OPTIMIZATION OF A SINGLE-EMBRYO TRANSFER IN PATIENTS WITH GOOD OVARIAN RESERVE

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Due to refinements of assisted reproductive technology, the number of multiple pregnancies has increased substantially. Time-lapse microscopy (TLM) is a tool for selecting quality embryos for transfer. This study aimed to assess the outcomes of single-embryo transfer of autologous oocytes performed on day 5 of embryo incubation in a TLM-equipped system in patients with good ovarian reserve. The study was carried out in 208 infertile women with good ovarian reserve (over 8 oocytes retrieved). Single-embryo transfer following incubation in a TLM-equipped incubator was performed in 95 patients, who formed the main group; the control group consisted of 113 patients undergoing single-embryo transfer following a traditional culture and embryo selection procedure. We assessed the quality of transferred embryos, the rates of clinical pregnancy and pregnancy loss. Two subgroups were identified in each group of the participants: the 5SET subgroup (nonelective single-embryo transfer), which included 45 patients from the main group and 67 controls, and the 5eSET subgroup (elective single-embryo transfer), which consisted of 50 main group patients and 46 controls. The groups did not differ in terms of age, infertility factors and infertility duration. The quality of transferred embryos was excellent or good in all main group patients (100%); in the control group, the quality of transferred embryos was excellent or good in 93.8% of cases (p = 0.037). Clinical pregnancies were achieved in 64.2% of women in the main group and in 60.2% of controls (p = 0.65). Delivery rates were 54% and 51.1% in the 5eSET and 5SET subgroups of the main group, respectively (p = 0.940). For the control group, delivery rates were 54.4% and 34.3% in the 5eSET and 5SET subgroups, respectively (p = 0.052, Fisher exact test). Elective single-embryo transfer (5eSET) and the use of TLM increased the chance of pregnancy 2.17-fold (p = 0.01).

Keywords: assisted reproductive technology, single-embryo transfer, elective blastocyst transfer, time-lapse microscopy

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ОПТИМИЗАЦИЯ ПЕРЕНОСА ОДНОГО ЭМБРИОНА У ПАЦИЕНТОК С ХОРОШИМ ОВАРИАЛЬНЫМ РЕЗЕРВОМ

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Совершенствование вспомогательных репродуктивных технологий привело к росту числа случаев многоплодной беременности. Один из инструментов выбора качественного эмбриона на перенос — использование time-lapse микроскопии (TLM). Целью работы было оценить исходы переноса одного эмбриона на пятые сутки культивирования у пациенток с хорошим овариальным резервом в программе ЭКО с использованием TLM. Исследовали 208 женщин с бесплодием, с хорошим овариальным резервом (при пункции фолликулов получено более восьми ооцитов): у 95 пациенток провели перенос одного эмбриона с использованием системы TLM (группа исследования); у 113 пациенток — с использованием традиционного культивирования и выбора эмбриона для переноса (группа контроля). Проведена оценка качества переносимых эмбрионов, частоты наступления клинической беременности, частоты достижения родов и случаев потери беременности. В каждой группе выделены две подгруппы: с неэлективным переносом одного эмбриона (подгруппа 5SET: 45 пациенток в группе исследования, 67 — в контрольной) и с элективным (подгруппа 5eSET: 50 пациенток в группе исследования, 46 — в контрольной). Группы не различались по среднему возрасту, фактору бесплодия, длительности бесплодия. В группе исследования в 100% случаев перенесены эмбрионы хорошего и отличного качества, в группе контроля — в 93,8% (p = 0,037). Частота наступления клинической беременности составила 64,2% в основной группе и 60,2% — в контрольной (p = 0,65). В группе исследования частота родов составила 54% в подгруппе 5eSET и 51,1% — в подгруппе 5SET (p = 0,940). В группе контроля в подгруппе 5eSET частота родов составила 54,4%, а в подгруппе 5SET — 34,3% (p = 0,052 по методу Фишера). Проведение элективного переноса эмбриона (5eSET) или использование TLM повышало вероятность родов в 2,17 раза (p = 0,01).

Ключевые слова: вспомогательные репродуктивные технологии, перенос одного эмбриона, элективный перенос бластоцисты, time-lapse микроскопия

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Due to advancements in assisted reproductive technology (ART), implantation rates have significantly improved in the past 15–20 years, resulting in an increased incidence of multiple pregnancies. A multiple pregnancy is a recognized high-risk factor for obstetric and neonatal complications [1–3]. Therefore, transfer of a single embryo, as opposed to multiple embryos, is a top-priority task in ART-based infertility treatment [4, 5].

Selecting an embryo with the best developmental potential is crucial to ART success. Selection allows reducing time to pregnancy and simplifies embryo grading for cryopreservation, which, in turn, ensures that high-quality embryos are transferred first [6, 7].

