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Incidentally Identified Basal Plate Myometrial Fibers and Hemorrhage Risk in the Subsequent Pregnancy

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Abstract: Background/Objectives: This study examines index pregnancies with histopathological diagnosis of placenta accreta, based on findings of basal plate myometrial fibers (BPMFs) without intervening decidua, and the risk of hemorrhagic morbidity and/or clinically adherent placenta in the subsequent pregnancy. Outcomes were compared between index pregnancies with incidental asymptomatic BPMF findings and those with symptoms based on hemorrhagic and placental factors. **Methods:** A retrospective cohort study was conducted at a large, integrated healthcare system from 2008 to 2019. All patients with an index finding of BPMF without intervening decidua and subsequent delivery of a live singleton were identified. Index pregnancies with BPMF were categorized as asymptomatic or symptomatic by the absence or presence of hemorrhagic morbidity and/or clinically adherent placenta. Rates of hemorrhagic morbidity and clinically adherent placenta in the subsequent pregnancy were compared among asymptomatic and symptomatic BPMF index pregnancies in bivariate analyses and multivariate models controlling for potential confounders. **Results:** A total of 140 patients were found to have BPMF and a subsequent delivery of a live singleton. Subsequent hemorrhagic morbidity/adherent placenta occurred in 28% of cases, with a lower incidence in asymptomatic patients (8% vs. 39%, $p < 0.0001$). Symptomatic BPMF was associated with increased odds of hemorrhagic morbidity/adherent placenta (aOR 10.2, 95% CI 2.7–38.4). Among 71 patients with subsequent placental pathology, 32% had recurrent BPMF, which correlated with higher morbidity compared to those without recurrence or those without placental pathology (61% vs. 40% vs. 9%, $p < 0.0001$). **Conclusions:** Incidentally identified BPMF was associated with a lower rate of subsequent hemorrhagic morbidity and/or adherent placenta compared to symptomatic BPMF. Symptomatic BPMF is highly associated with hemorrhagic morbidity and/or adherent placenta in the next pregnancy compared with incidentally identified BPMF, particularly if it is recurrent. These data can inform counseling and management of pregnant individuals with BPMF planning subsequent pregnancies.

Keywords: adherent placenta; hemorrhage risk; placenta accreta; pregnancy outcomes; occult accreta; basal plate myometrial fibers; preconception counseling

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1. Introduction

Placenta accreta spectrum (PAS) is the abnormal implantation of some or all of the placenta into the myometrium of the uterus. In its most severe form, PAS can lead to life-threatening peripartum hemorrhage. The incidence of PAS has increased from less than 1 per 1000 deliveries in the 1980s to as high as 11 per 1000 deliveries in the last two decades;

however, accurate estimates are limited due to challenges with consistency in defining PAS [1–3]. This trend correlates with the rise in the number of Cesarean deliveries, which is a significant risk factor for abnormal placentation [4]. Placenta accreta accounts for at least half of emergency peripartum hysterectomies and is associated with significant maternal morbidity and mortality [5]. Data suggest that prior history of clinically diagnosed placenta accreta based on adherent placenta at the time of delivery increases the risk of hemorrhagic morbidity in subsequent births compared to those without placenta accreta, with estimates up to 16% [6,7].

Evaluation of the placenta is often conducted in the setting of peripartum hemorrhage or when the placenta is adherent to the uterus. Histologically, PAS is evident when the decidua is absent between basal plate myometrial fibers and villous tissue on hysterectomy specimens. When incidentally identified on histopathologic analysis of fully delivered placenta (currently termed basal plate myometrial fibers (BPMFs) without intervening decidua), the clinical implications for subsequent pregnancies are unknown, including the contribution of BPMF to the development of clinically significant placenta accreta disorders [8,9]. A small number of observational studies suggested that histologic BPMF-like findings were associated with recurrence of placenta accreta or hemorrhage in subsequent births [9–15]. However, it is not well understood if an isolated finding of BPMF in the index pregnancy differs from symptomatic BPMF (sBPMF), defined as the presence of hemorrhagic morbidity and/or clinically adherent placenta in the index pregnancy. The objectives of this study were to describe the association of BPMF with subsequent pregnancy outcomes and to compare outcomes between pregnant individuals with asymptomatic incidentally identified BPMF (aBPMF) and those with sBPMF.

