Placenta accreta spectrum—A single-center retrospective observational cohort study of multidisciplinary management over time

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Abstract

Objective: To evaluate whether the results of a previous study that showed a decrease in blood loss and transfusions with a multidisciplinary approach, including a fixed team when delivering women diagnosed with placenta accreta spectrum at Sahlgrenska University Hospital, remained low throughout time, and to investigate hospital stay and maternal and neonatal complications during a time period with varying team structure compared with previous periods.

Methods: A retrospective observational cohort study comparing data from medical records including three cohorts of women diagnosed with placenta accreta spectrum between October 2003 and December 2020. Cohort 1 consisted of women delivered before the multidisciplinary approach was introduced. Cohort 2 and cohort 3 were both managed in a multidisciplinary manner, but while cohort 2 was managed by a fixed team, cohort 3 was managed by several different senior specialists. The data were analyzed using Kruskal-Wallis test.

Results: Blood loss and need for transfusion were significantly lower for cohort 3 and cohort 2 compared with cohort 1. No significant difference was found between cohort 3 and cohort 2.

Conclusion: The multidisciplinary management and surgical method employed at Sahlgrenska University Hospital have lowered blood loss and the need for transfusions, even over time.

Keywords: blood transfusion, cesarean hysterectomy, multidisciplinary management, placenta accreta spectrum, surgical blood loss

1 | INTRODUCTION

Placenta accreta spectrum (PAS) is a placental attachment disorder leading to an inability for the placenta to separate from the uterine wall after delivery, a condition caused by an abnormal ingrowth of trophoblasts into the myometrium.1 PAS is associated with increased morbidity and mortality of both women and infants, which are above all attributed to major blood loss during delivery.1-5 The strongest risk factor for developing PAS is previous cesarean section (CS).5,6

The optimal surgical approach for women with PAS is not yet clear, although the standard procedure is a planned cesarean hysterectomy, avoiding incision in the placenta, and removing the uterus...
with placenta in situ.\textsuperscript{1} Despite this approach, maternal morbidity can be considerable, due to a lack of prenatal diagnosis and a multidisciplinary team (MDT).\textsuperscript{7} The multidisciplinary approach and surgical method at the High-Risk Obstetric Unit at Sahlgrenska University Hospital (SU), a tertiary referral center, was introduced in 2011. Subsequently, this approach was evaluated by Lekic et al,\textsuperscript{7} reporting a striking decrease in blood loss and need for transfusion. Clearly, there is a need to try to reproduce such results; the importance of corroborating obtained data, particularly data from smaller series, has been firmly emphasized in recent years.\textsuperscript{9} Moreover, initially the team was fixed and did not vary between operations, a factor that calls for elucidation as to whether it has remained so over time. Several studies have shown that factors such as experience and consistency of staff are of paramount importance for a good outcome, but this can also be considered a reason for an additional evaluation to determine whether the results have persisted.\textsuperscript{9,10}

Our primary aim was to evaluate whether blood loss and need for transfusion have been kept low over time. Our secondary aims were to investigate duration of hospital stay and maternal as well as neonatal complications for women and children during the time period with varying team structure, compared with previous periods.

\section{Materials and Methods}

This was a retrospective observational cohort study, including women giving birth at SU who were diagnosed with the International Classification of Diseases 10th revision, Swedish version, (ICD-10 SE) for PAS (O43.2A, O42.2B, O43.2X) and intervention codes (MCA00, MCA30, MCA33) between 2003 to 2020. Data were acquired by searching the hospital medical records at SU using the relevant ICD-10 SE diagnosis and intervention codes between January 1, 2016 and December 31, 2020. Women included for the period of January 1, 2003 to December 31, 2015 were obtained from a previous study with the same inclusion criteria at SU.\textsuperscript{7} Women eligible for inclusion but not managed by the MDT or not requiring a peripartum hysterectomy were excluded, although women diagnosed intraoperatively, where the surgery was paused and the MDT was summoned, were included. Date of follow-up was not fixed; maternal complications during hospital stay or follow-up visits at the obstetric unit were included.

The type of placental adhesion was not consistently reported in the pathologic reports or in the medical records, especially not in the early cohort, so it was not possible to examine this.

