Contents lists available at ScienceDirect



American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

# Impact of point-of-care ultrasound on treatment time for ectopic pregnancy



Bethsabee S. Stone, MD<sup>a,\*</sup>, Krithika M. Muruganandan, MD<sup>b</sup>, Melinda M. Tonelli, MD<sup>b</sup>, Julianne N. Dugas, MPH<sup>c</sup>, Ivy E. Verriet<sup>d</sup>, Joseph R. Pare, MD, MHS<sup>b</sup>

<sup>a</sup> Pediatric Emergency Department, Boston Medical Center, Boston University School of Medicine, 1 Boston Medical Center Place, Boston, MA 02118, United States of America

<sup>b</sup> Emergency Department, Boston Medical Center, Boston University School of Medicine, 1 Boston Medical Center Place, Boston, MA 02118, United States of America

<sup>c</sup> Emergency Department, Boston Medical Center, 1 Boston Medical Center Place, Boston, MA 02118, United States of America

<sup>d</sup> Pediatric Emergency Department, Boston Medical Center, 1 Boston Medical Center Place, Boston, MA 02118, United States of America

## ARTICLE INFO

Article history: Received 30 January 2021 Received in revised form 13 May 2021 Accepted 27 May 2021 Available online xxxx

Keywords: Ultrasound Point-of-care Ectopic Rupture Pregnancy Radiology

# ABSTRACT

*Background:* Point-of-care ultrasound (POCUS) is useful in the evaluation of early pregnancy by confirming intrauterine pregnancy and recognizing hemorrhage from ectopic pregnancy. We sought to determine whether transabdominal POCUS by itself or in conjunction with consultative radiology ultrasound (RADUS), reduces Emergency Department (ED) treatment time for patients with ectopic pregnancy requiring operative care, when compared to RADUS alone. A secondary objective was to determine whether the incorporation of POCUS reduces time to operative care for patients with ruptured ectopic pregnancy specifically, when compared to RADUS alone.

*Methods:* We performed a retrospective review of patients admitted for operative management of ectopic pregnancy. We excluded patients with known ectopic pregnancy and/or imaging prior to arriving to the treatment area, found not to have an ectopic pregnancy, or did not undergo operative care. Descriptive statistics, classical and nonparametric statistical analysis, and linear regression were performed.

*Results*: There were 220 patients admitted with ectopic pregnancy, 111 met exclusion criteria, yielding 109 for analysis. Of 109, 36 received POCUS (23/36 also had RADUS), while 73 received RADUS only. Among the POCUS group 31/36 (86%) were classified as ruptured versus 47/73 (64%) in the RADUS group. The average ED treatment time in the POCUS group for all admitted ectopic pregnancies was 157.9 min (standard deviation [SD] 101.3) versus 206.3 min (SD 76.6) in the RADUS group (p = 0.0141). The median time to operating room (OR) for ruptured ectopic pregnancies was 203.0 min (interquartile range [IQR] 159.0) in the POCUS group versus 293.0 min (IQR 139.0) in the RADUS group (p = 0.0002). Regression analysis of the primary outcome was limited by multiple interactions and sample size. When controlling for race, positive shock index and ED visit time, POCUS was found to be associated with a significantly shorter time to OR among ruptured ectopic pregnancies compared to RADUS (p = 0.0052).

*Conclusion:* Compared to RADUS alone, incorporation of POCUS was associated with significantly faster ED treatment time for all ectopic pregnancies and significantly faster time to OR for ruptured ectopic pregnancies, even when combined with RADUS. When controlling for clinical differences, time to OR was still faster for patients who underwent POCUS. The integration of POCUS should be considered to expedite care for patients with ectopic pregnancy requiring operative care.

© 2021 Elsevier Inc. All rights reserved.

## 1. Introduction

deaths [1,2]. Given the potentially devastating outcomes from uncontrolled bleeding, timely evaluation of ectopic pregnancy is critical.

Point-of-care ultrasound (POCUS) has been shown to be key for the

Despite the reduction in mortality from ectopic pregnancy in recent decades, associated complications, primarily being intra-abdominal hemorrhage, continue to account for up to 10% of pregnancy-related

E-mail address: bethsabee.stone@gmail.com (B.S. Stone).

evaluation of early pregnancy as well as intra-abdominal hemorrhage. Importantly, POCUS is highly specific for the detection of intrauterine pregnancy (IUP) and its use can reduce Emergency Department (ED) length of stay [3]. The Focused Assessment with Sonography in Trauma (FAST) exam is broadly accepted to detect intraperitoneal hemorrhage in trauma and reduces time to operative care [4]. A number of studies advocate for acquiring limited FAST views as part of the POCUS

<sup>\*</sup> Corresponding author at: Care of: Joseph R. Pare, MD, BCD Building, 800 Harrison Ave, Boston, MA 02118, United State of America.

assessment of patients with symptoms of ectopic pregnancy to similarly detect intra-abdominal hemorrhage [3,5-9]. Patients with moderate to large free fluid (FF) in the pelvis are 3–9 times more likely to have an ectopic pregnancy, and identification of FF in the right upper quadrant (RUQ) on POCUS has been shown to decrease treatment time [7-10]. Furthermore, FF in the RUQ has a specificity of 99.5% for the associated diagnosis of ruptured ectopic pregnancy with a positive likelihood ratio (LR) of 112 for operative management [11]. The same study also reported the specificity of pelvic FF by POCUS to be 94% for ruptured ectopic pregnancy with a positive LR of 9.5 [11]. However, it has not been evaluated whether a combined pelvic and RUQ POCUS exam assessing for FF, when an IUP cannot be identified, results in expedited care for patients with ectopic pregnancy.

