Assessment of patients’ perceptions towards embryo disposition after donation of embryos to a research biobank

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Abstract

Purpose To explore perceptions towards embryo disposition among patients donating excess embryos to a research biobank.

Methods Cross-sectional study of survey responses collected as part of enrollment in a research biobank. Patients are asked questions regarding the difficulty of their disposition decision, their alternative disposition choice if donation to research was not available, quality of the counseling they received, and if additional counseling throughout their treatment would have been beneficial. Survey responses use 5-point Likert scales, with “1” being lowest/least and “5” being highest/most.

Results A total of 157 men and 163 women enrolled in the biobank. Median scores for difficulty of disposition decision were 3 for females and 2 for males, and for quality of counseling, the median scores were 4 for females and 3 for males. Seventy percent of patients would have chosen to discard their excess embryos had donation to research not been an option. Statistical analyses showed no significant difference in responses based on variations in race, religion, sexual orientation, and infertility diagnoses. Concordance of responses within heterosexual couples was tested and found to be poor to moderate.

Conclusions Assessing patients’ perceptions towards embryo disposition after donation of their excess embryos to a research biobank affords a unique perspective. The difficulty of the disposition decision, the tendency to discard embryos in the absence of a means for donation to research, and the poor agreement between heterosexual partners highlight the importance of donation to research as an accessible disposition option and the need for a personalized approach to counseling and consenting for embryo disposition.

Keyword Embryo disposition

Introduction

Improvements in efficiency of in vitro fertilization (IVF) cycles and establishment of single embryo transfers as standard practice result in excess embryos following 30% of IVF cycles [1, 2]. Patients have traditionally been presented with several disposition options for their excess embryos: continued storage, discard, donation to research, and donation to another patient. While these options have historically remained unchanged in the USA, other nations have varying laws regarding embryo disposition, including a complete ban on supernumerary embryos and on embryo research in some countries [3]. Traditionally, discarding excess embryos was the most common disposition, but donation to research has been increasing in popularity over the past decade, while donation to other couples consistently remains the least common disposition [2]. Issues with trust, communication, informed consent, and regulation remain the primary obstacles to patients choosing to donate their excess embryos to research [4–6]. Access limitations, in the form of a lack of availability of repositories dedicated to storage and collection of embryos, is another significant obstacle to more widespread donation of excess embryos to research [7].

Apart from access limitations, the disposition decision remains the most important factor for the fate of excess embryos.
embryos in storage. Previous studies have shown this decision to be of varying difficulties for patients, depending on numerous factors, such as where they are in their reproductive journeys, quality and quantity of embryos left, and personal values regarding embryo conceptualization [8–13]. While these prior studies evaluated perceptions of patients regarding embryo disposition, they have done so in a theoretical manner where no embryos were actually donated prior to perceptions being assessed, and few have specifically assessed patient perceptions at the end of their reproductive journeys [2, 13]. Our objective was to describe perceptions towards embryo disposition among patients who donated their excess embryos to a research biobank.

Materials and methods

Recruitment and survey methodology

Patients receive comprehensive counseling regarding excess embryos and available disposition options at the onset of their fertility treatment and are asked to indicate whether they are interested in donating excess embryos to research. Upon completion of family building, patients are given disposition options for remaining embryos, including discard, continued storage, donation to other couples, and donation to research. Those interested in donating excess embryos to research are contacted by the research team of a reproductive biobank (RENEW, Stanford, CA, USA), and a separate informed consent process is completed. As part of the enrollment and consent process for this biobank, all enrolled patients complete a questionnaire (Supplementary Table 1). Patients’ sources of funding for their reproductive treatments were not specifically assessed as part of recruitment into the biobank.

In this questionnaire, patients designate whether their excess embryos can be used for class I research (human development, embryo characteristics, IVF outcomes), class II research (induced pluripotent stem cell, iPS), or both classes of research. Patients are also asked to share their perceptions towards donation of embryos for research through four questions: the difficulty of their disposition decision; their alternative disposition if donation to research was not available; quality of the counseling they received; and if they believed additional counseling throughout their treatment would have been beneficial. The responses to these questions used a five-point Likert scale, from “1” being lowest/least to “5” being highest/most.

Patients also designate whether they would like to be contacted by the research team in case additional health information is requested or in the case relevant information for patients and/or their family is discovered from genetic testing done on the donated embryos. In this setting, a member of the research team attempts to contact the patient via contact information provided during the consent process. The patient identity is confirmed using multiple health identifiers, and the information is provided only to the patient themselves.

