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human reproduction **ORIGINAL ARTICLE** ***Infertility***

Self-operated endovaginal telemonitoring versus traditional monitoring of ovarian stimulation in assisted reproduction: an RCT

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STUDY QUESTION: Does self-operated endovaginal telemonitoring (SOET) of the ovarian stimulation phase in IVF/ICSI produce similar laboratory, clinical, patient reported and health-economic results as traditional monitoring (non-SOET)?

SUMMARY ANSWER: SOET is not inferior to traditional monitoring (non-SOET).

WHAT IS KNOWN ALREADY: Monitoring the follicular phase is needed to adapt gonadotrophin dose, detect threatening hyperstimulation and plan HCG administration. Currently, patients pay visits to care providers, entailing transportation costs and productivity loss. It stresses patients, partners, care providers and the environment. Patients living at great distance from centres have more difficult access to treatment. The logistics and stress during the follicular phase of assisted reproduction treatment (ART) is often an impediment for treatment.

STUDY DESIGNS, SIZE, DURATION: The study was a non-inferiority RCT between SOET and non-SOET performed between February 2012 and October 2013. Sample size calculations of number of metaphase II (MII) oocytes (the primary outcome): 81 patients were needed in each study arm for sufficient statistical power. Block randomization was used with allocation concealment through electronic files. The first sonogram was requested after 5 days of stimulation, after that mostly every 2 days and with a daily sonograms at the end.

PARTICIPANTS/MATERIALS, SETTINGS, METHODS: Inclusion criteria were age <41 years, undergoing ICSI, no poor response and having two ovaries. We used a small laptop with USB connected vaginal probe and developed a specific web site application. Sonographic training was given to all women at the initiation of a treatment attempt at the centre. The website contained demonstration material consisting of still images and video sequences, as well as written instructions regarding the use of the instrument and probe handling. In total, 185 eligible patients were recruited in four centres: 123 were randomized; 121 completed SOET ($n = 59$) or non-SOET ($n = 62$), and 62/185 (33%) eligible patients declined participation for various reasons.

MAIN RESULTS AND THE ROLE OF CHANCE: Patient characteristics were comparable. The clinical results showed similar conception rates ($P = 0.47$) and ongoing pregnancy rates (SOET: 15/59 = 25%; non-SOET: 16/62 = 26%) ($P = 1.00$) were obtained. Similar numbers of follicles >15 mm diameter at oocyte retrieval (OR), ova at OR, MII oocytes, $\log_2$ MII oocytes, embryos available at transfer, top quality embryos and embryos frozen were obtained in the two groups, indicating non-inferiority of SOET monitoring. Regarding patient-reported outcomes, a significantly higher contentedness of patient and partner ($P < 0.01$), a higher feeling of empowerment, discretion and more active partner participation ($P < 0.001$) as well as a trend towards less stress ($P = 0.06$) were observed in the S versus the NS group. In the economic analysis, the use of SOET led to reduced productivity loss, lower transportation costs, and lower sonogram and consultation costs (all $P < 0.001$ but higher personnel cost than NS).

LIMITATIONS, REASONS FOR CAUTION: The study was stopped (no further funding) before full sample size was reached. There were also a few cases of unexpected poor response, leading to a wider SD than anticipated in the power calculation. However, although the study was underpowered for these reasons, non-inferiority of SOET versus non-SOET was demonstrated.

WIDER IMPLICATIONS OF THE FINDINGS: Home monitoring using SOET may provide a patient-centred alternative to the standard methods. ART sonograms can be made, and then sent to the care provider for analysis at any appropriate time and from anywhere if an internet connection is available. This approach offers several advantages for patients as well as care providers, including similar results to the traditional methods with less logistical stress and potentially bringing care to patients in poor resource settings.

STUDY FUNDING/COMPETING INTEREST(S): Supported by an IOF (industrial research fund) of Ghent University (full protocol available at iBiTech) and as a demonstration project of Flanders Care (Flemish Government). There are no conflicts of interest to declare.

