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Effectiveness of Tranexamic Acid in Reducing Blood Loss during Placenta Accreta Spectrum, A Randomized Controlled Trial

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ABSTRACT

Background: Placenta accreta spectrum (PAS) represents a critical obstetric complication described as by the risk of massive hemorrhage. Tranexamic acid (TXA), an antifibrinolytic compound, has been demonstrated to effectively minimize blood loss in various surgical contexts, nevertheless its effectiveness in the management of PAS has not been thoroughly investigated.

Objective: This study aimed to assess the efficacy of prophylactic TXA in minimizing intraoperative blood loss and limiting transfusion requirements in cases with PAS undergoing Cesarean delivery.

Methods: A randomized controlled trial (RCT) was executed at Aswan University Hospital (October 2024–August 2025) involving 94 women with PAS scheduled for Cesarean delivery. Participants were allocated randomly to had either 1 g IV TXA (n=47) or saline (n=47) before skin incision. Intraoperative blood loss served as the primary endpoint, with operative time, transfusion requirement, and hospitalization duration defined as secondary endpoints.

Results: The TXA group (G) had significantly reduced mean hemorrhage (398.23 ± 133.25 mL vs. 533.81 ± 101.79 mL; P value = 0.0003), fewer PRBC infused (1.02 ± 0.87 vs. 2.17 ± 1.11 units; P value = 0.0002), and shorter hospital stays (4.89 ± 0.89 vs. 6.30 ± 1.08 days; P value = 0.0008). Operative time was reduced in the TXA G (44.79 ± 6.8 vs. 49.5 ± 6.5 minutes; P value = 0.002). No thromboembolic events or maternal deaths occurred.

Conclusion: Prophylactic TXA significantly reduces hemorrhage, requirement for blood transfusion, and hospital stay in PAS surgeries without increasing adverse events.

Keywords: Placenta accreta spectrum, Tranexamic acid, Postpartum hemorrhage, Cesarean section.

INTRODUCTION

Placenta accreta spectrum (PAS) is a major obstetric disorder characterized by abnormal placental invasion into the myometrium, either partial or complete, and is regarded as one of the most severe pregnancy-related complications [1-3]. The occurrence of PAS has risen in parallel with increasing Cesarean section (CS) rates over recent decades [1, 4]. Cases diagnosed with PAS are predisposed to significant, potentially fatal bleeding during and following delivery, with adverse maternal outcomes documented in approximately 60% of cases and maternal death in around 7% [5, 6].

Antifibrinolytic therapy represents a potential adjunctive approach to reduce bleeding in PAS cases [1]. As a potent antifibrinolytic agent, tranexamic acid (TXA) acts by attaching to lysine-binding sites of plasminogen, inhibiting fibrinolysis and consequently lowering hemorrhage, adverse outcomes, and mortality rates [7, 8]. TXA is extensively utilized in trauma, orthopedic, and cardiac surgery to control bleeding [5, 9]. Recent clinical evidence, including a multicenter randomized controlled trial in women with postpartum hemorrhage (PPH), has demonstrated that TXA effectively reduces bleeding-related mortality. Several additional studies further corroborate its efficacy in decreasing PPH [10-14].

Prophylactic administration of TXA following umbilical cord clamping has been shown to lower hemorrhage risk in PAS cases [5, 15]. Nonetheless, the available literature includes studies with limited sample sizes or design weaknesses, and although infrequent, severe complications such as postpartum renal cortical necrosis have been documented [15, 16]. Despite being acknowledged as an effective, safe, and cost-effective intervention for PPH [17], TXA has not achieved universal adoption in routine management, highlighting the importance of continued research [1]. Accordingly, this investigation aimed to assess the efficacy of prophylactic TXA in reducing intraoperative blood loss and transfusion requirements in women with PAS undergoing CS.

PATIENTS AND METHODS

This investigation was designed as a single-center, double-blind randomized controlled trial (RCT) performed at Aswan University Hospital.

Inclusion criteria: Women older than 18 years with a singleton pregnancy, an antenatal ultrasound-confirmed diagnosis of PAS, and planned CS or cesarean hysterectomy.