Our primary objective was to determine whether patients with ectopic pregnancy requiring operative care that received Emergency Physician (EP) transabdominal POCUS exams (which included pelvic and RUQ views) had a reduced ED length of stay. Our secondary objective was to determine if EP POCUS reduced time to operative management for patients found to have ruptured ectopic pregnancy. It was expected that an abnormal POCUS exam, including FF in pelvis and/or RUQ, when used as an early diagnostic tool, would lead to expedited medical care.

## 2. Methods

## 2.1. Study design and setting

This was a retrospective, observational, cohort study of patients diagnosed with ectopic pregnancy that underwent operative management, between January 2015 and September 2020.

The investigation was conducted at a large urban academic ED in the United States with an annual census of >140,000 visits per year. The facility is a level-1 trauma center with an emergency medicine residency, clinical ultrasound fellowship and pediatric emergency medicine fellowship. Consultative radiology performed ultrasound (RADUS) for pregnancy, including ectopic pregnancy evaluation, are available at all hours by in-house ultrasound technicians. In addition, the ED has six dedicated portable ultrasound machines available for point-of-care testing and an EP credentialed in POCUS is always present in the ED. EPs and residents are trained to perform POCUS for the evaluation of FF in the abdomen as well as to rule in IUP. Those performing POCUS are educated to describe FF in the pelvis as small or physiologic by visual assessment, which entails FF that does not extend more than 50% up the body of the uterus in the Pouch of Douglas. Curvilinear probes are available for the evaluation of pregnancy by POCUS in the ED, whereas RADUS additionally includes transvaginal imaging. Patients were classified as part of the POCUS cohort if they had both POCUS and RADUS performed and if the EP POCUS was performed prior to the result of the RADUS. Diagnostic requirements of an IUP for both POCUS and RADUS include a gestational sac with a yolk sac and/or fetal pole. It is standard practice at our institution to obtain RADUS for all patients with symptoms concerning for ectopic pregnancy that do not have an IUP detectable by POCUS and are hemodynamically stable. This study had institutional board approval and was guided by the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines as well as the best practices for retrospective chart reviews [12,13].

## 2.2. Selection of participants

We queried the institution's electronic medical record (EMR), EPIC (Verona, WI), to identify patients treated and admitted with a diagnosis of ectopic pregnancy from our ED (Appendix A). Subjects were included if they were admitted to the hospital for operative management of ectopic pregnancy. Subjects were excluded if they arrived with a known diagnosis of ectopic pregnancy, did not undergo operative treatment, were found not to have an ectopic pregnancy at surgery, or had imaging performed prior to arrival to the ED treatment area. This included

patients who had RADUS ordered from triage by a nurse after consultation with a physician. It is not the preferred workflow at our institution to have nurse consult with physicians to order RADUS from triage. However, during times of high volume with prolonged wait times, this can be done to expedite care.

# 2.3. Study protocol

All clinical data was collected from subjects' EMR, including ultrasound image storage software, Q-Path (Coquitlam, BC Canada) or OsiriX (Geneva, Switzerland). Data was directly entered into standardized data entry forms and stored on the institution's online database entry system REDCap (Nashville, TN) [14]. Clinical data from the EMR was entered into REDCap by two trained individuals (B.S·S., I.E.V.) who did not collect POCUS data. POCUS information was extracted by an individual with ultrasound fellowship training (J.R.P) based on documentation in Q-Path or as documented in the EMR by the performing EP. In order to determine the reliability of manual abstractions, a second blinded reviewer with clinical ultrasound training reviewed a random selection of 20% of the records for key datapoints related to the primary and secondary aims (M.M.T.). For any discrepancies, a third independent reviewer with clinical ultrasound fellowship training adjudicated the final results (K.M.M.).

## 2.4. Key measurements and definitions

Individual medical records were reviewed for ED visits corresponding to the admission diagnosis of ectopic pregnancy. EMR time stamps were recorded for ED arrival time, placement time in a treatment area, time to disposition (time stamp from being placed in treatment area to disposition order placed in EMR), and operation start time. RADUS findings were classified as IUP, no IUP, or indeterminate. FF was classified on RADUS as either positive in the pelvis (physiologic/small), positive in the pelvis (moderate/large), positive in RUQ and pelvis, positive in the RUQ only, or negative. POCUS findings were classified as IUP, no IUP, or indeterminate. Indeterminate POCUS and RADUS results were classified as no IUP for analysis since IUP is a rule in diagnosis. Pelvic FF on POCUS was classified as small/physiologic, moderate/large, or negative. POCUS RUQ FF was classified as positive, negative or not done. Indeterminate results for FF were classified as no FF for analysis since FF is a rule in diagnosis. The operative report was reviewed for findings, including location of ectopic pregnancy, amount of hemoperitoneum, and outcome of surgery. Hemoperitoneum was classified as small (<100 mL), moderate (100–250 mL), large (>250 mL), or none. We defined ruptured ectopic pregnancy as hemoperitoneum greater than 100 mL as specified in the operative report. Shock index, calculated as heart rate divided by systolic blood pressure, was considered positive if ≥0.9. Daytime hours were defined as ED visit from 7:00 am up to and including 4:59 pm, regardless of day.