TRIAL REGISTRATION NUMBER: EC/2011/669 (Ghent University Hospital), B670201112232 (Belgian registration) and NCT01781143 (clinical trials number).

Key words: telemonitoring / IVF/ICSI / vaginal sonography / health-economy / patient empowerment

Introduction

During the ovarian stimulation phase of assisted reproduction treatment (ART), the patient needs to be monitored for two main reasons: to increase or decrease the daily dose of gonadotrophins and to decide on the timely injection of HCG,. In addition, ovarian hyperstimulation syndrome (OHSS) can be prevented. Monitoring is achieved using serial vaginal sonograms, and counting the number and measuring the size of the follicles. The sonogram is performed by a gynaecologist, an IVF physician, a nurse or midwife and often is a very strenuous aspect of ART. Patients need to come, often from far away, to the centre for a relatively simple procedure. This entails an economic, logistic, emotional and potential environmental cost. For care providers sonograms represent a very routine procedure, reducing their time for more complex tasks.

Monitoring of ovarian stimulation is also based on serial measurements of serum estradiol (E_2), which is indeed essential in cases of OHSS but not for general use (Kwan *et al.*, 2009).

We have previously explored the possibility of monitoring patients at a distance, by teaching them to make their own vaginal sonograms at home (Gerris and De Sutter, 2010; Gerris *et al.*, 2009). We have conducted a prospective RCT comparing self-operated endovaginal telemonitoring (SOET) at home with traditional sonographic (non-SOET) follow-up.

Materials and Methods

This study was approved by the Ethical Committee of the University Hospital Ghent (EC/2011/669) and supported by an industrial research fund from Ghent University and a grant from the Flemish Government. Written consent was obtained from all patients.

Aim of the study

We hypothesized that self-monitoring (SOET) at home by the patient and traditional monitoring by medical staff (non-SOET) could result in similar laboratory and clinical outcomes, better patient-reported outcomes and a more favourable health-economic result for the S group. The primary outcome variable of the study, comparing the effect of ovarian stimulation, was the number of metaphase-II (MII) oocytes. Only ICSI attempts were therefore included, in which oocytes undergo denudation. Secondary outcome variables were patient-reported outcomes and health-economic variables. We wanted to compare two different *strategies* of monitoring, and therefore allowed all participating centres to use their own clinical and laboratory protocols.

Design of the study

A power calculation was performed prior to this RCT trial. Sample size calculations were based on the primary laboratory efficacy variable and calculated on the basis of historical data of numbers of metaphase-II oocytes at oocyte retrieval (OR) for women <41 years of age with at least four oocytes at OR at our centre. Poor responders were excluded. Because the distribution of numbers of metaphase-II oocytes was skewed to the right, the analysis was performed on the $\log_2$-transformed numbers of metaphase-II oocytes. A sample size of 81 patients per group would allow for 80% power to demonstrate non-inferiority for the SOET group in a two-sample T-test on the $\log_2$-transformed value of the primary outcome variable. Non-inferiority is defined as the SOET treatment having a number of metaphase-II oocytes at pick-up that is at least 80% of the number of metaphase-II oocytes at pick-up for standard monitoring (threshold limit for the difference of 0.32 on the $\log_2$-scale). Sample size calculation was performed under the further assumption that the true outcome of the SOET group is equal to the outcome of the standard nn-SOET stimulation.

Patient recruitment, study counselling, ovarian stimulation, sonographic follow-up, embryo transfer

Eligible patients had to fulfil the following inclusion criteria: <41 years of age, two ovaries, ICSI treatment. They needed a wireless internet connection at home and basic computer skills. Exclusion criteria were documented causes of severe distortion of the pelvic organs making sonography more difficult as well as poor responders (previously <4 oocytes) and serum anti-Mullerian hormone value <0.5 μIU/ml. Previous OHSS (at least 1 day of hospitalization in a previous ART attempt) and polycystic ovary syndrome (diagnosed using the Rotterdam criteria) were considered risk factors but not formal exclusion criteria.

Block randomization was conducted using electronic clinical research files, allotting each recruited patient at the time of enrolment to one of the groups.

