ARTICLE

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Fertility Preservation Programme in a Tertiary-Assisted Reproduction Unit in Hong Kong

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ABSTRACT

Background: Fertility preservation is increasingly important with improving cancer survival rates and the delay in childbearing in modern societies. The objective of our study was to review the experience of the fertility preservation programme in a tertiary-assisted reproduction unit in Hong Kong.

Methods: This is a retrospective study involving men and women who were seen at a tertiary-assisted reproduction unit for fertility preservation counselling before gonadotoxic treatment from January 2005 to December 2020. Their medical records in paper and electronic forms were reviewed.

Results: There were 75 consultations for female fertility preservation from 2010 to 2020 involving 72 women. Twenty women underwent 22 cycles of ovarian stimulation for oocyte or embryo cryopreservation, two of whom subsequently transported their oocytes abroad for further management and another two achieved natural conception. Additional four women who did not have oocyte or embryo cryopreservation achieved natural conception after cancer treatment. Eleven (15.2%) women were followed up at a reproductive endocrinology clinic after their cancer treatment. From 2005 to 2020, 265 men had sperm cryopreserved. Twenty-six (9.8%) came back to use the cryopreserved sperms, the wives of 13 (50.0%) of whom achieved an on-going pregnancy. Six of them transferred out and 40 discarded the cryopreserved sperms.

Conclusions: There was generally an increasing number of patient consultations for fertility preservation in our Centre over the past decade but a consistently low rate of utilisation of cryopreserved gametes for both women and men. Post-cancer treatment fertility evaluation and monitoring was a major area of deficiency in Hong Kong. More structured post-cancer treatment fertility follow-up is needed.

***Keywords*:** Cancer; Fertility Preservation; Oocyte Cryopreservation; Embryo Cryopreservation; Sperm Cryopreservation.

INTRODUCTION

Improvements in cancer treatment over the years have significantly improved the survival of patients suffering from different types of cancers. The 5-year survival rates of childhood and adolescent cancers have been improved to more than 80% in developed countries (Bhakta et al., 2019). However, surgery, chemotherapy and radiotherapy for cancer treatment can permanently destroy oocytes and sperm as well as cause DNA abnormalities in the gametes, rendering young women and men infertile after cancer treatment (Morgan et al., 2012). These young cancer survivors despite cure of their cancer often suffer the long-term mental and social consequences of gonadal dysfunction and infertility, which are in many cases irreversible (Geenen et al., 2007; Oeffinger et al., 2006).

Fertility preservation refers to procedures of saving or protecting the oocytes, sperm or reproductive tissue during gonadotoxic treatment so that the patient can use them to have biological children in the future. Fertility preservation before cancer treatment can allow cancer patients to focus on their treatment with the knowledge and hope that they can still create their desired family when they recover. The main fertility preservation options available include sperm cryopreservation for men, and oocyte, embryo or ovarian tissue cryopreservation for women. Recent guidelines from American Society of Clinical Oncology (ASCO) (Oktay et al., 2018), American Society for Reproductive Medicine (ASRM) (Practice Committee of the ASRM, Electronic address, 2019) and European Society of Human Reproduction and Embryology (ESHRE) (Preservation EGGoFF et al., 2020) all recognise the importance of counselling patients of reproductive age on the effects of cancer treatment on their fertility potential, and fertility preservation options before they undergo gonadotoxic cancer treatment.

Previous local studies in Hong Kong have demonstrated poor awareness of fertility preservation among local clinical oncologists,

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haematologists, gynaecologists, paediatricians and surgeons in public hospitals (Chung et al., 2017), as well as low utilisation of sperm cryopreservation in male cancer patients (Chung et al., 2013). In this retrospective study, we aim to review the experience of the fertility preservation programme in a tertiary-assisted reproduction unit. It is hoped that more insight can be gained into the local situation of fertility preservation over the years so as to improve fertility care before and after cancer treatment.

METHODS

This is a retrospective study involving men and women who were seen at the Centre of Assisted Reproduction and Embryology, The University of Hong Kong, Queen Mary Hospital, Hong Kong, for fertility preservation counselling before gonadotoxic treatment. Our study included data on sperm cryopreservation for men since 2005 and fertility preservation counselling for women since 2010 until December 2020. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

Patients who were going to receive cancer treatment were referred to our Centre from their parent medical teams if they expressed the wish to discuss about options of fertility preservation. Those who were planned to undergo cytotoxic treatment for benign diseases may also be eligible for fertility preservation as judged on an individual basis, and provided, in the cases of women, that their medical illness did not preclude future fitness for pregnancy. Non-medical or social oocyte freezing was not offered in the Centre.

