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FERTILITY PRESERVATION

Fertility preservation: ovarian response to freeze oocytes is not affected by different malignant diseases—an analysis of 992 stimulations

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Abstract

Purpose To study if ovarian response is affected by the type of disease if fertility preservation is required.

Methods A registry of the trinational fertility preservation network *Ferti*PROTEKT including 992 patients aged 18–40 years undergoing ovarian stimulation and follicle aspiration for fertility preservation from 1/2007 until 3/2016 was analysed. The number of collected oocytes, days of stimulation, total gonadotropin dosage and gonadotropin dosage per day were evaluated.

Results Total oocyte number was negatively correlated with increasing age ($r = 0.237$, $p < 0.0001$). Oocyte numbers were in women < 26 years 15.4 ± 8.8, 26–30 years 13.1 ± 8.5, 31–35 years 12.2 ± 7.7 and 36–40 years 9.9 ± 8.0. Age-adjusted oocyte numbers were not different in women with Hodgkin's lymphoma (12.6 ± 8.8), non-Hodgkin's lymphoma (12.4 ± 8.2), leukaemia (11.7 ± 8.2), sarcoma (11.8 ± 8.2), cerebral cancer (16.5 ± 8.1), gastrointestinal cancer (13.2 ± 8.1) gynaecological cancer (10.8 ± 8.2) and other types of malignancies (15.8 ± 8.1) apart from ovarian cancer with lower oocyte yield (7.3 ± 8.3, $p < 0.001$) compared to women with breast cancer (13.3 ± 8.8). The total gonadotropin dose used for stimulation was only elevated in Hodgkin's and non-Hodgkin's lymphoma compared to women with breast cancer ($p < 0.05$). Oocyte yield was lower in women with versus without ovarian cancer ($p < 0.0001$).

Conclusions As ovarian response is not affected by the type of cancer, ovarian stimulation can be performed with the same oocyte yield in different malignant diseases. However, oocyte yield is reduced if ovarian surgery is required and in older women.

Keywords Fertility preservation · Ovarian stimulation · Oocyte · Breast cancer · Hodgkin's lymphoma · Ovarian cancer

Introduction

Ovarian stimulation and cryopreservation of unfertilized or fertilised oocytes as well as cryopreservation of ovarian tissue are among the most frequently performed fertility conserving techniques before gonadotoxic treatment [1]. Ovarian stimulation is the more established of these two techniques. Ovarian stimulation is now possible with only a minimal risk of overstimulation using antagonist protocols and triggering of ovulation with GnRH agonists [2]. Furthermore, protocols for luteal phase stimulation have been established [3–5], double stimulation introduced [6] and stimulation directly after cryopreservation of ovarian tissue successfully tested [7]. Aromatase inhibitors have been introduced to reduce oestradiol serum concentrations in patients with oestrogen-dependent breast cancer [8]. Based on calculations from register data, the live birth rate after one stimulation cycle is approximately 35% in women around 30–35 years of age [9], a success rate which was confirmed in the first case series after the use of cryopreserved oocytes [10].

It is therefore important to know the disease-specific oocyte yield following ovarian stimulation to allow better counselling regarding the efficacy of this technique.

Existing smaller studies [10–18] are only of limited use for clinical practice as study results are controversial and no differentiation was made between the different malignancies. An

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exception is the recent publication on ovarian response in breast cancer patients. Quinn et al. [18] analysed the ovarian response in 191 breast cancer patients and compared the ovarian stimulation outcome with 589 women undergoing elective fertility preservation. They found similar oocyte numbers in both groups, even after adjustment for age.

The data from this analysis prompted us to use the ovarian response of breast cancer patients, the group with the greatest body of evidence, as a reference to compare the stimulation outcome data from a large trinational fertility preservation registry. We aimed to generate first age-specific data about the oocyte yield and second disease-specific data for different malignant diseases after age adjustment, to allow counselling regarding the oocyte yield of ovarian stimulation in cancer disease.

