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Review

Intracytoplasmic morphologically selected sperm injection results in improved clinical outcomes in couples with previous ICSI failures or male factor infertility: a meta-analysis

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ABSTRACT

The objective of this study was to perform the first meta-analysis to compare conventional intracytoplasmic sperm injection (ICSI) outcomes and intracytoplasmic morphologically selected sperm injection (IMSI) outcomes in couples with previous ICSI failures (IF) or male factor infertility (MF). A systematic review was performed by searching Medline database to identify articles reporting on the comparison between ICSI and IMSI outcomes in couples with IF or MF. The main outcome measures were the implantation, pregnancy and miscarriage rates. Thirteen studies fulfilled our predetermined criteria. The overall results of meta-analysis for implantation (OR: 2.88; CI: 2.13–3.89), pregnancy (OR: 2.07; CI: 1.22–3.50) and miscarriage rates (OR: 0.31; CI: 0.14–0.67) were in favor of IMSI in couples with IF. Additionally, the overall result of meta-analysis for implantation (OR: 1.56; CI: 1.11–2.18) and pregnancy rate (OR: 1.61; CI: 1.17–2.23) were in favor of IMSI in couples with MF. IMSI increases the odds of implantation by 50% and pregnancy by 60% in couples with MF. In light of improved clinical outcomes, we recommend promoting the IMSI method in couples with MF. Moreover, IMSI results in a 3-fold increase in implantation rate, a 2-fold increase in pregnancy rate and a 70% decrease in miscarriage rate as compared to ICSI in couples with IF, however, as no randomized evidence exists, randomized studies are needed to confirm the IMSI benefits in couples with IF.

Contents

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Introduction

In the last decade a new approach involving real-time, high-magnification observation of unstained spermatozoa, named 'motile sperm organelle morphology examination' (MSOME), has been introduced [1]. The incorporation of this technique together with a micromanipulation system has allowed the introduction of a modified intracytoplasmic sperm injection (ICSI) procedure, known as intracytoplasmic morphologically selected sperm injection (IMSI). This system of real-time detailed morphological sperm examination at high magnification, ranging from ×6600 to ×13,000 with Nomarski optics, enables the selection of the best available motile spermatozoa before oocyte injection [2–5].

Several studies have investigated the benefits of IMSI by comparing the results obtained using this technique with those obtained via ICSI; however, the results are controversial [2–18]. Nevertheless, numerous publications have reported that IMSI is positively associated with implantation and/or pregnancy rates [2–5,7–12,16–18] in couples with previous and repeated implantation failures and in patients with male factor infertility.

Meta-analysis provides an overall consensus from studies, resulting in a more precise estimate than any of the individual articles. A meta-analysis, published in 2010, comparing ICSI vs. IMSI outcomes concluded that IMSI not only significantly improves the percentage of top-quality embryos, implantation and pregnancy rates, but also significantly reduces miscarriage rates as compared with ICSI [19]. However, this previous meta-analysis included a single randomized controlled trial and two non-randomized studies. Similarly, a more recent meta-analysis showed a very-low-quality evidence that IMSI improves clinical pregnancy [20]. These two meta-analyses did not take into account the indications for ICSI; therefore, their results cannot be generalized for all the couples undergoing ICSI. Therefore, the aim of this study was to perform the first meta-analysis to compare conventional intracytoplasmic sperm injection (ICSI) outcomes and intracytoplasmic morphologically selected sperm injection (IMSI) outcomes in couples with previous ICSI failures (IF) or male factor infertility (MF).

Materials and methods

Literature search

A computerized search in MEDLINE (from January 2001 until April 2013) was performed to identify articles reporting on the comparison between ICSI and IMSI outcomes. Keywords used were: "Intracytoplasmic morphologically selected sperm injection", "motile sperm organelle morphology examination" "IMSI", "MSOME" and "high magnification ICSI". The search was not restricted for articles written in English. References detected with the related articles function in Pubmed were also checked to identify cited articles not captured by electronic searches. The reference lists of eligible primary studies were examined for identification of additional articles.

