

Title: Discarding IVF embryos: Reporting on global practices

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ABSTRACT

PURPOSE: To provide a global scale report on a representative sample of the clinical embryology community depicting the practice of discarding supernumerary IVF embryos.

METHODS: A web-based questionnaire titled ‘Anonymous questionnaire on embryo disposal practices’ was designed in order to ensure anonymous participation of practicing clinical embryologists around the world.

RESULTS: During a data collection period of 8 months, 703 filled in questionnaires from 65 countries were acquired. According to the data acquired, the majority of practitioners, dispose of embryos by placing them directly in a trash can strictly dedicated for embryo disposal for both fresh and frozen cycles (39% and 36.7% respectively). Moreover, 66.4% of practitioners discard the embryos separately-case by case-at different time points during the day. Over half of embryologists (54%) wait until Day 6 to discard the surplus embryos, while 65.5% do not implement a specially allocated incubator space as a designated waiting area prior to disposal. The majority of 63.1% reported that this is a witnessed procedure. The vast majority of embryologists (93%) do not employ different protocols for different groups of patients. Nonetheless, 17.8% reported the request to perform a ceremony for these embryos. Assessing the embryologists’ perspective, 59.5% of participants stated that the embryology practice would benefit from a universally accepted and practiced protocol.

CONCLUSION(S): This study uniquely provides insight into global embryo disposal practices and trends. Results highlight the divergence between reported practices, while indicating the significance on standardization of practice, with embryologists acknowledging the need for a universally accepted protocol implementation.

KEYWORDS: surplus embryos, embryo disposal practices, IVF

Introduction

During In Vitro Fertilization (IVF) treatment, embryos of the highest implantation potential are included in the embryo transfer or cryopreservation process. Studies show that the optimal number of oocytes retrieved per cycle is 15 [1], subsequently, supernumerary embryos are expected. The decision-making process regarding the fate of these embryos is considered to be the most challenging and crucial step during the entire IVF process [2]. From morphology grading to the emergence of prediction models [3], and the promise of artificial intelligence (AI) [4,5] the evolution of all these trends serves the era of personalized medicine by strengthening the practice of elective single embryo transfer (eSET) [6]. A byproduct of the eSET practice are surplus embryos [7].

Depending on their quality, the legal framework, the patients' will, and the respective family planning status, surplus embryos may be subjected to certain options. Common practice dictates that good quality embryos may be cryopreserved for future IVF cycles employing a frozen-thaw protocol [8].

With regards to cryopreserved stored embryos, in the case that that it is decided that no further fertility treatments will be pursued, couples are faced with the challenging decision regarding disposition of their frozen embryos also known as “embryo disposal decision” (EDD) [9]. A successful attempt in childbearing most commonly signals the designation of cryopreserved embryos as surplus material. Surplus cryopreserved embryos that are stored during the process of assisted reproduction are not always reclaimed by the patients. In Sweden, 30% of couples during a 3 year period did not use their cryopreserved embryos in a subsequent cycle [10], and similar reports are documented in France [11,12] and Denmark [13]. Interestingly, there is the matter of “abandoned embryos” in storage, this term refers to cases where the couple/person cannot be reached and/or fails to provide the clinic with a decision pertaining to the embryos' fate [14]. The safekeeping of “abandoned embryos” raises ethical and bureaucratic challenges

for IVF clinics worldwide as published reports indicate that frozen embryos in storage have reached numbers in the range of 52 000 (UK, 1996), 71 000 (Australia, 2000) and 400 000 (USA, 2003) [15,16]. To address the prospect of unclaimed embryos, many clinics ask couples to make dispositional decisions prior to initiating IVF treatment.

Good quality embryos may be donated to a research program especially in light of the most recent stem cell studies [17]. Additionally, the embryos may be donated to other couples facing infertility to known or anonymous persons [14]. Donating embryos to research or to a third-party experiencing infertility, or discarding consist of the three main options available in cases of fresh or cryopreserved embryos.

Poor quality embryos that fail to qualify for embryo transfer or cryopreservation, as well as embryos subjected to preimplantation genetic testing (PGT) cycles diagnosed with a genetic or chromosome abnormality are typically discarded. Interestingly, IVF professionals in countries such as USA where neither sex selection nor access to PGT is regulated also provide the option for 'social sexing' leading to the subsequent disposal of healthy embryos [18].

The current literature provides an adequate number of studies describing patients' views on the disposal procedure of their surplus embryos. Couples' conceptualization of embryos is complex and may range from picturing these embryos as a little more than cohort of cells, or a tissue, to considering them as their unborn children [19–22]. In 2009, McMahon and Saunders reported that patients' hesitancy to donate their embryos to other infertile couples, was related to the belief that these surplus embryos were not only their potential children, but were siblings to existing children. Patients indecisiveness and hesitation towards donation may be attributed to a feeling of responsibility for the well-being of the offspring [23]. Interestingly, more than one study reported that even though most couples view their surplus embryos as 'potential life', the majority of them chose an option resulting in the embryos' disposal, or donation to research. [8,24–26]. The disposition decision is known as being emotionally demanding for couples that

are understandably focused on the first goal of achieving a clinical pregnancy [8,20,27,28]. Some couples, who chose to discard their embryos, described their decision as a ‘last minute decision’, perhaps indicating their opposing views regarding embryo research and additionally the sentiment that they are unable to donate their embryos to another couple [8].

