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Blood product transfusion in major burned pediatric patients: A case-control study

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ABSTRACT

Objective: To evaluate the impact of blood product transfusions on clinical outcomes, including mortality, dialysis requirement, and infection, in pediatric patients with extensive burns.

Material and Methods: This case-control study included pediatric patients with ≥20% total body surface area burns who were treated at a university hospital burn center between 2012 and 2022. Deceased patients were classified as cases, and discharged patients as controls. The primary outcome was mortality, and the secondary outcomes were dialysis. Multivariable logistic regression was used to assess associations between blood product usage and clinical outcomes, adjusting for burn severity, surgical duration, and infection.

Results: One hundred-thirteen patients were analyzed, with 93 discharged and 20 deceased. Platelet transfusion in the intensive care unit (ICU) was associated with lower mortality (odds ratio: 0.663, 95% confidence interval: 0.484-0.909, p=0.011) but with increased dialysis requirements. Moreover, albumin, red blood cell, and fresh frozen plasma transfusions in the ICU were correlated with an increased risk of infection. Albumin administration in the ICU was associated with decreased mortality (hazard ratio =0.848, 95% confidence interval: 0.735-0.977, p=0.023).

Conclusion: The findings suggest that burn injury severity, the amount of blood products transfused, and the timing of transfusions are critical factors in determining patient outcomes. Future research should focus on establishing evidence-based transfusion thresholds.

Keywords: Pediatric burn, transfusion, mortality, dialysis, infection

INTRODUCTION

Blood transfusion remains a cornerstone in the management of anemia-related perfusion disorders, providing critical support in maintaining adequate oxygen delivery. However, transfusion-related complications continue to pose significant challenges in clinical practice, often leading to hesitation in their use (1,2). A restrictive transfusion strategy with a hemoglobin threshold of ≤7 g/dL has been associated with reduced mortality in critically ill patients compared to a more liberal approach (3). The critical-care study of transfusion requirements also demonstrated a reduction in mortality with a restrictive transfusion strategy (4).

Pediatric patients with major burn injuries often require substantial blood transfusions due to factors such as surgical blood loss, hemodilution from resuscitation fluids, reduced erythropoiesis, increased erythrocyte destruction, and frequent blood sampling (4). Despite advances in surgical techniques, equipment, and supportive care, managing blood loss during and after major burn surgeries remains challenging and often requires substantial transfusion support, particularly in children (5). However, limited data exist on the specific effects of blood and blood-product transfusions on outcomes in pediatric patients with extensive total body surface area (TBSA) burns. The interplay between transfusion practices and the recovery of pediatric burn patients, including mortality, morbidity, and long-term outcomes, has not been thoroughly explored (6). The exact impact of transfusions of blood and blood products on clinical outcomes, the optimal thresholds and strategies for

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their use, and the long-term effects of transfusion practices on recovery and quality of life in pediatric burn survivors remain to be thoroughly investigated. Understanding the effects of transfusion practices in this vulnerable population is critical for optimizing patient care and improving survival outcomes.

This case-control study aimed to assess the impact of blood product transfusions on clinical outcomes in pediatric patients with extensive burn injuries, particularly those with significant TBSA involvement. The primary aim of this study was to assess the association between blood product transfusions (red blood cells, fresh frozen plasma, and platelets) and mortality by comparing transfusion patterns between patients who died (cases) and those who survived (controls). The secondary aim was to evaluate the relationship between blood product transfusions and the requirement for dialysis among pediatric burn patients.

MATERIAL and METHODS

Study Design and Population

This case-control study used data from patients with burns treated at our university hospital's burn and wound care center from 2012 to 2022. This center is a well-equipped burn and wound facility with a total of thirty-six beds, including twenty burn unit beds, ten chronic wound unit beds, and six intensive care unit (ICU) beds. Cases were defined as burn patients who died, and controls as burn patients who survived. Patients were included in the study if they were younger than 18 years, had a TBSA greater than 20%, and presented to the clinic within 48 hours of the injury. Patients were excluded if they refused blood products, received blood at another center before admission, or had incomplete or inaccessible data. Additionally, patients who had hemoglobinopathies, electrical burn injuries, or who died in the first three days were excluded.

