Incidence of congenital heart defects in IVF/ICSI pregnancy: a systematic review and meta-analysis

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Objective
There is no consensus concerning the risk of congenital heart defects (CHD) in pregnancy obtained from IVF/ICSI. The aim of the study is to assess whether CHD occur more often with the use of IVF/ICSI technique, as compared to spontaneous pregnancies.

Methods
A systematic search for studies in PubMed/MEDLINE from 1990 to March 2017 was conducted. The search included the following MeSH terms alone or in different combinations: “IVF”, “IVF/ICSI”, “ART pregnancy”, “assisted conception”, “birth defect”, “congenital heart defects” and “congenital malformations or abnormalities”. Cohort studies comparing neonatal incidence of CHD in IVF/ICSI and spontaneous conceptions were included, with exclusion of other types of assisted reproductive technology (ART) and of studies without information concerning termination of pregnancy. Chromosomal anomalies were excluded whenever possible. Meta-analysis was conducted to estimate the pooled unadjusted odds ratio (OR) with a 95% confidence interval (CI) using the fixed effect model. Statistical heterogeneity among studies was evaluated by I^2 value and chi - squared-based Q - test. A p-value > 0.10 for the Q-test or an I^2 value less than 50% revealed no obvious heterogeneity across the studies.

Results
A total of 25,250 children obtained from IVF/ICSI techniques and 288,131 children spontaneously conceived, both in singleton and multiple pregnancies, were included in the analysis. The total CHD events were 381/25,250 (1.51%) and 3,079/288,131 (1.06%) in the IVF/ICSI and spontaneous conception groups, respectively. The pooled estimate OR for CHD was significantly increased in the IVF/ICSI group as compared to spontaneous conceptions (OR=1.44; 95% CI 1.27-1.63; p < 0.0001; I^2=45%; p = 0.07). In the subgroup of singleton IVF pregnancies the same significant difference was obtained (OR 1.46; 95% CI 1.21–1.76; I^2=36%; p = 0.18).

Conclusion
Fetuses conceived after IVF/ICSI methods are at increased risk of CHD, compared to spontaneous conceptions. However, this finding deserves further investigation, due to heterogeneity of both ART procedures and cardiac defects.