

Predictors of successful Methotrexate management of suspected and confirmed tubal ectopic pregnancies

Hikari Sakurai¹, Hanine Fourie¹, Romana Cuffolo¹, Apryll Chase¹

1. Royal Berkshire NHS Foundation Trust

Introduction

- Ectopic pregnancy (EP) occurs in 11:1000 pregnancies (1).
- Life threatening condition with 8 women dying from EP between 2018-2020 in the UK (2).
- Early diagnosis and treatment credited with decreasing case fatality in recent years
- Single dose IM Methotrexate is frequently used for treatment for small uncomplicated tubal ectopic pregnancies

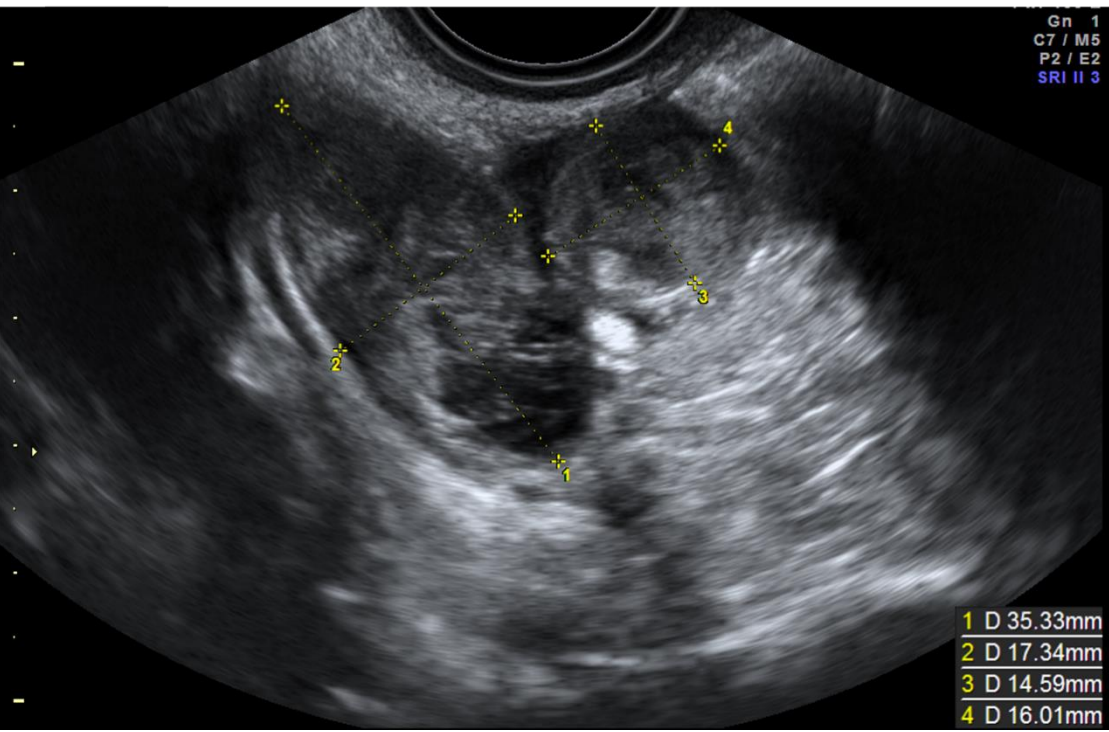
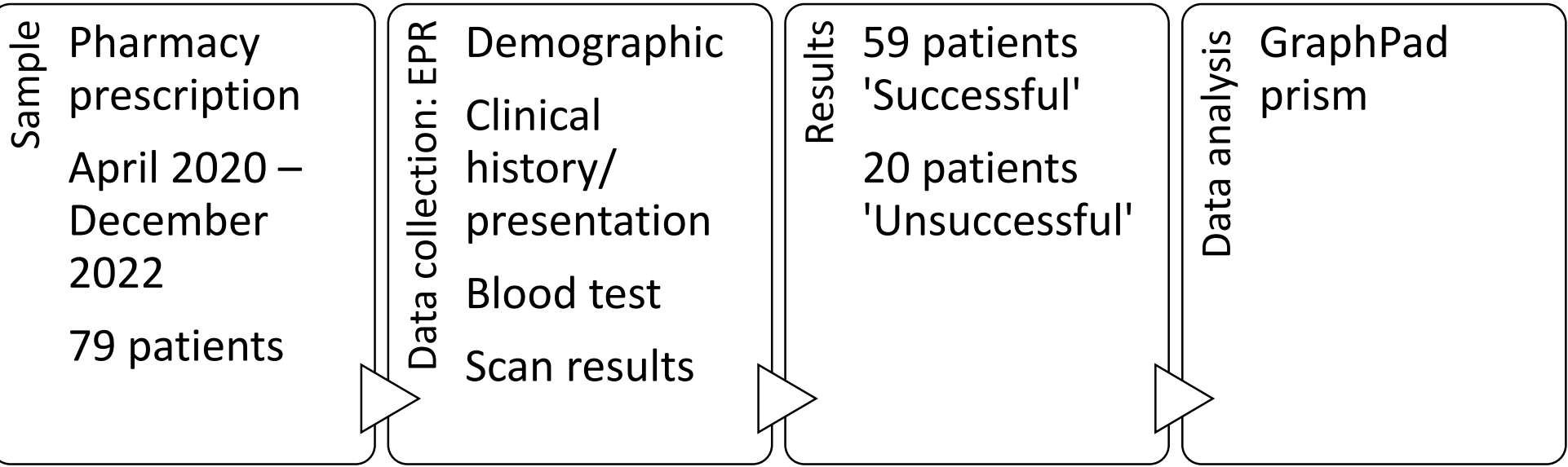