Eligible patients were given a first general explanation of the concept of SOET as well as a letter of information explaining aims, methods and expectations. Patients could be enrolled at the time of the initial sonogram. Those who agreed to participate, were electronically randomized to either the SOET or the non-SOET arm of the study.

Enrolled patients were given a diary to fill in the data for calculating direct and indirect costs. The CONSORT-diagram is shown in Figure 1.

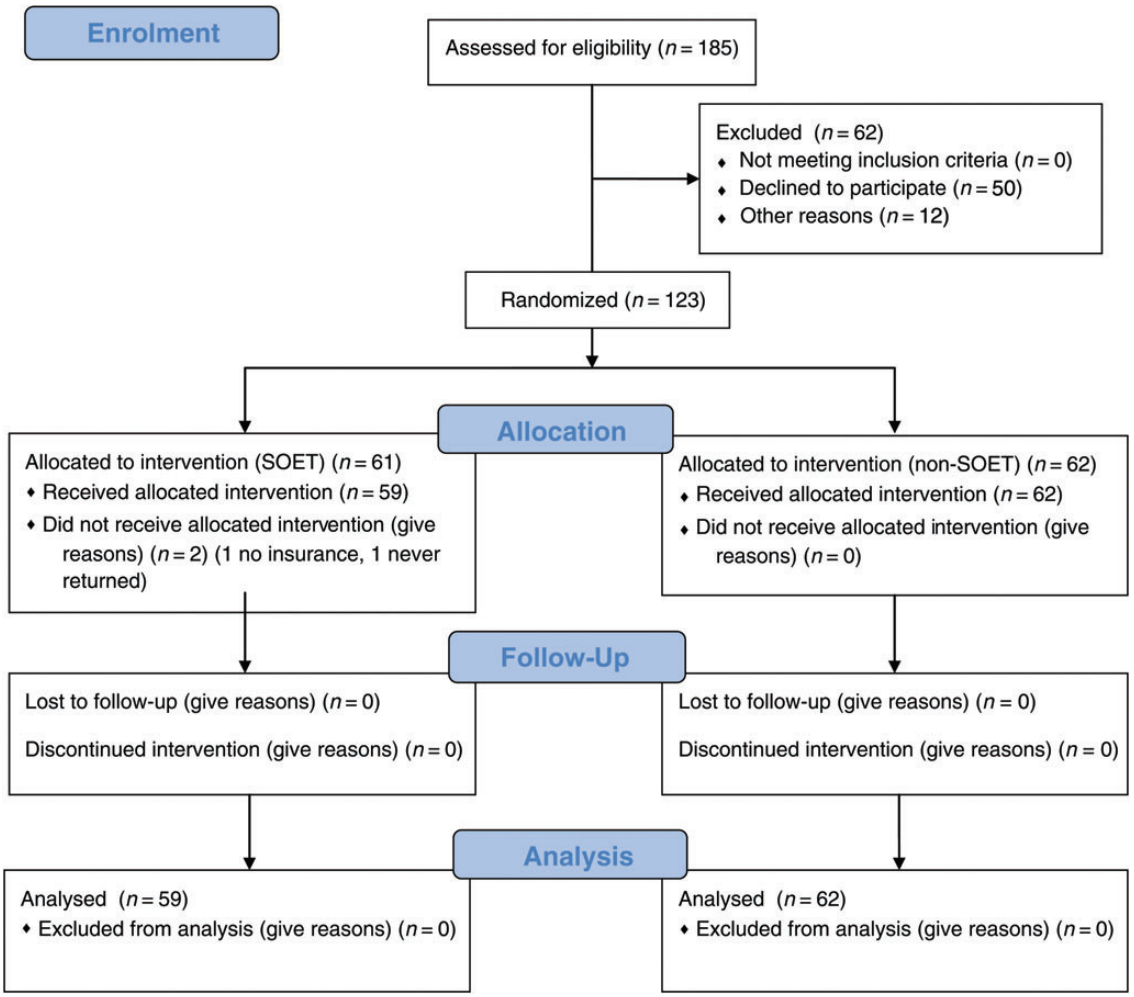

Figure 1 CONSORT flow diagram for a prospective RCT of self-operated endovaginal telemonitoring (SOET) versus traditional monitoring of ovarian stimulation in assisted reproduction.

