

Cryopreservation in reproductive medicine during the COVID-19 pandemic: rethinking policies and European safety regulations

Running title: COVID-19 and cryopreservation in ART

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Abstract

Cryopreservation of reproductive cells and tissues represents an essential aspect of ART practices that might be particularly strategic and helpful during SARS-CoV-2 emergency. However, recommendations on how and when to preserve reproductive tissues and cells during a novel severe pandemic are scanty. This paper uses a SWOT (strengths, weaknesses, opportunities and threats) analysis to identify favorable and unfavorable factors and to recognize challenges and obstacles related to the use of cryopreservation procedures during the spreading of a new virus. One of the strengths associated with the cryopreservation is represented by the availability of robust European guidelines on storage safety to prevent sample contamination or cross-contamination by pathogens. These recommendations should be deep-rooted in all ART laboratories. Weaknesses include uncertainties regarding the management of COVID-19 affected asymptomatic patients, the suboptimal accuracy of diagnostic tests for the disease, the nebulous prospective regarding the duration of the pandemic and the additional costs. The application of the strategy represents an opportunity to postpone pregnancy in order to avoid a severe infectious disease during gestation while concomitantly counteracting the possible detrimental effect of time. Critical threats, at present still undefined, are represented by potential adverse events for the mother and offspring due to infected gametes or embryos after thawing and, subsequently, the re-spreading of the virus.

Key words: ART, cryopreservation, SARS-CoV-2, COVID-19, SWOT analysis, risk assessment

Introduction

The novel infectious Coronavirus disease-2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is proving to be an unprecedented disaster for global health. Following the sweep of the disease, lockdowns and recommendations on containment have become commonplace in several countries. However, pathogenetic mechanisms of the virus remain poorly understood as well as how it spreads and whether and for how long an anti-viral immunity is established. The number of asymptomatic cases is still not well defined. According to the different studies, the proportion of asymptomatic individuals varies between 5% and 80% (Zhou *et al.*, 2020; Tian *et al.*, 2020; Day, 2020; Chau *et al.*, 2020). Moreover, no specific drugs for the virus have been developed. As a consequence, the effectiveness of the measures in the combat to contain the infection might be only transitory. The virus might stay for many months or even years before an effective vaccine or herd immunity will temper its effects.

Even in this situation, infertility represents an important public health issue that cannot be ignored. Social, political, ethical and psychological dimensions as well as economical considerations have contributed to the increased offer of worldwide access to infertility services (Dyer and Patel, 2012; Inhorn and Patrizio, 2015; Mladovsky and Sorenson, 2010). Unfortunately, due to the present uncertainties regarding viral spread and potential effects on pregnancy course, all ART centres worldwide are questioning how to safely manage infertility couples and whether or not to postpone treatments. Many months or years of delay could have a negative clinical impact as well as profound emotional effects on the couples' quality of life. Moreover, aiming at a SARS-CoV-2 free context of work is unrealistic and ART centres have to handle affected cases properly as well as anticipating the presence of undiagnosed cases when they resume their activity.

Cryopreservation of reproductive cells and tissues represents an important aspect of ART that might be particularly strategic and helpful in this scenario. While specific and detailed recommendations for patients' safety have been widely provided to the ART health community, scant attention has been paid to the possible role of cryopreservation of gametes, embryos and tissues. Thus, the analysis presented herein aims to provide a pragmatic tool to rethink critically the appropriateness and safety

of the cryopreservation procedures in ART centres in the context of the current SARS-CoV-2 pandemic.

Recommendations and position statement by Scientific Societies

In response to the virus spreading, prestigious Scientific Societies in the field have rapidly provided recommendations to mitigate the risk of patients' and staff infection. On March 19, the European Society of Human Reproduction and Embryology (ESHRE) published a statement supporting a precautionary approach in relation to pregnancy planning in the pandemic period. For ART treatments already ongoing, pregnancy was suggested to be deferred taking advantage of oocyte/ embryo cryopreservation. On April 2, to clarify their position, ESHRE confirmed the same recommendation but added some observations on the management of biological material (European Society of Human Reproduction and Embryology, 2020). The possibility for gametes/embryos to be infected by SARS-CoV-2 in the ART laboratory was assumed as minimal or non-existent. Indeed, the repeated washing steps in culture and freezing protocols were supposed to result in a very high dilution of any possible viral contaminant making it less dangerous. Even though no specific data are so far available, ESHRE also speculated that infection of gametes and embryos was unlikely due to the absence of SARS-CoV-2 receptors. The protective role of the zona pellucida (ZP) was thought to be crucial in this regard. Nonetheless, the need to adhere to good clinical and laboratory practice was also reiterated (De los Santos *et al.*, 2016).