Hitherto, there is a lack of evidence and data regarding the different practices adopted in order to discard embryos in IVF laboratories as there is no universal protocol or a respective guideline or dedicated section in any code of practice. A guideline defines a statement that aims to rationalize particular practices according to a set routine. The rationale fueling design of the present study is to present the IVF community with a descriptive study on the various practices entailed in discarding surplus embryos providing an international report. The lack of published data, along with no documented thesis in literature, prompted our team of experts to approach this subject aiming to shed light to what is reported as the existing practice. This original study aims to serve as a platform voicing the current practices and understand what may be lacking. The scope of this survey, in combination with a comprehensive literature review on this topic, was to present the similarities and discrepancies reported on a global scale regarding embryo disposal practices on fresh and cryopreserved embryos. The practice of preimplantation embryo disposal pertains to the clinical embryologist disposing of the embryos, along with the respective couple/person subjected to ART who ultimately determine the embryos’ fate. The authors do not attempt to approach the issue of potential advantages entailed in a practice characterized by a common universal protocol on embryo disposal. This is a descriptive survey and the questions included in the survey do not propose or evaluate potential benefits related to standardization of disposal practices. Nonetheless, such benefits may be entailed especially in light of the bioethical stance of the preimplantation embryo.

Materials and Methods

A web-based questionnaire titled ‘Anonymous questionnaire on embryo disposal practices’ was designed employing the “google-forms” format in order to ensure anonymous participation of IVF professionals around the world. The questionnaire can be found in supplementary material (Figure 1). Demographic information regarding the name of the country and the state, where applicable, the IVF clinic was based was acquired. The questionnaire was divided into three sections. The first section focused on how IVF practitioners perform embryo disposal of surplus embryos. The second assessed the various approaches employed in order to satisfy the patient requests or requirements in regards to embryo disposal, while the third section aimed to assess the embryologists’ perspective and view in regards to implementation of a universal protocol. The IVF professionals’ practice, patterns, and opinions were assessed through ‘Yes’, ‘No’, multiple choice questions and short answers.

In an effort to reach a worldwide audience, various approaches were adopted to ensure participation. The authors contacted 68 organizations and associations on IVF practice and Reproductive Medicine. The inclusive list of all organizations contacted is available in supplementary material presented in Table 6. The authors emailed the person responsible as indicated by the respective organizations. The email aimed to introduce the Academic affiliation involved in the study, describe the nature of the study and present the recipient Association/Organization with the request to forward the questionnaire to embryologists, in order to promote the survey. In continuation, the authors employed the contact platforms available online in websites of IVF clinics to reach IVF professionals worldwide. Three thousand seven hundred and twenty-four (3724) IVF clinics worldwide were contacted. Table 1 of the Results section provides information on the number of IVF clinics contacted per continent, along with the respective responses from individual practitioners. Finally, in order

to reach a wider audience and increase participation, the questionnaire link was posted online employing social media platforms such as special interest groups in LinkedIn and Facebook. It should be highlighted that providing a response rate could not be attempted herein. This is thoroughly explained in the dedicated limitation section that follows. The reason behind this limitation is that the responses correspond to individuals participating in the survey and are not representative of IVF units.

The answers were collected and analyzed in order to unfold trends and patterns on embryo disposal practices around the globe. Analysis of the responses was automatically conducted through the program employed by Google forms and was presented in the format of pie charts. Institutional Review Board approval was not required for this study as it did not involve human or animal subjects nor collection of personal data.

Results

Following contacting via email the 68 Reproductive Medicine Organizations and Associations, the authors proceeded with emailing IVF clinics on a world wide scale. Overall 3724 emails were sent. A total of 391 IVF units were contacted in USA, 86 in Canada, 87 in Central America and 297 in South America. A total of 1787 IVF units were contacted in Europe, 151 in Africa, 812 in Asia and 113 in Australia (Table 1). Subsequently, the authors proceeded with posting the questionnaire online in Social media platforms. Following an 8-month data collection period, the google form platform was inactivated to collect and analyze data. A total of 703 filled in questionnaires from 65 different countries that are listed alphabetically in supplementary material Table 1 were acquired. Overall, Europe followed by USA yielded the highest number of responses being 351 and 186 respectively. Number of responses are categorized by continent and county and are available in supplementary material presented in Table 2-5.

The results' analysis is presented categorizing the responses with regards to the three aspects that the questionnaire aimed to investigate and report on namely: "How and when embryos are discarded", "Approaches employed to accommodate patients' requests", and "Embryologists' perspectives on implementation of a universal protocol for discarding embryos".

With regards to the actual protocol, the preferred method regarding embryo disposal of surplus embryos of a fresh IVF cycle, was reported to be "place them in a trash can strictly dedicated for embryo disposal" (39%) followed by "leave them on the bench prior to disposing in a trash can" (30.8%) and "use ethanol prior to disposing them in a trash can" (3.4%) (Figure 1). The remaining 26.8% of respondents reported on a different practice for this procedure contributing to a list of different approaches documented herein (Table 2). Regarding cryopreserved embryos, the majority of embryologists opt to "place the carrier in a trash can strictly dedicated for embryo disposal while still frozen" (36.7%), followed by "leave the carrier on the bench

prior to disposing the embryos in a trash can” (22%). A 17.7% of practitioners opt to “thaw embryos and leave them on the bench prior to disposing in a trash can”. The remaining 20.3% responded by describing a different practice for this procedure contributing to a list of different approaches (Table 2).