2. Materials and Methods

This was a retrospective cohort study carried out at an integrated healthcare system in Northern California that serves four million patients and conducts over 40,000 deliveries per year. The demographic make-up of the patient community is representative of the population living in the geographical area served by this integrated healthcare system, except that the patient community has slightly lower representation at the extremes of income [16]. All healthcare is provided in an integrated system and captured in the electronic health record (EHR). This study included all index deliveries between January 2008 and December 2019.

The variability in the literature describing histological findings of placenta accreta led to the adoption of BPMF terminology in our study, as recommended in a recent consensus by an expert panel [8]. The panel suggests that examination of a placental specimen should separately categorize it as BPMF, defined as the presence of microscopic findings of myometrial smooth muscle fibers attached to the basal plate of the placental disk with or without intervening decidua. Reporting includes Stage 1 (decidua present), Stage 2 (decidua absent), size (linear dimension along the basal plate in the largest focus), and number of separate foci. In our study, we use the abbreviated term BPMF to mean findings without decidua (Stage 2).

Figure 1 outlines the process by which we identified all patients with a finding of BPMF in the index pregnancy and subsequent delivery of a live singleton between 2008 and 2019. A query of the CoPath pathology information system by Cerner was conducted to search all pathology reports with the word "accreta." In the pathology report, the word "accreta" was employed in the diagnosis and/or comment field when the microscopic examination revealed basal plate myometrial fibers (BPMFs) without intervening decidua at the maternal surface of the placenta. Among these cases, subsequent births were identified in the EHR. The medical record of each patient was then individually reviewed by an obstetrician–

gynecologist to confirm the presence of BPMF on pathology reports as well as recurrence of BPMF in subsequent pregnancy.