Study selection and data extraction

Grey literature (abstracts, unpublished studies, conference proceedings, graduate theses, book chapters, company reports, and applications) was not included in this meta-analysis. Studies dealing with azoospermia and sperm DNA fragmentation and studies in which patients acted as their own controls were excluded from the subsequent analysis. No strict selection according to the experimental designs or language was applied. The main outcome measures were implantation, pregnancy and miscarriage rates. Studies were selected in a two-stage process (illustrated in Fig. 1). At the first screening, the titles and abstracts from the electronic searches were scrutinized by two reviewers independently (A.S. and D.B.). Studies with lack of any relevance were excluded and full manuscripts of all citations that were likely to meet the predefined selection criteria were obtained. Second, final inclusion or exclusion decisions were made on examination of full manuscripts by both reviewers.

Two independent investigators (A.S. and D.B.) extracted the data from all eligible trials. Discrepancies were resolved by the involvement of another investigator (R.F.). From each eligible trial we recorded for both arms the following data: demographic

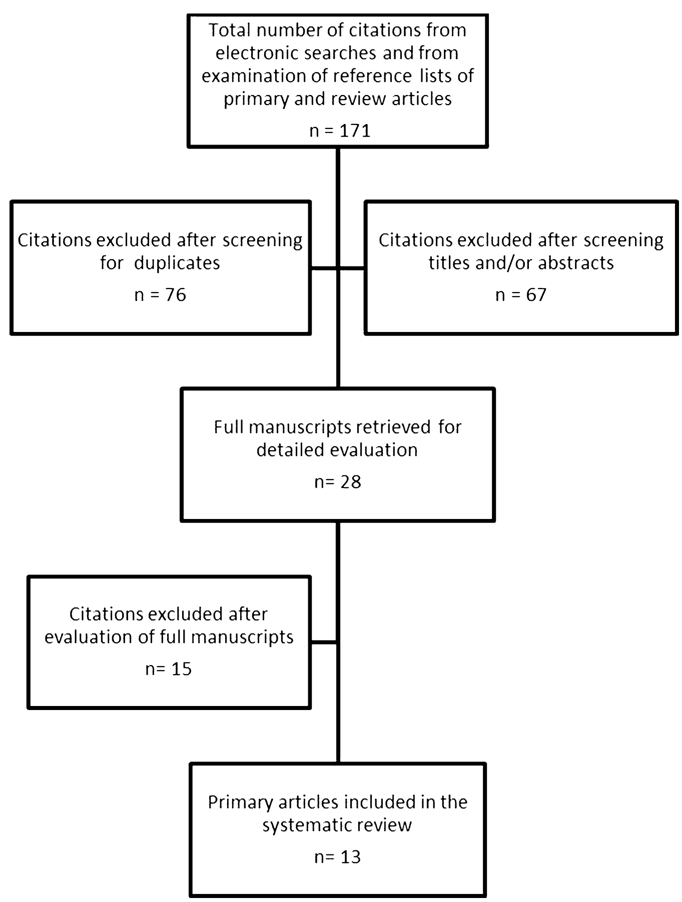


Fig. 1. Study selection process for systematic review.

(authors, type of study, country of origin, patients' mean age at enrollment and period of enrollment), procedural (number of patients included, inclusion and exclusion criteria for patients' populations) and outcome data (implantation, pregnancy and miscarriage rates).

The Newcastle–Ottawa Quality Assessment Scales for observational studies [21] were implemented. This instrument assesses the quality of nonrandomized studies in 3 broad categories (patient selection [4 criteria], comparability of study groups [1 criterion], and assessment of the outcome [3 criteria]). In this meta-analysis, following quality assessment standards of previous meta-analyses, studies that met 5 or more of the Newcastle–Ottawa Scale criteria were considered to be of higher quality.

