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Preoperative cystoscopy could determine the severity of placenta accreta spectrum disorders: An observational study

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Abstract

Aim: In the surgical treatment of placenta accreta spectrum disorders, cystoscopy for prophylactic stent placement is performed to protect the ureters from potential injury. Despite its frequent use, the use of cystoscopy in assessing the severity of these disorders has not been explored. Our objective was to find out if the abnormal findings documented during cystoscopy are associated with disease severity.

Methods: In this retrospective, observational cohort study ($n = 56$), the bladder wall was evaluated at the time of ureteral stent placement via cystoscopy in prenatally diagnosed placenta accreta spectrum cases. Three abnormal findings were commonly present in these cases: bulging of the posterior bladder wall, neovascularization and arterial pulsatility in the area of neovascularization. These findings were stratified according to severity in histologically confirmed specimens. Continuous variables were compared via twotailed t-tests and Wilcoxon rank sum tests. Categorical data were evaluated using logistic regression analysis.

Results: Neovascularization affected 84%, bulging 71% and pulsatility 54% of the cases. Bulging and neovascularization increased with disease severity. Pulsatility occurred exclusively in percreta. Bulging was associated with a 12-fold ($OR = 11.6$, 95% CI 2.94–46.33, $P = 0.0005$) increased likelihood of percreta and neovascularization with a 17-fold ($OR = 17.06$, 95% CI 2.98–97.79, $P = 0.0014$) increase. Neovascularization and/or the presence of bulging of the bladder have high positive predictive value for placenta increta and percreta (91.5% and 95.0%, respectively).

Cystoscopy can be used to assess the severity of placenta accreta spectrum cases preoperatively, especially when placentation is over the previous uterine scar and is in proximity to the bladder wall.

Keywords

cystoscopy; morbidly adherent placenta; percreta; placenta accreta; urinary bladder

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Disclosure

No author has any potential conflict of interest.

Introduction

Hemorrhage is the leading cause of maternal mortality worldwide^{1–3} and remains a leading cause of morbidity, even in developed countries.⁴ Hemorrhage incidence in the United States, as indicated by transfusion rates, increased by 90% from 1998–1999 to 2004–2005.⁵ Massive intrapartum or post-partum hemorrhage as a cause of maternal mortality in North America is now predominantly secondary to complications arising from invasive placentas,⁶ especially when the diagnosis is not made antenatally. In an effort to promote accurate and uniform terminology of the abnormally adherent (placenta creta) and invasive placenta disorders (placenta increta and percreta), we will refer to this range of conditions as Placenta Accreta Spectrum (PAS) disorders.^{7,8} The incidence of PAS is increasing rapidly, reaching as high as 1 in 600 pregnancies in patients who have had a prior cesarean section in the United States and Canada.^{9–11} Predelivery diagnosis and planned, preterm deliveries by an experienced team are known to reduce morbidity.^{10,12} Interdisciplinary, team-managed care for PAS results in better maternal outcomes, including reduced blood loss and ICU admissions.^{10,13}

Antenatal diagnosis typically requires high-quality ultrasound imaging and expert interpretation of soft ultrasound signs, preferably at a tertiary care facility.^{10,13} Despite obstetric ultrasonography being the standard for PAS diagnosis, the reported accuracy of ultrasonography varies greatly between facilities, experts and even nations.^{14,15} Magnetic resonance imaging (MRI) is sometimes used but has more variable accuracy, with higher costs and fewer radiology experts in PAS.¹⁴ Unfortunately, disease severity can often only be assessed definitively at the time of surgery and ultimately diagnosed by histopathology. Additional methods to evaluate the presence and/or severity of disease prior to surgery are critical for improving maternal outcomes. We propose that one such method is cystoscopy.

In obstetric practice, cystoscopy is mainly used for the detection and potential prevention of urinary tract injury in the setting of complicated pelvic surgeries.¹⁶ Cystoscopy and ureteral stent placement is recommended for prophylactic protection of the ureters during surgical intervention in PAS.¹³ In our Center for Abnormal Placentation (CAP), we perform cystoscopy for the placement of prophylactic ureteral stents immediately prior to surgery when ultrasound and/or MRI suggests the presence of PAS. Here, we report on our observational findings of the bladder during stent placement and its relationship to disease severity.

