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Improving female fertility preservation through assisted reproductive technologies: Strategies and promising outcomes

PhD Thesis

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TABLE OF CONTENT

This doctoral thesis is based on the following publications:

1. **Vesztergom D,** Téglás G, Nánássy L, Mátrai Z, Novák Z. A termékenység megőrzése daganatos betegségekben. Egy hazai felmérés tapasztalatai [Fertility preservation in cancer patients]. *Orv Hetil*. 2022;163(6):246-252. Published 2022 Feb 6. doi:10.1556/650.2022.32375. *Classification:* ***Q4***

2. **Vesztergom D**, Téglás G, Bahrehmand K, Torok A, Sipos M, Tandor Z, Zadori J, Balla L, Boga P, Forgacs V, Varnagy A, Manfai Z, Novék Z. Reducing radicality in fertility-sparing surgery is associated with improved in vitro fertilization outcome in early-stage cervical cancer: a national retrospective study. *Gynecologic Oncology.* 2024; 186: 35-41, doi.org/10.1016/j.ygyno.2024.03.024. *Classification:* ***D1***

3. **Vesztergom D**, Segers I, Mostinckx L, Blockeel C, De Vos M. Live births after in vitro maturation of oocytes in women who had suffered adnexal torsion and unilateral oophorectomy following conventional ovarian stimulation. *J Assist Reprod Genet*. 2021;38(6):1323-1329. doi:10.1007/s10815-021-02171-8 . *Classification:* ***Q1***

List of original publications connected to the PhD thesis:

1. **Vesztergom D**, Székely B, Hegyi B, et al. Daganatos nőbetegek termékenységének megőrzése II. [Fertility preservation in female cancer patients. Possibilities beside current treatments in different types of cancer]. *Orv Hetil*. 2023;164(29):1134-1145. Published 2023 Jul 23. doi:10.1556/650.2023.32824. *Classification: Q4*

2. **Vesztergom D**, Nánássy L, Polgár C, et al. Daganatos nőbetegek termékenységének megőrzése I. [Fertility preservation in female cancer patients. Gonadotoxicity of oncological therapies and possibilities of prevention]. *Orv Hetil*. 2023;164(28):1094-1101. Published 2023 Jul 16. doi:10.1556/650.2023.32823. *Classification: Q4*

3. **Vesztergom D,** Takács T, Bíró K, et al. Gyermek- és felnőttkorú daganatos férfiak nemzőképességének megőrzése [Fertility preservation of adult and prepubertal male

cancer patients]. Orv Hetil. 2023;164(51):2016-2023. Published 2023 Dec 24. doi:10.1556/650.2023.32953. *Classification: Q4*

4. **Vesztergom D**, Téglás Gy, Fónyad G, et al. A hazai meddőségi ellátás fejlesztési koncepciója [The concept for the development of infertility care in Hungary] *Nőgyógyászati és szülészeti továbbképző szemle*. 2023; 25(2), 45-50 (6).

5. Sipos M, Polgár Cs, **Vesztergom D,** et al. A Belügyminisztérium egészségügyi szakmai irányelve a daganatos nőbetegek termékenységének megőrzéséről. [Ministry of the Interior's health professional guide on fertility preservation for women with cancer] *Efészségügyi Közlöny*. 2024;74(5): 869-891.

6. Szigeti F, J., Soltész K., Sipos M., Juhász A., Szöllősi K., **Vesztergom D**., Ujma P. P., & Purebl, G. A pszichológiai szűrés és ellátás helye az asszisztált reprodukcióban [The role of psychological screening and care in assisted reproduction]. *Orv. Hetil.* 2024; *165*(12), 455–463. https://doi.org/10.1556/650.2024.33007 *D, Q Classification:* ***Q4***

