Supplementary

Table S1 The PICOS design structure for literature search strategy

Population
The males with high SDF in the ejaculate semen
Intervention
Testi-ICSI *vs.* Ejac-ICSI
Comparison
Primary pregnancy outcomes between Testi-ICSI and Ejac-ICSI among couples with high SDF in the ejaculate semen, and SDF level between the ejaculate semen and testicular sperm in above couples if provided available data
Outcomes
SDF level between the ejaculate semen and testicular sperm, primary pregnancy outcomes including live birth rate (per cycle), fertilization rate, clinical pregnancy rate, miscarriage rate and live birth rate, SDF level between the ejaculate semen and testicular sperm
Study
RCT and prospective or retrospective non-randomized observational studies that enrolled human participants

PICOS, Population, Intervention, Comparison, Outcomes, Study; SDF, sperm DNA fragmentation; Testi-ICSI, intracytoplasmic sperm injection with testicular sperm; Ejac-ICSI, intracytoplasmic sperm injection with ejaculated sperm; RCT, randomized controlled trial.

Table S2 Quality assessment of all included studies*

Study	The criteria for nonrandomized studies							
	Pre-intervention		At intervention	Post-intervention				Overall bias
	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurements of outcomes	Bias in selection of reported results	Risk of bias judgment
Prospective observational cohort								
Moskovtsev 2010	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Moskovtsev 2012	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Esteves 2015	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Arafa 2017	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Retrospective cohort								
Lewis 2004	Moderate risk	Serious risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	Serious risk
Greco 2005	Moderate risk	Serious risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Serious risk
Bradley 2016	Moderate risk	Moderate risk	Moderate risk	Low risk	Low risk*	Moderate risk	Low risk	Moderate risk
Pabuccu 2016	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zhang 2019	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Herrero 2019	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Alharbi 2020	Moderate risk	low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate risk

*, the ROBINS-I tool was used to rate risk of bias for all non-randomised included studies. ROBINS-I, Risk Of Bias In Non-randomized Studies of Interventions.

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Table S3 Sensitivity analysis for the effect of removal of individual studies on the mean SDF rates in testicular and ejaculated sperm

Included studies	Excluded study	Mean difference (95% CI)	I^2
All	None	–25.81 (–34.82, –16.81)	94%
Greco *et al.*, 2005	Esteves *et al.*, 2015	–21.83 (–27.28, –16.37)	43%
Moskovtsev *et al.*, 2010			
Moskovtsev *et al.*, 2012			
Esteves *et al.*, 2015	Greco *et al.*, 2005	–30.50 (–34.76, –26.25)	27%
Moskovtsev *et al.*, 2010			
Moskovtsev *et al.*, 2012			
Esteves *et al.*, 2015	Moskovtsev *et al.*, 2010	–25.65 (–36.45, –14.84)	96%
Greco *et al.*, 2005			
Moskovtsev *et al.*, 2012			
Esteves *et al.*, 2015	Moskovtsev *et al.*, 2012	–25.85 (–36.41, –15.29)	96%
Greco *et al.*, 2005			
Moskovtsev *et al.*, 2010			

SDF, sperm DNA fragmentation; CI, confidence interval.

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Table S4 Sensitivity analysis for the effect of removal of individual studies on fertilization rates

Included studies	Excluded study	Odds ratio (95% CI)	I^2
All	None	0.87 (0.61, 1.12)	81%
Arafa *et al.*, 2018	Alharbi *et al.*, 2020	0.86 (0.63, 1.18)	83%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Pabuccu *et al.*, 2017			
Alharbi *et al.*, 2020	Arafa *et al.*, 2018	0.83 (0.62, 1.10)	80%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Pabuccu *et al.*, 2017			
Alharbi *et al.*, 2020	Bradley *et al.*, 2016	0.93 (0.68, 1.27)	82%
Arafa *et al.*, 2018			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Pabuccu *et al.*, 2017			
Alharbi *et al.*, 2020	Esteves *et al.*, 2015	0.95 (0.75, 1.20)	68%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Greco *et al.*, 2005			
Pabuccu *et al.*, 2017			
Alharbi *et al.*, 2020	Greco *et al.*, 2005	0.82 (0.63, 1.28)	82%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Pabuccu *et al.*, 2017			
Alharbi *et al.*, 2020	Pabuccu *et al.*, 2017	0.82 (0.63, 1.09)	82%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			

CI, confidence interval.