Since the advent of in vitro fertilization (IVF), morphological evaluation has been the primary method exploited by embryologists to assess the development of human embryos and identify those with the highest implantation potential. Later, grading systems were proposed to estimate the viability of embryos, but their practical application was impeded by the rapid pace of embryo development in the preimplantation phase. In other words, it is possible that an embryo evaluated at 8:00 am will look very different in only a few hours [8]. So, it is very difficult to offer correct interpretation of the morphological data without analyzing the dynamicsdynamics of embryo development at a number of different time points.

Introduction of time-lapse microscopy (TLM) into IVF laboratories heralded a new age in embryology. TLM is a modern technique of embryo selection for subsequent implantation. It is used for continuous evaluation of embryo morphology in a series of images taken every few minutes [9–11].

Published reports on TLM results are conflicting. A retrospective study has demonstrated that incubation of human embryos in the EmbryoScope system can improve live birth rates whereas traditional culture techniques can negatively affect the development of embryos and their implantation potential [12]. Other retrospective and prospective studies point to the advantages of this promising technology [13–16], as well as to the absence of differences in outcomes in comparison with the conventional technique for morphological evaluation [17, 18].

The aim of our study was to assess the outcomes of single-embryo transfer following embryo incubation in a TLM-equipped incubator in patients with good ovarian reserve undergoing IVF.

METHODS

The study was conducted in 208 infertile women receiving a single-embryo transfer as part of their IVF treatment at the IDK Medical Company (Samara) in 2013–2015.

We analyzed 208 patients' clinical and embryo protocols using SPSS21 Statistics (License 20130626-3; IBM Company; USA) and Microsoft Excel (Microsoft; USA).

The following inclusion criteria were applied: participation in the IVF program, fresh autologous IVF cycles with 8 or more oocytes retrieved per cycle, embryo transfer on day 5 of incubation, and endometrial thickness of ≥ 8 mm on the day of transfer.

Exclusion criteria: participation in the ICSI program, donor oocyte cycles (with ≤ 8 oocytes), frozen-thawed embryo transfer, transfer on day 3 of incubation, multiple (2) embryo transfer, endometrial thickness of < 8 mm on the day of transfer.

There was no age limit applied. The lowest age was 20 years, whereas the highest, 42 years.

The patients were divided into two groups. The main group comprised 95 patients with good ovarian reserve undergoing a single-embryo transfer following embryo incubation in a TLM-equipped system.

The control group consisted of 113 patients with good ovarian reserve undergoing a single-embryo transfer following conventional embryo incubation and selection. The average age of the participants, infertility factors, the duration of infertility, and the number of the current IVF program did not differ between the groups. The average age was 31.40 ± 0.38 and 30.65 ± 0.37 years in the main and control groups, respectively ($p > 0.05$).

In the main group, embryo cultures were monitored using a Primo Vision time-lapse system (Vitrolife; Sweden).

In both groups, embryo quality was assessed using the alphanumeric blastocyst grading system proposed by Gardner and Schoolcraft in 1999 [19]. Grades AA, AB and BA represented excellent quality blastocysts; grade BB indicated good quality; grades AC, CA, BC, CB, and CC were considered to be satisfactory quality blastocysts.

Two subgroups were identified in each group based on the type of embryo transfer: a subgroup of nonelective single-embryo transfer on the 5th day of culture (the 5SET subgroup, which included 45 patients from the main group and 67 women from the control group) and a subgroup with elective single-embryo transfer on the 5th day of culture (the 5eSET subgroup consisting of 50 patients from the main subgroup and 46 controls). A transfer was classified as elective if there were 2 or more excellent quality embryos to choose from.

In the main group, embryos were selected for transfer based on their morphokinetic parameters. The following developmental events were assessed: time of the first cleavage division; an interval between the first and second divisions; time of the third cleavage; time of blastocyte formation. If these parameters fell within the reference range of the Primo Vision system and the embryo was of excellent or good quality, it was selected for transfer (a reference-positive embryo). The reference-positive subgroup comprised 52 patients. If one or more parameters of embryo development did not fall within the system's reference range, the standard morphological assessment technique for embryo selection was applied (a reference-negative embryo). The reference-negative subgroup included 43 patients.

In both groups, the embryos were cultured in a Continuous Single Culture medium (Irvine Scientific; USA). Embryo quality was assessed on day 5 of incubation, 116–118 h after fertilization.

RESULTS

We assessed the quality of transferred embryos and calculated the rates of successful pregnancies, delivery and pregnancy loss.

Patients of late reproductive age (≥ 35 years) made up 21.05% of women in the main group and 23.89% of women in the control group ($p > 0.05$). Because the study included only females with good ovarian reserve and a single-embryo transfer, our sample was dominated by patients of early reproductive age.