Typically, patients were prepared for ICSI using an oral contraceptive. After withdrawal, a GnRH agonist was started using a short protocol (e.g. Decapeptyl, 0.1 mg/day for 7 days); after 3 days of the agonist, gonadotrophin stimulation was started, 150 IU being the usual starting dose. In case of previous OHSS, lower starting doses were used; in case of unexpected low response, a higher initial dose, with a maximum of 300 IU/day, was used.

SOET patients were shown how the server based communication software, developed at the faculty of engineering of Ghent University, Belgium, and the imaging software (NuWav, Laborie, Canada), worked. Patients were shown how to make video images, an how to upload and send them to the centre. They were given a laptop on which only the communication software and the imaging software were installed, a vaginal sonography probe with USB connection, a mouse, a power connection, condoms and gel. We used a 7.5 MHz endocavity probe for vaginal application (Laborie Medical, Inc., Toronto, Canada). They were instructed to send a first video recording soon after withdrawal bleeding in order to establish functional communication with the centre.

The video recordings were made by the patients by manually sweeping the probe. All measurements were performed by the care provider following up the stimulation. Patients scanned first their right ovary, then the uterus, then the left ovary. Before making actual recordings, the patient could explore how to make the best sweep using the screen of their laptop. After recording the sweep, lasting between 60 and 90 s for each ovary, and 30 s for the uterus, they could check the recorded images before sending them. If images were not considered appropriate, another recording could be made. Most patients learned quickly, finding their ovaries increasingly easily once they knew how to handle the probe within the vagina. With this pre-industrial hardware configuration, each recording was carried out, files were compressed, uploaded and sent separately. This could take up to 1 h (depending on the band width) but less than the time to travel to and from the centre, and was usually performed during leisure time.

Patients entering the SOET arm were monitored using home-made sonograms exclusively. They were not seen by a care provider between the day of the initial sonogram and the day of OR. If needed for clinical purposes (e.g. threatening OHSS), serum E_2 measurements could be performed in a laboratory near to the patient's home. Criteria for threatening OHSS were >15 follicles with a diameter of ≥ 15 mm or serum E_2 values >3000 pg/ml. Patients entering the non-SOET arm were monitored as usual: some in-house, even if they lived at a distance from the centre; others by a 'satellite' centre or physician.

Videos were downloaded and opened in the imaging software in order to perform 2D-measurements of the follicles. All measurements were

performed by the principal investigators. Video images could be stopped, played forward or backward using two callipers in order to measure each follicle at its largest diameters. Using the report function of the website, the patient then obtained instruction concerning hormonal dose continuation or adjustment and planning of the subsequent sonogram. When follicles were considered mature, an instruction for HCG administration was given and the patient returned the system at the time of puncture. Each participating centre used its standard stimulation protocols and criteria for HCG administration. At any time, direct communication by e-mail or telephone was possible in both directions, creating a direct line between the centre (midwives, doctor) and the patient.

The midwives or nurse-practitioners taught the patients how to introduce and handle the probe, how to find the uterus and resting suppressed ovaries with hardly visible follicles at the start of the cycle, which was not always possible. At the patient's side of the study website, still images of follicles in different stages of development and a video demonstration were available at all times. The primary image quality criterion was to detect follicles that were identifiable and measurable in serial recordings. The patients took no responsibility whatsoever for measuring, interpreting or making decisions. The role of the midwives was to assist when the system was explained to patients, to communicate with the patient by mail or telephone if needed and to collect the diaries and fill out the patient reported outcomes (PRO) questionnaires during the post-study visit.

All centres had to adhere to the Belgian legislation concerning the number of embryos to transfer aimed at minimizing the percentage of multiple pregnancies (De Sutter *et al.*, 2003; Gerris 2005; Ombelet *et al.*, 2005; De Neubourg *et al.*, 2013; Peeraer *et al.*, 2013).

