

Risk factors for monozygotic twinning in IVF: a multicenter, cohort study

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Disclosures

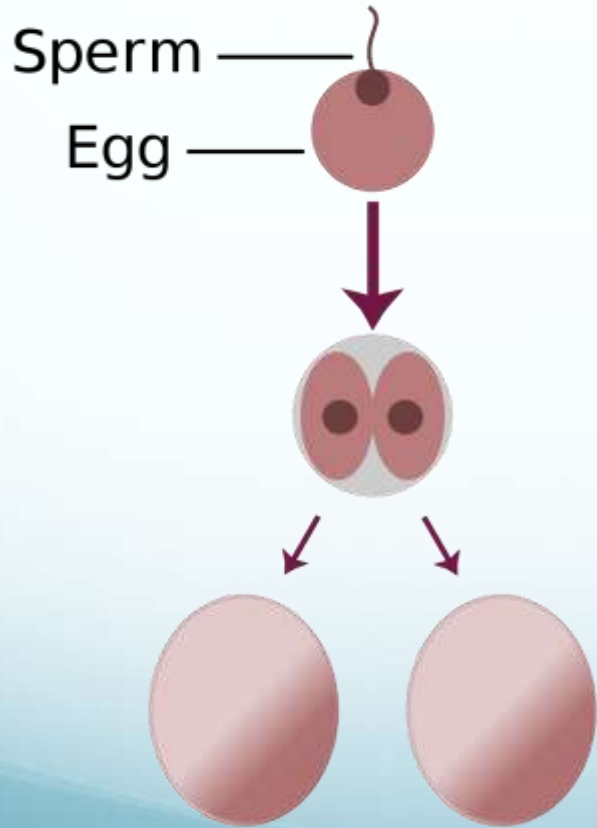
- Nothing to disclose

Objectives

- Background on monozygotic twinning (MZT)
- Preliminary results
- Future study plans
- Questions

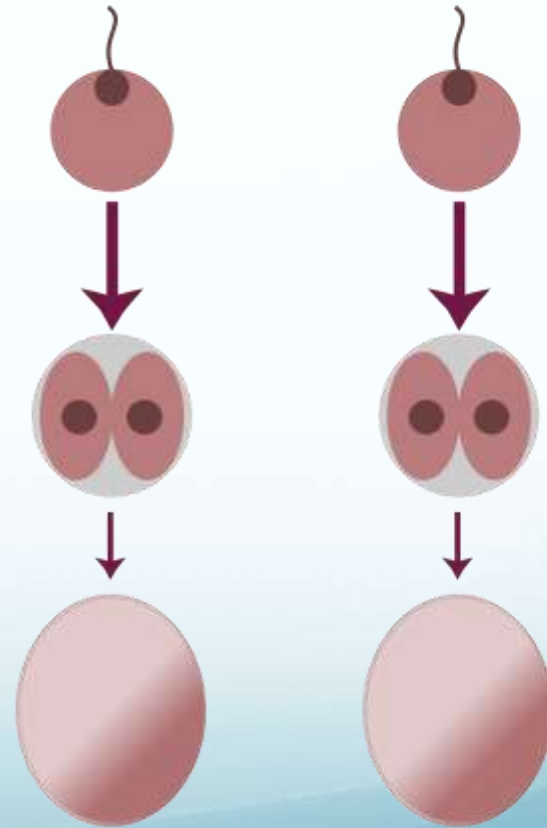
Background

Identical
(Monozygotic)



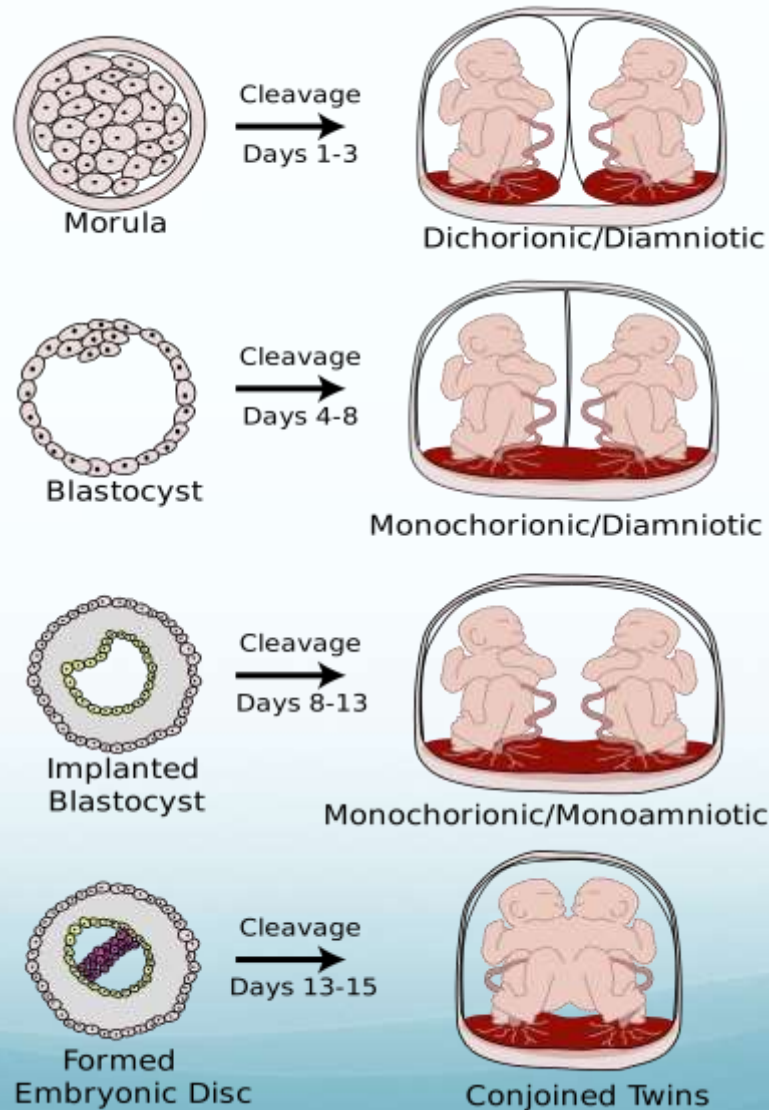
(Shared placenta)

