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Author(s)	Ebihara, Yuma; Kyogoku, Noriaki; Takano, Hironobu et al.
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Comparison of D2 and Non-D2 Lymphadenectomy in Older Patients (≥75 years) Undergoing Minimally Invasive Distal Gastrectomy for Gastric Cancer: A Multicenter Retrospective Propensity Score-matched Analysis

YUMA EBIHARA[1], NORIAKI KYOGOKU[2], HIRONOBU TAKANO[1], HIDEYUKI WADA[1], TAKEO NITTA[1], DAISUKE SAIKAWA[3], YOSHIYUKI YAMAMURA[4], MINORU TAKADA[5], TOSHIAKI SHICHINOHE[1] and SATOSHI HIRANO[1]

[1]Department of Gastroenterological Surgery II, Faculty of Medicine, Hokkaido University, Sapporo, Japan;

[2]Department of Surgery, Japanese Redcross Kitami Hospital, Kitami, Japan;

[3]Department of Surgery, Tonan Hospital, Sapporo, Japan;

[4]Department of Surgery, Obihiro-Kosei General Hospital, Obihiro, Japan;

[5]Department of Surgery, Teine Keijinkai Hospital, Sapporo, Japan

Correspondence to: Yuma Ebihara (ORCID 0000-0002-7317-8067), Department of Gastroenterological Surgery II, Hokkaido University Faculty of Medicine, Kita 15 Nishi 7, Kita-ku, Sapporo City, 060-8638, Japan. Tel: +81 117067714, Fax: +81 117067158, e-mail: yuma-ebi@wc4.so-net.ne.jp

Running title: D2 vs Non-D2 in MIDG for Older GC Patients

Abstract

Background/Aim: This multicenter retrospective cohort study with propensity score matching (PSM) evaluated

the surgical outcomes and prognosis of minimally invasive distal gastrectomy (MIDG) with D2 lymphadenectomy (LND) in older patients (≥75 years) with gastric cancer (GC).

Patients and Methods: We retrospectively enrolled 988 patients who underwent MIDG for GC at five institutions between January 2018 and December 2024. Older patients with GC (cN+ or ≥cT2) were categorized into two groups: those who received D2 LND (D2 group) and those who did not (Non-D2 group). PSM was performed using the following covariates: age, sex, body mass index, American Society of Anesthesiologists physical status classification, surgical approach (laparoscopic or robotic), reconstruction method (Billroth I, Billroth II, or Roux-en-Y), adjuvant chemotherapy, and clinical T/N stage according to the Japanese Classification of Gastric Carcinoma. Surgical outcomes and prognoses were compared between groups.

Results: A total of 186 eligible patients were identified (D2: 74; Non-D2: 112), and 82 patients (41 per group) were included after matching. Operation time was significantly shorter in the Non-D2 group [D2: 349 min (176–507) *vs*. Non-D2: 285 min (138–458); p=0.025). The incidence of postoperative complications (Clavien–Dindo grade ≥II) was comparable between groups. The median follow-up was 23.3 months (range=1–79.4) in the D2 group and 26.2 months (range=1–79.5 months) in the Non-D2 group. No significant differences were observed in 5-year overall survival (D2: 47.7% *vs*. Non-D2: 34.6%; p=0.143) or 5-year relapse-free survival (RFS) (D2: 34.3% *vs*. Non-D2: 27.2%; p=0.578). Multivariable analysis identified pathological lymph node metastasis as an independent prognostic factor for RFS (hazard ratio= 3.553; 95% confidence interval=1.263–9.996; p=0.016).

Conclusion: Among older patients (≥75 years) undergoing MIDG for GC, D2 LND was associated with longer operation time without significant differences in survival outcomes.

Key Words: Minimally invasive distal gastrectomy, gastric cancer, D2 lymph node dissection, prognosis.

According to the GLOBOCAN database, gastric cancer (GC) is the fifth most common malignancy and the third leading cause of cancer-related mortality worldwide, with incidence increasing markedly with age. In Japan, where 28.9% of the population is aged ≥65 years, the number of older patients with GC continues to rise (1, 2). For locally advanced GC, complete surgical resection (R0) with adequate lymphadenectomy remains the cornerstone of curative treatment. D2 lymphadenectomy (LND) is considered the standard procedure for resectable GC, as the extent of lymph node removal is a key prognostic factor. However, the necessity and safety of D2 dissection in older patients remain controversial (3–5). Minimally invasive gastrectomy (MIG), including laparoscopic and robotic approaches, has been increasingly adopted because it reduces surgical trauma while providing oncological outcomes comparable to those of open surgery (6, 7). Several studies have demonstrated its feasibility and safety in older patients (8, 9). Nevertheless, despite guidelines established by the Japanese Gastric Cancer Association (JGCA), surgical strategies for older patients with GC often vary according to patient-specific factors and institutional policies (10). Given the increasing longevity of this population, optimizing the balance between oncologic radicality and postoperative quality of life is crucial.

This multicenter retrospective study aimed to evaluate the therapeutic value of D2 LND in older patients (≥75 years) undergoing minimally invasive distal gastrectomy (MIDG). Using propensity score matching (PSM), we compared surgical outcomes and prognosis between patients who received D2 *versus* non-D2 LND.