Exclusion criteria: Cases with history of cardiovascular disease (coronary artery disease, severe arrhythmias and

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congestive heart failure, or myocardial infarction), bleeding disorders (antiphospholipid syndrome, renal or hepatic dysfunction, coagulation abnormalities, preoperative anemia (Hb < 8 g/dL); thrombocytopenia), preeclampsia or eclampsia during the current pregnancy or contraindications to TXA, including prior venous thromboembolism, hypersensitivity, ongoing thrombosis, seizure disorders, hematuria, acquired color vision defects and renal failure.

Eligible participants received counseling regarding the study, and informed consent was obtained either through self-reading of the information sheet or by having it read aloud. Randomization occurred prior to enrollment, with allocation determined by computer-generated random sequences concealed in opaque, sealed envelopes that were opened only after consent was provided. A total of 94 pregnant women scheduled for Cesarean delivery were enrolled and randomized into two groups. Cases in group I were administered 1 g of TXA intravenously, diluted (1 g/10 mL) in 20 mL of 5% glucose and infused over 10 minutes prior to skin incision. Group II, serving as the control group, was administered an equal volume of normal saline. Demographic and clinical baseline characteristics, including age, medical history, smoking status, and BMI, were recorded. Obstetric data (parity and gestational age) and preoperative vital signs (heart rate, respiratory rate, and blood pressure) were also documented. Preoperative laboratory values included hemoglobin (Hb) and hematocrit (Hct).

Ultrasound assessments, including the degree of PAS, were recorded and categorized as PAS1 (mild), PAS2 (moderate), or PAS3 (severe). The diagnosis and grading of PAS followed the FIGO classification system [18, 19], which stratifies severity based on defined ultrasound criteria in women with placenta previa.

- **PAS1 (mild):** Characterized by multiple placental lacunae (≥2), loss of the hypoechoic clear zone, and bladder wall irregularity.
- **PAS2 (moderate):** Encompassed all PAS1 findings, in addition to uterovesical hypervascularity in the lower uterine segment with parametrial extension.
- **PAS3 (severe):** Demonstrated PAS1 and PAS2 features, plus further enhancement of lower uterine segment vascularity with invasion into parametrial region.

The most recent pre-surgical ultrasound assessment examination was utilized to evaluate PAS-related findings and to determine the severity grade of the disorder. The cases were transferred to the operating room, where a calibrated plastic drape was positioned beneath them. Hemorrhage was recorded from the delivery of the placenta until the conclusion of the surgical procedure. Intraoperative hemorrhage (mL) during CS was determined as follows:
Hemorrhage = (weight of used surgical sponges − preoperative weight of sponges) + volume collected in suction bottle after placental delivery.

Hemorrhage during transfer to the postoperative care unit was measured using a calibrated plastic drape placed beneath the participant intraoperatively. Postoperative hemorrhage within the first 2 hours after surgery was assessed separately using one or two calibrated plastic drapes beneath the participant. The Hb and Hct values were measured afterwards.

Outcomes: The study's **primary outcome** was estimated intraoperative blood loss (EBL).

Secondary outcomes consisted of the number of packed red blood cells (PRBCs) and fresh frozen plasma (FFP) units transfused intraoperatively and in the first 24 hours postpartum. Additional endpoints encompassed operative time, surgical and postoperative complications—including hysterectomy—length of hospitalization, ICU stay duration, and discharge modality. Evaluated safety outcomes included minor adverse effects (nausea, vomiting, headache & skin reactions) and major clinical events such as thromboembolic complications, along with perioperative alterations in Hb and Hct.

Sample size: For both groups, sample size was derived using a significance level of $\alpha = 0.05$, a power of $1–\beta = 0.8$, and a presumed standard deviation of 1000 mL for hemorrhage in PAS.

Ethical approval: The study was conducted in full compliance with the ethical guidelines of The Faculty of Medicine's ethics committee in Aswan University. A confidential file was maintained for each participant, and data presentation adhered to a strict non-disclosure policy, ensuring that no identifying personal information was included. Participants received both verbal and written explanations of the study, and only those who provided documented informed consent were enrolled. The study was carried out in compliance with the World Medical Association's Code of Ethics (Declaration of Helsinki).