In line with ESHRE statements, on March 17, the American Society for Reproductive Medicine (ASRM) recommended to advise patients to defer pregnancy through oocyte or embryo cryopreservation. Only "urgent" treatments should go ahead. Universal precautions on how to handle specimens from COVID-19 infected individuals were also provided and, specifically for tissue storage, it was recommended to handle samples from infected patients in the same way as tissues derived from other infectious diseases. With an update provided on March 30, the ASRM Task Force has supported the safe storage of tissues/cells by referring to the guidance provided by the Society

for Assisted Reproductive Technologies (SART), however, this does not specifically mention how to safely store tissues and cells (American Society for Reproductive Medicine, 2020). The guidance produced by ESHRE on April 23 to minimize risks related to SARS-CoV-2-positive patients and staff at the restart of ART treatments was mostly based on a first triage questionnaire selection. In case of positive triage, patients would be rerouted to testing for SARS-CoV-2 IgM/IgG and/or RT-PCR. For cryopreservation, ESHRE suggested that high-security straws and/or vapour phase storage tanks should be implemented for SARS-CoV-2-positive patients (ESHRE COVID-19 Working Group, 2020). Recently, ESHRE, ASRM and the International Federation of Fertility Societies (IFFS) have joined supporting the importance for continued reproductive care during the COVID-19 pandemic (<https://www.eshre.eu/Home/COVID19WG>).

SWOT analysis of cryopreservation in a pandemic

This confused scenario on how and when to process, preserve and store reproductive tissues and cells correctly in the pandemic situation, is not only a consequence of the paucity of evidence but also the hidden or unconscious desire to avoid adding complexity to the management of a successful process in a period already full of uncertainties. On the other hand, we have to consider and minimize the risks of ART during this period. Consequences of wrong choices can be devastating. On these bases, a SWOT (Strengths, Weaknesses, Opportunities and Threats) analysis on the procedure of cryopreservation of reproductive samples during the COVID-19 pandemic has been conducted (Figure 1).

Strengths

Cryopreservation represents a strategic tool in ART treatments (Rienzi *et al.*, 2017; Viganò *et al.*, 2020) as it has numerous advantages: i) allowing personalized care for different patient populations; ii) increasing the safety of ART treatments by eliminating the risk of ovarian hyperstimulation

syndrome (OHSS); iii) improving the cumulative live birth rate by deferring embryo transfer to a subsequent frozen cycle, in particular for cases showing an excessive response or a premature rise in peripheral progesterone; iv) reducing the maternal and perinatal risks by facilitating an elective single embryo transfer policy; v) allowing male and female fertility preservation; vi) enabling oocyte and sperm banking for donations; vii) oocyte cryopreservation can avoid embryo overproduction in order to align with the ethical and religious beliefs of individuals who might object to embryo storage, viii) optimizing the treatment of absolute male infertility requiring sperm retrieval from the epididymis or the testis. Finally, cryopreservation represents an excellent tool to manage unexpected or disastrous events and, in a pandemic like COVID-19, to ix) postpone the embryo transfer thus efficiently preventing the potential risks of the disease during pregnancy.

ART centres have a vast literature and robust guidance on processing and storage safety.

First of all, procedures involving gamete or embryo manipulation should be performed in a controlled environment and systems for controlling air quality should comply with European and national guidelines and be monitored regularly. According to the EU Guidelines to Good Manufacturing Practice for medicinal products (known as GMP), aseptic processing must be done in a Grade A zone, with a background of at least GMP Grade D. A positive pressure should be created relative to adjacent cleanrooms of a lower grade, limiting the entry of contaminations into the cleanrooms of a higher cleanliness level. A microbiological monitoring of the environments and of the surfaces is also mandatory (European Directorate for the Quality of Medicines & HealthCare of the Council of Europe, 2019).