Patients and Methods

Patients. We retrospectively reviewed patients who underwent MIDG for GC at five institutions— Hokkaido University Hospital (HU), Teine Keijinkai Hospital (TKH), Obihiro-Kosei General Hospital (OKGH), Tonan Hospital (TH), and Japanese Red Cross Kitami Hospital (JRCKH)—between January 2018 and December 2024. All patients who underwent curative MIDG were included in the analysis. GC diagnosis was established using endoscopy, computed tomography (CT), or endoscopic ultrasonography. All participating institutions are high-volume centers specializing in MIDG for GC. Tumor staging followed the Japanese Classification of Gastric Carcinoma (JCGC) (4). LND was classified as either D2 dissection (D2) or non-D2 dissection (Non-D2) based on the Japanese gastric cancer treatment guidelines published by JGCA (4). In this study, patients with GC invading beyond the muscularis mucosae (≥T2) or with lymph node metastasis, including T1 tumors confined to the mucosa or submucosa with nodal involvement (T1, N+), were eligible for inclusion. Patients who underwent D2 LND were assigned to the D2 group, whereas those who underwent D1 or D1+ LND were assigned to the non-D2 group. The selection of LND extent was determined by the operating surgeon and institution, with the intent of achieving R0 resection. Non-D2 dissection was chosen primarily in cases with low suspicion of nodal metastasis on preoperative imaging or in older patients with significant comorbidities and higher operative risk.

In our cohort, candidates for D2 tended to be younger, have better physical status, and present with more advanced clinical nodal disease compared with non-D2 candidates.

***Data collection*.** Clinicopathological variables—including age, sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS), clinical stage, combined resection of other organs, LND, reconstruction method, time to recurrence, and prognosis—were collected. Surgical outcomes, including operation time, estimated blood loss, postoperative complications, and length of postoperative hospital stay, were also recorded. The study protocol was approved by the Institutional Review Board of Hokkaido University Hospital (No. 024-0219) and conducted in accordance with the principles of the Declaration of Helsinki.

Surgical procedure. The operative procedure (resection and reconstruction) and surgical approach (laparoscopic and robotic) were determined based on the experience and preference of surgeons accredited through the Endoscopic Surgical Skill Qualification System of the Japan Society for Endoscopic Surgery (JSES) (11). When the operating surgeon did not hold this accreditation, a qualified surgeon supervised the surgery. The extent of lymph node dissection was determined according to JGCA guidelines (4). Surgical robotic platforms used included the da Vinci Si, X, and Xi systems (Intuitive Surgical, Sunnyvale, CA, USA) and the hinotori^TM^ Surgical Robot System (Medicaroid Corporation, Kobe, Japan).

In this study, the extent of LND in MIDG was defined according to JGCA guidelines (4) as follows: D0, lymphadenectomy less than D1; D1, dissection of station Nos. 1, 3, 4sb, 4d, 5, 6, and 7; D1+, D1 plus Nos. 8a

and 9; and D2, D1 plus Nos. 8a, 9, 11p, and 12a. In principle, D2 LND is indicated for cN+ or ≥cT2 tumors, whereas D1 or D1+ LND is indicated for cT1N0 tumors. Specifically, D1 LND is indicated for cT1a tumors that do not meet the criteria for endoscopic resection (*i.e.,* differentiated-type adenocarcinoma without ulcerative findings) and for cT1bN0 tumors that are differentiated-type and ≤1.5 cm in diameter. D1+ LND is indicated for other cT1N0 tumors not meeting the criteria specified above. Based on these indications, patients with cN+ or ≥cT2 tumors were assigned to the D2 LND group, and those with cT1N0 tumors to the non-D2 LND (D1 or D1+) group. Distal gastrectomy was performed according to guideline recommendations, typically resecting approximately two-thirds of the stomach, including the pylorus. Following distal gastrectomy and LND, a longitudinal incision <10 cm in the middle abdomen was made to remove the specimen, and then intracorporeal or extracorporeal anastomosis was performed according to the surgeons' discretion. The brief modalities of anastomosis were as follows: (i) Billroth I (B-I) with delta-shaped anastomosis, (ii) Billroth II (B-II) with or without Braun anastomosis, and (iii) Roux-en-Y (R-Y) anastomosis (antecolic route).

Postoperative follow-up. All patients were observed every three months postoperatively. Hematological analyses (including tumor marker analysis for carcinoembryonic antigen and carbohydrate antigen 19-9) were performed at each visit. Abdominal CT was performed every six months or whenever clinical recurrence was suspected. Gastrointestinal endoscopy was performed at 1, 3, and 5 years postoperatively. Based on this surveillance, data on the 5-year overall survival (OS), relapse-free survival (RFS), and cancer-specific survival (CSS) were obtained. OS was defined as the time from surgery to death from any cause or loss to follow-up. RFS was defined as the

time from surgery to the first recurrence of GC, death from GC, or loss to follow-up. CSS was defined as the time from surgery to death specifically attributable to GC.

Complications. Postoperative complications included anastomotic leakage (including duodenal stump leakage), anastomotic stricture, anastomotic hemorrhage, intra-abdominal hemorrhage, ileus (including gastrointestinal obstruction and delayed gastric emptying), intra-abdominal abscess, peripancreatic fluid collection (due to pancreatic fistula or deep surgical site infection), wound infection, cardiac complications, pulmonary complications, urinary and renal complications, hepatobiliary complications, and other events. Anastomotic leakage was defined as the disruption of an anastomotic site and/or duodenal stump. Peripancreatic fluid collection was defined as fluid accumulation resulting from pancreatic fistula formation or deep surgical site infection, which are often difficult to distinguish (12). Delayed gastric emptying was defined according to the International Study Group of Pancreatic Surgery criteria (13). Pneumonia was diagnosed based on respiratory symptoms, blood tests, and imaging (X-ray or CT). Patients were classified into five groups based on Clavien–Dindo (CD) classification of postoperative complications, which ranks complications according to the therapeutic intervention required: Grade I (minor deviation from the normal postoperative course); Grade II (requiring pharmacological treatment); Grade III (requiring surgical, endoscopic, or radiological intervention); Grade IV (life-threatening complications requiring intensive care management); and Grade V (death) (14, 15).