## 2.5. Outcome measures

The primary outcome measure was to compare ED treatment time (placement time in a treatment area to disposition time, defined as disposition order entered in the EMR) for patients who received POCUS as a part of their ED care compared to RADUS only for ectopic pregnancies undergoing operative intervention. The secondary outcome was to determine whether POCUS patients with ruptured ectopic pregnancy had faster time to operating room (OR) than those who received RADUS only.

# 2.6. Data analysis

A sample size calculation was performed using a two-sample *t*-test with an alpha of 0.05. To achieve 80% power, 44 patients with a 1:3 ratio of POCUS to RADUS (11:33) would be needed to detect a difference

Demographic information.

	$\frac{\text{Overall}}{(n = 109)}$	$\frac{\text{POCUS}}{(n = 36)}$	$\frac{\text{RADUS}}{(n = 73)}$	<i>p</i> -value
Ruptured ectopic, n (%)	78 (71.6)	31 (86.1)	47 (64.4)	$0.0180^{*}$
Age (years), mean (sd)	31.2 (6.2)	32.1 (5.3)	30.7 (6.5)	0.2818 <sup>†</sup>
BMI (kg/m <sup>2</sup> ), median (IQR)	27.4 (8.8)	27.4 (9.4)	27.8 (8.1)	0.4309 <sup>‡</sup>
<b>Race</b> , <i>n</i> (%)				$0.0255^{*}$
White	17 (15.6)	11 (30.6)	6 (8.2)	
Black or African American	43 (39.4)	11 (30.6)	32 (43.8)	
Other	16 (14.7)	5 (13.9)	11 (15.1)	
Declined or not available	33 (30.3)	9 (25.0)	24 (32.9)	
Ethnicity, n (%)				0.0654 <sup>§</sup>
Hispanic or Latino	38 (34.9)	8 (22.2)	30 (41.1)	
Not Hispanic or Latino	70 (64.2)	28 (77.8)	42 (57.5)	
Declined	1 (0.9)	0 (0.0)	1 (1.4)	
HR (bpm), mean (sd)	89.1 (17.2)	93.1 (22.0)	87.0 (14.0)	0.1353 <sup>†</sup>
RR (rpm), median (IQR)	18.0 (2.0)	18.0 (3.0)	18.0 (2.0)	0.3354 <sup>‡</sup>
SBP ( <i>mmHg</i> ), mean (sd)	120.9 (20.7)	112.3 (19.9)	125.2 (19.8)	$0.0019^{\dagger}$
DBP (mmHg), mean (sd)	75.8 (13.7)	69.3 (12.9)	79.1 (12.9)	0.0003 <sup>†</sup>
<b>Positive shock index</b> , $\geq 0.9$ , <i>n</i> (%)	23 (21.1)	15 (41.7)	8 (11)	$0.0002^{*}$
<b>ESI</b> , <i>n</i> (%)				0.0006 <sup>§</sup>
1	1 (0.9)	1 (2.8)	0 (0.0)	
2	13 (11.9)	10 (27.8)	3 (4.1)	
3	92 (84.4)	25 (69.4)	67 (91.8)	
4	2 (1.8)	0 (0.0)	2 (2.7)	
Not listed	1 (0.9)	0 (0.0)	1 (1.4)	
English-speaking, n (%)	70 (64.2)	23 (63.9)	47 (64.4)	$0.9596^{*}$
Treatment area, n (%)	. ,			0.2666 <sup>§</sup>
Adult ED	100 (91.7)	35 (97.2)	65 (89.0)	
Pediatric ED	9 (8.3)	1 (2.8)	8 (11.0)	
Room in hallway, n (%)	42 (38.5)	12 (33.3)	30 (41.1)	$0.4335^{*}$
Triage time (min), median (IQR)	14.0 (30.0)	12.0 (11.5)	15.0 (34.0)	$0.0298^{\ddagger}$
Triage time among ruptured ectopics (min), median (IQR)	12.5 (19.0)	12.0 (11.0)	15.0 (31.0)	0.0721 <sup>‡</sup>
Relevant presenting symptoms, n (%)				
Vaginal bleeding	70 (64.2)	13 (36.1)	57 (78.1)	< 0.0001*
Abdominal pain	107 (98.2)	35 (97.2)	72 (98.6)	>0.9999§
Syncope	5 (4.6)	5 (13.9)	0 (0.0)	0.0032§
Vomiting	15 (13.8)	8 (22.2)	7 (9.6)	0.0834§
Other	15 (13.8)	5 (13.9)	10 (13.7)	>0.9999
Peritoneal signs on exam, n (%)	62 (56.9)	24 (66.7)	38 (52.1)	$0.1474^{*}$
Prior pelvic surgery, n (%)	38 (34.9)	11 (30.6)	27 (37.0)	$0.5076^{*}$
IUD in place, $n$ (%)	6 (5.5)	2 (5.6)	4 (5.5)	>0.9999
Prior pregnancy, n (%)	82 (75.2)	29 (80.6)	53 (72.6)	$0.3657^{*}$
<b>Gravida</b> <sup>a</sup> , <i>n</i> (%)	- 、 /	/		0.3071*
2	27 (24.8)	9 (25.0)	18 (24.7)	
3	19 (17.4)	6 (16.7)	13 (17.8)	
4	16 (14.7)	5 (13.9)	11 (15.1)	
5	11 (10.1)	7 (19.4)	4 (5.5)	
>5	9 (8.3)	2 (5.6)	7 (9.6)	
Prior ectopic pregnancy, n (%)	10 (9.2)	3 (8.3)	7 (9.6)	>0.9999
serum β-hCG ( <i>mIU/mL</i> ), median (IOR)	3055.0	6027.5 (10,435.0)	2124.0	0.0182 <sup>‡</sup>
	(9678.0)	0027.5 (10,455.0)	(6216.0)	0.0102

Abbreviations: SD: standard deviation, IQR: interquartile range, bpm: beats per minute, rpm: respirations per minute, min: minute, RADUS: Radiology performed Ultrasound, hCG: human chorionic gonadotropin, kg/m<sup>2</sup>: kilogram per meter squared, mIU/mL: mili-international units per milliliter.

