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Full length article

Ovarian response in natural cycle, minimal stimulation and conventional IVF protocols in relation to anti-mullerian hormone level – A multi-center study

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ABSTRACT

Background: In addition to conventional *in-vitro-fertilization* IVF (cIVF) alternative protocols such as natural cycle (NC–) and minimal stimulation (Min stim-) protocols allow individualized IVF and oocyte freezing treatments. The objective was to develop a model to predict ovarian response in relation to different stimulation protocols and anti-mullerian hormone (AMH) levels.

Methods: International multi-centre retrospective cohort study including 1504 NC-IVF, 1287 Min stim IVF and 2048 cIVF cycles performed 01.2022–03.2023. Min stim protocols consisted of oral compounds such as low dose clomiphene citrate or aromatase inhibitors alone or in combination with low dose gonadotropins. Negative binomial regression models were used to assess the effect of protocol and AMH level on the number of oocytes and secondarily on zygotes. Predictions of outcomes were derived across protocols and different AMH categories (<1, ≥1-<2, ≥2 ng/ml).

Results: AMH is an effective predictor of the number of oocytes in relation to IVF protocol. Number of oocytes increase in protocols including gonadotropins, but not in protocols with only oral compounds. Effect of stimulation increased with increasing AMH level but was less pronounced with low AMH level. For example, if AMH is < 1 ng/ml, the predicted number of oocytes is 0.85 and 4.04 in the NC– and cIVF protocols, whereas the difference is twice as large with AMH ≥ 2 ng/ml with predicted values of 0.83 and 10.54, respectively. Conclusion. Based on AMH level, Min stim-protocols can be individualized by selecting specific stimulation protocols according to the predicted ovarian response, especially in cases with low ovarian reserve.

Introduction

Over the past two decades, minimal stimulation IVF (Min stim-IVF) protocols using clomiphene citrate (CC), aromatase inhibitors (AI), low dose gonadotropins (human menopausal gonadotropins (hMG) or recombinant human follicle stimulating hormone (FSH) alone or in combination were developed and implemented as an alternative to conventional IVF (cIVF) and Natural cycles IVF (NC-IVF) treatments [1–5].

The purpose of Min stim-IVF protocols is, based on personal wishes

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of patients, to combine the benefits of NC-IVF with hardly any medical intervention, monthly treatments cycles, low treatment risks and no anesthesia with the benefits of cIVF with high oocyte yield and higher cumulative success rates per cycle [6–9]. Furthermore, these protocols also aim to better treat the increasing number of women with low ovarian reserve due to increased maternal age or due to medically or surgically induced reduction of ovarian reserve [10–14]. Studies analysing the treatment risks, the pain intensity of aspiration without anesthesia/analgesia and the treatment related stress of Min stim-IVF and NC-IVF have already been performed [9,15–18].

However, when considering the predicted ovarian response, no study has assessed so far the association between the anti-mullerian hormone (AMH) level and the expected number of oocytes or zygotes in Min stim-IVF stimulation protocols. AMH is currently only used to predict the response to ovarian stimulation in cIVF [19–22].

Based on the recurring call for more patient-friendly approaches, it is relevant to evaluate IVF protocols in relation to AMH levels and to investigate their impact on the predicted number of oocytes and zygotes. Our aim was to develop a prediction model to improve counselling regarding the most appropriate stimulation protocols and thereby individualize IVF stimulation but also individualize stimulation for medical and social freezing in cases with lower ovarian reserve. The model focused on the number of oocytes and zygotes as later developmental stages render a comparison impossible due to protocol specific modifications such as embryo selection, embryo freezing etc.

Materials and Methods

Study design, setting and study participants

This is a multi-centre international retrospective cohort study of women who underwent seven different IVF stimulation protocols between January 2022 and March 2023. Five outpatient fertility centres in Germany and three outpatient fertility centres in Switzerland participated in the data collection. The lead centre of the study was the Division of Gynaecological Endocrinology and Reproductive Medicine, University Women's Hospital, Inselspital, Bern, Switzerland. All the participating centres were part of the "IVF-Naturelle" network (https://www.IVF-Naturelle.com), a group of IVF centres also specialised in NC– and Min stim-IVF and performing the same IVF treatment protocols [9].