At the first consultation, a detailed history was taken and the indication for sperm, oocyte or embryo cryopreservation was identified. The fertility preservation options, procedures and risks, duration of freezing, disposal of frozen gametes and charging policy were gone through in detail should if the patient wished to proceed. Written consent was obtained from the patient or the guardian prior to freezing of the gametes or embryos. Embryo cryopreservation could only be offered to women who were legally married.

Men who wished to proceed with sperm cryopreservation prior to gonadotoxic treatment submitted one or two semen samples by masturbation. The samples were analysed before freezing according to the World Health Organisation laboratory manual for the examination of human semen and sperm-cervical mucus interaction (4th edition, 1999 or 5th edition, 2010) depending on the year the man was seen. When there were more than one semen samples saved, the one with a higher total motile count was used for analysis. The liquefied samples were mixed with freezing medium (TEST Yolk Buffer, Irvine Scientific, Santa Ana, USA) in 1:1 ratio. The mixture was aliquoted in cryogenic vials and was allowed to equilibrate for 15 minutes at room temperature. A programmable freezer (Kryo-360, Planer PLC, Sunbury-On-Thames, UK) was used to freeze the semen samples. The freezing programme consisted of five steps: (1) cooling from 20°C to 2°C (−1°C/minute); (2) holding for 5 minutes; (3) cooling from 2°C to −3°C (−10°C/minute); (4) cooling from −3°C to −20°C (−6°C/minute); (5) cooling from −20°C to −90°C (−10°C/minute). The vials were immersed into liquid nitrogen tank when the freezing program was completed.

For women who opted for oocyte or embryo cryopreservation, oocytes were retrieved in a stimulated cycle as previously described (Yeung et al., 2014). If they did not present close to the first day of their menstrual cycles, recombinant follicle stimulating hormone (FSH) for ovarian stimulation was started on any day of the menstrual cycle in either the follicular phase or the luteal phase ('random-start') using a gonadotrophin releasing hormone (GnRH) antagonist protocol. Double stimulation was not used. GnRH antagonist (subcutaneous ganirelix or cetrorelix) 0.25 mg daily was given from the sixth day of FSH administration. Letrozole was used throughout ovarian stimulation in cases of hormone sensitive cancers like breast cancer. Transvaginal ultrasound scan was performed for follicular tracking 7 days after the start of FSH injection and every 1–3 days thereafter, depending on the ovarian response. Recombinant hCG (human chorionic gonadotrophin Ovidrel®, Serono, Bari, Italy) 0.25 mg or GnRH agonist (0.2 mg subcutaneous triptorelin) was given when there were three follicles >17 mm in diameter.

Transvaginal ultrasound-guided oocyte retrieval under conscious sedation was scheduled 34–36 hours after hCG or GnRH agonist injection. Oocytes and blastocysts were cryopreserved by vitrification. Oocytes were immersed for 1 minute in basic solution (without cryoprotectant) and then gradually exposed to equilibration solution (consisted of 7.5% v/v dimethylsulphoxide (DMSO) and 7.5% v/v ethylene glycol) for 9 minutes. For blastocysts, they were exposed to equilibration solution for 10 minutes. The oocytes/blastocysts were then immersed in vitrification solution (consisting of 15% v/v DMSO, 15% v/v ethylene glycol, 0.5 mol/l sucrose) for 30 seconds before loading on the fibreplug (Cryologic, Victoria, Australia). Vitrification was carried out by direct contact to a sterile surface of a pre-chilled metal block for 15 seconds (Cyrologic). The fibreplug was then transferred to a liquid nitrogen tank. Cleavage stage embryos were frozen by slow freezing protocol by a programmable freezer (kryo-360). Sucrose and 1,2-propanediol were used as cryoprotectant. The freezing program consisted of four steps: (1) cooling from 20°C to −7°C (−2°C/minute); (2) soaking for 5 minutes followed by manual seeding and soaking for another 10 minutes; (3) cooling from −7°C to −30°C (−0.3°C/minute); (4) cooling from −30°C to −120°C (−30°C/minute). The straws were then transferred into a liquid nitrogen tank for long-term storage.

