

OBJECTIVE

The aim of this study is to determine if there is an optimal estradiol (E₂) level on the day of hCG triggering, which would predict absence of an oocyte at egg retrieval and later pregnancy in modified natural in vitro fertilization (mnIVF).

METHODS

We retrospectively reviewed mnIVF data for which an egg retrieval was scheduled between January 1, 2012 and June 30, 2013. Cycles for which we had no E₂ level or there was 2 or more dominant follicles the day of hCG triggering were excluded. Finally, 1074 mnIVF cycles of 581 women were analyzed.

STATISTICS

The lower levels of E₂ which result in no pregnancies were determined.

Using clinique ovo's empirical E₂ threshold of 500 pmol/mL, Fischer and Chi² tests were used to compare the absence of oocytes at egg retrieval and pregnancy rates in the E₂ < 500 pmol/mL group vs. ≥ 500 pmol/mL group. P < 0.05 is significant.

Univariate analyses were performed to determine whether E₂ levels on the day of hCG triggering could predict no oocyte at egg retrieval and pregnancy rate (PR). Sensitivity (Se) and specificity (Sp) analysis were done using ROC curves to screen for no oocyte at egg retrieval.

RESULTS

T1 : Population and cycle characteristics of patients undergoing mnIVF from January 2012 to June 2013

	Means (SD)
Female age, years	32.4 ± 3.5
AMH, ng/mL	1.7 ± 1.8
Cycles, n	1074
Indication for mnIVF (n = 581 patients)	
Unexplained*	241 (22.4%)
Decreased ovarian reserve	190 (17.7%)
Male factor	410 (38.2%)
Tubal-pelvis factor	195 (18.2%)
Other/multifactorial	38 (3.6%)
IVF procedure (n = 1074 cycles)	
IVF	455 (42.4%)
IVF-ICSI	618 (57.6%)
Follicle, mm	18.5 ± 1.2
Endometrium, mm	9.3 ± 1.9
Estradiol, pmol/mL	916.0 ± 303.4
Progesterone, nmol/L	1.6 ± 0.8
Total day of GnRH antagonist, days	2.5 ± 1.0
Oocyte obtained, n (%)	912 (84.9%)
Premature ovulation, n (%)	49 (4.6%)
No oocyte, at egg collection n (%)	102 (9.2%)
Mature oocytes (MII), n (%)	869 (80.9%)
Oocytes fertilized (2PN), n (%)	613 (57.1%)
Embryo transferred, n (%)	531 (49.4%)
Pregnancies per cycle, n (%)	
Biochemical [§]	191 (17.8%)
Clinical [¶]	174 (16.2%)
Pregnancies per embryo transfer, n (%)	
Biochemical [§]	191 (35.9%)
Clinical [¶]	174 (32.8%)

Results are expressed per cycle except if indicated.
*unexplained infertility, endometriosis stage I-II, polycystic ovaries or anovulatory polycystic ovaries; [§]biochemical pregnancy: positive pregnancy test; [¶]clinical pregnancy: positive foetal heart between 6 and 7 weeks.

T2 : Group comparison clinique ovo empirical threshold

	E ₂ < 500 pmol/mL (n=52)	E ₂ ≥ 500 pmol/mL (n=792)	p
No oocyte at egg retrieval	19.2% (10)	9.5% (75)	0.03 [¶]
Clinical pregnancy	23.1% (12)	16.3% (129)	0.28 [§]

[¶] Fischer test; [§] Chi² test; p ≤ 0,05 is significant.

