OBSTETRICS

The Society for Pediatric Pathology Task Force grading system for placenta accreta spectrum and its correlation with clinical outcomes

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BACKGROUND: The terminology and diagnostic criteria presently used by pathologists to report placenta accreta spectrum is inconsistent and does not reflect current knowledge of the pathogenesis of this disease.

OBJECTIVE: In 2020, the perinatal subcommittee of the Society for Pediatric Pathology Placenta Accreta Task Force proposed a new pathologic grading system for placenta accreta spectrum. We sought to correlate the clinical outcomes with the classification into each group in the new placenta accreta spectrum grading system.

STUDY DESIGN: The pathology reports of patients with histopathologic confirmation of placenta accreta spectrum were reviewed in 2 academic referral centers by placental pathologists. Pathologic grading was assigned based on the new grading system according to which placenta accreta spectrum is categorized into 5 groups depending on the depth of invasion, from grade p1 with no invasion into the uterine wall to grade p3E with invasion beyond the uterine wall to the adjacent organs. Patient characteristics and clinical outcomes were compared among these groups. A univariate analysis was performed, and a multivariate linear or binomial regression was employed when needed.

RESULTS: A total of 683 patients with placenta accreta spectrum were identified. Of those, 407 were included for histology review. There were 92 patients (23%) categorized into the grade p1 group, 74 (18%) in the grade p2 group, 84 (20%) in the grade p3A group, 121 (30%) in the grade p3D group, and 36 (9%) in the grade p3E group. There was a significant association between the pathology grading and the number of red blood cells transfused (β=1.14; 95% confidence interval, 0.48—1.79) and the postoperative complications including the rate of readmission (risk ratio, 1.93; 95% confidence interval, 1.26—2.94) and bladder injury (risk ratio, 1.81; 95% confidence interval, 1.23—2.68) after adjustment for antenatal diagnosis and other variables. The pathology grading was not associated with the estimated blood loss (P=.072).

CONCLUSION: The new pathology grading system accurately reflects maternal outcomes and complications of placenta accreta spectrum. We encourage the utilization of this new pathologic grading system because it is designed to omit discrepancies in placenta accreta spectrum reporting and to standardize communication.

Key words: clinical outcomes, maternal complications, pathology grading system, placenta accreta, placenta accreta spectrum

Introduction

Placenta accreta spectrum (PAS) is a well-known cause of serious maternal morbidity, leading to massive hemorrhage, blood transfusion, and hysterectomy. Over the past several decades, the incidence of PAS has been increasing substantially as a consequence of a continued rise in the rates of its major risk factor, cesarean delivery; in 2016, the PAS rate was 1 in 272 compared with a rate of 1 in 30,000 in the 1920s.[1–3] Thus, this once rare condition can now be expected to be encountered by obstetricians several times during their careers.

PAS has been categorized traditionally based on descriptive findings about the level of the invasion of chorionic villi into the uterine wall, from adherent placenta without intervening decidua (placenta accreta), to invasive into the myometrium (placenta increta), and, furthermore, to the uterine serosa and beyond (placenta percreta).[4,5] The term PAS is chosen to reflect the coexistence of adherent and invasive placenta in the pathophysiology of PAS as it is reflected in the histopathology and imaging findings.[6]

Recently, it has been shown that the high degree of heterogeneity reported in the prevalence of different levels of PAS invasion is primarily because of the variations in the histopathologic diagnostic criteria. Several methodological inconsistencies are described in the literature, including criteria for clinical diagnosis at birth, histopathologic confirmation, and differentiating between adherent and invasive placentation.[7] This was especially evident in cases involving minor degrees of invasion; consequently, 18% to 29% of patients with a clinical diagnosis have no pathologic confirmation.[8,9] In response, the Placenta Accreta Task Force was convened by the Society for Pediatric Pathology (SPP) and they developed a pathologic grading system that identifies clinically and biologically meaningful subcategories of PAS.[10] A summary of this system of classification is presented in the Figure. The proposed description of degree of placental invasion under the umbrella diagnosis of PAS replaced the

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AJOG at a Glance

Why was this study conducted?

Before widespread adoption of the new histopathology grading system for placenta accreta spectrum suggested by the Society for Pediatric Pathology Placenta Accreta Task Force, an evaluation of the association with clinical outcomes is necessary.

Key findings

The new grading system accurately reflects clinical severity and outcomes.

What does this add to what is known?