List of original publications directly not related to the PhD thesis

1. **Vesztergom D**, Vita E, Szekrényes Á, Krádi A, Szöllősi K. Miért fagyasszunk? A petesejtek krioprezervációjával kapcsolatos megfontolások [Why should we freeze? Considerations in oocyte cryopreservation] *Magyar Nőorvosok Lapja, 2024, 87 : 2 pp. 70-74. , 5 p.*
2. **Vesztergom D**, Sipos M, Illés A, et al. A mikrobiom és az infertilitás kérdései [The microbiome and infertility] *Magyar Nőorvosok Lapja*, 2021; 84(3), 128-135.
3. **Vesztergom D**, Szomszéd O, Nagy T, et al. A Magyar fiatalok termékenységtudatossága [Fertility awareness of Hungarian youth] *Kapocs.* 2021; 4:3-4, 3-20:17

Abbreviations

AFC	antral follicle count
AMH	Anti-Müllerian Hormone
ART	assisted reproductive technology
BMI	Body Mass Index
CLBR	cumulative live birth rate
COC	cumulus-oocyte complex
CPR	clinical pregnancy rate
DET	double embryo transfer
ET	embryo transfer
FET	frozen embryo transfer
FIGO	International Federation of Gynecology and Obstetrics
FP	fertility preservation
FSS	fertility-sparing surgery
HRT	hormone replacement therapy
ICSI	Intracytoplasmic sperm injection
IUI	intrauterine insemination
IVF	in vitro fertilization
IVM	in vitro maturation
MII	Metaphase II
NEAK	National Health Insurance Fund of Hungary
OHSS	Ovarian hyperstimulation syndrome
OS	ovarian stimulation
PCOM	polycystic ovarian morphology
PCOS	Polycystic ovary syndrome
PR	pregnancy rate
SET	single embryo transfer

I. Introduction

The incidence of cancer increases with age, and as family planning has been delayed over the last decade, there is an increasing number of cancer patients whose fertility may be affected by oncological treatments [1]. Recent advances in cancer treatment have greatly improved quality of life after treatment [2]. However, the potential loss of fertility is a significant emotional burden for many young people [3]. For women of reproductive age diagnosed with cancer, fertility preservation (FP) strategies have become an essential part of their treatment, offering hope for future motherhood.

The decision to use FP requires careful consideration, counselling and a comprehensive assessment of multiple factors. These strategies are primarily based on preserving the reproductive organs, cryopreserving reproductive cells and tissues, and selecting the most appropriate intervention based on the time available before cancer treatment.

The primary goal is to achieve oncological outcomes that are non-inferior to those without FP, while optimizing reproductive outcomes. Most FP techniques have been available to women of reproductive age for several decades.

International guidelines recommend that all cancer patients of reproductive age, including adolescents, should receive fertility preservation counselling. If indicated, fertility preservation procedures should be performed as part of their comprehensive cancer care.

In Hungary, approximately 2,066 women under the age of 40 are diagnosed with cancer each year, according to the National Cancer Registry [4]. Approximately two thirds of these patients require gonadotoxic treatment for their disease, which can potentially reduce their chances of conceiving and giving birth in the future. With an incidence of 16 cases per 100,000, there are approximately 230-250 new cases each year. This means that approximately 80 adolescents and young adults should be referred for FP treatment each year [3,5].

As a result of our work, we have just published the Hungarian professional guideline on fertility preservation in women with cancer [6]. Unfortunately, there is still no established oncofertility program and network in Hungary. This gap in resources and guidance poses a significant challenge for cancer patients of reproductive age who wish to preserve their fertility while undergoing essential treatment.

II. Aims and objectives

In oncofertility counselling, it's important to provide patients with accurate information to help them make informed decisions about their options for conceiving after cancer. However, there is limited knowledge about the effectiveness of assisted reproductive technology (ART) treatment in women who have undergone fertility-sparing surgery (FSS), and there are few reports of in vitro fertilization (IVF) outcomes following FSS. It is therefore essential to have comprehensive information on ART outcomes.

