21	4.3	
IIIB	158	11.6	23	1.5		27	5.5	22	4.4	
IIIC	233	17.2	9	0.6		13	2.6	9	1.8	

Abbreviations: BMI, body mass index; LG, laparoscopic gastrectomy; OG, open gastrectomy; SD, standard deviation.

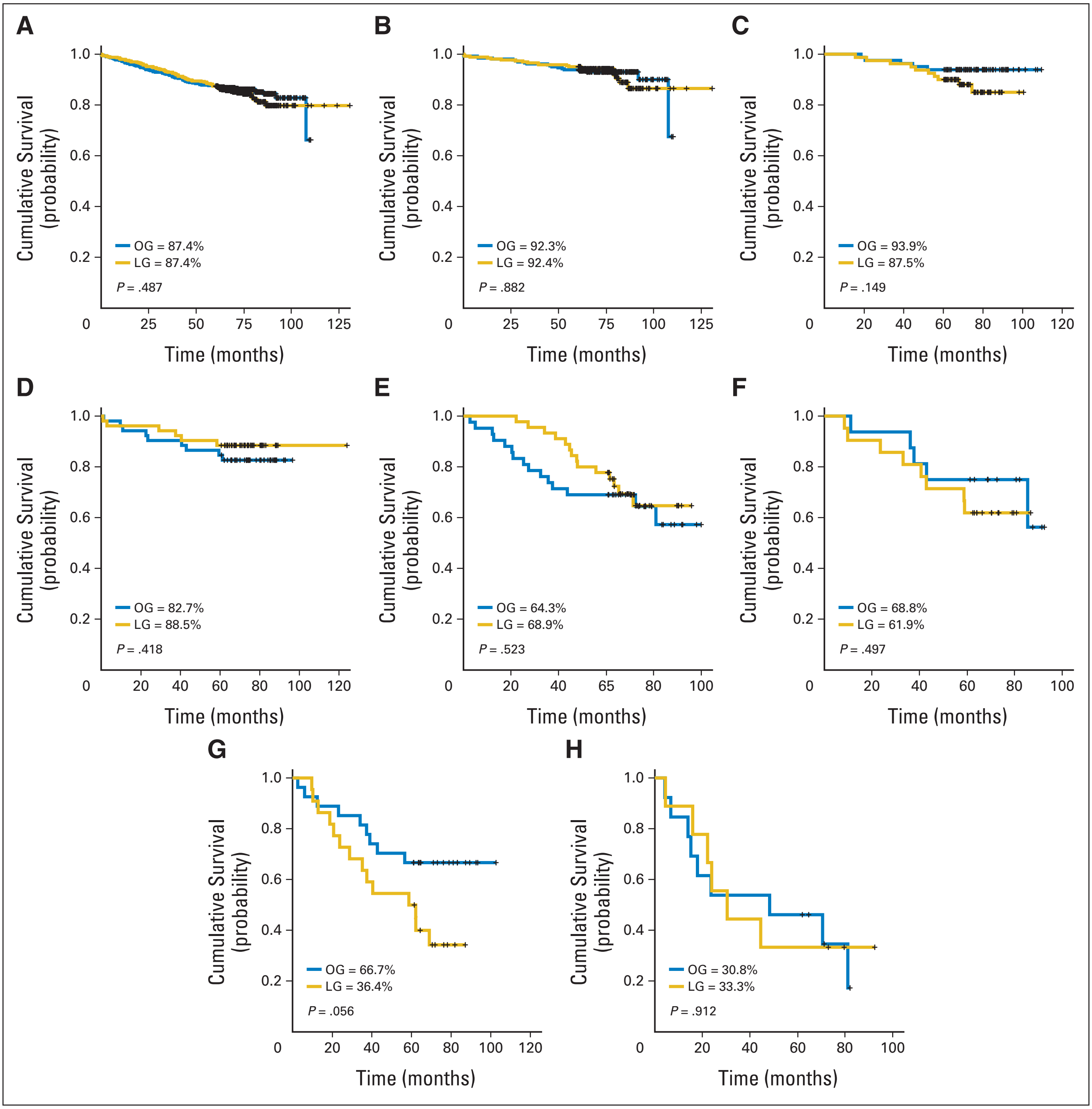

Fig A1. Comparison of overall long-term survival rate between open gastrectomy (OG) and laparoscopic gastrectomy (LG) according to stage after matching. (A) Overall survival; (B) stage IA; (C) stage IB; (D) stage IIA; (E) stage IIB; (F) stage IIIA; (G) stage IIIB; (H) stage IIIC.