The “ESHRE Guidelines for Good Practice in IVF Laboratories” also describes procedures to minimize risks for both the staff and biological materials based on the idea that “*all body fluids (blood, follicular fluid, semen, etc.) should be treated as potentially contaminated*” (De los Santos *et al.*, 2016). Furthermore, the Guide to the Quality and Safety of Tissues and Cells for Human Application suggests the use of Personal Protective Equipment (PPE) (hairnets and non-toxic, non-powdered gloves and masks) and the handling of biological material under vertical laminar flow benches in

order ensure aseptic conditions for tissue, gametes, and embryos (European Directorate for the Quality of Medicines & HealthCare of the Council of Europe, 2019).

Finally, reproductive cells and tissues must be cryopreserved and stored according to the European Tissue Directive 2006/17/EC (European Union [EU] Directive 2006/17/EC) to prevent the transmission or cross-contamination of samples by pathogens. Screening patients for blood borne viruses (BBVs) as HIV, Hepatitis B and C before gamete/embryo processing and cryopreservation, and the separate storage of reproductive cells and tissues for positive and negative patients, are mandatory. Also, periodic cleaning of storage vessels is considered a good laboratory practice (GLP) in order to decontaminate from viral and microbial agents (European Directorate for the Quality of Medicines & HealthCare of the Council of Europe, 2019).

Importantly, oocytes and embryos, being composed of a small number of cells (only one for eggs) and lacking any blood supply carry a minimal risk of acting as pathogen vectors (Pomeroy *et al.*, 2010). The routine rigorous washing of oocytes and embryos prior to cryopreservation represents an additional preventive measure. Finally, it is controversial whether the virus can cross the ZP or attach to it and be transferred to the embryo during hatching or implantation (Vanroose *et al.*, 2000; Queiroz-Castro *et al.*, 2019).

Overall, cryopreservation processing in ART practice is well-supported and robust from a safety standpoint. Adherence to the strict European regulations should avoid concerns even during a social calamity. The spread of a new virus should not have found us unprepared.

Weaknesses

An efficient risk management system implies a risk awareness. For this pandemic, the poor knowledge on the proportion of asymptomatic cases, the poor accuracy of the diagnostic testing and the concerns about the universal screening (Patel *et al.*, 2020) mean that we will have to live with the

virus for the foreseeable future, affected and non-affected subjects often being indistinguishable. This awareness has relevant implications in an ART laboratory.

Considering dedicated personnel first, it may be possible to decrease the number of laboratory staff to decrease the likelihood of virus transmission or to devise prevention strategies to limit the virus spread if an operator does become infected (De Santis *et al.*, 2020). The reducing staff in response to the reduction in workload due to the pandemic cannot fully overcome the potential hazard and a significant reduction in dedicated personnel may impair safety. The failure to observe GLP during critical steps (e.g. witnessing during cryopreservation), might increase the likelihood of mistakes with severe consequences. Another critical point to consider is represented by the liquid nitrogen supply especially when manual-fill tanks are used. In this case, a staff reduction during the pandemic might be the cause of cryostorage accidents. In addition, the potential for errors arises with the level of stress. In crisis management, the “human” factor represents a potential source of severe errors (Reason, 2000), particularly critical in ART laboratories. Also, in emergencies, the decision process of ART managers (e.g. Laboratory Directors) under stressful settings might be very different from the usual conditions (Cosgrave, 1996), leading to the introduction of new inappropriate procedures and/or changes in the processes.

Regardless of the paucity of evidence on the potential detrimental effects of COVID-19 in pregnancy (Chen *et al.*, 2020; Mullins *et al.*, 2020), avoiding a potentially devastating infection during gestation by cryopreserving oocytes or embryos is obviously wise. This option is in general considered mandatory for subjects developing COVID-19 during ART but may also be applied for the whole community of couples requiring ART treatments. There are however some downsides. A policy of universal freezing is inevitably linked to the idea of transferring embryos only once SARS-CoV-2 will be overcome or at least controlled. But, how long will we have to wait to declare the pandemic over? This may take months or years and couples would have to accept delaying their attempt to fulfil their desire of parenthood for a long time. The emotional and psychological impact of this approach is unknown but it is potentially harmful and cannot be neglected. Moreover, additional costs are

