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Only women's age and the duration of infertility are the prognostic factors for the success rate of natural cycle IVF

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Abstract

Purpose It is controversial who should be recommended to undergo natural cycle IVF (NC-IVF). Therefore, objective prognostic criteria which are already known at the time of counselling were defined.

Methods A retrospective observational study was performed with 201 couples (age 34.7 ± 4.1) undergoing 311 NC-IVF treatments with 201 transfers, corresponding to a transfer rate of 65.3%. The first cycle resulting in a transfer of one embryo was further analysed. Clinical pregnancy and live birth rates were analysed.

Results Pregnancy rate and live birth rates per first cycle were 21.9% and 13.2%, respectively. Groupwise comparison revealed the following clinical pregnancy/live birth rates per transfer cycle: duration of infertility 1–2 years 34.3/25.7%, 3–4 years 21.8/14.9% and > 4 years 9.1/4.5%. Women's age < 34 years 26.3/22.4%, 34–37 years 25.7/18.9% and 38–42 years 15.7/3.9%. Linear regression analysis showed that pregnancy and live birth rate correlated negatively with the duration of infertility and that live birth rate but not pregnancy rate correlated negatively with increasing female age. In contrast, AMH and infertility factors did not correlate with the success rate. Statistically significant correlations remained if a multivariate logistic regression analysis was performed, supporting further that the duration of infertility (OR 0.61, 95% CI 0.42–0.86) ($P = 0.006$) and female age (OR 0.87, 95% CI 0.78–0.95) ($P = 0.008$) are the predictors for live birth rates in NC-IVF transfer cycles.

Conclusions Based on the success rates, NC-IVF can especially be recommended for women with short duration of infertility and young age, whereas older women and those with long duration of infertility are not the best candidates for this technique.

Keywords Pregnancy rate · Live birth rate · Natural cycle IVF · Prognostic factors · Age

Introduction

Natural cycle IVF (NC-IVF) is being carried out with increasing frequency in many countries [1, 2], as psychological distress for women [3] as well as the risks and costs [4] per treatment cycle appear to be less compared to conventional IVF (cIVF) with gonadotropin stimulation.

However, the efficacy of NC-IVF compared to cIVF is still controversial. A Cochrane analysis tried to compare the efficacy of NC-IVF or modified NC-IVF with cIVF and came to the conclusion that no evidence of a statistically different live birth rates was found between both treatments (OR 0.68, 95% CI 0.46–1.01) [4]. However, the authors stated that they could not come to clear conclusions as too many different protocols and study populations were used. They also stated that NC-IVF might be particularly suitable for couples with male factor subfertility.

The authors suggested to perform large-scale randomised controlled trials to compare both treatments. However, the high variety of NC-IVF treatment protocols and the different indications make it almost impossible to perform such studies. It seems to be more feasible to define prognostic factors for the success of NC-IVF to allow balanced counselling for or against this technique.

Prognostic factors have already been intensively evaluated and defined in cIVF. A meta-analysis [6] revealed a negative association between pregnancy and female age (OR 0.95, 95% CI 0.94–0.96), duration of subfertility (OR

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0.99, 95% CI 0.98–1.0) and basal FSH (OR 0.94, 95% CI 0.88–1.0). It also described a positive association with the number of oocytes (OR 1.04, 95% CI 1.02–1.07) and better embryo quality was also associated with higher pregnancy chances. The relevance of the cause of infertility seems to be limited as shown by an Australian registry study [7], which showed a success rate of 22.0% in couples with a male factor compared to 19.2% with a female factor.

However, these prognostic factors have only been identified in cIVF and cannot be applied to NC-IVF treatments, as only one oocyte can be collected in NC-IVF. Therefore, prognostic factors need to be defined specifically for NC-IVF. Such factors have already been evaluated by Gonzales-Foruria et al. [8]. They confirmed age (OR 0.93, 95% CI 0.88–0.98), but not infertility, to be a prognostic factor in NC-IVF. However, this study included varying numbers of IVF cycles per patient and gonadotropin-stimulated cycles. Furthermore, the duration of infertility was not analysed and only pregnancies, but not live birth rates, were analysed.