Statistical analysis. PSM was performed using a logistic regression model to reduce selection bias. Variables

included in the PSM were age, sex, BMI, ASA-PS classification, surgical approach (laparoscopic or robotic), reconstruction method (Billroth I, Billroth II, or Roux-en-Y), adjuvant chemotherapy, and clinical T/N stage according to JCGC. Propensity scores were matched within 0.2 standard deviations of the logit, following the recommendations by Austin (16). Categorical variables were analyzed using the chi-square or Fisher's exact test, and continuous variables were examined using the Mann–Whitney U test, both before and after PSM. Survival curves were generated using the Kaplan–Meier method and compared using the log-rank test. Independent prognostic factors for survival were identified using the Cox proportional hazard regression model. Statistical significance was defined as $p<0.05$. All statistical analyses were performed using the JMP® 18.2.0 software (SAS Institute Inc., Cary, NC, USA).

Results

Clinical features and surgical outcomes of the study population. A total of 988 patients were screened. After applying the exclusion criteria (age ≤74 years, palliative surgery, resection of other organs, conversion or emergency surgery, neoadjuvant chemotherapy, and insufficient data), 186 patients were eligible for analysis. The D2 and non-D2 groups comprised 74 and 112 patients, respectively. After PSM, 41 patients in the D2 group were individually matched with 41 patients in the non-D2 group (Figure 1), yielding a final matched cohort of 82 patients (41 per group). The matched D2 group consisted of patients from HU (n=6), TKH (n=17), OKGH (n=6), TH (n=5), and JRCKH (n=7); the matched non-D2 group included HU (n=6), TKH (n=9), OKGH (n=6), TH (n=7), and JRCKH (n=13). Table I summarizes patient characteristics before (n=186) and after (n=82) matching.

Table II presents the surgical outcomes. In the matched cohort, the non-D2 group included three patients (7.3%) who underwent D1 and 38 patients (92.7%) who underwent D1+ LND. Operation time was significantly shorter in the non-D2 group [D2: 349 min (176–507 min) *vs*. non-D2: 285 min (138–458 min); p=0.025]. No significant between-group differences were observed in blood loss, surgical approach, clinical T category, reconstruction method, postoperative complications (CD ≥II), or the median number of harvested lymph nodes [blood loss: D2, 20 ml (0–600 ml) *vs.* non-D2, 0 ml (0–550 ml); p=0.071; surgical approach—laparoscopic/robotic: D2, 30/11 *vs*. non-D2, 30/11; p=1.00; reconstruction—B-I/B-II/R-Y: D2, 12/9/20 *vs*. non-D2, 10/8/23; p=0.798; postoperative complications: D2, 7/41 (17.1%) *vs*. non-D2, 13/41 (31.7%); p=0.123; median number of harvested lymph nodes: D2, 42 (12–76) *vs*. non-D2, 35 (11–70), p=0.087]. Median postoperative hospital stay was significantly shorter in the D2 group (D2: 10 days (5–26) *vs*. non-D2: 12 days (7–65); p=0.009). Table III shows no significant differences between groups in terms of postoperative complication types. Reoperation was required in one patient (1.4%) in the D2 group and two (1.8%) in the non-D2 group before PSM. After matching, no patients in the D2 group required reoperation, whereas one patient (2.4%) in the non-D2 group did.

Prognosis. After PSM, histological examination of resected specimens revealed no significant differences between groups; therefore, the pathological stages according to JCGC were similar (p=0.395). The median follow-up period was 23.3 months (range=1–79.4 months) for the D2 group and 26.2 months (range=1–79.5 months) for the non-D2 group. During follow-up, postoperative recurrence was observed in 13 patients (13/41, 31.7%) in the D2 group and 10 patients (10/41, 24.4%) in the non-D2 group, with no statistically significant difference (p=0.461).

No between-group differences were observed in the recurrence site or median time to recurrence [D2: 280 days (166–1534) *vs*. non-D2: 454 days (105–1283); p=0.535] (Table IV). The 5-year OS rates were 47.7% and 34.6% in the D2 and non-D2 groups, respectively. Kaplan–Meier analysis indicated no significant difference in OS between groups (p=0.143). The 5-year RFS rates were 34.3% and 27.2% in the D2 and non-D2 groups, respectively, with no significant difference observed in Kaplan–Meier analysis (p=0.578). The 5-year CSS rates were 63.6% and 61.4% in the D2 and non-D2 groups, respectively, also showing no significant difference between groups (p=0.795) (Figure 2). Table V presents the results of univariate and multivariate analyses assessing the risk factors for OS, RFS, and CSS. Univariate Cox regression analyses identified pathological lymph node metastasis (pN+) as significantly associated with worse relapse-free survival (RFS) [hazard ratio (HR)= 3.217, 95% confidence interval (CI)=1.231–8.403, p=0.017], whereas lymphadenectomy extent (D2 *vs*. non-D2) and depth of tumor invasion (pT) showed no significant associations with OS, RFS, or CSS. In multivariate analyses adjusting for these factors, pN(+) remained an independent prognostic factor for RFS (HR= 3.553, 95%CI=1.263–9.996, p=0.016), confirming the critical importance of nodal status in predicting disease recurrence. However, the extent of lymphadenectomy (D2 *vs*. non-D2) did not independently influence OS, RFS, or CSS in the multivariate model. Similarly, pN(+) showed a trend toward worse CSS (HR= 6.365, 95%CI=0.790–51.300, p=0.082), although this did not reach statistical significance, likely due to the limited number of cancer-specific deaths and relatively short follow-up period. These findings suggest that while pathological lymph node involvement strongly predicts recurrence risk, the choice between D2 and non-D2 dissection does not significantly impact survival outcomes in this elderly patient population.

