INPLASY

Selective Reduction in Selective Fetal Growth Restriction: A Meta-Analysis of Co-Twin Survival and Perinatal Outcomes

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 August 2025 and was last updated on 1 August 2025.

INTRODUCTION

Review question / Objective To assess co-twin loss, neonatal mortality, and overall perinatal outcomes following selective reduction in pregnancies complicated by selective fetal growth restriction (sFGR), and to compare these outcomes between radiofrequency ablation (RFA) and cord coagulation techniques.

Rationale Selective fetal growth restriction (sFGR) is a serious complication that affects a subset of monochorionic pregnancies, often due to unequal placental sharing and abnormal vascular connections. In more severe cases, one fetus experiences significant growth compromise and faces a high risk of intrauterine demise. Because of shared placental circulation, the co-fetus may also be at risk—particularly for neurological injury or sudden cardiovascular collapse if the smaller fetus dies. These scenarios pose extremely difficult clinical challenges and raise complex questions around how best to protect the healthier fetus.

One option in these high-risk situations is selective reduction. This intervention involves stopping blood flow to the compromised fetus, with the goal of reducing the chance of harm to the co-fetus. Two of the most commonly used techniques are radiofrequency ablation (RFA) and umbilical cord coagulation, including bipolar cord coagulation. While these methods differ in how they achieve vascular occlusion, both aim to isolate the affected fetus in order to prevent further complications.

Over the past decade, the use of selective reduction in cases of sFGR has grown, but outcomes reported across studies remain inconsistent. Some suggest that RFA may be linked to higher co-fetal survival and fewer complications, while others show no clear advantage between techniques. Reported outcomes vary and include fetal demise, neonatal death, preterm delivery, low birth weight, neurological complications, and NICU admission. Interpreting the available data is challenging, not only because of the diversity in clinical practice, but also due to differences in patient selection,

timing of intervention, and outcome definitions. Most studies are retrospective or observational, and there are no randomized controlled trials specifically comparing RFA and cord coagulation in this context.

Given these limitations, there's a clear need for a focused, well-designed meta-analysis that examines the outcomes of selective reduction for sFGR. By bringing together data from multiple studies, this review will offer a more comprehensive understanding of the risks and potential benefits associated with each technique. In particular, it will evaluate the rates of co-fetal loss, neonatal mortality, and broader perinatal outcomes, and provide a direct comparison between RFA and cord coagulation approaches.

Ultimately, the goal is to offer clearer evidence to support decision-making in one of the most complex areas of fetal medicine. Better data can improve how clinicians counsel families, guide procedural choices, and potentially shape future recommendations for practice. In pregnancies already facing heightened risks, having stronger evidence for when and how to intervene could make a meaningful difference in outcomes.

Condition being studied Selective fetal growth restriction (sFGR) is a condition that occurs in pregnancies with a shared placenta (typically monochorionic), where one fetus receives significantly less placental blood flow than the other. This imbalance leads to a marked difference in fetal growth, placing the smaller fetus at risk for intrauterine demise and long-term complications. Due to shared vascular connections, the death of one fetus can also endanger the surviving co-fetus, potentially resulting in neurological injury or death. sFGR is typically classified into three types based on umbilical artery Doppler patterns, with Type II and III associated with worse outcomes. Management options include expectant monitoring, laser ablation, or selective reduction in severe cases to protect the healthier fetus. This study focuses on evaluating outcomes following selective reduction for sFGR.

METHODS

Search strategy Selective fetal growth restriction (sFGR) is a complication unique to monochorionic pregnancies, where two fetuses share a single placenta and are connected by vascular anastomoses. It is defined by a significant discrepancy in estimated fetal weight (typically ≥25%) between the fetuses, where one fetus has an estimated fetal weight below the 10th percentile. Unlike generalized fetal growth restriction, sFGR arises due to unequal placental sharing and hemodynamic imbalances through inter-fetal vascular connections, leading to asymmetric growth and an increased risk of adverse outcomes.

sFGR is classified into three types based on umbilical artery Doppler flow patterns in the smaller fetus. Type I, with positive end-diastolic flow, is generally associated with more favorable outcomes and is usually managed expectantly. Type II, characterized by persistently absent or reversed end-diastolic flow, and Type III, defined by intermittent absent/reversed end-diastolic flow, carry a much higher risk of intrauterine fetal demise (IUFD) and neurological injury to the co-fetus due to the unstable placental circulation.