The histopathology grading system aligns with the currently established International Federation of Gynecology and Obstetrics clinical grading system and provides more detail than the standard 3-tiered pathology classification of "accreta, increta, and percreta."

traditional terminology (placenta accreta, increta, percreta [AIP]) with a new descriptive grading system that parallels the clinical grading guidelines endorsed by the International Federation of Gynaecology and Obstetrics (FIGO).[11] In addition, the nomenclature for hysterectomy specimens was separated from that of placentas delivered without hysterectomy and was designated basal plate myometrial fibers (BPMF).[12] It was the hope of these investigators that such a unified classification strategy would lead to improved communication and reporting.

In this study, we sought to investigate the association between the new SPP histopathology grading system for PAS and the clinical outcomes and to investigate the utility and potential practical relevance for clinical care of the grading system. A strong association between this new histopathology grading system and clinical findings would support the widespread use of this system and enhance standardization of histopathologic reporting. We believe that a well-established, detailed pathologic grading system that has a good correlation with outcomes could retrospectively identify clinical and imaging characteristics of high-risk patients, which will help to guide future surgical and clinical management strategies and research trials.

Materials and Methods

A retrospective cohort study was performed at 2 referral centers for PAS between 2010 and 2021 after approval was obtained from the respective institutional review boards. The pathology slides of patients with PAS, which were originally reviewed as part of clinical care and classified as placenta accreta, increta, or percreta, were once again reviewed by the perinatal pathologists and categorized based on the recommendations by the SPP (Figure) (the schematic figure was reproduced with permission of the owner).[10] A 5-tiered pathologic grading system was used to classify the samples as follows. Grade p1: gross adherence of the placenta without thinning of the uterine wall and histologic sections showing loss of the decidual layer between villi and myometrium. Grade p2: myometrial invasion and thinning of the uterine wall under the placenta with at least 25% preservation of the myometrial thickness. Grade p3A: myometrial invasion and thinning of the uterine wall under the placenta with <25% preservation of the myometrial thickness. Grade p3D: disruption of the uterine serosa. Grade p3E: invasion of extrauterine structures.

Only patients who underwent a hysterectomy and for whom histopathologic slides were available were included because the suggested grading system requires the full thickness of the uterine wall to be present at the time of evaluation for PAS. Uterine scar pregnancies were excluded. Retrospective chart review was performed to extract clinical information. Patient characteristics and clinical outcomes were compared based on the pathologic grade level assigned.

Statistical analysis was performed using IBM SPSS, version 22 (SPSS Inc, Chicago, IL). Univariate analyses were performed using chi-square and Kruskal-Wallis tests as appropriate. Multivariate analyses were performed using linear or binomial regression as needed, with adjustment for antenatal diagnosis of PAS based on prenatal imaging, which was shown previously to affect the clinical outcomes.[13,14] Adjustments were made for other relevant variables according to the demographic and clinical differences among the groups. For the purpose of the regression analysis, the reference groups for the variables were no previous cesarean delivery, absence of placenta previa, and no antenatal diagnosis of PAS. Differences were considered significant if the 2-sided P value was $<.05$.

Results

A total of 683 patients with PAS who underwent a hysterectomy were identified. Pathology slides were available for review for 407 of these patients. Pathologic grading according to the SPP system was as follows: 92 (23%) grade p1, 74 (18%) grade p2, 84 (20%) grade p3A, 121 (30%) grade p3D, and 36 (9%) grade p3E. The distribution of patients based on the SPP grading system was roughly consistent with the traditional histopathologic classification of placenta AIP (Table 1). Most of the grade p1 patients were previously reported to have placenta accreta (91%) and those of grade p2 patients were previously reported to have placenta increta (80%). Of the grade p3D patients, 82% were previously classified as having placenta percreta and 89% of p3E patients were previously also classified as having placenta percreta. However, grade p3A patients showed less consistency with 61% of the patients previously being reported to have placenta increta and 29% being reported to have placenta percreta.