Discussion

To our knowledge, this multicenter retrospective study using PSM is the first to compare surgical outcomes and prognosis between D2 and non-D2 LND in older patients (≥75 years) who underwent MIDG for GC. Our results showed that although D2 LND prolongs operation time, it does not increase postoperative complications. Moreover, D2 LND during MIDG may provide limited survival benefits in older patients with GC.

In recent years, population aging has progressed rapidly worldwide, particularly in Asian countries such as Japan (17). Consequently, the average age of patients undergoing gastrectomy for GC has risen accordingly. Conventionally, "older" is defined as individuals aged ≥65 years, with those aged 65–74 years classified as "pre-old age" and those aged ≥75 years classified as "old age" (18). Many recent GC studies involving older populations have targeted the ≥75-year-old group, and our study similarly focused on this "old age" cohort (9, 19). In our dataset, 40.7% (402/988) of patients were aged 65–74 years, and 38.1% (376/988) were aged ≥75 years, indicating that older individuals (≥65 years) comprised 78.7% (778/988) of the total cohort. Older patients commonly present with multiple comorbidities and reduced physiological reserve, making them more susceptible to postoperative complications (20), which can rapidly worsen their overall condition (21). In this study, late-older patients (≥75 years) tended to have poorer performance status (PS); however, after PSM, PS was not significantly associated with postoperative complications (p=0.216).

Previous studies have similarly shown that postoperative complications are adverse prognostic factors in GC (22, 23). In particular, older male patients are reportedly at higher risk of postoperative complications and worse

prognosis. Notably, limited surgery without complications has been shown to improve outcomes compared with standard surgery complicated by adverse events in this population (24). The observed sex difference may be related to anatomical and hormonal influences on intestinal microcirculation, although a definitive biological mechanism remains to be established. Before PSM, the study cohort included 123 men (66.1%, 123/186 cases) and 63 women (33.9%, 63/186 cases), reflecting a men predominance. The median age was 81 years (range=75–91 years) for men and 80 years (range=75–91 years) for women, with no significant difference (p=0.548). ASA-PS classification scores of 3–4 were observed in 22.8% (28/123 patients) of men and 12.7% (8/63 patients) of women, indicating a trend toward higher ASA-PS among men (p=0.091). Although postoperative complications (CD grade ≥ II) did not significantly differ by sex, their incidence tended to be higher in men (24.3%) than in women (12.7%) (p=0.054). In univariate analyses, neither postoperative complications nor sex was significantly associated with OS, RFS, or CSS. Further analyses are planned to explore potential sex-related differences in prognosis. The 2025 Gastric Cancer Treatment Guidelines of the JGCA state that "in older patients, reduced and less invasive surgery, such as limited LND, may be weakly recommended after considering the balance between benefits and harms" (10). In clinical practice, however, surgical indications for older patients with GC often depend on patient-specific factors, as well as surgeon and institutional policies. Consequently, the choice of procedure, reconstruction method, and surgical approach (open, laparoscopic, or robotic) is largely determined by the surgeon's experience and preference. This variability underscores the need for clearer, evidence-based guidelines for managing older patients with GC. In contrast, the European Society for Medical Oncology (ESMO) recommends basing treatment decisions on functional age, assessed through a geriatric assessment (GA), rather

than chronological age (25). GA provides a comprehensive evaluation of physical and cognitive function, psychological and nutritional status, comorbidities, polypharmacy, and social support to identify frailty and guide individualized treatment planning. In this study, patient condition was assessed using the ASA-PS classification; however, GA was not performed. Among older patients, ASA-PS classifications were as follows: PS 0 (n=1), PS 1 (n=10), PS 2 (n=139), PS 3 (n=34), and PS 4 (n=2). In the total cohort, 12.2% (120/988 patients) had PS ≥3, a proportion significantly higher among older patients (≥75 years) than non-older patients (<75 years) (17.8% *vs*. 8.7%, $p<0.001$). Given the anticipated growth of the older population, including individuals with multiple comorbidities, developing GC surgery guidelines tailored to this demographic is becoming increasingly important.

Since Dr. Kitano first introduced laparoscopic distal gastrectomy (LDG) for early GC in 1994, laparoscopic gastrectomy (LG) has become widely adopted due to technological advancements (26). Compared with open gastrectomy (OG), LG is associated with reduced surgical trauma, faster recovery, and comparable oncological outcomes, establishing it as an effective minimally invasive surgical option for both early and advanced GC (6, 27–29). In Japan, the adoption rate of LG increased from 6.6% in 2004 to 64.9% in 2019 (30). This trend particularly benefits older patients, who are more vulnerable to surgical stress. The LOC-A multicenter study similarly reported comparable complication rates between LG and OG, but faster recovery and shorter hospital stays in the LG group, with similar 5-year OS (31). Minimally invasive surgery may help preserve physiological reserve and reduce severe complications in frail patients. Immunological studies have shown that LG attenuates postoperative increase in inflammatory markers such as interleukin-6 and C-reactive protein, potentially reducing non-cancer-related mortality (32, 33). More recently, robotic gastrectomy (RG) has garnered attention for its