Outcome variables

For laboratory outcome we recorded the total number of oocytes at retrieval, the number of mature metaphase-II oocytes at retrieval, the percentage of metaphase-II oocytes over the number of follicles punctured, the total number of top quality embryos on Day 3 and Day 5 (Van Royen *et al.*, 1999; Van den Abbeel *et al.*, 2013) and the number of embryos transferred or cryopreserved (Day 5).

For clinical outcome we recorded the number of follicles $\geq$15 mm diameter prior to puncture, the total number of positive HCGs, and the number of ongoing pregnancies (>12 weeks, at least one fetus with cardiac beats). Conceptions and ongoing pregnancies were counted cumulatively: each conception resulting from a study cycle was counted. This allows us to include all conceptions both from fresh and from frozen/thawed embryo replacements. The conception with the longest gestation was considered as the one to include in the results.

Patient-reported outcome was assessed at the time of the SOET follow-up visit.

Input data for the health-economic analysis were collected through patient diaries. Costs related to these input data, calculated for the duration of the study, were obtained using published and unpublished sources.

Statistics

Primary non-inferiority efficacy analysis is based on the most conservative per protocol (PP) analysis, which strictly includes patients that performed at least one sonogram as determined by the randomization. Protocol violators are excluded from this analysis. Non-inferiority is only concluded for the primary end-point. Additional analyses based on the intention-to-treat (ITT) and as-treated analysis also support the non-inferiority conclusion.

In order to demonstrate non-inferiority with respect to the primary outcome variable, we needed to show that the number of M-II oocytes at OR was at least 80% of the number after standard monitoring.

A two-sided 95% confidence interval (CI) for the difference in mean $\log_2 n$ metaphase II oocytes of NS versus SOET monitoring was calculated, to evaluate the non-inferiority hypothesis. Clinical outcome measures, like proportions of positive HCG results and ongoing pregnancies, and PRO comparing SOET and non-SOET are compared using Fisher's exact tests.

Results

Patient characteristics

One hundred and eighty-five patients were recruited between February 2012 and October 2013, of whom 62 (34%) did not participate for a variety of reasons listed in Table I. Of 123 patients enrolled, 62 entered the non-SOET arm and 61 the SOET arm. Two patients, both belonging to the SOET arm, dropped out: one because she learned she had no insurance coverage and one who stopped treatment for unknown reasons. Two patients attributed to the SOET arm switched to traditional monitoring because of technical fall-out of the probe. In the ITT principle, they were analysed in the SOET arm. Table II describes the characteristics of 121 analysed patients (59 SOET, 62 non-SOET). Both groups were comparable with respect to age of the patient, age of the partner, BMI, smoking behaviour and duration of subfertility.

Laboratory results

Laboratory data are summarized in Table III (primary variables) and Table IV (secondary variables). The median of the number of M-II oocytes was eight in the SOET group versus seven in the non-SOET group (ITT analysis). After $\log_2$-transformation of the number of M-II oocytes, the mean is 3.01 (SD = 1.06) for the SOET arm versus 2.78 (SD = 1.37) for the non-SOET arm (ITT analysis). The 95% CI for the average difference in $\log_2 n$ M-II oocytes non-SOET versus SOET is −0.24 (−0.68; 0.19) ($P = 0.27$), indicating non-inferiority of SOET monitoring.

A *post hoc* power analysis based on the most conservative PP analysis shows that group sample sizes of 57 women in the SOET arm and 62 women in the non-SOET arm achieve 29% power to detect

Table I Reasons for not participating in the self-operated endovaginal telemonitoring (SOET) RCT in eligible patients.