Image: Ectopic pregnancy on transvaginal ultrasound scan

Method

- A retrospective review of patients who received intramuscular methotrexate for management of suspected (persistent pregnancy of unknown location (PPUL)) and confirmed tubal ectopic pregnancies at Royal Berkshire Hospital from April 2020 to December 2022. Patient list was obtained from pharmacy prescriptions.
- Data was obtained through electronic patient record and ultrasound reporting system.
- Patients were divided into 'Successful' and 'Unsuccessful' groups, defined by their outcomes. ('Successful' group: only requiring one dose of Methotrexate with subsequent reduction in β HCG to <20IU/L. 'Unsuccessful' group: requiring a further dose of Methotrexate or surgery)
- Statistical analysis was conducted using GraphPad Prism (GraphPad Software, Inc).



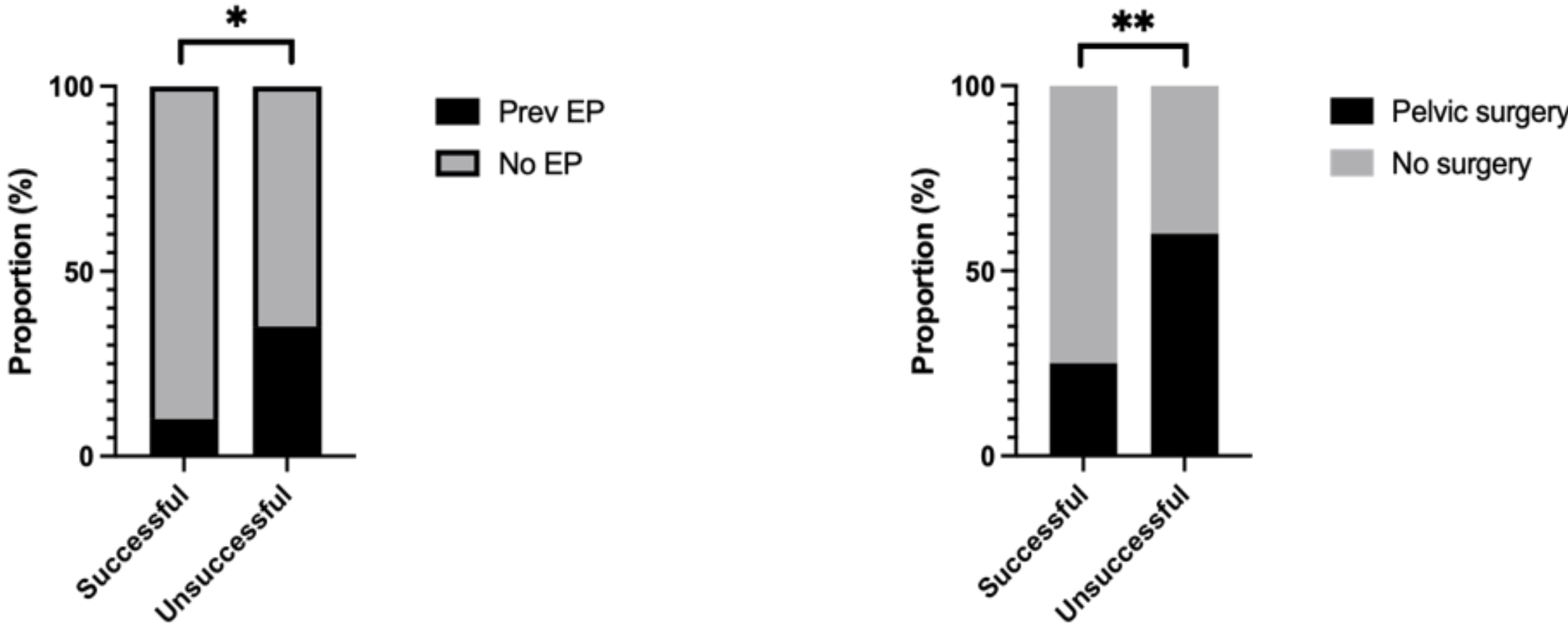
Results

Demographics

	Median	Range
Age (years)	33	19-47
Gravidity	2	1-6
Parity	1	0-5

Risk factors

- Previous EP and previous pelvic surgery were identified as risk factors associated with difference in outcome
 - Previous EP (successful 10% (6/59) vs unsuccessful 35% (7/20), $P < 0.02$)
 - Previous pelvic surgery (25.4% (15/59) vs 60% (12/20), $P < 0.007$)



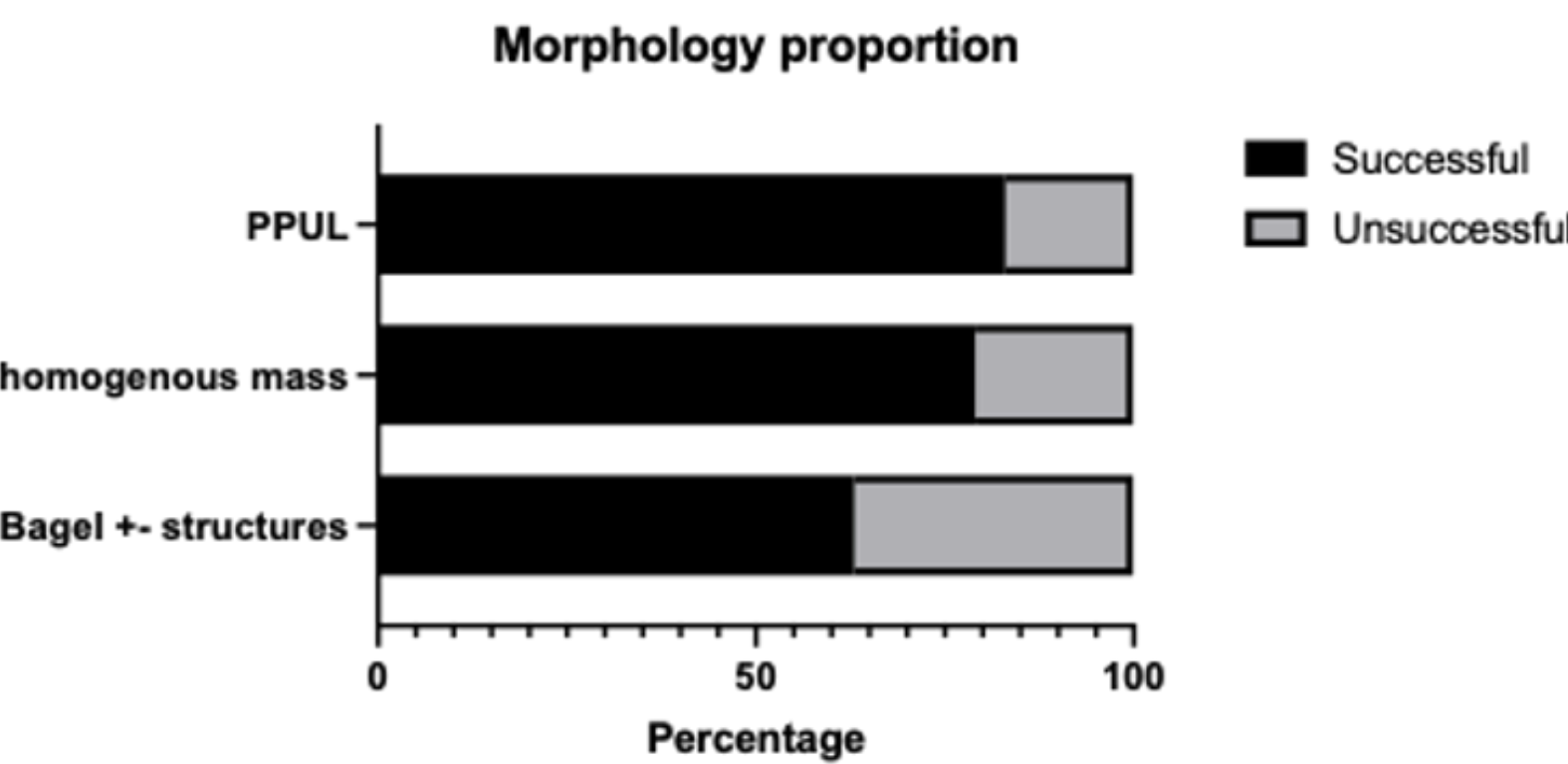
- No statistically significant difference in smoking history and pelvic inflammatory disease history in unsuccessful vs successful group

