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Physicians and patients' motivations to perform elective single or double-embryo transfers: A nationwide survey

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ABSTRACT

Objectives: To evaluate motivations to perform an elective single embryo transfer (e-SET).

Methods: Cross-sectional surveys to reproductive medicine specialists and to infertile patients undergoing assisted reproductive treatments.

Results: In the physician's survey (n=278), we found that the main reasons for not offering e-SET were the physicians' belief that patients prefer optimizing the pregnancy rates regardless of the potential complications (57.1%). Regarding the decision making process, 76.7% of physicians thought that patients and doctors should make these decisions together and 93.3% would like to have a more formal decision-aid to help with counseling. In the patients' survey (n=100), 21.3% chose e-SET, while 33% mentioned that complications associated to multiple pregnancies were insufficiently discussed. Among those patients, none chose to have e-SET, while 30% of those who had a full discussion selected e-SET (p=0.05).

Conclusions: Most physicians did not offer e-SET based on potential patients' negative feelings. Also, almost 30% take important decisions without the patient's participation. Patients that discussed more thoroughly this topic, more frequently selected e-SET. Almost all the physicians surveyed agreed that decision-aids could help in this important shared-decision process.

Practice implications: Decision aids about e-SET vs DET are needed to help patients in the decision making process.

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1. Introduction

During the last decade in the USA, a huge increase in elective single-embryo transfers (e-SET) has been observed since publication of the 2004 guidelines, where e-SET was strongly recommended [1]. Nowadays, legislation related to reproductive medicine in certain countries does not mention limits in the number of embryos to be transferred, while in others, a limit between one and three embryos was established [2–4]. An increasing number of guidelines promoted the reduction in the number of embryos to be transferred, as it is seen in USA, UK, Canada and Australia [5–7]. In Argentina, there is no specific limit mentioned in the Reproductive Medicine National Law, but our specific ART program promotes eSET in those patients with good

prognosis [2]. The Society for Assisted Reproductive Technology (SART) reported that, in 2014, 21.8% of the cycles with embryo transfer had e-SET, with a higher rate in women below 35 years old (32.5%) and a lower rate in women above 40 years old (10.7%). However, in the same year, 10.4% of the embryo transfers in women below 35 years old had twins and 0.3% triplets or more, while in women above 40, only 1.8% had twins and 0.1% had high-order multiple pregnancies [8].

Deciding on the number of embryos to be transferred, is a relevant decision to be made prior to transfer, and both, pros and cons coexist in each of the options. If e-SET is chosen, a lower live birth per transfer is achieved, compared to performing double-embryo transfer (DET) [9]. However, when DET is performed, the multiple pregnancy rate is higher and as a result, maternal and perinatal complications are increased [10–13,6]. There is low-quality evidence coming from a systematic review published in 2013, showing that sequential e-SETs got a cumulative live-birth rate that did not show statistically significant differences from a DET [9]. Based on this information, one can infer that sequential e-

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SET does not offer a lower live-birth rate per cycle, but it could generate a longer time-to-pregnancy and, be a bit more expensive process, due to the higher number of embryo transfers performed [9]. Of course, e-SET has the advantage of a lower incidence of multiple pregnancies and, therefore, a potential reduction in maternal and perinatal complications, such as preeclampsia, gestational diabetes and preterm birth, which are associated to a higher mortality and long-term morbidity, both for the mother and the newborn [14–16].

A Danish Health Technology Assessment [17] showed a better cost-effectiveness profile for e-SET, while a Spanish economic evaluation [18] showed similar effectiveness and costs for both interventions. The controversy about any superiority among both interventions suggests that the choice of strategy to be adopted, should be determined by the context of the health care system and the individual prognosis and preferences [18].

Despite the above-mentioned increment in e-SETs, it seems that the growth in the number of these procedures is not moving fast enough. There are physicians and patients that still prefer to transfer more than one embryo, accepting the risk of having a multiple gestation [19]. A recent study by Rai et al. showed that in one of the UK's largest independent fertility clinic, there was a high proportion of female patients that had a positive attitude toward having twins [20]. Also of significance, the patients undergoing their first IVF cycle had a more positive attitude towards e-SET (and negative toward having twins) than patients with several prior IVF failures.

Patient-centered decision-making is a paradigm that is gaining ground during the last decades. Both physicians and patients play a big role in this paradigm. Physicians have the responsibility to provide the information needed for the patients to make a properly informed decision. Patients have the opportunity to incorporate their values and preferences, and decide which option they like best.