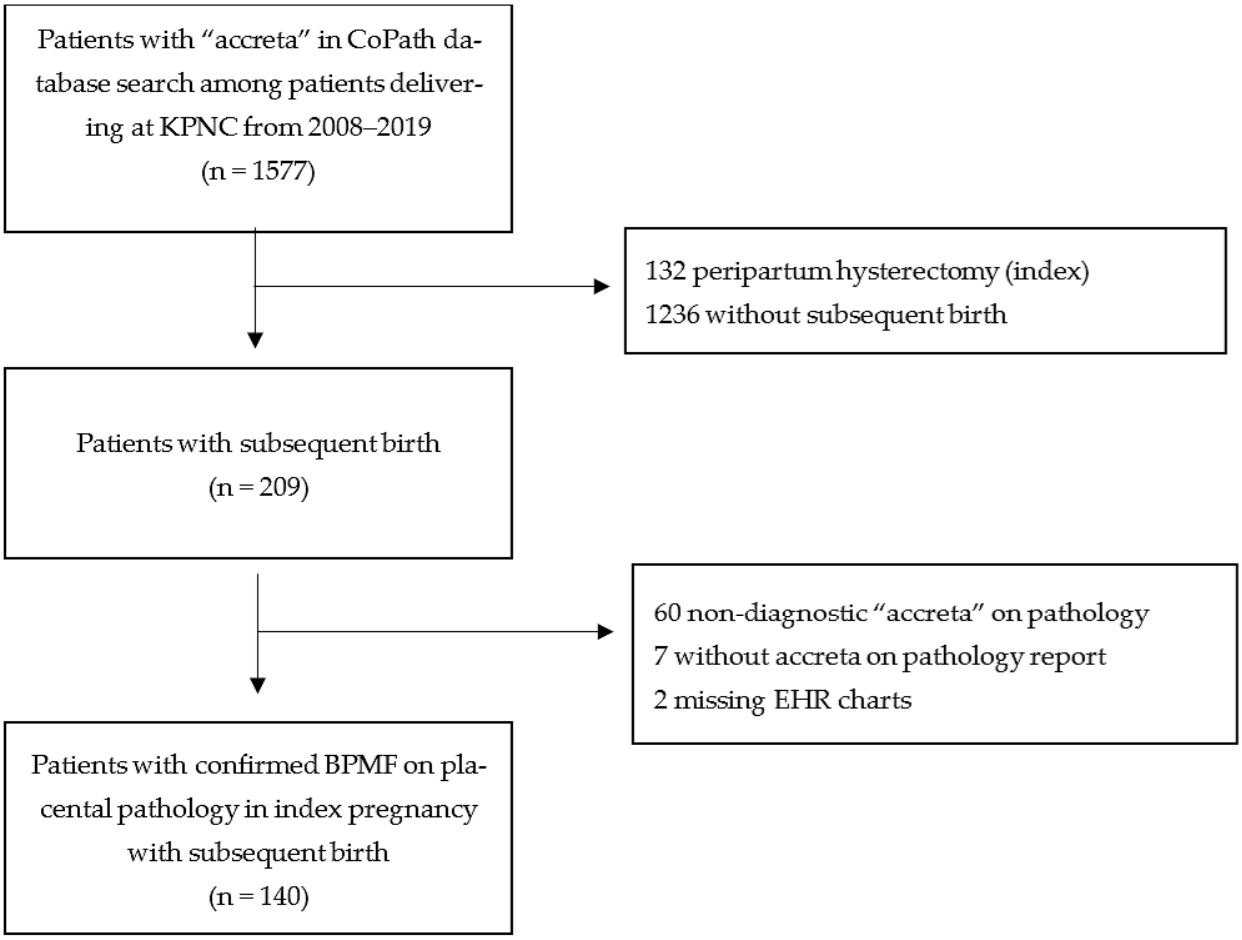

Figure 1. Study population selection: Flow diagram showing case selection for confirmed basal plate myometrial fibers (BPMFs) without intervening decidua among pregnant individuals delivering at Kaiser Permanente Northern California from 2008 to 2019. The selection process excluded patients without subsequent birth, with peripartum hysterectomy, non-diagnostic pathology, or missing electronic health records.

We extracted relevant patient characteristics at the time of the index and subsequent pregnancy from the EHR. Baseline demographic information consisted of age, parity, race/ethnicity, and body mass index (BMI). Obstetric characteristics included variables known or suggested to be risk factors for peripartum hemorrhage or PAS, such as prior uterine surgeries, placenta previa at the time of delivery, Cesarean section at the time of delivery, and in vitro fertilization (IVF). Placental and hemorrhagic characteristics were also extracted, and the chart was reviewed for both the index and subsequent pregnancy in the context described below. The practice within our integrated healthcare system was to not routinely send all placentas for analysis. Placentas were sent to pathology for a variety of clinical indications, including intraamniotic infection, fetal growth restriction, and suspected placenta accreta. Thus, incidental findings of aBPMF would be found on placentas sent for other clinical indications. During the study period, 16–23% of all placentas delivered within the system were examined by a pathologist.

For the exposure variables, we determined if those with BPMF in the index pregnancy were asymptomatic or symptomatic. sBPMF was defined as the presence of clinically adherent placenta or hemorrhagic morbidity. Clinically adherent placenta was determined by its description in the delivery notes based on the clinical judgment of an obstetrician–

gynecologist. Manual extraction of the placenta following a vaginal delivery was a stronger indicator of clinically adherent placenta compared to manual extraction during Cesarean delivery, as routine manual removal of the placenta during surgery is a variable practice and not suggestive of placental abnormalities. Hemorrhagic morbidity was defined as having at least one of the following: estimated blood loss (EBL) > 1500 mL, blood transfusion, intrauterine tamponade, dilation and curettage (D&C), uterine artery embolization (UAE), or intensive care unit (ICU) admission.

Adverse outcomes due to placental or hemorrhagic factors in the subsequent pregnancy were similarly defined, with peripartum hysterectomy within one month of delivery added to the criteria for hemorrhagic morbidity.

Rates of hemorrhagic morbidity and clinically adherent placenta in the subsequent pregnancy were reported overall and compared between aBPMF and sBPMF index pregnancies. Multivariable logistic regression analysis was performed to determine which factors were associated with hemorrhagic morbidity and/or adherent placenta in the subsequent pregnancy. The model was adjusted for a priori confounders, including maternal age, race/ethnicity, and Cesarean section at index delivery. Normally distributed continuous variables were compared using two-sample t tests. Chi-square tests or Fisher exact tests were performed for categorical variables. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA). *p*-values were 2-sided, with a significance threshold of 0.05. This study was approved by the Institutional Review Board, with a waiver of the requirement for informed consent.