The average number of retrieved oocytes was 11.87 ± 0.32 and 12.49 ± 0.40 in the main and control groups, respectively ($p > 0.05$).

It is known that the quality of transferred embryos significantly affects the chance of pregnancy in patients undergoing IVF treatment. It is reported that transfer of excellent or good quality embryos results in much higher pregnancy rates than observed for satisfactory quality embryos [20]. In the main group, transferred embryos were of either good (16) or excellent (79) quality in 100% of cases. In the control group, good (18) or excellent (88) quality embryos were transferred in 93.8% of cases ($p = 0.037$) (Fig. 1). Satisfactory quality embryos were transferred to 7 patients in the control group (6.2%).

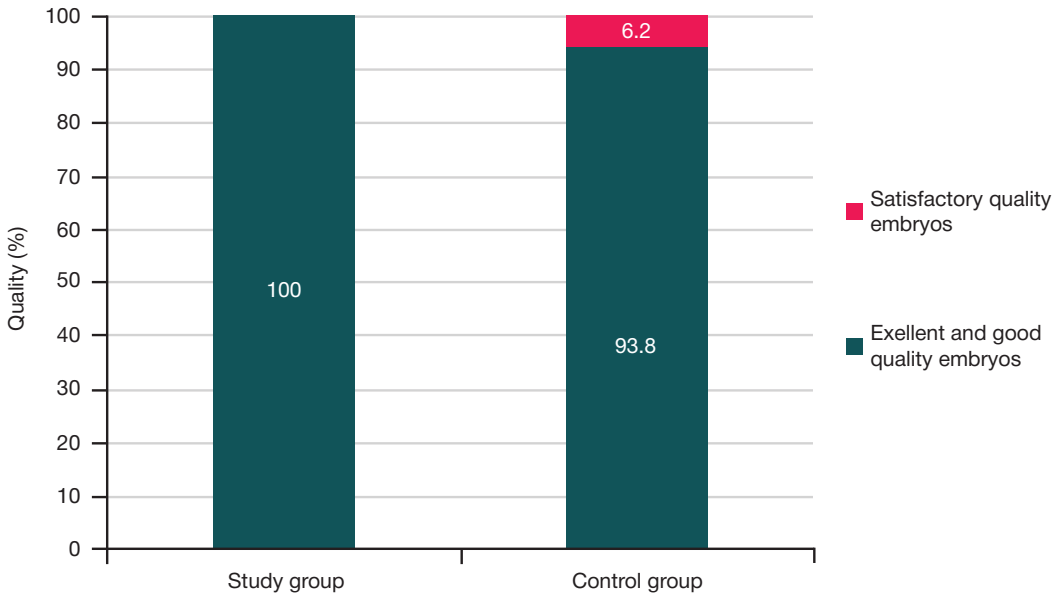

Fig. 1. Embryo quality in the main and control groups

The analysis of embryo quality did not reveal any significant differences between the reference-positive and reference-negative subgroups. In the reference-positive subgroup, 87.5% of embryo transfers were performed with excellent quality embryos, whereas in the reference-negative subgroup, the proportion of such cycles was 78.95% ($p = 0.44$).

Thus, the clinical pregnancy rate did not differ between the groups and was 64.2% in the main group and 60.2% in the control group ($p = 0.65$) (Table 1).

Live births accounted for 52.6% and 42.5% of all embryo transfer outcomes in the main and control groups, respectively ($p > 0.05$). Early pregnancy loss (biochemical pregnancy and pregnancy loss before gestational week 12) was observed in 11.6% of cases in the main group and in 17.7% of cases in the control group, but this difference was statistically insignificant.

No statistically significant differences were noted between the reference-positive and reference-negative subgroups in terms of clinical pregnancy rates (66.7% vs 60.5%, respectively) and delivery rates (50% vs 52.6%, respectively).

According to the literature, elective embryo transfer increases the probability of a positive outcome [21]; therefore, we decided to compare the delivery rate among patients who had undergone different types of transfer.

In the 5eSET subgroup (elective single-embryo transfer) of the main group, the delivery rate reached 54%; in the 5SET subgroup (nonelective single-embryo transfer), it was 51.1% ($p = 0.940$) (Fig. 2). In the control group, this parameter was significantly affected by the type of transfer: the delivery rates for the 5eSET and 5SET subgroups were 54.3% and 34.3%, respectively ($p = 0.052$, Fisher exact test). The difference in the delivery rate was 20.1 % (95%CI 1.5–37%), with OR = 2.28 (95%CI 1.06–4.91). Thus, the delivery rate was high in the TLM group, regardless of the type of transfer (54.0% and 51.1%), and did not differ significantly between the subgroups.