enhanced precision and articulated dexterity, which have been shown to decrease anastomotic leakage, intra-abdominal abscess formation, blood loss, and length of hospital stay (34). In the present study, all patients underwent MIDG, and half of them (501/988, 50.8%) had early-stage disease (T1N0). Several studies have assessed MIG for advanced GC. The JLSSG0901 (27) and CLASS-01 (6) trials both reported no significant differences in early or late complications between LDG and open distal gastrectomy, confirming the safety of LG in advanced disease. For invasive GC, D2 LND remains the standard, whereas D1 or D1+ LND is recommended for early GC not amenable to endoscopic resection (4). In older patients, survival declines with age regardless of LND extent, whereas the risk of postoperative complications increases with more extensive LND. Prior reports have shown that open D2 LND in older patients is associated with higher morbidity with limited survival benefit (35, 36). Similarly, laparoscopic series involving patients aged ≥75 years have demonstrated higher rates of pancreatic fistula and abscess with D2 dissection, without a corresponding survival advantage (37). Ongoing trials, including a Chinese randomized study evaluating laparoscopic D1 LND in older patients with advanced GC (≥cT2) (38), are expected to further elucidate its safety and feasibility. In our PSM-adjusted MIDG cohort, D2 LND was performed in 39.8% of patients (74/186). Before PSM, non-D2 LND was more frequently performed in patients with poorer general condition (p=0.044). After PSM, operation time was significantly longer in the D2 group (349 *vs*. 285 min, p=0.025), while blood loss (20 *vs*. 0 ml, p=0.071) and postoperative complication rates (CD grade ≥ II; 17.1 *vs*. 31.7%, p=0.123) did not differ significantly. Interestingly, postoperative hospital stay was shorter in the D2 group (median 10 *vs*. 12 days, p=0.009), possibly reflecting surgeon expertise, as D2 LND was frequently performed by JSES-certified specialists [D2:17/41 (41.5%) *vs*. 14/41 (34.2%), p=0.495] (11). However,

discharge criteria varied across institutions without standardized definitions, which may have influenced the length of hospital stay. RG was implemented at all participating institutions and performed in 27.9% of all cases (276/988 patients). The decision to perform RG or LG depended on the surgeon and institutional preferences. Before PSM, RG was performed in 23.7% (44/186) of patients—31.1% in the D2 group and 18.7% in the non-D2 group—indicating a non-significant but notable tendency toward more frequent use of RG in the D2 group (p=0.053). After PSM, operative time tended to be longer in robotic distal gastrectomy compared with LDG [median: 376 (274–507) *vs*. 357 (288–446) min, p=0.78]. Previous reports have suggested the usefulness of RG in facilitating precise D2 dissection, indicating that RG may increasingly become the preferred approach for such technically demanding procedures in the future (34). In this study, no significant differences were observed between the D2 and non-D2 groups in 5-year OS (47.7% *vs*. 34.6%, p=0.143), RFS (34.3% *vs*. 27.2%, p=0.578), or CSS (63.6% *vs*. 61.4%, p=0.795). Multivariate analysis identified pN(+) as an independent prognostic factor for RFS but not for OS or CSS (39). This discrepancy may be attributable to the high rate of non-cancer-related deaths (7/82 patients, 8.5%) and the relatively short follow-up (median 33.1 months). Among all patients (988 patients), non-cancer-related deaths were more common among patients aged ≥75 years (25/376 patients, 6.6%) compared with those <75 years (18/612 patients, 2.9%, p=0.005). These findings underscore the need to account for competing risks—particularly in older patients—when assessing the oncological benefit of extensive LND. Our results, therefore, suggest that D2 LND may confer limited survival benefit in older patients with GC, especially when balanced against the greater operative burden. Although an Italian study reported a higher number of retrieved lymph nodes in patients who underwent D2 dissection (40), our study demonstrated a similar trend

without statistical significance (D2 *vs*. non-D2: median, 42 *vs*. 35; p=0.087). The distinction between D1+ LND and D2 LND primarily lies in the inclusion of dissection at stations No.11p and No.12a. The clinical significance of dissecting these two stations should be carefully evaluated based on pathological factors such as tumor stage and histological subtype of the primary tumor. Therefore, an individualized approach to determine the extent of LND is essential, particularly in older patients. Considering these factors, D1+ LND may represent a less invasive, yet sufficiently effective therapeutic option for this population. Previous studies have suggested that retrieving at least 16 lymph nodes is required for accurate staging (41). In the present study, 40 of 41 patients (97.5%) in the D2 group and 36 of 41 patients (87.8%) in the non-D2 group met this threshold. Large international datasets have indicated that retrieval of at least 29 lymph nodes is associated with optimal survival outcomes. In our cohort, 34 patients (82.9%) in the D2 group and 26 (63.4%) in the non-D2 group had ≥29 dissected lymph nodes, which falls below this optimal threshold. Although some cases did not meet this criterion, the total number of retrieved lymph nodes may have confounded survival comparisons and should, therefore, be interpreted cautiously.

In recent years, enhanced recovery after surgery programs have been increasingly adopted since their introduction in 2014, demonstrating safety and benefit—even in older patients—through shorter hospital stays and reduced costs (42). However, treatment guidelines specifically tailored for older patients with GC remain limited, and few clinical trials have focused on this population. In our study, the length of hospital stay was longer in the non-D2 group compared with the D2 group [median: 10 (5–26) *vs*. 12 (7–65) days, p=0.009]. This prolonged hospitalization may be attributed to variations in discharge criteria across institutions and the lack of standardized fast-track protocols following MIDG. A reduction in food intake is frequently observed, and a body weight loss

of approximately 10–15% within one year after distal gastrectomy is common (43). Several studies have demonstrated the benefit of introducing enteral nutrition, suggesting that further investigation into preoperative interventions and nutritional indications is warranted. In addition, accumulating evidence supports the usefulness of prehabilitation in older patients. In gastrectomy, preoperative assessment of skeletal muscle mass has been particularly recommended (44). However, in the participating institutions of this study, the prehabilitation programs were not standardized, indicating the need for further studies to establish unified protocols. In older patients, the benefit of adjuvant chemotherapy remains controversial due to multiple comorbidities and reduced treatment tolerance. Several studies have investigated the efficacy of adjuvant chemotherapy in patients aged ≥75 years. Among the 988 patients enrolled in our study, 387 patients (39.5%, 387/988 patients) had pathological stage II or higher disease. Postoperative chemotherapy was administered to 69.5% (148/213 patients) of patients aged ≤74 years and 32.2% (56/174 patients) of those aged ≥75 years (p<0.001). After PSM, adjuvant chemotherapy was administered to 10 patients (24.4%) in the D2 group and nine patients (22.0%) in the non-D2 group. Among patients with pathological stage II or higher disease—those for whom adjuvant chemotherapy is recommended in the treatment guidelines (4)—administration rates were 31.3% (10/32 patients) in the D2 group and 30.0% (9/30 patients) in the non-D2 group. In Japan, established evidence supporting the use of neoadjuvant chemotherapy (NAC) remains insufficient, and NAC has not yet been adopted as a standard treatment. Although the ESMO guidelines recommend NAC, its application in older patients with poor general condition remains controversial. The Japanese Gastric Cancer Treatment Guidelines (2025) state that "there is no consensus regarding the introduction of NAC into routine clinical practice" (10). According to the ESMO guidelines, NAC with the FLOT