\*Chi-squared test; <sup>†</sup>Student's *t*-test; <sup>‡</sup>Wilcoxon ranked-sum test; <sup>§</sup>Fisher's Exact test.

<sup>a</sup> There were no patients with only 1 prior pregnancy.

of 30 min (2 h versus 2.5 h) with a SD of 30 min between cohorts. Summary statistics were calculated separately for patients that did and did not receive POCUS, as well as for all patients overall. Continuous values were compared between the two groups using either student's *t*-test or Wilcoxon ranked-sum test, and categorical values were compared either by chi-squared test or Fisher's Exact test. Agreement between the two reviewers was assessed using a simple kappa coefficient for categorical variables and Lin's concordance correlation coefficient for continuous variables [15]. Median ED treatment time and time to OR were calculated for each of the following three distinct groups: POCUS only, POCUS & RADUS, and RADUS only. Kruskal-Wallis tests were used to compare the values between the three groups. Multivariable linear regression was performed for the primary and secondary outcomes to adjust for confounding variables. Linear regression was performed for the primary and secondary outcomes to account for the fact that patients in the POCUS group may have significant differences (sicker or difference in arrival times). Covariates included in the regression analysis included ruptured ectopic (when applicable), positive shock index, race and ED visit time during off-hours. Covariates were selected by the authors based on their expected influence on the primary and secondary outcomes. All analyses were performed using SAS v9.4 (SAS Institute, Inc., Cary, NC).

# 3. Results

During the study period, a total of 220 patients were admitted with a diagnosis of ectopic pregnancy (Fig. 1). Of those, 111 patients were excluded, leaving a total of 109 patients for analysis. All patients underwent at least one imaging study, POCUS or RADUS, or both. Out of the 109, 73 had RADUS only and 36 had POCUS. From the 36 in the

Downloaded for Anonymous User (n/a) at The Baruch Padeh Medical Center Poriya from ClinicalKey.com by Elsevier on September 12, 2021. For personal use only. No other uses without permission. Copyright ©2021. Elsevier Inc. All rights reserved.





Fig. 2. ED treatment time for ruptured ectopic pregnancies. Abbreviations: POCUS: point-of-care ultrasound, RADUS: radiology performed ultrasound.

**Fig. 1.** Patient enrollment flow chart. Of the 36 patients in the POCUS group, 23/36 also received radiology ultrasound.

Abbreviations: EMR: electronic medical record, OR: operating room, US: ultrasound.

POCUS group, 23 also underwent RADUS, thus having both studies performed.

Baseline characteristics of the study population are shown in Table 1. There were 31/36 patients (86.1%) in the POCUS group and 47/73 patients (64.4%) in the RADUS group found to have a ruptured ectopic pregnancy by operating room (OR) findings. Both positive shock index and triage Emergency Severity Index (ESI) scored patients of higher acuity in the POCUS group compared to the RADUS group (p = 0.0002and p = 0.0006, respectively). There was no significant difference found between the groups in regards to prior pelvic surgeries, prior ectopic pregnancies, or prior intrauterine pregnancies. It is notable that approximately 5% of patients in both groups had an intrauterine device (IUD) at the time of diagnosis. The mean ED treatment time was significantly faster in the POCUS group at 158 min (standard deviation [SD] 101.3) compared to 206 min (SD 76.6) in the RADUS group (p = 0.0141, Table 2, Fig. 2). Similarly, patients in the POCUS group had a significantly faster time to operative management for ruptured ectopic pregnancy, 203 min (interquartile range [IQR] 159.0) versus 293 min (IQR 139.0) in the RADUS group (p = 0.0002, Table 2, Fig. 3). The median volume of hemoperitoneum measured at the time of surgery was 500 mL (IQR 1300) in the POCUS group and 200 mL (IQR 400) in the RADUS group (p = 0.0008).

In a subgroup analysis of the 3 groups, POCUS only, POCUS & RADUS, and RADUS only: the POCUS only (n = 13) median ED treatment time was 71.0 min (IQR 69.0), while the POCUS & RADUS group (n = 23) was 182.0 min (IQR 148.0), and RADUS only (n = 73) 195.0 min (IQR 76.0) (p = 0.0001). For time to OR among ruptured ectopic pregnancy, POCUS only (n = 13) median time was 129.0 min (IQR 66.0), POCUS & RADUS (n = 18) was 250.5 min (IQR 142), and RADUS only (n = 47) was 293.0 min (IQR 139.0) (p = 0.0001).

#### Table 2

Study outcomes findings.