Considering this finding, we analyzed a possible correlation between the positive outcome of an IVF cycle (live birth) and the following factors: the absence/presence of TLM and the type of embryo transfer (elective or nonelective; Table 2).

The delivery rate was as high as 53.2% in the group with the combination of two factors (5eSET in both groups and 5SET in the main group), whereas in the control group, it was lower (34.3%) ($p = 0.01$; OR = 2.17 (1.19–3.97)). Thus, it could be hypothesized that there is a positive trend showing an increase in live births in patients undergoing IVF treatment aided by TLM regardless of the embryo transfer type.

DISCUSSION

The TLM technology minimizes exposure of the incubated embryo to environmental factors, which might be a contributor to a higher implantation potential. Continuous monitoring within short time intervals provides more information about the kinetics and morphology of embryos in comparison with traditional

Table 1. Outcomes of embryo transfer in the main and control groups

		Main group		Control group		χ^2	p
		Абс.	%	Абс.	%		
Pregnancy	No	34	35.8%	45	39.8%	0.2	0.65
	Yes	61	64.2%	68	60.2%		
Outcomes	No pregnancy	34	35.8%	45	39.8%	3.7	0.443
	Early loss of pregnancy	11	11.6%	18	15.9%		
	Late loss of pregnancy			2	1.8%		
	Preterm delivery	1	1.1%	1	0.9%		
	Delivery at term	49	51.6%	47	41.6%		
Childbirth	No	45	47.4%	65	57.5%	1.7	0.186
	Yes	50	52.6%	48	42.5%		

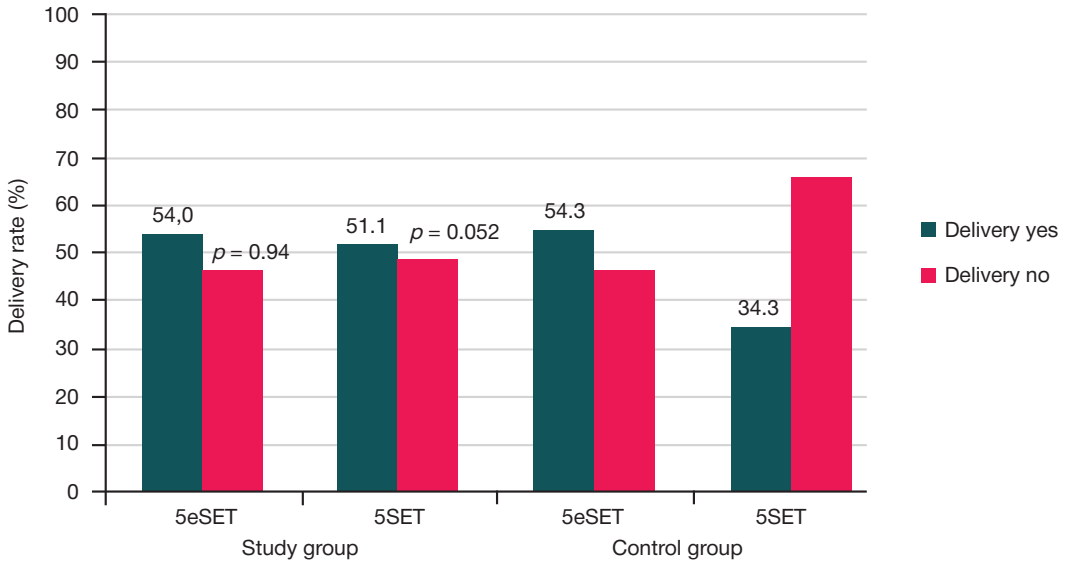

Fig. 2. Delivery rate depending on the type of the embryo transfer

morphological evaluation. So far, reports of the impact of TLM on IVF outcomes are conflicting.

We discovered that the quality of blastocytes in the TLM group was higher than in the case of traditional morphological evaluation, which is consistent with the findings of other authors [22, 23]. A study reports that in patients with good ovarian reserve, the proportion of good quality blastocytes and the number of cryopreserved embryos per patient was significantly lower in the control group than in the TLM group (50.7% and 1.72 ± 1.55 vs 60.1% and 2.64 ± 2.59, respectively; $p < 0.05$); however, no statistically significant differences were observed in the number of good quality embryos on day 3 of incubation, as well as in the rates of clinical pregnancy and implantation [23]. In our study, patients did not differ in terms of age, infertility factors and infertility duration; therefore, it could be hypothesized that the difference in the proportion of good and excellent quality embryos can be attributed to the absence of impact of environmental factors (ambient temperature, light, pH conditions) in the TLM group.

The efficacy of TLM might be determined by 2 factors: stable incubation conditions (there is no need to remove an embryo from an incubator for morphological evaluation) and the possibility of selecting an embryo for transfer using specialized software [24].