All patients treated in the participating centres were offered the opportunity to participate in the study. Briefly, patients were eligible for the study if they fulfilled the following criteria: (i) giving informed consent, (ii) undergoing IVF cycles (NC-IVF and/or Min stim-IVF and/or cIVF) with an intention to fresh transfer.

The "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) criteria were followed [23].

Objectives

The main objective of the study was to predict ovarian response, defined by the number of oocytes and zygotes, of different IVF protocols as a function of both the protocol and the level of AMH. The results are intended to be used in daily practice to inform patients and, eventually, guide the choice of IVF stimulation protocol.

The number of oocytes as a well-accepted marker of the ovarian response and the number of zygotes reflects the fertilization capacity of the oocytes and sperms and indirectly also the maturity of the oocytes. The zygote stage is the last stage of oocyte development before the above-mentioned IVF treatment modalities (NC-IVF, Min stim-IVF and cIVF) differ significantly due to embryo selection and embryo freezing in case of polyfollicular response. Outcomes were analysed per cycle.

Anti-mullerian hormone analysis

AMH serum levels were assessed in all women with a stable fully automated assay at the beginning of the cycle, alongside the usual hormonal analysis. AMH categories were chosen as follows: AMH < 1 ng/ml, AMH $\geq 1 - <2$ ng/ml and AMH ≥ 2 ng/ml. < 1 ng/ml is a recognized clinical threshold in infertile patient defined as expected poor response [24] and an AMH concentration of 2 ng/ml has also been used by other similar studies [25].

After the diagnostic phase and IVF-treatment counselling, an IVF protocol was attributed to each patient according to specific biological characteristics in accordance with the standard of care. Personal preferences were also considered. A change of IVF stimulation protocol was always possible during the process of infertility treatment.

Stimulation protocols

Natural cycle and minimal stimulation IVF

NC-IVF was defined as IVF treatment without any kind of stimulation, either gonadotropins or oral compounds. Only single gonadotropin-releasing hormone antagonist (GnRH antagonist) injections were given, if necessary, in order to avoid premature ovulation. Human chorionic gonadotropin (hCG) was regularly used to induce ovulation.

Min stim-IVF was defined as IVF treatments with $\leq$ 100 IU human menopausal gonadotropin (hMG) or recombinant human follicle stimulating hormone (FSH) per day combined or not with the oral compounds CC ($\leq$ 25 mg) or AI ($\leq$ 5 mg) per day. Protocols were standardised between centres to allow comparison. The following Min stim-IVF protocols were used and described elsewhere [9,17]. In brief:

Protocol "CC-IVF"

25 mg of CC per day was started around day 4 of the cycle until the day of the ovulation trigger.

Protocol "AI-IVF"

5 mg of letrozole per day was started around day 4 of the cycle for 5 days.

Protocol "hMG/FSH-IVF"

75–100 IU of hMG or FSH per day was started around day 4 of the cycle until the day before the ovulation trigger was given.

Protocol "CC + hMG/FSH-IVF"

The "CC-IVF" protocol was used and 75–100 IU per day of hMG of FSH was added from around day 4 of the cycle until the day before the ovulation trigger was given.

Protocol "AI + hMG/FSH-IVF"

The "AI-IVF" protocol was used and 75–100 IU per day of hMG of FSH was added from around day 4 of the cycle until the day before ovulation was induced.

Conventional IVF, cIVF

cIVF was defined as IVF treatment with hMG or FSH doses of 150 to 300 IU per day, corresponding to agonist or antagonist stimulation protocols.

Regardless of IVF protocols, follicle growth of each participant was monitored by transvaginal ultrasound and assessment of serum luteinising hormone and estradiol concentrations analysed by electrochemiluminescence. Oocyte retrieval was performed 36 h after hCG injection. The fertilisation technique used was either standard IVF or intracytoplasmic sperm injection (ICSI).