	$\frac{\text{Overall}}{(n = 109)}$	$\frac{\text{POCUS}}{(n = 36)}$	$\frac{\text{RADUS}}{(n = 73)}$	<i>p</i> -value
<b>ED treatment time</b> ( <i>min</i> ), mean (SD)	190.3 (88.1)	157.9 (101.3)	206.3 (76.6)	0.0141 <sup>†</sup>
ED time among ruptured ectopics <sup>a</sup> (min), mean (SD)	169.2 (73.8)	133.4 (78.1)	192.8 (60.8)	0.0003 <sup>†</sup>
Time to OR (min), median (IQR)	288.0 (164.0)	221.0 (220.5)	302.0 (147.0)	$0.0008^{\ddagger}$
Time to OR among ruptured ectopics <sup>a</sup> (min), median (IQR)	265.5 (155.0)	203.0 (159.0)	293.0 (139.0)	0.0002 <sup>‡</sup>
ED visit during daytime hours <sup>b</sup> , n (%)	48 (44.0)	17 (47.2)	31 (42.5)	0.6380*
<b>Ectopic location</b> , <i>n</i> (%)				0.2494 <sup>§</sup>
Ovary	3 (2.8)	2 (5.6)	1 (1.4)	
Tubal	100 (91.7)	34 (94.4)	66 (90.4)	
Cornual	4 (3.7)	0 (0.0)	4 (5.5)	
Other	2 (1.8)	0 (0.0)	2 (2.7)	
Hemoperitoneum, n (%)				0.0012*
Small	17 (15.6)	5 (13.9)	12 (16.4)	
Moderate	29 (26.6)	5 (13.9)	24 (32.9)	
Large	48 (44.0)	25 (69.4)	23 (31.5)	
None	15 (13.8)	1 (2.8)	14 (19.2)	
<b>Hemoperitoneum volume</b> <sup>c</sup> ( <i>mL</i> ), median (IQR)	300.0 (700.0)	500.0 (1300.0)	200.0 (400.0)	$0.0008^{\ddagger}$
Surgery outcome, n (%)		. ,		>0.9999 <sup>§</sup>
Salpingectomy	105 (96.3)	35 (97.2)	70 (95.9)	
Other	4 (3.7)	1 (2.8)	3 (4.1)	

Abbreviations: SD: standard deviation, IQR: interquartile range, min: minute, OR: operating room, RADUS: Radiology performed Ultrasound, mL: milliliters.

\*Chi-squared test; <sup>†</sup>Student's *t*-test; <sup>‡</sup>Wilcoxon ranked-sum test; <sup>§</sup>Fisher's Exact test.

<sup>a</sup> Total number of ruptured ectopic pregnancies: overall n = 78; POCUS n = 31; RADUS n = 47.

<sup>b</sup> Daytime hours defined as 7:00 am-4:59 pm daily.

<sup>c</sup> Hemoperitoneum volume missing for n = 2 patients, both of whom received RADUS.



Fig. 3. ED time to OR for ruptured ectopic pregnancy.

Abbreviations: POCUS: point-of-care ultrasound, RADUS: radiology performed ultrasound.

There were numerous significant interactions between the variables in the primary outcome model (POCUS and ruptured ectopic; POCUS and race; ruptured ectopic and race; and ruptured ectopic and off hour times). Due to the small sample size, further stratified models were not run, and we did not report a result for the primary outcome using linear regression. Linear regression was performed for the secondary outcome (time to OR for ruptured ectopic pregnancy). Among ruptured ectopic pregnancy only, there were no significant interactions between the covariates. POCUS was associated with significant shorter time to OR compared to RADUS, controlling for race, positive shock index and off-hours ED visits (p = 0.0052).

POCUS and RADUS findings are summarized in Table 3. Among ruptured ectopic pregnancies, 16% (5/31) of the patients in the POCUS group were found to have moderate to large amounts of FF in the pelvis only. In the RADUS group, 15% (10/65) had small pelvic FF, whereas 48% (31/65) had moderate to large FF without fluid in the RUQ. In the POCUS group, there was one encounter documented as FF in the pelvis that was found not to be ruptured at surgery. For the RADUS group, 16% (5/31) of

#### Table 3

POCUS versus RADUS findings.

POCUS $(n = 36)$		
	Ruptured $(n = 31)$	Not ruptured $(n = 5)$
IUP	0	0
No FF	5	3
Pelvic FF only: small/physiologic	0	0
Pelvic FF only: moderate/large	5	0
Pelvic + RUQ FF	20	0
Pelvic FF: moderate/large; RUQ not done	0	1
Indeterminate	1	1
Hemoperitoneum volume ( <i>mL</i> ), median (IQR)	1000.0 (1100.0)	35.0 (30.0)
RADUS ( $n = 96$ )		
	Ruptured	Not ruptured
	(n = 65)	(n = 31)
IUP	0	0
No FF	1	11
Pelvic FF only: small/physiologic	10	15
Pelvic FF only: moderate/large	31	5
Pelvic + RUQ FF	23	0
<b>Hemoperitoneum volume</b> ( <i>mL</i> ), median (IQR)	300.0 (300.0)	50.0 (15.0)

Abbreviations: IUP: intrauterine pregnancy, FF: free fluid, RUQ: right upper quadrant, IQR: interquartile range, min: minute, OR: operating room, RADUS: Radiology performed ultrasound, POCUS: point-of-care ultrasound, mL: milliliters.

the non-ruptured ectopic pregnancies were classified as moderate pelvic FF with no positive RUQ FF findings, 48% (15/31) were classified as FF being small or physiologic and 31% (11/31) as no FF. Interrater reliability was excellent for the nine key variables assessed related to the primary and secondary outcomes (range 0.77–1.0; Appendix B).

# 4. Discussion

Our results demonstrate that EP POCUS is associated with expedited care for life threatening hemorrhage in the evaluation and management of patients with suspected ectopic pregnancy. We found that EP POCUS is associated with faster ED treatment time and time to operative management. We believe that the presence and recognition of FF on POCUS expedited care, including for timely ordering of RADUS and obstetric consultation, as 83.3% of POCUS exams had moderate to large FF identified. This in turn likely lead to improved metrics for our primary and secondary outcomes.