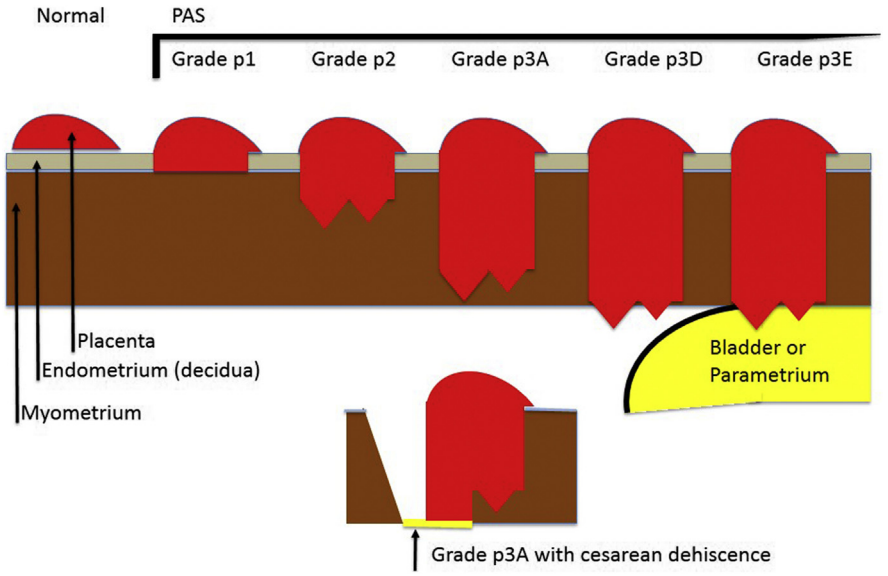
Table 2 summarizes the baseline demographic characteristics of the studied population. Maternal age ranged from a median of 37 years (interquartile range

[IQR], 32−41 years) for grade p1 patients to 34 years (IQR, 30−37) for grade p3E patients (P=.002). Patients with more severe forms of PAS tended to deliver earlier at a median gestation of 33 weeks (IQR, 30−34 weeks) for grade p3E patients compared with 34 weeks and 5 days (IQR, 32−37 weeks) for grade p1 patients (P<.001). Patients with different PAS grades have different numbers of previous pregnancies (P<.001). The number of previous cesarean deliveries was also different among patients with different PAS grades (P<.001), with 28% of grade p1 PAS patients having no history of cesarean delivery.

The frequency of patients with placenta previa was different among the PAS grades (P<.001), with 89% of the patients with grade p3E pathology having placenta previa. Among the grade p3E patients, 97% of cases had an antenatal diagnosis of abnormal placental implantation.

A review of the maternal outcomes based on the SPP pathologic grading system after adjustment for antenatal diagnosis, number of previous cesarean deliveries, and presence of placenta previa is provided in Table 3. Although the estimated blood loss was not associated with the PAS pathologic grading designation, patients with more severe invasion received more blood products including red blood cells (β=1.14; 95% confidence interval [CI], 0.48−1.79) and fresh frozen plasma (β=0.82; 95% CI, 0.37−1.28) based on the linear regression analysis. For each increasing pathologic grade of PAS severity, there was an increased risk for readmission (risk ratio [RR], 1.93; 95% CI, 1.26−2.94) and for unintentional cystotomy (RR, 1.81; 95% CI, 1.23−2.68) based on the binomial regression analysis.

FIGURE
SPP placenta accreta task force new grading system for PAS



Grade p1: gross adherence of the placenta without thinning of the uterine wall and histologic sections showing loss of the decidual layer between villi and myometrium. Grade p2: myometrial invasion and thinning of the uterine wall under the placenta with at least 25% preservation of the myometrial thickness. Grade p3A: myometrial invasion and thinning of the uterine wall under the placenta with <25% preservation of the myometrial thickness. Grade p3D: disruption of the uterine serosa. Grade p3E: invasion of extrauterine structures. The schematic figure is reproduced with permission from the owner, Hecht et al.[10]

PAS, placenta accreta spectrum; *SPP*, Society for Pediatric Pathology.

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Comment

Principal findings

Based on our results, the SPP pathologic grading system for PAS[10] demonstrated a correlation with clinical outcomes, including higher rates of red blood cell transfusions and maternal complications, as grade severity increased. The adverse clinical outcomes were largely driven by higher grades of pathology particularly among SPP grade p3E patients. These associations persisted after adjusting for antenatal diagnosis of abnormal placental invasion. The SPP system also correlated reasonably well with the traditional pathologic reporting system (placenta AIP) while also providing additional descriptive detail.