3. Results

From 1 January 2008 to 31 December 2019, we identified a cohort of 140 patients with confirmed BPMF in the index pregnancy who had a subsequent birth. This number was derived from an initial pool of 1577 patients that resulted from the CoPath database search for "accreta" in the pathology reports. We identified 209 patients who went on to have a subsequent birth of a singleton. Among the 69 excluded from the final cohort, 60 had "non-diagnostic" BPMF findings in the pathology report, 7 did not have BPMF, and 2 had missing charts (Figure 1).

In the index pregnancy, 90 (64%) had sBPMF and 50 (36%) had aBPMF (Table 1). The sBPMF and aBPMF groups did not significantly differ in parity, prior uterine surgery, or presence of previa during the index pregnancy (Table 1). Most patients were nulliparous or had one previous birth (87%) and were less than 35 years old (82%) at the index pregnancy. Patients with aBPMF were more likely to have delivered by Cesarean section in the index pregnancy compared to those with sBPMF (64% vs. 20%, $p < 0.0001$). The indication for placental examination differed between the two groups: suspected accreta was higher in the sBPMF group (93% vs. 10%, $p < 0.001$) and all other reasons were higher in the aBPMF group (Table 1).

In the subsequent pregnancy, 39 (28%) had clinically adherent placenta or hemorrhagic morbidity overall. The combined morbidity in subsequent pregnancies for aBPMF was 8% compared to 39% for sBPMF ($p < 0.0001$; Table 2). Among the 39 patients with an adverse outcome in the subsequent pregnancy, 35 had sBPMF in the index pregnancy. After adjusting for potential confounders—age, race/ethnicity, parity, BMI, IVF, prior uterine surgery, Cesarean delivery, and placenta previa—the odds of adverse outcomes at a subsequent pregnancy were higher for patients with sBPMF in the index pregnancy compared to those with aBPMF (adjusted odds ratio (aOR) 10.2, 95% confidence interval (CI) 2.7–38.4; Table 3).

Table 1. Selected characteristics according to symptomatic (s) vs. asymptomatic (a) basal plate myometrial fibers (BPMFs) in index pregnancy (N = 140).

Selected Characteristics	Total (N = 140) n (%) or Mean (SD)	sBPMF (N = 90, 64%) n (%) or Mean (SD)	aBPMF (N = 50, 36%) n (%) or Mean (SD)	*p*-Value
Maternal age (Year) at the first prenatal visit				
Mean (Year)	30.8 (4.9)	31.5 (4.6)	29.5 (5.3)	0.023
<35 years old	115 (82.1)	72 (80.0)	43 (86.0)	0.374
≥35 years old	25 (17.9)	18 (20.0)	7 (14.0)	
Parity				0.452
0–1 births >20 weeks	122 (87.1)	77 (85.6)	45 (90.0)	
>1 birth >20 weeks	18 (12.9)	13 (14.4)	5 (10.0)	
Race/Ethnicity				0.031
White	76 (54.3)	53 (58.9)	23 (46.0)	
Black	13 (9.3)	4 (4.4)	9 (18.0)	
Hispanic non-Black	22 (15.7)	12 (13.3)	10 (20.0)	
Asian or Pacific Islander	25 (17.9)	17 (18.9)	8 (16.0)	
Native American/Multiracial/ Other/Unknown	4 (2.9)	4 (4.4)	0	
Body mass index (BMI)				0.939
<30	106 (75.7)	67 (74.4)	39 (78.0)	
30–34	23 (16.4)	16 (17.8)	7 (14.0)	
35–39	6 (4.3)	4 (4.4)	2 (4.0)	
≥40	5 (3.6)	3 (3.3)	2 (4.0)	
Prior uterine surgery	15 (10.7)	9 (10.0)	6 (12.0)	0.714
Placenta previa at time of delivery	1 (0.7)	1 (1.1)	0 (0.0)	1.000
Cesarean at time of delivery	50 (35.7)	18 (20.0)	32 (64)	<0.001
In vitro fertilization (IVF)				0.901
Yes	6 (4.3)	4 (4.4)	2 (4.0)	
No	134 (95.7)	86 (95.6)	48 (96.0)	
Indication for pathologic examination				<0.001
Suspected accreta *	89 (63.6)	84 (93.3)	5 (10.0)	
Placental abruption	3 (2.1)	0 (0)	3 (6.0)	
Infection	7 (5.0)	0 (0)	7 (14.0)	
Preterm labor	2 (1.4)	0 (0)	2 (4.0)	
PPROM	6 (4.3)	1 (1.1)	5 (10.0)	
IUGR	10 (7.1)	0 (0)	10 (20.0)	
HTN	7 (5.0)	3 (3.3)	4 (8.0)	
GDM	2 (1.4)	0 (0)	2 (4.0)	