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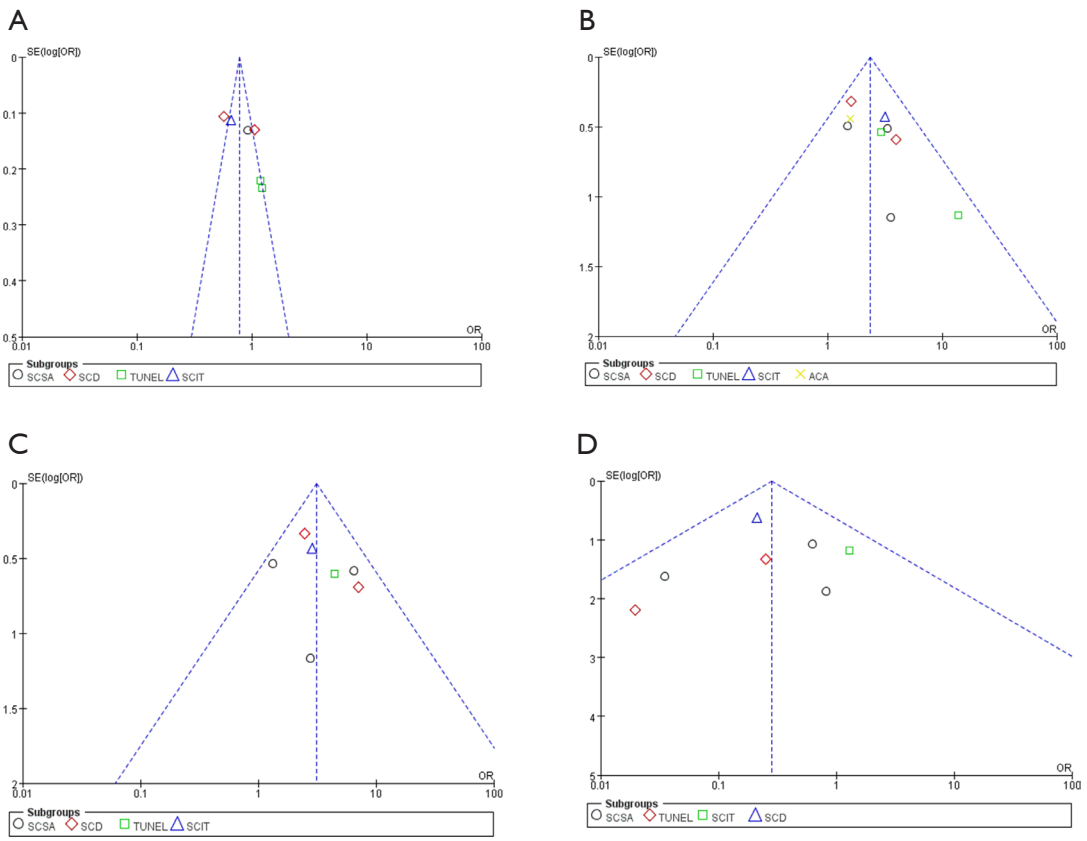

Figure S1 Funnel plots were constructed for Publication bias: (A) fertilization rates; (B) clinical pregnancy rates; (C) live birth rates; (D) miscarriage rates. SCSA, sperm chromatin structure assay; SCD, sperm chromatin dispersion; TUNEL, terminal deoxynucleotidyl transferase dUTP nick end labelling; SCIT, sperm chromatin integrity test; ACA, alkaline comet assay; OR, odds ratio; SE, standard error.

Table S5 Sensitivity analysis for the effect of removal of individual studies on clinical pregnancy rates

Included studies	Excluded study	Odds ratio (95% CI)	I^2
All	None	2.36 (1.71, 3.24)	0%
Arafa *et al.*, 2018	Alharbi *et al.*, 2020	2.49 (1.77, 3.49)	0%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Lewis *et al.*, 2004			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			

Table S5 (*continued*)

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Table S5 (*continued*)

Included studies	Excluded study	Odds ratio (95% CI)	I^2
Alharbi *et al.*, 2020	Arafa *et al.*, 2018	2.25 (1.62, 3.14)	0%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Lewis *et al.*, 2004			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Bradley *et al.*, 2016	2.24 (1.58, 3.16)	0%
Arafa *et al.*, 2018			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Lewis *et al.*, 2004			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Esteves *et al.*, 2015	2.70 (1.86, 3.93)	0%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Lewis *et al.*, 2004			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Greco *et al.*, 2005	2.31 (1.65, 3.23)	4%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Herrero *et al.*, 2019			
Lewis *et al.*, 2004			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			

Table S5 (*continued*)

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Table S5 (*continued*)

Included studies	Excluded study	Odds ratio (95% CI)	I^2
Alharbi *et al.*, 2020	Herrero *et al.*, 2019	2.33 (1.69, 3.22)	5%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Lewis *et al.*, 2004			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Lewis *et al.*, 2004	2.51 (1.78, 3.54)	0%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Pabuccu *et al.*, 2017	2.23 (1.61, 3.09)	0%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Lewis *et al.*, 2004			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Zhang *et al.*, 2019	2.26 (1.62, 3.17)	0%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Lewis *et al.*, 2004			
Pabuccu *et al.*, 2017			

CI, confidence interval.

