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ASSISTED REPRODUCTION TECHNOLOGIES

Recent trends in embryo disposition choices made by patients following in vitro fertilization

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Abstract

Purpose To assess longitudinal trends in in vitro fertilization (IVF) patients' choices for disposing of cryopreserved embryos.

Methods This is a retrospective cohort study of embryo disposition forms submitted between January 2000 and February 2020 at a university-based fertility clinic. Primary outcome was disposition decision. Binary and multivariable logistic regression were performed to determine odds ratios (OR) for decisions according to female age, education, race, religion, state of residence, area deprivation index based on zip code, and IVF pregnancy history. We also assessed disposition year, storage duration, and number of stored embryos.

Results Forms were reviewed from 615 patients; 50.6% chose to discard embryos, 45.4% donated to research, and 4.1% chose reproductive donation. In the regression model, two factors were significantly associated with donation to research: female listing "no preference" or declining to list religious preference (OR 2.56, 95%CI 1.44–4.54) and live birth of multiples after IVF (OR 1.58, 95%CI 1.05–2.36). Before 2012, females younger than age 30 at storage were equally likely to choose to donate embryos to research as discard them. However, between 2013 and 2020, females younger than 30 were significantly more likely to discard than donate embryos for research (OR 2.87, 95%CI 1.13–7.28).

Conclusion Since 2013, the majority of patients younger than 30 at storage have chosen to discard cryopreserved embryos. Before then, patients were more likely to donate embryos for research. To ensure sufficient embryos are available for research, young patients, who are most likely to have cryopreserved embryos, should be counseled about options for donation.

Keywords Embryo disposition · Cryopreserved embryos

Introduction

In 2016, US fertility clinics performed nearly 200,000 assisted reproductive technology procedures with the intent to transfer at least one embryo [1]. In many of these procedures, excess embryos were produced and cryopreserved. Although patients initially cryopreserve their embryos in the hopes of increasing their chances for a future live birth, up to 40% of cryopreserved embryos are unused [2]. When patients choose to end cryostorage for their embryos, fertility clinics customarily ask that patients express their wishes regarding the disposition of embryos. Options include donating them to another patient or couple for reproduction, discarding them, or donating them for research. In the 1990s, patients commonly chose to discard their embryos. In the early 2000s, patients began to instead choose to donate their embryos for research [3–5]. For example, Lanzendorf et al. examined disposition forms at our institution between 2002 and 2007 and reported that 59% of 149 patients chose to donate their embryos to research.

In 2002, a survey of clinics found that 400,000 embryos remained in long-term storage, and this number has increased annually [6]. Over the last 10 years, at least three significant changes have increased the number of embryos available for cryopreservation. First, improved laboratory conditions have allowed for extended culture techniques and increased the numbers of high-quality blastocysts [7]. Second, single embryo transfer has been increasingly used in the USA, especially since 2013, resulting in couples transferring fewer of the

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generated embryos [8]. Third, improvements in vitrification techniques have allowed more efficient cryopreservation of embryos [9]. Given these changes in practice, we sought to determine whether patients' disposition decisions have changed over time and to identify factors associated with patient choice for embryo disposition. We were especially interested in women who were under age 30 at the time of embryo cryopreservation, as women in this group are very likely to have high-quality embryos.

Materials and methods

Disposition practices at our institution

All patients who are currently storing embryos at our facility are sent a final disposition consent form annually, just before yearly billing for storage. When a patient or couple decides to end cryostorage, they are asked to choose one of the following options for their embryos: (1) discard, (2) donate to research that has been approved by our Institutional Review Board (IRB), or (3) transfer to another facility for reproductive donation. The same disposition option must be chosen by both partners. Couples are not required to receive outside counseling or psychological screening before finalizing this decision. The patient is educated that all embryos donated to research are used for scientific research that has been approved by the IRB at Washington University and if the embryos cannot be used for research, they will be discarded.

Ethical review, methods, and data collected

This study was approved by the Washington University School of Medicine in St. Louis IRB. A retrospective cohort study was conducted of embryo disposition forms submitted between January 2000 and February 2020. Additionally, patients' available electronic medical records were queried. Data were collected on the female patient age (at the time of storage and disposition), education, race, religion, whether or not the female resided in a state mandating infertility insurance coverage at the time of storage, disposition year, duration of storage, total number of oocyte retrievals, number of embryos in storage, use of donor gametes, live birth outcomes (whether from IVF or spontaneous), and area deprivation index (ADI). Same-sex male couples were not included in this data collection. The ADI is a comprehensive tool that allows rankings of addresses by socioeconomic disadvantage and reflects key employment, housing quality, and poverty measures. ADI was defined according to the patient's residential zip code at the time of embryo cryopreservation [10]. Religious categories listed in the electronic medical record were no religion listed (blank), no preference, Christian or Protestant, Catholic, or other (Muslim, Hindu, Judaism, Mormon, Greek Orthodox, or Other Religion). Any write-in information (for instance, their reason for disposition) the patients provided on the disposition form was recorded. One author (VA) coded the responses into four categories.