Statistical analysis

From each study, outcome data were extracted in 2 × 2 tables by the two reviewers (A.S. and D.B.). The measure of heterogeneity (non-combinability) was evaluated by I^2. For a non-significant I^2 result a fixed model was used. For a significant I^2 result, a random model (DerSimonian and Laird) was used. The results were pulled using Mantel–Haenszel statistic model and are expressed as ORs with 95% confidence intervals (CIs). The meta-analysis was conducted using the RevMan 5.2 Software (Cochrane Collaboration, Oxford, UK).

Results

Literature identification and study characteristics

The process of literature identification and selection is summarized in Fig. 1. A total of 171 studies were initially retrieved from the literature. At first screening, after removing duplicates ($n = 76$) and excluding citations after screening titles and/or abstracts ($n = 67$), a total of 28 published studies, which compared IMSI and ICSI outcomes, were considered for inclusion [2–16,18,22–33]. After the second screening, out of the 28 studies, 13 fulfilled our predetermined criteria [2,5–8,10–12,14–16,22,33]. The included studies and their characteristics, as well as the results for the Newcastle–Ottawa quality assessment scales for non-randomized studies are listed in Table 1.

Data on ICSI outcomes

The 13 selected studies comprised 1715 IMSI cycles and 2750 ICSI cycles. The quality and the main characteristics of the included studies are presented in Table 1. The overall result of the meta-analysis is displayed in Fig. 2.

Couples with previous implantation failures

Out of the thirteen selected studies, six investigated couples with previous implantation failures [2,5,7,8,10,14]. The six studies comprised 440 IMSI cycles and 667 ICSI cycles.

Implantation rate

Four studies reported their implantation rates. A total of 181 gestational sacs resulted from 680 transferred embryos (26.6%) in IMSI cycles compared with 76 out of 635 in ICSI cycles (12.0%). The overall result of meta-analysis was in favor of IMSI and considered as statistically significant (OR: 2.88; CI: 2.13–3.89) (Fig. 2.1a).

Pregnancy rate

Six studies reported their pregnancy rates. In IMSI group, a total of 188 pregnancies were obtained out of 440 cycles (47.0%) and 189 out of 667 ICSI cycles (28.3%). The overall result of meta-analysis was in favor of IMSI and considered as statistically significant (OR: 2.07; CI: 1.22–3.50) (Fig. 2.1b).

Miscarriage rate

Four studies reported their miscarriage rates. In IMSI cycles, 15 miscarriages occurred out of 114 pregnancies (13.2%) compared with 19 out of 58 in ICSI cycles (32.8%). The overall result of meta-analysis was in favor of IMSI and considered as statistically significant (OR: 0.31; CI: 0.14–0.67) (Fig. 2.1c).

Couples with male factor infertility

Out of the thirteen selected studies, ten investigated couples with male factor infertility [6,7,10–12,14–16,22,33]. The ten studies comprised 1275 IMSI cycles and 2083 ICSI cycles.

Implantation rate

Seven studies reported their implantation rates. A total of 417 gestational sacs resulted from 1908 transferred embryos (21.9%) in IMSI cycles compared with 314 out of 1838 in ICSI cycles (17.1%). The overall result of meta-analysis was in favor of IMSI and considered as statistically significant (OR: 1.56; CI: 1.11–2.18) (Fig. 2.2a).

Pregnancy rate

Nine studies reported their pregnancy rates. In IMSI group, a total of 534 pregnancies were obtained out of 1234 cycles (43.3%) and 782 out of 2029 ICSI cycles (38.5%). The overall result of meta-analysis was in favor of IMSI and considered as statistically significant (OR: 1.61; CI: 1.17–2.23) (Fig. 2.2b).

Miscarriage rate

Six studies reported their miscarriage rates. In IMSI cycles, 53 miscarriages occurred out of 369 pregnancies (14.4%) compared with 50 out of 289 in ICSI cycles (17.3%). No significant difference was observed between the IMSI and ICSI groups (OR: 0.86; CI: 0.56–1.32) (Fig. 2.2c).

Comment

This is the first meta-analysis that draws together the reports of the ICSI × IMSI outcomes, addressing couples with IF or MF. Out of 28 relevant studies identified in the current literature, 13 studies met the eligibility criteria and were identified as suitable for this meta-analysis. The overall results of our meta-analysis for implantation, pregnancy and miscarriage rates were in favor of IMSI in couples with IF. Additionally, the overall result of our meta-analysis for implantation and pregnancy rate was in favor of IMSI in couples with MF.