As in previous reports, detection of RUQ FF correlates to significant hemoperitoneum, hence assessment of the RUQ during POCUS is crucial to identifying signs of ruptured ectopic pregnancy [9-11]. Multiple previous studies have shown that higher amounts of intraperitoneal FF are needed to detect fluid in the RUQ, whereas the threshold for pelvic FF is closer to 100 mL [5,6,8,16]. It has been shown that approximately 42% of patients with ectopic pregnancies may have isolated FF in the cul-de-sac [7]. Our results also show that a significant number of patients with ruptured ectopic pregnancy will have FF in the pelvis classified as moderate or large and no RUQ FF detected (POCUS: 16%, RADUS: 48%). This is not unexpected as isolated pelvic FF is likely an early precursor to having FF in the RUQ and should not be overlooked.

All 36 patients in the POCUS group had POCUS prior to RADUS (if performed), except for 1 patient who had RADUS first. In this case, POCUS was done prior to obtaining RADUS results and the patient was expedited to the OR based on POCUS demonstrating RUQ and pelvic FF. Notably, 13 patients in the POCUS group did not have a RADUS performed. All 13 patients were found to have positive RUQ and moderate to large pelvic FF on POCUS and diagnosed with ruptured ectopic pregnancy, with an average of 1200 mL of hemoperitoneum found at surgery. RADUS was initially ordered in 46% of those 13 patients, then after POCUS was performed, RADUS was canceled. The degree of hemoperitoneum in the group that only had POCUS highlights how ill these patients were in comparison to the group that only had RADUS. The choice to perform RADUS may be perceived as unsafe when significant abdominal FF has been identified on POCUS. As a result, our findings reflect the difference in illness severity between patients in the RADUS only and POCUS only groups, as well as the reason why RADUS was canceled after POCUS was performed.

Although it appears the POCUS group was comprised of sicker patients, it reinforces the importance and utility of POCUS evaluation of the pelvis and RUQ for early evaluation of ectopic pregnancy. Particularly among these patients, POCUS can be performed to identify life threatening hemorrhage within minutes at the bedside by trained EPs. After controlling for clinical findings which may bias care, we found that POCUS saved on average 90 min between the two groups for time to OR, thus expediting care for the patients at highest risk of having a poor outcome.

To our knowledge, there is no explicit acronym for the use of "limited FAST" evaluation of patients presenting with symptoms concerning for ectopic pregnancy. As such, we would like to introduce the acronym RUPTURE, which stands for **R**ight **U**pper and **P**elvis **T**imely **U**ltrasound for **R**uptured **E**ctopic. This exam includes three parts: 1) evaluation for IUP, 2) evaluation for FF in the pelvis, and 3) evaluation for FF in the RUQ. As outlined above, we believe that a thorough EP POCUS investigation, as done with the RUPTURE exam, is warranted in all patients presenting to the ED with suspected ectopic pregnancy, in order to avoid delays in care for patients with ruptured ectopic pregnancy. Additionally, we also found that among ruptured ectopic pregnancy, 16% of patients in the POCUS group and 38% in the RADUS group had hCG level below the discriminatory zone of detection on ultrasound of 1000–1500 mIU/mL, with a lowest hCG level of 140 and 142 in their respective groups [17,18]. Furthermore, none of those patients were found to have ultrasound findings diagnostic of IUP or ectopic pregnancy and all of them, except one, had intraperitoneal FF. This suggests that POCUS should be performed regardless of the serum hCG level [19,20]. It is our opinion that EPs should not wait for a serum hCG level when pregnancy has already been confirmed or is suspected, as detection of significant FF in the pelvis or RUQ should immediately raise concern for ruptured ectopic pregnancy.

Lastly, we recognize that isolated pelvic FF may not be a result of ruptured ectopic pregnancy and could be due to other causes, such as physiologic FF or ruptured ovarian cysts. Thus, we emphasize the importance of recognizing early warning signs of intra-abdominal hemorrhage on the RUPTURE exam in order to expedite obstetric consultation and consultative RADUS (as clinically appropriate) to accelerate care, rather than recommend operative management based solely on isolated pelvic FF. Actions that may be advisable for patients with isolated FF may include closer monitoring, ensuring an active type and screen, obtaining more than one large bore IV access, and speaking with radiology and obstetric physicians to expedite patient care. Finally, if an EP works in a facility where obstetric consultation or consultative imaging is not available, the use of the RUPTURE exam may also help to identify patients that require more rapid transfer.

### 5. Limitations

As is known with retrospective studies, it is unclear how variations in documentation in the EMR may have affected our findings. Specifically, it was not possible to accurately extract the correct time to obstetric physician consult from the EMR given that it was not systematically documented. Another limitation is the definition of ruptured ectopic pregnancy as hemoperitoneum greater than 100 mL as specified in the OR note. This could have biased our results toward a larger sample of ruptured ectopic pregnancies. However, multiple studies have used that hemoperitoneum threshold and shown that it accurately correlates with ultrasound findings [21,22]. Additionally, most patients in the POCUS group had more abnormal vital signs, which could have biased the results toward decreased ED treatment time and time to OR. However, it is important to note that 64% (23/36) of patients in the POCUS group went on to get RADUS and the treatment time remained shorter on average. The POCUS only group comprised 13 patients and a subgroup regression analysis was not done given its small size.