With regards to the timing and the routine of the discard practice, the vast majority of practitioners opt to “discard embryos separately, case by case at different time points during the day” (66.4%) (Figure 1). Nineteen-point seven percent (19.7%) “discard embryos cumulatively, at the end of the day (including all cases)”, and 5.4% are performing a “single embryo disposal”, while 8.5% of the practitioners responded by describing a different practice (Table 2). The preferred time-point for embryo disposal was “wait until Day 6 of the embryo development and then discard the embryos” (54%). A 19.2 % of the embryologists discard the surplus embryos “following cryopreservation-if employed” whereas a 7.9% discard the embryos “following embryo transfer”. Interestingly, 18.9% responded by describing a different approach (Table 2). The majority of IVF laboratories do not opt for a set-up employing a special incubator allocated as a waiting space (65.5%). Most importantly, embryo disposal in most laboratories is a witnessed procedure (63.1%), which is in compliance with a detailed Standard Operating Procedure (SOP) (54.3%).

Following on the report on “Approaches employed to accommodate patients’ requests”, the vast majority of laboratories does not operate different disposal protocols for different groups of patients (93%) and has not been asked to perform any special ceremony (82.2%) (Figure 2). The ceremonies that have been requested are presented in Table 2.

Considering the final part of the survey reporting on the “Embryologists’ perspectives on a universal protocol for discarding of embryos”, it appears that most of the participants believe that the embryology practice would benefit from a universal protocol regarding embryo disposal (59.5%) (Figure 3).

Table 1: Number of IVF units contacted per continent along with respective responses contributed by individual practitioners.

	No of IVF units contacted	No of Practitioners Responding
IVF Units (Worldwide)	3724	703
<i>America</i>	861	235
<i>Canada</i>	86	23
<i>USA</i>	391	186
<i>Central America</i>	87	1
<i>South America</i>	297	25
<i>Europe</i>	1787	351
<i>Africa</i>	151	21
<i>Asia</i>	812	89
<i>Australia</i>	113	7

Table 2: A representative list of responses reporting on the section of the questionnaire that inquired on “different practices”.

Different responses on how IVF laboratories perform embryo disposal of surplus embryos of a fresh IVF cycle	Different responses on how IVF laboratories perform embryo disposal of cryopreserved embryos.	Different responses on the time point that practitioners perform disposal of the embryos	Different responses on special ceremonies performed
“Place the embryos in a trash can dedicated for biological waste”	“Exposure of the straws to ambient temperature and disposal of the embryos employing secure medical waste containers”	“Day 6 or Day 7 (depending on embryo quality)”	“Request of a prayer by a Catholic priest before the disposal procedure”
“Add sterile water and then discard embryos in biohazard bag”	“24-hour exposure period at room temperature for the embryo carriers before disposal into the designated trash can”	“7 days following completion of the cycle”	“A Jewish prayer book to be placed near the incubator”

“Expose the embryos to high temperature”	“Leave embryos to thaw and expose them to high temperature”	“After Day 7 or 48 hours following developmental arrest”	“Read a prayer before the disposal procedure”
“Place the embryos in the general trash can”	“Unload embryos from cryo-carrier and allow to lyse in water prior to placing in clinical waste bin”	“Wait until day 8”	“Blessing embryos before the disposal procedure”
“No disposal procedure in place, all embryos are vitrified and stored”	“Place straws in standard clinical waste bin”	“Wait till day 9 or 10”	“Have a moment of silence before the disposal procedure”
“Collect embryos and send them for burial service”	“Unwanted embryos are donated to the laboratory for training purposes prior disposal”	“4 days following last day in culture”	“Allow patients a moment with their embryos prior to the disposal procedure”
“Unwanted embryos are donated to the laboratory for training purposes prior to disposal”	“By prior consent, all patients who do not wish to use their frozen embryos donate them to another couple via a National embryo donation service”	“After at least day 10 of culture”	“Arrange for a Christian burial service”
	“Frozen embryos are sent to a company that disposes of the embryos for the patient for a fee”	“After keeping them for at least another week in a separate incubator”	“Arrange for a burial service through a Catholic organization providing a ceremony for the embryos free of charge to the couples”
	“Frozen embryos are given to the patients in a can”	“Following the pint that embryo presents with signs of degeneration”	“Arrange for the presence of a religious representative during the procedure”

	“No disposal procedure in place, all embryos are being delivered to long term storage banks”	“3 years following freezing”	“Fulfilling the patients’ request to be allowed to bury their embryos”
		“According to each case and patients’ will”	“Request to release the embryos to the patient in order for them to be buried with the deceased wife”
			“Given to patient in order for the embryos to be buried in their back yard”
			“Patient documenting their intention to plant a tree at the burial site”
			“Discard the embryos at a specific time so that relatives can acknowledge and honor the moment of disposal”
			“Sing a song to the embryos before the disposal procedure”

Limitations of the study

It may be presumed that despite the anonymity ascertained through the format of the questionnaire, social reasons may have led some respondents not to disclose practices that are less than socially acceptable. Debating on an issue of bioethical nature, it is understandable that the opinions of non-respondents may have varied significantly from those of respondents. In an effort to reach IVF professionals the anonymous questionnaire was forwarded via email on communication platforms addressing Associations, organizations, and IVF clinics, and individual practitioners were invited to participate. Throughout this process, difficulties were encountered in conducting this research in the context of ascertaining responses or even ascertaining acknowledgment of the invitation to participate. This fact, lead to the authors not being in a position to report on which organizations may have forwarded the questionnaire, introducing possible bias. Ultimately, it was not possible to reach a greater audience through Associations and Societies, which may have enabled collection of a larger dataset. Failing to receive the volume of feedback that was originally anticipated by the authors, may have been attributed to such difficulties.