We, therefore, performed a systematic evaluation of all possible prognostic factors which are already available at the time of IVF counselling and which have shown to be potentially relevant, such as women's age, duration of infertility, ovarian reserve and cause of infertility. Furthermore, we tried to exclude the influence of technically related confounders such as risk of premature ovulation and oocyte retrieval rate, etc., by restricting our study to transfer cycles, as these confounders can be expected to vary among IVF centres. Furthermore, outcome criteria were not only clinical pregnancy but also live birth rates.

Materials and methods

Study population and participants

The retrospective, observational single university centre study was performed with couples starting NC-IVF therapy between 2012 and 2015. NC-IVF was defined as IVF/ICSI without ovarian stimulation but with modifications to prevent premature ovulation. Women 18–42 years of age with regular menstrual cycles (24–32 days) and basal FSH concentrations < 10 IU/L undergoing their first three NC-IVF cycle treatments were evaluated. The first cycle resulting in a transfer of one embryo was included in the analysis. Only one cycle per patient was included. Transfer was performed in 56.7% of the cases in the first cycle at the age of 34.8 years ± 3.6, in 31.8% of the cases in the second cycle at the age of 33.8 years ± 4.7 and in 11.4% of the cases in the third cycle at the age of 33.7 years ± 4.2. Comprehensive statistical calculation was limited to transfer cycles to reduce the influence of other treatment-related factors such as premature ovulation, etc. Patients' characteristics such as age, AMH concentration, duration of infertility and infertility factors were determined. Oocyte quality and endometrial thickness were excluded as thin endometrium is a negative prognostic factor not only in cIVF [9], but also in NC-IVF [10].

The study was approved by the local ethical committee and patient's approval was given by written consent.

Couples were divided into different groups defined by the duration of infertility (1–2, 3–4 and > 4 years), women's age (< 34, 34–37 and 38–42 years), concentration of AMH (< 1, 1–5 and > 5 ng/ml) and by the cause of infertility such as severe male infertility (SMI) with sperm concentration < 5 Mill/ml, mild/moderate male infertility (MMI) with sperm concentration 5 to < 15 Mill/ml and/or total motility < 40%, other infertility factors (OI) included unilateral or bilateral tubal pathology diagnosed by hysterosalpingography or laparoscopy, endometriosis rASRM > II° diagnosed by sonography or laparoscopy and mixed pathologies and idiopathic infertility (II) without the diagnosis of any of the mentioned pathologies.

Furthermore, couples were divided into those with and without a clinical pregnancy and live birth rate, respectively.

Natural cycle IVF treatment

NC-IVF treatment was performed as follows: patients were monitored using ultrasound and analysis of luteinizing hormone (LH) and E_2 concentrations. First monitoring consultation was scheduled on cycle day 10 ± 1 in patients menstruating every 26–27 days and day 11 ± 1 if menstruation took place every 28–30 days. Slight variations in the first day of consultation resulted from the patients' own agendas and to avoid consultations at weekends.

Women did not receive ovarian stimulation apart from clomifene citrate 25 mg/day (46.3% of the cases), starting at day 6 or 7 of the cycle until ovulation induction [11]. In cases of previous premature ovulation, single injection of GnRH antagonists the day before ovulation triggering (18.4% of the cases) to avoid aspirations on Sundays, and ibuprofen three times 400–600 mg per day starting on the day of ovulation triggering (6.0% of the cases), if LH already increased on the day of follicle monitoring to postpone ovulation [11], and to enable the aspiration to be performed 2 days later. When the follicle diameter reached at least 18 mm and E_2 concentration was expected to be ≥ 800 pmol/L, 5000 IU of hCG (Pregnyl®, MSD Merck Sharp and Dohme GmbH, Lucerne, Switzerland) was administered and patients were scheduled 36 h later for oocyte retrieval. Follicles were aspirated without anaesthesia and without analgesia using 19G single lumen needles (220 mmHg) as described elsewhere [12]. After initial aspiration, follicles were flushed and aspirated three times each with 2–5 ml flushing medium with heparin (SynVitro® Flush, Origio, Berlin, Germany). The flushing

volume was adapted according to the size of the follicle. Fertilisation was achieved by standard ICSI. Biochemical and clinical pregnancy rates, defined by ultrasound diagnosis of an amniotic sac, as well as the live birth rate were analysed per transfer in relation to women's age and infertility factor.