Our research efforts are focused on three main aims:

1. Evaluation of oncofertility practices in Hungary:

- To evaluate the knowledge, attitudes and existing clinical practices of Hungarian oncologists in the field of oncofertility.

- To identify factors that may prevent young women with cancer from accessing fertility preservation programs.

- To develop an educational program tailored for clinicians (oncologists and fertility specialists) with the aim of improving network accessibility for cancer patients.

2. IVF outcomes in early stage cervical cancer:

- To evaluate the results of in vitro fertilization (IVF) in patients with early-stage cervical cancer who have undergone fertility-sparing procedures.

- To compare outcomes between radical and non-radical approaches in specific cases of oncofertility.

3. To explore innovative approaches to fertility preservation:

- To investigate the feasibility of incorporating new methods, such as in vitro maturation (IVM), into a fertility preservation program.

By addressing these objectives, our research aims to fill critical gaps in the understanding of oncofertility, contribute to informed patient decision making, and pave the way for improved fertility preservation options and accessibility in Hungary.

III. Materials and Methods

1. Evaluation of oncofertility practices in Hungary:

An online questionnaire on fertility prevention was sent to members of the Hungarian Oncology Society (MOT) in November 2020. The survey was completed in full by 94 oncology specialists and the data received were analyzed using R statistical software (v4.1.0).

2. IVF Outcomes in Early-Stage Cervical Cancer

Our retrospective analysis was based on data from Hungary's National Health Insurance Fund (2004-2022) from patients who underwent IVF treatment following FSS for early-stage cervical cancer at ten Hungarian fertility clinics. Patients were classified into radical and non-radical surgical groups, with the uterine arteries being spared in the non-radical procedures. RStudio (R software version: 4.2.2) was used for statistical analysis. Student’s t-test was used to compare group means, and Fisher's exact test was applied to assess independence and distributions between categorical variables, and to estimate odds.

3. Exploring Innovative Approaches in Fertility Preservation

Data abstraction was performed from medical records of two subfertile women with excessive functional ovarian reserve. Both women had previously received gonadotropins for ovulation induction or ovarian stimulation, resulting in ovarian torsion. They were offered IVM of oocytes retrieved from antral follicles after mild ovarian stimulation, fertilisation of mature oocytes using ICSI, and embryo transfer. Outcome measures were the incidence of complications and live birth after fertility treatment.

IV. Results

1. Evaluation of oncofertility practices in Hungary:

The majority (77%) of Hungarian oncologists who responded discuss the impact of cancer treatment on fertility with their patients, but only a small number of patients of childbearing age are actually referred. Half of the respondents said they rarely or never refer their patients to an infertility center, citing the lack of a fertility prevention network, adequate training and national guidelines. Oncologists and infertility specialists in Hungary should work more closely together, according to the majority of respondents (86%).

Barriers to patient referral for fertility preservation are summarized in Table 1.