Maintaining the anonymity of the participants was imperative and was ensured through the employment of the google forms platform. In turn, this approach enabled reflection of the individual practitioners' opinion and current practice. This data corresponds only to the stated country of practice and not to an individual IVF clinic. Further to that, methodology could not warrant that a party did not respond twice. This equally presents as a limitation. The general rules that apply when forwarding a questionnaire and collecting electronically sourced data stand for this approach similarly. The value of the analysis is based on the principle that a participant will provide true data on an individual basis as requested.

As indicated previously, responses do not correspond to IVF units but rather to IVF professionals. This may be serving as a confounder in analyzing the results, and translating

them in trends representing IVF units. It is the authors' perspective presenting this study, that the individual practitioners' opinion must be voiced and evaluated in order to improve the scientific and clinical practice. In the current study the currency is not the IVF practice, but rather the IVF practitioner.

The authors cannot provide the reader with a true response rate. This could not be possible primarily due to the fact the questionnaire was distributed through organization, associations, IVF units and social media platforms. One cannot extrapolate that the communication effort referring to a single email sent on behalf of the authors corresponds to a single response.

An additional limitation in this survey is the language employed in the anonymous questionnaire. The English language is the lingua franca in the clinical and scientific field [29]. Nonetheless, the language barrier may be assumed to have served as an obstacle in sourcing data and reaching countries where English is not spoken, possibly resulting to lack of contribution from certain parts of the world.

Discussion

This study highlights the existing diversity in human embryo disposal protocols employed in IVF laboratories worldwide. Following a comprehensive review of the literature little has been published on embryo disposal practices on a worldwide scale. Gurmankin et al in 2004 reported-for the first time-on the current embryo disposal practices in IVF clinics in the United States (U.S.). This study highlighted the diversity regarding this laboratory procedure and the direct association to the existing controversial moral status of the human embryo particularly in the U.S. During their survey, Gurmankin et al., mailed anonymous self-administered questionnaires to directors of 341 American IVF units yielding 217 responses [30]. In this report, authors underline the variety documented regarding equally the laboratory practices for embryo disposal, along with the management of providing respective information to the

couples, and their subsequent decision. Additionally, this study raises questions with respect to the rationale behind certain practices. “Could the moral sensitivity, ethical considerations and the controversial moral status of the human embryo in vitro influence and drive the practice?” The undefined moral status of the human embryo remains to be one of the most significant ethical dilemmas that has surfaced in the world of Assisted Reproduction Technology (ART) [31]. Although this immensely complicated issue, is substantially discussed in the bioethical and philosophical literature, it remains unclear [31]. According to the current legislation dictating employment of human embryos in the United States, Australia, United Kingdom and Europe, the human preimplantation embryo has very little or no independent moral status [32].

Both Thomas Douglas and Professor Julian Savulescu are renowned bioethicists and have contributed significant work which is recognized as world leading research in the field of medical and practical ethics. Addressing this complex subject of morality in human embryo research in 2009, they reported that all embryos are defined by a special moral value. This moral value is a pivotal component in the plan to form or extend a family, and should be viewed as an essential factor when designing a study to fulfill a research purpose [33].

Clinical embryologists are being trained to culture, transfer, cryopreserve or to discard human preimplantation embryos, while the moral status of human embryos in the very beginning of forming life, remains undefined. Clinical embryologists may be viewed by some as acting to serve a higher purpose in an otherwise “grey” bioethical zone. In an effort to clarify this complex subject in 2017, John Janez Miklavcic and Paul Flaman exploring the personhood status of the human zygote, the embryo and the fetus, presenting as an undoubtable bioethical dilemma, argued that it is most reasonable to support the belief that the personhood status may be acquired-at the point of human fertilization [34]. Based on the above, the bioethical status of the preimplantation embryo is undoubtable and deserves the respective courtesy and

consideration. Even though, aspects of practical nature may account as drivers of this diversity in shaping various practices of embryo disposal, nonetheless, considerations of moral and bioethical nature may be certainly implicated exerting a strong influence in defining practice. Perhaps the standing variety on disposal protocols, as evident by data sourced herein, may be potentially attributed to moral and bioethical perceptions surrounding the preimplantation embryo's bioethical stance. Nonetheless, the present study does not allow for any direct associations to be drawn.

According to the "World Population Review" there are 195 countries in the world hosting a population of 7,632,819,325 people that may inquire on infertility treatment in more than 3,564 IVF clinics worldwide. The standing legislation in the IVF World regarding embryo disposal protocols contributes significantly to a portraying a landscape of diversity. Legal frameworks vary between countries providing IVF services, a fact that serves as a restriction in clinical practice in certain cases, while at the same time fueling cross border reproductive care. Malta for instance is one of the countries that legislation does not permit embryo discarding. Instead embryologists are allowed to inseminate up to 3 oocytes while all resulting embryos are required to be transferred [35,36]. It is this diversity indicated through data presented in this study that may strengthen the need for a common protocol on human embryo disposal.