The study was approved by the local ethical board committee (Internal Review Board, Inselspital Berne, 13-042).

Statistical analysis

Patients' baseline characteristics were compared for two groups using the Mann–Whitney *U* test and for three to four groups by the Kruskal–Wallis test. Fisher's exact test was used for categorical variables. Correlation of patients' characteristics was confirmed by non-parametric regression analysis. A multivariate logistic regression model (adjusted by the four prognostic factors) was used to identify independent variables that could most accurately predict pregnancy and live birth rate. $P < 0.05$ was considered statistically significant. The statistical analysis was performed with SPSS version 22.

Results

269 couples (18–42 years) undergoing NC-IVF treatment and fulfilling inclusion criteria were screened. 68 women (25.3%) were excluded due to missing transfer, resulting in 201 couples, undergoing 311 IVF cycles (overall transfer rate 65.3%) to be included in the final analysis. Characteristics of trial participants are shown in Table 1.

Pregnancy rate and live birth rates after up to three cycles (mean 1.55 ± 0.69 cycles) resulted in an overall pregnancy rate of 23.4% and live birth rate of 16.4% per patient. Pregnancy rate and live birth rates per first cycle were 21.9% and 13.2%, respectively. Transfer rate was 65.3% (Table 1).

Women were divided into different groups according to the duration of infertility (Table 1) and female age (Table 2). Characteristics of participants were, apart from lower AMH concentrations in older women (Table 2), not significantly different in the groups as shown by groupwise comparison and confirmed by correlation analysis. Women were also divided into groups according to AMH concentration (< 1 ng/ml: $n = 74$; 1–5 ng/ml: $n = 109$; > 5 ng/ml: $n = 18$) and cause of infertility (SMI: $n = 54$; MMI: $n = 44$; OI: $n = 44$ and II: $n = 59$) (data not shown). Characteristics in these groups were also not significantly different.

Groupwise comparison in relation to the duration of infertility revealed the following clinical pregnancy/live birth rates per transfer: 1–2 years 34.3/25.7%, 3–4 years 21.8/14.9% and > 4 years 9.1/4.5% (Table 1, Fig. 1). Accordingly, miscarriage rates per transfer were 25% (1–2 years), 31.6% (3–4 years) and 50% (> 4 years). Clinical pregnancy/live birth rates in relation to women's age per transfer were: < 34 years 26.3/22.4%, 34–37 years 25.7/18.9% and 38–42 years 15.7/3.9%. (Table 2, Fig. 2). Accordingly,

Table 1 Patient's characteristics in different "Duration of infertility" groups for transfer cycles (above) and treatment cycles (below)