regimen (fluorouracil, leucovorin, oxaliplatin, and docetaxel) is regarded as a standard treatment (5). Recent trials, including PRODIGY (45), JCOG1704 (46), and MATTERHORN (47), have shown promising outcomes, potentially paving the way for the future adoption of NAC in Japan.

Limitations. First, it was a retrospective observational study, and most procedures were performed by, or under the supervision of, surgeons specialized in MIDG. The choice of surgical approach and extent of procedure varied depending on institutional protocols and surgeon preferences. Second, 87.8% (867/988) of patients were classified as ASA-PS 1 or 2, indicating relatively good general condition and suggesting potential selection bias. Moreover, the exclusive use of ASA-PS to assess surgical fitness, without incorporating more comprehensive indices, further limits the ability to rule out selection bias, as patients with higher operative risk may have been preferentially assigned to less invasive non-D2 LND. Third, the median postoperative follow-up differed slightly between groups (23.3 months in the D2 group *vs*. 26.2 months in the non-D2 group), and the overall duration was relatively short for evaluating 5-year OS and RFS. Consequently, the reliability of the Kaplan–Meier–estimated 5-year survival rates should be interpreted with caution. Additionally, seven (8.5%) non-cancer-related deaths occurred during follow-up after PSM (D2: 1 patient, non-D2:6 patients). These findings underscore the importance of accounting for non-cancer-related mortality when managing GC in older patients. Comprehensive geriatric assessment (CGA) was not performed, and patients were not stratified by frailty status (fit, pre-frail, or frail). CGA, which evaluates comorbidities, nutritional and psychological status, social support, and polypharmacy, has been reported to improve postoperative outcomes (48, 49). Several studies have also demonstrated an association between frailty and postoperative adverse events (50, 51). Finally, this study covered a relatively long period

(2018–2024), during which evolving treatment strategies and perioperative management may have introduced historical bias. The lower major complication rate observed compared with previous reports (30) suggests that surgeons may have empirically selected less extensive procedures for patients at higher risk. Future studies should aim to develop risk-adapted strategies to identify patients unlikely to tolerate D2 LND and to determine the optimal extent of lymphadenectomy in older or frail populations.

Conclusion

In this PSM analysis of older patients with GC (≥75 years) undergoing MIDG, D2 LND was associated with longer operative time but did not confer a significant survival advantage over non-D2 LND. These findings suggest that, in appropriately selected older patients, a non-D2 LND approach can be safely performed without compromising oncological outcomes. Therefore, the extent of LND in this vulnerable population should be carefully individualized, weighing the perioperative risks against potential oncological benefits.

Conflicts of Interest

The Authors declare that they have no competing interests relevant to this article.

Authors' Contributions

Study conception and design: Yuma Ebihara and Noriaki Kyogoku; Acquisition of data: Yuma Ebihara; Analysis and interpretation of data: Yuma Ebihara and Noriaki Kyogoku; Drafting of manuscript: Yuma Ebihara; Critical revision of the manuscript: Yuma Ebihara, Noriaki Kyogoku, Hironobu Takano, Hideyuki Wada, Takeo Nitta,

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Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

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Figure legends

Figure 1. Study enrollment. NAC: Neoadjuvant therapy.

Older patients diagnosed with gastric cancer (cN+ or ≥cT2) were eligible for inclusion and were assigned to one of two groups based on propensity score matching: those who underwent D2 lymphadenectomy (D2) and those who did not (Non-D2).

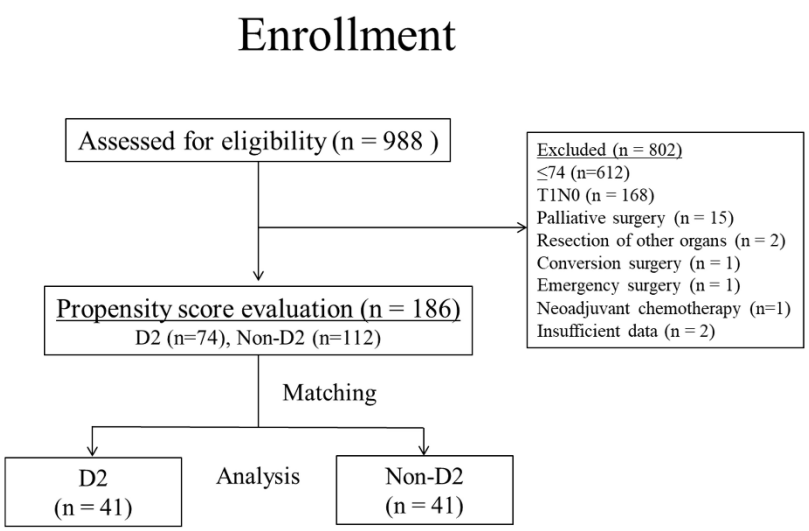


Figure 2. Prognosis of patients who underwent minimally invasive distal gastrectomy for gastric cancer according to D2 versus non-D2 lymphadenectomy. (A) Overall, (B) relapse-free survival, and (C) cancer-specific survival.