The authors purposefully refrain from justifying or extrapolating on the responses collected, nonetheless a critical analysis is attempted herein. This survey could be theoretically divided in three sections aiming to all-inclusively investigate the worldwide practice. The first section, including questions 1 to 6 and 8, focuses on how IVF practitioners perform embryo disposal of surplus embryos. In both fresh and frozen cycles, the majority of practitioners (39% regarding fresh and 36.7% regarding frozen cycles) dispose of the embryos by placing them directly in a trash can without thawing the embryos first in case of frozen embryos (Figure 1). This, may be viewed as the most straightforward and time-efficient option of performing the

disposal. Such a practice maybe attributed to accommodating the hectic, time-demanding schedule commonly associated with IVF laboratories.

Information regarding the timing each laboratory chooses to discard the embryos as part of the disposal protocol was documented. Furthermore, 66.4% of practitioners discard the embryos separately, case by case, at different time points during the day, which similarly strengthens the scenario of favoring a straightforward practice instead of dedicating a special time during the day to perform this as a separate procedure (Figure 1). In Table 2 among other practices, a longer than Day 6 incubation time, prior to discarding the embryos, has been reported. Fifty-four percent (54%) of embryologists wait until Day 6 to discard the surplus embryos (Figure 1). Such an approach may ensure practicing the act of disposal in a safe fashion, as D6 signals the end of the embryo culture. The longest time reported in this study was the 14-day suspension of surplus embryos in the incubator environment, always in accordance to the 14-day limit with regards to maintaining human embryos in culture [37]. It has been years since the paper published by “Nature” on being able to study embryos in the laboratory for 14 days. Understandably, the possible requirement to amend the 14-Day rule, or change it to a 28-Day rule [38] has already been reported [39].

As reported in Table 2 there are various protocols employed worldwide for discarding human embryos in fresh and in cryopreserved cycles during infertility treatment. Ethanol or water may be implemented in order to proceed with degeneration of embryos on the bench. Implementation of the “grave yard” incubator was described in our results. Nonetheless, sixty-five-point five percent (65.5%) of practitioners do not use a special allocated incubator as a “waiting space” prior to the disposal procedure (Figure 2). A specially allocated waiting space could perhaps not be a feasible option for an IVF laboratory where allocating incubator space may be difficult.

Through this survey 63.1% of embryologists reported that embryo disposal is a witnessed procedure, while 54.3% reported that a detailed SOP for this procedure is in place (Figure 2). Although, the majority of the clinics (54.3%) refer to the procedure employing an SOP, this result may signal an alert and classify this as non-optimal practice. Ideally, percentages referring to both witnessing of the procedure and employing a detailed SOP for the disposal procedure, should be closer to 100% ensuing a safe and effective practice minimizing room for error.

In the second part of the survey, questions 7, 9 and 10, assess the various approaches employed in order to satisfy patient requests or requirements in regards to embryo disposal (Figure 2). As mentioned above, in order to mitigate the “abandoned embryos” scenario, IVF clinics request that couples proceed with an embryo disposition decision (EDD). Embarking on such a decision may be highly challenging for couples as they may encounter difficulties in committing to any of the provided options. They may often get emotional experiencing feelings of regret about making the wrong decision. Occasionally, further options may be required to be presented if the standard protocol of embryo discarding fails to meet the couples’ needs [31]. The couples’ psychology during infertility treatment is of utmost importance and respective attention must be provided. It has been reported that couples may consider their embryos as their unborn children or even existing children [24,40–42] hence the process of grief for the loss when their embryos have to be discarded is a reality. Taking into consideration this psychological perceptive it may come as no surprise that this survey verifies –as anticipated- that it is not rare for IVF practitioners worldwide to be asked for burial services, prayers prior to discarding the surplus embryos, or even the option for the embryos to be released to the couple presenting them with a “take-home” option. The general population is familiar with the options that death may be followed by burial or cremation according to the person’s beliefs and will [43]. Interestingly, optional burial services can nowadays be provided

by specific funeral homes that offer a service described as a corporal and spiritual care for the so-called “embryonic human beings”. In recent years the option of swirling ashes into glass art creations available from companies has even become available and communicated through social media. Should the preimplantation embryo be allowed the same burial options? Should human life be considered equal from the first hours of the zygote formation to the point that death by natural causes takes place? May such questions claim answers or at least a thesis from the scientific community of clinical embryologists who are being called to discard the supernumerary preimplantation embryos? These questions merit an analysis on the bioethical perspectives raised in this context. Nonetheless, such an approach is not attempted herein, as this study focuses on presenting the various practices, trends and opinions, rather than analyzing the respective issues stemming from this practice in light of the bioethical stance of the preimplantation embryo.

Notably, the majority of practitioners (93%) responded that they do not employ different protocols for different groups of patients, while 17.8% reported that they have been asked to perform some kind of a ceremony for disposal of these embryos (Figure 2). In particular, some practitioners have reported performing a religious or quasi-religious disposal ceremony. Some clinics require the couple’s participation in disposal, some allow it but do not require it, while other clinics discourage or forbid it. All these documented requests from patients with different religious concerns raise questions on whether and how could religious ceremonies be adopted in IVF clinical routine practice. If so, should these ceremonies be practiced as an individual exception treatment following a special request, or should all couples irrespectively be presented with the option in a horizontal fashion?