It is now well established that the sperm is necessary not only for the key events of fertilization, such as the activation of oocyte, but also for embryonic development from the initial cleavages to the activation of the embryonic genome. It has been demonstrated that spermatozoa have an early and a late paternal effect on embryonic development [34]. The early paternal effect can influence fertilization and early stages of embryo development and is the consequence of sperm cytoplasmic content. The late

Table 1
Characteristics and quality of the included studies comparing ICSI and IMSI outcomes.

References	Design	ICSI cycles	IMSI cycles	Indication	Inclusion criteria	Methods	Implantation rate (%)	Pregnancy rate (%)	Miscarriage rate (%)	Newcastle–Ottawa scale S, C, O
[33]	Randomized study	39	38	Unselected infertile population and a subpopulation with MF	Unselected infertile population	Couples were randomized to ICSI and IMSI groups	ICSI: 15.2 IMSI: 29.6[c]	X	X	X
[1]	Comparative study	50	50	IF	Female age ≤37 years, >3 retrieved ova, male infertility, previous failure of ≥2 ICSI cycles	The IMSI outcomes were matched with ICSI outcomes from similar couples	ICSI: 9.5 IMSI: 27.9[c]	ICSI: 30.0 IMSI: 66.0[c]	ICSI: 33.0 IMSI: 9.0[c]	2,1,3
[4]	Comparative study	80	80	IF	Female age ≤37 years, >3 retrieved ova, male infertility, previous failure of ≥2 ICSI cycles	The IMSI outcomes were matched with ICSI outcomes from similar couples	ICSI: 9.4 IMSI: 31.3[c]	ICSI: 25.0 IMSI: 60.0[c]	ICSI: 14.0 IMSI: 40.0[c]	2,1,3
[22]	Randomized study	219	227	MF	Female age ≤35 years, severe oligoasthenoteratozoo spermia	Couples were randomized to ICSI and IMSI groups	ICSI: 11.3 IMSI: 17.3[c]	ICSI: 26.5 IMSI: 39.2[c]	ICSI: 24.1 IMSI: 16.9[a]	X
[8]	Cohort study	30	30	IF	Female age <38 years, previous failure of ≥2 ICSI cycles	The IMSI outcomes were matched with ICSI outcomes from similar couples	ICSI: 29.7 IMSI: 44.8[c]	ICSI: 50.0 IMSI: 63.0[a]	ICSI: 26.6 IMSI: 15.7[a]	2,1,2
[12]	Randomized study	37	20	MF	Poor semen quality and all arrested embryos following a prolonged 5-day culture in previous ICSI cycles	Couples were randomized into ICSI and IMSI groups	ICSI: 6.8 IMSI: 17.1[a]	ICSI: 8.1 IMSI: 25.0[a]	X	X
[14]	Comparative study	55	63	IF	Female age ≤39 years, ≥4 retrieved ova in previous cycles, previous failure of ≥2 ICSI cycles with good quality embryos	Couples were divided into ICSI and IMSI groups and the outcomes were compared	ICSI: 9.8 IMSI: 13.6[a]	ICSI: 19.0 IMSI: 26.0[a]	ICSI: 31.6 IMSI: 15.4[a]	3,1,2
	Comparative study	45	37	IF and a subpopulation with MF	Female age ≤39 years, ≥4 retrieved ova in previous cycles, patients with male factor with ≥2 ICSI attempts	Couples were divided into ICSI and IMSI groups and the outcomes were compared	ICSI: 11.2 IMSI: 11.8[a]	ICSI: 24.4 IMSI: 32.4[a]	ICSI: 36.4 IMSI: 16.7[a]	
References	Design	ICSI cycles	IMSI cycles	Indication	Inclusion criteria	Methods	Implantation rate (%)	Pregnancy rate (%)	Miscarriage rate (%)	Newcastle–Ottawa scale S, C, O
[15]	Randomized study	250	250	MF	Isolated male factor infertility, ≥6 oocytes available on retrieval	Couples were randomized into ICSI and IMSI groups	ICSI: 25.4 IMSI: 23.8[a]	ICSI: 36.8 IMSI: 37.2[a]	ICSI: 17.9 IMSI: 18.4[a]	X
[16]	Randomized study	125	125	MF	Sperm concentration between 1×10^6/ml and 20×10^6/ml	Patients were randomized to ICSI or IMSI techniques and outcomes were compared	ICSI: 14.8 IMSI: 24.2[c]	ICSI: 40.0 IMSI: 65.6[c]	X	X
[11]	Randomized study	70	52	MF	Isolated teratozoospermia, ≥6 mature oocytes available on retrieval	Patients were randomized to ICSI or IMSI techniques and outcomes were compared	ICSI: 29.0 IMSI:16.5[c]	ICSI: 24.0 IMSI: 48.0[c]	ICSI: 11.8 IMSI: 20.0[a]	X
[6]	Randomized study	139	125	MF	Female age <38 years, at least 2 and no more than 20 mature oocytes. Cycles with fresh ejaculated spermatozoa with concentration ≥0.1 million/ml were included	The oocytes were split into ICSI (n = 1548) and IMSI groups (n = 1557) and the fertilization and percentage of high-quality embryos were compared between the groups	ICSI: 32.2 IMSI: 30.3[a]	ICSI: 36.7 IMSI: 34.4[a]	ICSI: 2.0 IMSI: 7.0[a]	X