According to a recent Cochrane review that analyzed the data on 2,995 couples, there is no convincing evidence about the advantage of TLM over the conventional culture technique: no significant differences were observed in terms of clinical pregnancy rates (OR 0.95; 95%CI 0.78–1.16) and live birth rates (OR 1.12; 95%CI 0.92–1.36) [25].

By contrast, in a meta-analysis of data of 1,637 patients, TLM was shown to have an advantage over traditional incubation and morphological evaluation procedures [26]. This study reports high rates of clinical pregnancies (51.0 vs 39.9%; OR 1.54, 95%CI 1.21–1.97) and live births (44.2 vs 31.3%; OR 1.67, 95%CI 1.13–2.46) and lower rates of pregnancy loss (15.3 vs 21.3%; OR 0.66, 95%CI 0.47–0.94).

In our study, pregnancy rats were high in both groups (64.2% in the main group and 60.2% in the control group), which may suggest the absence of TLM negative effect on the incubated embryos. The use of time-lapse microscopy resulted in a reduction in the number of early pregnancy losses.

The absence of differences between the groups in terms of pregnancy rates, delivery rates and early pregnancy loss in our study might be associated with a small sample size (95 patients in the TLM group).

In another retrospective cohort study, the TLM group demonstrated an increase in clinical pregnancy rates (+15.7% per embryo transfer) [27]. However, unlike ours, that study was heterogenous in terms of patient sample (IVF cycles with donor oocytes were also included), number of transferred embryos (1–3) and time of transfer (in the majority of cases in the TLM group transfer was performed on day 3 of incubation, which decreased the overall pregnancy rate). In the TLM group, clinical pregnancies achieved after performing transfer of retrieved oocytes on the 5th day of culture were observed in 50% of cases, whereas for our patients, the pregnancy rate (embryo transfer on day 5 of incubation) was as high as 64.2%. One of the strengths of our study is a prognostic mathematical model developed by the authors of this work. The model predicted a 15.7% increase in pregnancy rates per transfer achieved through the use of TLM. Ever better outcomes can be achieved by increasing the number of IVF cycles with TLM to ≥ 200.

Like many technological advances, TLM may not ensure immediate results in every laboratory, and some standardization might be required. Indeed, TLM does not always demonstrate an advantage in terms of embryo selection [22]. However, its growing value for continuous incubation and embryo biopsy scheduling cannot be overestimated [28, 29].

At present, there are attempts to integrate artificial intelligence into TLM in order to identify the right combination of parameters predicting the potential of the embryo for implantation and live birth [24].

Table 2. Delivery rates in the absence/presence of TLM for different types of embryo transfer

Delivery	Transfer type				χ^2	p
	5eSET in both groups + 5SET in the main group		5SET in the control group			
	Abs.	%	Abs.	%		
No	66	46.8%	44	65.7%	5.75	0.01
Yes	75	53.2%	23	34.3%		

CONCLUSIONS

Our study did not reveal any differences in the rates of clinical pregnancies, delivery and early pregnancy loss between the TLM group and patients with traditional embryo incubation. This might be explained by a small number of patients in the TLM group. With TLM incubation, delivery rates were high regardless of the type of embryo transfer (selective or nonselective) and there were no differences in terms of pregnancy rates and early pregnancy losses. With traditional embryo incubation and selection, the transfer type significantly affected the delivery rate: in the elective transfer subgroup, the delivery rate was higher than in the nonelective transfer subgroup (p = 0.052; Fisher exact test). Performing elective embryo transfer on day 5 of incubation (5eSET) and the use of TLM regardless of transfer type were favorable factors and increased the chance for live birth (p = 0.01).

Our findings hold promise for exploring advantages of TLM in patients of different age groups with reduced ovarian reserve. Further accumulation of data is required to assess cumulative pregnancy rates following IVF with the use of TLM and to monitor the long-term results of this technology. There is no doubt that complex systems will soon be created for noninvasive evaluation of embryo quality (morphology, kinetics and metabolism) allowing automatization of embryo selection for transfer. They will reduce the probability of negative impact of environmental factors and thereby increase the rate of live births following embryo transfer.

