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Oncological Significance of Proximal Resection Margin Length in Proximal Gastric and Gastroesophageal Junction Adenocarcinoma: A Single-center Retrospective Analysis

Proksimal Mide ve Gastroözofageal Bileşke Adenokarsinomunda Proksimal Rezeksiyon Sınırı Uzunluğunun Onkolojik Önemi: Tek Merkezli Retrospektif Bir Analiz

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Abstract

Objectives: The proximal margin required for oncologically sound resection of proximal gastric and gastroesophageal junction (GEJ) adenocarcinoma has not been established. We examined whether the pathological distance from the tumor to the proximal transection line was associated with postoperative oncological outcomes after curative-intent surgery.

Material and Methods: We retrospectively evaluated 186 patients who underwent total gastrectomy, distal esophagectomy, and lymphadenectomy for proximal gastric or GEJ adenocarcinoma at a single center. Clinicopathological data, relapse patterns, and survival were reviewed. Multivariable Cox proportional hazards models were used to determine factors independently associated with recurrence and overall survival.

Results: The pathological proximal margin averaged 2.5±1.0 cm. Over a mean follow-up of 26.3±22.8 months, 51 patients (27.4%) experienced recurrence and 88 (47.3%) died. Margin distance was comparable between the recurrence and non-recurrence groups (p=0.081) and did not independently predict relapse. Recurrence was independently associated with limited lymphadenectomy [recorded as "palliative lymphadenectomy" in the operative records; hazard ratio (HR): 2.99, p=0.014], pathological N3 stage (HR: 5.60, p<0.001), and splenectomy (HR: 2.74, p=0.007). Overall survival was independently associated with neural invasion, metastatic lymph node burden, recurrence, and the length of esophagus resected.

Conclusion: Among patients undergoing curative-intent resection of proximal gastric or GEJ adenocarcinoma, pathological proximal-margin distance was not independently associated with recurrence after microscopic clearance (R0) was achieved. Because no margin cut-off analysis was performed, the observed mean distance of 2.5 cm should not be interpreted as a definitive adequacy threshold.

Keywords: Gastric adenocarcinoma, gastroesophageal junction neoplasms, surgical margins, lymph node dissection, tumor recurrence, survival analysis

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Öz

Giriş / Amaç: Proksimal mide ve gastroözofageal bileşke (GEJ) adenokarsinomlarının onkolojik açıdan uygun rezeksiyonu için gerekli proksimal cerrahi sınır mesafesi henüz belirlenmemiştir. Bu çalışmada, tümörden proksimal transeksiyon hattına kadar olan patolojik mesafenin, küratif amaçla gerçekleştirilen cerrahi sonrasındaki onkolojik sonuçlarla ilişkili olup olmadığını değerlendirdik.

Gereç ve Yöntem: Tek bir merkezde proksimal mide veya GEJ adenokarsinomu nedeniyle total gastrektomi, distal özofajektomi ve lenfadenektomi uygulanan 186 hasta retrospektif olarak değerlendirildi. Klinikopatolojik veriler, nüks paternleri ve sağkalım sonuçları incelendi. Nüks ve genel sağkalımla bağımsız olarak ilişkili faktörleri belirlemek için çok değişkenli Cox orantısal risk modelleri kullanıldı.

Bulgular: Patolojik proksimal cerrahi sınır mesafesi ortalama 2,5±1,0 cm idi. Ortalama 26,3±22,8 aylık takip süresince 51 hastada (%27,4) nüks gelişti ve 88 hasta (%47,3) yaşamını yitirdi. Cerrahi sınır mesafesi nüks gelişen ve gelişmeyen gruplar arasında benzerdi (p=0,081) ve nüksü bağımsız olarak öngörmedi. Nüks; sınırlı lenfadenektomi [ameliyat kayıtlarında "palyatif lenfadenektomi" olarak belirtilen; tehlike oranı (HR): 2,99, p=0,014], patolojik N3 evresi (HR: 5,60, p<0,001) ve splenektomi (HR: 2,74, p=0,007) ile bağımsız olarak ilişkiliydi. Genel sağkalım ise perinöral invazyon, metastatik lenf nodu yükü, nüks ve rezeke edilen özofagus uzunluğu ile bağımsız olarak ilişkiliydi.

