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Association of congenital anomalies with NICU course and early outcomes in neonates with esophageal atresia

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MAIN POINTS

- In this tertiary NICU cohort of neonates with esophageal atresia, overall in-hospital mortality was 27.3%, indicating that EA remains associated with substantial mortality despite modern neonatal care.
- Infants with esophageal atresia and associated congenital anomalies required longer mechanical ventilation and experienced delayed nutritional recovery, characterized by a prolonged time to reach full enteral feeding and an extended duration of postoperative TPN.
- The presence of additional anomalies was associated with increased surgical complications (OR 4.71) and increased mortality (33.3% vs 20%).

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ABSTRACT

Aim: Esophageal atresia (EA) is a serious congenital malformation that requires early surgical intervention during the neonatal period and is frequently associated with additional structural anomalies. This study aimed to evaluate the impact of accompanying major congenital anomalies on the neonatal intensive care unit (NICU) course and early clinical outcomes in neonates with EA.

Materials and Methods: In this retrospective cohort study, neonates who were diagnosed with EA and managed in a tertiary-level NICU between January 2010 and December 2025 were reviewed. Patients were categorized into two groups based on the presence of major structural anomalies: those with EA without associated anomalies and those with EA with associated anomalies. Demographic and perinatal characteristics, surgical variables, and NICU-related parameters were analyzed. The primary outcome measures were the durations of mechanical ventilation and total parenteral nutrition (TPN), and the time to achieve full enteral feeding. Secondary outcomes included surgical complication rates and mortality.

Results: A total of 33 patients were included in the analysis. At least one major congenital anomaly was identified in 54.5% of the cases. Compared with infants with EA without associated anomalies, infants with EA and associated anomalies had significantly longer durations of mechanical ventilation (p = 0.049), postoperative total parenteral nutrition (p = 0.007), and time to achieve full enteral feeding (p = 0.009). Although the risk of short-term surgical complications was greater in patients with associated anomalies (OR: 4,71; 95% CI: 0.94–23.68), this finding did not reach statistical significance (p = 0.052). The mortality rates did not differ significantly between the groups (p = 0.392).

Conclusion: The presence of major concomitant congenital anomalies in neonates with EA is associated with increased postoperative morbidity and a prolonged NICU course. These findings underscore the importance of incorporating comorbidity burden into prognostic assessment and clinical management strategies in this high-risk population.

Keywords: Esophageal atresia, Congenital abnormalities, Newborn, Mechanical ventilation, Parenteral nutrition

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INTRODUCTION

Esophageal atresia represents a relatively rare congenital malformation of the upper gastrointestinal tract, with an estimated incidence of 1 per 2,500–4,000 live births. Infants with esophageal atresia generally require early surgical intervention, and the neonatal course is often complicated by substantial morbidity, primarily related to respiratory instability, difficulties in establishing enteral feeding, and infection-related complications [1,2]. Over the past three decades, advances in neonatal intensive care practices, improvements in ventilatory technologies, and the standardization of perioperative management have led to a significant increase in survival rates. In developed countries, mortality has decreased to very low levels among term infants without major associated congenital anomalies, with survival approaching nearly 100% [3]. However, mortality rates range between 30% and 80% in

the presence of prematurity, low birth weight, major anomalies, or resource-limited settings [4,5]. Despite these improvements in survival, the burden of postoperative morbidity and prolonged intensive care hospitalization remains clinically significant [2,6].

A substantial proportion of infants with EA have associated anomalies involving the cardiovascular, gastrointestinal, renal, central nervous system, and musculoskeletal systems. Cardiac anomalies, in particular, are among the principal determinants of mortality and contribute to increased hemodynamic vulnerability during the perioperative period [7-9]. These anomalies should not be regarded solely as anatomical associations; rather, they represent clinical modifiers that diminish physiological reserve, reduce tolerance to surgical stress, and prolong the recovery process.