Data analysis

IBM SPSS 24 software was used to analyze data. Bivariate analyses used the chi-square test for categorical variables and Student's t test for continuous variables. $P < 0.05$ was considered statistically significant. Multivariate logistic regression analyses were performed to estimate odds ratios (ORs) and examine the effects of patient characteristics on disposition decision. Variables with a $P < 0.05$ were entered as covariates. Comparisons were carried out between all three groups and then between one group and the other two (discard vs. donate to research plus reproductive donation; reproductive donation vs. discard plus donate to research; and donate to research vs. discard plus reproductive donation). Bivariate analysis was also performed for the disposition year. Multivariate logistic regression analysis was performed to examine the effect of disposition year (2000–2012 or 2013–2020) on disposition decision by patients in different age groups. Changes in disposition over time were analyzed using a general linear model (GLM), with disposition decision as the dependent variable and disposition year as a fixed factor. Results of the GLM are shown as estimated marginal means.

Results

We reviewed 615 unique disposition forms and found that 316 (50.6%) patients chose to discard their embryos, 270 (45.4%) donated to research, and 25 (4.1%) chose reproductive donation. Demographic and clinical data for female patients discontinuing storage are shown in Table 1. The majority listed no religion or noted no preference, were white, had a college education, lived in the upper two state ADI quintiles, had five or fewer embryos stored, and had undergone only one egg retrieval. About one-third of the patients underwent two or more egg retrievals. As shown in Table 2, at the time of submitting their embryo disposition forms, the largest fraction of patients (40.8%) had two children (including those conceived spontaneously and via IVF), and 12.7% had not conceived. Each year between 2006 and 2019, between 2.6 and 18.1% of patients who were sent a cryopreservation bill discontinued storage (see Table 3). (Billing data was not available for the years 2013–2017.)

The following factors were not associated with disposition choice: whether pregnancy was achieved with IVF, whether two or more live births were achieved (either spontaneous or via IVF), number of egg retrievals, use of donor gametes, number of embryos in storage, duration of storage, residence

Table 1 Demographics

Characteristic	*N*	%
Religion ($n = 615$)		
No religion listed	161	26.2
No preference	159	25.9
Christian or Protestant	132	21.5
Catholic	117	19.0
Other religion (Muslim, Hindu, Judaism, Mormon, Greek Orthodox, Other)	46	7.5
Race ($n = 615$)		
White	552	89.8
Asian	39	6.3
Black	17	2.8
Other	7	1.1
Donor gametes used	25	4.1
Residence in a state mandating infertility coverage		
Yes	320	52.0
No	295	47.9
< 30	172	27.9
31–34	224	36.4
35–38	148	24.1
> 39	71	11.5
Number of embryos stored		
≤ 5	523	85.0
6–10	74	12.0
11–15	16	2.6
≥ 16	2	0.3
Yes	514	83.6
No	58	9.4
Unknown	43	7.0
Number of egg retrievals		
1	408	66.3
2	144	23.4
3	48	7.8
≥ 4	15	2.4
State area deprivation index quintile		
1	155	25.2
2	226	36.7
3	103	16.7
4	86	14.0
5	45	7.3
Duration of storage		
≤ 3.5 years	333	54.1
> 3.5 years	282	45.9

in a state mandating fertility insurance coverage, race, possession of a college degree, and ADI (Table 4).

In our regression model, patients were significantly more likely to choose reproductive donation over other options if the woman was older than 37 at the time of disposition or had undergone exactly one egg retrieval (Table 5). In the regression model, patients were more likely to donate embryos to research than to discard them if the woman listed "no preference" or declined to list a religious preference, or had had a live birth of multiples (Table 5). Finally, patients were more likely to discard embryos than to donate them to research if they listed "Catholic" as their religion than if they listed no religion or no preference for a religion (OR 2.02, 95% CI 1.03–4.06, $P = 0.04$).