Presentation

- Majority presented with pain and bleeding (59.5%, $n=47$). 17.7% ($n=14$) presented with pain only, and 18.9% ($n=15$) with bleeding only
- Others were diagnosed with an asymptomatic PUL at specialist clinics (termination / fertility, $n=3$)

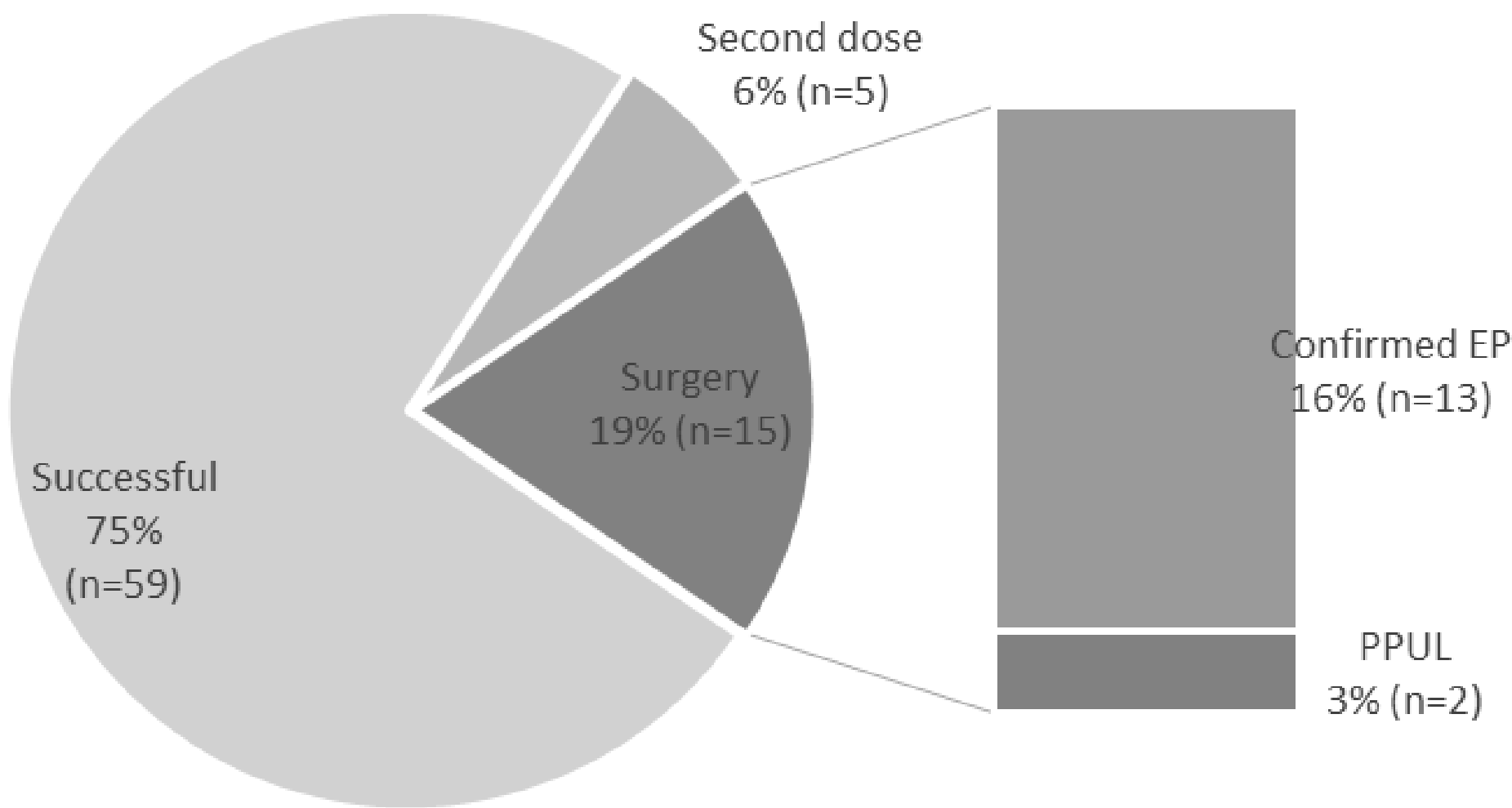
Ultrasound scan

- 54 confirmed tubal ectopic on scan
- No statistically significant difference in median ectopic size (successful 15.49mm vs unsuccessful 14.50mm) or presence of free fluid between the two groups ($p > 0.05$)