Duration of infertility	All participants	1–2 years	3–4 years	> 4 years	Groupwise comparison *P* value	Correlation analysis *r* (*P* value)
Transfers, *n*	201	70	87	44		
Age, years ± SD	34.7 ± 4.1	34.4 ± 4.0	34.8 ± 4.0	35.1 ± 4.3	0.713	0.050 (0.485)
AMH, pmol/l ± SD	15.4 ± 14.7	18.5 ± 17.1	13.4 ± 11.9	14.5 ± 15.2	0.081	−0.162 (0.022)
SMI, *n*	54 (26.9%)	26 (37.1%)	18 (20.7%)	10 (22.7%)	0.169	0.107 (0.131)
MMI, *n*	44 (21.9%)	10 (14.3%)	21 (24.1%)	13 (29.5%)		
OI, *n*	44 (21.9%)	17 (24.3%)	18 (20.7%)	9 (20.5%)		
II, *n*	59 (29.4%)	17 (24.3%)	30 (34.5%)	12 (27.3%)		
Pregnancies, *n*	47 (23.4%)	24 (34.3%)	19 (21.8%)	4 (9.1%)	0.007	−0.223 (0.001)
Live births, *n*	33 (16.4%)	18 (25.7%)	13 (14.9%)	2 (4.5%)	0.008	−0.217 (0.002)
Data per treatment cycle						
Treatment cycles, *n*	311	111	122	78		
Performed cycles until first transfer, *n* ± SD	1.55 ± 0.69	1.59 ± 0.79	1.44 ± 0.56	1.70 ± 0.73	0.163	0.060 (0.397)
Transfer rate	65.3%	58.3%	69.6%	58.7%	–	–
Pregnancies, *n*/cycles all cycles ($n = 311$)	47/311 (15.1%)	24/111 (21.6%)	19/122 (15.6%)	4/78 (5.1%)	–	–
Pregnancies, *n*/cycles first cycles ($n = 114$)	25/114 (21.9%)	11/42 (26.2%)	13/52 (25.0%)	1/20 (5.0%)	0.127	−0.144 (0.126)
Live births, *n*/cycles all cycles ($n = 311$)	33/311 (10.6%)	18/111 (16.2%)	13/122 (10.7%)	2/78 (2.6%)	–	–
Live births, *n*/cycles first cycles ($n = 114$)	15/114 (13.2%)	7/42 (16.7%)	8/52 (15.4%)	0/20 (0.0%)	0.136	−0.140 (0.137)

SMI severe male infertility, *MM* mild/moderate male infertility, *OI* other causes of Infertility, *II* idiopathic infertility

Table 2 Patient's characteristics in different age groups for transfer cycles (above) and treatment cycles (below)

Female age	< 34 year	34–37 years	38–42 years	Groupwise comparison *P* value	Correlation analysis *r* (*P* value)
Transfers, *n*	76	74	51		
Duration of infertility, years ± SD	3.11 ± 1.29	3.59 ± 2.14	3.67 ± 2.26	0.537	0.099 (0.485)
AMH, pmol/l ± SD	19.9 ± 14.4	16.5 ± 16.8	7.1 ± 6.5	< 0.001	− 0.434 (< 0.001)
SMI, *n* (%)	27 (35.5%)	16 (21.6%)	11 (21.6%)	0.458	0.118 (0.095)
MMI, *n* (%)	13 (17.1%)	17 (23.0%)	14 (27.5%)		
OI, *n* (%)	15 (19.7%)	19 (25.7%)	10 (19.6%)		
II, *n* (%)	21 (27.6%)	22 (29.7%)	16 (31.4%)		
Pregnancies, *n* (%)	20 (26.3%)	19 (25.7%)	8 (15.7%)	0.335	− 0.093 (0.188)
Live births, *n* (%)	17 (22.4%)	14 (18.9%)	2 (3.9%)	0.010	− 0.221 (0.002)
Data per treatment cycle					
Treatment cycles, *n*	121	108	82		
Performed cycles until first transfer, *n* ± SD	1.59 ± 0.70	1.46 ± 0.67	1.61 ± 0.72	0.346	− 0.014 (0.844)
Pregnancies, *n*/cycles all cycles (*n* = 311)	20/121 (16.5%)	19/108 (17.6%)	8/82 (9.8%)	–	–
Pregnancies, *n*/cycles first cycles (*n* = 114)	11/40 (27.5%)	11/47 (23.4%)	3/27 (11.1%)	0.275	− 0.089 (0.208)
Live births, *n*/cycles all cycles (*n* = 311)	15/121 (12.4%)	12/108 (11.1%)	6/82 (7.3%)	–	–
Live births, *n*/cycles first cycles (*n* = 114)	8/40 (20.0%)	6/47 (12.8%)	1/27 (3.7%)	0.170	− 0.180 (0.055)

SMI severe male infertility, *MM* mild/moderate male infertility, *OI* other causes of infertility, *II* idiopathic infertility