Tartışma / Sonuç: Proksimal mide veya GEJ adenokarsinomu nedeniyle küratif amaçlı rezeksiyon uygulanan hastalarda, mikroskobik cerrahi sınır negatifliği (R0) sağlandıktan sonra patolojik proksimal cerrahi sınır mesafesi nüks ile bağımsız olarak ilişkili bulunmadı. Herhangi bir cerrahi sınır eşik değeri analizi yapılmadığından, gözlenen ortalama 2,5 cm'lik mesafe kesin bir yeterlilik eşiği olarak yorumlanmamalıdır.

Anahtar Kelimeler: Mide adenokarsinomu, gastroözofageal bileşke neoplazileri, cerrahi sınırlar, lenf nodu diseksiyonu, tümör nüksü, sağkalım analizi

Introduction

Although the overall incidence of gastric cancer has declined over recent decades, it continues to account for a substantial proportion of cancer deaths worldwide. Its anatomical distribution has also changed: lesions of the proximal stomach and gastroesophageal junction (GEJ) now constitute a relatively greater share of cases, especially in Western populations (1,2). This shift has intensified interest in how best to resect these technically demanding tumors.

For localized gastric and GEJ adenocarcinoma, the principal curative option is complete surgical excision with tumor-free margins (3,4). Proximal clearance warrants particular attention because malignant cells can extend through submucosal or lymphatic channels beyond the macroscopically apparent margin. Microscopic involvement of the proximal margin has been linked to more local failures and poorer long-term outcomes (5).

The amount of gross proximal clearance needed to secure a negative microscopic margin remains uncertain. Traditional recommendations called for at least 5 cm in intestinal-type cancers and an even greater distance in diffuse tumors because occult intramural extension may be longer in the latter group (6,7). Such recommendations encouraged surgeons to resect a substantial segment of the esophagus to achieve adequate clearance.

More recent evidence has prompted reconsideration of these broad distance thresholds. Improvements in staging, intraoperative evaluation, specimen assessment, and perioperative systemic therapy allow surgeons to target an R0 resection without automatically maximizing the length of esophagus removed (8,9). Contemporary cohorts have accordingly described acceptable cancer control with shorter margins when the transection line is microscopically negative (10).

This question is especially consequential in Siewert II and III disease, where the tumor spans the anatomical transition between the distal esophagus and the proximal stomach. In this setting, both the operative route and the length of proximal esophageal resection remain debated (2,4). Guidelines consistently require microscopic margin negativity, yet they offer limited high-level evidence for a single distance that reliably prevents recurrence (3,8).

We therefore assessed whether the measured pathological proximal margin was associated with recurrence or overall survival after total gastrectomy and distal esophagectomy for proximal gastric or GEJ adenocarcinoma. The specific objective was to determine whether shorter, but histologically negative, proximal margins compromised oncological outcomes.

Materials and Methods

Study Design and Ethical Approval

This single-center retrospective cohort study was conducted in the Department of General Surgery at Van Yüzüncü Yıl University Faculty of Medicine. Approval was granted by the Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (approval no: 2020/10-03, date: 11.12.2020). All study procedures conformed to the Declaration of Helsinki. Because

existing records were analyzed retrospectively, the committee waived individual informed consent.

Patient Population

Institutional operative reports, pathology reports, oncology follow-up records, and electronic medical records were searched to identify consecutive patients who had undergone surgery with curative-intent for adenocarcinoma of the proximal stomach or GEJ.

Inclusion required histological confirmation of proximal gastric or GEJ adenocarcinoma, treatment consisting of total gastrectomy with distal esophagectomy and regional lymphadenectomy, a documented pathological measurement of the proximal margin, and sufficient postoperative follow-up information.

We excluded patients with any of the following: metastases at presentation; who underwent palliative operations; macroscopic residual tumor (R2); recurrent disease; a histological diagnosis other than adenocarcinoma; a synchronous malignant tumor; a complete pathological response after neoadjuvant therapy that precluded margin measurement; or missing clinicopathological data.

Surgical Treatment

Operations were performed by surgeons experienced in upper gastrointestinal oncology. Selection of the operative approach took into account tumor position and local extension, patient-related factors, and the operating surgeon's judgment.