Statistical analysis

First, the characteristics of patients and cycles were summarized in tables stratified by IVF protocol (three main categories: NC-IVF, Min stim-IVF and cIVF). Categorical variables were summarized as number and proportion, continuous variables as a range (minimum and maximum), median with interquartile range (IQR) and mean with standard deviation (SD), as appropriate.

Secondly, negative binomial regression models were used to model the effects of the IVF protocol and the level of AMH on the number of oocytes and zygotes. The model included the outcomes as dependent variables, the effect of the IVF protocol (categorical) and AMH level (<1 ng/ml, ≥1 − <2 ng/ml, ≥2 ng/ml), and was adjusted for the most recognized influencing factors [26–32]: age (continuous, years) and Body mass index (BMI) (continuous variable, kg/m^2). To account for the structure of the dataset and manage arbitrary correlation among observations within a patient we used a cluster of robust variance estimators. The results of the models were used to derive the predicted outcomes' counts for each protocol and AMH levels category along with the associated 95 % prediction intervals. All analyses were performed using R version 4.2.3.

Ethical approval

Ethical approval was given by the cantonal ethics committee of Bern, for Switzerland (ID KEK 2021–01689, 04.10.2021) and by the ethics committees of Germany (Baden-Württemberg (ID F-2024–068, 22.08.2024), Niedersachsen (ID Grae/080/2024, 30.08.2024), Bavaria

Table 1
Baseline characteristics of patients stratified by IVF protocol and overall.

	Overall	NC-IVF	CC-IVF	AI-IVF	hMG/ FSH-IVF	CC + hMG/ FSH-IVF	AI + hMG/ FSH-IVF	cIVF
Characteristics								
Number of Patients per protocol, n	2530[a]	588[b]	255[b]	106[b]	109[b]	178[b]	233[b]	1541[b]
Median [IQR]	1.0 [1.0,2.0]	2.0 [1.0,3.0]	1.0 [1.0,2.0]	1.0 [1.0,2.0]	1.0 [1.0,2.0]	1.0 [1.0,1.0]	1.0 [1.0,1.0]	1.0 [1.0,2.0]
Range [min, max]	[1.0,12.0]	[1.0,10.0]	[1.0,10.0]	[1.0,4.0]	[1.0,11.0]	[1.0,4.0]	[1.0,7.0]	[1.0,8.0]
Female age at 1st OPU, years								
Mean (±SD)	35.9 (±4.3)	36.6 (±3.9)	36.1 (±4.5)	35.8 (±4.8)	37.2 (±3.7)	36.7 (±4.4)	36.7 (±4.5)	35.6 (±4.4)
Range [min, max]	[21.0,48.0]	[23.0,46.0]	[24.0,46.0]	[24.0,46.0]	[27.0,45.0]	[22.0,46.0]	[22.0,46.0]	[21.0,48.0]
BMI (Kg/m^2)								
Mean (SD)	24.1 (4.7)	23.0 (4.1)	24.0 (4.7)	23.3 (4.4)	22.9 (4.7)	24.4 (4.9)	24.3 (4.7)	24.4 (4.9)
Range [min, max]	[15.4,46.7]	[15.8,44.2]	[15.4,40.6]	[16.2,39.4]	[15.4,44.2]	[16.8,44.2]	[16.3,42.7]	[15.4,46.7]
Missing	9	2	0	1	0	0	0	7
Duration of infertility, years								
Median [IQR]	3.0 [2.0,4.0]	3.0 [2.0,4.0]	3.0 [2.0,4.0]	3.0 [2.0,4.0]	3.0 [2.0,5.0]	3.0 [2.0,4.0]	3.0 [2.0,4.0]	3.0 [2.0,4.0]
Range [min, max]	[1.0,17.0]	[1.0,15.0]	[1.0,10.0]	[1.0,10.0]	[1.0,10.0]	[1.0,15.0]	[1.0,13.0]	[1.0,17.0]
Missing	5	0	1	0	0	1	0	4
Causes of infertility, n (%)								
Male factor	956 (38 %)	156 (27 %)	95 (37 %)	26 (25 %)	36 (33 %)	46 (26 %)	60 (26 %)	681 (44 %)
Female factor	617 (24 %)	175 (30 %)	44 (17 %)	28 (26 %)	30 (28 %)	49 (28 %)	73 (31 %)	342 (22 %)
Male & female	507 (20 %)	111 (19 %)	71 (28 %)	29 (27 %)	18 (17 %)	37 (21 %)	54 (23 %)	286 (19 %)
Idiopathic	355 (14 %)	137 (23 %)	40 (16 %)	20 (19 %)	22 (20 %)	28 (16 %)	31 (13 %)	178 (12 %)
Homosexuality	95 (3.8 %)	9 (1.5 %)	5 (2.0 %)	3 (2.8 %)	3 (2.8 %)	18 (10 %)	15 (6.4 %)	54 (3.5 %)
AMH level (ng/ml)								
Median [IQR]	2.0 [1.0,3.7]	1.8 [0.7,3.1]	2.0 [1.0,3.9]	1.8 [0.4,3.5]	1.6 [0.8,3.3]	1.6 [0.7,3.3]	1.6 [0.5,3.2]	2.2 [1.1,4.0]
Range [min, max]	[0.0,21.0]	[0.0,15.0]	[0.0,16.8]	[0.0,12.5]	[0.0,21.0]	[0.0,14.1]	[0.0,15.0]	[0.0,21.0]
<1	625 (25 %)	191 (33 %)	61 (24 %)	40 (38 %)	33 (30 %)	56 (32 %)	84 (36 %)	307 (20 %)
≥1-<2	578 (23 %)	133 (23 %)	53 (21 %)	15 (14 %)	30 (28 %)	45 (26 %)	46 (20 %)	371 (24 %)
≥ 2	1302 (52 %)	258 (44 %)	139 (55 %)	50 (48 %)	46 (42 %)	73 (42 %)	102 (44 %)	8151 (56 %)
Missing	25	6	2	1	0	4	1	12