Although numerous studies have focused on mortality and survival, and several have demonstrated the impact of associated anomalies on overall outcomes in esophageal atresia, data specifically addressing the neonatal intensive care unit course remain relatively limited. In particular, relatively few studies have directly compared infants with isolated esophageal atresia and those with associated major congenital anomalies using objective indicators of postoperative morbidity. The available data are heterogeneous, and further evidence is needed regarding clinically relevant parameters such as the duration of mechanical ventilation, progression to enteral feeding, total parenteral nutrition (TPN) requirements, and length of intensive care stay. Therefore, a more detailed evaluation of the impact of associated anomalies on these clinical outcomes may contribute to prognostic assessment and help optimize perioperative management strategies.

In this study, neonates with esophageal atresia treated at our center were categorized as having EA without associated anomalies or EA with associated anomalies. We hypothesized that compared with infants without associated anomalies, infants with associated major congenital anomalies would experience a more complicated NICU course and increased postoperative morbidity. Accordingly, demographic and clinical characteristics and intensive care parameters were analyzed, and the effects of associated anomalies on morbidity and mortality were evaluated using objective, quantitative outcome measures.

MATERIALS AND METHODS

Study design and setting

This retrospective cohort study was conducted in the neonatal intensive care unit of a tertiary referral center. All consecutive neonates diagnosed with esophageal atresia (EA) who were followed in the NICU from January 2010 to December 2025 were screened. Patients who met the predefined eligibility criteria were included in the analysis.

The study protocol was approved by the Clinical Research Ethics Committee of Inonu University Faculty of Medicine (Approval No: 2026/9522, Date: 24.02.2026). Given the study's retrospective design, the ethics committee waived the requirement for informed consent. The investigation was performed in accordance with the principles of the Declaration of Helsinki. All the data were anonymized prior to analysis, and patient confidentiality was strictly maintained.

Sample size

Owing to the retrospective nature of the study, a sample size calculation was not applicable. Therefore, the study population consisted of all consecutive infants diagnosed with esophageal atresia who met the inclusion criteria during the study period.

Participants

Inclusion criteria

- Clinically and radiologically confirmed diagnosis of esophageal atresia,
- Initial preoperative admission to the study center during the specified study period,
- Availability of complete clinical records.

Exclusion criteria

- Patients transferred from another center during the postoperative period,
- Patients who died before surgical intervention,
- Cases with missing data regarding critical study variables.

Grouping and definitions

The study population was categorized according to the presence or absence of associated major congenital anomalies.

1. EA without associated major congenital anomalies: Patients without any clinically significant additional major structural anomalies.

2. EA with associated major congenital anomalies: Patients with at least one major structural congenital anomaly.

Major structural anomalies were defined as congenital defects involving the cardiovascular system, renal system, gastrointestinal system, central nervous system, or musculoskeletal system that required clinical follow-up, medical treatment, or surgical intervention. Minor anomalies and clinically insignificant anatomical variations were not considered in this classification.

Data collection and outcome measures

Demographic, perinatal, and clinical data were retrospectively extracted from patient medical files and the institutional electronic medical records system.

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Demographic, perinatal, and clinical information was retrospectively obtained from patient charts and the institutional electronic medical database. The collected baseline variables included gestational age at birth, birth weight, sex, mode of delivery (cesarean or vaginal birth), and small for gestational age (SGA) status. SGA was defined as a birth weight below the 10th percentile for gestational age.

Clinical characteristics included prenatal diagnosis, intubation in the delivery room, respiratory distress, tracheoesophageal fistula (TEF), and associated congenital anomalies. Associated anomalies were subclassified into gastrointestinal, cardiovascular, central nervous system, renal, or limb anomalies.

NICU-related variables included: duration of mechanical ventilation (days), requirement for mechanical ventilation lasting longer than seven days, duration of total parenteral nutrition (TPN) (days), day of initiation of enteral feeding, day of achievement of full enteral feeding, and total length of hospital stay (days). The presence of sepsis, early postoperative mortality within the first seven days, and overall in-hospital mortality were evaluated. Episodes were categorized as culture-confirmed or clinical sepsis. Culture-confirmed sepsis was diagnosed when blood culture positivity was accompanied by clinical findings compatible with systemic infection. Clinical sepsis was defined as the presence of clinical and laboratory features suggestive of sepsis that required intravenous antibiotic therapy for at least 5 days despite the absence of microbiological growth in blood cultures.