* Based on clinically adherent placenta, history of accreta, or unexplained bleeding during delivery.

Table 2. Clinical outcomes in subsequent pregnancy by presence of symptomatic (s) vs. asymptomatic (a) basal plate myometrial fibers (BPMFs) in index pregnancy (N = 140).

Outcome in Subsequent Pregnancy (N (%))	Total (N = 140)	sBPMF * (N = 90)	aBPMF (N = 50)	*p*-Value
Hemorrhagic morbidity and/or adherent placenta	39 (27.9)	35 (38.9)	4 (8.0)	<0.0001
Adherent placenta only	13	11	2	
Hemorrhagic morbidity only †	12	10	2	
Both	14	14	0	
None	101 (72.1)	55 (61.1)	46 (92.0)	

* Symptomatic if any of the following present: clinically adherent placenta, EBL ≥ 1500 mL, blood transfusion, intrauterine tamponade, D&C, UAE, ICU admission. † Hemorrhagic morbidity includes any of the following: EBL ≥ 1500 mL, blood transfusion, intrauterine tamponade, D&C, UAE, ICU admission, and peripartum hysterectomy.

Table 3. Multivariable logistic regression: Odds ratios and 95% confidence intervals (CIs) of placental or hemorrhagic morbidity in subsequent pregnancies according to presence of symptomatic (s) vs. asymptomatic (a) basal plate myometrial fibers (BPMFs) in index pregnancy.

	Any Placental or Hemorrhagic Morbidity Outcome in Subsequent Pregnancy			
Presence of Accreta Symptoms in Index Pregnancy	Crude Odds Ratio (95% CI)	*p*-Value	Adjusted Odds Ratio (95% CI) *	*p*-Value
sBPMF †	7.32 (2.42–22.12)	<0.001	10.2 (2.7–38.4)	<0.001
aBPMF (reference)	1.0		1.0	
Model c-statistics	0.676		0.735	

* Adjusted for maternal age, race and ethnicity, and c-section at index delivery. † Symptomatic if any of the following present: clinically adherent placenta, EBL ≥ 1500 mL, blood transfusion, intrauterine tamponade, D&C, UAE, and ICU admission.

Additionally, we identified 71 patients with placental pathology performed in the subsequent pregnancy. Among these, 23 had recurrent BPMF and 48 did not have recurrent BPMF. Recurrent BPMF was associated with increased morbidity compared to those without recurrence or those with no placental pathology (61% vs. 40% vs. 9%, $p < 0.0001$; Table 4).

Table 4. Clinical outcomes by pathological findings in subsequent pregnancy (N = 140).

	Total Subsequent Pregnancies (N = 140)	Hemorrhagic Morbidity * and/or Adherent Placenta (N = 39)	None (N = 101)	*p*-Value
Indication for placenta pathology in subsequent pregnancy, *n* (%)				
No placental pathology	69	6 (8.7)	63 (91.3)	<0.0001
Yes placental pathology	71			
Recurrent BPMF	23	14 (60.9)	9 (39.1)	
No Recurrent BPMF	48	19 (39.6)	29 (60.4)	

* Hemorrhagic morbidity includes any of the following: EBL ≥ 1500 mL, blood transfusion, intrauterine tamponade, D&C, UAE, ICU admission, and peripartum hysterectomy.