Material and methods

Study population

A retrospective analysis was performed of all 1200 documented ovarian stimulations in the F*erti*PROTEKT network registry (www.fertiprotekt.com) performed in around 89 IVF centres for medical reasons from 1/2007 until 3/2016. The network *Ferti*PROTEKT is a multicentre network of centres in Germany, Austria and Switzerland. Each woman underwent one stimulation cycle due to underlying malignant or non-malignant disease requiring gonadotoxic treatment or possibly losing ovarian function due to ovary destructing diseases such as borderline ovarian tumours. One hundred and thirty eight stimulation cycles were excluded from analysis due to age > 40 years ($n = 16$), missing data ($n = 6$), no gonadotoxic therapy or ovarian surgery such as Turner syndrome and endometriosis ($n = 6$), incomplete data sets ($n = 100$) and cancelled stimulations ($n = 9$) (breast cancer ($n = 4$) , Hodgkin‘s lymphoma ($n = 1$), non-Hodgkin’s lymphoma ($n = 1$) and leukaemia ($n = 1$)) resulting in 1062 stimulation cycles with follicle aspiration. Of those, cycles performed in women without malignant diseases ($n = 71$) were also excluded resulting in 992 women to be further analysed.

Analysed parameters

Dependent on the underlying type of cancer (breast cancer, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, leukaemia, sarcoma, cerebral cancer, gastrointestinal cancer, ovarian cancer, gynaecological cancers (cervical, vulvar and endometrial cancer) and other types of malignancies (thyroid cancer, lung cancer, Wilms tumour, peritoneal cancer, etc.)), stimulation and outcome parameters were analysed according to age (total, ≤ 25, 26–30, 31–35, 36–40 years). The analysed parameters included number of oocytes retrieved (n), number of oocytes retrieved adjusted for age, days of stimulation (n), days of stimulation adjusted for age, gonadotropin dose used (IU), gonadotropin dose used adjusted for age, gonadotropin dose (IU)/day and gonadotropin dose /day adjusted for age.

Statistical analysis

Difference of oocyte numbers and stimulation parameters in different age groups were compared by Pearson’s correlation coefficients Spearman’s rank correlation analysis. For calculation of statistical significance between the disease groups, age-adjusted values were calculated and 95% confidence intervals were defined. The difference between the groups was calculated using analysis of covariance, and the age was treated as a continuous variable (ANCOVA). Outcome parameters of women with individual malignant diseases were compared to breast cancer patients, as ovarian stimulation outcome in breast cancer patients has been shown to be comparable to women undergoing elective fertility preservation [18]. A $p < 0.05$ was considered to be statistically significant. Age-adjusted parameters (number of oocytes, stimulation days, gonadotropin dose and gonadotropin dose/day) as well as all other parameters are depicted as mean ± standard deviation (SD).

Results

Total oocyte number was negatively correlated with increasing female age ($r = 0.234$, $p < 0.0001$). Oocyte number was in women < 26 years 15.4 ± 8.8, 26–30 years 13.1 ± 8.5, 31–35 years 12.2 ± 7.7 and 36–40 years 9.9 ± 8.0. Total gonadotropin dose and total gonadotropin dose/day were higher in older age groups (Table 1).

Compared to patients with breast cancer, women with other malignant diseases were almost all, with the exception of gastrointestinal and gynaecological cancer, significantly younger (Table 2). The age-adjusted number of collected oocytes was not different in most groups of malignant diseases compared to breast cancer patients. Only the ovarian cancer group had a significantly lower number of − 6.0 oocytes [95% CI − 9.0, − 3.1]. The number of stimulation days was also similar in most groups of malignant diseases compared to patients with breast cancer, with the exception of Hodgkin’s lymphoma and non-Hodgkin’s lymphoma, which required 0.8 [95% CI 0.4, 1.2] and 0.8 [95% CI 0.2, 1.4] more stimulation days. Additionally, the total gonadotropin dosage was also higher in women with Hodgkin’s lymphoma (+ 225.9 IU [95% CI 54.7, 397.1]) and in women with non-Hodgkin’s lymphoma (+ 266.8 IU [95% CI 43.2, 490.4]), whereas the total gonadotropin dosage in the other groups of malignant diseases were not different compared to breast cancer patients.