The use of monthly or three-monthly GnRH agonist during chemotherapy as an option for ovarian function protection was discussed for those who had to undergo chemotherapy. Women were advised to be referred back to our reproductive endocrinology clinic for assessment of ovarian function and review and consideration of hormone replacement therapy after completion of cancer treatment. Men were advised to have a semen analysis 1–2 years after completion of chemotherapy.

The provision of reproductive technology procedures, the handling, storing or disposal of gametes or embryos used or intended to be used in connection of a reproductive technology procedure is regulated by the Code of Practice of the Council on Human Reproductive Technology in Hong Kong. The maximum period for storing sperm or oocytes for medical reasons is 10 years or until the patient reaches the age of 55 years, whichever is later, but a shorter storage period can be specified by the patient. There is no minimal age for storage of sperm or oocytes. In general, parental consent is sought for persons below 18 years old, but the situation is assessed on an individual basis and younger people can also consent to fertility preservation if Gillick competent. The storage period is renewed every 2 years in the Centre. The stored gametes can be used for assisted reproductive procedures only when the patient is legally married. Post-humous use of gametes or embryos is not allowed in Hong Kong. The gametes will be discarded or donated for research after the death of the patient or when the agreed storage period has elapsed.

Starting from August 2020, a public-funded fertility preservation service was introduced for patients in the Centre. Eligibility criteria for public funding included current age being less than 35 years, absence of a living child, having a high risk of gonadal insufficiency after cancer treatment, predicted survival rate of more than 50% after

cancer treatment, having no prior chemotherapy or radiotherapy, as well as having antral follicle count of more than seven on pelvic scanning. The newly established public-funded programme currently does not include benign diseases other than cancer (e.g. systemic lupus erythematosus) that are treated with gonadotoxic drugs or genetic conditions (e.g. Turner syndrome) owing to limited resources.

The medical records in paper and electronic forms were reviewed for demographic data, type of cancer, cancer treatment, fertility preservation method chosen, cycle characteristics of ovarian stimulation, semen analysis, reproductive outcome and follow up if available. In Hong Kong, an electronic patient health record platform enables authorised healthcare providing organisations in all clinics and hospitals in the public sector (and recently some private providers) to access and share participating patients' electronic health records for healthcare purpose.

STATISTICS

Data were analysed using IBM SPSS software (SPSS 26.0, IBM Corporation, NY, USA) and presented as median (25th–75th percentile or range as specified) or number (percentage).

RESULTS

The number of consultations for fertility preservation counselling per year for women and the number of sperm freezing per year for men in the study period were shown in Figs. 1 and 2, respectively.

Women

There were 75 consultations for female fertility preservation from 2010 to 2020 involving 72 women. Three women were consulted twice as they were seen again when the disease was better controlled. Two women were excluded from further analysis–one who had hypogonadotrophic hypogonadism and one who received one single dose of chemotherapy for suspected gestational trophoblastic disease. The demographics and cancer outcomes of these women are shown in Table 1.

Twenty women underwent 22 cycles of ovarian stimulation for oocyte or embryo cryopreservation (Table 2), of which two women underwent two stimulation cycles each. Among them, 12 cryopreserved oocytes, 7 cryopreserved embryos/blastocysts (4 at cleavage stage and 3 at blastocyst stage) and one quit after start of ovarian stimulation because of change in condition of her haematological malignancy. The median time (25th–75th percentile) between the consultation and oocyte retrieval was 17 (13–30) days. Six women with breast cancer had letrozole co-treatment during ovarian stimulation. Seven women decided against embryo or oocyte cryopreservation after counselling because of personal reproductive choice, cost and low antral follicle count. Two women have returned for use of frozen oocytes, and both transported their frozen oocytes abroad for further fertility management. Another two women who had frozen oocytes/embryos had livebirths from natural conception (see below). There were no complications arising from ovarian stimulation and oocyte retrieval procedures. Among these 20 women, 13 women are in remission of their cancer (including 2 who subsequently underwent hysterectomy), 6 women are still on hormonal therapy for breast cancer and 1 woman with Turner syndrome is having irregular menstrual cycles.

Forty-one out of the 67 women (61.2%) who were to receive chemotherapy had GnRH agonist during chemotherapy. Among those who did not receive GnRH agonist, three declined GnRH agonist, four already had chemotherapy or pelvic radiotherapy, chemotherapy was not needed in another three and one was pending to receive pelvic radiotherapy. Four women declined chemotherapy or adjuvant therapy because of fertility concerns. The reasons for not receiving GnRH agonist were not cited in the others but 9 of those who did not receive GnRH agonist had oocyte or embryo cryopreservation.