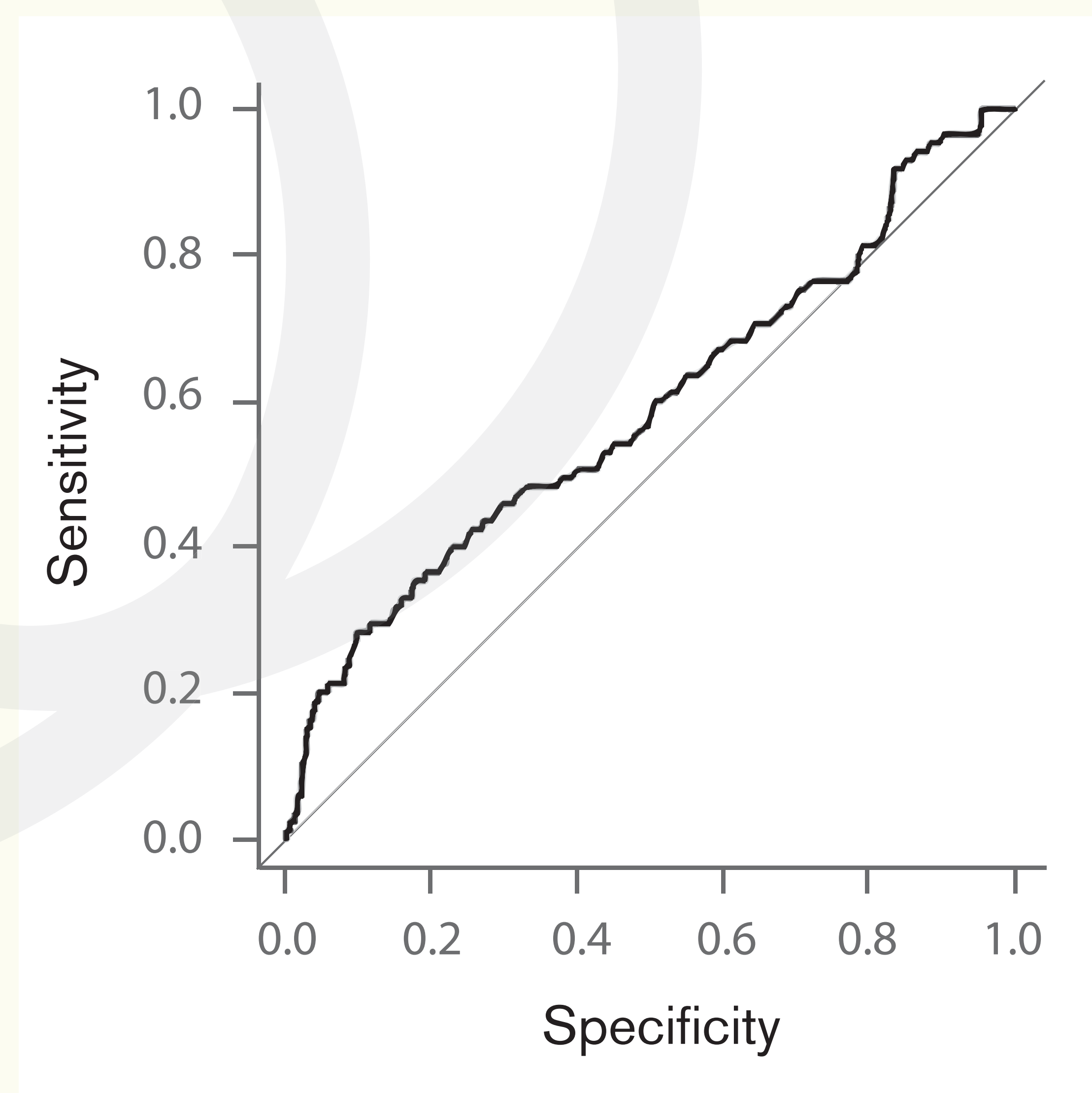
No pregnancies were observed when E₂ level the day of triggering was below 380 pmol/mL.

T3 : E₂ level on the day of hCG triggering and no oocyte at egg retrieval and biochemical pregnancy predictors

	No oocyte at egg retrieval		Biochemical pregnancy	
	Odd Ratio	p	Odd Ratio	p
E ₂ level on the day of hCG	0.99 (0.99 - 0.99)	0.004	1.00 (0.99 - 1.00)	0.56
E ₂ level ≥ 500 pmol/mL on the day of hCG	0.43 (0.21 - 0.90)	0.02	0.66 (0.29 - 1.48)	0.31

Univariate analysis by univariate mixed model with patient as random factor, p ≤ 0,05 is significant. Results are same for clinical pregnancy predictors.

F1 : E₂ Cut-off analysis for no oocyte at egg retrieval - ROC curve



There is no clear E₂ threshold cut-off for no oocyte at egg retrieval.

By choosing E₂ cut-off of 500 pmol/mL as used as clinique ovo, we obtained a sensitivity of 11.8% and a specificity of 94.5% for predicting no oocyte at egg retrieval.

CONCLUSIONS

E₂ level and E₂ level ≥ 500 pmol/mL on the day of hCG triggering are not significant predictors of pregnancy using multivariate analysis, even with the consideration of confounding factors (diagnosis of infertility, number of GnRH antagonists days, AMH and age).

One of the main challenge in mnIVF is having an oocyte at egg retrieval. Our results suggest that an E₂ threshold of 500 pmol/mL during the monitoring of mnIVF is acceptable. Therefore, our recommendation is: withhold triggering if E₂ below 380 pmol/mL and consider cancelling cycle or repeat E₂ level the following day.

The next step in this study is to evaluate the relevance of progesterone level on the day of hCG triggering in a decisional algorithm.

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