Table 1 Comparison of oocyte yield and stimulation parameters in different age groups of all women

	Total, $n = 992$	< 26 years, $n = 240$	26–30 years, $n = 300$	31–35 years, $n = 297$	36–40 years, $n = 155$	Correlation coefficient[1], p value
Mean age (years ± SD)	29.6 ± 5.6	22.0 ± 2.5	28.3 ± 1.4	32.9 ± 1.4	37.6 ± 1.3	
Oocytes total (n ± SD)	12.9 ± 8.4	15.4 ± 8.8	13.1 ± 8.5	12.2 ± 7.7	9.9 ± 8.0	− 0.234 < 0.0001
Days of stimulation (days ± SD)	10.8 ± 2.4	11.4 ± 2.4	10.7 ± 2.2	10.6 ± 2.4	10.6 ± 2.6	− 0.119 0.0002
Total gonadotropin dose (IU ± SD)	2563 ± 952	2430 ± 820	2443 ± 909	2680 ± 1000	2777 ± 1064	0.138 < 0.0001
Total gonadotropin dose/day (IU ± SD)	237.3 ± 71.3	214.8 ± 60.3	227.2 ± 71.7	252.7 ± 73.1	261.9 ± 69.0	0.251 < 0.0001

[1] Pearson's correlation with age (years)

The most common diseases within the group of malignant diseases were breast cancer ($n = 493$, 49.7%), Hodgkin's lymphoma ($n = 224$, 22.6%) and non-Hodgkin's lymphoma ($n = 84$, 8.5%). Therefore, an individual age group-dependent analysis was additionally performed in these groups (Table 3).

Within the individual age groups, no difference was noted regarding the oocyte yield. The total stimulation dosage was also similar in all groups. Only women with Hodgkin's lymphoma at the age of < 26 years and women with non-Hodgkin's lymphoma at the age of 26–30 years received a slightly higher gonadotropin dosage of 486 IU [95% CI 144, 827] and 402 IU [95% CI 18, 786] respectively (Table 3).

As women with ovarian surgery can be expected to have a lower oocyte yield, a subanalysis was performed comparing women without and with ovarian surgery (Table 4). The age-adjusted oocyte yield was significantly lower in diseases requiring ovarian surgery ($p < 0.0001$).

Discussion

Our study revealed that oocyte yield is negatively correlated with increasing female age and that it is not reduced in malignant diseases apart from ovarian cancer with lower oocyte number. It also revealed that women with ovarian surgery have a lower oocyte yield compared to women receiving gonadotoxic therapies such as chemotherapy and radiotherapy. The analysis was based on data from a trinational fertility preservation registry from Germany, Austria and Switzerland which has already successfully been used in previous studies [1, 5].

Apart from the large number of cycles that made a disease-specific analysis possible, the large registry also allowed transferability of the data by largely eliminating the influence of centre-specific characteristics. However, the analysis of registry data is also a weakness of the present study, because a registry analysis does not allow a very detailed data analysis and thus the evaluation is limited to the number of oocytes, the duration of the stimulation (stimulation days) and the stimulation dose. Nevertheless, since the success rate of a stimulation closely correlates with the oocyte count [19] and further data such as the rate of metaphase II oocytes or the rate of fertilisation would hardly likely to increase the general outcome of the study, the evaluation of the oocyte count in combination with the gonadotropin dose appears to be a reliable parameter for assessing the oocyte yield.

A further weakness is the missing concentrations of anti-Mullerian hormone (AMH) or antral follicle counts (AFC), which were not provided by the registry. However, even if these parameters had been provided, due to the variability of the AFC in different centres and the variability of AMH concentrations before automated AMH assays were introduced, these values would possibly not have added reliable information.

Statistically, it needs to be noted that we did not adjust for multiple comparisons in this observational registry study, as this might have inflated the type 1 error.

In a recently published study, it was shown that the ovarian response in breast cancer patients is not reduced when compared to healthy women [18]; therefore, our analysis related the data from the different diseases to the data obtained from the breast cancer patients. Our study showed that in almost all malignancies, the oocyte yield is similar. The number of oocytes was only significantly reduced in women with ovarian cancer. This reduction is either due to the fact that tumour removal led to a reduction in the ovarian reserve and/or due to ovarian tumour reducing ovarian function per se, which is proven for tumours of the testes in which a clear reduction in sperm quality could be demonstrated [20].