Abbreviations: AI, aromatase inhibitor; AMH, anti-mullerian hormone; BMI, body mass index; CC, Clomiphene citrate; cIVF; conventional IVF; FSH, follicle stimulating hormone; hMG, human menopausal gonadotropin; IQR, interquartile range; IVF, *in-vitro-fertilisation*; min, minimum; max, maximum; NC-IVF, Natural Cycle-IVF; OPU, oocyte pick-up; SD, standard deviation.

[a] Number of patients.

[b] Number of patients per protocol. As some patients underwent many IVF protocols, the overall population is not the sum of each IVF protocol population

(ID mb24043, 12.09.2024) and Nordrhein-Westfalen (ID 2024 194, 30.10.2024)).

Results

This specific analysis included 2530 patients from 8 outpatient fertility centres who underwent 4839 cycles, of which 1504 cycles were NC-IVF, 1287 cycles were Min stim-IVF and 2048 cycles were cIVF cycles.

Patients' demographics data are shown in Table 1. The baseline patients' characteristics were comparable between different IVF protocols. Cycles characteristics are shown in Table S1.

Results of the statistical regression model for the number of oocytes and the number of zygotes are shown in Table 2 and Supplementary Table S2, respectively. For the two outcomes, the models revealed a significant interaction effect between IVF protocol and AMH ($p < 0.001$). This effect shows that both the protocol and the AMH values can affect the ovarian response and that the effect of the protocol depends on the AMH level (or reciprocally that the effect of AMH depends on the protocol).