With respect to surgical and postoperative parameters, the day of the operation, additional surgical procedures (gastrostomy, cervical esophagostomy, or colostomy),and surgical complications were recorded. Surgical complications were defined as radiologically or clinically confirmed anastomotic leakage, anastomotic stricture, or perforation occurring during the postoperative period.

The primary outcome measures were duration of mechanical ventilation, duration of total parenteral nutrition, and time to full enteral feeding. Secondary outcomes included surgical complication rates and mortality.

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics version 26 (IBM, USA). The distributional characteristics of the continuous variables were examined with the Shapiro–Wilk test. Variables demonstrating a normal distribution are reported as the mean ± standard deviation, whereas variables not meeting normality assumptions are presented as medians with ranges (minimum–maximum).

For group comparisons, the independent-samples t-test was used for normally distributed continuous variables, and the Mann–Whitney U test was used for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Odds ratios (ORs) and 95% confidence intervals (CIs) for surgical complications and mortality were calculated using 2×2 contingency tables. A two-tailed p value of <0.05 was considered to indicate statistical significance.

RESULTS

During the study period, 36 neonates diagnosed with esophageal atresia (EA) were admitted to our unit. Three patients who died during the preoperative period were excluded, leaving 33 patients in the final analysis. Thirteen infants (39.4%) had been referred from outside the province.

Among the study population, 51.5% were female. The median gestational age was 37 weeks (range: 28–40), and 48.5% of the infants were born before 37 weeks of gestation. The mean birth weight was 2280 ± 536 grams, and 48.5% were classified as SGA. Cesarean delivery was performed in 84.8% of the cases, and a prenatal diagnosis was established in 39.4% of the cases. Intubation in the delivery room was required for 36.4% of patients, while respiratory distress during follow-up was documented in 60.6%. A tracheoesophageal fistula was present in 84.8% of the infants. Early postoperative mortality within the first 7 days was 12.1%, and overall in-hospital mortality was 27.3%. The median length of hospital stay was 35 days (range: 15–110). Reported surgical complications included anastomotic stricture (20%), anastomotic leakage (16.7%), and esophageal perforation (3.3%) (Table 1).

The study population was categorized into two groups: infants with esophageal atresia without associated major congenital anomalies (n = 15) and those with associated major congenital anomalies (n = 18). Baseline comparisons revealed no statistically significant differences between the groups in demographic characteristics, gestational age, birth weight, prenatal diagnosis, the presence of a tracheoesophageal fistula, or early mortality (Table 2).

Late-onset sepsis was identified in 22 of 33 infants (66.7%). Among these, 11 infants (33.3%) were classified as having clinical sepsis, and 11 (33.3%) had culture-proven sepsis. The frequency and distribution of sepsis subgroups were comparable between the study groups, with no statistically significant differences detected (p = 0.333).

Analysis of NICU-related parameters showed that the duration of mechanical ventilation was significantly longer in the group with associated anomalies (p = 0.049). The time to initiation of postoperative enteral feeding was comparable between the groups (p = 0.852). However, the time to achieve full enteral feeding (p = 0.009) and the duration of postoperative total parenteral nutrition were significantly prolonged in patients with associated anomalies (p = 0.007).

A subgroup analysis comparing inborn and outborn infants revealed no statistically significant differences in mortality, the presence of associated anomalies, the duration of mechanical ventilation, postoperative TPN duration, or the time to achieve full enteral feeding. The cesarean delivery rate was

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Table 1. Demographic, clinical and intensive care characteristics of patients with esophageal atresia.