The women were divided into three exposure groups. Cohort 1 (C1) consisted of nine women delivered before the introduction of the multidisciplinary approach, October 2003 to October 2012. Cohort 2 (C2) and cohort 3 (C3) were both managed in a multidisciplinary manner. C2 included 10 women delivered between June 2011 and December 2015 with a fixed surgical team, and C3 included 14 women delivered between January 2016 and December 2020 with a team consisting of experienced specialists, but not fixed. In C2, five obstetricians, four urologists, and five gynecologists were involved. In C3 the same number of obstetricians and urologists were involved, but seven different gynecologists.

Detailed preparation for hysterectomy was carried out before delivery, minimizing the hysterectomy duration after delivery, and performed as follows. A lower midline abdominal incision was performed, after which the bladder was carefully dissected free from the uterus. The dissection was halted immediately upon recognition or suspicion of placental growth into the bladder wall. In such a case, a cystotomy was performed immediately anterior to the position of the placental ingrowth, after which the dissection was resumed until the ingrowing placenta was completely surrounded, with care being taken not to come into conflict with the placenta or its vascularization. The entire part of the bladder that appeared engaged by the invasive placenta was cut free from the rest of the bladder, hence hanging by the placenta to the isthmus uteri. The dissection was then completed, including the identification of both ureters and the iliac vessels, so preparing, as far as possible, for the anticipated hysterectomy. Hysterotomy was performed at the level of the upper corpus, taking care to maintain a safe distance to the upper margin of the placenta. The baby was delivered and the umbilical cord was ligated, cut, and replaced in the uterine cavity. No attempt was made to manually detach the placenta and, as a rule, uterine contracting agents were not administered. The mother was given full general anesthesia and muscle relaxation after the delivery. Uterotomy was followed by hysterectomy, which was performed in a standardized fashion, after which reconstruction of the urinary tract, if applicable, was undertaken. Using the anesthesiology records, the composition of the MDT was assessed for each and every procedure. If multiple clinicians in one specialty were present, the clinician with highest experience with PAS was reported.

The sample size was decided by the size of the data set. Comparisons between groups were made using the Kruskal–Wallis test. If a significant difference was found, further analyses were made using the Mann–Whitney U test. To correct for multiple comparisons, the Bonferroni method was used. Categorical outcomes were analyzed by calculating relative risk and 95\% confidence interval. Confounding factors were not examined because of the small sample study. No multiple comparison correction was made for secondary outcomes. The data were analyzed using SPSS, version 26.0 (IBM).

Ethical approval was waived by the Swedish Ethical Review Authority on March 24, 2021 (Dnr 2021–01053). The database was coded and registered in accordance with the Personal Data Act and approved by the Data Protection Officer at SU.

\section{Results}

Inclusion of women in the study is shown in the flowchart (Figure 1). All women in C3 had a histopathologic diagnosis of PAS, whereas in C2 and C1 the numbers of histopathologic diagnoses were 7 (70\%) and 4 (44.4\%), respectively (Figure 2). There were differences in frequency of previous uterine surgery (CS excluded), placenta
previa, smoking during pregnancy, country of origin other than Nordic, method of diagnosis, time of diagnosis, premature birth, and low birth weight (Table 1).

All women were examined with ultrasound; in C2 and C3 the majority were performed by a consultant obstetrician with special training in obstetric ultrasound. Acute CS was most frequent in C1 (4; 44.4%), compared with C2 (3; 30.0%) and C3 (5; 35.7%) (Table 1).

Most cases in C2 were managed by one obstetrician and one urologist, whereas two from each specialty managed the majority of cases in C3 (Figure 3). In C3 seven specialists were involved in the MDT and none were present at more than five surgeries.

The estimated intraoperative blood loss and need for transfusion were significantly lower in C3 and C2 compared with C1 ($P = 0.002$ and $P = 0.001$, respectively) (Table 2). No significant difference in blood loss or transfusions could be found between C3 and C2 ($P = 0.169$).

In C1 the frequency of perioperative and postoperative complications was highest—5 (55.6%) and 7 (77.8%), respectively, many of whom had more than one complication each (Table 3). In C2 the lowest rate of postoperative complications was recorded—2 (22.2%): one case of suspected postoperative bleeding into the abdomen not leading to reoperation and one case of catheter blockage. In C3, 6 (46.2%) women suffered from postoperative complications, but of Clavien-Dindo low grade. Only one Clavien-Dindo Grade IIIb complication was found in C3, the development of a vesicovaginal fistula necessitating closure under general anesthesia.