The predicted numbers of oocytes and zygotes stratified by AMH category (category <1, $\geq 1 - <2$, ≥ 2 ng/ml) and IVF protocols are given in Tables 3 and 4 and displayed in Figs. S1 and S2. Predicted values clearly illustrate the interaction effect between the different IVF stimulation protocol and the AMH category. In patients with high AMH levels, the effect of treatment (i.e. increased ovarian response in IVF protocols with higher simulation levels) is significantly more pronounced. For example, in patients with AMH < 1 ng/ml, the predicted number of oocytes is equal to 0.85 [0, 3] and 4.04 [0, 10], in the NC and cIVF protocols, respectively, whereas the difference is twice as large, when considering patients with AMH ≥ 2 ng/ml (i.e. predicted values of 0.83 [0, 3] and 10.54 [2,24], respectively). For Min stim-IVF stimulation protocols the predicted values are between the values of NC and cIVF protocols and are lowest in protocols with only oral compounds and highest in protocols with the combination of oral compounds and gonadotropin stimulation (Tables 3 and 4, Fig. S1 and S2). Specifically, in CC– and AI-IVF protocols the number of zygotes did not increase in women with increasing AMH category (0.85, 0.93, 0.96 for CC-IVF; and 0.79, 0.77, 0.68 for AI-IVF). In contrast, in IVF protocols using gonadotropins the number of zygotes increased with increasing category of AMH levels (1.08, 1.25, 2.45 for hMG/FSH-IVF; 1.30, 1.72, 2.74 for CC + hMG/FSH-IVF; 1.34, 2.71, 3.25 for AI + hMG/FSH-VF).

Table 2
Regression model for the number of oocyte.

Characteristics	IRR	95 % CI	p-value
NC-IVF, Min stim IVF and cIVF, protocols			**<0.001**
NC-IVF	–	–	
CC-IVF	1.71	1.50, 1.96	
AI-IVF	1.67	1.36, 2.05	
hMG/FSH-IVF	1.76	1.41, 2.19	
CC + hMG/FSH-IVF	2.33	1.94, 2.80	
AI + hMG/FSH-IVF	2.52	2.13, 2.98	
cIVF	4.75	4.31, 5.23	
AMH (ng/ml)			**0.059**
<1	–	–	
≥1 − <2	1.07	0.98, 0.17	
≥2	0.98	0.91, 1.05	
Protocol x AMH			**<0.001**
CC-IVF x AMH ≥ 1 − <2	0.97	0.80, 1.18	
AI-IVF x AMH ≥ 1-<2	0.71	0.49, 1.05	
hMG/FSH-IVF x AMH ≥ 1 − <2	1.34	0.95, 1.91	
CC + hMG/FSH-IVF x AMH ≥ 1 − <2	1.38	1.04, 1.83	
AI + hMG/FSH-IVF x AMH ≥ 1 − <2	1.83	1.34, 2.49	
cIVF x AMH ≥ 1 − <2	1.58	1.39, 1.80	
CC-IVF x AMH ≥ 2	1.00	0.84, 1.19	
AI-IVF x AMH ≥ 2	0.89	0.69, 1.14	
hMG/FSH-IVF x AMH ≥ 2	2.67	1.90, 3.75	
CC + hMG/FSH-IVF x AMH ≥ 2	2.23	1.75, 2.86	
AI + hMG/FSH-IVF x AMH ≥ 2	2.36	1.91, 2.91	
cIVF x AMH ≥ 2	2.67	2.39, 2.98	
BMI (Kg/m^2)	0.99	0.98, 0.99	**<0.001**
Women's age (year)	0.98	0.97, 0.98	**<0.001**

Abbreviations: AI, aromatase inhibitor; AMH, Anti-mullerian hormone; BMI, body mass index; CC, Clomiphene citrate; CI, confidence interval; cIVF, conventional IVF; FSH, follicle stimulating hormone; hMG, human menopausal gonadotropin; IRR, Incidence Rate Ratio; IVF, *in-vitro-fertilisation*; NC-IVF, Natural Cycle-IVF.

Table 3
Predicted values for the number of oocytes according to the prediction model.