The previous studies have shown in malignant diseases both lower and unchanged oocyte numbers. A meta-analysis of 7 studies conducted between 1998 and 2011, involving 227 women, showed a lower oocyte count [13]. The studies by Das et al. [12] with 41 women, by Almog et al. [14] with 81 women, by Johnson et al. [21] with 50 women and by Garcia-Velasco et al. [16] with 355 women all showed no difference in the oocyte count compared to a control group. However, no disease-specific analysis was performed in any of these

Table 2 Stimulation parameters and oocyte yield of women with malignant disease according to the individual disease. Significant numbers are shown in italics

Diseases	Breast cancer, $n = 493$	Hodgkin's lymphoma, $n = 224$	Non-Hodgkin's lymphoma, $n = 84$	Leukaemia, $n = 25$	Sarcoma, $n = 37$	Cerebral cancer, $n = 32$	Gastrointestinal cancer, $n = 32$	Ovarian cancer, $n = 34$	Gynaecological cancer, $n = 11$	Other types of malignancies, $n = 20$
Age (years ± SD)	32.3 ± 4.2	25.5 ± 4.9	28.4 ± 5.7	27.6 ± 6.1	26.2 ± 5.0	28.7 ± 4.5	30.3 ± 4.6	25.1 ± 5.4	32.9 ± 4.3	28.8 ± 7.0
Difference [95% CI]**		*− 6.8 [− 7.5; − 6.0]*$^{\alpha}$	*− 3.9 [− 5.0; −2.8]*$^{\alpha}$	*− 4.7 [− 6.6; − 2.8]*$^{\alpha}$	*− 6.0 [− 7.6; − 4.5]*$^{\alpha}$	*− 3.6 [− 5.3; − 1.9]*$^{\alpha}$	*− 2.0 [− 3.7; − 0.3]*	*− 7.2 [− 8.8; − 5.6]*$^{\alpha}$	0.6 [− 2.2; 3.4]	*− 3.5 [− 5.7; − 1.4]*$^{\beta}$
Oocytes total (n ± SD)	12.2 ± 8.4	14.3 ± 8.7	12.9 ± 7.8	12.6 ± 9.4	13.1 ± 6.8	16.5 ± 10.5	12.9 ± 6.6	9.1 ± 5.1	9.5 ± 7.6	16.1 ± 9.6
Oocyte total (n ± SD)*	13.3 ± 8.8	12.6 ± 8.8	12.4 ± 8.2	11.7 ± 8.2	11.8 ± 8.2	16.1 ± 8.1	13.2 ± 8.1	7.3 ± 8.3	10.8 ± 8.2	15.8 ± 8.1
Difference [95% CI]**		− 0.7 [− 2.1; 0.8]	− 0.9 [− 2.9; 1.0]	− 1.6 [− 4.9; 1.7]	− 1.6 [− 4.4; 1.2]	2.8 [− 0.1; 5.8]	− 0.1 [− 3.0; 2.8]	*− 6.0 [− 9.0; − 3.1]*$^{\alpha}$	− 2.5 [− 7.4; 2.3]	2.4 [− 1.2; 6.1]
Days of stimulation (n ± SD)	10.5 ± 2.3	11.3 ± 2.7	11.3 ± 2.3	10.6 ± 2.8	10.8 ± 2.0	10.9 ± 1.7	10.5 ± 2.0	11.2 ± 2.5	10.6 ± 1.9	11.6 ± 1.6
Days of stimulation (n ± SD)*	10.6 ± 2.6	11.2 ± 2.6	11.3 ± 2.4	10.6 ± 2.4	10.7 ± 2.4	10.9 ± 2.4	10.5 ± 2.4	11.1 ± 2.4	10.6 ± 2.4	11.6 ± 2.4
Difference [95% CI]**		*0.6 [0.2; 1.0]*$^{\Omega}$	*0.7 [0.1; 1.3]*$^{\Omega}$	0.0 [− 1.0; 10]	0.1 [− 0.7; 1.0]	0.3 [− 0.5; 1.2]	− 0.1 [− 0.9; 0.8]	0.5 [− 0.4; 1.3]	0.1 [− 1.4; 1.5]	1.0 [0.0; 2.1]$^{\Omega}$
Total gonadotropin dose (IU ± SD)	2550 ± 1002	2551 ± 952	2686 ± 799	2763 ± 1437	2550 ± 829	2523 ± 898	2539 ± 615	2449 ± 737	2545 ± 616	2561 ± 823
Total gonadotropin dose (IU ± SDE)*	2460 ± 1016	2686 ± 1018	2727 ± 945	2829 ± 944	2661 ± 951	2552 ± 942	2516 ± 942	2599 ± 957	2435 ± 944	2589 ± 942
Difference [95% CI]**		*225.9 [54.7; 397.1]*$^{\Omega}$	*266.8 [43.2; 490.4]*$^{\Omega}$	369.0 [− 14.35; 752.4]	200.9 [− 123.0; 524.9]	91.38 [− 248.7; 431.5]	55.7 [− 282.4; 393.7]	138.5 [− 201.3; 478.3]	− 25.6 [− 589.1; 537.9]	128.2 [− 295.6; 552.1]
Gonadotropin dose/day (IU ± SD)	242 ± 73	228 ± 76	239 ± 55	255 ± 98	235 ± 62	232 ± 73	244 ± 47	222 ± 57	244 ± 58	220 ± 64
Gonadotropin dose/day (IU ± SD)*	232 ± 75	243 ± 75	243 ± 69	263 ± 69	247 ± 70	236 ± 69	241 ± 69	238 ± 70	232 ± 69	224 ± 69
Difference [95% CI]**		11.3 [− 1.3; 23.9]	11.5 [− 4.9; 27.9]	*30.6 [2.5; 58.8]*$^{\Omega}$	15.3 [− 8.5; 39.0]	3.7 [− 21.2; 28.7]	9.4 [− 15.4; 34.2]	6.3 [− 18.6; 31.2]	− 0.2 [− 41.6; 41.1]	− 8.4 [− 39.5; 22.7]