Data were collected by clinical staff in the clinic. Institutional Review Board (IRB) of University of Health Sciences Türkiye, Kartal Dr. Lütfi Kırdar City Hospital approval was secured before data collection (protocol no: 2021/514/204/20, date: 22.06.2021), and the study adhered to all relevant IRB guidelines for patient confidentiality and ethical research conduct. Collected data included patient demographics, total blood and blood product transfusion volumes, number of surgical procedures, and laboratory values of hemoglobin, platelet count, INR, and creatinine at admission and discharge. In this context, "discharge" refers to the final recorded laboratory values prior to either hospital discharge or in-hospital mortality. Additional variables recorded included the need for mechanical ventilation in the ICU, duration of hospital and ICU stays, dialysis requirements, frequency of infectious episodes, mortality rates, and complications such as pneumonia and wound infections. Data on transfusions of erythrocytes, fresh frozen plasma, platelet suspensions, albumin, and cryoprecipitate during hospitalization and ICU care were also documented. All patients received transfusions in accordance with the institution's established algorithm for blood product administration.

Covariates

We constructed directed acyclic graphs to identify the minimum set of variables required for adjustment to assess the unconfounded association between blood transfusion and clinical outcomes. For the primary and secondary outcomes (mortality and dialysis requirement, respectively), the necessary adjustment variables were surgery duration and burn severity. These variables were selected based on data availability and their established role in influencing mortality and adverse clinical outcomes. Burn severity was adjusted using TBSA and burn degree, and infection was adjusted using sepsis and pneumonia.

Statistical Analysis

Each patient was assigned a unique protocol number that was used to retrieve the required data from the system. The extracted data were de-identified and recorded in an Excel file for analysis, ensuring patient confidentiality.

The statistical analyses were conducted using STATA version 18. The normality of variable distributions was assessed using visual methods (histograms and Q-Q plots). Data that did not follow a normal distribution were reported as medians [with interquartile ranges (IQR)], while categorical variables were presented as frequencies and percentages. We used Pearson chi-square test to analyze differences between categorical groups, with Fisher's exact test applied when necessary. To compare medians between two independent groups that did not conform to a normal distribution, the Mann-Whitney U test was employed.

To assess the association between blood product transfusion and adverse clinical outcomes, we used multivariable logistic regression adjusted for surgery duration, burn severity, and infection. Results are reported as adjusted odds ratios (aOR), 95% confidence intervals (95% CI) and p-values.

A Cox proportional hazards regression model was used to assess the association between blood product transfusion and patient survival time. The model was adjusted for surgery duration, burn severity (TBSA and degree), and the presence of pneumonia. Results are reported as adjusted hazard ratios (aHRs) with 95% CIs and p-values.

RESULTS

Demographic Data and Clinical Characteristics

During the ten-year study period, data were collected for 209 patients. A CONSORT flow diagram showing the number of patients considered for study inclusion and those excluded, along with the reasons for exclusion, is shown in Figure 1.

Six patients were excluded due to electrical burns. Upon re-evaluation, twenty-six patients were excluded as their burn injuries were deemed ineligible for the study. Fourteen patients were not treated within the first 48 hours, and twenty-one patients had incomplete records. Additionally, twenty-nine patients who died within the first three days were excluded. The study included 113 patients.

Table 1 presents the baseline characteristics of the 113 individuals analyzed. Among them, 93 were discharged (37 females, 56 males) and 20 were deceased (6 females, 14 males). The median age was 2 years in the discharged group and 2.5 years in the deceased group. American Society of Anesthesiologists class I was observed in 80.5% of discharged patients and 16.8% of deceased patients. The median TBSA burned was significantly higher in the deceased group (40%; IQR 30-51) than in the discharged group (30%; IQR 24-37) (p=0.006). First-degree burns were observed in 39.8% of patients in the discharged group and in 25% of patients in the deceased group. Second-degree burns were the most common, affecting 58% of those discharged and 65% of those who died. Third-degree burns were present in 2.2% of the discharged group and 10% of the deceased group.

Furthermore, regarding the occurrence of infection, pneumonia was reported in 4.3% of the discharged group and in 45% of the deceased group. Sepsis occurred in 90.3% of the discharged group, but in 100% of the deceased group. Notably, all patients in both groups developed wound infections.