In the case of gamete donors, intended parents answered the questionnaire based on their own beliefs and same-sex couples indicated their sex on the questionnaire accordingly. One patient had a deceased partner and utilized a known sperm donor, so in this single instance, the donor filled out the questionnaire in place of the patient’s partner, but the disposition decision was made by the intended parent.

The complete methodology for this reproductive research biobank has been previously described [7].

The biobank, the included questionnaires, and this work are approved by the Stanford IRB (#IRB-10466) and the Stem Cells Research Oversight panel (SCRO-795).

Statistical analysis

Kruskal–Wallis and Mann–Whitney U tests were used to test for significant differences among Likert scales in the survey based on demographic factors, including race, religion, sexual orientation, and infertility diagnosis. For the purpose of statistical analysis, demographic factors were divided into the distinct categories: Race was divided into Asian, White, and others; religion was divided into Christian and non-religious/atheist; sexual orientation was divided into heterosexual and homosexual/bisexual; and infertility diagnosis was divided into male factor, unexplained, and others. When reported, embryo status was also categorized as all aneuploid, some aneuploid, and no aneuploid. Kruskal–Wallis test was used to assess for significant differences among survey responses based on race, ploidy, and infertility diagnoses; Mann–Whitney U test was used for religion and sexual orientation; and Fisher’s exact test was used to assess responses to the alternative disposition survey question for all demographic and embryo factors.

Weighted kappa statistic (WKC) was applied to test the concordance of survey responses within heterosexual couples and reported as single values with 95% confidence intervals (CI) based on the Fleiss-Cohen weight. WKC results are interpreted as none (<0.20), minimal (0.21–0.39), weak (0.40–0.59), moderate (0.60–0.79), strong (0.80–0.90), or almost perfect (>0.90) [14]. For the purposes of this analysis, if one member of a couple self-identified as heterosexual while the other member self-identified as homosexual or bisexual, these couples were excluded from this analysis (n = 2). If one member of a couple identified as heterosexual and the other member chose not to disclose their sexual orientation and/or did not respond to the question, these couples were included in the analysis (n = 4). This analysis was restricted to heterosexual couples due to the low number of
non-heterosexual couples in the cohort. All statistical analyses were performed using R Project (v4.2.0, 2022).

Results

This is a cross-sectional survey study of 157 men and 163 women (157 heterosexual couples and 6 single women) who completed enrollment in a reproductive research biobank from September 2020 to March 2022 and donated their embryos. The average age of female and male partners is 36 and 37 years old, respectively. This is a highly educated cohort who primarily identifies as Caucasian (77% of females, 83% of males) and heterosexual (91% of females and 92% of males) with a variety of religious backgrounds and underlying infertility diagnoses. Seventy-five percent of the cohorts’ donated embryos did not have a known ploidy status. Full patient demographics are listed in Table 1.

All patients completed the questionnaire, with results listed in Supplementary Table 2. Seventy-nine percent of couples consented to their embryos being used for class II research, which includes creation and use of stem cells. While some couples specifically opted for class I research only (12.3%), the remainder (8.6%) were restricted to class I due to use of donor gametes and the associated regulatory constraints with third party reproduction. Most couples also consented to be contacted by the research team in the future for additional health-related information (81.6%) and for disclosure of results from genetic testing (84%).

The responses to survey questions are listed in Table 2. The median difficulty of disposition decision was 3 for female and 2 for male patients, and 39.5% of male patients found the decision to be difficult at all compared to 28.8% of female patients.

Discarding excess embryos was the most likely alternative disposition choice, with 68.7% of females and 70.7% of males indicating that if donation to research was not an available option, they would have discarded their remaining embryos (Table 2). Female patients equally favored continual storage and donation to other couples (12.3% and 15.3%, respectively), while male patients favored donation to other couples over continual storage (15.9% and 8.9%, respectively).

Female patients were satisfied with the quality of counseling they received regarding their disposition options (median score 4) but were more neutral regarding benefits of additional counseling, ongoing counseling. Male patients were neutral towards the quality of counseling (median score 3), yet they did not believe additional counseling would have been beneficial (median score 2) (Table 2).

Statistical analyses did not reveal any significant differences in Likert scales for difficulty of disposition decision, quality of counseling, benefits of additional counseling, or alternative disposition choice based on race, religion, sexual orientation, infertility diagnoses, and embryo status (Supplementary Table 3).

Concordance of Likert scale responses within each couple is shown in Table 3. The extent of agreement within couples was weak for difficulty of disposition decision and for alternative disposition choice and moderate for quality of counseling and benefits of additional counseling.