Statistical analysis

Statistical analyses were conducted using SPSS version 26. Continuous variables were expressed as mean ± SD, while categorical variables were reported as frequencies and percentages. Group comparisons were made using Chi-square or Fisher's exact test for categorical data, and Student's t test or Mann–Whitney U test for continuous data. Associations between quantitative variables were examined with partial

Spearman correlation coefficients. Statistical significance was defined as a two-sided P value < 0.05.

RESULTS

This study encompassed 94 pregnant women undergoing Cesarean delivery who were meeting the inclusion criteria. The study group pregnant women for whom TXA was given (47) and controls (47) pregnant women. The demographic characteristics of these women in comparing both groups were shown in table (1).

The baseline maternal and neonatal traits were similar among both groups, indicating appropriate randomization and minimizing potential selection bias. The mean maternal age did not differ substantially between the TXA group (26.8 ± 4.3 years) and controls (27.43 ± 4.51 years; p = 0.483). Similarly, the mean BMI was nearly identical in both groups (31.2 ± 3.8 kg/m² vs. 31.46 ± 4.4 kg/m²; p = 0.727). The gestational age at delivery was also consistent across groups (39.36 ± 1.2 weeks in the TXA group vs. 39.34 ± 1.08 weeks in controls; p = 0.787). Obstetric history as reflected by the number of previous CSs, showed no significant difference (1.06 ± 0.99 in TXA group vs. 1.3 ± 1.1 in controls; p = 0.281). Neonatal outcomes at birth were comparable, with mean birth weights of 3193.62 ± 452.72 g in the TXA group and 3182.98 ± 455.08 g in controls (p = 0.910). The data demonstrated that both groups were well matched at baseline, reducing the likelihood of confounding from demographic or perinatal variables in subsequent outcome analyses.

Table (1): Demographic distribution based on subject characteristics in the two groups

Variable	TXA group (n = 47)	Control group (n = 47)	P-value
Maternal Age (years)	26.8 ± 4.3	27.43 ± 4.51	0.483
BMI (kg/m²)	31.2± 3.8	31.46 ± 4.4	0.727
Gestational age (weeks)	39.36 ± 1.2	39.34 ± 1.08	0.787
Number of previous CS	1.06 ± 0.987	1.3 ± 1.1	0.281
Birth weight	3193.62± 452.723	3182.98± 455.08	0.910

In table (2), the distribution of PAS grades was equivalent in the two groups, showing no statistically meaningful variations was observed. Grade 1 PAS was identified in 2 cases (4.3%) in the TXA G and 4 participants (8.5%) in controls (p = 0.654). Grade 2 PAS was manifested in 12 participants (25.5%) in TXA group and 10 participants (21.3%) in controls (p = 0.650). Grade 3 PAS was the predominant type in both groups, affecting 33 participants (70.2%) in each (p = 0.732). Preoperative laboratory parameters were comparable among groups. The average Hb level was 10.98 ± 1.07 g/dL in the TXA group and 11.12 ± 0.99 g/dL in controls (p = 0.497), while the average Hct values were 34.21 ± 3.10% and 34.50 ± 2.50% respectively (p = 0.609). Similarly, baseline hemodynamic measurements showed no marked differences. The mean pre-systolic blood pressure was marginally reduced in the TXA group (116.81 ± 8.87 mmHg) relative with the controls (120.43 ± 9.10 mmHg), but this variation neared, although was not significant (p = 0.054). Pre-diastolic blood pressure was 73.40 ± 5.63 mmHg in the TXA group and 74.47 ± 6.50 mmHg in controls (p = 0.400). The average preoperative heart rate was nearly identical among both groups (85.81 ± 3.40 bpm vs. 86.00 ± 5.03 bpm; p = 0.819).

Table (2): Comparison between preoperative PAS grading, pulse and blood pressure, HB, and HT

Variable	TXA group (n = 47)	Control group (n = 47)	P-value
PAS* Grade (1/2/3) • Grade 1 PAS • Grade 2 PAS • Grade 3 PAS	 **2 (4.3%)** **12 (25.5%)** **33 (70.2%)**	 **4 (8.5%)** **10 (21.3%)** **33 (70.2%)**	 **0.654** **0.650** **0.732**
Preoperative Hemoglobin (g/dL)	**10.98 ±1.07**	**11.12 ± 0.99**	**0.497**
Preoperative Hematocrit (%)	**34.213 ± 3.1**	**34.5 ± 2.5**	**0.609**
Presystolic Blood Pressure (mmHg)	**116.81 ±8.87**	**120.43± 9.1**	**0.054**
Prediastolic Blood Pressure (mmHg)	**73.4 ± 5.63**	**74.47 ± 6.5**	**0.400**
Preoperative Heart Rate (bpm)	**85.81 ± 3.4**	**86. ±5.028**	**0.819**