Table 2 Live birth outcomes before the decision to dispose of embryos

Live births	*N*	%
Live birth from IVF?		
Yes	537	87.3
No	78	12.6
Live birth outcome from IVF		
Multiples	186	34.6
Singletons only	351	65.3
Number of live births from IVF		
Zero	85	13.8
One	393	63.9
Two	121	19.7
≥ three	16	2.6
Total number of live births, including spontaneous and IVF ($n = 612$)		
Zero	78	12.7
One	171	27.8
Two	251	40.8
Three	98	15.9
Four	14	2.3

Among women who were under age 30 at the time of cryopreservation, those who submitted their disposition form in 2013 or later were more likely to discard their embryos (over donating for research or reproductive donation) than those who submitted their forms before 2013 (Table 5). Additionally, the trends of disposition decisions of women in all age groups have changed over the years (Fig. 1). In general, in the last decade, there have been a growing proportion of patients choosing to discard their embryos rather than donate them to research. Before 2013, women under age 30 were equally likely to donate to research as to choose one of the other options (OR 1.18, 95%CI 0.58–2.38, $p = 0.653$). However, between 2013 and 2020, women in this group were more likely to discard embryos than donate them for research or choose reproductive donation (OR 2.87, 95%CI 1.13–7.28, $P = 0.026$). The trend in decision of women under 30 choosing to discard embryos over donating them to research is seen in the increase in the estimated marginal means of disposition decisions over time since 2012 (Fig. 2).

Table 3 Percent of patients discontinuing storage

Year	Total *N*	Discontinuing storage, *N* (%)
2006	308	46 (14.9)
2007	238	33 (13.9)
2008	209	32 (15.3)
2009	253	26 (10.3)
2010	262	42 (16.0)
2011	284	31 (10.9)
2012	238	43 (18.1)
2013	–	34
2014	–	42
2015	–	25
2016	–	82
2017	–	63
2018	623	61 (9.8)
2019	881	23 (2.6)

Of the 49 patients who provided a reason for ending storage of embryos, the majority cited feeling their "family was complete," whereas others noted that they had conceived on their own without IVF, wanted to avoid further assisted reproductive technology because of costs or invasiveness of the procedure, or felt "too old" to undergo assisted reproductive technology or to be a parent (Table 6).

Discussion

In the overall study population, we found that over the last decade, there have been a smaller proportion of patients choosing to donate embryos to research compared with the prior decade. This trend has been most pronounced among younger women. Since 2013, patients at our university-based fertility clinic who were age 30 and under at the time of cryostorage have been more likely to discard their cryopreserved embryos than donate them to research or reproductive donation. This is in contrast to findings in studies in the early 2000s, in which patients were more likely to donate their embryos for research. One such study by Lanzendorf et al. at our institution reported a review of 149 disposition request forms between 2002 and 2007 and found that 59% of patients donated embryos to research and 38% elected to discard [3]. In comparison, we found that every year since 2013, at least 40% of patients have elected to discard their embryos. Our findings from 2013 through 2020 are more similar to findings from studies performed in the 1990s, in which patients had low rates of donating embryos to research [4].

Like Lanzendorf et al., we found there was no significant impact of obtaining a delivery on the disposition decisions. However, Lanzendorf et al. also found there was no effect on choice seen with regard to the age of the female patient at retrieval (they found those who chose to discard had a mean age at retrieval of 31.8 years; and those who chose to donate to research had a mean age at retrieval of 33.9 years) [3]. In contrast, we found that age at retrieval significantly correlated with disposition decision. Since the publication of that paper, many technological advances, such as embryo vitrification and improved post-thaw survival rates, have occurred and may have contributed to this change in finding.

We did not collect information about why couples chose a particular disposition option for their embryos. However, couples may be responding to a changing political and cultural

Table 4 Logistic regression/odds ratio of donation to research

Predictor	OR	95% confidence interval	*P* value
In decision to donate to research (over discard)			
Pregnancy achieved with IVF	0.66	0.32–1.36	0.26
Two or more live births	0.96	0.58–1.61	0.89
Two or more egg retrievals	1.10	0.75–1.60	0.63
Use of donor gamete	0.67	0.27–1.68	0.39
≥ 2 of embryos in cryostorage	1.45	0.84–2.51	0.18
Duration of storage ≥ 3.5 years	1.18	0.68–2.06	0.56
Possession of a college degree	1.35	0.77–2.37	0.295
Race			
White*			
Black	0.43	0.14–1.32	0.14
Asian	0.55	0.26–1.18	0.12
Other	0.94	0.18–4.99	0.94
Residence in state mandating fertility insurance coverage	0.75	0.47–1.21	0.24
Residence in lowest state ADI quintile (compared to highest)	0.73	0.23–2.33	0.59

NOTE: * Reference category; *ADI*, area deprivation index

environment in which an embryo may be regarded as a person, property, or potential (an intermediate position between human person and human tissue) [11]. Additionally, a person's beliefs about the moral status of embryos may guide their views about the acceptability of certain disposition outcomes.