This survey additionally raises questions regarding the rationale, the driver and the need fueling certain clinical practices. Why do certain protocols require cryopreserved embryos to thaw prior to their disposal? Do they regard this practice as one following a more natural course

regarding the physiology of the embryo? How does the scientific community respond to certain protocols allowing and encouraging couples to proceed with discarding their own surplus embryos, while other protocols consider this practice as deviating from standard procedure? Such major discrepancies may significantly differentiate the clinics, and what may merit further investigation is whether disclosure of the embryo disposal protocol by the clinics could serve as an incentive for couples in reaching an informed decision when contemplating which IVF unit to pursue treatment in. As literature fails to provide evidence, while nothing systematic has been reported, the couples' role in this remains ambiguous.

The third and last section of the survey, including question 11, aims to assess the embryologists' perspective. As a result, more than half of the practitioners (59.5%) contributing to this survey reported that the embryology practice would benefit from a universal protocol (Figure 3).

Our results, along with the practices presented in Table 2, highlight the divergence between the reported practices. This is heightened in light of the fact that all the reported percentages are close to 50% indicating that there is clearly "room" for variety in practice. Notably, no option achieved a true majority status by percentages over 50%. Albeit practicing clinical embryology may entail that diversity is acceptable and in fact a coveted quality trait in an embryologist, nonetheless on the subject of embryo disposal practices the clinical embryology field would certainly benefit from more consistency rather than diversity. The majority of IVF clinics worldwide identify as a principal priority cryopreservation of surplus embryos. Our results present that practitioners diverse in protocols regarding management of supernumerary embryos, responsibility for disposal, and use of ceremonies employed during the disposal procedure. Variation was also noted in allowing the couples' involvement in the disposal procedure itself or alternatively in keeping it strictly a laboratory routine procedure. Despite its limitations, this study uniquely provides insight into global embryo disposal practices and

trends, and raises questions bearing on the standardization and perhaps the possibility of regulation of clinical practices, while strengthening the need for defining and concurring on a commonly accepted universal protocol. From another perspective, the practice of embryo disposal may unquestionably harbor religious concerns which may influence and define practice accordingly [44]. Nonetheless, concerns of bioethical nature related to the practice may be argued in light of the fact that the process employed to discard an embryo may not be viewed as being associated or affecting the final status of the embryo. This perspective may render the presently documented divergence on the disposal practices as of limited consequence. A key parameter in attempting to define optimal practices in discarding IVF embryos is concurring on the status of the preimplantation embryo. As this remains unclear, the need for adopting a universally accepted practice may be in return strengthened.

In regards to the standing diversity on disposal protocols, this data may serve as the trigger for design and conduction of innovative multi-sectional studies. Future studies may attempt a multifactorial approach in depicting the current status on embryo disposal practices. This would enable an all-inclusive portrait encompassing various levels of the practice and their respective associations. Surveys could focus on evaluating practical issues regarding embryology practice, along with quality and safety issues, and further entailing psychological perspectives, ethical reflections, along with religious concerns surrounding the practice of disposal in light of the bioethical stance of the preimplantation embryo. Most importantly, it would be interesting to analyze viewpoints focusing on the perceptions concerning equally both sides, the practicing embryologists and the patients. Overall, this article contributes significantly to the literature addressing disposition of surplus embryos. The authors attempt to highlight the notable variability among IVF practice on a global scale. This study may serve as an incentive to consider the value of a commonly accepted protocol, especially as results articulate the importance of implementing standardization regarding embryo discard practices.

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SUPPLEMENTARY MATERIAL

Table 1: List of countries contributing data to the survey.

Countries					
1	Albania	24	Hungary	47	Romania
2	Algeria	25	India	48	Russia
3	Argentina	26	Indonesia	49	Saudi Arabia
4	Australia	27	Iran	50	Serbia
5	Bangladesh	28	Ireland	51	Slovakia
6	Belgium	29	Italy	52	Slovenia
7	Bosnia and Herzegovina	30	Japan	53	South Africa
8	Brazil	31	Jordan	54	Spain
9	Bulgaria	32	Kuwait	55	Sri Lanka
10	Canada	33	Latvia	56	Sweden
11	Chile	34	Lebanon	57	Switzerland
12	China	35	Malaysia	58	Taiwan
13	Colombia	36	Mexico	59	Thailand
14	Croatia	37	Montenegro	60	Turkey
15	Cyprus	38	Netherlands	61	Ukraine
16	Czech Republic	39	Nigeria	62	United Arab Emirates
17	Denmark	40	Norway	63	United Kingdom, UK
18	Egypt	41	Oman	64	United States of America, USA
19	Finland	42	Pakistan	65	Venezuela
20	France	43	Palestine		
21	Georgia	44	Poland		
22	Germany	45	Portugal		
23	Greece	46	Kazakhstan		

Table 2: Number of IVF units contacted that yielded responses. Data is presented per country in the continent of **America**

AMERICA	No of IVF units contacted	No of Practitioners Responding
NORTH AMERICA	477	209
<i>Canada</i>	86	23
<i>USA</i>	391	186
CENTRAL AMERICA	64	1
<i>Mexico</i>	64	1
SOUTH AMERICA	251	25
<i>Argentina</i>	52	2
<i>Brazil</i>	139	14
<i>Chile</i>	14	1
<i>Colombia</i>	27	1
<i>Venezuela</i>	19	7