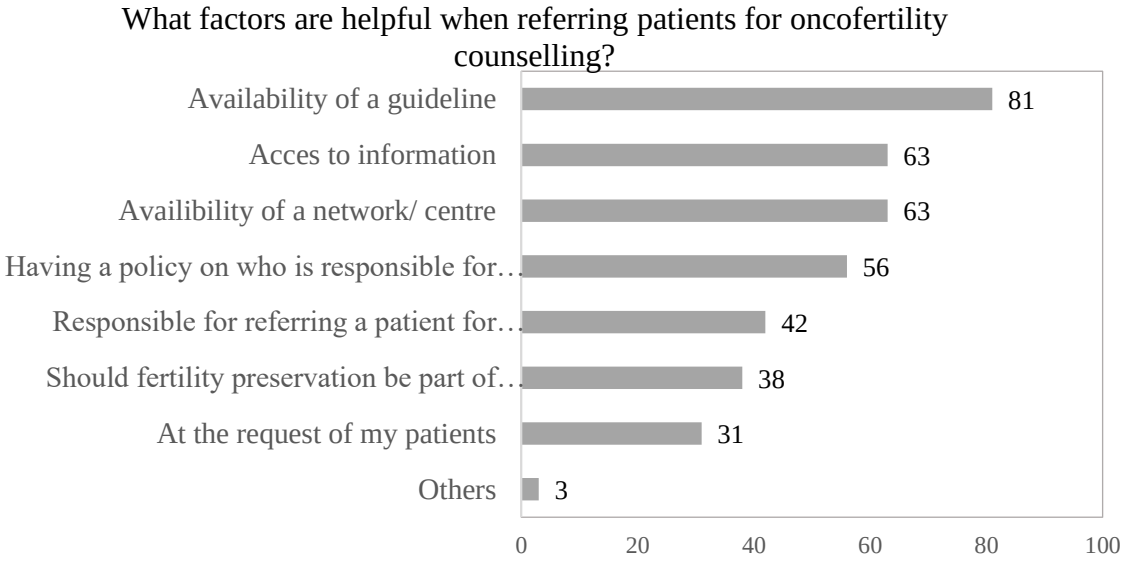
Table 1. Factors leading to oncologists not referring patients for assisted reproduction

Main reasons for not referring a patient for fertility preservation treatment

Response	(n)
Insufficient collaboration between oncologist/fertility specialist.	64
There is no time for fertility preservation because the tumor needs urgent treatment.	58
Cancer treatment is more important than fertility preservation.	55
The information I have about fertility preservation is not up to date.	54
Lack of fertility preservation network.	53
Patients don't know that cancer treatment and fertility preservation can co-exist.	51
When a tumor is detected, the psychological burden of dealing with the loss of fertility is high.	35
Ovarian stimulation is considered dangerous in hormone receptor-positive gynaecological and breast cancers.	32
Short consultation time.	29
I don't think it's clear who has to tell the patient.	24
In the case of breast cancer, I am concerned about the oncological risk of subsequent pregnancies.	16
The patient is frightened by the prospect of fertility treatment.	8
I think the success rate of assisted reproduction is low.	2
Other	7

Regarding referral practices, 86% of respondents felt that a multidisciplinary oncofertility guideline would be beneficial. Targeted education of professionals, an oncofertility network and accessible contacts (hotline) were identified as critical factors that would facilitate patient referral for fertility preservation, as shown in Figure 1.

Figure 1: Factors influencing referral for oncofertility treatment



In terms of geographical differences, oncologists in the capital showed greater awareness of assisted reproduction centers (55%) than their rural counterparts (39%).

2. IVF Outcomes in Early-Stage Cervical Cancer

In our study we analyzed data from 122 IVF treatment cycles involving 36 patients. The non-radical group had a significantly higher live birth rate (83%, 5/6) compared to the radical group (17%, 5/30). Additionally, the non-radical group had a significantly higher implantation rate and cumulative live birth rate per oocyte retrieval (37%, 7/19 and 55%, 6/11 respectively) compared to the radical group (8%, 12/148 and 6%, 5/80 respectively).

Table 2. summarizes patient and tumor characteristics.

Table 3. summarizes the ovarian stimulation outcomes and patient characteristics

Table 4. summarizes the IVF outcomes after fertility-sparing surgery.

