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ARTICLE

Fertility-preservation counselling and treatment for medical reasons: data from a multinational network of over 5000 women

Michael von Wolff [a,*,1], Ralf Dittrich [b,1], Jana Liebenthron [c,1], Frank Nawroth [d,1], Andreas N Schüring [e,1], Thomas Bruckner [f], Ariane Germeyer [g,1]

[a] *Division of Gynaecological Endocrinology and Reproductive Medicine, Women's University Hospital, Effingerstrasse 102, 3010 Berne, Switzerland;* [b] *Women's University Hospital, Friedrich-Alexander University of Erlangen–Nuremberg, Universitätsstraße 21-23, 91054 Erlangen, Germany;* [c] *Division of Gynaecological Endocrinology and Reproductive Medicine, Women's University Hospital, Sigmund-Freud-Str. 25, 53127 Bonn, Germany;* [d] *Centre for Fertility, Prenatal Medicine, Endocrinology and Osteology, amedes, Mönckebergstraße 10 (Barkhofpassage), 20095 Hamburg, Germany;* [e] *Infertility Center, Women's University Hospital, Albert-Schweitzer-Campus 1, Building D11, Münster, Germany;* [f] *Institute of Medical Biometry and Informatics, University of Heidelberg, Im Neuenheimer Feld 105, 69120 Heidelberg, Germany;* [g] *Division of Gynaecological Endocrinology and Reproductive Medicine, Women's University Hospital, Im Neuenheimer Feld 440, 69120 Heidelberg, Germany*

* Corresponding author. *E-mail address:* michael.vonwolff@insel.ch (M von Wolff). [1] Representing the network *Ferti*PROTEKT.

Professor Michael von Wolff is Head of the Division of Gynaecology and Reproductive Medicine at the Women's University Hospital, Berne, Switzerland. He trained in Aachen, Munich and Heidelberg in Germany as well as in London, New York and Switzerland. His main interests are the regulation of folliculogenesis, natural cycle IVF and fertility preservation in women. He initiated the ESHRE Task Force for fertility preservation. Furthermore he established and is head of the German speaking network FertPROTEKT (www.fertiprotekt.com), one of the largest networks for fertility preservation.

Abstract Fertility-preservation techniques for medical reasons are increasingly offered in national networks. Knowledge of the characteristics of counselled patients and techniques used are essential. The *Ferti*PROTEKT network registry was analysed between 2007 and 2013, and included up to 85 university and non-university centres in Germany, Austria and Switzerland; 5159 women were counselled and 4060 women underwent fertility preservation. In 2013, fertility-preservation counselling for medical reasons increased significantly among nullipara and women aged between 21 and 35 years ($n = 1043$; $P < 0.001$). Frequency of GnRH applications slowly decreased, whereas tissue, oocytes and zygote cryopreservation increased. In 2013, women with breast cancer mainly opted for tissue freezing, whereas women with lymphoma opted for GnRH agonist. Women younger than 20 years predominantly opted for GnRH agonists and ovarian tissue cryopreservation; women aged between 20 and 40 years underwent a variety of techniques; and women over 40 years opted for GnRH agonists. The average number of aspirated oocytes per stimulation cycle decreased as age increased (<30 years: 12.9; 31–35 years: 12.3; 36–46: 9.0; > 41 years: 5.7). For ovarian tissue cryopreservation, removal and cryopreservation of fewer than one ovary was preferred and carried out in 97% of cases in 2013.

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Introduction

The report of the first live birth following transplantation of ovarian tissue in 2004 (Donnez et al., 2004) has substantially accelerated the implementation of fertility preservation programmes for medical reasons. Furthermore, since the first reviews about the putative protective effect of gonadotrophin-releasing hormone (GnRH) agonists on ovarian function in 2008 (Blumenfeld and von Wolff, 2008), and the report about the high efficacy of unfertilized vitrified oocytes in 2010 (Rienzi et al., 2010), the reproductive physician can currently choose between a broad spectrum of fertility-preservation techniques. These techniques allow treatment approaches to be individualized according to patient's age, to the gonadotoxicity of the treatments, and to the available time frame.