We propose that the standard cystoscopy procedure has the ability to provide useful information about the extent of disease in suspected PAS cases, either in the presence of a complete previa or anterior placentation underlying the previous uterine scar, both of which are in proximity to the posterior bladder wall. Furthermore, our findings suggest that, in settings where advanced imaging or an expert diagnostician is not available, clinical scenarios of morbid obesity and extensive abdominal scar tissue (where prenatal diagnosis is exceedingly difficult), cystoscopy may be an advantageous supplementary diagnostic tool.

Methods

There were 56 patients included in the cohort. Inclusion criteria consisted of evaluation and treatment in the CAP from 2009 to 2016, antenatal diagnosis of suspected PAS, cystoscopy performed with appropriate documentation and video images, singleton pregnancy, cesarean–hysterectomy and confirmation of PAS diagnosis by histopathology. All included patients have had at least one prior cesarean section and presented with either placenta previa ($n = 44$) or anterior placentation overlying the previous cesarean section scar with close proximity to the posterior bladder wall ($n = 12$). Cystoscopy was only performed in such cases of PAS. At the time of routine ureteral stent placement, video clips and photos were used to document the bladder wall findings. Institutional Review Board (IRB) approval was obtained for retrospective analysis of the cystoscopy findings in relation to PAS diagnosis.

Cystoscopic findings were categorized by a dichotomous descriptive classification of three signs that, in the course of 10 years of CAP-managed interdisciplinary care, surgeons and urologists noted in PAS surgeries as abnormal. These signs were: the presence of posterior bladder wall bulging, neovascularization and arterial pulsatility in the area of neovascularization. The term neovascularization is used as a generic term encompassing either elaboration/remodeling of extant blood vessels or the growth of new blood vessels. Neovascularization and angiogenesis cannot be distinguished from each other in this study, and both are likely to be present in PAS (Fig. 1). The blood vessels appear to be large venous and/or arterial plexuses located mostly on the posterior bladder wall, which arise from the anterior uterine surface and infiltrate the bladder serosa. These formations are not to be confused with hyperemia of the bladder, which can be seen in Figures 1a,b and 2.

In our center, when ultrasound and/or MRI is suggestive of PAS involving the bladder, we perform cystoscopy in the operating room immediately prior to delivery. A rigid 22-French 30° scope (Storz, Tuttlingen, Germany) is used to visualize the bladder wall. Three different urologists performed the procedure across the study period (even though successful cystoscopies can also be performed by experienced gynecologists, urogynecologists or surgeons who are credentialed for the procedure).¹⁷ All patients provided appropriate consent and were counseled regarding the risks (urinary tract infection and injury/perforation of the bladder or ureters)¹⁷ of the cystoscopy procedure with ureteral stent placement. The documented findings of bulging, neovascularization and pulsatility were examined for association with the histopathological outcomes of placenta creta, increta and percreta.

Data were summarized using descriptive statistics. Continuous variables were presented as mean (standard deviation) or median (interquartile range) and range [$n - n$], depending on whether the data were normally distributed, as indicated by the Shapiro–Wilk test of normality. Categorical data were expressed as counts (percentages). Comparisons of continuous variables were conducted using two-tailed t tests and Wilcoxon rank-sum tests, as appropriate. Comparisons of and associations between categorical data (the occurrence of placental creta, increta and percreta), as indicated by pathology, were analyzed using logistic

regression analysis, with results reported as odds ratio (OR), 95% confidence interval (CI) and *P* value.

Results

The characteristics of the 56 patients who underwent cystoscopy and were histologically diagnosed with PAS are given in Table 1. Of the 56 cases, 16% were histologically diagnosed as creta, 10% as increta and 73% as percreta. The disproportionate number of severe percreta cases is a result of CAP's status as a tertiary referral center for PAS. There were no maternal or neonatal deaths and all mothers and their infants were discharged home in a stable condition.

The most commonly noted abnormality on cystoscopy was neovascularization (Fig. 1, Table 2), which affected 84% of the entire sample and increased in prevalence with severity of disease. Bulging of the posterior bladder wall was less common, affecting 71% of all PAS cases (Figs 2–3, Table 2), and also increased in prevalence with severity of disease. Arterial pulsatility in the area of neovascularization was the least common of the three cystoscopic findings; however, it was exclusively observed in percretas (Table 2). None of the three cystoscopic signs were seen in 6 of 9 cretas, 2 of 6 incretas and 2 of 41 percretas.