Reason	*N* patients
Uncertain they could produce good videos	26
First attempts	11
Last attempts	4
Pregnant after FRET	4
Practical reasons (timing)	8
Interruption of treatment	4
Previous OHSS	1
Spontaneous pregnancy	1
Changed therapy to AID	1
Intervening malignancy	1
Did not accept ICSI	1

FRET, frozen embryo transfer; AID, artificial insemination by donor sperm; OHSS, ovarian hyperstimulation syndrome.

non-inferiority using a two-sided 95% CI for the difference in means, assuming a common SD of 1.24, a true difference in means of 0 and a non-inferiority limit of 0.32 on the $\log_2$-scale, comparing non-SOET versus SOET. Although underpowered, this study still shows non-inferiority of SOET versus non-SOET monitoring of ovarian stimulation in ART.

Results calculated for the PP analysis, excluding attempts with OR but without embryo transfer (either no eggs or no transferable embryos) (SOET: $n = 52$; non-SOET: $n = 57$), indicate non-inferiority for SOET in this scenario as well (−0.21 (−0.57; 0.14)).

Table II Patient characteristics at the time of randomization.

Patient characteristics	SOET ($n = 59$)	Non-SOET ($n = 62$)
Age (years)	33 (3.6)	33 (4.2)
Age of the partner (years)	38 (6.4)	36 (5.9)
BMI (kg/m^2)	24.3 (3.91)	23.8 (4.08)
Smoking behaviour Smoker *n* (%)	5 (8)	2 (3)
Subfertility (months)	42 (24.3)	37 (16.3)
*Rank of attempt Median (Q1;Q3) [min,max]	1 (1;3) [1;5]	2 (1;4) [1;6]
AMH in serum (μg/ml) Mean (SD)	5.2 (3.83)	4.0 (2.91)

AMH, anti-Mullerian hormone, Q1, quartile1.
All data are Mean (SD) unless stated otherwise.
*Rank of attempt refers to the rank of the stimulated ART cycle; an attempt may include one 'fresh' and one or more cryo-transfers.

Clinical results

All patients finished their treatment attempt, except for two drop-outs. Two patients from the S group had a technical fall-out of their probe and continued in the traditional monitoring, coming to the centre. In two patients, imaging remained uncertain and they were asked to come to the centre. One was a poor responder who had her daily dose increased and continued successfully with home follow-up. The other had follicles that were almost mature, and received HCG the day after the routine sonogram. This is the only patient where the SOET approach can be considered to have failed, because the patient did not succeed in identifying the follicles. In all the other patients, no extra visits were needed between the initial sonogram and the OR. Almost all patients experienced stress of uncertainty for some days, especially when follicles were still small (<12 mm). Once the follicles became clearly visible, patients succeeded in recording adequate video sequences.

In the SOET group there were 58/61 OR procedures (one cancellation) and 54/61 embryo transfers (four patients with either no or only bad quality embryos). In the non-SOET group there were 59/62 retrievals and 57/62 transfers. All results are calculated per started attempt.

In the SOET arm, 26/59 (44%) attempts resulted in a positive HCG versus 32/62 (52%) in the non-SOET arm ($P = 0.47$). The difference in 95% CI in the proportion of conceptions between study arms was −0.08 [−0.25; 0.10]. In the SOET group there were 15/59 ongoing pregnancies (25%) versus 16/62 (26%) in the non-SOET group ($P = 1.00$). The difference with 95% CI in the proportion of ongoing pregnancies between study arms was −0.01 [−0.16; 0.15]. Clinical outcome measures are not statistically different between SOET and non-SOET monitoring.

Table III Overview of laboratory results in patients after SOET/non-SOET for assisted reproduction treatment (ART): primary end variables, analysed without two protocol violators who were treated in the non-randomized arm (Per Protocol – analysis), analysed with these two in the as-treated arm (As-Treated – analysis) and analysed in the randomized arm (Intention To Treat – analysis).