*Placenta accreta spectrum

Data in table (30 showing the estimated surgical hemorrhage that was markedly decreased in TXA group relative with the controls. The average hemorrhage in TXA group was 398.23 ± 133.25 mL, whereas the controls had an average of 533.81 ± 101.79 mL. This variation was meaningful in statistical terms (p = 0.0003), showing a substantial decrease in surgical bleeding associated with TXA administration. **(Table 3 and figure 1).**

Table (3) Estimated blood loss between the two groups

Outcome	TXA group (n=47)	Control group (n=47)	P-value
Estimated Blood Loss (mL)	398.23 ± 133.25	533.81 ± 101.79	0.0003

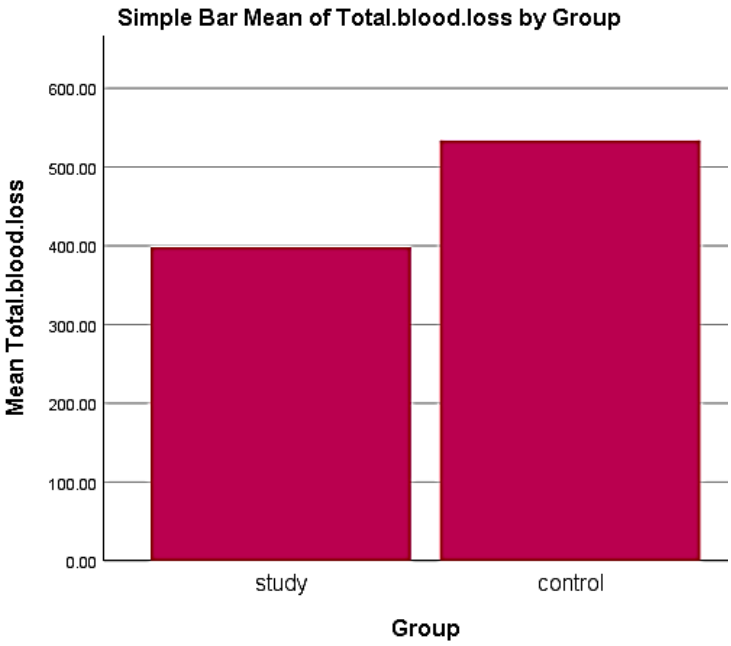

Figure 1. Bar chart showing ESL among the two Gs

Regarding surgical interventions, no meaningful difference was detected among TXA group and controls (Fisher's exact test, p = 0.0887). In the TXA group, 4.3% of cases required no intervention, 29.8% underwent hemostatic suturing and 66% required uterine artery ligation. Whereas in the controls, 8.5% underwent hemostatic suturing, and 89.4% required uterine artery ligation. One participant (2.1%) in controls required hysterectomy but, in this case, hysterectomy was done as the case had previous 5 CS and completed her family not from intractable bleeding. Blood product utilization was substantially reduced in TXA group.

The mean number of packed red blood cell (PRBC) units infused was 1.02 ± 0.87 in the TXA group relative with 2.17 ± 1.11 in the controls (p = 0.0002). Likewise, the average number of FFP units infused was 0.09 ± 0.28 versus 0.51 ± 0.69, in respective manner (p = 0.0002). The period of surgery was significantly reduced in the TXA group (44.79 ± 6.8 minutes) compared to the controls (49.5 ± 6.5 minutes; p = 0.002). Post-surgery Hb concentrations were greater in the TXA group (10.33 ± 0.8 g/dL) than in the controls (9.67 ± 0.7 g/dL; p = 0.0001). The mean Hb drop was significantly less with TXA (0.64 ± 0.5 g/dL) compared to controls (1.4 ± 0.6 g/dL; p = 0.0005). Postoperative Hct and Hct drop were comparable across both groups (p = 0.774 and p = 0.452 respectively).