- Morphologically developed EPs with presence of structures had lower success rates



Results

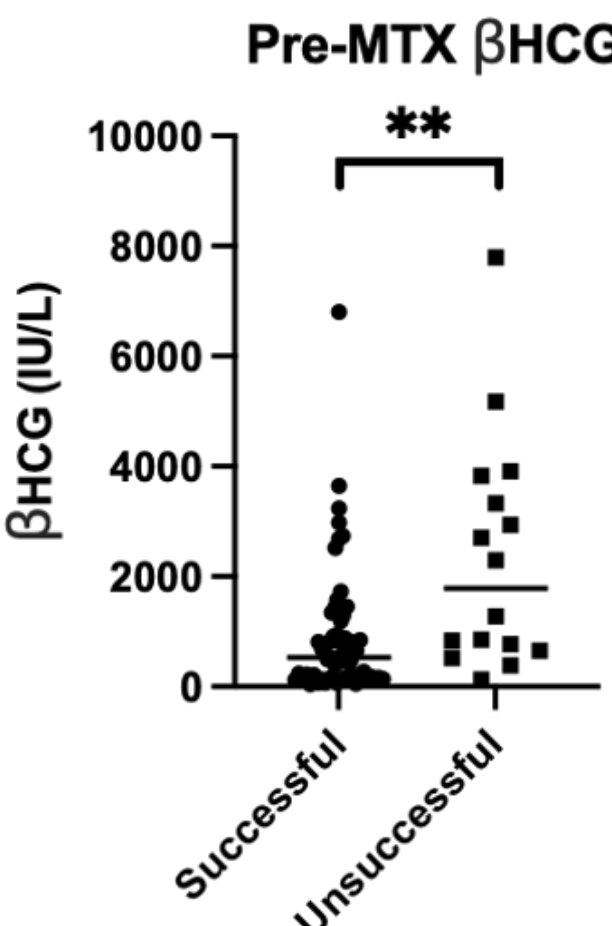
Management



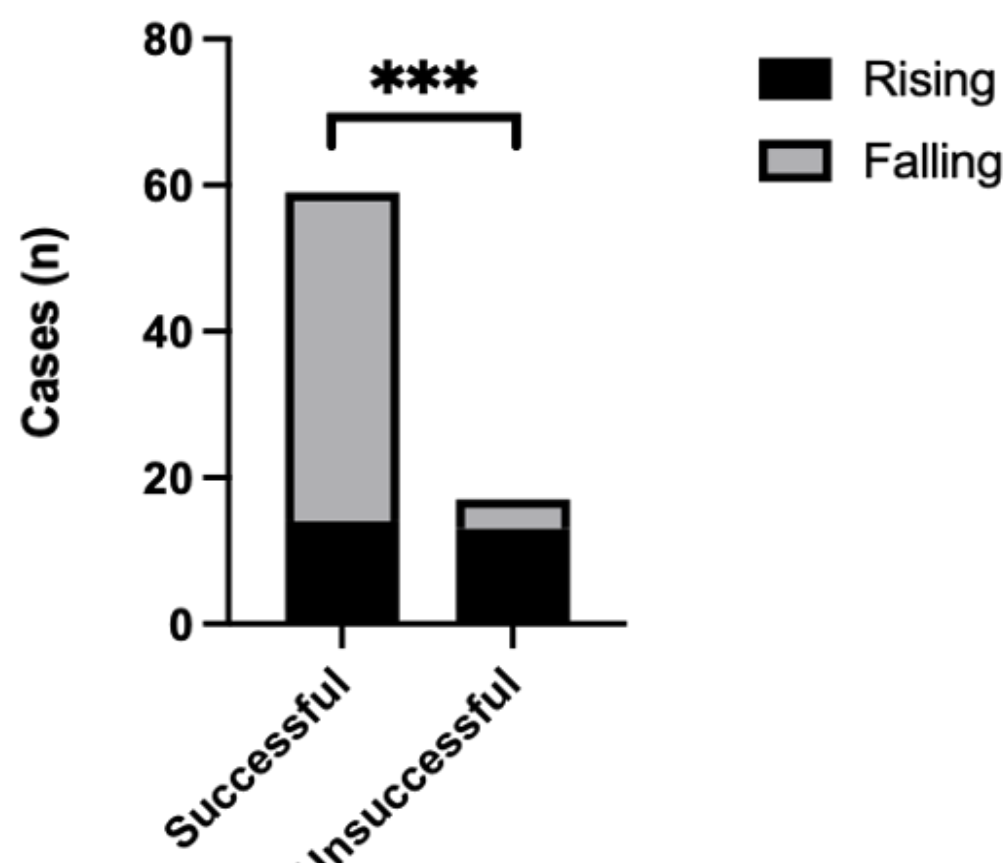
- Overall, 19.0% ($n=15$) required surgical intervention (6/15 for tubal rupture, 7/15 pain post-MTX, 1/15 rising β HCG, 1/15 EP on repeat USS)
- There was no difference in gestational age at time of first MTX (median 7+4wks vs 7+0wks, $P > 0.05$)
- The mean time to resolution for successful treatment after one dose of methotrexate was 24.5 days (median 22.5, range 7-65). 3 patients were lost to follow up.