Comparison of the admission and final laboratory values (Table 2) between the discharged and deceased groups showed that survivors had a median admission creatinine of 0.33 compared with 0.445 in the deceased group (p=0.041). The final creatinine readings for survivors and non-survivors were 0.24 and 0.515,

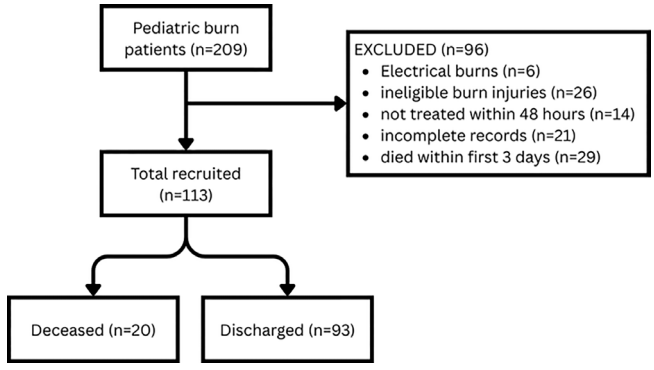

Figure 1. CONSORT flow diagram.

Table 1. Relationship between demographic values and mortality

	n (%)	Discharge (n=93)	Exitus (n=20)	p-value
Male	70 (61.9)	56 (49.6)	14 (12.7)	0.411
Female	43 (38.1)	37 (32.7)	6 (5.3)	
Age [median (IQR)]		2 (1-5)	2.5 (1-10)	0.587
Weight (kg) [median (IQR)]		12 (10-20)	15 (11-25)	0.411
ASA 1	111 (98.2)	91 (80.5)	20 (18.0)	0.414
ASA >2	2 (1.8)	2 (1.8)	0 (0.0)	
TBSA [median (IQR)]		30 (24-37)	40 (30-51)	0.006
1st degree burn	42 (37.2)	37 (32.7)	5 (4.4)	0.138
2nd degree burn	67 (59.3)	54 (47.8)	13 (11.5)	
3rd degree burn	4 (3.5)	2 (1.8)	2 (1.8)	
Hospital stay (day) [median (IQR)]		28 (21-40)	13.5 (8-24)	<0.001
ICU stay (day) [median (IQR)]		8 (4-16)	10.5 (7.5-24)	0.059
Mechanical ventilation duration (day) [median (IQR)]		0 (0-2)	8 (3.5-14)	<0.001
Pneumonia	13 (11.5)	4 (3.5)	9 (7.96)	<0.001
Sepsis	104 (104)	84 (74.3)	20 (17.7)	0.150
Wound infection		93	20	
Dialysis	3 (2.7)	0 (0)	3 (2.7)	<0.001
Number of total procedures [median (IQR)]		3 (2-5)	1 (1-3.75)	0.005
Fasciotomy & escharotomy [median (IQR)]		1 (0-1)	1 (1)	0.100
Debridement & graft [median (IQR)]		2 (1-4)	0 (0-2)	<0.001
Dressing [median (IQR)]		11 (8-15)	5 (2-9.75)	<0.001

ASA: American Society of Anesthesiologists, TBSA: Total body surface area, ICU: Intensive care unit, IQR: Interquartile ranges.

respectively (p-value 0.001). Both groups had similar median hemoglobin levels on admission (13.5 vs. 13.45 g/dL), but had statistically significant differences at discharge (10.5 vs. 8.65 g/dL, p-value <0.001). On admission, both groups had similar median international normalised ratio (INR) values (1.17 vs. 1.15); however, on discharge, survivors had a median INR of 1.0 compared with 1.6 in non-survivors (p<0.001). Survivors had lower platelet counts on admission than non-survivors (377 vs. 437.5), but at discharge survivors had significantly higher platelet counts (503 vs. 62; p<0.001).

Table 3 presents the adjusted odds ratios (ORs) for mortality, infection, and dialysis associated with blood product transfusions and albumin administration. Among the variables analyzed, platelet transfusion in the ICU was significantly associated with decreased odds of mortality (OR: 0.663; 95% CI: 0.484-0.909; p=0.011). This suggests a potential protective effect of platelet transfusion in critically ill pediatric burn patients. Although red blood cell (RBC) transfusion in the ward (OR: 10.662, 95% CI: 0.877-129.597, p=0.063) and in the operating theatre (OT) (OR: 2.175, 95% CI: 0.942-5.021, p=0.069) were associated with trends toward increased mortality, these associations did not reach statistical significance.