Table 3: Number of IVF units contacted that yielded responses. Data is presented per country in the continent of **Europe**

EUROPE	No of IVF units contacted	No of Practitioners Responding
<i>Albania</i>	7	5
<i>Belgium</i>	59	1
<i>Bosnia and Herzegovina</i>	4	3
<i>Bulgaria</i>	20	8
<i>Croatia</i>	12	5
<i>Cyprus</i>	21	1
<i>Czech Republic</i>	37	10
<i>Denmark</i>	28	24
<i>Finland</i>	20	7
<i>France</i>	73	15
<i>Georgia</i>	7	3
<i>Germany</i>	166	11
<i>Greece</i>	46	68
<i>Hungary</i>	13	1
<i>Ireland</i>	7	13
<i>Italy</i>	412	23
<i>Latvia</i>	4	3
<i>Montenegro</i>	4	6
<i>Netherlands</i>	129	7
<i>Norway</i>	21	3
<i>Poland</i>	28	5
<i>Portugal</i>	51	9
<i>Romania</i>	13	15
<i>Serbia</i>	17	8
<i>Slovakia</i>	10	4
<i>Slovenia</i>	4	4

<i>Spain</i>	244	18
<i>Sweden</i>	20	8
<i>Switzerland</i>	39	12
<i>Ukraine</i>	28	8
<i>United Kingdom (UK)</i>	173	43

Table 4: Number of IVF units contacted that yielded responses. Data is presented per country in the continent of **Africa**

AFRICA	No of IVF units contacted	No of Practitioners Responding
<i>Algeria</i>	2	7
<i>Egypt</i>	41	10
<i>Nigeria</i>	11	4

Table 5: Number of IVF units contacted that yielded responses. Data is presented per country in the continent of **Asia**

ASIA	No of IVF units contacted	No of Practitioners Responding
<i>Bangladesh</i>	4	1
<i>China</i>	17	7
<i>India</i>	266	9
<i>Indonesia</i>	5	5
<i>Iran</i>	15	1
<i>Japan</i>	15	1
<i>Jordan</i>	11	4
<i>Kuwait</i>	6	6
<i>Kazakhstan</i>	2	3
<i>Lebanon</i>	14	2
<i>Malaysia</i>	57	2
<i>Oman</i>	1	4
<i>Pakistan</i>	13	5
<i>Palestine</i>	1	2
<i>Russia</i>	41	19
<i>Saudi Arabia</i>	17	2
<i>Sri Lanka</i>	1	1
<i>Taiwan</i>	8	4
<i>Thailand</i>	17	5
<i>Turkey</i>	80	2
<i>United Arab Emirates</i>	8	4

Table 6: Reproductive Medicine Organizations, Associations and Societies that were contacted to promote the survey.

Reproductive Medicine Organizations, Associations and Societies	
1	American Society for Reproductive Medicine, USA
2	Argentine Society of Reproductive Medicine - SAMeR, Argentina
3	Association for Fertility and Reproductive Health (AFRH), Nigeria
4	Austrian Society of Sterility, Fertility and Endocrinology, Austria
5	Bangladesh Fertility Society (BFS), Bangladesh
6	Belgian Society for Reproductive Medicine, Belgium
7	Brazilian Society of Human Reproduction, Brazil
8	British Fertility Society, United Kingdom
9	Bulgarian Association of Sterility & Reproductive Health, Bulgaria
10	Canadian Fertility and Andrology Society, Canada
11	Chilean Society of Reproductive Medicine (SOCMER), Chile
12	Chinese Society of Reproductive Medicine, China
13	Colombian Association of Fertility and Reproductive Medicine (ACFE), Colombia
14	Czech Society for Sterility and Assisted Reproduction, Czech Republic
15	Ecuadorean Federation of Gynecological Societies (FESGO), Ecuador
16	Ecuadorian Society of Reproductive Medicine (SEMER), Ecuador
17	Egyptian Fertility and Sterility Society, Egypt
18	Fertility and Sterility Society of Bangladesh, Bangladesh
19	Fertility Society of Australia, Australia
20	Finnish Gynecological Association, Finland
21	French Society for the Study of Fertility, France
22	Georgian Association of Reproductive Health, Georgia
23	German Society of Reproductive Medicine (DGRM), Germany
24	Fertility Society of Ghana (FERSOG), Ghana
25	Guatemalan Association of Fertility and Human Reproduction, Guatemala
26	Hellenic Fertility and Sterility Society, Greece
27	Hungarian Society of Assisted Reproduction (MART), Hungary
28	Indian Fertility Society (IFS), India
29	Indian Society for Assisted Reproduction (ISAR), India
30	Indonesian Association of In Vitro Fertilization (PERFITRI), Indonesia
31	Iranian Society for Reproductive Medicine, Iran
32	Iraqi Fertility Society, Iraq
33	Irish Fertility Society, Ireland
34	Israel Fertility Association, Israel
35	Italian Society of Fertility, Sterility and Reproductive Medicine (SIFES), Italy
36	Japan Society of Reproductive Medicine (JSRM), Japan
37	The Jordanian Society for Fertility and Genetics, Jordan