associated with a policy of universal freezing. The procedures of cryopreservation are complex and the additional costs compared to fresh interventions are appreciable (Cassettari *et al.*, 2016; Papaleo *et al.*, 2017; Le *et al.*, 2018; Alteri *et al.*, 2019; Somigliana *et al.*, 2019). This issue is gaining even more relevance in the context of an imminent devastating economical crisis, for both private and public health assistances. Moreover, freezing oocytes or embryos to postpone pregnancy poses another additional crucial query. How many cycles should we perform? In general, in fertility preservation of oocytes, this issue tends to be neglected because most women generally do not perform more than 1-2 cycles either because they have not sufficient time (for cancer patients) or cannot afford more (for non-medical reasons). Overall, universal freezing for all couples requiring ART during the COVID-19 pandemic could be foreseen but is unrealistic. Increased costs and complexity as well as possible patients' concerns regarding long-term delay in parenthood hamper its widespread diffusion.

Opportunities

As suggested by many scientific societies, oocyte and embryo cryopreservation should be maintained during the COVID-19 pandemic, even during a lockdown context.

As mentioned earlier, while universal freezing for all couples requiring ART is impracticable, on the other hand, Some infertile couples may consider this as an opportunity to avoid focusing on the health emergency during the planning of a pregnancy. Cryopreservation could prevent the detrimental effects of women aging (Van Voorhis, 2007) and couples could reasonably be reassured that the delay in time will not affect their chances of parenthood if they decide to freeze oocytes or embryos.

More importantly, cryopreservation of embryos during a ART cycle represents an opportunity for both patients and clinicians to avoid dealing with the possible complications associated with pregnancies during the pandemic. Available data do not support a higher risk of severe illness in COVID-19 affected pregnant women compared with the general population (Chen *et al.*, 2020; Della Gatta *et al.*, 2020; Parazzini *et al.*, 2020). However, severe maternal morbidity as a result of COVID-

19 infection can occur and may require premature delivery and the associated inevitable threats for the newborns (Della Gatta *et al.*, 2020; Zaigham and Andersson, 2020; Parazzini *et al.*, 2020). The disease may also complicate clinical management because of the overlap with some main obstetric complications (Gidlöf *et al.*, 2020). Finally, potential detrimental effects of COVID-19 on long-term newborns health, in particular for exposures during the early phases of pregnancies, are unknown.

COVID-19 might also negatively impact male fertility. Spermatogonia, Leydig and Sertoli cells display the ACE2 receptor, a possible target for SARS-CoV-2 infection and one may infer possible effects (Wang *et al.*, 2020) but knowledge is too preliminary and lacunar for meaningful conclusions (Paoli *et al.*, 2020; Song *et al.*, 2020; Pan *et al.*, 2020; Li *et al.*, 2020; Holtmann *et al.*, 2020). If more robust evidence on long-term specific or non-specific (for instance fever) detrimental effects on spermatogenesis of COVID-19 will emerge, one might foresee the need for semen cryopreservation in reproductive age men interested in parenthood, either at the beginning of the COVID-19 symptoms or as a general policy for this population. To date, however, this cannot be justified.

Finally, one may also underline that the policy of elective cryopreservation may facilitate social distancing. Numbers of referral to the ART centres could be reduced as fresh embryo transfers would not be performed and semen cryopreservation could avoid the male partner needing to attend the ART centre on the day of oocyte retrieval.

Threats

Analyzing the cryopreservation procedures during the COVID-19 pandemic highlights several critical points that represent severe threats. A crucial point is to accept or not a 'theoretical risk'. A theoretical risk is defined as something dangerous that possibly could happen according to theory, but for which there is no evidence it has ever happened in reality. The ECDC has taken into account precautionary measures to mitigate the theoretical risk of agent transmission for substances of human origin (SoHO) including human blood, blood components, tissues, reproductive and non-reproductive

cells and organs, as defined in EU/EEA Directives (European Centre for Disease prevention and Control, 2020).

Although SARS-CoV-2 virus is transmitted from human to human via droplets (Morawska and Milton, 2020; Zhang *et al.*, 2020), uncertainties about the presence of the virus in the blood and bodily fluids of an asymptomatic donor may be considered as a potential threat to the safety of SoHO. All respiratory viruses, except adenoviruses (Zhang and Bergelson, 2005), normally attach to receptors in the airways and therefore the possibility of their blood-borne transmission is unknown. Their transmission by transfusion or transplantation has not been reported (Chang *et al.*, 2020). Based on current knowledge, the possibility of COVID-19 transmission through SoHO appears to be theoretical. Nonetheless, the precautionary measures implemented by SoHO establishments and plasma collection centres included: i) non eligibility for donors diagnosed with confirmed COVID-19 to a donation of any type of SoHO; ii) deferring of donors recovering from confirmed COVID-19 from donation for at least 14 days after symptoms resolution and negative results of repeated testing. In ART centres, no precautionary measures have been recommended to prevent the theoretical risk of transmission of SARS-CoV-2 to the offspring and to the woman through infected gametes or embryos.