Variables	(n=33)
Demographic and Perinatal Characteristics	
Female sex, n (%)	17 (51.5)
Gestational age, weeks*	37 (28–40)
<37 weeks, n (%)	16 (48.5)
≥37 weeks, n (%)	17 (51.5)
Birth weight, g**	2280 ± 536
SGA, n (%)	16 (48.5)
Cesarean delivery, n (%)	28 (84.8)
Prenatal diagnosis, n (%)	13 (39.4)
Clinical Characteristics	
Delivery room intubation, n (%)	12 (36.4)
Respiratory distress, n (%)	20 (60.6)
Presence of tracheoesophageal fistula, n (%)	28 (84.8)
Late-onset sepsis, n (%)	22 (66.6)
Culture-proven sepsis n (%)	11 (33.3)
Clinical sepsis n (%)	11 (33.3)
Day of operation*	2 (1–15)
Need for intubation >7 days, n (%)	11 (36.7)
Duration of mechanical ventilation, days*	5 (2–30)
Postoperative enteral feeding initiation day*	6 (2–17)
Time to full enteral feeding, days*	14 (10–30)
Postoperative TPN duration, days**	11.1 ± 5.2
Length of hospital stay, days*	35 (15–110)
Associated Anomalies, n (%)	
Gastrointestinal anomaly	8 (24.2)
Cardiovascular anomaly	7 (21.2)
Central nervous system anomaly	3 (9.1)
Renal anomaly	3 (9.1)
Limb anomaly	3 (9.1)
Gross Classification, n (%)	
Type A	5 (15.6)
Type C	27 (84.4)
Surgical Outcomes, n (%)	
Gastrostomy	8 (24.2)
Cervical esophagostomy	5 (15.2)
Colostomy	4 (12.1)
Surgical complications, n (%)	
Anastomotic stricture	6 (20.0)
Anastomotic leakage	5 (16.7)
Perforation	1 (3.3)
Mortality, n (%)	
Early postoperative 7-day mortality	4 (12.1)
Total mortality	9 (27.3)

Gross classification data were available for 32 patients. Surgical complication data were available for 30 patients (14 patients without associated anomalies and 16 patients with associated anomalies). *Values are presented as the median(minimum–maximum).**Values are presented as the mean ± standard deviation.

significantly higher among inborn infants (p = 0.003), which likely reflects the impact of prenatal diagnosis and planned perinatal management at our tertiary referral center. Although outborn infants underwent surgery at a relatively later postnatal age, this difference did not reach statistical significance (p = 0.057).

Although the short-term risk of surgical complications appeared to be greater among patients with associated anomalies (OR: 4,71; 95% CI: 0.94–23.68), this association did not reach statistical significance (p = 0.052).

Overall mortality was higher in the EA with associated anomalies group than in the EA without associated anomalies group (33.3% vs. 20%); however, the difference was not statistically significant (p = 0.392; OR: 2.18; 95% CI: 0.44–10.8).

The association between Spitz risk classification and mortality was also evaluated. An overall increase in mortality rates was

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Table 2. Comparison of clinical characteristics between patients with and without associated anomalies

Variables	EA without Associated Anomalies (n=15)	EA with Associated Anomalies (n=18)	p
Demographic and Perinatal Characteristics			
Female sex, n (%)	8 (53.3)	9 (50.0)	0.849
Gestational age, weeks*	37 (30--40)	37 (28--39)	0.898
<37 weeks, n (%)	7 (46.7)	9 (50.0)	0.849
≥37 weeks, n (%)	8 (53.3)	9 (50.0)	0.849
Birth weight, g**	2150 ± 546	2250 ± 614	0.626
SGA, n (%)	10 (66.7)	6 (33.3)	0.056
Cesarean delivery, n (%)	13 (86.7)	15 (83.3)	0.790
Prenatal diagnosis, n (%)	5 (33.3)	8 (44.4)	0.515
Clinical Characteristics			
Delivery room intubation, n (%)	4 (26.7)	8 (44.4)	0.290
Respiratory distress, n (%)	8 (53.3)	12 (66.7)	0.435
Presence of TEF, n (%)	13 (86.7)	15 (83.3)	1.000
Late-onset sepsis			
Culture-proven sepsis n (%)	3 (20.0)	8 (44.4)	0.333
Clinical sepsis n (%)	6 (40.0)	5 (27.8)	
Day of operation*	2 (1--4)	2 (1--15)	0.610
Need for intubation >7 days, n (%)	4 (28.6)	7 (43.8)	0.389
Duration of mechanical ventilation, days*	4.5 (2--13)	6 (3--30)	**0.049**
Postoperative enteral feeding day*	6 (2--10)	6 (3--17)	0.852
Time to full enteral feeding, days*	13 (10--20)	22 (10--30)	**0.009**
Postoperative TPN duration, days**	8.5 ± 3.0	13 ± 5.7	**0.007**
Length of hospital stay, days*	27 (15--110)	60 (22--90)	0.193
Gross Classification			
Type A	2 (13.3)	3 (17.6)	1.000
Type C	13 (86.7)	14 (82.4)	
Surgical Outcomes, n (%)			
Gastrostomy, n (%)	2 (13.3)	6 (33.4)	0.182
Cervical esophagostomy, n (%)	1 (6.7)	4 (22.2)	0.215
Colostomy, n (%)	0 (0.0)	4 (22.8)	0.051
Surgical complication, n (%)	3 (21.4)	9 (56.3)	0.052
Mortality, n (%)			
Early postoperative 7-day mortality, n (%)	2 (13.3)	2 (11.1)	0.846
Total mortality, n (%)	3 (20.0)	6 (33.3)	0.392

