

CUMULATIVE IMPLANTATION AND LIVE BIRTH AFTER RECURRENT IMPLANTATION FAILURE: OUTCOMES OF SIX CONSECUTIVE SINGLE EUPLOID EMBRYO TRANSFERS IN A COHORT OF 20,536 PATIENTS

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BACKGROUND: Recurrent implantation failure (RIF), or repeated failed sustained implantation (SI), occurs in fewer than 5% of patients undergoing in vitro fertilization (1). Recent studies report cumulative SI (cSI) of 95.2% and cumulative live birth (cLB) of 92.6% and 98.1% after 3 and 5 single euploid embryo transfers (SEETs), respectively (2,3). Still, whether there is a threshold number of SEET cycles beyond which the likelihood of SI or LB declines remains unclear.

OBJECTIVE: This study evaluates clinical outcomes and predictors of SI in patients undergoing up to 6 consecutive SEETs.

MATERIALS AND METHODS: This multi-center retrospective study included patients who underwent up to 6 consecutive SEETs from 2014-2024. Patients had satisfactory uterine cavity evaluation prior to SEET. Exclusion criteria were uterine factor, uterine anomalies, and gestational carrier use. Primary outcomes were SI (intrauterine gestation with cardiac activity at 7 weeks) and cSI (proportion of SEETs resulting in SI across all transfer attempts). SI was selected as the primary outcome to align with prior literature (1). Secondary outcomes included positive hCG, LB, and cLB. Generalized linear mixed-effects Poisson regression and Cox proportional hazards models were used to evaluate outcomes across SEETs, adjusting for age, BMI, endometrial thickness (EMT), and clinical site. Adjusted relative risks (RR), hazard ratios (HR), and 95% CI were calculated. Survival curves were generated for cSI and cLB.

RESULTS: The study included 28,165 SEET cycles from 20,536 patients, with 20,536 cycles comprising the 1st SEET. Subsequent SEETs after initial SI failure included: 2nd (n=5,463 cycles), 3rd (n=1,562), 4th (n=452), 5th (n=120), and 6th (n=32). SI declined across successive SEETs: 56.8% (1st), 48.7% (2nd), 41.6% (3rd), 41.6% (4th), 35.0% (5th), and 28.1% (6th). Age-adjusted RRs for SI similarly declined: 2nd SEET RR 0.87 [0.83–0.90]; 3rd RR 0.74 [0.69–0.81]; 4th RR 0.74 [0.64–0.86]; 5th RR 0.64 [0.47–0.87]; and 6th RR 0.52 [0.27–1.0]. Still, cSI reached 98.7% [97.8–99.2%] after 6 SEETs. Positive hCG from 1 to 6 SEETs were: 74.7%, 68.9%, 62.8%, 60.8%, 55.8%, and 50.0%. Corresponding LB were: 52.5%, 44.8%, 38.7%, 37.3%, 30.4%, and 25.0%. While age-adjusted LB per cycle declined similarly to SI, cLB reached 97.8% [96.5–98.7%] by the 6th SEET. In evaluating predictors of SI, patients in age groups 35-37, 38-40, 41-42, and >42 had reduced likelihood of SI compared to those <35 (HR 0.93 [0.89-0.96], HR 0.86 [0.82-0.89], HR 0.8 [0.75-0.85], and 0.73 [0.68-0.78], respectively), even in this

cohort limited to SEETs. Despite this, by the 6th SEET, cSI remained high in all age groups, reaching 96% in patients >42 years, and ET remained nonfutile, with a 25% LB in the cohort undergoing a 6th SEET (n=32).

CONCLUSIONS: While probability of SI and LB decline with each successive SEET, cumulative outcomes demonstrated that 98.7% of patients achieved SI by the 6th transfer. Accordingly, the study observed a cumulative RIF rate of 1.3% after 6 SEETs. Patients who experience RIF should be advised to continue treatment up to 6 SEETs, as SI and LB demonstrate very high cumulative success rates.

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References:

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