References

1. Kalinkina OB, Spiridonova NV, Junusova JuR, Aravina OR. Mnogofaktornyj analiz riska razvitija akusherskih i perinatal'nyh oslozhnenij u pacientok s ozhireniem i izbytochnoj massoj tela. Izvestija Samarskogo nauchnogo centra RAN. 2015; 17 (5–3): 793–7.
2. Anderson P, Doyle LW. Victorian Infant Collaborative Study Group. Neurobehavioral outcomes of school-age children born extremely low birth weight or very preterm in the 1990s. J Am Med Assoc. 2003; 289: 3264–72.
3. Ombelet W, De Sutter P, Van der Elst J, Martens G. Multiple gestation and infertility treatment: registration, reflection and reaction-the Belgian project. Hum Reprod Update. 2005; 11: 3–14.
4. De Sutter P, Van der Elst J, Coetsier T, Dhont M. Single embryo transfer and multiple pregnancy rate reduction in IVF/ICSI: a 5-year appraisal. Reprod Biomed Online. 2003; 7: 464–9.
5. Thurin A, Hausken J, Hillensjo T, Jablonowska B, Pinborg A, Strandell A, Bergh C. Elective single-embryo transfer versus double-embryo transfer in in vitro fertilization. N Engl J Med. 2004; 351: 2392–402.
6. Bergh C. Single embryo transfer: a mini-review. Hum Reprod. 2005; 20: 323–7.
7. Gardner DK, Meseguer M, Rubio C, Treff NR. Diagnosis of human preimplantation embryo viability. Hum Reprod Update. 2015; 21: 727–47.
8. Bavister BD. Culture of preimplantation embryos: facts and artifacts. Hum Reprod Update. 1995; 1: 91–148.
9. Meseguer M. Time-lapse: the remaining questions to be answered. Fertil Steril. 2016; 105 (2): 295–6.
10. Pribenszkya C, Matyasb S, Kovacsb P, Losonczic E, Zádori J, Vajta G. Pregnancy achieved by transfer of a single blastocyst selected by time-lapse monitoring. Reprod Biomed Online. 2010; 21 (4): 533–6.
11. Wang SX. The past, present, and future of embryo selection in in vitro fertilization: Frontiers in Reproduction Conference. Yale J Biol Med. 2011; 84 (4): 487–90.
12. McEvoy K, Brison D, Roberts S, Turner C, Adeniyi T, Wood L, et al. A one year retrospective analysis comparing live birth outcomes from embryos grown and transferred from an undisturbed time-lapse culture system with a conventional culture system. Human reproduction. 2016; 31: i174–i175.
13. Shurygina OV, Saraeva NV, Tugushev MT, Pekarev VA, Bajzarova AA, Krasnova OV, et al. Otdalennye rezultaty programm VRT s ispolzovaniem sistemy nepreryvnogo videonabljudenija na jembriologichekom jetape. V sbornike: Reproduktivnye tehnologii segodnja i zavtra. Materialy XXVII mezhdunarodnoj konferencii Rossijskoj Associacii Reprodukcii Cheloveka; 6–9 centjabrja 2017 g. M.: Media Sfera, 2017; 328 s.
14. Adamson GD, Abusief ME, Palao LM, Gvakharia M. Improved implantation rates of day 3 embryo transfers with the use of an automated time-lapse–enabled test to aid in embryo selection. Fertil Steril. 2015; 105: 369–75.
15. Diamond MP, Suraj V, Behnke EJ, Yang X, Angle MJ, Lambe-Steinmiller JC, et al. Using the Eeva Test™ adjunctively to traditional day 3 morphology is informative for consistent embryo assessment within a panel of embryologists with diverse experience. J Assist Reprod Genet. 2015; 32: 61–68.
16. Ver Milyea MD, Tan Lei, Joshua TA, Conaghan J, Ivani K, Gvakharia M, et al. Computer-automated time-lapse analysis results correlate with embryo implantation and clinical pregnancy: A blinded, multi-centre study. Reprod Biomed Online. 2014; 29 (6): 729–36.
17. Kirkegaard K, Hindkjaer JJ, Grøndahl ML, Kesmodel US, Ingerslev HJ. A randomized clinical trial comparing embryo culture in a conventional incubator with a time-lapse incubator. J Assist Reprod Genet. 2012; 29 (6): 565–72.
18. Minasi MG, Colasante A, Riccio T, Ruberti A, Casciani V, Scarselli F, et al. Correlation between aneuploidy, standard morphology evaluation and morphokinetic development in 1730 biopsied blastocysts: a consecutive case series study. Hum Reprod. 2016; 31 (10): 2245–54.
19. Gardner DK, Schoolcraft WB. Culture and transfer of human blastocysts. Curr Opin Obstet Gynecol. 1999 Jun; 11 (3): 307–11.
20. Gardner DK, Lane M, Stevens J, Schlenker T, Schoolcraft WB. Blastocyst score affects implantation and pregnancy outcome: towards a single blastocyst transfer. Fertil Steril. 2000; 73: 1155–8.
21. Lee AM, Connell MT, Csokmay JM, Styer AK. Elective single embryo transfer — the power of one. Contracept Reprod Med. 2016; 1: 11.
22. Goodman LR, Goldberg J, Falcone T, Austin C, Desai N. Does the addition of time-lapse morphokinetics in the selection of embryos for transfer improve pregnancy rates? A randomized controlled trial. Fertil Steril. 2016; 105 (2): 275–85.
23. Zhang JQ, Li XL, Peng Y, Guo X, Heng BC, Tong GQ. Reduction in exposure of human embryos outside the incubator enhances embryo quality and blastulation rate. Reprod Biomed Online. 2010; 20: 510–15.
24. Apter S, Ebner T, Freour T, Guns Y, Kovacic B, Le Clef N, et al. Good practice recommendations for the use of time-lapse technology. Human Reproduction Open. 2020; 2020 (2: hoaa008. Available from: https://doi.org/10.1093/hropen/hoaa008.
25. Armstrong S, Bhide P, Jordan V, Pacey A, Marjoribanks J, Farquhar C. Time-lapse systems for embryo incubation and assessment in assisted reproduction. Cochrane Database of Systematic Reviews. 2018; 25 (5): CD011320. DOI: 10.1002/14651858.CD011320.pub4.
26. Pribenszkya C, Nilselid AM, Montag M. Time-lapse culture with morphokinetic embryo selection improves pregnancy and live birth chances and reduces early pregnancy loss: a meta-analysis. Reprod Biomed Online. 2017 Nov; 35 (5): 511–520.
27. Meseguer M, Rubio I, Cruz M, Basile N, Marcos J, Requena A. Embryo incubation and selection in a time-lapse monitoring system improves pregnancy outcome compared with a standard