It is also important to note that there were significant interactions in the regression analysis of ED treatment time, including POCUS and ruptured ectopic pregnancy. It is not surprising that sicker patients would be more likely to receive POCUS, however we did not expect to find the interactions based on race and ruptured ectopic pregnancy as well as race and POCUS. It is unclear why patients that identified as white were more likely to have ruptured ectopic pregnancies and were more likely to undergo POCUS. While white patients in our cohort were more frequently found to have ruptured ectopic pregnancy, this may not fully account for differences based on race. This finding has prompted our ED to investigate these findings further.

We did not review each physician's prior ultrasound experience; however, this study was conducted over 5 years by numerous EPs performing POCUS, which suggests our results to be generalizable to most EPs with basic POCUS training. This is supported by the fact that evaluation of IUP and FF on FAST are core emergency medicine POCUS skills [23]. We also want to highlight that EP POCUS was only performed transabdominally using curvilinear probes and did not include a transvaginal exam. Our resources likely are representative of most EDs using only curvilinear probes, but transvaginal POCUS imaging warrants further scientific investigation. It is also important to recognize the pitfalls of heterotopic pregnancy, and results must be considered in the entire clinical presentation. Future studies, including prospective validation, are needed to support the use of the RUPTURE exam for patients presenting to the ED with symptoms concerning for ectopic pregnancy.

# 6. Conclusion

This investigation demonstrates that patients with ruptured and non-ruptured ectopic pregnancy requiring operative care who received EP POCUS have significantly faster ED treatment time and time to operative management. We introduce a new terminology, the RUPTURE exam, to designate the use of POCUS with limited views from the FAST exam and evaluation for IUP in patients with suspected ruptured ectopic pregnancy. We believe that the RUPTURE exam should be performed early in the care of all patients presenting to the ED with symptoms suggestive of ectopic pregnancy.

# Author credit

Conceptualization: B.S.S. and J.R.P.; Methodology: B.S.S., J.R.P. and J.N.D.; Investigation and Data Curation: B.S.S., J.R.P., M.M.T., I.E.V. and J.N.D.; Analysis: B.S.S., J.R.P. and J.N.D.; Manuscript writing and review: all authors.

# Funding

Study data were collected and managed using REDCap electronic data capture tools hosted at Boston University, CTSI 1UL1TR001430.

## **Declaration of Competing Interest**

No conflict of interest.

# Appendix A. EPIC extraction diagnoses for "ectopic pregnancy"

Ectopic fetus Ectopic pregnancy Ectopic pregnancy of ovary Ectopic pregnancy with intrauterine pregnancy Ectopic pregnancy with intrauterine pregnancy, unspecified location Ectopic pregnancy without intrauterine pregnancy Ectopic pregnancy, tubal Ectopic pregnancy, unspecified location Ectopic pregnancy, unspecified location, unspecified whether IUP is present Other ectopic pregnancy Other ectopic pregnancy with intrauterine pregnancy Other ectopic pregnancy without intrauterine pregnancy Ovarian ectopic pregnancy Ovarian ectopic pregnancy, unspecified laterality, unspecified whether IUP is present Pregnancy, ectopic, cornual or cervical Pregnancy, ectopic, tubal Pregnancy, ectopic, with intrauterine pregnancy Unspecified ectopic pregnancy with intrauterine pregnancy Unspecified ectopic pregnancy without intrauterine pregnancy Unspecified ectopic pregnancy Tuboovarian ectopic pregnancy Tubal ectopic pregnancy, unspecified laterality, unspecified whether IUP is present Tubal ectopic pregnancy

Shock due to ectopic pregnancy

Shock after ectopic pregnancy

Ruptured right tubal ectopic pregnancy causing hemoperitoneum Ruptured left tubal ectopic pregnancy causing hemoperitoneum Tubal pregnancy

Tubal pregnancy with intrauterine pregnancy

Tubal pregnancy with intrauterine pregnancy, unspecified laterality Tubal pregnancy without intrauterine pregnancy

Tubal pregnancy without intrauterine pregnancy, unspecified laterality

Tubal pregnancy, rupture of Right tubal pregnancy Left tubal pregnancy Ruptured tubal pregnancy Unruptured tubal pregnancy Pregnancy, tubal

Pregnancy, tubal with rupture

# Appendix B. Interrater reliability assessment

Value	Coefficient	Value	95% CI
Heart rate	CCC	1.000	1.000-1.000
Systolic blood pressure	CCC	1.000	1.000-1.000
ED arrival time	CCC	1.000	1.000-1.000
Emergency Severity Index	K	0.889	0.675-1.000
ED room time	CCC	1.000	1.000-1.000
ED disposition time	CCC	0.998	0.996-0.999
OR date time	CCC	1.000	1.000-1.000
Point-of-care ultrasound	К	1.000	1.000-1.000
OR findings: hemoperitoneum	К	0.774	0.503-1.000