Surgery time did not differ between the groups, but time to delivery was significantly longer for C3 and C2 compared with C1.
Time to delivery was also longer for C3 compared with C2, but not significantly ($P = 0.057$).

No significant differences could be found between the groups concerning the neonatal complications (Table 4). In C3, all of the neonates suffering from complications were prematurely delivered. Similarly, in C2, all but one of the seven neonates suffering from complications were delivered prematurely. This was also the case for admittance to the neonatal intensive care unit, all children in C3 and C2 admitted to neonatal intensive care were premature. In C3, there was one case of intrauterine death at gestational week 29, which was known before delivery, and so was not associated with the surgical procedure.

### DISCUSSION

In the present study we found that the estimated blood loss and need for transfusion were consistently significantly reduced since...
the introduction of multidisciplinary management and a new surgical technique in 2011, also when the surgical team had a varying team structure. There were no differences in maternal or neonatal complications, except for a prolonged time to delivery with the new surgical technique. However, in recent years a number of changes have been made in the management of PAS, above all regarding screening. The increase in prenatal diagnosis could be a contributing factor to these positive results.

The decision to implement a formal multidisciplinary management strategy, using a modified surgical approach including the
### TABLE 3 Secondary outcomes

| Risk estimate                                      | Cohort 1 (n = 9) | Cohort 2 (n = 10) | Cohort 3 (n = 14) | Cohort 3 Cohort 1 | Cohort 2 Cohort 1 | Cohort 1 Cohort 1 | Pairwise comparison |
|---------------------------------------------------|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---------------------|
| Complications                                     |                  |                   |                   |                   |                   |                   |                     |
| Perioperative complications                       | 5 (55.6)         | 2 (20.0)          | 4 (28.6)          | 0.51 (0.19–1.42)  | 1.43 (0.32–6.34)  | 0.36 (0.09–1.42)  |                     |
| Bladder wall damage                               | 5 (55.6)         | 2 (22.2)          | 2 (15.4)          |                   |                   |                   |                     |
| Ureteric damage                                   | 2 (22.2)         | 1 (11.1)          | 1 (7.7)           |                   |                   |                   |                     |
| Vaginal wall damage                               | 0 (0.0)          | 0 (0.0)           | 1 (7.7)           |                   |                   |                   |                     |
| Postoperative complications                       | 7 (77.8)         | 2 (22.2)          | 6 (46.2)          | 0.59 (0.30–1.18)  | 2.08 (0.54–8.06)  | 0.29 (0.08–1.02)  |                     |
| Infection                                         | 4 (44.4)         | 0 (0.0)           | 3 (23.1)          |                   |                   |                   |                     |
| Pressure ulcer                                    | 1 (11.1)         | 0 (0.0)           | 1 (7.7)           |                   |                   |                   |                     |
| Urinary incontinence                              | 1 (11.1)         | 0 (0.0)           | 0 (0.0)           |                   |                   |                   |                     |
| PPH                                               | 2 (22.2)         | 0 (0.0)           | 0 (0.0)           |                   |                   |                   |                     |
| Hernia at the place of incision                   | 1 (11.1)         | 0 (0.0)           | 0 (0.0)           |                   |                   |                   |                     |
| Vesicovaginal fistula                             | 1 (11.1)         | 0 (0.0)           | 1 (7.7)           |                   |                   |                   |                     |
| Missing                                           | 0 (0.0)          | 1 (10.0)          | 1 (7.1)           |                   |                   |                   |                     |
| Length of hospital stay, days                     | 8 (4–42)         | 7 (4–15)          | 6 (2–9)           | 0.120             |                   |                   |                     |
| Missing                                           | 0 (0.0)          | 1 (10.0)          | 1 (7.1)           |                   |                   |                   |                     |
| Surgery time, min                                 | 131 (25–543)     | 183 (114–408)     | 247 (166–438)     | 0.119             |                   |                   |                     |
| Missing                                           | 0 (0.0)          | 0 (0.0)           | 0 (0.0)           |                   |                   |                   |                     |
| Time to delivery, min                             | 4 (1–42)         | 44 (6–119)        | 77 (31–173)       | 0.000             | 3–1               | 0.000             |                     |
| Missing                                           | 0 (0.0)          | 0 (0.0)           | 0 (0.0)           |                   | 3–2               | 0.057             |                     |
|                                                 |                  |                   |                   |                   |                   | 2–1               | 0.002               |

Abbreviations: PPH, postpartum hemorrhage.