Observing neovascularization upon cystoscopy was associated with a 17-fold increased likelihood of percreta (OR = 17.06, 95% CI, 2.98–97.79, *P* = 0.0014). The presence of bulging in the posterior bladder wall was associated with a 12-fold increased likelihood of percreta (OR = 11.67, 95% CI, 2.94–46.33, *P* = 0.0005). As pulsatility was present only in percreta, OR could not be calculated. While this study was not designed to provide data on diagnostic power, it is useful to know whether the cystoscopy signs might be of diagnostic utility. We found that neovascularization has a sensitivity of 91.5% (95% CI 83.5–99.5%) for the combined pathologies of increta and percreta and a specificity of 55.6% (95% CI 21.2–86.3%). Bulging is 80.9% sensitive (69.6–92.1%) and 77.8% specific (40.0–97.2%). Pulsatility, being only observed in percretas, had a sensitivity of 63.8% for combined increta/percreta but had 100% specificity.

Discussion

To our knowledge, this is the first report correlating the findings observed during cystoscopy to the pathological severity of PAS. Our retrospective calculations of sensitivity and specificity of the three cystoscopy findings suggest that they could be useful in PAS diagnosis; they could even be equivalent to the efficacy of reading gray-scale, soft ultrasonographic signs widely considered to be the primary modality of antenatal PAS diagnostics.¹⁸ Gray-scale signs include the presence of placental lacunae, interruption of the uterine and bladder interface, increased vascularity and thinning of the myometrium at the area of placentation.^{19–21} Recent efforts to define, standardize and even quantify these gray-scale signs²² may improve the gross diagnostic variability across sites and geographic areas, which is reflected in widely variant sensitivity and specificity reported for them in the diagnosis of PAS. The need for diagnostic modalities, such as cystoscopy, that are easily accessible and executed with promising specificity and sensitivity is evident.

In 2014, an NIH consensus panel reviewed vital statistics for the ultrasonographic diagnosis of PAS.¹⁸ In the best of the studies, interrogating only women with placenta previa and a history of cesarean or myomectomy, a combination of several gray-scale markers had a sensitivity of 77%, specificity of 96%, PPV of 65% and an NPV of 98%.²¹ Ultimately, the conclusion was that the ultrasound should be the primary tool for the diagnosis of PAS. Geographic variation in PAS diagnosis and treatment results in the inconsistent reporting of ultrasonographic accuracy¹⁵, perhaps because the European preference for conservative management leads to a lack of international goldstandard diagnosis, and therefore questionable diagnostic accuracy altogether. For example, a French group recently reported that ultrasound had a sensitivity of 100% for diagnosis of PAS, while MRI had only 76.9%.¹⁵ Both modalities had low specificity: 38% and 50%, respectively. However, only 11 of 26 cases were histologically confirmed, and the authors did not indicate whether these were cretas, incretas or percretas. Ultimately, the utility of the gray-scale markers for determining the severity of PAS could not be addressed in the context of the ultrasound or MRI measures reported.¹⁵

In addition, the efficacy of ultrasound decreases in patient populations such as the morbidly obese, those with uterine myomas or a history of multiple prior surgeries (due to extensive scar tissue), which may also result in placental previas.²³ In obese patients, ultrasounds can lose visual accuracy due to increased signal attenuation from absorption, dispersion and backscatter, producing suboptimal images and likely difficult PAS diagnosis.²⁴ Myomas or extensive scar tissue due to prior pelvic and/or obstetric surgeries may also result in suboptimal transabdominal ultrasonographic imaging, even with attempted transvaginal ultrasound, due to visual obstruction and/or uterine tethering.²⁵ A placental previa diagnosis in women with a history of cesarean delivery also means an 11–67% clinical likelihood of PAS, with risk increasing as the number of prior CS increases.²⁶ The use of cystoscopy in these groups of patients could potentially provide critical information for PAS diagnosis.

The proposed pathophysiology for PAS involves endomyometrial damage from prior surgery(ies), resulting in myometrial interface distortion and inadequate healing.²⁷ The molecular pathology for PAS includes abnormally deep invasion by the extravillous trophoblast cells of the placenta, which carry out the vascular remodeling required for normal pregnancy, far deeper into the myometrial blood vessels than is normal.^{28,29} Given the effects of trophoblast invasion on spiral artery enlargement and increased blood flow, the relationship between PAS and the risk of massive hemorrhage is obvious. It is extensive aberrant neovascularization/angiogenesis that underlies many of the subjective ultrasound soft signs for PAS.