Every patient underwent total gastrectomy and distal esophagectomy. The regional lymph node dissection followed the gastric cancer standards applicable during the treatment period, and continuity was restored with a Roux-en-Y esophagojejunostomy. For this study, the term "palliative lymphadenectomy", as retained from the operative records, denoted a lymph node dissection less extensive than a standard D1 or D2 dissection because of intraoperative technical or patient-related constraints. Nevertheless, these procedures were performed with curative-intent and without macroscopic residual tumor. The term did not refer to a palliative resection. In the manuscript, this category is described as limited lymphadenectomy (recorded as "palliative lymphadenectomy").

The gross cranial extent of the lesion was assessed intraoperatively by visual inspection and palpation. Surgeons selected a proximal transection point intended to balance technical practicality with achieving a tumor-free, oncologically acceptable margin.

Pathological Evaluation

Dedicated gastrointestinal pathologists evaluated all surgical specimens. After opening and fixation in accordance with local laboratory procedures, the specimens were assessed for tumor dimensions, histological type and grade, lymphovascular and perineural invasion, nodal metastases, pathological stage, and involvement of resection margins.

For this analysis, the pathological proximal margin was defined as the minimum microscopic distance between the most proximal tumor focus and the cut end of the specimen. Distances documented in millimeters were converted to centimeters before statistical analysis.

Resections were categorized by the presence or absence of microscopic residual disease. R0 denoted the absence of tumor at every examined margin, whereas R1 denoted the presence of microscopic cancer at one or more margins.

Pathological T and N categories were assigned using the edition of the American Joint Committee on Cancer (AJCC) tumor-node-metastasis system that was current when each specimen was reported.

Data Collection

The dataset included age, sex, tumor site, histological category, differentiation, pathological T and N categories, lymphovascular and perineural invasion, numbers of examined and of metastatic lymph nodes, proximal margin distance, receipt of adjuvant treatment, recurrence, and survival status.

Follow-up Protocol

Postoperative surveillance was performed through the institutional gastric cancer follow-up program. Assessments consisted of clinical examination and laboratory tests; upper gastrointestinal endoscopy, thoracoabdominal computed tomography, or other imaging were obtained when clinically indicated.

Relapse was recorded when supported by radiological, endoscopic, histological, or clinical evidence following curative resection. Disease at the anastomosis or operative bed was considered local recurrence; hematogenous and peritoneal spread were categorized as distant recurrence.

Overall survival was measured from surgery until death from any cause, with living patients censored at their most recent follow-up. Disease-free survival was measured from surgery to the first recurrence or death.

Statistical Analysis

Analyses were conducted with IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA).

Continuous-variable distributions were examined graphically with histograms and probability plots, and were also tested using the Kolmogorov-Smirnov procedure. Normally distributed data are reported as mean $\pm$ standard deviation; skewed data are given as median with minimum and maximum values. Counts and percentages describe categorical data.

For two-group comparisons, normally distributed continuous measures were analyzed with the independent-samples Student's t-test and non-normally distributed measures were analyzed with the Mann-Whitney U test. Pearson's chi-square test was used for categorical comparisons unless sparse cell counts required Fisher's exact test.

Kaplan-Meier estimates were used to construct overall and disease-free survival curves, and differences between curves were assessed by the log-rank test.

Candidate variables that were associated with recurrence or survival at $p<0.10$ in univariable testing were entered into multivariable Cox proportional hazards models. Effect estimates are presented as hazard ratios (HRs) with 95% confidence intervals (CIs).

All hypothesis tests were two-tailed, with $p<0.05$ defining statistical significance.

Results

The analysis included 186 patients who were treated with curative-intent for proximal gastric or GEJ adenocarcinoma. Mean age was 61.0±10.5 years, and 114 participants (61.3%) were men. The proximal pathological margin averaged 2.5±1.0 cm and the distal margin 9.5±3.0 cm. Patients had a median of 3 metastatic lymph nodes and a mean of 28.2±13.4 nodes examined. Mean observation time after surgery was 26.3±22.8 months. Baseline demographic, pathological, and follow-up data are detailed in Table 1.