Table 1 (*Continued*)

References	Design	ICSI cycles	IMSI cycles	Indication	Inclusion criteria	Methods	Implantation rate (%)	Pregnancy rate (%)	Miscarriage rate (%)	Newcastle–Ottawa scale S, C, O
[7]	Prospective non-randomized study	130	90	IF	Couples with mild male factor who had at least two implantation failures after transfers of good-quality embryos	Couples were divided into ICSI and IMSI groups and the outcomes were compared	ICSI: 28.8 IMSI: 34.4[a]	ICSI: 26.0 IMSI: 24.0[a]	X	4,1,3
		126	132	MF	Patients with severe teratozoospermia at their first or second attempt	Couples were divided into ICSI and IMSI groups and the outcomes were compared	ICSI: 20.1 IMSI: 30.7[c]	ICSI: 26.0 IMSI: 46.0[c]	X	
References	Design	ICSI cycles	IMSI cycles	Indication	Inclusion criteria	Methods	Implantation rate (%)	Pregnancy rate (%)	Miscarriage rate (%)	Newcastle–Ottawa scale S, C, O
[10]	Cohort study	322	127	IF	Failed fertilization or less than 20% fertilization rate in a previous IVF treatment, total motile count <1.5 million after sperm wash and preparation or normal morphology of <2% and>90% head defects (WHO 2010 criteria) or <5% and >90% head defects	Couples were divided into ICSI and IMSI groups and the outcomes were compared	X	ICSI: 38.0 IMSI: 56.0[c]	X	4,1,3
		1033	269	MF	Failed fertilization or less than 20% fertilization rate in a previous IVF treatment, total motile count <1.5 million after sperm wash and preparation or normal morphology of <2% and>90% head defects or <5% and >90% head defects	Couples were divided into ICSI and IMSI groups and the outcomes were compared	X	ICSI: 46.0 IMSI: 47.0[a]	X	

Note: IF—implantation failure; MF—male factor.

[a] Not significantly different from ICSI.

[b]Not applicable.

[c] Significantly different from ICSI.