If a couple thinks of their embryos as potential persons, they may be more likely to discard them than donate them for reproduction donation. For example, Zeifel et al. documented changes in the attitudes of anonymous oocyte donors towards reproductive donation pre- and post-donation, and they postulated that invasive IVF procedures may "increase the reality" for a patient that a potential child could result [12]. Similarly, Lyerly et al. noted that infertility patients may feel they have an obligation to their embryos that "precludes allowing them to develop into children without the knowledge, participation, or love of those who created them" [13]. They also found those ascribing high importance to concerns about a future child were more likely to discard embryos than to choose reproductive donation [2]. It is possible this thinking may have increased in the last decade. Thus, patients may prefer to discard embryos rather than feel pressured to find "acceptable" parents for their cryopreserved embryos [12].

If a person thinks of their embryos as potential persons, they may also be more likely to discard them than to donate them for research. Although ethical guidelines clearly prohibit the use of human embryonic stem cells for reproductive cloning and forbid the creation of such stem cell lines without appropriate informed consent [14, 15], some patients may believe otherwise, and social media may propagate misinformation about what occurs after the donation of reproductive tissues to research [14–16]. In fact, a 2018 study in China cited a "distrust in science" as one of the major reasons that patients decline to donate embryos to research [17]. We found that women listing no preference or no religion were significantly more likely to donate embryos to research than to discard them. In contrast, those identifying as Catholic were significantly less likely to donate embryos to research than to discard them. These results are consistent with findings in Australia

Table 5 Logistic regression /odds ratio of the decision specified over other options

Predictor	OR	95% confidence interval	*P* value
Choose reproductive donation (over discard or donation to research)			
Age of female older than 37 at time of disposition	2.47	1.03–5.95	0.043
Underwent exactly one oocyte retrieval	2.78	1.04–8.22	0.05
Choose to donate to research (over discard or reproductive donation)			
No preference or no religion listed	2.56	1.44–4.54	0.001
Live birth of multiples	1.58	1.05–2.36	0.028
Choose discard (over donation to research or reproductive donation)			
Disposition form in 2013–2020 (after cryopreserving under age 30)	2.87	1.13–7.28	0.026

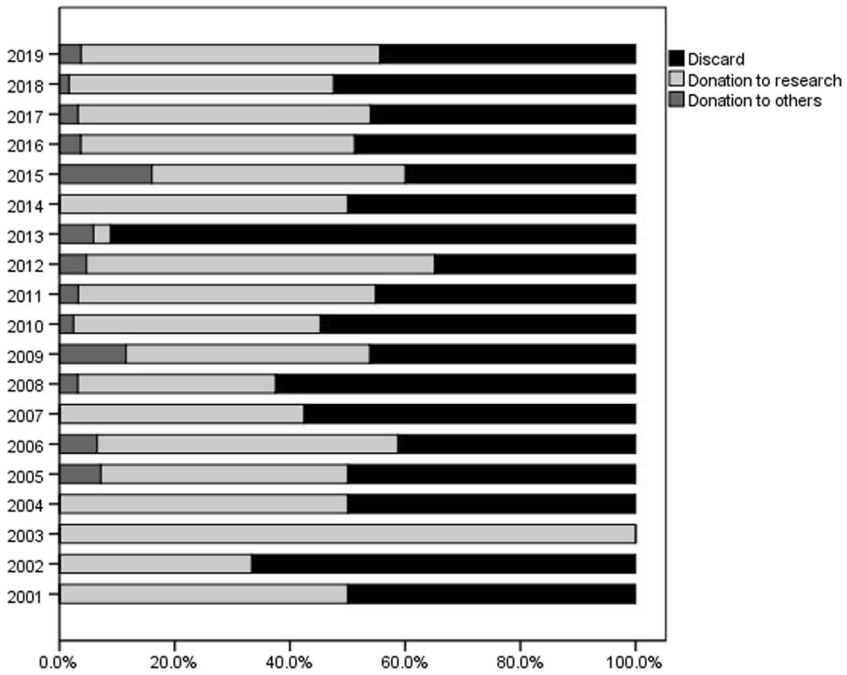

Fig. 1 Proportion of final embryo disposition decisions selected over the years (2001–2019; $N = 615$, made with SPSS)

and Europe that women who held moderate to strong religious beliefs were significantly less likely to donate to research than those whose religious beliefs were not strong [18].