Table 1. Baseline clinicopathological characteristics of the study population (n=186)

Variable	Value
Age (years), mean ± SD	61.0±10.5
Male sex, n (%)	114 (61.3)
Female sex, n (%)	72 (38.7)
Tumor diameter (cm), mean ± SD	4.8±2.7
Tumor volume (cm^3), mean ± SD	37.5±60.6
Positive lymph nodes, median (range)	3 (0-48)
Retrieved lymph nodes, mean ± SD	28.2±13.4
Resected esophageal segment (cm), mean ± SD	8.4±1.5
PCS (cm), mean ± SD	2.5±1.0
DCS (cm), mean ± SD	9.5±3.0
Follow-up duration (months), mean ± SD	26.3±22.8
Recurrence, n (%)	51 (27.4)
Mortality, n (%)	88 (47.3)

PCS: Proximal resection margin, DCS: Distal resection margin, SD: Standard deviation

Extended total gastrectomy accounted for 81.2% of procedures. Lymphadenectomy was classified as D2 in 59.1% of cases, D1 in 30.6%, and limited (recorded as "palliative lymphadenectomy") in 10.2%. 31.7% of patients received neoadjuvant treatment, and 95.7% received postoperative adjuvant therapy. Table 2 provides the complete distribution of operative and treatment variables.

Recurrence was documented in 51 patients (27.4%); no recurrence was recorded in 135 patients (72.6%). Locoregional disease alone occurred in 21 patients (11.3%), distant metastasis alone in 21 patients (11.3%), and both components in 5 patients (2.7%). By the end of follow-up, 88 patients (47.3%) had died.

The recurrence group had features indicative of more advanced disease. Its median metastatic node count was 7 (2-12), compared with 2 (0-5) in patients without recurrence ($p<0.001$). Splenectomy was more frequent in the recurrence group (23.5% vs. 8.9%, $p=0.016$), as was mortality (78.4% vs. 35.6%, $p<0.001$). Recurrence was unrelated to distal margin distance or to the length of esophagus resected. The pathological proximal margin was also similar between groups: 2.2 cm (2.0-3.0) in patients with recurrence and 2.5 cm (2.0-3.0) in patients without recurrence ($p=0.081$). Group comparisons are summarized in Table 3.

Factors associated with recurrence in preliminary analyses were jointly evaluated in a Cox model. Relative to D2 dissection, limited lymphadenectomy (recorded as "palliative lymphadenectomy") was associated with a higher recurrence hazard (HR: 2.99, 95% CI: 1.24-7.20, $p=0.014$). The hazard was also greater for pathological N3 disease than for N0 disease (HR: 5.60, 95% CI: 2.22-14.15, $p<0.001$) and for patients undergoing splenectomy (HR: 2.74, 95% CI: 1.32-5.69, $p=0.007$). Proximal margin distance did not remain in the model as an independent predictor. Full model estimates appear in Table 4.

Table 2. Surgical and treatment characteristics

Variable	n (%)
Extended total gastrectomy	151 (81.2)
ETG+splenectomy	22 (11.8)
ETG+phrenolaparotomy	8 (4.3)
Total gastrectomy	3 (1.6)
ETG+splenectomy+pancreatectomy	2 (1.1)
D2 lymphadenectomy	110 (59.1)
D1 lymphadenectomy	57 (30.6)
Palliative lymphadenectomy	19 (10.2)
Neoadjuvant therapy	59 (31.7)
No neoadjuvant therapy	124 (66.7)
Adjuvant therapy	178 (95.7)
No adjuvant therapy	4 (2.2)

ETG: Extended total gastrectomy

Table 3. Clinicopathological characteristics according to recurrence status

Variable	No recurrence (n=135)	Recurrence (n=51)	p-value
Positive lymph nodes	2 (0-5)	7 (2-12)	<0.001
Retrieved lymph nodes	28 (19-36)	21 (15-34)	0.063
Resected esophageal segment (cm)	8 (8-9.5)	8 (7-10)	0.249
PCS (cm)	2.5 (2-3)	2.2 (2-3)	0.081
DCS (cm)	9 (8-12)	10 (7-12)	0.581
Splenectomy, n (%)	12 (8.9)	12 (23.5)	0.016
Mortality, n (%)	48 (35.6)	40 (78.4)	<0.001

PCS: Proximal resection margin, DCS: Distal resection margin

Table 4. Independent predictors of recurrence

Variable	HR	95% CI	p-value
D1 vs D2 lymphadenectomy	1.55	0.825-2.917	0.173
Palliative vs. D2 lymphadenectomy	2.99	1.244-7.202	0.014
N1 vs. N0	1.19	0.414-3.397	0.751
N2 vs. N0	2.18	0.754-6.323	0.150
N3 vs. N0	5.60	2.217-14.145	<0.001
Splenectomy	2.74	1.324-5.688	0.007