incubator: a retrospective cohort study. Fertil Steril. 2012 Dec; 98 (6): 1481–9.
28. Athayde Wirka K, Chen AA, Conaghan J, Ivani K, Gvakharia M, Behr B, et al. Atypical embryo phenotypes identified by time-lapse microscopy: high prevalence and association with embryo development. Fertil Steril. 2014; 101 (6): 1637–48.
29. Liu Yanhe, Chapple V, Feenan K, Roberts P, Matson P. Time-lapse deselection model for human day 3 in vitro fertilization embryos: the combination of qualitative and quantitative measures of embryo growth. Fertil Steril. 2016; 105 (3): 656–62.

Литература

1. Калинкина О. Б., Спиридонова Н. В., Юнусова Ю. Р., Аравина О. Р. Многофакторный анализ риска развития акушерских и перинатальных осложнений у пациенток с ожирением и избыточной массой тела. Известия Самарского научного центра РАН. 2015; 17 (5–3): 793–7.
2. Anderson P, Doyle LW. Victorian Infant Collaborative Study Group. Neurobehavioral outcomes of school-age children born extremely low birth weight or very preterm in the 1990s. J Am Med Assoc. 2003; 289: 3264–72.
3. Ombelet W, De Sutter P, Van der Elst J, Martens G. Multiple gestation and infertility treatment: registration, reflection and reaction-the Belgian project. Hum Reprod Update. 2005; 11: 3–14.
4. De Sutter P, Van der Elst J, Coetsier T, Dhont M. Single embryo transfer and multiple pregnancy rate reduction in IVF/ICSI: a 5-year appraisal. Reprod Biomed Online. 2003; 7: 464–9.
5. Thurin A, Hausken J, Hillensjo T, Jablonowska B, Pinborg A, Strandell A, Bergh C. Elective single-embryo transfer versus double-embryo transfer in in vitro fertilization. N Engl J Med. 2004; 351: 2392–402.
6. Bergh C. Single embryo transfer: a mini-review. Hum Reprod. 2005; 20: 323–7.
7. Gardner DK, Meseguer M, Rubio C, Treff NR. Diagnosis of human preimplantation embryo viability. Hum Reprod Update. 2015; 21: 727–47.
8. Bavister BD. Culture of preimplantation embryos: facts and artifacts. Hum Reprod Update. 1995; 1: 91–148.
9. Meseguer M. Time-lapse: the remaining questions to be answered. Fertil Steril. 2016; 105 (2): 295–6.
10. Pribenszkya C, Matyasb S, Kovacsb P, Losonczic E, Zádori J, Vajta G. Pregnancy achieved by transfer of a single blastocyst selected by time-lapse monitoring. Reprod Biomed Online. 2010; 21 (4): 533–6.
11. Wang SX. The past, present, and future of embryo selection in in vitro fertilization: Frontiers in Reproduction Conference. Yale J Biol Med. 2011; 84 (4): 487–90.
12. McEvoy K, Brison D, Roberts S, Turner C, Adeniyi T, Wood L, et al. A one year retrospective analysis comparing live birth outcomes from embryos grown and transferred from an undisturbed time-lapse culture system with a conventional culture system. Human reproduction. 2016; 31: i174–i175.
13. Шурыгина О. В., Сараева Н. В., Тугушев М. Т., Пекарев В. А., Байзарова А. А., Краснова О. В., и др. Отдаленные результаты программ ВРТ с использованием системы непрерывного видеонаблюдения на эмбриологическом этапе. В сборнике: Репродуктивные технологии сегодня и завтра. Материалы XXVII международной конференции Российской ассоциации репродукции человека; 6–9 сентября 2017 г.; М.: Медиа Сфера, 2017; 328 с.
14. Adamson GD, Abusief ME, Palao LM, Gvakharia M. Improved implantation rates of day 3 embryo transfers with the use of an automated time-lapse–enabled test to aid in embryo selection. Fertil Steril. 2015; 105: 369–75.