Fig.2A

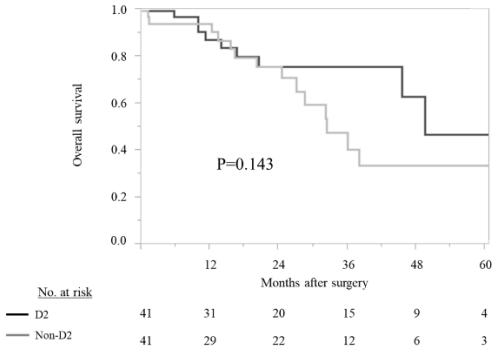


Fig.2B

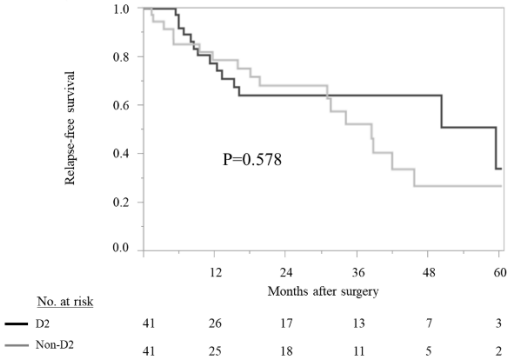


Fig.2C

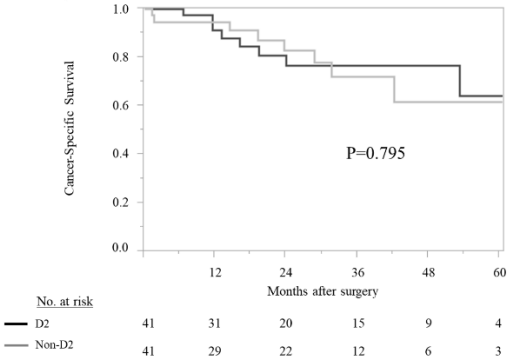


Table I. Baseline characteristics of patients who underwent minimally invasive distal gastrectomy before and after propensity score matching.

	All patients (n=186)			Propensity-matched patients (n=82)		
	D2 (n=74)	Non-D2 (n=112)	*p*-Value	D2 (n=41)	Non-D2 (n=41)	*p*-Value
Age, median (range)	78 (75-87)	82 (75-91)	< 0.001	81 (75-87)	80 (75-87)	0.828
Sex (%)			0.540			0.639
Male	47 (63.5)	76 (67.9)		28 (68.3)	27 (65.9)	
Female	27 (36.5)	36 (32.1)		13 (31.7)	14 (34.1)	
BMI†(kg/m^2), median (range)	23.0 (16.0-36.7)	22.6 (16.4-32.3)	0.905	23.1 (16.0-36.7)	22.6 (16.4-31.9)	0.689
ASA-PS*, n (%)			0.044			1.000
1-2	65 (87.8)	85 (75.9)		34 (82.9)	35 (85.4)	
3-4	9 (12.2)	27 (24.1)		7 (17.1)	6 (14.6)	
Clinical T stage**, n (%)			0.002			0.840
T1b	2 (2.7)	3 (2.7)		2 (4.9)	1 (2.4)	
T2	13 (17.6)	50 (44.6)		9 (21.9)	12 (29.3)	
T3	52 (70.2)	49 (43.8)		27 (65.9)	25 (61.0)	
T4	7 (9.5)	10 (8.9)		3 (7.3)	3 (7.3)	
Clinical N stage**, n (%)			< 0.001			0.658
N-	33 (44.6)	86 (76.8)		21 (51.2)	23 (56.1)	
N+	41 (55.4)	26 (23.2)		20 (48.8)	18 (43.9)	

†Body mass index, *The American Society of Anaesthesiologist's physical status, **According to the Japanese classification of gastric carcinoma: 6th English edition.

Table II. Surgical outcomes and postoperative course in patients who underwent a minimally invasive distal gastrectomy before and after propensity score matching.

	All patients (n=186)			Propensity-matched patients (n=82)		
	D2 (n=74)	Non-D2 (n=112)	*p*-Value	D2 (n=41)	Non-D2 (n=41)	*p*-Value
Operation time (min), median (range)	339 (176-531)	273.5 (109-458)	< 0.001	349 (176-507)	285 (138-458)	0.025
Blood loss (ml), median (range)	20 (0-600)	0 (0-550)	0.001	20 (0-600)	0 (0-550)	0.071
Approach, n (%)			0.053			1.000
Laparoscopic	51 (68.9)	91 (81.3)		30 (73.2)	30 (73.2)	
Robotic	23 (31.1)	21 (18.7)		11 (26.8)	11 (26.8)	
Lymphadenectomy, n (%)						
D1	0	11 (9.8)		0	3 (7.3)	
D1+	0	101 (90.2)		0	38 (92.7)	
D2	74	0		41	0	
Reconstruction, n (%)			0.543			0.798
Billroth I	12 (29.3)	28 (25.0)		12 (29.2)	10 (24.4)	
Billroth II	9 (22.0)	30 (26.8)		9 (22.0)	8 (19.5)	
Roux-en-Y	20 (48.7)	54 (48.2)		20 (48.8)	23 (56.1)	
Postoperative complication (CD[§] ≥ II), n (%)	12 (16.2)	26 (23.2)	0.247	7 (17.1)	13 (31.7)	0.123
Number of harvested lymph nodes, median (range)	40 (12-78)	37.5 (7-81)	0.273	42 (12-78)	35 (11-71)	0.087
Postoperative hospital stay (day), median (range)	9.5 (4-26)	12 (6-110)	< 0.001	10 (5-26)	12 (7-65)	0.009
Mortality (within 30 days)	1	1		0	1	

[§]Clavien-Dindo, classification

Table III. Postoperative complication types.