Overall, at this stage, there is insufficient knowledge to rule out the theoretical risk of SARS-Cov-2 transmission to the offspring through infected gametes or embryos. While no data on SARS-Cov-2 are available in oocytes or embryos, controversial findings have been reported on the presence of SARS-CoV-2 in the semen (Pan *et al.*, 2020; Paoli *et al.*, 2020; Song *et al.*, 2020; Li *et al.*, 2020; Holtmann *et al.*, 2020).

Regarding the potential risk of transmission to the mother through infected gametes or embryos, a preliminary answer may derive from animals. Embryos have been exposed to pathogens and then transferred into livestock to clarify whether there was a transmission into the recipient. In all the experimental cases, the pathogens were not detected in the mother (Wrathall *et al.*, 1979; Singh *et al.*, 1982; Hare *et al.*, 1985; Gilbert *et al.*, 1987). In line, there have been no substantiated reports

anywhere in the world of disease transmission to an uninfected recipient by commercial transfer in the livestock industry.

Although the transmission of the virus through infected gametes or embryos is associated only with a theoretical risk, the subsequent re-diffusion of the virus after the pandemic following the thawing of the infected reproductive samples maybe years later should be considered. If SARS-CoV-2 is present in the stored material and survive the freezing/thawing processes, one may claim a potential threat even years later. This could be particularly relevant for men storing their semen for oncological indications. One may speculate that the woman who will receive the semen could get infected and develop COVID-19. Theoretically, this could be the trigger for a new epidemic years from now.

Another concern that cannot be ruled out is represented by the risk of cross-contamination in the storage of potentially infected frozen gametes and embryos derived from SARS-CoV-2 carrier patients. Indeed, the European Tissue Directive 2006/17/EC often cited the term “risk of cross-contamination”, that is averted by blood testing for patients and using of dedicated tanks for BBVs infected patients. Viruses can survive in liquid nitrogen, deriving from the environment or from an infected sample in case of a storage container (straw or vial) damage. Concerns about the dangers of reproductive cells and tissues storage emerged after the incident occurred in United Kingdom about 25 years ago involving a Hepatitis B virus cross-contamination by blood samples stored in the same liquid nitrogen container (Tedder *et al.*, 1995). In addition, the possibility of cross-contamination was reported in experimental conditions using very high titers of microbial agents introduced into the cryo-system, conditions which are however very different from embryo cultures or the cryopreservation setting in a ART laboratory (Piasecka-Serafin, 1972; Bielanski *et al.*, 2000; Letur-Konirsch *et al.*, 2003; Bielanski *et al.*, 2003). Let’s consider in detail the series of events that should occur for a cross-contamination of a pathogen in the liquid nitrogen in a ART laboratory: i) damage of a storage container containing infected oocytes/embryos/sperm; ii) virus entry in another storage container; iii) virus interaction with the still non-infected oocytes/embryos/sperm. While, as previously mentioned, for oocytes and embryos, the possibility to act as pathogen vectors is trivial,

the potential for semen to act as a vector may be less theoretical. The semen is not collected as a sterile tissue and can contain other blood components that can be infected by pathogens. In case of an infected sperm sample, viruses should be able to contaminate other semen samples in liquid nitrogen with possible entry or contact with the membrane. A consequent injection of the virus with the sperm into the egg cytoplasm should theoretically occur.

Notwithstanding a theoretical risk cannot be completely excluded, ART centres have applied very few precautionary measures, for instance the use of high-security straws for SARS-CoV-2-positive patients, in order to prevent the possibility of cross-contamination derived from SARS-CoV-2 carrier patients.

Overall, differently from other institutions and due to the paucity of evidence, it has to be recognized that ART centres are not completely recognizing and thus controlling all the possible theoretical risks of severe adverse events associated with cryopreservation procedures during COVID-19 pandemic.