Among the women who were seen by us for fertility preservation counselling, only 11 (15.2%) were followed up at a reproductive endocrinology clinic after their cancer treatment. Another seven were seen by gynaecologists for follow-up of their gynaecological malignancy. Six were deceased, three were still on cancer treatment (excluding those on adjuvant hormonal therapy for breast cancer) and 45 women had no follow-up.

Among the women seen by us for fertility preservation counselling (including those who did not have cryopreservation of oocytes or embryos), six patients had natural conception resulting in nine live births at full term. One patient had termination of pregnancy for anxiety state. Among these six women, two had immature teratoma and four had lymphoma.

Men

From 1995 to 2020, 265 men had sperm cryopreserved. The diagnoses and cancer outcomes of men consulted for fertility preservation are shown in Table 3. The median age (25th–75th percentile) of the men was 28 (23–35) years. The median number of sperm cryopreserved (25th–75th percentile) was 6 (6–6) vials. The median total motile sperms recovered (25th–75th percentile) was 29.4 million (4.9–93.8 million). Six of them transferred out and 40 discarded the cryopreserved sperms. Twenty-six (9.8%) came back

Fig. 1. The number of consultations for fertility preservation counselling per year for women from 2010 to 2020.

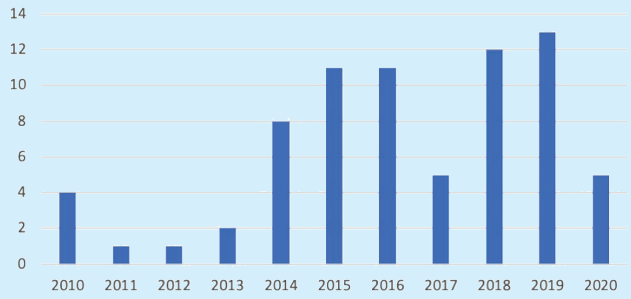

Fig. 2. The number of men who underwent sperm freezing per year for men from 2005 to 2020.

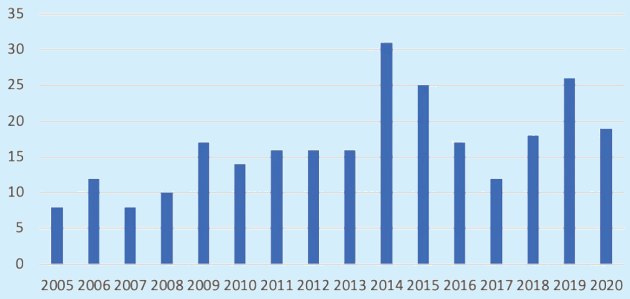

Table 1. Characteristics of women who consulted for fertility preservation.

n = 70		Cancer outcomes			
		In remission/ stable disease	On treatment	Deceased	Lost to follow up^
Age (years)	31 (25–36)				
Indication for fertility preservation					
Benign diseases	8 (11.4%)				
Malignancy	62 (88.6%)				
Diagnoses of women consulted for fertility preservation					
Haematological cancers	39 (55.7%)	31 (79.5%)	3 (7.7%)	4 (10.2%)	1 (2.6%)
– Acute leukaemia	10				
– Hodgkin's lymphoma	11				
– Non-Hodgkin's lymphoma	14				
– Others	4				
Carcinoma of the breast	12 (17.1%)	1 (8.3%)	10[a] (83.3%)	1[#] (8.3%)	
Gynaecological cancers	10 (14.3%)	8 (80.0%)		1 (10.0%)	1 (10.0%)
– Carcinoma of the cervix	3				
– Carcinoma of the uterine corpus	1				
– Ovarian cancer	6				
Nasopharyngeal carcinoma	1	1 (100.0%)			
Soft tissue sarcoma	1				1[#] (100%)
Carcinoma of the lung	1			1 (100%)	
Central nervous system glioma	1	1 (100.0%)			
Genetic (Turner syndrome)	1	1 (100.0%)			
Autoimmune disease	4	2 (50.0%)	2 (50.0%)		
Previous chemotherapy	13 (18.6%)				
Single	46 (65.7%)				
Nulliparous	65 (92.9%)				

Data presented as median (25th–75th percentile) or number (percentage).

