Radiological criteria for selecting candidates for neoadjuvant chemotherapy for gastric cancer: An exploratory analysis from the PRODIGY study

Hyung-Don Kim[1], Jong Seok Lee[2], Jeong Hwan Yook[3], Min-Hee Ryu[1], Young-Kyu Park[4], Jin Young Kim[5], Young-Woo Kim[6], Sang Cheul Oh[7]
Jong Gwang Kim[8], Jae-Ho Cheong[9], Oh Jeong[4], Sung Hoon Noh[9] and Yoon-Koo Kang[1]

1 Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea 2 Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea 3 Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea 4 Department of Surgery, Chonnam National University Medical School, Hwasun, Republic of Korea 5 Division of Hemato-Oncology, Department of Internal Medicine, Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Republic of Korea 6 Center for Gastric Cancer, Research Institute & Hospital, National Cancer Center, Graduate School of Cancer Science and Policy, Goyang, Republic of Korea 7 Department of Internal Medicine, Korea University Guro Hospital, Seoul, Republic of Korea
8 Department of Internal Medicine, Kyungpook National University, Daegu, Republic of Korea 9 Department of Surgery, Yonsei University College of Medicine, Seoul, 03722, Republic of Korea

Introduction

- In the phase 3 PRODIGY study, we demonstrated that patients who received additional neoadjuvant chemotherapy followed by surgical resection and adjuvant S-1 exhibited significantly improved progression-free survival (PFS) compared to those who received standard therapy with surgical resection and adjuvant S-1 only.
- Although the PRODIGY study included patients with locally advanced disease by clinical assessment (i.e., cT2/3N+ or cT4/Nany), these radiological criteria were associated with a non-negligible proportion of pathological stage (pStage) I disease (11%) in the SC group.
- We aimed to define the radiological criteria to identify patients with gastric cancer who may derive maximal clinical benefit from neoadjuvant chemotherapy.

Methods

- There were 246 patients allocated to receive surgery followed by adjuvant S-1 (SC group) and 238 allocated to receive neoadjuvant chemotherapy (CSC group).
- As the PRODIGY's radiological method of lymph node (LN) evaluation considers short diameter and morphology (size and morphology method), a method considering only short diameter was also employed (size-only method).
  - **Size and morphology method**: LNs were considered positive when the short axis was ≥ 8 mm or the shortest diameter was ≥ 5 mm with central necrosis, a round shape, perinodal infiltration, and/or prominent enhancement
  - **Size-only method**: lymph node-positive when they had lymph nodes with a short axis of ≥ 8 mm regardless of their morphologic features
- In the SC group, the correlation between radiologic and pathologic findings was analyzed.
- The hazard ratio (HR) for the PFS of the CSC group was analyzed in subgroups with different cT/N stages

Results

Table 1. Clinical characteristics of the study patients

	SC group (N=246)	CSC group (N=238)	P value
Age (years)	58 (26-75)	58 (27-75)	0.728
Male sex	200 (81.3%)	184 (77.3%)	0.278
ECOG performance status			0.028
0	177 (72.0%)	149 (62.6%)	
1	69 (28.0%)	89 (37.4%)	
Clinical T stage			0.872
T2	13 (5.3%)	12 (5.0%)	
T3	56 (22.8%)	60 (25.2%)	
T4a	159 (64.6%)	146 (61.3%)	
T4b	18 (7.3%)	20 (8.4%)	
Clinical N+ by size and morphology method	238 (96.7%)	234 (98.3%)	0.413
Clinical N+ by size-only method	142 (58.2%)	136 (57.1%)	0.970

Figure 1. Concordance between clinical and pathological T stage (A) and overall pathological stage (B)

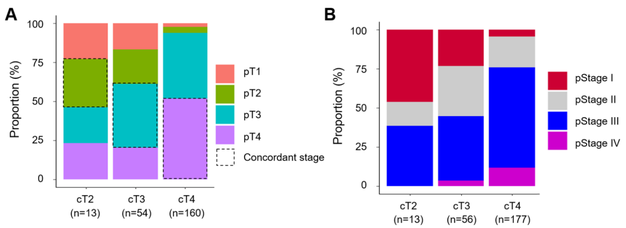

Figure 2. Distribution of pathological stages according to clinical T and N stages based on the size and morphology method (A) and size-only method (B).