*aCategorical data are presented as number (percentage) with risk estimate (95% confidence interval). Numerical data are presented as median (minimum–maximum) and analyzed using Kruskal-Wallis, if \( P < 0.05 \) pairwise comparisons were performed using Mann–Whitney’s U test. The data has not been adjusted for multiplicity. Missing data not included.
assistance of an experienced urologist, was prompted by our clinical experience, which included several massive hemorrhages as illustrated by the control group. The reason to adopt precisely our chosen strategy was neither founded on a solid review of the literature, nor really evidence-based. The introduction of the present strategy was made step by step and a remarkable improvement was recognized. Similar studies investigating the use of a standardized multidisciplinary approach have shown comparable results; however, the use of elective hysterectomy and surgical techniques differ between the centers described by Shamshirsaz et al., Smulian et al, and Al-Khan et al.11–13 The management of PAS has developed during the past years but there is still no definite answer concerning details of the optimal management without compromising the neonatal outcomes; however, the use of an MDT at a tertiary center is generally agreed upon.9,10,14 The method described by Shamshirsaz et al11 was similar to that at SU, but no urologist was present at delivery and the bladder dissection and eventual cystotomy were performed after the CS. They reported a median estimated blood loss of 2.1 L (range 0.5–18 L) for their multidisciplinarily managed group.11 The method described by Al-Khan et al13 was of a more mixed nature. They reported results slightly superior to ours regarding estimated blood loss (0.8 L, range 0.6–1.5 L). Smulian et al12 described a cesarean hysterectomy performed primarily by a maternal-fetal medicine specialist and a gynecologic oncologist with an estimated blood loss of 1.2 L (range 0.5–7.5 L). In 63.2% of the cases a urologist was present. In contrast to SU, they used uterine artery embolization and ureteral stents if they were considered necessary. It could not be shown that these interventions were responsible for the improved outcome.12 The use of both interventional radiology and ureteral stents has been debated, and neither have been clearly shown to improve the outcomes during cesarean hysterectomies. The overall recommendations state that the benefits of ureteral stents do not outweigh

### Table 4: Neonatal outcomes

| Risk estimate                              | Cohort 1 (n = 9) | Cohort 2 (n = 10) | Cohort 3 (n = 14) | Cohort 1 | Cohort 2 | Cohort 1 | Cohort 2 | Cohort 1 | Cohort 2 |
|--------------------------------------------|------------------|-------------------|------------------|----------|----------|----------|----------|----------|----------|
| Neonatal complications                     | 4 (44.4)         | 7 (70.0)          | 7 (53.8)         | 1.21     | 0.77     | 1.58     | 0.68     |
| Respiratory stress syndrome                | 0 (0.0)          | 1 (10.0)          | 5 (35.7)         |          |          |          |          |
| Other respiratory distress of newborn      | 0 (0.0)          | 3 (30.0)          | 0 (0.0)          |          |          |          |          |
| Sepsis                                     | 0 (0.0)          | 1 (10.0)          | 0 (0.0)          |          |          |          |          |
| Fetal and neonatal death                   | 0 (0.0)          | 0 (0.0)           | 1 (7.7)          |          |          |          |          |
| Other diagnoses                            | 4 (44.4)         | 4 (40.0)          | 6 (46.2)         |          |          |          |          |
| Missing                                    | 0 (0.0)          | 0 (0.0)           | 1 (7.1)          |          |          |          |          |
| Stay at NICU                               | 4 (44.4)         | 6 (60.0)          | 4 (30.8)         | 0.69     | 0.51     | 1.35     | 0.56     |
| Missing                                    | 0 (0.0)          | 0 (0.0)           | 1 (7.1)          |          |          |          |          |
| Length of hospital stay, child, days       | 8 (4–42)         | 7 (4–26)          | 7 (3–14)         | 0.485    |          |          |          |
| Missing                                    | 0 (0.0)          | 2 (20.0)          | 6 (42.9)         |          |          |          |          |
| APGAR score at 5 min                       | 10 (8–10)        | 10 (6–10)         | 9 (0–10)         | 0.421    |          |          |          |
| Missing                                    | 0 (0.0)          | 0 (0.0)           | 0 (0.0)          |          |          |          |          |
| Umbilical cord pH (venous)                 | 7.34 (7.24–7.40) | 7.32 (7.26–7.37) | 7.31 (7.29–7.35) | 0.534    |          |          |          |
| Missing                                    | 4 (44.4)         | 3 (30.0)          | 5 (35.7)         |          |          |          |          |
| Umbilical cord pH (arterial)               | 7.29 (7.13–7.36) | 7.34 (7.24–7.38) | 7.25 (7.18–7.35) | 0.125    |          |          |          |
| Missing                                    | 5 (55.6)         | 2 (20.0)          | 5 (35.7)         |          |          |          |          |