*2 excluded (one for hypogonadotrophic hypogonadism and one for suspected gestational trophoblastic disease).

[#]declined chemotherapy.

^includes those who were lost to follow up, opted for follow up in the private sector or went abroad for further management.

[a]hormonal therapy.

to use the cryopreserved sperm, the wives of 13 (50%) of whom achieved an on-going pregnancy. In addition, among the wives of these 26 men, one had a miscarriage and one had live birth from natural conception. Twenty-five men passed away and 19 still have frozen sperm in our lab pending disposal. All other patients were still in touch with us.

DISCUSSION

Our study showed a generally increasing number of patient consultations for fertility preservation in our Centre over the years but a consistently low rate of utilisation of cryopreserved gametes (~10%) for both women and men.

The increasing number of consultations was likely related to improving awareness of fertility preservation. Although in many countries, programmes for fertility counselling and preservation exist, fertility preservation services can be quite variable and remain as one of the top five unmet needs for young cancer patients (Klosky et al., 2015; Macklon and Fauser, 2019). This is especially so in many Asian countries, where fertility preservation is still developing (Harzif et al., 2019; Takae et al., 2019). The Asian Society for Fertility Preservation (ASFP) was established in 2015 and the field is becoming more widespread. In Hong Kong, fertility preservation is available in two university-affiliated and some private-assisted reproduction centres.

The pre-requisites of a successful fertility preservation programme include rapid access to the service preferably before the start of gonadotoxic treatment and strong multidisciplinary team collaboration involving reproductive medicine specialists with expertise on fertility preservation, embryologists and urologists, and referring specialists including oncologists, haematologists, physicians, surgeons and paediatricians (Stern and Agresta, 2019). The lack of referral pathways and financial cost had been identified as barriers to providing fertility preservation in our locality (Chung et al., 2017). On the medical practitioner's side, the reasons for not referring suitable patients for fertility preservation included time constraints before cancer treatment commencement, prognostic factors related to the disease, priority towards cancer treatment and lack of awareness of the fertility preservation service (Chung et al., 2017). In the past few years, we recognised the limitations of non-referral from missed opportunities for fertility preservation, and have liaised with adult and paediatric oncology units of various public hospitals to increase awareness and set up referral pathways for patients requiring fertility preservation, as well as developed patient information leaflets and multimedia content on social

Table 2. Characteristics of those who underwent ovarian stimulation for oocyte/embryo cryopreservation.

n = 20 (22 cycles)	
Age (years)	31 (26–34)
Body weight (kg)	51 (49–59)
Previous chemotherapy	2 (10%)
Antral follicle count	14 (6–20)
Duration of ovarian stimulation (days)	11 (10–14)
Peak oestradiol level (pmol/L)	4538 (2554–7949)
Oocyte maturation trigger*	
– hCG	12/21 (57.1%)
– GnRH agonist	9/21 (42.9%)
Number of follicles aspirated	16 (6–30)
Number of oocytes cryopreserved	8 (3–20)
Number of embryos cryopreserved	
– Cleavage stage embryos	2 (1–2)
– Blastocysts	8 (2–13)

GnRH: gonadotrophin releasing hormone, hCG: human chorionic gonadotrophin.
Data presented as median (25th–75th percentile) or number (percentage).
*1 cancelled cycle after start of ovarian stimulation due to change in condition of malignancy.

media to help young men and women make an informed choice regarding fertility preservation within the limited time frame. Our flexible clinic setting and a 'reproductive medicine specialist' roster allowed urgent slotting in of cases into our existing clinic framework 5 days per week if required. Our close working relationship with associated specialists enabled us to promptly see referrals for fertility preservation counselling within 1 week so as to start fertility preservation with minimal delay to cancer treatment.

Cancer treatment is costly and both physically and emotionally challenging. When faced with the sudden potentially life-threatening diagnosis, anticipated upcoming series of treatment procedures and potential loss of earning power during or after cancer treatment, some young women and their families may not be able to bear the additional financial burden of fertility preservation and have to forgo oocyte or embryo freezing. This may represent a missed opportunity and can even lead to regret further down the line. The decision for fertility preservation had to occur within a short window of opportunity, during which cancer treatment would naturally take priority. With the delay in marriage and childbearing in modern societies, many young cancer patients may not have completed their family or even have a partner. Studies have shown that young women with a pre-treatment desire for children retain this desire years after their cancer diagnosis, and that failing to fulfil this desire is associated with worse mental health and social consequences (Armuand et al., 2014; Nilsson et al., 2014). Previously, fertility preservation was only available in our locality as a private service. The newly introduced programme for public-funded oocyte freezing allowed patients to undergo the egg/embryo freezing cycle at one-third of the cost of private services. Since the start of our public-funded fertility preservation service last year, 11 men and 6 women have been seen for fertility preservation counselling. Increased public funding is needed to extend the fertility preservation service to women with benign diseases who need to receive gonadotoxic treatment.