To investigate further the motivations leading to the performance of e-SET vs DET, and if a process of share-decision making about the number of embryos to be transferred is usually followed, we performed a nationwide survey among reproductive medicine specialists in Argentina, and also among patients at a large university-affiliated fertility center in Buenos Aires.

2. Materials and methods

This is a cross-sectional study that includes two separate surveys: one for physicians and one for patients. The specific STROBE statement was followed for reporting [21]. Institutional Review Board (IRB) approval was obtained from our institution.

2.1. Survey for physicians

All physician-members of the Argentine Society for Reproductive Medicine (SAMER) received a survey through email in June 2016. They are all infertility specialists that perform ART procedures. It was an anonymous survey that included the following domains: personal data, routine practice, barriers for performing e-SET, decision making process, knowledge about the patients preferences, and decision aid tool. A total of 676 e-mail addresses were contacted using Survey Monkey. After the first surveys were delivered, 3 weekly reminders were sent to those physicians that did not answer the survey, or to those that sent incomplete reporting.

2.2. Survey for patients

A survey was conducted in a University-affiliated infertility clinic in Buenos Aires, Argentina, between May/2016 and July/

2016. This survey was given to all patients undergoing a controlled ovarian hyperstimulation for an ART procedure, or an endometrial preparation for a frozen-embryo transfer or an egg-donor cycle. Patients received the survey during their first monitoring appointment. The IRB for the study was approved by the Institution Ethics Committee. The domains included in the survey were personal data, intention about the number of embryos to be transferred, preferences about having a singleton or a twin gestation, time spent during the consultation discussing the number of embryos to be transferred, knowledge of complications associated with multiple pregnancies, satisfaction on the information received about making a decision on the number of embryos to be transferred. For an estimated e-SET election of 20%, based on a pilot study, 95%CI and a precision of $\pm 8\%$, we calculated a sample size of 96 patients. As we expected some incomplete responses, we administered these surveys until 100 patients completed them.

We used proportions and 95% confidence interval to describe each of the evaluated parameters. To test differences between proportions we used chi square test with Fisher's exact test. For statistical analysis we used software STATA 11.2.

3. Results

3.1. Infertility specialists

A total of 676 e-mails were sent to the whole database of physicians/members of the Argentine Society for Reproductive Medicine (SAMER). A total of 279 (45.1%) responded to the anonymous survey. See Table 1 for the sample characteristics.

In Table 2, the survey shows that physicians do e-SET more frequently in younger patients and, especially, when a blastocyst is transferred. It can be seen that embryos stage of development was the most relevant variable helping them make a decision, but female age also played an important role. Participants were also asked if they offered all their patients e-SETs, and 76% (200/263) responded negatively.

The main reason, given by 57.1% (109/191) of these physicians, was their belief that "ART patients value more positively a pregnancy, than their negative perception of a potential complication". A total of 46.9% (89/190) of the responders also thought that "patients feel frustrated when they need to repeat embryo transfers" and 42.4% (81/191) assumed that "cumulative

Table 1
Doctors' characteristics (n=279).

	Mean% (n)
Gender	
Female	49.8% (138)
Male	50.2% (139)
Time in reproductive medicine	
<10%	3.2% (9)
10–50%	23.9% (66)
50–80%	35.9% (99)
>80%	37% (102)
Working position	
Staff at an infertility clinic	62.2% (171)
Own office	37.8% (104)
Clinic's characteristic (IVF cycles per year)	
<100	17.7% (48)
100–300	18% (49)
300–1000	31.6% (86)
>1000	32.7% (89)
Doctor's experience (number of ET per year)	
<20	20.6% (56)
20–50	37.1% (101)
50–100	22.4% (61)
>100	19.9% (54)

Table 2

Physicians' responses to scenarios about choice of eSET or DET based on maternal age and stage of development of the embryo.

Clinical scenario Physician responses (Mean%)	
<38years old & cleavage stage	
1 embryo	6%
2 embryos	90.2%
≥2 embryos	3.8%
<38years old & blastocyst stage	
1 embryo	59.6%
2 embryos	40.4%
≥2 embryos	0%
≥38 years old & cleavage stage	
1 embryo	1.9%
2 embryos	81.9%
≥2 embryos	16.2%
≥38 years old & blastocyst stage	
1 embryo	29.7%
2 embryos	68.8%
≥2 embryos	1.5%

*All cases are with own eggs and without preimplantation genetic testing (PGT).

pregnancy rate in two e-SETs is lower than a double fresh embryo transfer". Finally, 11% (21/191) stated that "complications from multiple-pregnancies are severe but infrequent" and 7.4% (14/190) believed that "complications from multiple-pregnancies are not that important".