No instances of primary PPH were reported in either group. ICU admission rates were identical at 91.5% in both groups but our hospital guidelines were ICU admission for every case of PAS. The average period of hospital stay was substantially decreased in TXA group (4.89 ± 0.89 days) relative to controls (6.30 ± 1.08 days; p = 0.0008). No major adverse events, encompassing pulmonary embolism (PE) or deep vein thrombosis (DVT) were reported, and there were no cases of maternal mortality in either group.

Table (4): Intraoperative surgical intervention and blood products transfusion

Outcome	TXA group (n = 47)	Control group (n = 47)	P-value
Surgical intervention:			**P-value (Fisher's exact) = 0.0887**
No intervention	**2 (4.3%)**	**0%**	
hemostatic sutures	**14 (29.8%)**	**4 (8.5%)**	
balloon dilatation	**0%**	**0%**	
uterine artery ligation	**31 (66%)**	**42 (89.4%)**	
internal iliac artery ligation	**0%**	**0%**	
Need for Hysterectomy	**0%**	**1 (2.1%)**	
PRBC Units Transfused	**1.02 ± 0.87**	**2.17 ± 1.11**	**0.0002**
FFP Units Transfused	**0.09 ± 0.28**	**0.51 ± 0.688**	**0.0002**
Duration of Surgery (minutes)	**44.79± 6.8**	**49.5 ± 6.5**	**0.002**
Postoperative Hb (g/dL)	**10.33 ± 0.8**	**9.67 ± 0.7**	**0.0001**
Hb Drop (g/dL)	**0.64 ± 0.5**	**1.4 ± 0.6**	**0.0005**
Postoperative Hct (%)	**33.91 ± 2.9**	**34.07 ± 2.4**	**0.774**
Hct Drop (%)	**0.3 ± 0.86**	**0.4 ± 0.9**	**0.452**
Primary postpartum	**0 (%)**	**0 (%)**	**NS**
ICU Admission (n, %)	**43(91.5%)**	**43 (91.5%)**	**NS**
Duration of Hospital Stay (days)	**4.89± 0.89**	**6.30± 1.08**	**0.0008**
Major side effects (DVT/PE) (n, %)	**0 (%)**	**0 (%)**	**NS**
Mortality (if any)	**0 (%)**	**0 (%)**	**NS**

Table (5) showed Pearson's correlation analysis, which demonstrated that total blood loss was highly positively associated with surgery time (r = 0.65) and moderately linearly linked with Hct difference (r = 0.58) indicating that higher blood loss was associated with longer operative times and greater postoperative Hct drops. A weak positive correlation was observed between total blood loss and neonatal birth weight (r = 0.42). Weak inverse association were found among total blood loss and pre-surgical Hb (r = –0.37) and between total blood loss and preoperative Hct (r = – 0.32), suggesting that higher baseline hematologic values may offer some protection against excessive blood loss. Total blood loss showed only a weak correlation with BMI (r = 0.18). Surgery time showed a moderate linear link with Hct difference (r = 0.51). As expected, preoperative Hb and preoperative Hct revealed a very strong linear link (r = 0.92), reflecting their close physiological relationship.

Table (5): Correlation Coefficients (Pearson's *r*) between variables

Variables	variables	Correlation (*r*)	Interpretation
Total Blood Loss	**Surgery Time**	**0.65**	**Strong positive**
Total Blood Loss	**HCT Difference**	**0.58**	**Moderate positive**
Total Blood Loss	**Baby Weight (B.W)**	**0.42**	**Weak positive**
Total Blood Loss	**Pre-op Hemoglobin**	**-0.37**	**Weak negative**
Total Blood Loss	**Pre-op Hematocrit**	**-0.32**	**Weak negative**
Total Blood Loss	**BMI**	**0.18**	**Very weak**
Surgery Time	**HCT Difference**	**0.51**	**Moderate positive**
Pre-op Hemoglobin	**Pre-op Hematocrit**	**0.92**	**Very strong positive**

DISCUSSION

This RCT demonstrated that prophylactic intravenous TXA (1g) administered prior to skin incision significantly reduced intraoperative hemorrhage, necessity of transfusion, and hospital stay length among women undergoing CS for PAS, without increasing thromboembolic or other major adverse events.

