MONOCHORIONIC TWIN PREGNANCY: SELECTIVE FETAL GROWTH RESTRICTION (sFGR)

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1. INTRODUCTION: DEFINITION AND PATHOPHYSIOLOGY

Selective fetal growth restriction (sFGR) affects 10-15% of monochorionic (MC) twin pregnancies, and it is mainly caused by an asymmetric placental distribution between fetuses. Due to the existence of vascular anastomoses between fetuses, the natural history of sFGR can be very different as compared with FGR in singletons or dichorionic (DC) twins. sFGR is associated with a high risk of intrauterine fetal demise and neurologic complications for the FGR twin but also for the appropriate for gestational age (AGA) twin.

The number and type of intertwin vascular anastomoses in the MC placenta play an important role in the clinical course and prognosis. Most sFGR cases can be classified into three types, defined by the characteristics of Umbilical Artery (UA) Doppler in the FGR twin, which correlate with certain gross patterns of vascular anastomosis and with distinct clinical behaviour (Table 1):

- Type I: Normal flow
- Type II: Persistently absent or reversed end-diastolic flow (AREDF)
- Type III: Intermittently absent or reversed flow end-diastolic flow (iAREDF)

Table 1. Correlations between the sFGR type and the pattern of placental anastomoses

Type sFGR	UA Doppler	AV/VA anastomosis	AA anastomosis
Type I	Normal	Several in both directions	Possible, but of small size
Type II	AREDF	Few and small	Absent, if present very small size.
Type III	iAREDF	Variable	At least one large AA (>2mm)

Doppler UA examination in MC twins with sFGR should be performed as close as possible to the placental insertion. If done properly and according to the good practice recommendations for a Doppler examination (i.e. respecting a correct angle of insonation<30, proper magnification, avoiding maternal breathing movements, and location close to the placenta), the examinations are reproducible. In most cases (>90%), the type of sFGR established at the moment of diagnosis will remain the same during pregnancy.

2. DIAGNOSIS OF sFGR

The diagnosis of sFGR in a MC pregnancy requires first ruling out TTTS (Table 2). Amniotic fluid discordance is a common finding in sFGR, but the criteria for TTTS must not be met. It is possible to have TTTS and sFGR, but the case must be managed as TTTS.

As a rule, the diagnosis of sFGR should be considered when one fetus has an estimated fetal weight <10 centile. This finding should lead to closer follow-up and Doppler examination of both fetuses, and classification into types according to the UA Doppler of the smaller fetus.

A more refined classification has been proposed according to combinations of criteria, but the clinical implications do not change in relation with the previous simplified criterion.

- As a single criterion: Estimated fetal weight (EFW) <3rd percentile
- Combined criteria: If EFW >3rd percentile, 2 of the 3 following criteria:
  - EFW < 10th percentile (or abdominal circumference <24weeks < 10th percentile)
  - Intertwin EFW discordance (or AC discordance) ≥ 25%, calculated as (EFW of larger twin – EFW smaller) / (EFW larger)
  - UA-Pulsatility Index in FGR >95th percentile.

Figure. Differential diagnosis algorithm for MC twins with suspected TTTS and/or sFGR

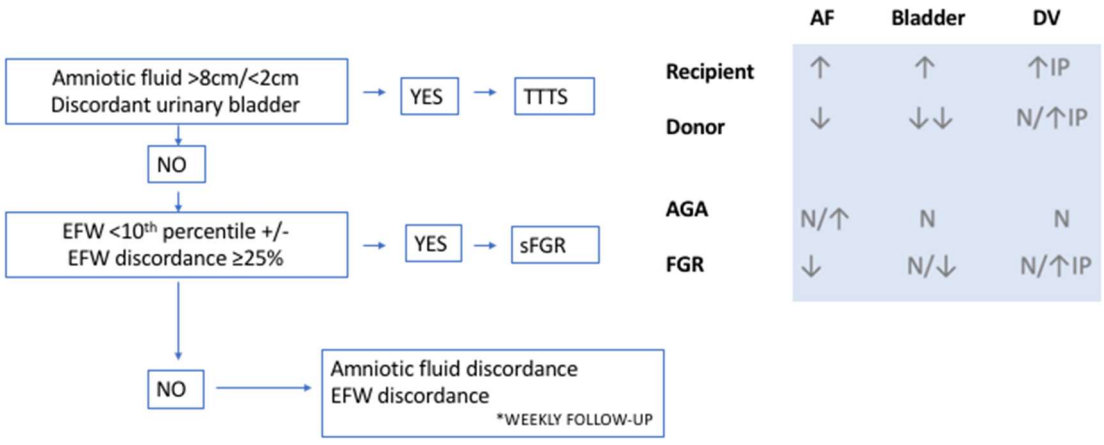


Table 2. Clinical characteristics in the differential diagnosis between sFGR and TTTS