	All patients (n=186)						Propensity-matched patients (n=82)					
	D2 (n=74)			Non-D2 (n=112)			D2 (n=41)			Non-D2 (n=41)		
	All grades	≥ II	≥ III	All grades	≥ II	≥ III	All grades	≥ II	≥ III	All grades	≥ II	≥ III
Anastomotic leakage	3	3	0	2	2	2	2	2	0	0	0	0
Anastomotic stricture	0	0	0	0	0	0	0	0	0	0	0	0
Anastomotic hemorrhage	0	0	0	0	0	0	0	0	0	0	0	0
Intra-abdominal hemorrhage	0	0	0	3	3	1	0	0	0	2	2	1
Ileus (including DGE*)	4	3	1	6	6	1	0	0	0	3	3	0
Intra-abdominal abscess	0	0	0	4	3	1	0	0	0	2	2	1
Peripancreatic fluid collection	2	2	0	3	3	1	1	1	0	2	2	1
Cardiac complications	0	0	0	2	2	1	0	0	0	0	0	0
Pulmonary complications	1	1	0	4	4	0	1	1	0	1	1	0
Urinary and renal complication	1	0	0	1	1	0	0	0	0	1	1	0
Hepatobiliary complications	2	2	0	0	0	0	2	2	0	0	0	0
Other	1	1	0	2	2	1	1	1	0	2	2	1
All, n (%)	14 (18.9)	12 (16.2)	1 (1.4)	27 (24.1)	26 (23.2)	8 (7.1)	7 (17.1)	7 (17.1)	0	13 (31.7)	13 (31.7)	4 (9.8)
Reoperation, n (%)		1 (1.4)			2 (1.8)			0			1 (2.4)	

Table IV. Pathological results, postoperative recurrence site, and time to recurrence.

	All patients (n=186)			Propensity-matched patients (n=82)		
	D2 (n=74)	Non-D2 (n=112)	*p*-Value	D2 (n=41)	Non-D2 (n=41)	*p*-Value
Pathological T stage*, n (%)			0.155			0.735
T1	13 (17.6)	34 (30.4)		10 (24.4)	12 (29.3)	
T2	15 (20.3)	22 (19.6)		8 (19.5)	6 (14.6)	
T3	24 (32.4)	35 (31.3)		12 (29.3)	15 (36.6)	
T4	22 (29.7)	21 (18.7)		11 (26.8)	8 (19.5)	
Pathological N stage*, n (%)			0.042			0.304
N0	22 (29.7)	57 (50.9)		9 (22.0)	16 (39.0)	
N1	18 (24.3)	18 (16.1)		10 (24.4)	10 (24.4)	
N2	18 (24.3)	19 (16.9)		11 (26.8)	6 (14.6)	
N3	16 (21.7)	18 (16.1)		11 (26.8)	9 (22.0)	
Pathological JCGC stage*, n (%)			0.023			0.395
I	15 (20.3)	39 (34.8)		9 (22.0)	10 (24.4)	
II	26 (35.1)	43 (38.4)		13 (31.7)	17 (41.5)	
III	33 (44.6)	30 (26.8)		19 (46.3)	14 (34.1)	
Adjuvant chemotherapy, n (%)	25 (33.8)	15 (13.4)	0.001	10 (24.4)	9 (22.0)	0.794
Recurrence, n (%)	18 (24.3)	21 (18.8)	0.024	13 (31.7)	10 (24.4)	0.461
Days until recurrence (day), median (range)	357 (166-1534)	206 (69-1283)	0.378	280 (166-1534)	454 (105-1283)	0.535

Death from other causes, n (%)	3 (4.1)	13 (11.6)	0.154	1 (2.4)	6 (14.6)	0.106
Recurrence site, n						
LN (Para Ao/Distant)	6	6		5	3	
Peritoneum dissemination	10	5		7	3	
Liver metastasis	1	6		1	3	
Lung metastasis	0	1		0	0	
Skin metastasis	0	1		0	0	
Anastomotic lesion (remnant stomach)	1	2		0	1	

*According to the Japanese classification of gastric carcinoma: 6th English edition.

Table V. Univariate and multivariate Cox regression analyses for overall survival/relapse-free survival/ cancer-specific survival after propensity score matching.

	Overall survival				Relapse-free survival				Cancer-specific survival			
	Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis	
	HR（95%CI）	*p*-Value	HR（95%CI）	*p*-Value	HR（95%CI）	*p*-Value	HR（95%CI）	*p*-Value	HR（95%CI）	*p*-Value	HR（95%CI）	*p*-Value
Lymphadenectomy (D2 / Non-D2)	0.538 (0.232-1.249)	0.149	0.499 (0.212-1.172)	0.111	0.695 (0.341-1.416)	0.316	0.553 (0.266-1.152)	0.114	0.878 (0.328-2.349)	0.795	0.695 (0.258-1.874)	0.472
pT** (1,2 / 3,4)	0.567 (0.243-1.317)	0.187	0.702 (0.253-1.948)	0.497	0.589 (0.284-1.221)	0.155	0.881 (0.405-1.914)	0.749	0.313 (0.101-0.978)	0.046	0.211 (0.147-1.525)	0.211
pN** (Y / N)	1.458 (0.572-3.717)	0.429	1.606 (0.651-3.965)	0.304	3.217 (1.231-8.403)	0.017	3.553 (1.263-9.996)	0.016	7.793 (1.023-59.095)	0.047	6.365 (0.790-51.300)	0.082

*The American Society of Anaesthesiologist's physical status, [§]Clavien-Dindo, classification, **According to the Japanese classification of gastric carcinoma: 6th English edition. HR: Hazard ratio; CI: confidence interval; pT: pathological tumor depth; pN: pathological node metastasis.