At that time, it also became apparent that because of the complexity of the involved treatments, and because of the need to integrate fertility-preservation counselling and treatment into the oncological treatment protocols, local, national or even international co-operation and multidisciplinary networks were urgently required. Accordingly, networks such as *Ferti*PROTEKT (2014), covering Germany, Austria and Switzerland, and the Oncofertility Consortium (2015), covering the USA, were founded in 2006 and 2007, respectively.

Furthermore, to support physicians and oncologists in this rapidly evolving complex area, these networks (von Wolff et al., 2011) as well as national (Loren et al., 2013; Practice Committee of American Society for Reproductive Medicine, 2013) and international (ISFP Practice Committee et al, 2012) societies have published several recommendations. According to these recommendations, the technique most frequently recommended is ovarian stimulation to cryopreserve oocytes, zygotes or embryos. Those techniques not explicitly recommended, such as cryopreservation of ovarian tissue and GnRH agonists, have also recently been suggested to be effective (Dittrich et al., 2015; Donnez et al., 2013; Liebenthron et al., 2015; Moore et al., 2015). In addition, ethics committees of national societies have prepared several statements about the ethical issues related to the welfare of patients and offspring (Ethics Committee of American Society for Reproductive Medicine, 2013).

In contrast, data about the actual number of patients being counselled and treated by fertility- preservation techniques, the distribution of the applied techniques and patients' characteristics are limited. The network *Ferti*PROTEKT has published preliminary data, but analysis has not been conducted longitudinally in recent years. Rather it has been limited to women aged between 15 and 40 years, and a detailed analysis about the relationship between patients' characteristics and the type of treatment selected, as well as any changes throughout the years, has not been carried out (Lawrenz et al., 2011).

Data from representative multinational registries are essential for understanding the current status of fertility preservation so that fertility-preservation programmes can be improved. Data from the *Ferti*PROTEKT network registry (FertiPROTEKT), which involves 85 documenting centres, were analysed. The duration of analysis was from the start of fertility preservation in 2007 until 2013, when these techniques were already implemented in many oncological treatment protocols.

Materials and methods

The *Ferti*PROTEKT network

The *Ferti*PROTEKT network was founded in 2006 to offer fertility-preserving techniques, initially in Germany, then also to neighbouring German-speaking countries, Austria and Switzerland. The aim was to scientifically evaluate and improve the techniques and make them part of oncological treatment protocols. Initially, all university fertility clinics were included; private fertility centres were subsequently incorporated.

To ensure high-quality counselling and treatment, and to keep up to date with the rapid developments in the specialty, all centres were required to attend an annual 2-day workshop. Standardized storage of ovarian tissue is ensured through central cryobanks. Support in treatments is further given by the recommendations made by the network, which are published internationally (von Wolff et al., 2011), and by a bilingual website in German and English (www.fertiprotekt.com), which is available for doctors and patients.

The network's registry

A registry, which includes details of all treatments given, complications and pregnancies was established in 2007. Physicians are required to complete a questionnaire about basic patient information, such as age, disease and oncological treatment. Furthermore, details about the fertility-preservation technique selected are added. In cases of ovarian tissue cryopreservation, type of abdominal surgery, amount of ovarian tissue removed and site of storage are documented. In cases of ovarian stimulation, timing of ovarian stimulation, number of stimulation days, gonadotrophin dosage, number of collected oocytes, fertilization technique and number of fertilized oocytes are included. In addition, use of GnRH agonist, any combination of the specified therapies and data about complications are documented. Finally, data about ovarian tissue retransplantation and embryo transfers are added. The data sheets are sent to a centrally located university-based infertility centre, where data are added to the registry's software on a weekly basis.

The data are analysed annually, presented at an annual workshop held by the network, and basic data are made publicly available through the *Ferti*PROTEKT website. For this present study, data from 5159 counselled women were analysed. Data concerning the final outcome of the treatments, such as ovarian tissue retransplantation, have been described elsewhere (Dittrich et al., 2015; Liebenthron et al., 2015).

For clarity, first total numbers of counselling sessions and treatments were calculated (**Figure 1**). Patients'

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