4. Discussion

In this retrospective cohort study, we found that patients with sBPMF had 10-fold increased odds of postpartum hemorrhage and/or adherent placenta in the subsequent pregnancy compared to patients with an incidentally identified aBPMF. aBPMF was associ-

ated with low but non-negligible rates of hemorrhagic morbidity and/or adherent placenta in subsequent pregnancies. These findings suggest that the clinical context of the index pregnancy where BPMF is found plays an important role in assessing obstetric morbidity in future pregnancy.

Previous studies established that histological BPMF was associated with placenta accreta or hemorrhage recurrence in subsequent deliveries. However, these studies largely focus on symptomatic BPMF, leaving providers with clinical uncertainty regarding subsequent pregnancy outcomes in patients with incidentally found BPMF. Our investigation of BPMF builds upon prior work seeking to understand the clinical significance of abnormal histological findings suggestive of PAS. The absence of intervening decidua between chorionic tissue from the placenta and myometrium of the uterus defines placenta accreta. While a hysterectomy specimen allows for the most complete assessment of abnormal placentation and reflects the most severe cases of PAS, milder forms of placenta accreta, or occult accreta, based on placental specimen evaluation have been reported in the scientific literature [10,17,18]. One descriptive report reviewed 36 placentas with microscopic foci of myometrial tissue adherent to the basal plate, which is the maternal interface of the placenta after delivery [17]. Only 4 cases had a clinical diagnosis of placenta accreta, 8 of 15 vaginal births underwent manual removal due to adherent placenta at the time of delivery, and 3 experienced postpartum hemorrhage. A retrospective observational study of 491 clinically adherent placentas found 20% with a pathologic diagnosis of occult accreta, and compared to controls, occult accreta had higher rates of prior Cesarean delivery (19% vs. 11%), prior uterine surgery (35% vs. 20%), postpartum hemorrhage (59% vs. 32%), hysterectomy (21% vs. 0.3%), recurrence of accreta (30% vs. 7%), and retained placenta in subsequent pregnancy (43% vs. 19%) [10]. The variables in this work contributed to the formulation of the obstetric outcomes in our study as well as the risk factors used in our adjusted models.

Further investigation of abnormal attachment of myometrial fibers to the basal plate (BPMYO) was conducted in three case–control studies specifically to associate BPMYO with pathologically diagnosed placenta accreta and morbidly adherent placenta in a subsequent pregnancy. The first study analyzed 25 cases of morbidly adherent placenta and 100 controls and found BPMYO in 61% of cases compared to 39% in controls ($p < 0.001$) after adjusting for confounders [11]. In the second study, an analysis of 50 cases with accreta on pathology and 100 controls found that cases were twice as likely to have BPMYO in their prior pregnancies (84% vs. 42%, $p < 0.001$), were more likely to have higher stages of BPMYO (38% vs. 2%, $p < 0.001$) and had a greater number of BPMYO foci (6.2% vs. 7%, $p < 0.001$) [12]. In the third study, recurrence of BPMF in a subsequent pregnancy was reported to be 100%, with half of these progressing in severity in the subsequent pregnancy and a tenth of the recurrent cases leading to a hysterectomy [15].

Estimates of the recurrence rate of placenta accreta varies widely in the literature due to variability in study designs, inclusion criteria for the study population, and the definition of placenta accreta by pathologic or clinical diagnosis. A population-based study in New South Wales using birth and hospital records reported a recurrence rate of 4.7% [19]. A literature review of six papers and 407 pregnancies with placenta accreta found a recurrence rate of 20% [20]. Our estimate of recurrence provides more nuanced risk stratification that allows for more precise evaluation and counseling.

Furthermore, the risk of postpartum hemorrhage in subsequent pregnancies among those with aBPMF resembles estimates of postpartum hemorrhage in subsequent births among a general population of pregnant individuals without a history of obstetric hemorrhage [21,22]. The rate of hemorrhagic morbidity in subsequent pregnancy among sBPMF reflects the estimated rates of postpartum hemorrhage recurrence among those with a

history of PPH [21,22]. These findings suggest that a histologic finding of BPMF alone is not a clinically meaningful predictor of morbidity in subsequent pregnancies. However, the population studies on postpartum hemorrhage cited above utilize a lower threshold for inclusion (i.e., EBL > 1000), whereas the criteria for the outcomes in our study aim to define clinically meaningful hemorrhage morbidity.