Per Protocol analysis	SOET (59)	non-SOET ($n = 62$)
N metaphase II-ova (nMII) Median (Q1;Q3) [Min;Max]	9.0 (5.0;13.0) [0.0;24.0]	7.0 (4.3;13.0) [0.0;30.0]
$\log_2$ *n* metaphase II-ova Mean (SD)	**3.03** (1.077)	**2.78** (1.374)
Mean difference in $\log_2$ *n* metaphase II-ova (95% CI), comparing non-SOET versus SOET	−0.25 (−0.70;0.18)	
As-Treated analysis	SOET ($n = 59$)	non-SOET ($n = 64$)
N metaphase II-ova (nMII) Median (Q1;Q3) [Min;Max]	9.0 (5.0;13.0) [0.0;24.0]	7.0 (4.8;13.0) [0.0;30.0]
$\log_2$ *n* metaphase II-ova Mean(SD)	**3.03** (1.077)	**2.76** (1.317)
Mean difference in $\log_2$ *n* metaphase II-ova (95% CI), comparing non-SOET versus SOET	−0.27 (−0.70;0.16)	
Intention To Treat analysis	SOET ($n = 59$)	non-SOET ($n = 62$)
N metaphase II-ova (nMII) Median (Q1;Q3) [Min;Max]	8.0 (5.0;13.0) [0.0;24.0]	7.0 (4.3;13.0) [0.0;30.0]
$\log_2$ *n* metaphase II-ova Mean(SD)	**3.01** (1.064)	**2.78** (1.374)
Mean difference in $\log_2$ *n* metaphase II-ova (95% CI), comparing non-SOET versus SOET	−0.08 (−0.25;0.10)	

Mean difference in $\log_2$ n is indicated in bold.

Table IV Laboratory results in patients after SOET/non-SOET for ART: secondary end variables.

Secondary outcome variables	SOET ($n = 59$)	NON-SOET ($n = 62$)	*P*-value MW U test
N follicles > 15 mm at OPU (NF)			0.741
Mean (SD)	8.1 (3.64)	8.7 (4.96)	
Median (Q1;Q3) [Min;Max]	8 (5;11) [0;16]	8 (5;12) [0;20]	
N oocytes at OPU (NOR)			0.458
Mean (SD)	12.2 (7.31)	11.3 (7.44)	
Median (Q1;Q3) [Min;Max]	11 (5;16) [0;29]	10.5 (6;15) [0;37]	
Proportion (nMII/NOR)			0.432
Mean (SD)	78 (13.9)	77 (22.4)	
Median (Q1;Q3) [Min;Max]	75 (68;88) [50;100]	81 (67;97) [14;100]	
N embryos available			0.743
Mean (SD)	4.8 (3.89)	4.5 (3.74)	
Median (Q1;Q3) [Min;Max]	4 (1;7) [0;14]	4 (2;6) [0;14]	
N top quality embryo's at ET			0.698
Mean (SD)	1.3 (0.72)	1.2 (0.70)	
Median (Q1;Q3) [Min;Max]	1 (1;2) [0;3]	1 (1;2) [0;3]	
N embryos cryopreserved			0.846
Mean (SD)	1.5 (2.08)	1.5 (2.42)	
Median (Q1;Q3) [Min;Max]	0 (0;2) [0;7]	0 (0; 3) [0;10]	

Table V Average total cost per treatment attempt (€).

	NON-SOET ($N = 62$)	SOET ($N = 59$)
Ultrasound – paid by insurance	€143 (66)	€32 (44)
Ultrasound – paid by patient	€35 (16)	€8 (11)
Transport – paid by patient	€190 (265)	€51 (81)
Material – paid by insurance and/or patient	€0 (0)	€69 (0)
Productivity loss – paid by employer	€423 (381)	€96 (184)
Labour costs medical staff – paid by employer	€103 (39)	€199 (42)
Total	€894 (654)	€455 (284)

Data were analysed using official cost data during the study period (February 2012–October 2013).
Data are Cost (SD).

Patient-reported outcomes

All patients were seen at a post-treatment consultation and asked to assess six outcome measures: satisfaction of the patient and of the partner, feeling of empowerment, active participation of the partner, stress and discretion. In five out of these six variables SOET scored better than non-SOET attempts (*P*-value <0.001), while for stress the *P*-value was 0.06, indicating a trend. Almost all women indicated they experienced two types of stress. For stress that was related to organizational and logistic aspects of monitoring stimulation, they felt SOET scored better. However, the application of a novel technique induced stress, which disappeared as follicles became more clearly visible on the screen as days went by.