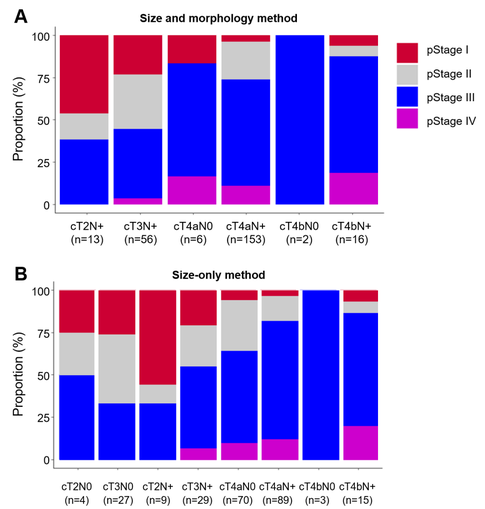

Figure 3. Relative risk reduction of the CSC group for PFS in subgroups determined by different T/N stages.

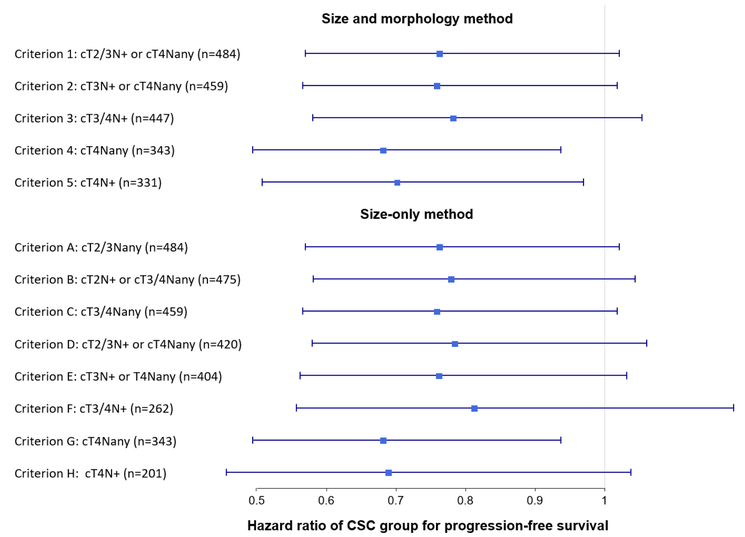

Table 2. Proportion of pathological stage I disease and sensitivity for pathological stage III disease by criteria based on each radiological method of evaluating lymph node

Criteria by size and morphology method	pStage I (%)	Sensitivity for pStage III	Criteria by size-only method	pStage I (%)	Sensitivity for pStage III
-	-	-	Criterion A: cT2/3Nany (n=227)	27 (11.9%)	100.0%
-	-	-	Criterion B: cT2N+ or cT3/4Nany (n=223)	26 (11.7%)	98.6%
-	-	-	Criterion C: cT3/4Nany (n=214)	21 (9.3%)	96.5%
Criterion 1: cT2/3N+ or cT4Nany (n=227)	27 (11.9%)	100.0%	Criterion D: cT2/3N+ or cT4Nany (n=196)	19 (9.7%)	92.2%
Criterion 2: cT3N+ or cT4Nany (n=214)	21 (9.3%)	96.5%	Criterion E: cT3/4N+ or T4Nany (n=187)	14 (7.4%)	90.1%
Criterion 3: cT3/4N+ (n=207)	20 (9.7%)	92.2%	Criterion F: cT3/4N+ (n=124)	10 (8.1%)	61.0%
Criterion 4: cT4Nany (n=160)	8 (5.0%)	80.1%	Criterion G: cT4Nany (n=160)	8 (5.0%)	80.1%
Criterion 5: cT4N+ (n=155)	7 (4.5%)	75.9%	Criterion H: cT4N+ (n=97)	4 (4.3%)	51.1%

Conclusions

- Gastric cancer patients with cT4Nany disease may preferentially benefit from neoadjuvant chemotherapy in the PRODIGY study.
- The cT4-based criterion may help select patients for neoadjuvant chemotherapy and guide future clinical studies of neoadjuvant chemotherapy, especially in Asia.
- Our findings require further investigation and validation in independent cohorts with different neoadjuvant regimens. .

Conflict of Interest: Nothing directly related to this work. Out of this work, YKK has served as a consultant for ALX Oncology, Zymeworks, Amgen, Novartis, Macrogenics, Daehwa, Blueprint, Surface Oncolgy, BMS, Merck (MSD). MHR received honoraria from DAEHWA Pharmaceutical, Bristol Myers Squibb, Lilly, Ono Pharmaceutical, MSD, Taiho Pharmaceutical, Novartis, Daiichi Sankyo and AstraZeneca, and served as a consultant for DAEHWA Pharmaceutical, Bristol Myers Squibb, Lilly and Ono Pharmaceutical. JHC is a founder and shareholder of NOVOMICS.

Acknowledgement: The data analyzed were from the PRODIGY study which was a Sanofi sponsored study.

ESMO 2021 Congress, ePoster Session, presentation number: 1396P, corresponding author: Prof. Yoon-Koo Kang ykkang@amc.seoul.kr