HR: Hazard ratio, CI: Confidence interval

Table 5. Multivariable Cox regression analysis for overall survival

Variable	HR	95% CI	p-value
Neural invasion	2.00	1.169–3.412	0.011
Positive lymph node count	2.36	1.521–3.670	<0.001
Resected esophageal segment length	0.62	0.397–0.959	0.032
Recurrence	2.43	1.577–3.754	<0.001

Cox proportional hazards regression model (Omnibus test p<0.001)
HR: Hazard ratio, CI: Confidence interval

A separate multivariable model evaluated overall survival. Neural invasion was associated with a twofold increase in mortality hazard (HR: 2.00, 95% CI: 1.17-3.41, p=0.011), and greater metastatic node burden predicted poorer survival (HR: 2.36, 95% CI: 1.52-3.67, p<0.001). Recurrence conferred an approximately 2.4-fold increase in mortality hazard (HR: 2.43, 95% CI: 1.58-3.75, p<0.001). In contrast, a longer resected esophageal segment was associated with a lower hazard of death (HR: 0.62, 95% CI: 0.40-0.96, p=0.032). Table 5 lists the complete results.

Taken together, recurrence and survival were driven mainly by nodal burden, lymphadenectomy category, splenectomy, neural invasion, and relapse. After an R0 resection had been obtained, the measured proximal margin distance showed no independent association with recurrence.

Discussion

The increasing proportion of cancers arising in the proximal stomach and GEJ has sustained debate over the operation and resection extent most likely to provide durable cancer control (1,2). Complete excision remains essential, but the minimum acceptable proximal margin has not been determined. International recommendations prioritize R0 status while acknowledging uncertainty about the distance required for long-term safety (3,4).

Our central observation was the lack of an independent association between pathological proximal margin distance and recurrence after achieving microscopically negative margins. The margin was numerically shorter in patients who relapsed; however, the between-group difference was not statistically significant and was no longer evident in adjusted analyses. The cohort therefore provides no evidence that routinely removing a wider proximal segment improves oncological outcome after R0 resection. However, because proximal margin distance was analyzed as an observed continuous measure and no cut-off analysis was performed, the mean value of approximately 2.5 cm cannot be considered a definitive minimum adequate margin.

Concern about occult intramural extension historically favored generous proximal resections. Data published more recently do not uniformly support that practice. In the multi-institutional analysis by Postlewait et al. (11), proximal margin distance did not independently determine survival after resection of proximal gastric adenocarcinoma. Mine et al. (12) likewise reported acceptable outcomes in Siewert II and III cancers managed with limited proximal margins when histological clearance was confirmed. Our results align with those studies and suggest that the presence or absence of a tumor at the margin is more informative than distance alone.

Anatomical and biological heterogeneity across the esophagogastric junction partly explains why operative strategies remain variable. Changes incorporated into the AJCC system have affected how GEJ tumors are staged (13), whereas surgeons continue to use the Siewert categories when selecting an operative approach (14). Histological diversity within the junction further complicates uniform decision-making (15). Accordingly, institutions differ in their choice of access, the extent of esophageal resection, and nodal dissection.

Nodal status had a much stronger association with recurrence than did proximal margin distance. Pathological N3 disease was associated with a marked excess of relapse compared with N0 disease, consistent with the established prognostic importance of nodal burden in proximal gastric and GEJ cancer (16,17). Hasegawa et al. (16) used lymphatic dissemination patterns to define priorities for dissection in Siewert II/III tumors, and Barbour et al. (17) emphasized that an adequate nodal harvest

improves both staging and prognostic assessment in GEJ adenocarcinoma.

The category of nodal dissection was also relevant: patients in the limited lymphadenectomy category (recorded as "palliative lymphadenectomy" in the operative records) had a higher adjusted recurrence hazard. This label described a dissection less extensive than standard D1 or D2 lymphadenectomy and did not indicate that the gastric resection itself was palliative. The association should therefore be interpreted as reflecting both reduced nodal clearance and the adverse clinical or technical circumstances that led to a limited dissection. Previous work has similarly linked patterns of lymphatic spread and the extent of dissection to outcomes in junctional malignancies (18,19). Yamashita et al. (18) evaluated the optimal nodal field for Siewert II tumors, while Song et al. (19) showed that depth and site influence nodal distribution. These observations favor tailoring lymphadenectomy to disease anatomy rather than applying an identical field to every patient.