The random start of ovarian stimulation can shorten the delay due to ovarian stimulation without affecting the number and quality of the eggs (Preservation EGGoFF et al., 2020). Even with flexible ovarian stimulation protocols, around 2 weeks was needed for one cycle of ovarian stimulation for oocyte or embryo cryopreservation. The median (25th–75th percentile) number of oocytes retrieved

Table 3. Diagnoses of men who consulted for fertility preservation.

		Cancer outcomes			
n = 265		**In remission/ stable disease**	**On treatment**	**Deceased**	**Lost to follow up^**
Haematological cancer	99 (37.4%)	76 (76.8%)	11 (11.1%)	9 (9.1%)	3 (3.0%)
– Acute leukaemia	25				
– Hodgkin lymphoma	32				
– Non-Hodgkin lymphoma	36				
– Others	6				
Urological cancer	89 (33.6%)	69 (77.5%)	3 (3.4%)	2 (2.2%)	15 (16.9%)
– Testicular cancer	83				
– Prostate cancer	4				
– Others	2				
Cancer of the central nervous system	15 (5.6%)	14 (93.3%)		1 (6.7%)	
Oro/Nasopharyngeal carcinoma	15 (5.6%)	9 (60.0%)	2 (13.3%)	2 (13.3%)	2 (13.3%)
Sarcoma	15 (5.6%)	8 (53.3%)	2 (13.3%)	4 (26.7%)	1 (6.7%)
Carcinoma of the gastrointestinal tract	13 (4.9%)	6 (46.1%)		5 (38.5%)	2 (15.4%)
Mediastinal germ cell tumour	4 (1.5%)	3 (75.0%)		1 (25.0%)	
Autoimmune disease	4 (1.5%)	3 (75.0%)	1 (25.0%)		
Genetic (Klinefelter syndrome)	2 (0.8%)	2 (100.0%)			
Miscellaneous	9 (3.5%)	6 (66.7%)	1 (11.1%)	1 (11.1%)	1 (11.1%)

Data presented as number (percentage).
^includes those who were lost to follow up, opted for follow up in the private sector or went abroad for further management.

was 8 (5–13) in a cohort of women from 2013 to 2016 in our centre excluding donor oocyte IVF, in vitro maturation, fertility cryopreservation and pre-implantation genetic testing. The median ovarian response in patients seen for fertility preservation was similar to that of our usual women undergoing ovarian stimulation for infertility at our centre, but the range of ovarian response was wider-on the high end because of generally higher starting dose of gonadotrophins used to maximise stimulation; on the other end, some women who had previous chemotherapy had poor ovarian response despite ovarian stimulation. For some patients, even a 2-week delay was too long for their cancer treatment. Ovarian tissue cryopreservation does not require ovarian stimulation and may be the only option for pre-pubertal girls or those who have to start chemotherapy immediately. Despite ovarian tissue cryopreservation no longer being experimental in recent guidelines, our Centre is not offering it yet because of the constraints of the laboratory condition. Further development of tissue freezing is also important in Hong Kong, as this is the only means available for pre-pubertal girls. GnRH agonist is commonly discussed in women who have to undergo chemotherapy but should not be used in place of fertility cryopreservation methods as there is limited evidence on their protective effect on the ovarian reserve and future reproductive potential (Practice Committee of the ASRM, 2019; Preservation EGGoFF et al., 2020). Despite the limited evidence, most of our patients still opted for GnRH agonist during chemotherapy. More data is needed on the long-term gonadal function and fertility after GnRH agonist administration. In our series, 18.6% of women who could not afford to delay chemotherapy were seen by us after chemotherapy when their disease was under control. Realistic fertility counselling could always be offered and oocyte or embryo cryopreservation could still be considered on a case-by-case basis. Of note, some patients refuse appropriate cancer therapy because of fertility concerns. One of the worst consequences of missing a discussion on fertility preservation is suboptimal cancer treatment, which could affect the life expectancy of the patient.