X—not evaluated; S—selection; C—comparability; O—outcome.

paternal effect reflects DNA contents and can impair embryo development from day 3 to day 5. Several DNA abnormalities have been associated with the occurrence of sperm nuclear vacuoles. Consequently, it may be suggested that the improvements in clinical outcomes after IMSI compared with ICSI is explained by an optimal selection of spermatozoa free of vacuoles having the best chances to produce a viable blastocyst with higher implantation potential. In fact, Delaroche et al. [35] recently observed that the number of extended embryo culture cycles and the mean number of blastocysts obtained were higher in IMSI cycles than in ICSI cycles. In a recent study investigating the effects of sperm vacuoles in early and late outcomes, Greco et al. [36] observed that statistically significant differences were detected in the "late" outcomes, such as pregnancy, implantation, and live birth rates. The use of IMSI has also been associated with decreased likelihood of malformations in offspring [37,38].

The first meta-analysis on ICSI × IMSI outcomes was published in 2010, and concluded that IMSI not only significantly improves the percentage of top-quality embryos, implantation and pregnancy rates, but also significantly reduces miscarriage rates as compared with ICSI [19]. However, only 3 studies (one randomized and two nonrandomized studies) that fitted the predetermined criteria were available at the time. More recently, a new meta-analysis showed that the evidence that IMSI improves clinical pregnancy is of very low quality [20]. Moreover, no evidence of effect on live birth or miscarriage was observed. The authors suggested that further trials are necessary to improve the evidence quality before recommending IMSI in clinical practice. One could argue why this previous meta-analysis and ours have such different results and recommendations, given that only randomized clinical trials were included in Teixeira's study and therefore our grounds are less solid. The meta-analysis of Teixeira et al. did not take into account the indications for ICSI; therefore, their results cannot be generalized for all the couples undergoing ICSI which might explain the discrepancies in the findings and conclusions.

A weakness of this meta-analysis is related to the lack of consensus among the included studies regarding the number of previous ICSI attempts and the definition of male factor, which could have introduced a bias. In addition, prior failures in ICSI cycles constituted an inclusion criterion in several studies employing IMSI. Additionally, the implantation rate may be underestimated because it was not calculate per patient but per transferred embryos.