38	The Korean Society for Reproductive Medicine, Korea
39	Mexican Association of Reproductive Medicine, Mexico
40	Mongolian Reproductive Endocrinology and Infertility Society
41	Moroccan Society of Fertility and Contraception, Morocco
42	Obstetrical and Gynecological Society of Myanmar
43	National Hospital of Obstetrics and Gynecology, Vietnam
44	Obstetrical and Gynaecological Society of Malaysia (OGSM), Malaysia
45	Obstetrical and Gynecological Society of Singapore (OGSS), Singapore
46	Paraguayan Fertility Society, Paraguay
47	Peruvian Fertility Society, Peru
48	Philippine Society of Reproductive Medicine (PSRMI), Philippines
49	Polish Gynaecological Association Section of Fertility and Sterility (SPiN), Poland
50	Portuguese Society of Reproductive Medicine (SPMR), Portugal
51	Romanian Association of Human Reproduction, Romania
52	Russian Association of Human Reproduction (RAHR), Russia
53	Salvadoran Society of Gynecological Endoscopy and Medicine, El Salvador
54	Saudi Arabian Fertility Society, Saudi Arabia
55	Serbian Association for Human Reproduction, Serbia
56	Slovenian Society of Reproductive Medicine, Slovenia
57	Southern African Society for Reproductive Science and Surgery, South Africa
58	Spanish Fertility Society, Spain
59	Sudan Human Reproduction and Embryology Society
60	Swedish Society of Obstetrics and Gynecology (SFOG), Sweden
61	Swiss Society for Reproductive Medicine (SGRM), Switzerland
62	Taiwanese Society for Reproductive Medicine, Taiwan
63	Tunisian Society of Fertility and Sterility, Tunisia
64	Turkish Infertility Foundation, Turkey
65	Turkish Society for Reproductive Medicine (TSRM), Turkey
66	Uganda Fertility Society, Uganda
67	Uruguayan Society of Human Reproduction (SURH), Uruguay
68	Venezuelan Society of Obstetrics and Gynecology (SOGVZLA), Venezuela

Figure 1: The questionnaire on embryo disposal practices

(<https://goo.gl/forms/UhC7soezcdaJGKpr2>)

The image shows a Google Form titled "Anonymous questionnaire on embryo disposal practices". The form is divided into three vertical panels. The first panel contains the title, a subtitle "Research regarding embryo disposal practices in the IVF laboratory", a "Required" field for "Country", and a "State" field. Below these are two multiple-choice questions: "1. How do you perform embryo disposal of surplus embryos of a fresh IVF cycle?" and "2. How do you perform embryo disposal of cryopreserved embryos?". Each question has four options (A, B, C, D) and a "Different practice" option. The second panel contains question "3. Does your disposal protocol include perishing the embryos?" with four options (A, B, C, D) and a "Different practice" option. It also includes a "When do you perish embryos?" question with four options (A, B, C, D) and another "Different practice" option. The third panel contains question "4. Do you have a detailed SOP in order to perish the surplus embryos?" with two options (Yes/No), question "5. Have you been asked to perform any kind of ceremony for these embryos?" with two options (Yes/No), question "6. What kind of ceremony?" with a text input field, and question "7. Do you believe that the embryology practice would benefit from a universal protocol regarding embryo disposal?" with two options (Yes/No). At the bottom of the third panel, there is a "Thank you for your contribution!" message, a "SUBMIT" button, a progress bar, and the text "Page 1 of 1".

Anonymous questionnaire on embryo disposal practices

Research regarding embryo disposal practices in the IVF laboratory

* Required

Country: *

Your answer

State:

Your answer

1. How do you perform embryo disposal of surplus embryos of a fresh IVF cycle?

A. Leave on the bench prior to disposing in a trash can

B. Use of ethanol prior to disposing in a trash can

C. Place them in a trash can strictly dedicated for embryo disposal

D. Different practice

In case of "Different practice", please give details:

Your answer

2. How do you perform embryo disposal of cryopreserved embryos?

A. Thaw embryos and leave on the bench prior to disposing in a trash can

B. Thaw embryos and use ethanol prior to disposing in a trash can

C. Leave the carrier on the bench prior to disposing in a trash can

D. Place the carrier in a trash can strictly dedicated for embryo disposal while still frozen

E. Different practice

In case of "Different practice", please give details:

Your answer

3. Does your disposal protocol include perishing the embryos:

A. Cumulatively, at the end of the day (including all cases)

B. Separately, case by case at different time points during the day

C. Single embryo disposal

D. Different practice

In case of "Different practice", please give details:

Your answer

4. When do you perish embryos?

A. Following embryo transfer

B. Following cryopreservation if employed

C. Wait until Day 6

D. Different practice

In case of "Different practice", please give details:

Your answer

5. Do you move the embryos to be perished in a special allocated incubator "waiting space" prior to the disposal procedure?

Yes

No

6. Is disposal of embryos a witnessed procedure?

Yes

No

7. Do you have different disposal protocols/practices for different groups of patients?

Yes

No

If YES please specify:

Your answer

8. Do you have a detailed SOP in order to perish the surplus embryos?

Yes

No

9. Have you been asked to perform any kind of ceremony for these embryos?

Yes

No

10. What kind of ceremony?

Your answer

11. Do you believe that the embryology practice would benefit from a universal protocol regarding embryo disposal?

Yes

No

Thank you for your contribution!

SUBMIT

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