For men, sperm cryopreservation is the only option and can be arranged easily without delay to their cancer treatment in most cases. In our cohort, the most common diagnoses for men attending for fertility preservation were testicular cancers and haematological cancers, probably due to relatively young age of those affected and high awareness of the impact on fertility, especially for testicular cancers. For pre-pubertal boys, testicular tissue cryopreservation is still experimental and not available in our Centre.

Alarmingly, only less than 20% of female cancer survivors were followed up at a reproductive endocrinology clinic after cancer treatment. The number was likely to be even lower for men. We did not provide routine follow up consultation to men who have cryopreserved sperms at our Centre because they were previously seen as a private service, and resources are limited even with the current public-funded fertility preservation programme. Instead, they are asked to have a semen analysis 1–2 years after completion of chemotherapy, and to rebook in our clinic if they need to utilise the cryopreserved sperm when they wish to start a family and their cancer treatment was complete. For women, we advise referral to our reproductive endocrinology clinic after completion of their cancer treatment for management if there are clinical features of premature ovarian insufficiency. Fertility preservation should not only be about cryopreserving gametes or reproductive tissue but should always include post-treatment follow-up visits for fertility assessment and counselling on hormone replacement therapy and general reproductive health (Macklon and Fauser, 2019; Massarotti et al., 2019) as post-cancer survival reproductive care is still a neglected area (Fidler et al., 2019). In a busy oncology clinic, patients may not be asked specifically about their gonadal health after cancer treatment. It is insufficient to rely on their own recall of fertility information and advice given at their cancer diagnosis, a time when they were emotionally overwhelmed and information loaded by details of the cancer diagnosis, investigations and treatment. Close liaison between oncologists and reproductive medicine specialists is important to ensure high awareness of reproductive care amongst healthcare providers and that cancer survivors are referred back to reproductive specialists after cancer treatment. In many places including Hong Kong, there are no concrete guidelines as to when post-treatment fertility assessment and counselling should be provided. Further efforts should look into these areas. The establishment of a centrally coordinated referral system for more structured fertility preservation and post-treatment follow up may be able to overcome some of these difficulties.

The low utilisation of frozen gametes in our Centre was consistent with previous publications both locally and internationally (Blackhall et al., 2002; Chung et al., 2013; Kelleher et al., 2001). The majority of frozen samples were kept for many years without being used, unless the patient succumbs. The reason for non-usage was not known in the majority of our cases and worth further exploration, but medical, psychological and social factors may play a part. For some, it may be a reminder of past cancer experience. In a cross-sectional questionnaire study of 499 cancer survivors between April 2008 and December 2010, men who declined to return for semen analysis after cancer treatment were more likely to have a negative experience of banking sperm and a negative attitude towards disposal of their stored semen than those who attended (Pacey et al., 2012). In a more recent questionnaire study involving 45 male childhood cancer survivors aged 15–25 years, two-thirds of them were interested in learning more about their fertility post-treatment (6). We noted that some patients (or their partners) have had natural conceptions without assisted reproductive treatment but the proportion documented on our medical system may not be representative of the complete picture if not asked systematically during oncology follow up, especially for men. Some patients may have changed their mind and opted not to embark on pregnancy. Some of our patients transported gametes abroad for further treatment. For these patients, it is important to note that the laws for gamete usage differ in different countries.

The strength of this paper was that we looked into the evolution of fertility preservation over the past 10–15 years at a university-affiliated tertiary-assisted reproduction centre. Our Centre has started to offer sperm cryopreservation in 1996, embryo cryopreservation in 2010 and oocyte cryopreservation in 2013. Limitations include the retrospective nature and the single-centred basis. Although the electronic patient records linked up all hospitals under the Hospital Authority and some private clinics, there would still be missing information if the patients were seen in the private sector. Some men and women might have been missed in the database if they defaulted.

CONCLUSIONS

There was generally an increasing number of patient consultations for fertility preservation in our Centre over the years but a consistently low rate of utilisation of cryopreserved gametes for both women and men. Post-cancer treatment fertility evaluation and monitoring was a major area of deficiency in Hong Kong. Increased public funding and more structured post-cancer treatment fertility follow-up are urgently needed.

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CONFLICT OF INTEREST

All authors have disclosed no conflicts of interest.

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