Surgical complication data were available for 30 patients (14 patients without associated anomalies and 16 patients with associated anomalies). *Values are presented as the median (minimum–maximum). **Values are presented as the mean ± standard deviation. SGA: Small for gestational age; TPN: Total parenteral nutrition; TEF: Tracheoesophageal fistula.

observed across higher-risk categories: 18.7% (3/16) in Spitz Type 1, 33.3% (3/9) in Spitz Type 2, 25% (1/4) in Spitz Type 3, and 50% (2/4) in Spitz Type 4. Overall, mortality tended to increase across higher Spitz risk categories.

Gross classification could be determined in 32 of 33 infants. Among these, 5 infants (15.6%) had gross type A lesions, and 27 infants (84.4%) had gross type C lesions. The gross type distribution did not differ significantly between infants with EA without associated anomalies and those with associated anomalies (p = 1.000).

DISCUSSION

Esophageal atresia (EA) is a complex congenital disorder frequently accompanied by multisystem anomalies, which are important determinants of clinical outcomes. In our cohort, associated congenital anomalies were identified in 54.5% of patients, which is consistent with previously reported rates ranging from 40% to 60% [8-10]. These findings support the clinical relevance of the comorbidity burden in shaping the neonatal intensive care course of infants with EA.

Associated anomalies may directly affect the NICU course by reducing the physiological reserve during the perioperative period. In our study, at least one major congenital anomaly was identified in 54.5% of the patients (n = 18), with gastrointestinal and cardiovascular pathologies being the most common. VACTERL association was identified in two patients, and no chromosomal abnormalities were detected in these patients. These findings are consistent with previously reported data and further support the clinical relevance of the comorbidity burden in infants with esophageal atresia [11,12].

Postoperative mechanical ventilation requirements and duration are important determinants of the clinical course. In our

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cohort, 36.4% of patients required invasive ventilatory support for longer than 7 days. When infants with esophageal atresia without associated anomalies were compared with those with associated anomalies, the duration of mechanical ventilation was significantly longer in the latter group (p = 0.049). These findings suggest that concomitant anomalies may impair cardiopulmonary stabilization during the postoperative period and increase the need for respiratory support. Consistent with our findings, Piro et al. [12] reported prolonged durations of invasive mechanical ventilation (IMV) in infants with associated congenital anomalies, with the duration of IMV extending to 9 days in the subgroup of infants with more than one associated anomaly. In addition, prolonged mechanical ventilation has been associated with postoperative morbidities such as pneumonia and atelectasis [13,14].

In our cohort, the median duration to achieve full enteral feeding was 14 days (range, 10–30 days), whereas the mean duration of total parenteral nutrition (TPN) was 11.1 ± 5.2 days. Compared with those without associated anomalies, infants with esophageal atresia and associated major congenital anomalies had a significantly delayed progression to full enteral feeding (p = 0.009) and a significantly longer requirement for TPN support (p = 0.007). These findings suggest that comorbid anomalies may delay gastrointestinal adaptation and impair feeding tolerance during the postoperative period. Consistent with our findings, Piro et al. [12] reported that the duration of TPN extended to 13 days in infants with esophageal atresia and associated anomalies, with significant differences compared with that in isolated cases. Similarly, Lees et al. [15] demonstrated that structural cardiac anomalies were associated with delayed feeding progression and prolonged parenteral nutritional support.