The major clinical concern in sFGR is that the intrauterine demise of the growth-restricted fetus can acutely compromise the surviving fetus. In monochorionic pregnancies, the death of one fetus can result in abrupt hemodynamic shifts across shared placental anastomoses, potentially causing hypotension, hypoxic-ischemic injury, or even death in the co-fetus. As a result, the management of severe sFGR—particularly Types II and III—often requires careful consideration of interventional options aimed at reducing the risk to the unaffected fetus.

Selective reduction is one such option, primarily offered when the risk to the co-fetus becomes unacceptably high due to progressive deterioration of the growth-restricted fetus. The procedure involves targeted interruption of the umbilical circulation to the compromised fetus, thereby isolating it from the shared placental system. Commonly used techniques for selective reduction include radiofrequency ablation (RFA) and umbilical cord coagulation (UCC), such as bipolar cord occlusion. Both approaches aim to minimize procedural risks while maximizing the chance of survival and intact neurodevelopment in the co-fetus.

While selective reduction is increasingly performed in specialized fetal therapy centers, outcomes vary significantly across studies. Co-fetal survival, neonatal death, preterm birth, and neurologic morbidity are among the most commonly reported outcomes, but findings remain inconsistent, and direct comparisons between techniques are limited. Most available data come from small, retrospective cohorts, and there is a lack of high-quality evidence to guide clinical decisions in this setting.

This study focuses specifically on pregnancies complicated by sFGR managed with selective reduction, aiming to evaluate and compare perinatal outcomes—particularly co-fetal survival—across different procedural techniques. Understanding these outcomes is essential to improving counseling, procedural planning, and overall management strategies in this high-risk population.

Participant or population This review will include pregnant individuals with monochorionic diamniotic pregnancies complicated exclusively by selective fetal growth restriction (sFGR) who underwent selective fetal reduction. Only cases in which sFGR was the sole indication for intervention will be included. Pregnancies with additional complications such as twin-to-twin transfusion syndrome (TTTS), twin reversed arterial perfusion (TRAP) sequence, twin anemia-polycythemia sequence (TAPS), or discordant structural anomalies will be excluded unless outcome data for isolated sFGR cases are reported separately.

Eligible studies must define sFGR based on established criteria, typically including an estimated fetal weight (EFW) below the 10th percentile in one fetus and an inter-twin discordance of ≥25%. Studies that use Doppler-based classification systems (Types I, II, or III) for sFGR will also be included, provided they focus on cases where no coexisting conditions are present.

The population of interest is patients who underwent selective reduction via radiofrequency ablation (RFA) or umbilical cord coagulation techniques (e.g., bipolar cord occlusion), specifically for the management of isolated sFGR. Only studies that report perinatal outcomes of the surviving co-fetus—such as intrauterine fetal demise (IUFD), neonatal death, gestational age at delivery, and/or neonatal morbidity—will be included.

All included studies must provide sufficient detail to confirm that selective reduction was performed solely due to sFGR, with no overlapping indications. Multiple gestations other than monochorionic diamniotic pregnancies (e.g., dichorionic twins or monochorionic triplets) will be excluded unless outcomes for MCDA sFGR cases are clearly separable.

Intervention The intervention under evaluation is selective fetal reduction performed in monochorionic diamniotic pregnancies complicated solely by selective fetal growth restriction (sFGR). Specifically, the review will assess and compare outcomes following two commonly used techniques for vascular occlusion:

Radiofrequency ablation (RFA) – a minimally invasive procedure that uses thermal energy to coagulate fetal vessels and interrupt blood flow to the compromised fetus.

Umbilical cord coagulation – including bipolar cord coagulation and other methods aimed at occluding the umbilical cord using direct energy delivery via fetoscopy or ultrasound guidance.

Only interventions performed for the indication of isolated sFGR—without concurrent conditions such as twin-to-twin transfusion syndrome (TTTS), TRAP sequence, or structural anomalies—will be considered. The review will focus on evaluating perinatal outcomes of the co-fetus following these procedures.

Comparator The primary comparator in this review is the type of selective reduction technique used for managing isolated selective fetal growth restriction (sFGR) in monochorionic diamniotic pregnancies. Specifically, outcomes will be compared between:

Radiofrequency ablation (RFA)
versus

Umbilical cord coagulation (UCC), including bipolar cord coagulation

The review will compare perinatal outcomes of the surviving co-fetus—such as intrauterine fetal demise (IUFD), neonatal death, gestational age at delivery, and other morbidities—across these two procedural techniques.