*Individual parameters are listed as age-adjusted values

**Difference [95% CI] is calculated in comparison to breast cancer

Statistical significant values (ANOVA) are as follows: $^{\alpha}p < 0.001$; $^{\beta}p < 0.005$; $^{\Omega}p < 0.05$

Table 3 Age-dependent oocyte yield and stimulation doses used in breast cancer, Hodgkin's lymphoma and non-Hodgkin's lymphoma. Significant numbers are shown in italics

Diseases	Breast cancer, $n = 493$	Hodgkin's lymphoma, $n = 224$	non-Hodgkin's lymphoma, $n = 84$
< 26 years (n)	30	118	26
Oocyte yield ($n \pm$ SD)	17.5 ± 9.1	15.5 ± 8.8	14.7 ± 9.9
Oocyte yield ($n \pm$ SD)*	18.3 ± 9.3	15.4 ± 9.0	14.4 ± 9.0
Difference [95% CI]**		− 2.9 [− 6.6; 0.9]	− 3.9 [− 8.8; 1.0]
Total gonadotropin dose (IU ± SD)	2056 ± 649	2479 ± 868	2417 ± 742
Total gonadotropin dose (IU ± SD)*	2002 ± 844	2488 ± 818	2438 ± 819
Difference [95% CI]**		*486* [*144*; *827*]$^{\Omega}$	436 [− 8; 881]
26–30 years (n)	140	69	27
Oocyte yield ($n \pm$ SD)	12.9 ± 9.1	13.4 ± 8.9	13.9 ± 7.4
Oocyte yield ($n \pm$ SD)*	13.3 ± 8.8	12.6 ± 9.0	14.0 ± 8.7
Difference [95% CI]**		− 0.7 [− 3.3; 2.0]	0.7 [− 2.88; 4.33]
Total gonadotropin dose (IU ± SD)	2355 ± 909	2521 ± 1035	2746 ± 705
Total gonadotropin dose (IU ± SD)*	2336 ± 940	2564 ± 959	2738 ± 926
Difference [95% CI]**		228 [− 55;510]	*402* [*18*; *786*]$^{\Omega}$
31–35 years (n)	198	34	22
Oocyte yield ($n \pm$ SD)	12.0 ± 7.4	12.6 ± 7.7	11.4 ± 5.6
Oocyte yield ($n \pm$ SD)*	12.0 ± 7.2	12.7 ± 7.2	11.5 ± 7.2
Difference [95% CI]**		0.8 [− 1.9; 3.4]	− 0.5 [− 3.7; 2.7]
Total gonadotropin dose (IU ± SD)	2610 ± 981	2781 ± 1024	2868 ± 948
Total gonadotropin dose (IU ± SD)*	2611 ± 976	2773 ± 977	2859 ± 977
Difference [95% CI]**		161 [− 196;518]	247 [− 185;680]
36–40 years (n)	125	3	9
Oocyte yield ($n \pm$ SD)	10.5 ± 8.5	7.0 ± 3.6	8.6 ± 5.4
Oocyte yield ($n \pm$ SD)*	10.5 ± 8.3	8.9 ± 8.5	8.0 ± 8.3
Difference [95% CI]**		− 1.6 [− 11.4; 8.2]	− 2.5 [− 8.2; 3.1]
Total gonadotropin dose (IU ± SD)	2793 ± 1125	3450 ± 834	2844 ± 752
Total gonadotropin dose (IU ± SD)*	2792 ± 1101	3614 ± 1131	2796 ± 1109
Difference [95% CI]**		822 [− 484;2128]	4 [− 753;760]