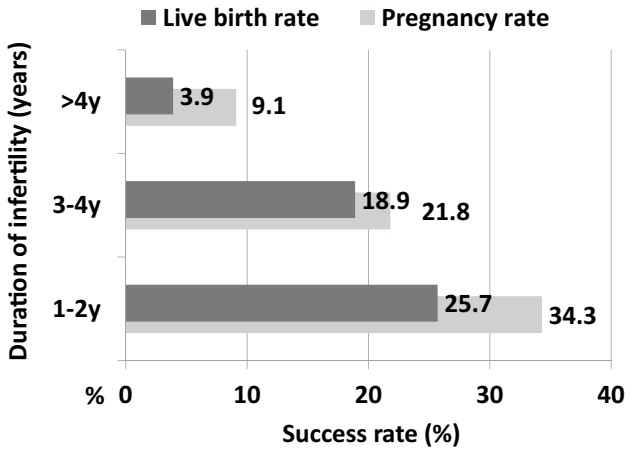

Fig. 1 Clinical pregnancy ($P < 0.05$) and live birth ($P < 0.05$) rates per transfer in women in relation to the duration of infertility (transfer rates per cycle: 1–2 years: 58.3%; 3–4 years: 69.6%; > 4 years: 58.7%)

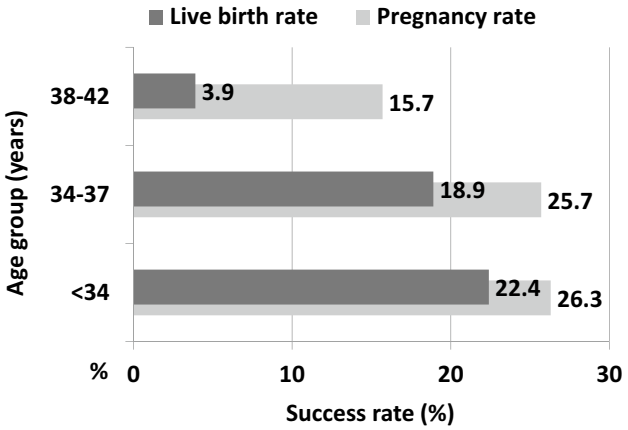

Fig. 2 Clinical pregnancy and live birth ($P < 0.05$) rates per transfer in women in relation to women's age (transfer rates per cycle: < 34 years: 63.9%; 34–37 years: 69.2%; 38–42 years: 62.2%)

miscarriage rates per transfer were 15% (< 34 years), 26.3% (34–37 years) and 75% (38–42 years). The miscarriage rates in women 38–42 years were very high, which might be attributed to small number of patients in this group.

Groupwise and linear regression analysis did show that pregnancy and live birth rate correlated negatively with the duration of infertility (Table 1) and that live birth rate but not pregnancy rate correlated negatively with increasing female age (Table 2). In contrast, AMH and infertility factors did not correlate with the success rate.

Characteristics of women without and with clinical pregnancies (Table 3) and without and with live births (Table 4) were also not significantly different regarding AMH concentration and infertility factors. In contrast, regarding the IVF success rate, differences were found in non-pregnant versus pregnant women (Table 3) for the duration of infertility (3.66 ± 2.05 years vs. 2.68 ± 1.06; $P = 0.002$). For non-pregnant versus live birth women (Table 4), differences were found for both duration of infertility (3.60 ± 2.01 years vs. 2.58 ± 0.94 years; $P = 0.002$) and female age (35.1 ± 4.1 years vs. 32.7 ± 3.4 years; $P = 0.002$).

Table 3 Patient's characteristics in women with and without a clinical pregnancy (transfer cycles)

Clinical pregnancy	Yes ($n=47$)	No ($n=154$)	P value
Age, years ± SD	34.0 ± 4.0	34.9 ± 4.1	0.188
AMH, pmol/l ± SD	18.1 ± 17.1	14.6 ± 13.9	0.125
Duration of infertility, years ± SD	2.68 ± 1.06	3.66 ± 2.05	0.002
SMI	15 (31.9%)	39 (25.3%)	0.609
MMI	9 (19.1%)	35 (22.7%)	
OI	12 (25.5%)	32 (20.8%)	
II	11 (23.4%)	48 (31.2%)	

SMI severe male infertility, *MM* mild/moderate male infertility, *OI* other causes of infertility, *II* idiopathic infertility

Table 4 Patient's characteristics in women with and without a live birth (transfer cycles)