Secondly, among variables analyzed for association with infection, RBC transfusion in the ICU (OR: 1.426, 95% CI: 1.044-1.948, p=0.025) and fresh frozen plasma (FFP) transfusion in the ICU (OR: 1.448, 95% CI: 1.052-1.993, p=0.023) were significantly associated with an increased risk of infection. Additionally, albumin transfusion in the ICU was associated with a higher risk of infection (OR: 1.378, 95% CI: 1.034-1.837, p=0.028). These findings indicate that blood product transfusions in the ICU, particularly RBC, FFP, and albumin, may contribute to an increased risk of infection in pediatric burn patients.

Thirdly, platelet transfusion in the ICU was significantly associated with a increased likelihood of requiring dialysis (OR: 1.388, 95% CI: 1.012-1.904, p=0.042). Although RBC transfusion (OR: 1.423, 95% CI: 0.906-2.234, p=0.125) and FFP transfusion (OR: 1.537, 95% CI: 0.878-2.688, p=0.132) in the ICU were associated with increased odds of requiring dialysis, these associations were not statistically significant. These findings highlight a potential association between transfusions of platelets and other blood

Table 2. Impact of laboratory values on mortality/discharge

Lab values	Total number of the patients (n=113) median (IQR)	Discharge (n=93) median (IQR)	Exitus (n=20) median (IQR)	p-value
Admission creatinine [median (IQR)]	0.35 (0.23-0.48)	0.33 (0.23, 0.46)	0.445 (0.335, 0.505)	0.041
Admission INR [median (IQR)]	1.17 (1-1.41)	1.17 (1.05, 1.43)	1.15 (1, 1.355)	0.596
Admission hematocrit [median (IQR)]	40.2 (36.8-44.5)	40.1 (36.9, 44.5)	40.65 (36.2, 45.8)	0.857
Admission hemoglobin [median (IQR)]	13.5 (12-15)	13.5 (12, 14.8)	13.45 (12.3, 15.6)	0.767
Admission platelet (x10^3) [median (IQR)]	385 (304-498)	377 (305, 493)	437.5 (277.5, 522.5)	0.496
Discharge creatinine [median (IQR)]	0.26 (0.17-0.36)	0.24 (0.16, 0.33)	0.515 (0.3, 1.085)	<0.001
Discharge INR [median (IQR)]	1 (0.95-1.11)	1 (0.95, 1.02)	1.6 (1.41, 2.125)	<0.001
Discharge hematocrit [median (IQR)]	30.6 (27.7-33.8)	31.8 (28.7, 34.25)	25.3 (22, 28.1)	<0.001
Discharge hemoglobin [median (IQR)]	10.2 (8.9-11.25)	10.5 (9.6, 11.3)	8.65 (6.95, 9.15)	<0.001
Discharge platelet (x10^3) [median (IQR)]	467 (306-607)	503 (399, 640)	62 (31.5, 132)	<0.001

IQR: Interquartile range, INR: International normalized ratio.

Table 3. Logistic regression-outcome: death, infection, dialysis

	OR (death)	95% CI (death)	p	OR (infection)	95% CI (infection)	p	OR (dialysis)	95% CI (dialysis)	p
RBC tx in ICU	0.949	0.709-1.269	**0.725**	1.426	1.044-1.948	**0.025**	1.423	0.906-2.234	**0.125**
FFP tx in ICU	1.040	0.737-1.467	0.821	1.448	1.052-1.993	0.023	1.537	0.878-2.688	0.132
Plt tx in ICU	0.663	0.484-0.909	0.011	0.916	0.716-1.172	0.489	1.388	1.012-1.904	0.042
RBC tx in OT	2.175	0.942-5.021	**0.069**	0.973	0.656-1.443	**0.893**	0.543	0.077-3.834	**0.541**
FFP tx in OT	1.762	0.831-3.738	0.140	1.038	0.692-1.557	0.855	0.594	0.075-4.711	0.623
RBC tx in the ward	10.662	0.877-129.597	0.063	1.262	0.651-2.446	0.490			
Albumin in ICU	0.818	0.584-1.147	**0.245**	1.378	1.034-1.837	**0.028**	1.284	0.823-2.004	**0.270**

IQR: Interquartile range, RBC tx: Red blood cell transfusion, FFP tx: Fresh frozen plasma transfusion, Plt tx: Platelet transfusion, OT: Operating theatre, ICU: Intensive care unit, OR: Odds ratio, CI: Confidence interval.

products and renal dysfunction among critically ill pediatric burn patients, which warrants further investigation.