Discussion

This work describes perceptions regarding embryo disposition after patients had donated their excess embryos to a research biobank. Our findings illustrate that disposition of excess embryos is a personal, and sometimes difficult, choice.

Generally, the factors that contribute to a patients’ disposition decision have been related to the value patients ascribe to the embryo, their understanding of how embryos can be used in research, and their relationship with their providers and with the healthcare system as a whole [4]. In our experience, 79% of patients consented for their embryos to be used in stem cell research and 70% would have discarded their embryos had donation to research not been an option. Traditionally, patients were more likely to elect to discard their remaining embryos rather than donate them to research or to another couple. Over the past two decades, there has been an increase in the proportion of patients who prefer donation to research [5]. Increased public awareness of stem cell research and its benefit has likely contributed to this trend [5], but awareness does not necessarily imply support in the form of embryo donation to research [15]. Our findings corroborate the importance of having accessible means of donating excess embryos to research to match the growing demand for this disposition option and avoid discarding of embryos that could have contributed to scientific progress.

Patients’ relationship with their providers and the medical system is also an important contributor to a willingness to donate excess embryos to research [16]. The foundation of this relationship is trust and communication. Recruiting patients at the conclusion of family building harnesses the longitudinal trust developed between patients and their providers who counsel them throughout this journey. When performed as part of enrollment in a dedicated reproductive research biobank, this counseling is comprehensive and includes a detailed description of the types of research that could be conducted on donated embryos while also communicating the uncertainty, the unknown, and untapped potential that the future may bring. The consent process utilized by this biobank is a multi-step process [17] that accounts for the likely possibility of patients changing their disposition...
Table 1  Demographics

|                              | Female (n = 163)* | Male (n = 157) |
|------------------------------|-------------------|----------------|
| **Race**                     |                   |                |
| Asian                        | 39 (23.9%)        | 24 (15.3%)     |
| Black or African American    | 3 (1.8%)          | 1 (0.6%)       |
| White                        | 125 (76.7%)       | 130 (82.8%)    |
| Other                        | 5 (3.0%)          | 6 (2.7%)       |
| **Ethnicity**                |                   |                |
| Not Hispanic/Latinx          | 155 (95.1%)       | 148 (94.3%)    |
| Hispanic/Latinx              | 6 (3.7%)          | 8 (5.1%)       |
| Unknown/not reported         | 2 (1.2%)          | 1 (0.6%)       |
| **Gender***                  |                   |                |
| Female (cisgender)           | 162 (99.4%)       | 1 (0.6%)       |
| Male (cisgender)             | 1 (0.6%)          | 156 (99.4%)    |
| **Sexual orientation**       |                   |                |
| Heterosexual/straight        | 148 (90.8%)       | 144 (92%)      |
| Non-heterosexual             | 14 (8.6%)         | 12 (7.4%)      |
| Unknown                      | 1 (0.6%)          | 1 (0.6%)       |
| **Religious affiliation**    |                   |                |
| Christian                    | 74 (45.4%)        | 63 (40.1%)     |
| Hindu                        | 8 (4.9%)          | 8 (5.1%)       |
| Jewish                       | 11 (6.7%)         | 6 (3.8%)       |
| Not religious/atheist        | 37 (22.7%)        | 51 (32.5%)     |
| Other                        | 10 (5.1%)         | 12 (7.7%)      |
| Choose not to disclose       | 21 (12.9%)        | 13 (8.3%)      |
| Unknown/not reported         | 2 (1.2%)          | 1 (0.6%)       |
| **Highest education level**  |                   |                |
| High school and/or some college | 9 (5.5%)        | 24 (15.3%)     |
| Bachelor’s degree            | 60 (36.8%)        | 62 (39.5%)     |
| Master’s degree              | 65 (39.9%)        | 43 (27.4%)     |
| Doctoral/professional degree (PhD, MD, JD) | 23 (14.1%) | 24 (15.3%)     |
| Choose not to disclose       | 6 (3.7%)          | 4 (2.5%)       |
| **Infertility diagnosis****  |                   |                |
| Female infertility           | 54 (34.2%)        |                |
| Male infertility             | 29 (18.5%)        |                |
| Unexplained infertility      | 44 (28.0%)        |                |
| Other                        | 25 (15.9%)        |                |
| Not applicable               | 19 (12.1%)        |                |
| Unknown/not reported         | 19 (12.1%)        |                |
| **Embryo ploidy status**     |                   |                |
| All aneuploid                | 12 (7.4%)         | 11 (7.0%)      |
| Some aneuploid               | 19 (12%)          | 17 (11%)       |
| None aneuploid               | 9 (5.5%)          | 9 (5.7%)       |
| Unknown                      | 123 (75%)         | 120 (76%)      |