Live birth	Yes ($n=33$)	No ($n=168$)	P value
Age, years ± SD	32.7 ± 3.4	35.1 ± 4.1	0.002
AMH, pmol/l ± SD	19.8 ± 18.5	14.5 ± 13.8	0.070
Duration of infertility, years ± SD	2.58 ± 0.94	3.60 ± 2.01	0.002
SMI	10 (30.3%)	44 (26.2%)	0.968
MMI	7 (21.2%)	37 (22.0%)	
OI	7 (21.2%)	37 (22.0%)	
II	9 (27.3%)	50 (29.8%)	

SMI severe male infertility, *MM* mild/moderate male infertility, *OI* other causes of infertility, *II* idiopathic infertility

Table 5 Multivariate logistic regression analysis of pregnancy rate (above) and live birth rate (below) per transfer for different patient's characteristics

Variable	OR (95% CI)	P value
Pregnancy rate		
Female age	0.97 (0.89–1.06)	0.468
AMH	1.01 (0.98–1.03)	0.551
Duration of infertility	0.68 (0.51–0.89)	0.005
Cause of infertility	> 1.21	> 0.4
Live birth rate		
Female age	0.87 (0.78–0.95)	0.008
AMH	1.01 (0.98–1.03)	0.683
Duration of infertility	0.61 (0.42–0.86)	0.006
Cause of infertility	> 0.77	> 0.7

Multivariate logistic regression analysis confirmed that the duration of infertility (OR 0.68, 95% CI 0.51–0.89) ($P=0.005$) is a predictor for clinical pregnancy rate in NC-IVF transfer cycles (Table 5). Multivariate logistic regression analysis further confirmed that not only the duration of infertility (OR 0.61, 95% CI 0.42–0.86) ($P=0.006$), but also the female age (OR 0.87, 95% CI 0.78–0.95) ($P=0.008$) are the predictors for the live birth rate (Table 5). Accordingly, in couples with infertility duration of 1–2 years and women's age < 34, 11/30 (36.7%) women delivered a baby in contrast to 0/13 (0%) couples with infertility duration > 4 years and women's age 38–42 years.

Discussion

Our study revealed that female age and the duration of infertility are the only prognostic factors for the live birth rate in NC-IVF. Our study only evaluated factors which are available at the time of counselling such as the duration of infertility, female age, AMH concentration and cause of infertility and which are relevant for counselling.

The comprehensive statistical analysis was restricted to embryo transfer cycles to exclude technical influences such as risk of premature ovulation and oocyte retrieval rate as these confounders can be expected to vary among IVF centres. It might be argued that this restriction is a limiting factor of the study, as the cycle performance before the transfer might also have an impact on prognostic factors. However, as female age has been shown not to influence the risk of premature ovulation, oocyte yield and the rate of embryo transfer [9], it can be assumed that excluding cycles without a transfer did not have a significant effect on the overall outcome of the study. In contrast, including only cycles with an embryo transfer and thereby excluding the influence of factors which vary individually and within different centres, we were able to address more specifically those factors which are already known before the IVF treatment and which are relevant for counselling for or against NC-IVF. However, to allow comparison of success rates with other studies or with other IVF therapies, success rates per treatment cycle were also included (Tables 1, 2).

Another weakness of our study might be the limited number of women. However, as first the above-mentioned factors were excluded by only including transfer cycles and as second we found significant correlations for the duration of infertility and female's age which remained significant even after adding several variables in the multivariate regression analysis we think that the results are sufficiently robust to be used in clinical practice.

Our study was initiated as NC-IVF is still controversially discussed. The reasons for this are manifold: NC-IVF has many advantages, such as lower psychological distress for women (lower risks and costs per achieved pregnancy [4]), which might not be obvious in less specialised centres. Furthermore, health care systems, reimbursing only a limited number of cycles, may reduce the motivation to perform NC-IVF. As the efficacy per cycle is lower in NC-IVF, more cycles are usually needed, which could lead to higher costs

for the patients as not all cycles are reimbursed. Cultural factors or personal interests might also play a role. Some couples prefer twin pregnancies and would, therefore, favour cIVF.