Health-economic analysis

A health-economic analysis was performed, with the aim to establish whether the cost for society and for the patient is different between SOET and non-SOET. A total of 121 cycles were analysed (62 NS, 59 S). The two drop-out cycles were excluded. Two other patients, who started in the S arm but continued in the standard way, were analysed in the SOET group.

We summarized the most important findings in Table V.

An average of 3.0 sonograms was performed in non-SOET cycles by care providers versus 5.4 sonograms in SOET cycles ($P < 0.001$). All patients used their car as means of transportation. In the non-SOET group, an average of 530 km (min: 26 km; max 5520 km) was covered versus 146 km (min.: 0 km; max.: 900 km) in the SOET group ($P < 0.001$). With a cost of €0.3456€/km (Fedweb, 2013), average transportation cost was calculated at €183 per non-SOET cycle (min €9, max €1908) versus €51 per SOET cycle.

Based on an average cost of €280 per day absence from work, the average cost related to productivity loss was €423 per non-SOET attempt (min €0, max €2169) versus €96 per SOET attempt (min €0, max €837) ($P < 0.001$)

More time was spent by care providers, on average, on SOET than on non-SOET attempts. However, midwives found their time was better structured: they spent more time at the start of the stimulation but much less at each monitoring session.

When all costs were added the average total cost per SOET attempt is approximately half that of a non-SOET attempt: €455 (95% CI = €382–€529; min €199; max €1499) versus €894 (95% CI €729–

€1058; min €121, max €4428). The largest difference between groups lies with the loss of productivity and the transportation costs, favouring the home sonography.

Discussion

The monitoring of ovarian stimulation for ART using home sonography performed by the patient and her partner, compares favourably with the traditional follow-up method in which the patient has to present herself for each sonogram to a care provider. Patients and their partners were more satisfied; they felt empowered and experienced a higher sense of discretion. Active participation of the partner was higher and, overall, the couple experienced less stress. Total costs were approximately halved when using SOET, creating the possibility of a shift of the cost of transportation or productivity loss experienced by the employer towards a reasonable service cost for the patient.

Although the present study is a RCT and the results are statistically valid, the trial was finally underpowered. Technological improvements must still be made and tested with respect to both hard- and software. External validation in luminary sites is important. Not all patients are interested in using the system.

The low-end apparatus to be further developed for this application must not necessarily yield the same high-quality images as existing sonographic instruments; It should produce images that will allow the clinician to make the same clinical decisions as those made using the high-end devices.

Recent publications have reported attempts to automate follicular size measurements, based on 3D or volumetric measurements rather than on routinely used 2D measurements (Raine-Fenning *et al.*, 2007, 2008, 2009, 2010; Deutch *et al.*, 2009; Salama *et al.*, 2010; Ata and Tulandi, 2011; Ata *et al.*, 2011; Vandekerckhove *et al.*, 2013). In the future, the application of post-processing technology will further facilitate the analysis of patient-generated video sequences.

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Authors' roles

J.G.: conceiving the solution, creating the system, pre-study development, main investigator of the trial, recruitment and follow-up of patients, analysis and writing. A.D.: co-creator, recruitment and follow-up of patients, text reviewing. N.D.: co-creator, recruitment and follow-up of patients, text reviewing. F.V.: recruitment and follow-up of patients, text reviewing. B.M.: reproductive and study nurse, counselling, taking study interviews, communication with patients. M.B.: reproductive and study nurse, counselling, taking study interviews, communication with patients. J.N.: reproductive and study nurse, counselling, taking study interviews, communication with patients. E.D.: all statistical issues (study design, power calculation, analysis, text reviewing). D.D.B.: all statistical issues (study design, power calculation, analysis, text reviewing). L.P.: all health-economic issues (journal development, data, collection and calculation, text reviewing). L.A.: supervision of all health-economic issues (journal development, data, collection and calculation, text reviewing). W.V.: recruitment and follow-up of patients. P.D.S.: recruitment, text reviewing.

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Conflict of interest

None declared.

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