Abbreviations: C1, Cohort 1; C2, Cohort 2; C3, Cohort 3; CS, Cesarean section; Dnr, diary number; ICD, International classification of diseases; MDT, Multidisciplinary team; NICU, Neonatal intensive care unit; PAS, Placenta accreta spectrum; SU, Sahlgrenska University Hospital.

aData are presented as number (percentage) and risk ratio (95% confidence interval) or as median (minimum–maximum) and analyzed using Kruskal-Wallis, if \( P < 0.05 \) pairwise comparisons were performed using Mann-Whitney’s \( U \) test. Missing not included in percentage.

bIntrauterine fetal death known before CS, not attributed to PAS.

cOther diagnoses included: neonatal jaundice, neonatal hypoglycemia, neonatal hypocalcemia, transient tachypnea, cardiac murmur, retinopathy of prematurity, bronchopulmonary dysplasia, delayed closure of ductus arteriosus, neonatal conjunctivitis and dacryocystitis, transient neonatal thrombocytopenia, anemia of prematurity, transitory disorders of carbohydrate metabolism, meconium plug syndrome, hydrocephalus, asphyxia, apnea of newborn, intraventricular (nontraumatic) hemorrhage, Rh isoimmunization of newborn, disturbance of temperature regulation, congenital hypotonia.
the risks such as infection or malposition.\textsuperscript{9,15} Interventional radiology is not recommended because there are few studies and varying results.\textsuperscript{9,14,15} Some advocate the assistance of an intervention radiologist\textsuperscript{11-13,16}; however, it is important to develop methods not dependent on this because not all hospitals have access to interventional radiology. In the present series, the decrease in need for transfusions for C3 and C2 compared with C1 was expected and the use of packed red blood cell transfusions is comparable to that in other studies (2.35 L, range 0.65–4.4 L).\textsuperscript{11-13,17}

As mentioned above, the surgeons varied slightly more in C3 compared with C2. Nevertheless, before assuming full responsibility the new urologists and obstetricians in C3 were subjected to a thorough introduction by the experienced participants from C2. Another possible explanation is that the method in itself renders favorable outcomes, rather than the participating individuals, providing that these individuals firmly adhere to the strategy decided. Moreover, the variation in team members was not pronounced to a degree that they should affect the results considerably.

In the present series, the occurrence of serious complications improved with the employment of multidisciplinary management; serious complications such as postoperative blood loss and repeated surgery were only found in C1, compared with only one Clavien-Dindo grade III complication of vesicovaginal fistula in C3. There were complications in all three cohorts, but the vast majority were mild. This indicates improvement regarding the severity of the complications.

Despite the high rate of antenatal diagnosis in C3 and C2, with planned delivery according to guidelines, the occurrence of acute CS was high. Notably, other studies have shown a decrease in acute delivery after implementing a multidisciplinary approach, even in those with similar median gestational week at delivery.\textsuperscript{11,12,18} The steepest decrease in acute delivery was found by Stanleigh et al.,\textsuperscript{18} who showed a complete elimination of acute deliveries. Acute delivery has been shown to increase maternal morbidity such as transfusions and complications, but this does not generally seem to be the case when managed by an MDT.\textsuperscript{19,20}