However, such manifold factors are difficult to include in the assessment of NC-IVF. We, therefore, focussed on clinically relevant prognostic factors and did not take economic, political and cultural aspects into account.

Our study was limited to NC-IVF treatment cycles without any additional mild stimulation, as the accuracy of defining prognostic factors could otherwise have been reduced. We only included cycles with modifications such as low-dose clomifene citrate [9] and non-steroidal anti-inflammatory drugs to reduce premature ovulation [13], but excluded any cycles with high doses of clomifene citrate and with gonadotropin stimulation.

Our study revealed that female age is a prognostic factor for the live birth rate which has already been shown in cIVF (OR 0.95, 95% CI 0.94–0.96) [6]. This has also been demonstrated in NC-IVF by Gonzales-Foruria et al. [8] (OR 0.93, 95% CI 0.88–0.98). In their study, varying numbers of IVF cycles per patient and gonadotropin-stimulated cycles were included, limiting the accuracy of the results. Even more importantly, this study evaluated only clinical pregnancy but not live birth rates. Our study revealed that the analysed factors had a significant effect on live birth but not the clinical pregnancy rate. This indicates that the miscarriage rate has a substantial effect on the outcome of NC-IVF and stresses the importance of defining the live birth rate as a parameter of success.

Our study also revealed that the duration of infertility is a strong prognostic factor in NC-IVF. This had also already been shown in cIVF (OR 0.99, 95% CI 0.98–1.0) [6]. One might speculate that this factor could be influenced by the cause of infertility, as severe male factors might more frequently lead to an instant start of IVF treatments, without time-consuming alternatives such as intrauterine insemination. However, this could not be shown in our study as the proportions of men with severe male factors were not correlated with the duration of infertility.

Our study did not reveal an association between AMH concentrations and the success of NC-IVF. In cIVF, the number of oocytes had been defined as a prognostic factor (OR 1.04, 95% CI 1.02–1.07) [6]. As high AMH leads to higher number of oocytes it can be speculated that AMH might also be a prognostic factor in cIVF.

We only included cycles with the transfer of one embryo, excluding embryo selection. Therefore, AMH concentration could only have an impact on the success rate in our study due to other potentially AMH-associated criteria such as oocyte quality. However, as AMH was not associated with pregnancy and live birth rates, such criteria do not seem to be relevant.

Our study also did not reveal an association of infertility factors with the success of NC-IVF. In cIVF, infertility factors also could not be identified as prognostic factors [6]. A Cochrane analysis stated that NC-IVF might be particularly suitable for couples with male factor subfertility [5]. However, this assumption could not be confirmed in our study, even though we tried to increase the accuracy of our analysis by subdividing the couples into groups with male infertility (severe male factor) and with male subfertility (mild/moderate male factor).

What are the clinical consequences of this study?

First, our study might explain the controversial attitudes of many clinicians regarding the success rates of NC-IVF. If NC-IVF is seen as a kind of last resort in infertility treatment and, therefore, if only couples with low prognostic criteria are recommended for NC-IVF, the success rate can be expected to be very low. This was confirmed in our study as live birth rate was only 0% (0/13 couples) in couples with infertility > 4 years and women's age 38–42 years. In contrast, in couples with good prognostic criteria such as infertility 1–2 years and women's age < 34 years, live birth per transfer was 36.7% (11/30 couples).

Second, knowledge about prognostic factors in NC-IVF and cIVF can allow more objective counselling for or against this kind of treatment. Couples with short duration of infertility and low female age are suitable for NC-IVF, especially if lower costs and treatments without gonadotropin stimulation are favoured. In contrast, couples with higher female age are less suitable for NC-IVF and should rather be counselled for cIVF, especially if ovarian reserve is still high to allow the collection of many oocytes.

In conclusion, NC-IVF is most successful in couples with short duration of infertility and low female age. Therefore, couples could be counselled for NC-IVF in the case of short duration of infertility and low female age, but should rather opt for cIVF in the case of long duration of infertility and high female age if ovarian reserve is still high. Accordingly, NC-IVF is a complimentary IVF treatment option, especially for good prognostic cases [14].

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Compliance with ethical standards

Conflict of interest None of the authors have declared a conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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