*Individual parameters are listed as age adjusted values

**Difference [95% CI] is calculated in comparison to breast cancer

Statistical significant values (ANOVA) is $^{\Omega} p < 0.05$

Table 4 Comparison of oocyte yield and stimulation parameters in all women separated in subgroups of women with chemo and/or radiotherapy compared to ovarian surgery

	Total ($n = 992$)	Chemo- and/or radiotherapy ($n = 958$)	Ovarian surgery[1] ($n = 34$)	Difference (95% CI)	p value*
Age (years ± SD)	29.6 ± 5.6	29.8 ± 5.5	25.1 ± 5.4	4.7 [2.8; 6.6]	< 0.0001
Oocytes total (age adjusted) ($n \pm$ SD)**	12.9 ± 8.2	13.1 ± 8.1	7.4 ± 8.2	5.7 [2.9; 8.5]	< 0.0001
Days of stimulation (age adjusted) (n ± SD)**	10.8 ± 2.4	10.8 ± 2.4	10.9 ± 2.4	− 0.1 [− 1.0; 0.7]	0.768
Total gonadotropin dose (age adjusted) (IU ± SD)**	2563 ± 943	2563 ± 944	2554 ± 954	8.5 [− 319; 335]	0.960
Total gonadotropin dose/day (age adjusted) (IU ± SD)**	237 ± 69	237 ± 69	236 ± 70	1.4 [− 22.5; 25.4]	0.907

Entities:

[1] Ovarian cancer (incl. dysgerminoma, teratoma, germ cell tumour)

*Statistical analysis was performed using ANOVA. A p value < 0.05 was considered significant

**Age-adjusted values

studies. Alvarez and Ramanathan [10] conducted a disease-specific study in 306 women and found lower oocyte numbers in 34 women with gynaecological (ovarian, endometrial and cervical malignancies, ovarian borderline tumours) compared with haematological and breast cancer patients. However, they did not perform an adjustment for age, even though patients with breast cancer were older. It is to be assumed that the controversial data is based on small patient groups and the lack of disease-specific evaluation.

Lawrenz et al. [15] and Lekovich et al. [17] described a significantly lower oocyte number and Sonigo et al. 2018 a lower antral follicle responsiveness to FSH but the same oocyte yield in women with lymphoma disease. To better compare these data with our data, we added both lymphoma groups and compared the oocyte yield with breast cancer patients. The number of oocytes was 1.2 oocytes lower in the total lymphoma group compared to the breast cancer group but the difference was not significant. A power analysis revealed that 884 women per group were required to reach the statistical significance for the difference of 1.2 ± 9 oocytes (two-tailed t test, alpha = 0.05, beta = 0.2). Therefore, the oocyte yield seems to be slightly reduced in lymphoma patients, but this effect is rather marginal and the clinical relevance is questionable.

What is the consequence of the study results?

On the one hand, they are reassuring, since the oocyte yield does not seem to be reduced in most malignant diseases. A lower oocyte yield is only to be assumed in the case of ovarian cancer. An adaptation of the stimulation dosage is otherwise only necessary in luteal phase stimulation, since this requires a somewhat longer stimulation duration and a higher daily gonadotropin dosage [3–5].

On the other hand, this data allows an improvement in counselling, since the oocyte yield of a stimulation treatment can be estimated well for the various malignancies and a lower than expected oocyte count can be indicated in some cases. According to theoretical calculations based on register data [9] as well as according to the first-case series [10], approximately one in three women may have a child after undergoing one stimulation cycle using these oocytes. However, as this study also clearly demonstrated, female age has always to be taken into account as the number of oocytes is negatively correlated with increasing female age.

In conclusion, the register analysis confirmed an age-related decline of oocyte yield. However, the oocyte yield is not significantly impaired in different malignant diseases after age adjustment, with the exception of diseases requiring ovarian surgery. Ovarian stimulation can therefore be expected to result in similar oocyte numbers in most malignant diseases.

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Compliance with ethical standards

As anonymized registry data were analysed, ethical approval was not required.

Conflict of interest The authors declare that they have no conflict of interest.

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