Abbreviations: CCC: concordance correlation coefficient, K: kappa

## References

- Creanga AA, Shapiro-Mendoza CK, Bish CL, Zane S, Berg CJ, Callaghan WM. Trends in ectopic pregnancy mortality in the United States: 1980-2007. Obstet Gynecol. 2011; 117(4):837–43. https://doi.org/10.1097/AOG.0b013e3182113c10.
- [2] Current Trends Ectopic Pregnancy United States. https://www.cdc.gov/mmwr/ preview/mmwrhtml/00035709.htm; 1990-1992.
- [3] McRae A, Murray H, Edmonds M. Diagnostic accuracy and clinical utility of emergency department targeted ultrasonography in the evaluation of first-trimester pelvic pain and bleeding: a systematic review. CJEM. 2009;11(4):355–64. https://doi. org/10.1017/s1481803500011416.
- [4] Melniker LA, Leibner E, McKenney MG, Lopez P, Briggs WM, Mancuso CA. Randomized controlled clinical trial of point-of-care, limited ultrasonography for trauma in the emergency department: the first sonography outcomes assessment program trial. Ann Emerg Med. 2006;48(3):227–35. https://doi.org/10.1016/j. annemergmed.2006.01.008.
- [5] Fauconnier A, Mabrouk A, Salomon IJ, Bernard J-P, Ville Y. Ultrasound assessment of haemoperitoneum in ectopic pregnancy: derivation of a prediction model. World J Emerg Surg WJES. 2007;2:23. https://doi.org/10.1186/1749-7922-2-23.

- [6] Thorsen MK, Lawson TL, Aiman EJ, et al. Diagnosis of ectopic pregnancy: endovaginal vs transabdominal sonography. Am J Roentgenol. 1990;155(2):307–10. https://doi. org/10.2214/ajr.155.2.2115257.
- [7] Dart R, McLean SA, Dart L. Isolated fluid in the cul-de-sac: how well does it predict ectopic pregnancy? Am J Emerg Med. 2002;20(1):1–4. https://doi.org/10.1053/ ajem.2002.30101.
- [8] Tang S, Zhou Q, Zhang Y, et al. Ultrasound measured depth of pelvic free fluid correlates well with blood loss volume in patients with ectopic pregnancy. Emerg Med Int. 2020;2020. https://doi.org/10.1155/2020/8874581.
- [9] Nyberg DA, Hughes MP, Mack LA, Wang KY. Extrauterine findings of ectopic pregnancy at transvaginal US: importance of echogenic fluid. J Diagn Med Sonogr. 1991;7(4):241. https://doi.org/10.1177/875647939100700438.
- [10] Rodgerson JD, Heegaard WG, Plummer D, Hicks J, Clinton J, Sterner S. Emergency department right upper quadrant ultrasound is associated with a reduced time to diagnosis and treatment of ruptured ectopic pregnancies. Acad Emerg Med. 2001;8(4): 331–6. https://doi.org/10.1111/j.1553-2712.2001.tb02110.x.
- [11] Moore C, Todd WM, O'Brien E, Lin H. Free fluid in Morison's pouch on bedside ultrasound predicts need for operative intervention in suspected ectopic pregnancy. Acad Emerg Med Off J Soc Acad Emerg Med. 2007;14(8):755–8. https://doi.org/10.1197/j. aem.2007.04.010.
- [12] Gilbert EH, Lowenstein SR, Koziol-McLain J, Barta DC, Steiner J. Chart reviews in emergency medicine research: where are the methods? Ann Emerg Med. 1996; 27(3):305–8. https://doi.org/10.1016/s0196-0644(96)70264-0.
- [13] Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. Ann Emerg Med. 2014;64(3):292–8. https://doi.org/10.1016/j.annemergmed.2014.03.025.
- [14] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42 (2):377–81. https://doi.org/10.1016/j.jbi.2008.08.010.
- [15] Lin LI. A concordance correlation coefficient to evaluate reproducibility. Biometrics. 1989;45(1):255–68https://doi.org/10.2307/2532051.
- [16] Jehle DVK, Stiller G, Wagner D. Sensitivity in detecting free Intraperitoneal fluid with the pelvic views of the FAST exam. Am J Emerg Med. 2003, Oct;21(6):476–8. https:// doi.org/10.1016/s0735-6757(03)00162-1.
- [17] Kaplan BC, Dart RG, Moskos M, et al. Ectopic pregnancy: prospective study with improved diagnostic accuracy. Ann Emerg Med. 1996;28(1):10–7. https://doi.org/10. 1016/S0196-0644(96)70131-2.
- [18] Barnhart KT, Simhan H, Kamelle SA. Diagnostic accuracy of ultrasound above and below the beta-hCG discriminatory zone. Obstet Gynecol. 1999;94(4):583–7. https://doi.org/10.1016/s0029-7844(99)00347-6.
- [19] Thamburaj R, Sivitz A. Does the use of bedside pelvic ultrasound decrease length of stay in the emergency department? Pediatr Emerg Care. 2013;29(1):67–70. https:// doi.org/10.1097/PEC.0b013e31827b53f9.
- [20] Tayal VS. Outcome of patients with an indeterminate emergency department firsttrimester pelvic ultrasound to rule out ectopic pregnancy. Acad Emerg Med. 2004; 11(9):912–7. https://doi.org/10.1197/j.aem.2004.03.017.
- [21] Popowski T, Huchon C, Toret-Labeeuw F, Chantry AA, Aegerter P, Fauconnier A. Hemoperitoneum assessment in ectopic pregnancy. Int J Gynecol Obstet. 2012;116 (2):97–100. https://doi.org/10.1016/j.ijgo.2011.09.019.
- [22] Dhombres F, Maurice P, Friszer S, et al. Developing a knowledge base to support the annotation of ultrasound images of ectopic pregnancy. J Biomed Semant. 2017;8. https://doi.org/10.1186/s13326-017-0117-1.
- [23] Ultrasound guidelines: emergency, point-of-care and clinical ultrasound guidelines in medicine. Ann Emerg Med. 2017;69(5):e27–54. https://doi.org/10.1016/j. annemergmed.2016.08.457.