Clinical and research implications

It is well known that PAS is a major risk factor for maternal morbidity, with the histopathologic depth of placental invasion being a consistent determinant of clinical outcomes.[15−17] However, wide variation exists in the reported frequency of various degrees of invasion; such variation likely reflects a degree of ambiguity intrinsic to the traditional definitions of placenta accreta, increta, and percreta. We have shown previously that the traditional categorization of PAS into accreta, increta, and percreta correlates poorly with the clinical findings when compared with the FIGO grading system.[18] In the former, all subcategories of FIGO grade 3 are simply reported as placenta percreta without a detailed presentation of the severity of disease; superficial serosal involvement is clearly a very different clinical condition from bladder and pelvic sidewall invasion. We believe that the use of the SPP pathologic grading system, which we have shown to have a good correlation with clinical outcomes, will help to improve the reproducibility of pathologic evaluation and reporting. Furthermore, it provides a more detailed description of the findings than the traditional reporting paradigm. It can also provide guiding information to retrospectively identify clinical and imaging findings for patients who are at higher risk to better plan future clinical and surgical management strategies and to help with future research investigations. The lack of close correlation between the AIP system and

TABLE 1
Cases of placenta accreta spectrum classified using the previous 3-point criteria (accreta, increta, percreta) vs the Society for Pediatric Pathology classification

	SPP Grade					
PAS	p1	p2	p3A	p3D	p3E	Total
Pathology						
Accreta	84 (91)	8 (11)	9 (10)	7 (6)	1 (3)	109 (27)
Increta	6 (7)	59 (80)	51 (61)	15 (12)	3 (8)	134 (33)
Percreta	2 (2)	7 (9)	24 (29)	99 (82)	32 (89)	164 (40)
Total	92	74	84	121	36	407

Data are reported as number (percentage).

PAS, placenta accreta spectrum; *SPP*, Society for Pediatric Pathology.

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the new SPP system illustrates the deficiency in the AIP definitions instead of highlighting mistakes made by the original pathologist. Resolving this problem was one of the main reasons for the SPP pathology consensus conference. Cases originally classified as accreta in this cohort correlated well with the grade p1 category because interpretation is straightforward in specimens with minimal surgical disruption and a regular smooth interface between the placenta and myometrium. Cases with invasion (increta, percreta) show an irregular interface with variable depth of invasion and involvement of scar dehiscence or surgical disruption that lead to heterogeneity in the classification.[19] This is best illustrated by cases graded as p3A among which 61% were previously reported as having placenta increta and 29% were reported as having placenta percreta. These cases invariably involved invasion into a cesarean scar with only a thin rim of tissue binding the placenta. To some, this represents invasion beyond the myometrium (percreta), whereas others only diagnose percreta with microscopic

TABLE 2
Demographic and clinical characteristics compared with the new proposed placenta accreta spectrum classification

Demographic and clinical variables	SPP grade					*P* value
	p1 (n=92)	p2 (n=74)	p3A (n=84)	p3D (n=121)	p3E (n=36)	
Age (y)	37 (32–41)	35 (31–39)	35 (31–39)	33 (30–37)	34 (30–37)	.002
GA at delivery (wk)	34.7 (32.6–37.1)	34.3 (32.6–35.7)	34.5 (32.6–35.4)	33.1 (31.3–34.6)	33.0 (30.2–34.7)	<.001
Parity						
Nulliparous	11 (12)	3 (4)	3 (4)	1 (1)	0	<.001
Primiparous	31 (34)	16 (22)	28 (33)	8 (6)	8 (22)	
Multiparous	50 (54)	55 (74)	53 (63)	112 (93)	28 (78)	
Number of previous CDs						
None	26 (28)	5 (7)	2 (2)	1 (1)	0	<.001
1	25 (27)	19 (25)	31 (37)	11 (9)	7 (20)	
2	25 (27)	28 (38)	28 (33)	50 (41)	17 (47)	
≥3	16 (18)	22 (30)	23 (28)	59 (49)	12 (33)	
Previous D&C	28 (32)	16 (22)	23 (30)	26 (21)	13 (36)	.216
Previous myomectomy	2 (2)	3 (4)	6 (7)	8 (7)	4 (11)	.267
Placenta previa	58 (63)	58 (78)	67 (80)	111 (92)	32 (89)	<.001
Antenatal diagnosis	46 (50)	43 (59)	62 (75)	110 (91)	35 (97)	<.001

Variables are reported as median (interquartile range) (Kruskal-Wallis test) or number (percentage) (chi-square test).

CD, cesarean delivery; *D&C*, dilation and curettage; *GA*, estimated-gestational age; *SPP*, Society for Pediatric Pathology.