Table 2. Patient and tumor characteristics

	Group			
	All patients	**Non-radical group**	**Radical group**	***P* value**
Number of patients, n	36	6	30	
Mean age at FSS, y (range)	31.7 (23-37)	31 (26-35)	30.2 (23-37)	
Nulliparous, n (%)	31 (86.1%)	5 (83.3%)	26 (86.7%)	
Stage distribution (FIGO 2018)				**<0.01**
IA1, n (%)	4 (11.1%)	4 (66.7%)	0 (0%)	
IA2, n (%)	3 (8.3%)	1 (16.7%)	2 (6.7%)	
IB1, n (%)	24 (66.7%)	1 (16.7%)	23 (76.7%)	
IB2, n (%)	3 (8.3%)	0 (0%)	3 (10%)	
IB3, n (%)	2 (5.6%)	0 (0%)	2 (6.7%)	
Histology				
Squamous cell carcinoma	20 (55.6%)	3 (50%)	17 (56.7%)	
Adenocarcinoma	12 (33.3%)	1 (16.7%)	11 (36.7%)	
Adenosquamous carcinoma	2 (5.6%)	2 (33.3%)	0 (0%)	
Other epithelial tumors	2 (5.6%)	0 (0%)	2 (6.7%)	
Type of FSS				
ART with bilateral ligation of uterine arteries, n (%)	30 (83.3%)	0 (0%)	30 (100%)	N/A
ART with preservation of uterine arteries non-radical, n (%)	1 (2.8%)	1 (16.7%)	0 (0%)	
Simple trachelectomy non-radical, n (%)	5 (13.9%)	5 (16.7%)	0 (0%)	
Cervical stenosis, n (%)	6 (16.7 %)	1 (16.7 %)	5 (16.7 %)	**1**
Median follow-up , y	13.6	16.4	13.2	
Note: FSS= Fertility-sparing surgery ; ART= Abdominal radical trachelectomy				

Table 3. Ovarian stimulation outcomes and patient characteristics

	Group			
	All patients	**Non-radical**	**Radical**	***P* value**
Mean time interval from FSS to first oocyte retrieval, days	1681	1864	1644	**0.6938**
Mean age at the first oocyte retrieval, y	35.1	36.2	34.9	**0.4703**
BMI, mean (kg/m^2)	22.9	24.3	22.7	**0.2264**
AMH, mean (ng/ml)	2.5	4.1	2.3	**0.2878**
Male infertility	4 (11.1%)	0 (0%)	4 (13.3%)	
Other causes of infertility in women	12 (33.3%)	2 (33.3%)	10 (33.3%)	
Stimulation cycles	91	11	80	

Mean number of ovarian stimulation cycles (per patient)	2.4	1.7	2.7	
Mean number of retrieved oocytes in the first cycle	7.1	8.3	6.8	**0.4647**
Fertilization rate	53% (311/585)	55% (37/67)	53% (274/518)	
Mean FSH dosage at the 1. cycle (IU)	1811	1800	1815	**0.9597**
OS response (mean FSH dosage per matured oocyte at the 1. cycle) (IU)	282	243	303	
Note: OS= Ovarian stimulation; FSS=Fertility-sparing surgery				

Table 4. Outcomes of in vitro fertilization after fertility-sparing surgery in the non-radical compared to the radical group

	Group			
	All patients	**Non-radical group**	**Radical group**	***P* value**
Patients, n	36	6	30	
Stimulation cycles, n	91	11	80	
Embryos, n	311	37	274	
Embryo transfers, n	95	11	84	
Pregnancies, n	17	7	10	
Miscarriage, n (%)	35% (6/17)	17% (1/7)	50% (5/10)	**0.3043**
1 st trimester miscarriage, n	4	1	3	
2 st trimester miscarriage, n	2	0	2	
Implantation rate, %	11% (19/167)	37% (7/19)	8% (12/148)	**0.0017**
CLBR per oocyte retrieval, %	12% (11/91)	55% (6/11)	6% (5/80)	**0.0002**
Clinical PR per embryo transfer, %	18% (17/95)	64% (7/11)	12% (10/84)	**0.0004**
Women with live birth, %	28% (10/36)	83% (5/6)	17% (5/30)	**0.0035**
Preterm birth <37 weeks of pregnancy, n (%)	63.6 % (7/11)	50 % (3/6)	100 % (5/5)	**0.1818**
24-32 weeks	14.3% (1/7)	0% (0/3)	40% (2/5)	
32-37 weeks	85.7% (6/7)	100% (3/3)	60% (3/5)	
Average gestational age at birth, w	33.5	35.5	31	**0.0758**
Average fetal birth weight, g	2203	2787	1473	**0.0515**
Note: CLBR= cumulative live birth rate; FSS= Fertility-sparing surgery; PR = pregnancy rate.				