IVF protocol	AMH (ng/ml) <1	≥1 − <2	≥2
NC-IVF	0.85 [0, 3][a]	0.91 [0, 3] [a]	0.83 [0, 3] [a]
CC-IVF	1.46 [0, 5] [a]	1.52 [0, 5] [a]	1.42 [0, 5] [a]
AI-IVF	1.42 [0, 5] [a]	1.09 [0, 4] [a]	1.23 [0, 4] [a]
hMG/FSH-IVF	1.50 [0, 5] [a]	2.15 [0, 7] [a]	3.91 [0, 10] [a]
CC + hMG/FSH-IVF	1.99 [0, 6] [a]	2.94 [0, 9] [a]	4.34 [0, 11] [a]
AI + hMG/FSH-IVF	2.14 [0, 6] [a]	4.2 [0, 11] [a]	4.95 [0, 13] [a]
cIVF	4.04 [0, 10] [a]	6.84 [1,17] [a]	10.54 [2,24] [a]

Abbreviations: AI, aromatase inhibitor; AMH, Anti-mullerian hormone; CC, Clomiphene citrate; cIVF, conventional IVF; FSH, follicle stimulating hormone; hMG, human menopausal gonadotropin; IVF, *in-vitro-fertilisation*; NC-IVF, Natural Cycle-IVF.

[a] 95% Prediction interval for women with BMI 24 and age 37.

Table 4
Predicted values for the number of zygotes according to the prediction model.

IVF protocol	AMH (ng/ml) <1	≥1 − <2	≥2
NC-IVF	0.59 [0, 3][a]	0.68 [0, 3] [a]	0.61 [0, 3] [a]
CC-IVF	0.85 [0, 3] [a]	0.93 [0, 4] [a]	0.96 [0, 4] [a]
AI-IVF	0.79 [0, 3] [a]	0.77 [0, 3] [a]	0.68 [0, 3] [a]
hMG/FSH-IVF	1.08 [0, 4] [a]	1.25 [0, 4] [a]	2.45 [0, 7] [a]
CC + hMG/FSH-IVF	1.3 [0, 5] [a]	1.72 [0, 6] [a]	2.74 [0, 8] [a]
AI + hMG/FSH-IVF	1.34 [0, 4] [a]	2.71 [0, 8] [a]	3.25 [0, 8] [a]
cIVF	2.28 [0, 7] [a]	3.68 [1,10] [a]	5.56 [1,15] [a]

Abbreviations: AI, aromatase inhibitor; AMH, Anti-mullerian hormone; CC, Clomiphene citrate; cIVF, conventional IVF; FSH, follicle stimulating hormone; hMG, human menopausal gonadotropin; IVF, *in-vitro-fertilisation*; NC-IVF, Natural Cycle-IVF.

[a] 95% Prediction interval for women with BMI 24 and age 37.

Discussion

Our study showed that the effect of AMH on the ovarian response, defined by the number of oocytes and zygotes, is IVF stimulation protocol dependent. More specifically, Min stim-IVF protocols based on low dose hMG/FSH with or without oral compounds produce more oocytes and zygotes than Min stim-IVF protocols with only oral compounds such as CC and AI. However, the effect of additional stimulation appears to be less in patients with low AMH levels.

The strength of our study is its large multi-centre design providing "real world data". Furthermore, we analysed a broad spectrum of Min stim-IVF stimulation protocols. To the best of our knowledge this is the first study assessing five different Min stim-IVF protocols, along with NC-IVF and cIVF in relation to three AMH level categories. The data provided allows the reproductive physician to counsel patients on the expected ovarian response of seven different IVF protocols and thereby to individualize IVF treatments based on personal wishes and AMH level.

A weakness of our study is its observational, retrospective design, and the fact that patients were not randomized to IVF protocols and

were included multiple times. Furthermore, even when measuring AMH using an automated assay, differences in assay coefficients between centers cannot be ruled out. Ultimately, we were unable to distinguish between mature and immature oocytes, which resulted in a combined measurement of both. As mentioned above Min stim-IVF protocols have not been analysed in relation to the AMH level before. Most of the existing literature refers to the value of AMH levels to predict the ovarian response in cIVF, expressed as the number of oocytes. In contrast, studies on the predictive value of AMH levels on the ovarian response in Min stim-IVF are rare [25,33–35].