We found that those with multiple births after IVF were significantly more likely to donate their embryos to research than to discard them. In our center, the majority of patients having multiples from IVF were unlikely to have had at least two good-quality embryos and thus were unlikely to be counseled to undergo single-embryo transfer. Thus, consistent with previous data suggesting that couples are more willing to donate lower-quality embryos to research [19], patients at our center who had multiples from IVF may have deemed their lower quality embryos as acceptable for research.

A limitation of this study is that our patient population was largely homogenous with respect to race and religion, so our findings may not be generalizable to other centers. One

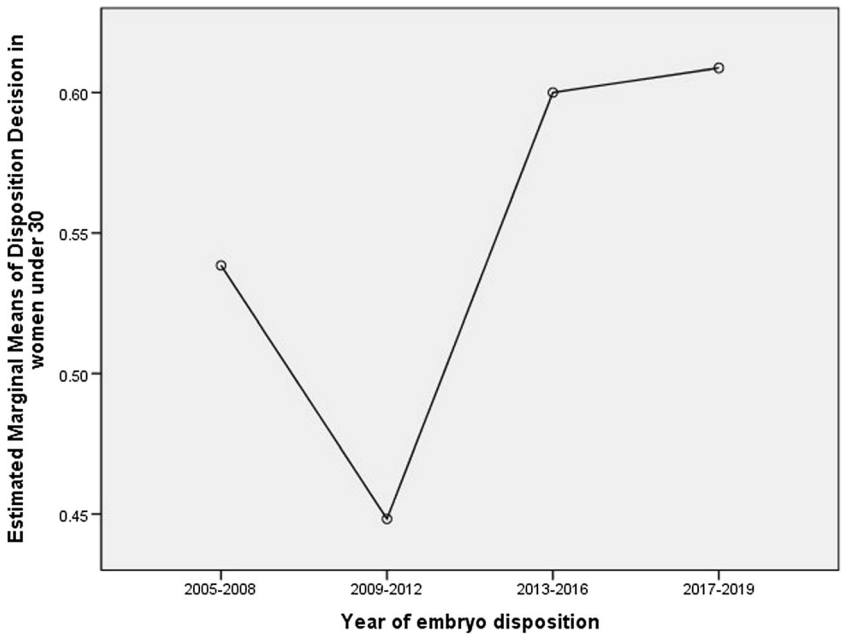

Fig. 2 Changes over time in the estimated marginal means of a decision to discard embryos (value 1) or donate embryos to research (value 0) for women under age 30 at the time of embryo storage ($N = 172$; made with SPSS). By proxy, an increasing value in the estimated marginal means over 0.5 indicates a majority selected discarding of embryos during that time period

Table 6 Reasons for ending storage ($n = 49$)

Reason	*N*	%
Family complete	32	65.3
Conceived spontaneously (without IVF)	6	12.2
Desire to avoid further ART (due to costs or procedure invasiveness)	7	14.3
Feeling "too old" to do ART or be a parent	4	8.1

strength of our study is the large number of final disposition forms available for review. Additionally, fewer than 3% of patients (86 out of 2458) transferred their cryopreserved embryos to either a long-term storage facility or another fertility center. Other strengths include access to medical records dating back nearly 20 years and a comparison study at our same site 10 years earlier. Finally, our academic center is in St. Louis, MO, and attracts many patients from IL, a state that mandates fertility coverage in medical insurance. Thus, we were able to determine that whether or not a woman resided in a state with mandated fertility coverage did not affect her decision regarding how her embryos should be disposed.

Conclusion

In conclusion, we found that, among women who choose to no longer cryopreserve their embryos, discarding them has been the most popular option in the last decade. In the early 2000s, young women were more likely to donate their embryos for research. This shift may reflect changes in the political and scientific environment in the USA. Research on donated human embryos can provide valuable insight into the mechanisms involved in implantation and infertility. Thus, to ensure that sufficient embryos are available for research, it may be necessary to counsel young patients—those most likely to have cryopreserved embryos—about options for donation and to dispel any misinformation they have regarding embryo research.

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Data availability The data that support the findings of this study are available from the corresponding author, VMA, upon reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval This study was approved by the Washington University School of Medicine in St. Louis Institutional Review Board (IRB). This study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Code availability Not applicable.

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