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TABLE 3
Clinical outcomes compared with the newly proposed pathologic placenta accreta spectrum classification

Clinical outcome variables	SPP grade					*P*crude	Regression
	p1 (n=92)	p2 (n=74)	p3A (n=84)	p3D (n=121)	p3E (n=36)		
EBL, mL	1725 (900–2500)	1500 (1085–2940)	1800 (1196–3000)	1500 (1000–3000)	2700 (1400–4000)	.072	618.39[a] (−124.66 to 1361.45)
Number of RBC units transfused	2 (0–3)	0 (0–3)	1.5 (0–3)	2 (0–5)	3.5 (1–6.75)	.003	1.14[a] (0.48–1.79)
Number of platelet units transfused	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–1)	.098	0.20[a] (0.06–0.34)
Number of FFP units transfused	0 (0–1)	0 (0–0)	0 (0–0.75)	0 (0–2)	1.5 (0–4)	.001	0.82[a] (0.37–1.28)
Readmission	4 (4)	1 (1)	3 (4)	5 (4)	7 (19)	.001	1.93[b] (1.26–2.94)
Unintentional cystotomy	1 (1)	4 (5)	5 (6)	6 (5)	6 (17)	.015	1.81[b] (1.23–2.68)
Ureter injury	1 (1)	1 (1)	1 (1)	1 (1)	3 (8)	.036	1.45[b] (0.71–2.99)
Acute renal injury	1 (1)	0	2 (2)	0	0	.290	1.07[b] (0.38–3.01)
Maternal death	0	0	0	1 (1)	0	.668	2.03[b] (0.26–15.68)

Data are reported as median (interquartile range) (Kruskal-Wallis Test) or number (percentage) (chi-square or Fisher exact test).

EBL, estimated blood loss; *FFP*, fresh frozen plasma; *NA*, not applicable; *PAS*, placenta accreta spectrum; *RBC*, red blood cell; *SPP*, Society for Pediatric Pathology.

[a] Regression analyses were adjusted for antenatal diagnosis, number of previous cesarean deliveries, and presence of placenta previa using linear regression analysis presented as β (95% confidence interval); [b] Binomial regression analyses are presented as the risk ratio (95% confidence interval).

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involvement of the bladder serosa, bladder mucosa, or in the setting of surgical disruption of the serosa.

Interestingly, we found a higher rate of antenatal diagnosis with higher grades of PAS invasion. This likely reflects a deficiency in the current diagnostic imaging for the diagnosis of less severe forms of PAS, which, nonetheless, may be associated with significant clinical morbidity. Our findings also revealed that lower grades of PAS are more frequently found in patients without placenta previa. This is of significant concern because standard teaching and practice today generally reserve suspicion for PAS and the application of more sophisticated imaging techniques to patients with both previous uterine surgery and current placenta previa. Clearly there is a need for additional research into the antepartum diagnosis of and clinical risk factors unique to lower grades of PAS.

Strengths and limitations

This study examined the association between the newly proposed SPP histopathologic grading system and the clinical outcomes in PAS. It included a large sample size from 2 separate referral centers that may represent a more generalizable population than results from a single center. An additional strength of our study is the direct evaluation of the pathologic slides by placental pathologists familiar with both AIP and the new pathologic grading system. One limitation of our study is that our data did not include patients for whom the pathology slide was not available for review; this may affect the analyses of cases for which a hysterectomy was performed, however, our data still included a large number of our overall cohort and are likely a reasonable representation of our full cohort. Cases managed with focal myometrial resection were excluded. We believe that the SPP pathology system provides more detail in reporting and may therefore also be useful for such cases, and further studies are warranted. The data from these patients and BPMF cases will be analyzed and reported separately. Because our data originated from

specialized referral centers, the clinical outcomes observed, particularly for those cases in which PAS was not suspected before delivery, cannot be interpreted to represent the expected outcomes for similar cases in other medical settings. Finally, this was a retrospective review, however, histopathologic evaluation of specimens occurred after clinical treatment was rendered and therefore is similarly retrospective by design. We anticipate that if adopted, the correlation of clinical outcomes with histopathologic grading will be similarly robust.

Conclusions

With the incidence of PAS on the rise, accurate assessment and standardization of both clinical and histopathologic categorization of the disease is of increasing importance so that we may enhance our understanding and ultimately improve treatment of this condition. After years of traditional categorization of PAS into 3 somewhat ambiguously defined groups, a new pathologic grading system that correlates better with intraoperative clinical findings and maternal outcomes is desirable. Our data suggest that the SPP pathologic grading system is a promising alternative as reflected by a consistent and useful association between its detailed subcategories and the clinical outcomes. ■

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