Ishii and colleagues performed a study which was most similar to ours [25]. They compared cycles, stimulated with CC at a dosage of 50 to 100 mg per day from the 3rd day of the cycle to the day before ovulation induction, CC cycles with additional low dose gonadotropins stimulation, short cIVF protocols as well as antagonist cIVF protocols and analysed oocyte numbers. The 1112 included patients were stratified according to four AMH levels (<1; ≥1 – ≤2; >2 – ≤3, >3 ng/ml). CC-IVF protocols showed only a very weak and non-significant correlation between AMH level and the number of retrieved oocytes but CC + low dose gonadotropin protocols revealed a moderate and significant correlation ($p < 0.01$) [25].

However, our study was much more comprehensive. We included a wide range of Min stim-IVF protocols and also analysed zygotes.Our study addresses a treatment concept that has been the subject of much debate. This concept involves several consecutive NC– or Min stim-IVF protocols, as opposed to one or a few fully stimulated cycles. The advantages and disadvantages of lower stimulation dosages, the absence of anaesthesia or embryo freezing and the lower costs per cycle must be discussed with couples. However, the need for more treatment cycles must also be considered [36]. Ultimately, the decision lies with the patients. Nevertheless, physicians must provide data on potential success rates based on this and other studies.

Our study therefore provides data that can be used to personalise treatment strategies based on the number of oocytes and zygotes of different protocols in relation to different AMH levels. NC– and/or Min stim-IVF can be used for IVF treatments and other treatments, such as secondary medical freezing after cancer therapy with low or very low ovarian reserve.

However, when using the data from our study for counselling purposes, it should be noted that success rates cannot be based solely on the number of oocytes or zygotes. It is important to take into account that first, the development potential of oocytes, zygotes and embryos appears to be greater in cycles involving low stimulation doses. It has been shown that the development potential, of oocytes and embryos obtained in NC-IVF is significantly higher than in cIVF cycles [18,37]. Second, very high stimulation in poor responders do not lead to better outcomes [38]. Third, the cost per cycle, as well as the cost per achieved pregnancy and live birth, may also be important, particularly if treatments are not reimbursed. Fourth, low stimulation treatments such as NC-IVF treatments are less stressful [15] and fifth, NC– or Min stim-IVF might possibly be lead to better health outcomes of the offspring [39,40], which however, has not yet been proven.

All these aspects show that patients can be advised on NC– and Min stim-IVF stimulation protocols, but the choice of the adequate protocol and strategy is complex and needs to include many different aspects.

Conclusion

AMH is an effective predictor for the number of oocytes and zygotes in relation to specific IVF stimulation protocols. Our findings could contribute to a more accurate counselling about the expected response of IVF stimulation protocols that differ from the standard conventionally stimulated IVF protocol. They are also of value for counselling for medical and social oocyte freezing, especially in cases with low ovarian reserve. However, further studies analyzing also pregnancy and live birth rates and success rates in relation to defined treatment time and costs are welcome to further improve counselling and individualization of IVF treatments.

Data availability.

The data underlying this article will be shared on reasonable request to the corresponding author.

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CRediT authorship contribution statement

I. Magaton: Writing – review & editing, Writing – original draft, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **A. Arni:** Writing – review & editing, Validation, Data curation. **L. von Arnim:** Writing – review & editing, Validation, Data curation. **M. Nordin:** Writing – review & editing, Validation, Project administration, Data curation. **I. Siercks:** Writing – review & editing, Validation, Project administration, Data curation. **RM. Popovici:** Writing – review & editing, Validation, Project administration, Data curation. **U. Bohlen:** Writing – review & editing, Validation, Project administration, Data curation. **S. Eisenhardt:** Writing – review & editing, Validation, Project administration, Data curation. **N. Reeka:** Writing – review & editing, Validation, Project administration, Data curation. **J-S. Lanowski:** Validation, Project administration, Data curation. **B. Lühr:** Writing – review & editing, Validation, Project administration, Data curation. **M. Roumet:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation. **M. von Wolff:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Von Wolff Michael reports financial support was provided by IBSA. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2025.114668.

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