No comparisons will be made with expectant management or other interventions (e.g., laser for TTTS), as the review is limited to cases undergoing selective reduction for isolated sFGR.

Study designs to be included This review will include prospective and retrospective cohort studies, case series with ≥5 cases, and comparative observational studies that report perinatal outcomes following selective reduction for isolated sFGR. Randomized controlled trials (RCTs) will also be included if available. Case reports, reviews, editorials, and studies with mixed indications that cannot be separated will be excluded.

Eligibility criteria Inclusion criteria:

Studies involving monochorionic diamniotic pregnancies complicated by isolated selective fetal growth restriction (sFGR)

Selective fetal reduction performed using radiofrequency ablation (RFA) or umbilical cord coagulation (UCC) techniques

Reported perinatal outcomes of the surviving fetus, including intrauterine fetal demise (IUFD), neonatal death, gestational age at delivery, or neonatal morbidity

Prospective or retrospective cohort studies, or case series with five or more cases

Articles published in English

Exclusion criteria:

Cases with additional complications such as twin-to-twin transfusion syndrome (TTTS), twin reversed arterial perfusion (TRAP), twin anemia polycythemia sequence (TAPS), or discordant structural anomalies

Elective reductions without medical indication

Case reports, narrative reviews, editorials, or conference abstracts without full data

Studies lacking extractable data on perinatal outcomes of the surviving fetus.

Information sources We will conduct a comprehensive literature search across the following electronic databases: PubMed/MEDLINE, Embase, Scopus, and the Web of Science Core Collection (ISI) from inception to the present. Additional sources will include reference lists of eligible studies and relevant review articles to identify any studies missed in the database search. If necessary, we will also contact study authors to obtain unpublished or clarifying data. No grey literature, trial registries, or non-peer-reviewed sources will be included. Only studies published in English will be considered.

Main outcome(s) The primary outcome of this review is the perinatal survival of the co-twin following selective fetal reduction for isolated selective fetal growth restriction (sFGR) in monochorionic diamniotic pregnancies. Perinatal survival will be defined as the absence of intrauterine fetal demise (IUFD) and neonatal death of the surviving fetus.
Secondary outcomes include:

Co-twin loss, defined as either intrauterine or neonatal death of the surviving fetus
Gestational age at delivery
Rates of neonatal morbidity, including pulmonary complications, sepsis, and adverse neurological outcomes (as reported by individual studies)
Effect measures will include pooled proportions (e.g., survival rate, co-twin loss rate, neonatal death rate) and mean or median differences (e.g., gestational age). Outcomes will be analyzed and, where possible, stratified by reduction technique and gestational age at intervention..

Quality assessment / Risk of bias analysis The risk of bias in included studies will be assessed using the Newcastle–Ottawa Scale (NOS), which is specifically designed for non-randomized studies. The NOS evaluates three key domains:
1. Selection of study groups
2. Comparability of groups
3. Outcome assessment (for cohort studies)
Each study will be scored based on a star system, with a maximum of 9 stars indicating highest quality. Studies will be categorized as low, moderate, or high risk of bias based on total NOS scores. Two reviewers will independently assess each study, and any discrepancies will be resolved by consensus or with input from a third reviewer.

Strategy of data synthesis Data synthesis will be conducted using a random-effects meta-analysis model, given the expected clinical and methodological heterogeneity across studies. Pooled proportions and 95% confidence intervals will be calculated for outcomes such as co-twin survival, intrauterine fetal demise, neonatal death, and other perinatal complications. For continuous outcomes (e.g., gestational age at delivery), pooled means and standard deviations will be analyzed when data are available.

Subgroup analyses will be performed to compare outcomes between different intervention techniques (e.g., RFA vs. umbilical cord coagulation) and by timing of the procedure where possible.

Subgroup analysis Subgroup analysis will be conducted based on the type of intervention technique used for selective reduction. Specifically, outcomes will be compared between:

Radiofrequency ablation (RFA)

Umbilical cord coagulation (UCC), including bipolar cord coagulation

This analysis will evaluate whether the choice of technique impacts co-twin survival, neonatal death, and other perinatal outcomes. Subgroup-specific effect estimates will be calculated where sufficient data are available.

Sensitivity analysis Not applicable. No sensitivity analysis is planned for this review.

Country(ies) involved USA.

Keywords Selective fetal growth restriction; sFGR; monochorionic pregnancy; selective reduction; radiofrequency ablation; umbilical cord coagulation; co-twin survival; perinatal outcome; fetal therapy.

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