Table 4 presents the Cox proportional-hazards model hazard ratios (HRs) for various blood product transfusions and albumin administration in the ICU. RBC transfusion in the ICU was associated with a slight decrease in mortality risk (HR =0.897, 95% CI 0.798-1.007, p=0.068); however, this did not reach statistical significance. FFP transfusion in the ICU (HR =0.907, 95% CI 0.798-1.032, p=0.140) and platelet transfusion in the ICU (HR =0.918, 95% CI 0.724-1.163, p=0.481) also showed no significant association with mortality. Similarly, RBC (HR =0.909, 95% CI 0.767-1.078, p=0.276) and FFP (HR =0.896, 95% CI 0.754-1.066, p=0.217) transfusions in the OT were not significantly associated with mortality. However, albumin administration in the ICU was significantly associated with a reduced mortality risk (HR =0.848, 95% CI 0.735-0.977, p=0.023), suggesting a potential protective effect.

DISCUSSION

In this case-control study, we examined the impact of blood transfusion on critically ill pediatric burn patients. The observed mortality rate was 17.7%. While RBC, FFP, or albumin transfusion in the ICU was not significantly associated with mortality or dialysis requirements, it was linked to an increased risk of infection. Conversely, platelet transfusion in the ICU was significantly associated with lower odds of mortality and an increased likelihood of requiring dialysis. However, it was not linked to the incidence of infection.

Moreover, deceased patients received significantly higher amounts of RBCs, FFP, platelet suspension, and albumin during their stay in the intensive care unit. This suggests that these critically ill patients had more severe clinical presentations, likely requiring greater support, such as transfusion of blood products, to manage ongoing blood loss and complications, including hypovolemia, coagulopathy, and anemia. It is important to note that the higher blood product use in the deceased group does not necessarily indicate a causal relationship with mortality; however, it may be indicative of the severity of their burn injuries and associated complications.

Table 4. Survival analysis

	Hazard ratio	95% CI	p
RBC tx in ICU	0.897	0.798-1.007	**0.068**
FFP tx in ICU	0.907	0.798-1.032	0.140
Plt tx in ICU	0.918	0.724-1.163	0.481
RBC tx in OR	0.909	0.767-1.078	**0.276**
FFP tx in OR	0.896	0.754-1.066	0.217
Albumin in ICU	0.848	0.735-0.977	**0.023**

IQR: Interquartile range, RBC tx: Red blood cell transfusion, FFP tx: Fresh frozen plasma transfusion, Plt tx: Platelet transfusion, OR: Operating room, CI: Confidence interval, ICU: Intensive care unit.

Furthermore, patients receiving RBC and FFP in the ICU had higher odds of requiring dialysis and developing infection. Platelet transfusion in the ICU was associated with higher odds of requiring dialysis. The lower hemoglobin levels in deceased patients compared with discharged patients appear to be multifactorial and primarily associated with the severity of their clinical condition. Deceased patients had a higher mean TBSA burned (40%) than discharged patients (30%). This result indicated that more extensive injuries likely led to greater blood loss and a higher risk of complications during critical illness, such as coagulopathy or destruction of red blood cells.

It should also be noted that the transfusion thresholds for pediatric burn patients vary depending on the clinical context, but general guidelines are often adapted from critical care and burn-specific recommendations (7). These thresholds aim to balance the risks and benefits of transfusion, including ensuring adequate oxygen delivery while minimizing complications such as infections, immune modulation, and volume overload. Each pediatric burn patient is unique, and transfusion decisions should be individualized based on hemodynamic stability, clinical symptoms, laboratory findings, the extent of burn injury, and associated complications (8,9). Close monitoring of the patient's response to transfusions, together with a multidisciplinary team approach, is essential to optimize patient outcomes. Studies focusing on children with burn injuries demonstrated that a restrictive blood transfusion protocol, with a hemoglobin threshold of 7 g/dL, is safe in acute pediatric burn care, potentially reducing medical risks and lowering healthcare costs (10,11). During our study period, The observed mean Hb level was lower in deceased patients (8.6 g/dL) than in discharged patients (10.5 g/dL). This result indicates that a restrictive transfusion strategy may not lead to significantly improved outcomes in critically ill patients with severe burns. While restrictive strategies reduce complications and costs in less critical populations, their impact on survival in high-risk burn patients requires further investigation. We believe that threshold Hb values should be reassessed for transfusion of blood products in this specific patient population.

