223

Key predictors of usable blastocyst yield in highly purified human menopausal gonadotropin (hp-hMG) only cycles: A multicenter machine learning analysis

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OBJECTIVE

Use machine learning to determine the strongest predictive clinical and laboratory factors of usable blastocyst yield in HP-hMG-only ICSI cycles

KEY TAKEAWAYS

1. **2PN count, maternal age, and MII oocyte number emerged as the dominant predictors of usable blastocyst yield, outweighing all other clinical variables**
2. **Ovarian response to stimulation is the decisive driver of usable blastocyst yield, making stimulation strategy the highest-leverage point for improving outcomes**
3. **Robustly validated across 1,319 IVF cycles — trained on 974 cycles from clinics in Europe, North America, and Asia, and confirmed on an independent 345-cycle dataset**

Abbreviations

2PN, 2 pronuclei (fertilization); **AFC**, antral follicle count; **AI**, artificial intelligence; **AMH**, anti-Müllerian hormone; **BMI**, body mass index; **CR**, complete response; **E2**, estradiol; **HP-hMG**, highly purified human menopausal gonadotropins; **ICSI**, intracytoplasmic sperm injection; **IVF**, in vitro fertilization; **MAE**, mean absolute error; **MII**, metaphase II (mature oocyte); **P4**, progesterone; **R2**, co-efficient of determination.

References

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Disclosures

NI is an employee of FertilAI Ltd. **AL** is an employee, board member, and shareholder of FertilAI Ltd. **RH** is an employee, shareholder, and board member of FertilAI Ltd. **MYoungster** has nothing to disclose. **AHochberg** has nothing to disclose. **MB** received consulting feeds from FertilAI Ltd., and received support from Ferring and Merck Serono to attend meetings and/or travel. **EM** is a shareholder and board member of FertilAI Ltd., and received support from Merck Serono to attend meetings and/or travel. **DCBA** is an employee of Ferring Pharmaceuticals, Inc. **MYu** is an employee of Ferring Pharmaceuticals, Inc. **WZ** is an employee of Ferring Pharmaceuticals, Inc. **KB** was an employee of Ferring Pharmaceuticals, Inc. at the time of the study. **EH** is an advisor to Cercle.AI, Inc. and Alife Health. **NP** is a stockholder of Alife and FertilAI, and has received grants, consulting fees, and/or honoraria for lectures from Merck, Ferring, Organon, Besins, Theramex, IBSA and/or Roche Diagnostics. **AHourvitz** is a shareholder and board member and received from consulting fees from FertilAI Ltd., and received support from Ferring and Merck Serono to attend meetings and/or travel.

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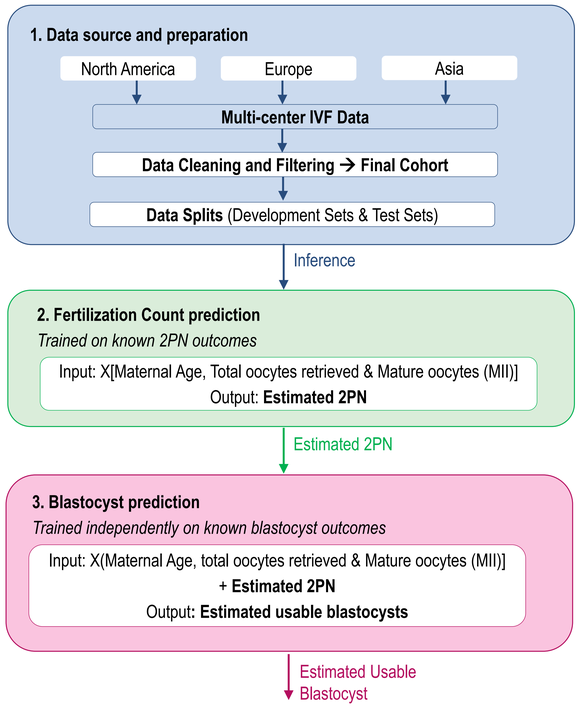
BACKGROUND

- Estimates of usable blastocyst yield are critical for patient counseling and laboratory planning[1]
- Age, ovarian reserve markers, and oocyte counts can help estimate blastocyst yield,[2] but often fail to capture blastocyst attrition that occurs between oocyte retrieval and culture Day 5
- Existing artificial intelligence (AI) models focus on predicting oocyte yield or pregnancy outcomes[3]
- AI models can
  - Identify the contribution of clinical and patient factors to the blastulation rate
  - Improve prediction capabilities, inform clinical decision-making, and possibly fine-tune future treatments for better outcomes

METHODS

- Retrospective data collected from IVF clinics in Europe, North America, and Asia (2014–2024).
- All patients were treated with highly purified human menopausal gonadotropin (HP-hMG)
- Model developed on data from 974 cycles with complete records (**Figure 1**)
- Inputs: age, BMI, AMH, AFC, trigger-day hormone levels (E2, P4), follicle counts, starting HP-hMG dose, and retrieved oocytes (Total/MII)
- Predictive performance evaluated based on coefficient of determination (R2) and Mean Absolute Error (MAE)
- Model validation performed on an independent test set of 345 cycles with complete fertilization and usable blastocyst outcomes

FIGURE 1 Methods



- **An XGBoost regression model predicted usable blastocyst count using various clinical factors plus fertilization (2PN) data**
- **Feature (factor) importance was analyzed to rank by contribution to the model's predictive accuracy**

RESULTS

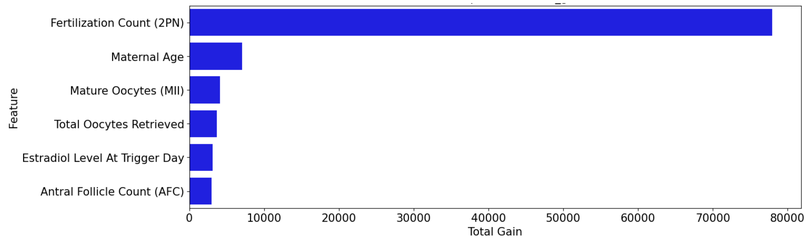
Independent test set (n=345)

- Mean yield: 2.56 usable blastocysts
- Model demonstrated reliable predictive performance (R2=0.55 and MAE=1.23)

Feature importance analysis

- Dominant predictors: fertilization count (2PN), maternal age and mature (MII) oocyte number (Figure 2)
- BMI was not a strong predictor, possibly due to personalized HP-hMG dose adjustments during stimulation

FIGURE 2 Factor Importance Analysis



Final usable blastocyst yield is not determined by fertilization success alone but is modulated by patient age, ovarian response, and treatment characteristics.

CONCLUSION

- This model accurately predicts blastulation outcomes within HP-hMG stimulation cycles by integrating fertilization data with age, ovarian reserve markers, and treatment parameters - delivering robust, clinically meaningful predictive power.
- Variability in laboratory procedures and the retrospective design remain key caveats to be weighed when interpreting the findings.
- Prospective external validation is the essential next step toward broader clinical implementation.

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