3. Exploring Innovative Approaches in Fertility Preservation

Both patients underwent transvaginal retrieval of cumulus-oocyte complexes from a single ovary. One patient had a singleton live birth after vitrified embryo transfer in her second IVM cycle. The other patient had a singleton live birth after fresh blastocyst transfer in her first IVM cycle.

Table 5 summarizes patient characteristics and IVM cycle outcomes.

Table 5: Baseline patient characteristics and IVM cycle outcome

	Patient 1		Patient 2
Baseline patient characteristics*			
Age (years)	25		30
BMI (kg/m^2)	16.5		19.4
AMH (ng/mL)	24.5		12.3
AFC (*N*)	60		30
FSH (IU/L)	<0.1		7.5
LH (IU/L)	<0.1		8.8
Progesterone (nmol/L)	1.34		0.64
E2 (ng/L)	32.0		28.0
IVM cycle outcome	Cycle 1	Cycle 2	
COC retrieved (*N*)	70	77	30
MII oocytes (*N*)	35	37	25
2PN oocytes (*N*)	25	22	21
Cleavage-stage embryos (*N*)	17	7	20
Cryopreserved embryos (*N*/stage)	0	7 (d3)	7 (d5)
Fresh ET (*N*/stage)	1/BL4BB (d5)	0	1/BL4AA (d5)***
eFET (*N*/stage)**	N/A	4	N/A
eFET no. 1		1/8c gr2 (d4)	
eFET no. 2		1/C2 gr1 (d4)	
eFET no. 3		1/5c gr3 (d4)	
eFET no. 4		2/BL1 gr2, C2 gr2 (d4)***	
Live birth	0	1	1

COC cumulus-oocyte complex, *MII* metaphase II, *2PN* two pronuclei, *ET* embryo transfer, *SET* single embryo transfer, *DET* double embryo transfer, *Y* yes, *N* no

*Patient characteristics at intake (after unilateral oophorectomy)

**Cleavage-stage embryos were vitrified on day 3; embryo transfer was performed 1 day after embryo warming

***Resulting in live birth

V. Discussion

1. Evaluation of oncofertility practices in Hungary

This study provides a comprehensive overview of oncofertility treatment in Hungary through a questionnaire survey of oncologists.

In general, respondents demonstrate a proactive approach to fertility preservation, the majority of the responding oncologists actively consider the possibility of fertility preservation for their young female and male cancer patients. In 77% of cases, respondents inquire whether patients under the age of 40 express a desire to have children in the future, while 79% systematically consider the gonadotoxic effects of treatment and discuss them with patients in 85% of cases. However, the actual referral rate to fertility centers remains low [7]. Almost half of the respondents (45%) said that they do not or rarely refer their patients to a fertility center, and 13% do not mention fertility preservation methods to patients undergoing oncological treatment. The majority of oncologists are unsure about who is responsible for providing fertility preservation treatment, and a significant proportion do not know of any institution in Hungary that deals with this issue.

Our study emphasizes the need for patient education and counseling based on established professional guidelines. There were no established professional guidelines for fertility preservation in Hungary at the time of our survey. In addition to the lack of professional guidelines, a notable challenge is the limited awareness among oncologists of the different fertility preservation techniques. Satisfaction with knowledge ranges from 5% to 25%, depending on the method [8]. This is highlighted by the remarkable perception of half of the oncologists that embryo cryopreservation is not an available method, although it is one of the most commonly used assisted reproductive techniques. A significant majority of Hungarian oncologists surveyed (60%) believe that it would be beneficial to provide patients with adequate information in this area. According to our study, poor collaboration between oncologists and infertility specialists, lack of dedicated network and lack of up-to-date information are barriers in the patient pathway. In contrast, countries such as the UK have better collaboration due to the existence of networks, and the main factor influencing the oncologist's decision to refer a patient for FP is the patient's clinical condition alone [9].