Additionally, our logistic regression analysis identified that the deceased group had a threefold higher frequency of dialysis requirement and a sevenfold greater number of days of mechanical ventilation. Higher rates of dialysis and mechanical ventilation in the deceased group suggest significant organ dysfunction, including impaired erythropoiesis due to renal insufficiency and systemic inflammation. These factors highlight the complexity of managing anemia and transfusions in pediatric burn patients, particularly in those with severe injuries and multi-organ involvement. Deceased patients had a significantly higher

TBSA burned, which likely led to severe systemic inflammatory responses and multi-organ failure, including acute kidney injury. Other contributing factors could include inflammatory and metabolic complications along with hemodynamic instability. On the other hand, the discharged group had significantly lower creatinine at hospitalization, creatinine at discharge, and INR at discharge than the deceased group. This was consistent with improved renal and coagulation functions. These findings reinforce the importance of early identification and management of organ dysfunction in critically ill pediatric burn patients.

Overall, the study emphasized the critical role of blood transfusions in the management of pediatric burn patients and recognized the need for careful assessment of risks and benefits to optimize outcomes. Further research is required to establish evidence-based transfusion thresholds and strategies specific to this vulnerable population. Our study underscored the challenges in optimizing transfusion strategies for pediatric burn patients. The role of restrictive versus liberal transfusion strategies in this population remains an area of ongoing research. Its applicability in pediatric burn patients requires further investigation.

Study Limitations

This study has several limitations that should be acknowledged. First, as a case-control study, it is inherently subject to biases, such as selection and information biases, which may affect the generalizability of the findings. Additionally, because this study had a retrospective design and data were obtained from medical records that may have contained inconsistencies or missing information, the accuracy and comprehensiveness of the data analysis were inherently limited. Second, the study was conducted at a single-center, which may not reflect practices and outcomes at other institutions that employ different protocols for managing pediatric burn patients. The findings may not be directly applicable to other populations with varying demographic, clinical, or institutional factors. Third, while the study explored the association between blood product transfusions and mortality, causation cannot be established due to the observational design. The higher use of blood products in the deceased group likely reflects the severity of illness rather than a direct causal relationship with mortality. Confounding factors such as the extent of burn injuries, systemic inflammatory responses, and organ dysfunction may have influenced the outcomes, but these variables were not fully accounted for in the analysis. Fourth, the study did not assess long-term outcomes, such as quality of life or functional recovery, which are crucial in understanding the broader implications of transfusion practices in pediatric burn patients. Future studies with larger cohorts and prospective designs are needed to validate the findings and explore the mechanisms underlying the observed associations.

Despite the limitations, the study provides valuable insights into transfusion practices and clinical outcomes among pediatric burn patients and underscores the need for further research to optimize management strategies for this vulnerable population.

CONCLUSION

In conclusion, this case-control study provides valuable insights into the impact of blood product transfusions on clinical outcomes in pediatric patients with extensive TBSA burns. The findings suggest that the severity of burn injury, the amount of blood products transfused, and the timing of transfusions are critical factors in determining patient outcomes. While blood transfusions remain a cornerstone in the management of major burns, further research is needed to define optimal transfusion strategies, identify risk factors for transfusion-related complications, and explore long-term outcomes in pediatric burn survivors. Additionally, the potential for personalized transfusion protocols based on burn severity and individual patient factors warrants further investigation. This study contributes to the growing body of evidence aimed at improving care and survival outcomes for pediatric burn patients.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Türkiye, Kartal Dr. Lütfi Kirdar City Hospital Clinical Research Ethics Committee, İstanbul, Türkiye, under protocol number 2021/514/204/20, dated 22 June 2021.

Informed Consent: Retrospective study.

Footnotes

Author Contributions

Concept - A.S., E.H.Ü., K.T.S.; Design - A.S., E.H.Ü., K.T.S.; Data Collection or Processing - E.H.Ü., S.Y., T.Ş., G.F., M.D., K.T.S.; Analysis or Interpretation - A.S., E.H.Ü., F.R.M., T.Ş., A.Z., K.T.S.; Literature Search - A.S., S.Y., F.R.M., T.Ş., A.Z., K.T.S.; Writing - A.S., F.R.M., K.T.S.

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