Fraternal
(Dizygotic)



(Separate placentas)

Background



Background

- Monozygotic (MZ) twins carry a significantly higher risk of perinatal morbidity and mortality than singleton and dizygotic twins^{1,2}
- Increased risk of premature delivery¹
- Growth discordance³
- Developmental anomalies⁴
- Mortality¹

Background

- Incidence of MZ twinning (MZT) is greatly increased amongst IVF patients compared to the general population (0.7-13% vs. 0.45%, respectively)
- Reason for this remains unclear^{5,6}

Background

- Prolonged embryo culture, appears to be a risk factor⁶
- Studies have also hypothesized that media characteristics—such as glucose⁷ or glutathione levels—may affect MZT rates.
- Zona Pellucida micromanipulation may be involved
- Others have suggested that the high incidence of MZT in infertility patients is conditioned by hereditary factors⁸

Study Objective

- Create a large, multicenter database to include data on monozygotic twinning in IVF
- To investigate risk factors for MZT

Methods

- Using an electronic medical record system (eIVF, PracticeHwy), clinical pregnancy data (confirmation of a gestational sac(s) and presence of a fetal pole with a heartbeat(s) on ultrasound)
- Data from 10 large IVF clinics in the U.S from January 1st 2000 to January 31st 2017 were retrospectively reviewed.
- Both fresh and thaw cycles were included

Methods

- MZT: when the number of fetal poles with cardiac activity seen and recorded exceeded the number of embryos transferred
- A binary logistic regression was performed to ascertain risk factors for MZT within our cohort

Results

- >124,000 clinical pregnancies identified in the database
- 61,924 clinical pregnancies met criteria for modeling
- 50,215 pregnancies resulted from fresh transfers
- 11,709 pregnancies resulting from thaw transfers

Cohort characteristics (n=61,924)

(n=

	Fresh	Frozen	Total
Age at cycle start	36.14 +/- 5.04	37.48 +/- 5.8	36.39 +/- 5.2
Transfer Day			
2-3 days	28240 (45.6%)	1022 (1.7%)	29262 (47.3%)
4-7 days	21975 (35.5%)	10687 (17.3%)	32662 (52.7%)
PGD performed	2140 (3.5%)	501 (0.8%)	2641 (4.3%)
Embryos transferred	2.13 +/- 1.06	0.93 +/- 1.84	1.9 +/- 1.12
IVF performed	25201 (40.7%)	0	25201 (40.7%)
ICSI performed	28566 (46.1%)	0	28566 (46.1%)
Assisted hatching performed	9573 (15.5%)	0	9573 (15.5%)

Results

- 352 cycles (0.57%) resulted in MZ twins
- 198 in the fresh cycle group
- 154 in the thaw cycle group

Monozygotic Twin Cohort Characteristics (n=352, 0.57%)

	MZT	Non-MZT	Total
Age at cycle start	35.8 +/- 5.76	36.4 +/- 5.22	36.39 +/- 5.2
Transfer Day			
2-3 days	49 (0.1%)	29213 (47.2%)	29262 (47.2%)
4-7 days	303 (0.5%)	32359 (52.3%)	32662 (52.7%)
PGD performed	28 (0.04%)	2613 (4.2%)	2641 (4.3%)
Embryos transferred	1.25 +/- 0.7	1.91 +/- 1.1	1.9 +/- 1.12
Any embryo biopsy (ICSI, assisted hatching, PDG)	133 (0.2%)	30062 (48.2%)	30195 (48.8%)

Table 1. Risk Factors for MZT events among 61,920 IVF cycles from Jan 2000 through Dec 2016. Adjusted odds ratios and p-values from multivariable logistic regression.

	OR (95% CI)	p value
Age at cycle start	0.99 (0.97-1.00)	0.15
Transfer Day	1.44 (1.26-1.60)	<0.0001
Thaw cycle	1.94 (1.37-2.7)	<0.0001
Assisted hatching	0.97 (0.93-1.02)	0.27
ICSI	0.99 (0.97-1.01)	0.38
PGS	1.39 (0.91-2.11)	0.13
Number of oocytes retrieved	1.03 (1.02-1.05)	<0.0001
Number embryos transferred	0.66 (0.57-0.77)	<0.0001

Conclusions (Preliminary)

- We have validated the hypothesis that prolonged embryo culture is a major risk factor for MZT
- For each additional day in culture the OR for MZT increases by 1.4
- Thaw cycles appear to be twice as likely to result in MZT

Future Studies

- Further investigate potential risk factors behind the increase in likelihood of MZT
- Investigate our clustering theory across all clinics independently
- Identify laboratory or clinical changes which may increase the risk of monozygotic clinic

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Thank you