Parallel to the current study, **Ibrahim *et al.*** [5] investigated the efficacy of TXA in reducing blood loss during and after Cesarean delivery in women with PAS. Their findings showed significantly less intraoperative hemorrhage in the TXA cohort compared to controls (2232 mL vs. 3405 mL). They further reported a marked reduction in the requirement for transfusion of PRBCs, FFP, and platelets both intraoperatively and within the first 24 hours postoperatively. **Kremer and Cortez** [15] reported a lower mean EBL in the TXA group (3.11 ± 3.94 mL) compared to the placebo group (9.42 ± 12.47 mL). However, this variation did not reach statistical significance (P = 0.3). Notably, the study included only 11 participants, which restricted the statistical power to identify differences in EBL. Similarly, the mean volume of PRBC infused during surgery was reduced in TXA group than in controls**.**

In a separate study, administration of TXA during umbilical cord ligation resulted in a substantial reduction in mean ESL (672 mL) versus controls (1072 mL) [13]. These results align with our findings, suggesting that TXA may serve as an effective prophylactic measure to prevent hemorrhage and related adverse events in females at probability of postpartum bleeding. A clinical trial assessing the effect of TXA on blood loss during scheduled CS found that average intra and postoperative hemorrhage was lower in the TXA group relative to controls (241.6 vs. 510 mL). Moreover, cases receiving TXA exhibited significantly elevated Hb and Hct levels. The investigators indicated that TXA might be of particular value in women with anemia or in those for whom transfusion is not feasible [20].

A meta-analysis of nine clinical trials involving 2,365 participants demonstrated that TXA administration prior to Cesarean delivery significantly reduced the incidence of PPH, transfusion requirements during and after surgery, Hb decline, and severe PPH, without evidence of significant adverse effects [1]. A separate meta-analysis incorporating 12 studies demonstrated that TXA substantially reduced blood loss in women undergoing either Cesarean delivery or vaginal birth [21]. Furthermore, three additional controlled trials reported that administration of TXA immediately before to CS reduced intraoperative and postoperative blood loss without causing maternal adverse effects or neonatal complications [22-24].

Similarly, **Sentilhes *et al.*** [25] observed that prophylactic TXA decreased vaginal PPH. Collectively, these studies underscore the efficacy of TXA in minimizing hemorrhage.

Our findings also demonstrated that both the period of surgery and the length of hospitalization were markedly shorter in PAS women who received TXA relative to controls who showed higher incidence of PPH and greater transfusion requirements.

In contrast, **Abdel-Aleem and colleagues** [20] reported no substantial variation in hospitalization duration between women undergoing elective CS who received TXA and those given a placebo. The discrepancy with our results may be attributed to differences in study populations: Our study focused on women with a diagnosis of PAS, whereas **Abdel-Aleem *et al.*** [20] included

females underwent routine scheduled Cesarean delivery. Nonetheless, both studies consistently documented decreased bleeding within and after delivery in TXA group. In our study, hysterectomy was also executed for one case in controls and performed not for intractable bleeding but electively as the case had previous 5 CSs and completed her family. **Shakur *et al.*** [8] also documented that TXA application in females with postnatal bleeding had no marked impact on the necessity of hysterectomy [8].

In our study, no complications were documented during and post- surgery in both groups. In two studies by **Sadek *et al.*** [8] and **Shakur *et al.*** [13] showed that complications encompassing thromboembolism had not been documented in medication regimen of TXA prophylaxis.

LIMITATIONS

- Single-center design: Conducted at Aswan University Hospital; generalizability to other settings requires validation.
- Short-term follow-up: Lack of data on long-term complications or neonatal outcomes.
- Predominance of severe PAS: 70% Grade 3 cases may limit applicability to milder forms, though this reflects real-world high-risk cohorts.
- Universal ICU admission policy: High ICU admission rate (91.5%) limits assessment of TXA's impact on critical care needs.

CONCLUSION

This study demonstrated that IV TXA was both effective and safe in women with PAS, substantially reducing intraoperative bleeding and transfusion requirements while being associated with shorter hospital stay. No adverse events were reported. The main limitations included the small sample size per group and the administration of a fixed 1 g dose rather than weight-adjusted dosing. Larger, adequately powered studies employing weight-based dosing protocols are needed to confirm these observations and enhance clinical applicability.

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