*Single mothers and lesbian couples using donor sperm

**Some patients identified as more than one race. Other includes the following: Middle Eastern/North African, American Indian/Alaska Native, and Native Hawaiian/Other Pacific Islander

***No patients indicated that they identify as transgender or genderqueer/non-binary/gender non-conforming

****Twenty-three couples (14.6%) had multiple infertility diagnoses. “Female Infertility” encompasses diminished ovarian reserve, endometriosis, hypothalamic amenorrhea, polycystic ovarian syndrome, recurrent pregnancy loss, tubal factor, and uterine factor
decision by the time they conclude fertility treatment [18].
While a dynamic, narrative consent model has previously
been proposed [19] to mirror the changing values of patients
over time, most patients who donated to the biobank were
satisfied with the counseling they received and there was
no clear indication that patients would have benefited from
additional, ongoing counseling.
Prior studies that have surveyed patients at various stages
of their reproductive journeys to assess how difficult they
find their disposition decision have generally revealed this
to be a difficult decision. Our cohort’s opinions match those
of another study to specifically survey patients at the con-
clusion of their fertility treatments, where about a third of
patients found the decision difficult [13]. Our study further
complements these findings by showing that male patients
have less difficulty with this decision than female patients,
which could be attributed to differences in embryo repre-
sentation. Our findings also dispel the hypothesis that the
disposition decision may be less difficult if patients are sur-
veyed after having already made the decision and donated
their embryos to research. The overall variation in degree
of difficulty that our patients reported with their disposi-
tion decision was not explained by any demographic factor
and, when viewed in the context of the largely homogenous
population of the biobank, suggests that the difficulty of this
decision is intrinsic to the core values of an individual and
unable to be adequately appreciated in aggregated data.
As expected, limited data suggests that the most desired
disposition for aneuploid embryos is donation to research
[20]. In our cohort, the survey responses were not signifi-
cantly affected by the ploidy status of the donated embryos.
However, this analysis was limited in power since 75% of
this cohort did not have a known ploidy status.
An interesting element of these findings reflects the tem-
poral correlation of enrollment into the biobank and dona-
tion of embryos with the COVID-19 pandemic. While the
pandemic-induced disruptions to fertility treatments nega-
tively impacted patients [21, 22], our findings did not reflect
a propensity towards continual storage of embryos as one
might expect from these disruptions. This is likely a reflec-
tion of this cohort being surveyed after completion of their
family building such that disruptions to fertility treatments
did not directly affect them or their disposition decision. An
assessment of the impact of the pandemic on disposition per-
ceptions would be a valuable addition to existing literature.
Our study statistically assesses concordance of
responses within heterosexual couples regarding disposi-
tion of excess embryos at the conclusion of fertility treat-
ment. Previously, evaluation of factors that potentially

Table 2  Survey responses

| Survey question                              | Responses, n (%) |
|---------------------------------------------|------------------|
|                                             | Female | Male |
| **Difficulty of disposition decision**      |         |      |
| 1 (least difficult)                         | 47 (29) | 62 (39) |
| 2                                           | 32 (20) | 39 (25) |
| 3                                           | 33 (20) | 28 (18) |
| 4                                           | 28 (17) | 15 (10) |
| 5 (most difficult)                          | 23 (14) | 13 (8) |
| **Alternative disposition choice**          |         |      |
| Continue to store them                      | 20 (12) | 14 (9) |
| Discard them                                | 112 (69) | 111 (71) |
| Donate them to another couple               | 25 (15) | 25 (16) |
| Other                                       | 6 (4) | 7 (4) |
| **Quality of counseling received**          |         |      |
| 1 (least helpful)                           | 24 (15) | 21 (13) |
| 2                                           | 24 (15) | 20 (13) |
| 3                                           | 30 (18) | 40 (25) |
| 4                                           | 32 (20) | 25 (16) |
| 5 (most helpful)                            | 53 (33) | 51 (32) |
| **Desire for additional counseling**        |         |      |
| 1 (least beneficial)                        | 53 (33) | 63 (40) |
| 2                                           | 22 (13) | 21 (13) |
| 3                                           | 31 (19) | 31 (20) |
| 4                                           | 26 (16) | 19 (12) |
| 5 (most beneficial)                         | 31 (19) | 23 (15) |