Splenectomy was independently associated with a greater risk of recurrence. The procedure was historically added to permit clearance of splenic hilar nodes, but routine splenectomy has been questioned because it increases morbidity without a consistent survival advantage (20,21). In our cohort, the association probably reflects selection of patients for splenectomy who have more locally advanced, biologically aggressive tumors, rather than a direct causal effect of organ removal.

The survival model identified neural invasion, metastatic node burden, and recurrence as adverse factors. This pattern is consistent with evidence that biological aggressiveness and the extent of nodal disease dominate prognosis after curative-intent resection (22,23). The magnitude of the effect of recurrence on mortality further underscores the need for effective local and systemic control.

A longer esophageal segment in the specimen was associated with better overall survival. Comparative studies of gastrectomy and esophagectomy for junctional cancer have also raised the possibility that a broader mediastinal component may benefit selected patients (24). However, this finding should be interpreted with caution because a retrospective cohort study cannot establish whether the length of the esophagus removed directly improves survival.

Study Limitations

Interpretation of these findings requires consideration of several limitations. The retrospective design permits selection bias and unmeasured confounding, and does not support causal inference. Results from one institution may not be extrapolated to centers with different case mixes or treatment pathways. The study covered a period during which staging, operative practice, perioperative care, and systemic therapy changed. Margin distance may have been influenced by tissue contraction and non-uniform specimen processing. No receiver operating characteristic, spline, or other cut-off analysis was performed; consequently, the observed mean proximal margin cannot establish a minimum adequate threshold. The limited lymphadenectomy category was based on terminology used in the operative records and may also reflect residual confounding from clinical or technical factors that prompted a less extensive dissection. Information on the precise pattern of recurrence and on adherence to adjuvant treatment was incomplete for some patients, and the number of relapse events limited the power of subgroup analyses.

The study nevertheless provides a comparatively large and clinically consistent series of patients who underwent total gastrectomy and distal esophagectomy. Detailed pathological margin measurements and parallel analyses of recurrence and mortality permitted a focused assessment of whether proximal margin distance contributes prognostic information beyond that provided by established disease-related factors.

Conclusion

Pathological proximal margin distance did not independently predict recurrence after curative-intent R0 resection of proximal gastric or GEJ adenocarcinoma. The observed mean proximal margin of approximately 2.5 cm describes this cohort and should not be interpreted as a definitive adequacy threshold.

Prognosis was more closely related to the biological and nodal extent of disease. Pathological N3 category, limited lymphadenectomy (recorded as "palliative lymphadenectomy"), and splenectomy were independently associated with recurrence; neural invasion, metastatic node burden, recurrence, and esophageal specimen length were independently associated with overall survival.

These results support an operative objective of microscopic tumor clearance combined with an appropriate lymphadenectomy, rather than the routine pursuit of an arbitrarily long proximal margin. Prospective multicenter studies incorporating prespecified margin cut-off analyses are warranted to define patient-specific resection requirements for proximal gastric and GEJ adenocarcinoma.

Ethics

Ethics Committee Approval: Approval was granted by the Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (approval no: 2020/10-03, date: 11.12.2020).

Informed Consent: Because existing records were analyzed retrospectively, the committee waived individual informed consent.

Footnotes

A generative artificial intelligence tool was used solely to assist with language revision and rephrasing. It was not used to design the study, generate or analyze data, or interpret the results. The authors reviewed and approved the final text and accepted full responsibility for its content.

Authorship Contributions

Concept/Design: O.O., M.B.Y., S.B., A.Ö., İ.Ö., İ.Ç., M.Ç.K., Data Collection or Processing: O.O., A.R.K., A.Ö., F.A., İ.Ç., M.Ç.K., Analysis or Interpretation: O.O., M.B.Y., S.B., A.Ö., İ.Ö., İ.Ç., R.K., M.Ç.K., Literature Review: O.O., M.B.Y., S.B., F.A., R.K., M.Ç.K., Writing, Reviewing and Editing: O.O., M.B.Y., S.B., A.R.K., İ.Ö., İ.Ç., M.Ç.K.

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