Regarding who has the responsibility of deciding on the number of embryos to be transferred, 76.7% (198/258) answered that it should be decided by both, patients and physicians, while 22.9% (59/258) thought that it should be decided only by the provider, and 0.4% (1/258) only by the patient. Physicians that spent more than 80% of their time working on reproductive medicine showed no important differences on this topic when compared with those that spent less time (only the physician should make the decision: 26.5% vs. 20.9% respectively, $p=0.43$). However, a small difference was noted when they responded as to who actually makes the decision in everyday practice, and they mentioned in 70.5% (95%CI 64.6–76.0) both physicians and patients together, and in 29.5% (95%CI 24.0–35.4) only the physician. A total of 37.3% (95/255) of the providers said that they do not discuss or discuss very briefly, the number of embryos to be transferred, and 16% (41/255) felt that the time dedicated to discuss complications of the treatment was minimal.

However, on the reverse, 58.4% (149/255) thought that they should hold a more prolonged discussion about complications of multiple pregnancies, while 9.5% said that they believe patients

would not understand the nature of the complications, and 7.5% answered that they do not usually have enough time to review potential complications.

Finally, physicians were asked about tools for communicating risks and benefits, and 56.7% (144/244) were not aware of any specific tools for reproductive medicine. However, none of the 43.3% that responded knowing those tools, actually knew of any decision-aids. A total of 71.4% (180/253) responded that never or only very occasionally used a tool to help explain risks and benefits, but 93.3% (239/256) would like to have a formal decision-aid available.

3.2. Patients

One hundred and three surveys were administered and 100 patients fully completed our survey. Eighty-three patients were going to have IVF using their own oocytes, while 17 were undergoing an egg donation cycle. The answers in the surveys represented the answers from the women alone in 50% and from couples in 50% of the responses. Table 3 shows patients' characteristics while Table 4 shows patients' opinions about the number of embryos to transfer. Using e-SET (all at the blastocyst stage) was chosen by 13/61 (21.3%, 95% CI 11.9–33.7) of the respondents, while 40/61 (65.6%, 95% CI 52.3–77.3) wanted at least two embryos transferred. The rest were undecided on this issue. We found that e-SET was more frequent in egg donor cycles, where all the embryo transfers were performed at the blastocyst stage, than in cycles using the patient's own oocytes (63.6% vs 12.8%, $p < 0.01$), where only half transferred at the blastocyst stage. It is important to consider that our own program, has a strict policy recommending e-SET in all oocyte-donation cycles. Besides, all the transfers on day 3 were done with two embryos while 32% of the blastocysts transfers were e-SET ($p=0.06$).

Regarding the desire for having a singleton or multiple pregnancy, 55/97 (56.7%, 95% CI 46.2–66.7) wanted a singleton, 31/97 (32.0%, 95% CI 23.0–42.2) preferred twins, and the rest were not sure. Reasons most commonly cited for choosing a singleton were: multiple pregnancies are associated with more complications in 25/55 (45.5%, 95% CI 32.0–59.4) and raising twins is too difficult in 10/55 (18.2%, 95% CI 9.1–30.9). Reasons most commonly cited for choosing twins were: "we like twins" in 17/31 (54.8%, 95% CI 36.0–72.7) and "we resolve the infertility problem at once" in 10/31 (32.2%, 95% CI 16.7–51.4).

When patients were asked about the time dedicated to discuss the number of embryos to transfer, 33.0% (95%CI 23.8–43.3)

Table 3

Characteristics of the patients who responded to the survey (n=100).

	Mean% (95% confidence interval)
Respondents	
Women alone	50%
Couples	50%
Age	
Own oocytes	37.3 ± 3.8 years old
Donor oocytes	42.4 ± 4.8 years old
PGS (only own oocytes)	
No	91.1%
Yes	8.9%
First IVF cycle	
Yes	75%
No	25%
Already have children	
Yes	30%
No	70%
Previous pregnancies	
Maternal complication	52.4%
Neonatal complication	22.2%

Table 4

Patients' responses to the how they would decide on number of embryos to be transferred.