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Table S6 Sensitivity analysis for the effect of removal of individual studies on live birth rates

Included studies	Excluded study	Odds ratio (95% CI)	I^2
All	None	3.10 (2.13, 4.51)	4%
Arafa *et al.*, 2018	Alharbi *et al.*, 2020	3.50 (2.33, 5.25)	0%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Arafa *et al.*, 2018	2.86 (1.93, 4.24)	0%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Bradley *et al.*, 2016	3.16 (2.08, 4.80)	20%
Arafa *et al.*, 2018			
Esteves *et al.*, 2015			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Esteves *et al.*, 2015	3.45 (2.18, 5.48)	12%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Herrero *et al.*, 2019	3.11 (2.12, 4.55)	20%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			

Table S6 (*continued*)

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Table S6 (*continued*)

Included studies	Excluded study	Odds ratio (95% CI)	I^2
Alharbi *et al.*, 2020	Pabuccu *et al.*, 2017	2.98 (2.00, 4.43)	14%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Herrero *et al.*, 2019			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Zhang *et al.*, 2019	2.78 (1.86, 4.15)	0%
Arafa *et al.*, 2018			
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			

CI, confidence interval.

Table S7 Sensitivity analysis for the effect of removal of individual studies on miscarriage rates

Included studies	Excluded study	Odds ratio (95% CI)	I^2
All	None	0.28 (0.13, 0.60)	0%
Bradley *et al.*, 2016	Alharbi *et al.*, 2020	0.25 (0.11, 0.57)	4%
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Bradley *et al.*, 2016	0.22 (0.09, 0.52)	0%
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Esteves *et al.*, 2015	0.34 (0.13, 0.91)	9%
Bradley *et al.*, 2016			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			

Table S7 (*continued*)

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Table S7 (*continued*)

Included studies	Excluded study	Odds ratio (95% CI)	I^2
Alharbi *et al.*, 2020	Greco *et al.*, 2005	0.31 (0.14, 0.68)	0%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Herrero *et al.*, 2019	0.27 (0.12, 0.59)	9%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Pabuccu *et al.*, 2017			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Pabuccu *et al.*, 2017	0.28 (0.13, 0.63)	14%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Zhang *et al.*, 2019			
Alharbi *et al.*, 2020	Zhang *et al.*, 2019	0.33 (0.15, 0.93)	0%
Bradley *et al.*, 2016			
Esteves *et al.*, 2015			
Greco *et al.*, 2005			
Herrero *et al.*, 2019			
Pabuccu *et al.*, 2017			

CI, confidence interval.

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Table S8 Certainty of evidence and summary effect estimates assessed by GRADE frame of the study outcomes*

Outcomes	Summary of findings		Quality assessment					Certainty of evidence#
	No. studies	OR (95% CI)	Study design*	Inconsistency†	Indirectness‡	Imprecision‖	Other consideration	
SDF	4	25.8 (16.81, 34.82)	Serious	Serious	Serious	Serious	Large effect size (OR >2)	⊕○○○ (very low)
FR	6	0.87 (0.67, 1.12)	Not serious	Serious	Serious	Serious	None	⊕○○○ (very low)
CPR	8	2.36 (1.71, 3.24)	Serious	Not serious	Serious	Not serious	Large effect size (OR >2)	⊕⊕○○ (low)
LBR	6	3.10 (2.13, 4.51)	Serious	Not serious	Serious	Not serious	Large effect size (OR >2)	⊕⊕○○ (low)
MR	6	0.28 (0.13, 0.60)	Serious	Not serious	Serious	Not serious	None	⊕⊕○○ (low)

*, downgraded by one level if >25% of participants in this comparison were from studies at high risk of bias; †, downgraded by one level if heterogeneity (I^2) >50%; ‡, downgraded by one level if >25% of included studies were monocenter-based; ‖, downgraded by one level if the limits of the 95% CI for risk estimates are wide or cross a minimally important difference of 10% for outcomes (RR: 0.9–1.1); #, high quality: very confident that the true effect lies close to that of the estimate of the effect; moderate quality: moderately confident in the effect estimate, and the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; low quality: confidence in the effect estimate is limited, and the true effect could be substantially different from the estimate of the effect; very low quality: very little confidence in the effect estimate, and the true effect is likely to be substantially different from the estimate of effect. GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; OR, odds ratio; CI, confidence interval; SDF, sperm DNA fragmentation; FR, fertilization rate; CPR, clinical pregnancy rate; LBR, live birth rate; MR, miscarriage rate; RR, relative risk.

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