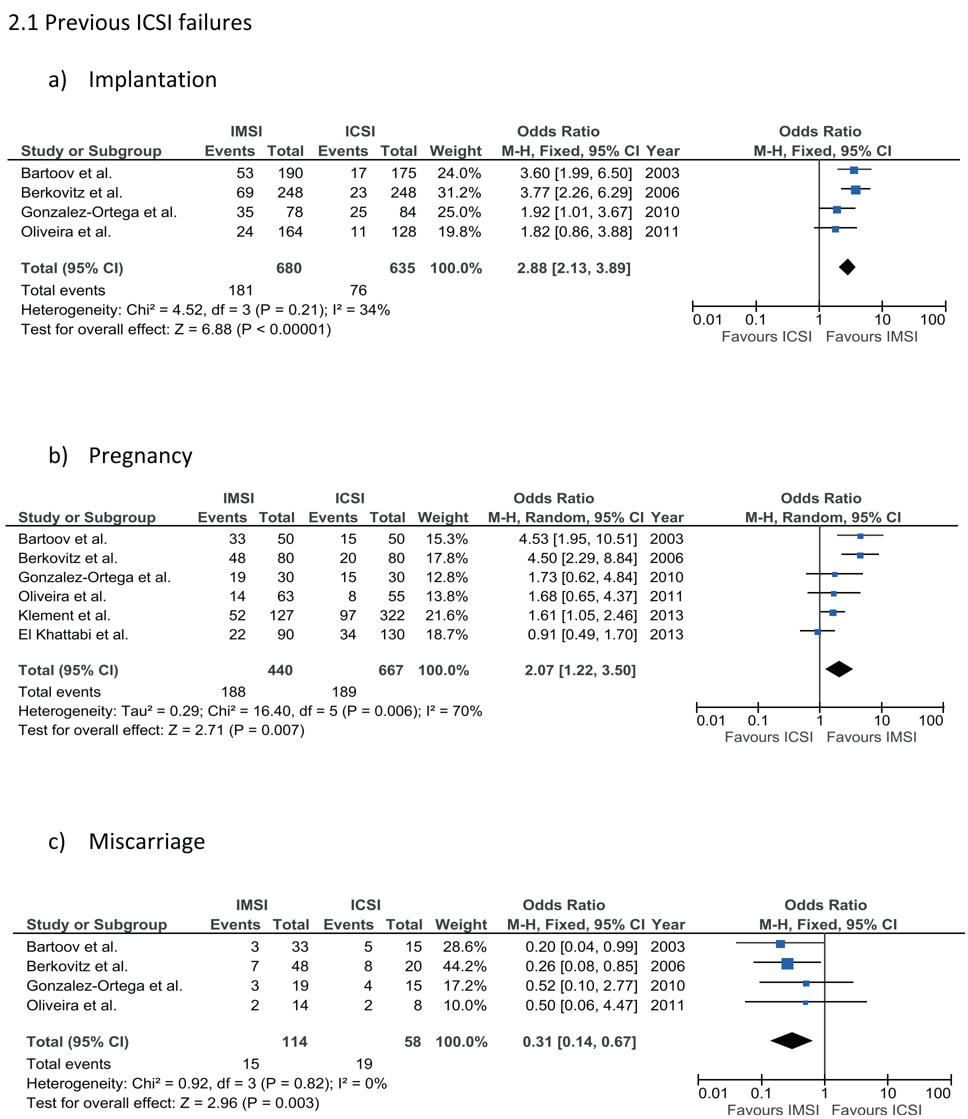


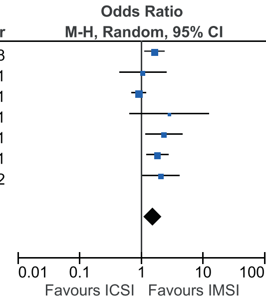
Fig. 2. Meta-analysis. Results are expressed as odds ratios (OR) with 95% of confidence intervals (CI). Fixed and random models assume homogenous and heterogeneous studies, respectively.

2.2 Male factor

a) Implantation rate

Study or Subgroup	IMSI Events	IMSI Total	ICSI Events	ICSI Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Antinori et al.	97	560	59	521	19.9%	1.64 [1.16, 2.32]	2008
Oliveira et al.	11	93	13	116	9.6%	1.06 [0.45, 2.50]	2011
Setti et al.	158	664	156	613	22.0%	0.91 [0.71, 1.18]	2011
Knez et al.	6	35	3	44	4.4%	2.83 [0.65, 12.24]	2011
Balaban et al.	32	108	16	105	12.6%	2.34 [1.19, 4.59]	2011
Wilding et al.	86	355	48	324	18.8%	1.84 [1.24, 2.72]	2011
Knez et al.	27	93	19	115	12.7%	2.07 [1.06, 4.02]	2012
Total (95% CI)		**1908**		**1838**	**100.0%**	**1.56 [1.11, 2.18]**	
Total events	417		314				

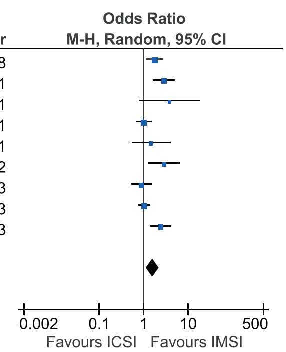
Heterogeneity: Tau² = 0.12; Chi² = 17.98, df = 6 (P = 0.006); I² = 67%
Test for overall effect: Z = 2.58 (P = 0.010)



b) Pregnancy rate

Study or Subgroup	IMSI Events	IMSI Total	ICSI Events	ICSI Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Antinori et al.	89	227	58	219	14.0%	1.79 [1.20, 2.67]	2008
Wilding et al.	80	122	44	110	12.0%	2.86 [1.68, 4.87]	2011
Knez et al.	5	20	3	37	3.5%	3.78 [0.80, 17.89]	2011
Setti et al.	93	250	92	250	14.5%	1.02 [0.71, 1.46]	2011
Oliveira et al.	12	37	11	45	6.9%	1.48 [0.56, 3.90]	2011
Knez et al.	25	52	17	70	8.8%	2.89 [1.34, 6.24]	2012
De Vos et al.	43	125	51	139	12.4%	0.90 [0.55, 1.50]	2013
Klement et al.	126	269	473	1033	15.8%	1.04 [0.80, 1.37]	2013
El Khattabi et al.	61	132	33	126	12.1%	2.42 [1.43, 4.09]	2013
Total (95% CI)		**1234**		**2029**	**100.0%**	**1.61 [1.17, 2.23]**	
Total events	534		782				