Table 3  Intra-couple survey response correlation

| Survey question                                                                 | Weighted kappa statistic (95% CI) | p value |
|---------------------------------------------------------------------------------|-----------------------------------|---------|
| On a scale of 1–5 (5 being the most difficult), how difficult was your decision to donate? | 0.59 (0.47, 0.73) | < 0.001 |
| Please rate the quality of your counseling regarding what to do with embryos still in storage upon completion of your fertility treatment on a scale of 1–5 (5 being the best) | 0.73 (0.63, 0.84) | < 0.001 |
| Do you think that you would have benefitted from additional counseling throughout your treatment regarding what to do with embryos in storage upon completion of your fertility treatment? Please rate the degree to which you believe you would have benefitted from additional counseling on a scale of 1–5 (5 being the largest benefit) | 0.68 (0.57, 0.79) | < 0.001 |
| If you did not have the option to donate your embryos to research what would be your second choice? | 0.59 (0.46, 0.72) | < 0.001 |

*A total of 145 heterosexual couples were utilized from the dataset for this analysis
impact the difficulty of the disposition decision has either focused on the couple as a single unit [4], on the female member exclusively [4], or failed to statistically quantify discordance [13]. Given the heterogeneous responses between female and male patients in our cohort, we sought to elucidate whether there is statistical correlation between the two individuals that comprise a couple. The concordance being weak for difficulty of disposition decision and the alternative disposition choice suggests the factors influencing this decision may be different for female and male patients. While limited data suggests that embryo representation is similar between partners, additional research is necessary to further investigate these differences [13]. It is also possible that the poor concordance observed may be due to other confounding demographic differences within a couple unrelated to the sex/gender of the patients. However, we were unable to identify statistically significant differences in Likert scale responses based on demographic differences for our cohort.

The concordance within heterosexual couples for quality of counseling received and the benefits of additional counseling was moderate. Interestingly, while male patients rated their counseling as lower quality than female patients did, they were also more reluctant to desire additional counseling. These findings indicate that it may be beneficial to alter the approach to counseling patients. Rather than exclusively counsel them as a single couple, it may be more effective to counsel each partner individually as well as a couple. While all counseling in this study and biobank was performed by physicians, the inclusion of other providers, such as genetic counselors and psychologists, may enhance the counseling experience for patients. Such a personalized approach can also provide additional data to better elucidate the different factors that can make the disposition decision difficult for male vs female patients. Prospective studies comparing these different counseling approaches could help clarify the significance of counseling in the difficulty and outcome of the disposition decision.

Our study’s strength lies in assessing the perceptions of patients who have already donated their embryos to a research biobank and who have completed their fertility treatments. This cohort is also unique in representing a diverse geography from various parts of the USA, including patients from both academic and private practices [7]. The geographic heterogeneity of the patients is also complemented by the centralization of the consenting and recruitment process through a dedicated reproductive biobank. The granularity of the questionnaire responses also allowed for statistically testing concordance of responses within each couple.

Limitations of our study include the lack of targeted recruitment of patients for a research study which precludes availability of a response rate. All patients who enrolled in the biobank did complete the questionnaire. Apart from the geographic heterogeneity, this cohort is largely homogeneous, particularly with low representation of minorities. However, the diversity of the biobank population will improve over time as recruitment continues to increase nationally. Our study also lacks the qualitative data to elucidate the reasons underlying the patients’ survey responses regarding the difficulty of their disposition decision and their opinions on the counseling they received. We were unable to assess concordance of survey responses among non-heterosexual couples due to the small sample size of these couples in our cohort at the time of this manuscript.

Conclusions

The growing prevalence of excess embryos as a byproduct of reproductive treatment necessitates the availability of disposition options for patients. With a clear trend towards greater interest in donation of excess embryos to research, the need for facilitating and nurturing this altruistic desire is equally great, especially since discarding embryos remains the most likely alternative disposition. Biobanks that are dedicated to collection, storage, and distribution of embryos for research are uniquely positioned to meet this growing demand.

The disposition decision can be difficult even for patients who have already donated their excess embryos to research at the conclusion of their reproductive treatments. Inadequate counseling does not seem to be a major factor in contributing to this difficulty, but the lack of agreement among heterosexual partners regarding embryo disposition implies that the approach to counseling may be a contributor. Our results demonstrate the potential for further personalizing counseling for individual partners rather than exclusively focusing on the couple as a single unit, and our findings also emphasize the value of a larger, more demographically diverse cohort to be studied.

Supplementary Information

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Author contribution

All authors contributed to the study conception and design. Material preparation and data collection were performed by Arian Khorsid and Anjali Wignarajah. Statistical analysis was performed by Jiaqi Zhang. The first draft of the manuscript was written by Arian Khorsid, and all authors edited the manuscript. All authors read and approved the final manuscript. The principal investigator overseeing this work was Gayathree Murugappan.

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