Finally, our findings are consistent with and extend the results of existing research examining our precise study questions. A descriptive study of 39 patients from Brigham and Women's Hospital demonstrated that patients with pathologically diagnosed placenta accreta during an index pregnancy complicated by a hemorrhagic outcome were more likely to have hemorrhagic recurrence in a subsequent pregnancy compared to patients without hemorrhagic complications in their index pregnancy [13]. Similarly, our study found that there was a statistically significant difference in hemorrhagic outcomes of subsequent pregnancies in patients with pathologically diagnosed placenta accreta who were clinically symptomatic compared to those without symptoms, with an aOR of 10.2. Furthermore, 32% of the 71 patients with placenta pathology in subsequent pregnancy had recurrent BPMF, with recurrent BPMF being associated with increased morbidity. This is consistent with the trend found in the study by Rutger's University [15].

While our study aimed to better describe the association between sBPMF and hemorrhagic morbidity in subsequent pregnancy, more robust studies are needed to substantiate our findings and reflect the new pathologic reporting guidelines detailed above. The most scientifically sound manner to determine this would be to prospectively collect a large number of placentas from all deliveries with subsequent pregnancies and compare the outcomes of subsequent pregnancy between those with BPMF and those without; however, this would require a significant research investment, as the practice of universal placental examination is not widely implemented.

5. Strengths and Limitations

This is the largest study examining BPMF as a risk factor for morbidity in subsequent pregnancy. This study expands the small body of literature by including a larger and more contemporary study population. This is also the only study that included a comparison group and used multivariate analysis to adjust for potential confounders.

A significant limitation of our study is that the comparison group did not include all patients without an indication for placental examination, as this was technically not feasible. Because placental pathology was sent only when there was an indication or suspicion of an indication, we were not able to conclude that these findings are necessarily reflective of real-world findings, even though we adjusted for potential confounding variables. Thus, the number of aBPMF cases was potentially underestimated. The study findings would be more robust if it were possible to have the pathology of every placenta to determine the true incidence of aBPMF and assess its association with subsequent morbidity. Additionally, it was not feasible to ascertain the rate of postpartum hemorrhage outcomes in the entire patient population within the integrated healthcare system to compare to the aBPMF group. However, estimates of postpartum hemorrhage outcomes in the United States suggest that the rate is similar to the rate seen among the asymptomatic group [23]. Lastly, our study has inherent limitations due to its retrospective cohort design; there may have been important factors contributing to characteristics and outcomes of both study groups that we were unable to collect and analyze.

6. Conclusions

In conclusion, symptomatic BPMF was associated with increased subsequent pregnancy hemorrhagic morbidity and/or adherent placenta compared with incidentally iden-

tified BPMF, particularly when BPMF was recurrent. Conclusions on whether incidental BPMF is independently associated with subsequent hemorrhagic morbidity and/or clinically adherent placenta are limited by the retrospective design and lack of a comprehensive comparison group including patients without clinical indication for placental examination. Nevertheless, this is the largest study to our knowledge using a comparison group and multivariate analysis to control for confounders that examines features of BPMF associated with morbidity in subsequent pregnancies. These data have important implications for counseling, pathology reporting, and the management of individuals with BPMF who are planning subsequent pregnancies. History of symptomatic BPMF or recurrent BPMF may inform the perception of risk and screening practices, such as advanced ultrasound to detect gross placental invasion [24]. The clinical context of a BPMF finding should be considered during counseling on subsequent pregnancy risks.

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Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Kaiser Permanente Northern California Region (protocol code 583397-1 and date of approval 1 April 2020).

Informed Consent Statement: Patient consent was waived due to the retrospective nature of this study.

Data Availability Statement: Data supporting reported results can be requested via emails to the corresponding author.

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Abbreviations

The following abbreviations are used in this manuscript:

EHR	electronic health record
KPNC	Kaiser Permanente Northern California
BPMF	basal plate myometrial fiber
PAS	placenta accreta spectrum

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