15. Diamond MP, Suraj V, Behnke EJ, Yang X, Angle MJ, Lambe-Steinmiller JC, et al. Using the Eeva Test™ adjunctively to traditional day 3 morphology is informative for consistent embryo assessment within a panel of embryologists with diverse experience. J Assist Reprod Genet. 2015; 32: 61–68.
16. Ver Milyea MD, Tan Lei, Joshua TA, Conaghan J, Ivani K, Gvakharia M, et al. Computer-automated time-lapse analysis results correlate with embryo implantation and clinical pregnancy: A blinded, multi-centre study. Reprod Biomed Online. 2014; 29 (6): 729–36.
17. Kirkegaard K, Hindkjaer JJ, Grøndahl ML, Kesmodel US, Ingerslev HJ. A randomized clinical trial comparing embryo culture in a conventional incubator with a time-lapse incubator. J Assist Reprod Genet. 2012; 29 (6): 565–72.
18. Minasi MG, Colasante A, Riccio T, Ruberti A, Casciani V, Scarselli F, et al. Correlation between aneuploidy, standard morphology evaluation and morphokinetic development in 1730 biopsied blastocysts: a consecutive case series study. Hum Reprod. 2016; 31 (10): 2245–54.
19. Gardner DK, Schoolcraft WB. Culture and transfer of human blastocysts. Curr Opin Obstet Gynecol. 1999 Jun; 11 (3): 307–11.
20. Gardner DK, Lane M, Stevens J, Schlenker T, Schoolcraft WB. Blastocyst score affects implantation and pregnancy outcome: towards a single blastocyst transfer. Fertil Steril. 2000; 73: 1155–8.
21. Lee AM, Connell MT, Csokmay JM, Styer AK. Elective single embryo transfer — the power of one. Contracept Reprod Med. 2016; 1: 11.
22. Goodman LR, Goldberg J, Falcone T, Austin C, Desai N. Does the addition of time-lapse morphokinetics in the selection of embryos for transfer improve pregnancy rates? A randomized controlled trial. Fertil Steril. 2016; 105 (2): 275–85.
23. Zhang JQ, Li XL, Peng Y, Guo X, Heng BC, Tong GQ. Reduction in exposure of human embryos outside the incubator enhances embryo quality and blastulation rate. Reprod Biomed Online. 2010; 20: 510–15.
24. Apter S, Ebner T, Freour T, Guns Y, Kovacic B, Le Clef N, et al. Good practice recommendations for the use of time-lapse technology. Human Reproduction Open. 2020; 2020 (2: hoaa008. Available from: https://doi.org/10.1093/hropen/hoaa008.
25. Armstrong S, Bhide P, Jordan V, Pacey A, Marjoribanks J, Farquhar C. Time-lapse systems for embryo incubation and assessment in assisted reproduction. Cochrane Database of Systematic Reviews. 2018; 25 (5): CD011320. DOI: 10.1002/14651858.CD011320.pub4.
26. Pribenszkya C, Nilselid AM, Montag M. Time-lapse culture with morphokinetic embryo selection improves pregnancy and live birth chances and reduces early pregnancy loss: a meta-analysis. Reprod Biomed Online. 2017 Nov; 35 (5): 511–520.
27. Meseguer M, Rubio I, Cruz M, Basile N, Marcos J, Requena A. Embryo incubation and selection in a time-lapse monitoring system improves pregnancy outcome compared with a standard incubator: a retrospective cohort study. Fertil Steril. 2012 Dec; 98 (6): 1481–9.
28. Athayde Wirka K, Chen AA, Conaghan J, Ivani K, Gvakharia M, Behr B, et al. Atypical embryo phenotypes identified by time-lapse microscopy: high prevalence and association with embryo development. Fertil Steril. 2014; 101 (6): 1637–48.
29. Liu Yanhe, Chapple V, Feenan K, Roberts P, Matson P. Time-lapse deselection model for human day 3 in vitro fertilization embryos: the combination of qualitative and quantitative measures of embryo growth. Fertil Steril. 2016; 105 (3): 656–62.