Heterogeneity: Tau² = 0.15; Chi² = 27.87, df = 8 (P = 0.0005); I² = 71%
Test for overall effect: Z = 2.90 (P = 0.004)



c) Miscarriage rate

Study or Subgroup	IMSI Events	IMSI Total	ICSI Events	ICSI Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Antinori et al.	15	89	14	58	31.2%	0.64 [0.28, 1.44]	2008
Wilding et al.	1	80	0	44	1.4%	1.68 [0.07, 42.09]	2011
Knez et al.	1	5	2	3	4.4%	0.13 [0.00, 3.22]	2011
Setti et al.	29	158	28	156	51.0%	1.03 [0.58, 1.82]	2011
Oliveira et al.	2	12	4	11	7.7%	0.35 [0.05, 2.47]	2011
Knez et al.	5	25	2	17	4.2%	1.88 [0.32, 11.02]	2012
Total (95% CI)		**369**		**289**	**100.0%**	**0.86 [0.56, 1.32]**	
Total events	53		50				

Heterogeneity: Chi² = 3.96, df = 5 (P = 0.55); I² = 0%
Test for overall effect: Z = 0.70 (P = 0.48)

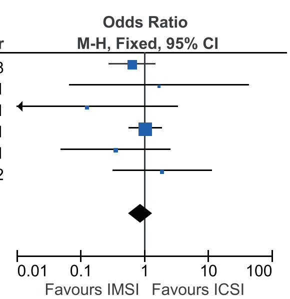


Fig. 2. (*Continued*).

Six studies included in the present meta-analysis were non-randomized. All the randomized studies evaluated couples with MF, thus, the results obtained for couples with IF are based on solely non-randomized studies. It is important to highlight that the results for the IF group are based on nonrandomized studies only, hence a low quality evidence has been observed. Conversely, in a recent review of IMSI indications, Boitrelle et al. [39] concluded that the only confirmed indication for IMSI is recurrent implantation failure following ICSI and that all other potential indications require further investigation.

In this study, we could have tried to minimize the heterogeneity by limiting the meta-analysis to a small more homogeneous group of studies. However, this limits the scope of the meta-analysis and essentially throws away useful information [40]. Moreover, it has been suggested that heterogeneity improves the generalizability of the results of the meta-analysis [41,42]. Therefore, it was decided to maintain all the included studies and use, whenever appropriate, the random effect model developed by DerSimonian and Laird [43], which incorporates the heterogeneity in the analysis of the overall result.

The IMSI method itself has its drawbacks; it is important to emphasize that switching between the glass-bottomed dish that is appropriate for Nomarski microscopy and the plastic-bottomed dish that works with Hoffman modulation contrast requires additional time, delaying the injection procedure. In addition, high magnification requires the use of an appropriate video camera and software system, an aspect that make MSOME and IMSI very expensive approaches. Having said that, the extra time necessary for sperm selection and the elevated equipment costs are a limitation to a more widespread use of IMSI [44].

Based on our results we conclude that IMSI increases the odds of implantation by 50% and pregnancy by 60% in couples with MF. In light of improved clinical outcomes, we recommend promoting the IMSI method in couples with MF. Moreover, IMSI results in a 3-fold increase in implantation rate, a 2-fold increase in pregnancy rate and a 70% decrease in miscarriage rate as compared to ICSI in couples with IF, however, as no randomized evidence exists, randomized studies are needed to confirm the IMSI benefits in couples with IF.

Condensation

IMSI increases the odds of implantation by 50% and pregnancy by 60% in couples with MF, and results in a 3-fold increase in implantation rate, a 2-fold increase in pregnancy rate and a 70% decrease in miscarriage rate as compared to ICSI in couples with IF.

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