In conclusion, a well-functioning system should facilitate the counseling of patients for fertility preservation. In order to improve referral rates and to ensure comprehensive care for patients

with cancer, it is essential to improve education and cooperation between oncologists and fertility preservation networks.

2. IVF Outcomes in Early-Stage Cervical Cancer

This is the largest retrospective study evaluating IVF outcomes in young, infertile cervical cancer survivors who had previously undergone FSS. All patients included underwent FSS for early-stage cervical cancer followed by IVF treatment at 10 different fertility clinics in Hungary between 2006 and 2022.

The live birth rate following IVF treatment was almost five times higher in the non-radical group than in the radical group. This statistically significant difference underlines the major impact of the radicality of fertility-sparing surgery on reproductive outcomes. Both the pregnancy rate per embryo transfer (PR) and the cumulative live birth rate per oocyte retrieval (CLBR) were significantly higher in the non-radical group.

In general, age is the primary factor affecting fertility, influencing both the quantity and quality of oocytes. Remarkably, in our study, the radical group had a lower mean age at the first oocyte retrieval but achieved a significantly lower CLBR following IVF treatment.

Cervical stenosis is a well-known cause of infertility after FSS [10,11], occurred in similar proportions in both surgical groups. These results suggest that it is not the cervical stenosis itself but the radicality of the surgical procedure that may be associated with reduced fertility.

According to our results, although higher doses of gonadotropins may be required, ovarian stimulation results and fertilization rates are similar in both radical and non-radical FSS groups.

Infertility may also be due to factors such as cervical shortening and changes in cervical mucus characteristics [12]. In addition, recent research has shown that conization can affect the vaginal microbiota, potentially leading to an increased risk of preterm birth [13]. Furthermore, a dysbiotic microbiota profile in the female reproductive tract is associated with poor reproductive outcomes in patients undergoing assisted reproduction [14].

Other factors, such as impaired uterine perfusion and lower implantation rates in the radical group, may also contribute to lower IVF success [15–17]. Despite comparable ovarian response, patients who underwent radical FSS had significantly lower implantation rates, probably due to the extensive surgical approach leading to myometrial and endometrial ischaemia. This may be this is the key factor explaining the poorer IVF outcome in patients in whom the uterine arteries were sacrificed during FSS. Studies evaluating pregnancy outcomes after FSS report variable

success rates depending on the surgical approach, with non-radical approaches showing better reproductive outcomes [18, 19]. A study by Plante et al showed that only 16% of patients had fertility problems after non-radical surgery [20].

In terms of obstetric outcomes, higher rates of prematurity and miscarriage were observed in the radical group, highlighting the potential risks associated with extensive surgical procedures. [21]. The study highlights the safety of conservative surgery for early, low-risk cervical cancer, which is supported by recent trials showing comparable oncological outcomes with fewer side effects and potentially better quality of life.

Strengths of the study include its comprehensive patient coverage, meticulous data collection, centralized patient management, and long-term follow-up. However, limitations such as the retrospective design, small sample size in the non-radical group, and differences in tumor stage distribution require larger prospective studies to provide definitive results on the impact of radical and non-radical FSS on reproductive and obstetric outcomes in cervical cancer survivors.

3. Exploring Innovative Approaches in Fertility Preservation

Our study sheds light on the safe and successful use of in vitro maturation (IVM) in patients with high functional ovarian reserve. These patients are not only at risk of ovarian hyperstimulation syndrome (OHSS), a common adverse event associated with ovarian stimulation (OS), but also face other potentially serious complications of fertility treatment. We would like to emphasize the importance of remaining vigilant in the management of these high responders, even in the era of low incidence of OHSS.