Consistent with previous reports, esophageal atresia type C has been described as the most common anatomical subtype [6,10], and the frequency of tracheoesophageal fistulas has been reported to be comparable between isolated cases and those with associated anomalies [1]. Similarly, in our cohort, type C was the predominant anatomical subtype, and no significant association was observed between the presence of major associated anomalies and either the gross anatomical subtype distribution or the presence of a tracheoesophageal fistula. These findings suggest that the clinical differences observed between the groups may be more closely related to the burden of comorbidities than to the anatomical subtype itself.

The Spitz classification remains among the most widely used prognostic tools in infants with esophageal atresia [9]. In our cohort, mortality progressively increased with higher Spitz categories, reaching 50% in the Type 4 group. Although statistical significance could not be demonstrated because of the limited sample size, this trend supports the prognostic relevance of the Spitz classification. Further studies with larger cohorts are needed to clarify its potential role in predicting morbidity and postoperative clinical outcomes.

Previous studies have consistently identified associated congenital anomalies, particularly cardiac defects, as major determinants of mortality in infants with esophageal atresia [1,7,16]. In our cohort, early postoperative mortality was comparable between the groups. Although overall mortality was numerically higher in infants with associated anomalies than in those without, this difference was not statistically significant. Nevertheless, the observed trend suggests that comorbidity burden may contribute to adverse clinical outcomes and that further validation in larger cohorts is needed.

In our cohort, infants with associated anomalies had higher rates of early postoperative complications. However, these observations did not reach statistical significance and should be interpreted with caution, given the limited sample size and a wide confidence interval. Similarly, the absence of a significant difference in mortality should not be interpreted as evidence of no clinical association, as the study may have been underpowered to detect clinically meaningful differences. Therefore, larger multicenter studies are warranted to further clarify the impact of associated anomalies on postoperative morbidity and survival in infants with esophageal atresia.

A key strength of the present study lies in its comparative cohort design, allowing direct assessment of the clinical course and postoperative outcomes in infants with esophageal atresia according to the presence or absence of associated major congenital anomalies. The analysis extended beyond mortality to include morbidity-related clinical parameters, such as the duration of mechanical ventilation and nutritional adaptation, thereby providing a more comprehensive assessment of the postoperative clinical course. Furthermore, the inclusion of a relatively homogeneous patient cohort managed at a single center under comparable surgical techniques and standardized intensive care protocols may have reduced practice-related variability and supported the consistency of the findings.

Limitations

The main limitations of our study include its retrospective, single-center design and its relatively small sample size. In particular, the limited number of patients within high-risk categories may have reduced the statistical power of mortality analyses and should therefore be considered when interpreting statistically nonsignificant findings in subgroup comparisons. Excluding neonates who died within the first 24 hours may have introduced selection bias by omitting the most critically ill patients. However, their inclusion could also have confounded the interpretation of postoperative outcomes, including duration of mechanical ventilation, duration of TPN, and enteral feeding parameters. Referral status may represent a potential confounding factor, as differences in prenatal diagnosis, transfer timing, and preoperative management may influence the clinical course in infants with

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esophageal atresia and limit the generalizability of our findings.

CONCLUSION

Overall, our findings indicate that associated anomalies play a central role in shaping the clinical trajectory of esophageal atresia. The significantly prolonged duration of mechanical ventilation and the delayed nutritional adaptation observed in infants with additional anomalies highlight the comorbidity burden as an important determinant of postoperative morbidity. However, no statistically significant difference in mortality was observed between the groups. These findings underscore the importance of careful clinical assessment of comorbidity burden in infants with esophageal atresia as part of postoperative management.

Ethics Committee Approval: The study protocol was approved by the Clinical Research Ethics Committee of Inonu University Faculty of Medicine (Approval No: 2026/9522, Date: 24.02.2026).

Informed Consent: Owing to the retrospective nature of the study, informed consent was waived.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Author Contributions: H.T.: Study conception and Design, Data collection, Statistical analysis, Literature review and Writing. E.Y.: Materials, Data collection, Data interpretation. R.Ö. : Study conception and Design, Supervision, Critical revision of the manuscript. T.Ç. : Design, Data collection, Literature review. N.A.: Design, Data collection, Literature review.

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