	Mean% (95% confidence interval)
Number of embryos they wanted to transfer	
1	21% (11.9–33.7)
1 or 2 (not sure yet)	5%
2	61%
2 or 3 (not sure yet)	3%
3	2%
Not sure yet	8%
At time of final decision	
Before the egg retrieval	56%
After the egg retrieval	44%
Main reason for the decision	
Doctor's opinion	45.2%
Doctor's opinion and embryos quality	19.3%
Embryo quality/quantity	64.5%
Who will take the decision	
Patients & doctor	72.4% (62.5–81.0)
Only patients	18.4% (11.3–27.5)
Only doctor	9.2% (4.3–16.7)

mentioned that it was not discussed at all, or it was only briefly discussed. When patients were asked about the time dedicated to discuss treatment complications in relation to effectiveness, 72.0% (95%CI 61.8–80.9) said that their physicians discussed mostly effectiveness, but minimally possible complications. Patients that perceived that had little discussion on the number of embryos to transfer, also felt that there was not enough time to discuss complications of multiple pregnancies (9.3%), while those that held longer discussions, on embryos to be transferred, also had more discussion about complications (35.4%, $p < 0.01$). Of interest, we found an association between patients that considered that they had spent enough time discussing with their physician the number of embryos to be transferred and the rate of e-SET, in comparison to those that had no discussion of the subject (30.2% vs 0%, $p = 0.05$). Finally, after the survey 9/82 (9.3%, CI 95% 4.3–18.3) mentioned they would have to think again about how many embryos they would like to have transferred (these were all patients that originally decided on transferring more than one embryo).

4. Discussion and conclusions

4.1. Discussion

In the survey to physicians, most respondents did not offer e-SET to all their patients, basing this decision on the assumption that patients value more getting pregnant than they value or consider negatively a potential complication, and also on the assumption that cumulative pregnancy rates in two sequential e-SETs are lower than doing a single DET. Almost 30% of physicians decided on how many embryos to transfer without consulting the patient, and more than one third did not even know if their patients prefer a singleton or a twin gestation. When we analyzed if there was any association between the experience of physicians and their type of assessment, we could not show any relevant difference among them. However, this study cannot discard important differences since statistical power is not enough for those outcomes. Lastly, almost none of the physicians know about a decision aid for this field of medicine and most would like to have one to help them better explain risks and benefits. We found that patients spending more time discussing decision issues, chose more frequently transferring electively a single embryo, in comparison with patients that felt that were not so well informed. In this set of patients, both, those who received stronger recommendations provided by our policy in egg donation of e-SET (an absolute difference of 50%), and those who had spent more

time, discussing with the physician about the number of embryos to transfer (an absolute difference of 30%), decided to transfer one embryo in most instances. These differences were both clinically and statistically significant. Finally, a large proportion of patients felt that information about pregnancy complications was minimal or none.

There are published studies that evaluated which were the barriers in some countries to increase the number of e-SET. In 2008, Peperstraten et al., in a national survey in the Netherlands, found similar results as we did, showing that main barriers were the perception of suboptimal success rates associated with embryo cryopreservation and also not seeing twin pregnancies as a complication [22]. The same author published another study based on in-depth interviews of Dutch physicians and patients showing that some of the factors negatively influencing on the use of e-SET, are the uncertainty about the e-SET technique, patients lack of knowledge about essential e-SET aspects and inferior cryopreservation success rates [23]. A study by Hojgaard et al. in, in which an anonymous survey was conducted in patients living in Denmark, to study what the attitude of patients were towards having twins, and concluded that more than half preferred having twins rather than singleton pregnancies [24]. Blennborn et al. showed that females are more aware of risks and more satisfied with information about it than males. Spare embryos to freeze, improvement of pregnancy rate in single embryo transfer and young age of the woman are predictive of choosing SET [25]. In 2010, Leese et al. reviewed 20 relevant papers about attitudes towards single embryo transfer, and found that, in order to improve acceptance of e-SET, it is recommended to show that SET has good success rates, that cryopreservation programs work properly, suggest including the partner when providing risk information and start performing e-SET especially in younger patients [26]. It is interesting to see that these authors found useful that physicians educate patients about it, consistently with the agreement of the physicians that we surveyed, who would like to have a tool to help them explain better this issues. Curiously, in contrast, many of those same physicians do not share with patients the decision of the number of embryo to transfer.

Shared-decision making process is the current paradigm. However it is a decision that is not easy to take. It requires physicians to be fully informed on ART success and possible pregnancy complications. And they should also have the ability to communicate this information and help in the decision making process. However, not all the physicians might know this detailed information and, even when they know it, there are no wide-known validated tools in this knowledge area to help them to communicate this information. In addition, not all the physicians agree that patients should participate in this type of decisions. Also, it is concerning that more than one sixth of the patients believe that they could take this decision without the participation of the healthcare provider. Clearly, the American College of Obstetricians and Gynecologists (ACOG) shared decisions to improve the effectiveness of patient-physician communication [27].