Our clinical–observational findings, along with what is known at the molecular level of PAS pathology, are consistent with our cystoscopic findings. The neovascularization shown in Figure 1 and the bulging shown in Figure 2 are consistent with our prior report indicating that grossly visible hypervascularity of the lower uterine segment is characteristic of two-thirds of incretas and all percretas but only a third of cretas.¹⁰ This is also consistent with immunohistochemistry studies showing trophoblast invasion of the deep myometrial blood vessels only in cases of increta and percreta, but not creta.^{28,29} Whether what we see in the bladder is the result of direct interaction with the trophoblast cells that have breached the

uterine serosa in percreta or a paracrine effect is unknown. Further studies on the type of interaction underlying the abnormal signs observed in the bladder wall of PAS cases could further help elucidate our understanding of the molecular pathology of PAS.

The retrospective nature of this study and lack of a control group is a major limitation of this observational report. Although we could not ethically obtain data from healthy controls for comparison, we performed comparisons with those PAS cases in which the three findings were absent to offset this limitation. The majority of these cases lacking all three signs were creta, the mildest form of PAS. Limitations also include the performance of cystoscopy only at the time of delivery/surgery and not across gestational age. In addition, cystoscopy is not routinely performed in pregnancy, and its use may be limited to pregnancy in which there is a clinical benefit, such as in the placement of ureteral stents for refractory renal colic. Some studies have proven the safety of ureteral stents placement in pregnancy, which is a more invasive procedure than solely a diagnostic cystoscopy.^{30,31}

Unfortunately, in PAS cases where the placenta implantation is away from the uterine–bladder interface (i.e. fundal implantation), cystoscopy may not be particularly useful. The cystoscopic visualization of the abnormal neovascularization into the bladder occurs in the setting of disease that is infiltrating into the bladder. This generally accounts for a large portion of patients with PAS as we know the major risk factor for PAS is a prior uterine scar (most commonly, a lower uterine transverse incision, which is usually in close proximity to the posterior bladder wall).

Strengths of our study include the analysis of only histologically confirmed cases and a large number of percretas within the study's sample size. As a tertiary referral center, we see significantly more severe than mild cases, strengthening our expertise in diagnosing and treating the gamut of PAS disease severity.

In conclusion, our study shows that cystoscopy can be a valuable supplement to routine imaging modalities in select patients when determining the severity of PAS. In the event of these abnormal cystoscopy findings, high-risk patients could be transferred to a tertiary care facility that is experienced in the surgical management of PAS. Moreover, cystoscopy in PAS could significantly aid in boosting the surgical preparedness of the interdisciplinary team.

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Figure 1.

(a) Normal cystoscopy image showing the posterior bladder wall in a 32-week pregnant woman with renal colic. (b) Cystoscopy image of the bladder wall in a patient with placenta accreta spectrum (PAS)-percreta at 34 weeks' gestation, prior to CS-hysterectomy. Notice the increased size of the blood vessels.

Figure 2. Bulging, dilated blood vessels seen on the surface of the lower uterine segment in most percreta and increta at surgery are visualized through the bladder wall on cystoscopy (*, arterial; **, venous).

Figure 3.
Distortion of the posterior bladder wall, showing bulging indicated by the arrows.

Table 1Maternal characteristics—mean $\pm$ SD (range) or median (IQ range)

Age (years)	36.3 $\pm$ 5.8 (23–48)
Height (cm)	161 $\pm$ 6 (149–175)
Body mass index (kg/m ²)	27 (17–43)
In Vitro Fertilization (IVF)	11%
Placenta previa	78%
Prior Cesarean	
1	24 (43%)
2	16 (28.5%)
>3	16 (28.5%)
Gestational age at delivery (weeks) [range]	34.0 (33.0, 34.0) [28.1–38.0]

Table 2

Cystoscopy findings by placenta accreta spectrum (PAS) diagnostic category

	All PAS (n = 56)	Creta (n = 9) 16%	Increta (n = 6) 11%	Percreta (n = 41) 73%
Neovascularization	84%	33%	67%	95%
Posterior bladder wall bulging	71%	22%	50%	90%
Arterial pulsatility in areas of neovascularization	54%	0	0	73%
No signs	18%	67%	33%	5%