Although rare (0.08 to 0.2% [22]), ovarian torsion remains a significant fertility problem with potential consequences including ovarian loss [23–25]. We emphasize the need for a conservative surgical approach when torsion occurs, as unilateral oophorectomy may adversely affect fertility outcomes. Although ovarian stimulation is a known risk factor for torsion due to ovarian hypertrophy, early diagnosis and intervention are essential to preserve ovarian viability.

Patients with polycystic ovarian morphology (PCOM) and polycystic ovarian syndrome (PCOS) are particularly at risk of developing OHSS following OS [26,27]. Although pre-stimulation parameters such as antral follicle count (AFC) and anti-Müllerian hormone (AMH) levels can predict a high ovarian response, their utility in predicting OHSS and torsion risk remains limited. Our findings underscore the lack of correlation between ovarian parameters and torsion risk and highlight the need for further research in this area. Patients with severe

functional ovarian reserve, IVM is emerging as a safe alternative to conventional OS [28–34]. Proper patient selection is crucial, as high responders can provide sufficient immature oocytes for IVM, compensating for its lower efficiency compared to standard IVF.

VI. Conclusions

1. Evaluation of oncofertility practices in Hungary:

Our study is the first step in the establishment of a national oncofertility network and highlights the importance of effective communication and collaboration between oncologists and reproductive specialists for successful fertility preservation.

Encouragingly, the majority of oncologists surveyed are interested in fertility preservation. They take patients' preferences into account, discuss treatment-related fertility risks and refer patients for counselling when necessary. However, the results highlight the need for further education and training of oncologists in this area. The establishment of common guidelines and a national fertility preservation network is considered crucial to ensure better patient access to fertility preservation treatments before starting cancer treatment.

2. IVF Outcomes in Early-Stage Cervical Cancer

For women of reproductive age with early-stage cervical cancer, fertility-sparing strategies have become essential to offer the prospect of future motherhood. Fertility-sparing surgery (FSS) aims to maintain oncological efficacy while optimizing reproductive outcomes. However, radical approaches carry significant morbidity risks, leading to a recent trend towards less aggressive surgical approaches for low-risk cervical cancer.

Our study suggests that non-radical FSS in patients with low-risk cervical cancer is associated with improved IVF outcomes compared with radical surgery. Radical procedures with uterine artery ligation were associated with a lower implantation rate and cumulative live birth rate. These findings highlight the importance of considering both oncological safety and reproductive outcomes when choosing an FSS for patients with early-stage cervical cancer. They also emphasize the need for comprehensive patient counselling and clinical decision-making. Further research is needed to strengthen the evidence for both the oncological safety and reduced morbidity of these approaches.

3. Exploring Innovative Approaches in Fertility Preservation.

In fertility preservation programs, in vitro maturation (IVM) may be offered as an alternative approach when conventional ovarian stimulation is not feasible or when conventional ovarian stimulation is contraindicated or when there is insufficient time to delay the initiation of gonadotoxic treatment for ovarian stimulation. However, due to its innovative nature, IVM requires specialized expertise [35]. Our study highlights the potential of IVM as a patient-friendly approach for high responders at risk of serious complications with conventional OS. However, further research is warranted to validate the safety and efficacy of IVM in a larger cohort of predicted high responders.

IVM following ex vivo oocyte retrieval from ovarian specimens maximizes the potential for fertility preservation in patients undergoing surgical removal of ovarian tissue. Immature oocytes can be retrieved from ovariectomy specimens during tissue processing for cryopreservation. This is particularly useful in cases such as ovarian cancer treatment. However, it's important to note that IVM after ex vivo retrieval is experimental and requires approval from a medical research ethics committee [35].

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VIII. References

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