Implementing solutions and lessons learned

Based on a SWOT analysis, a strategic plan should be constructed. Specifically, for this analysis of the procedures of cryopreservation of reproductive samples during the COVID-19 pandemic, some strategic solutions for weaknesses and threats may be proposed. Other high priority areas need to be more in depth discussed. On the other hand, we have left some points as unsolved since, given the current limited knowledge of the pandemic characteristics, suggesting plans would have implied too many speculations.

Reduced available staff

In case of substantial reduction in laboratory staff, to minimize the need of physical witnessing in the absence of electronic witnessing systems, De Santis and coworkers suggested to establish lean protocols as telematic witnessing or backing external personnel properly equipped (De Santis *et al.*,

2020). This approach could improve the ART laboratory management especially in centres with a low number of personnel. However, it has not been tested in clinical practice and remains speculative.

Increased risks of staff errors

The arrangement of mutually non-overlapping teams but each with the ability to manage all tasks may allow to minimize contacts maintaining service standards and reducing both stress and error risks (Chua *et al.*, 2020). Members within teams should remain constant and be equally balanced in terms of seniority of embryologists.

Effectiveness of preventing aging

Once informed, couples may opt for freezing oocytes or embryos while waiting for the end of the epidemic. In particular for older women, this could overcome the detrimental effects of aging (in particular if the epidemic will last several months or years). However, ART centres need utmost and documented expertise in freezing or the advantages can be easily wasted by the inefficiency of the process. To note, in older women, six months delay in initiating treatments is not expected to markedly hamper the rate of success (Somigliana *et al.*, 2020). Moreover, within oocytes or embryos freezing programs, patients and physicians will have to face the additional difficulty of the number of cycles to be planned. Even if some recent publications provided predictive models linking age, oocytes and chance of live birth (Cobo *et al.*, 2015; Goldman *et al.*, 2017), these models lack external validation and the counseling will inevitably remain theoretical and imprecise.

Potential risk of cross-contamination

The possible risk of cross-contamination considered by EU directives seems to be overstated for reproductive tissues and cells as the cascade of events to achieve a cross-contamination episode would seem to have a near zero probability. There are no reports so far on cross-contaminations among reproductive cells and tissues stored in cryogenic tanks. Cobo and coworkers showed no detection of viral sequences (HIV, HBV, and HCV) in samples of liquid nitrogen from containers containing oocytes and embryos from chronically infected patients (Cobo *et al.*, 2012). Moreover, semen preparation techniques permit to select only spermatozoa, removing the blood components and

contribute to significantly shrink the viral load. However, it is important not to confound the absence of evidence for evidence of the absence. As a matter of fact, no one has yet performed a quantified risk assessment for infection or cross-contamination of cryopreserved human embryos or gametes, supporting the idea that this risk is worldwide considered negligible. For COVID-19, this issue will be solved completely with the availability of a vaccine.

Conclusions

Cryopreservation of semen, oocytes and embryos could play a role in the therapeutic armamentarium to be used in the management of infertile couples during the COVID-19 pandemic. Cryostorage could be an opportunity and seems generally safe, in particular for the possible concerns regarding oocytes and embryos infection.

However, the lack of robust evidence prevents the diffusion of strong recommendations as well as of stringent warnings. In this uncertain context, precautionary principles should receive utmost attention but cannot prevail since a fully protective attitude may ultimately damage the patients.

After COVID-19 pandemic, we will be able to verify whether our decisions in cryopreservation balancing patients' care and risk prevention have been totally adequate in terms of efficiency and safety. This will allow to set up a standardized model to face up similar situations in the future.

In the meantime, the situation is rapidly evolving from both an epidemiological and cultural perspective and healthcare providers are called to remain adjourned more than ever to the rapid evolution of knowledge and to adopt an elastic clinical attitude. The COVID-19 crisis found them unprepared being suddenly deprived from their certainties and being called to take decisions in an unusual situation full of doubts. At present, patients' empowerment is even more fundamental than ever. There is the strong and insurmountable necessity to provide available knowledge to the patients and to discuss in depth with them about opportunities, risks, threats and uncertainties. Even if definitive recommendations cannot be drawn, cryopreservation techniques certainly deserve utmost

consideration in the decision-making process. Information should be transparent, balanced and honest.

Authors' roles

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Figure legends

Figure 1. SWOT (strengths, weaknesses, opportunities and threats) analysis of cryopreservation in the COVID-19 pandemic.



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