Serum analysis

- The median D0 β HCG was higher in the unsuccessful group (median 1110IU/L vs 526IU/L, $P < 0.002$.)
- A falling β HCG trend between day 0 to 4 was more common in the successful group (76.3%, 45/59 vs 23.5%, 4/17, $P < 0.0001$)
- The difference in day 4 to 7 β HCG percentage change was greater in the successful group (median drop of 34.6% vs 13.2%, $P < 0.007$)
- There was no statistically significant difference in initial progesterone level (11.9 ng/ml vs 16.8 ng/ml)



Binary hCG trend day 0-4



Discussion

The outcomes of our review support findings from previous studies, highlighting predictors of successful methotrexate management including low initial serum hCG (3), declining trend from day 1 to 4 serum hCG (4), and morphologically less developed EP on USS (5). In our study, only 24.1% of confirmed tubal ectopics required surgical intervention, and 5.6% required a second dose, which is comparable to published literature (6).

The RCOG suggests conservative management in cases where hCG is less than 1500, however our study found 40% of ectopic pregnancies that required further management had a hCG below 1500 (1). This highlights the importance of taking the overall clinical picture of the patient into account and offer medical management as appropriate.

Conclusions

- 1 dose of Methotrexate was successful in 74.7% of cases
- Factors associated with success was first EP, no previous pelvic surgery, a low initial β HCG and a falling trend between day 0 and 4
- Individualised care with consultant input on off-protocol use of methotrexate provides a valuable option

References

- Elson CJ, Kirk EJ, Chetty M, Potdar N, Salim R. Diagnosis and management of ectopic pregnancy. BJOG: An International Journal of Obstetrics & Gynaecology. 2016;123(13).
- Knight M, Bunch K, Patel R, Shakespeare J, Kotnis R, Kenyon S, Kurinczuk JJ (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care Core Report - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2018-20. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2022
- Lipscomb GH, McCord ML, Stovall TG, Huff G, Portera SG, Ling FW. Predictors of success of methotrexate treatment in women with tubal ectopic pregnancies. New England Journal of Medicine. 1999;341(26):1974–8.
- Levin G, Dior U, Shushan A, Gilad R, Benshushan A, Rottenstreich A. Early prediction of the success of Methotrexate Treatment Success by 24–Hour Pretreatment Increment in HCG and Day 1–4 change in HCG. Reproductive BioMedicine Online. 2019;39(1):149–54.
- Potter MB, Lepine LA, Jamieson DJ. Predictors of success with methotrexate treatment of tubal ectopic pregnancy at Grady Memorial Hospital. American Journal of Obstetrics and Gynecology. 2003;188(5):1192–4.
- Horne AW, Tong S, Moakes CA, Middleton LJ, Duncan WC, Mol BW, et al. Combination of gefitinib and methotrexate to treat tubal ectopic pregnancy (GEM3): A multicentre, randomised, double-blind, placebo-controlled trial. The Lancet. 2023;401(10377):655–63.