It can be argued that the prolonged time to delivery could be unfavorable for the neonates, even if general anesthesia during pregnancy has not been associated with impaired neurologic development for the fetus and maternal surgery under general anesthesia is recommended for selected conditions during pregnancy.\textsuperscript{21} The time to delivery did not differ significantly between C3 and C2, but the time was increased in C3. Speculatively, a difference could have been found with a larger study group. However, time to delivery is above all dependent on the dissection of the bladder and the uterus performed by the urologist, and in the present series this time varied even for the most experienced surgeons. The necessity of using the technique adopted at SU and by others (Brennan et al.\textsuperscript{22}), comprising extensive dissection before delivery allowing for a rapid control of hemorrhage, can of course be subjected to questioning. Perhaps it is of no obvious advantage in most cases, but throughout the years a few cases of partial detachment of an abnormally invasive placenta immediately after delivery have been encountered. The bleeding that occurred in these cases was, as anticipated, pronounced and difficult to control but this did not matter very much, because the meticulous preparation before delivery, including intentional cystotomy, allowed for very fast and uneventful hysterectomies.

It has been pointed out that it is not clear which component led to the results in the study by Lekic et al.,\textsuperscript{7,23} as several factors have changed in the management of women with PAS in recent years. As concluded by Lekic et al.,\textsuperscript{7} it is not possible to say if the improvement is caused by a combination of factors or if one single component is of more importance. However, intentional cystotomy does not seem to cause any increased bleeding; on the contrary it enables a rapid and uneventful hysterectomy should bleeding occur even if manual detachment of the placenta is refrained from. As mentioned above, time to delivery is prolonged, as a consequence of the meticulous dissection of the bladder, but not the total operational time and we could not find anything indicating that this is of disadvantage for the neonates. Hence, we are comfortable with upholding our contention that the employment of the urologist-assisted team leads to considerable improvement in the management of women with PAS.\textsuperscript{24}

The sample size was smaller than expected in all cohorts. SU has the largest obstetric service in Sweden with approximately 10 000 deliveries per year; the rate of PAS expected was five in 10 000. The small sample size could be attributed to a low rate of prenatal diagnosis; it has been found to be low in the Nordic countries.\textsuperscript{25} Also, many of the women with suspected PAS diagnosis were diagnosed intraoperatively and did not go through the multidisciplinary management, so they were excluded from the present study. Furthermore, the exclusion of women not receiving a hysterectomy and multidisciplinary management could mean that women with placenta increta and percreta were included to a greater extent than accreta in C3 and C2 compared with C1.

The proportion of cases with histopathologic diagnosis of PAS was greater in C3 than C2 and C1 (Figure 2). In C1, many records of histopathology were missing. Also, in this group, attempts to remove the placenta manually were made more often, making a histopathologic examination of the placenta impossible. Furthermore, in recent years a perinatal pathologist has been evaluating the placentas instead of a general pathologist, making the pathologic examination more certain. Due to the time frame of the investigated period other variables that could affect the care of mothers and neonates have changed, e.g. during the later years of the present study additional light neonatal intensive care units have opened, resulting in a stricter admission to the neonatal intensive care unit. The neonates admitted today might have a worse general condition than the average at the beginning of the study, making comparison uncertain.

The groups were not entirely comparable regarding the patient characteristics. Data for smoking and body mass index were missing from C1, two variables that are probably important for the tendency to bleed. Also, it is notable that women with a country of origin other than the Nordic countries were overrepresented and increased with time. This could be explained by immigration from countries with a higher use of CS. The optimal surgical approach for PAS is still not clear, but future studies of surgical approach for PAS should be evaluated in a larger cohort, enabling adjusted analyses to limit bias.
In conclusion, we have shown that the positive results regarding blood loss and need for transfusion with a standardized multidisciplinary approach have been consistent over time, although the small sample size limited the possibility to adjust for confounders. Serious complications such as reoperation because of postoperative hemorrhage were only present before the introduction of the MDT. Furthermore, complications in the neonates were attributed to prematurity and not to the surgical technique itself.

**AUTHOR CONTRIBUTIONS**
All authors have fulfilled the criteria for authorship according to ICMJE. AU took part in data extraction and interpretation, and writing the manuscript. YC, OK, RP, and TS took part in study set-up, interpreting the data, and writing the manuscript.

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**CONFLICT OF INTEREST**
The authors have no conflicts of interest.

**DATA AVAILABILITY STATEMENT**
Research data are not shared.

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