Patient-centered care is increasingly advocated as the best standard of care in IVF programs [28,29], and tools to support shared decision-making are needed to help infertility patients with their treatment choices [26–29]. Success outcomes such as live birth rate, as well as adverse effects, like multiple pregnancy rate, perinatal morbidity-mortality, coexist in these types of treatments. In the initial consultation, patient tend to focus their questions on success rates, while often remaining less aware of possible risks and complications (i.e. related to severe prematurity) [30]. Trustworthy estimates of benefits and harms are often not readily available, or presented in formats that are understandable to patients. An additional challenge specific to reproductive medicine

counseling is also that these estimates vary substantially with patient's age and clinical history [14,31,32], but also important features such as embryo developmental stage and the chromosomal evaluation of the embryos [33–35], which could have a major impact on the decision of transferring one or more embryos [9,34,36]. Considering all variables required for counseling patients, giving the correct advice on numbers is not easy. Patients and clinicians need decision aids based on trustworthy summaries of current best evidence to support both informed and meaningful discussions. Currently health providers do not have a decision tool that incorporates all these variables to make the exchange of information easier and more transparent for the patients, and therefore facilitating the shared decision-making. In 2015, the American Society for Reproductive Medicine (ASRM) released the on-line patient predictor of IVF success tool (<https://www.sartcorsonline.com/Predictor/Patient>). It allows the patient to enter some parameters and calculate the live birth and multiple pregnancy rates, if one or two embryos are transferred. This is a preliminary approach, but according to our study, it is far from patients and physicians' needs. A comprehensive decision aid should show patients important outcomes, rather than intermediate outcomes, and display estimates of benefits using sound presentation formats, to enhance patients understanding. Moreover, traditionally decision aids have been primarily designed for patients to consult on their own, in preparation for clinical encounters. Few tools exist to support meaningful interactions during counseling sessions [37] by enhancing meaningful clinical conversation.

One limitation in the survey to patients is the external validity. The sample came from consecutive patients surveyed at a single large university-affiliated fertility clinic in Buenos Aires, Argentina, and extrapolating these results to the rest of the population could be a limiting factor. However, as this kind of decisions may be based to a degree in cultural background, having focalized studies are important, to help understanding different settings where IVF procedures are performed. Another limitation is that the sample size was unpowered to find statistical significant differences in outcomes, such as the relative time discussing both, effectiveness and pregnancy complications. However, the study showed significant clinical differences, even in the lower limits of the confidence intervals, and that should be tested in future studies. One of the strengths of the design was that several different REI physicians within the clinic attended the participating patients, giving heterogeneity to the sample. Another point to remark is that our clinic, where the patient survey was conducted, cares for more than half of the patients referred from other cities in Argentina and other countries in South America, improving the external validity. In the survey given to the physicians, a 45% response rate is suboptimal, however its extensive national coverage, as well as the heterogeneity seen in the participants' characteristics, diminish the chances of obtaining biased results.

4.2. Conclusion

Most physicians did not offer e-SET to their patients because they assumed that e-SET was associated with lower cumulative pregnancy rates. Besides, they consider that patients valued more the positive effect of getting pregnant than the negative effect of having pregnancy complications. Also, almost one third of the physicians answered, that they make decisions without considering the patient's opinion. Finally, decision aids were not known by most of the physicians, yet most felt that they would like to have one available. In the patients' survey, we found that patients that discussed more thoroughly the number of embryos to be transferred, more frequently selected e-SET in comparison to those less informed.

4.3. Practice implications

Considering that most of the physicians surveyed agreed that decision aids could help promoting a shared-decision process, developing these kind of tools should be encouraged. Decision aids will ultimately help the physicians to better explain, and patients to better understand, the options available and their potential risks. As seen in the patients' survey, those that had a thorough discussion on the number of embryos to be transferred, had e-SET more frequently, which would help decrease the incidence of complications associated with multiple pregnancies.

Authors' contributions

Study concept and design: Demián Glujovsky, Stella Lancuba, Gustavo Martinez and Agustín Ciapponi and Carlos Sueldo.

Data collection: Demián Glujovsky, Andrea Coscia, Paula De Carvalho, Stella Lancuba, Gustavo Martinez.

Analysis and interpretation of data: Demián Glujovsky and Agustín Ciapponi.

Drafting of the manuscript: Demián Glujovsky and Agustín Ciapponi.

Revision of the manuscript: Demián Glujovsky, Carlos Sueldo, Andrea Coscia, Paula De Carvalho, Stella Lancuba, Gustavo Martinez and Agustín Ciapponi.

Conflict of interest

The authors have no conflicts of interest to report.

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