	sFGR	TTTS
EFW discordance	≥25% and EFW <10th percentile	Variable
AGA*/recipient fetus		
Amniotic fluid	Normal or slightly increased	> 8cm before 20 weeks/
Urinary bladder	Normal	>10cm after 20 weeks
Ductus venosus	Normal	Enlarged
		Variable (elevated PI)
FGR/donor fetus		
Amniotic fluid	Normal or slightly reduced	<2cm
Urinary bladder	Normal or slightly reduced	Very reduced/No visible

3. CLASSIFICATION, FOLLOW-UP AND MANAGEMENT

3.1. Type I sFGR

Definition: sFGR fetus with present diastolic flow in the UA Doppler waveform.

Clinical evolution: Generally, favourable. Usually the small fetus presents a linear growth curve without signs suggestive of deterioration, even in very small fetuses. Perinatal outcomes are generally good with rates of mortality (2-4%) and neurological damage (<5%) similar to those of MC twins.

Management: expectant management and close follow-up, normally 1/week.

- Fetal biometry every 2 weeks.
- Doppler surveillance (UA, middle cerebral artery (MCA) and ductus venosus (DV)) every evaluation. UA-PI Doppler >95th percentile is very uncommon but if present it may indicate potential progression to type II.
- Fetal functional echocardiography: preferably at 28-30 weeks.
- Neurosonography: preferably at 30-32 weeks.

Delivery (see Algorithm 1):

Delivery will be scheduled between 34 and 36 weeks depending on the degree of discordance and the Doppler findings.

In cases presenting any of the following criteria, delivery should be performed from 34 weeks onwards, after fetal lung maturation, according to the following protocol:

- Doppler abnormalities:
  - Persistent UA-PI > 95th percentile
  - Persistent DV-PI > 95th percentile
  - Persistent MCA-PI or CPR <5th percentile
- EFW discordance ≥ 35%.

The preferred mode of delivery will be by elective caesarean section, although in some very selected cases with small EFW discordances and favourable fetal presentations, a vaginal delivery could be discussed with parents.

3.2. Type II sFGR

Definition: sFGR fetus with persistently absent/reversed end-diastolic flow (AREDF) in the UA Doppler waveform

Clinical features: Similar to FGR in singletons or DC twins, the FGR fetus will present a progressive deterioration of Doppler findings (UA, MCA and DV). The rates of perinatal mortality and neurological sequelae are substantially higher than in type I sFGR, and the average gestational age at delivery is <30 weeks in most clinical series.

Management: See Algorithm 2. The following options can be discussed with parents:

- Expectant management: 1/week or more frequently if signs of fetal deterioration.
  - Fetal biometry every 2 weeks.
  - Weekly Doppler surveillance (UA, ACM, DV) to detect early signs of fetal deterioration in the next few days: reversed flow in UA, reversed or absent flow in DV. The presence of Doppler abnormalities should be confirmed within the next 24 hours, including fetal CTG after viability.
  - Fetal functional echocardiography: preferably at 28-30 weeks.
  - Neurosonography: preferably at 30-32 weeks.
- Fetal therapy (to be considered if Severity Criteria, see Table 3 and Algorithm 2). Therapeutic options are:

- Cord occlusion of the sFGR fetus: ≥90% survival of the AGA fetus.
- Fetoscopic laser coagulation of placental anastomoses: survival of 70-80% of the AGA and 30-40% of FGR fetus.

Criteria for Delivery (see Algorithm 1):

In cases with expectant management, delivery will be by elective caesarean section. Delivery will be planned between 30-34 weeks, depending on Doppler abnormalities, after fetal lung maturation and neuroprotection.

- No severity criteria: 33-34 weeks.
- Severity criteria: 30-32 weeks.
- Absent atrial flow in the DV or spontaneous decelerations in fetal CTG: delivery at any time could be considered, depending on gestational age and parents' wishes.

In cases with active management, delivery will depend on the type of treatment and the number of surviving fetuses:

- Cord occlusion or intrauterine fetal demise of the FGR fetus after laser treatment: 36-37 weeks, or earlier if maternal-fetal complications. The mode of delivery will depend on obstetric conditions.
- Laser treatment with survival of both fetuses: elective caesarean section.

3.3. Type III sFGR:

Definition: sFGR fetus with intermittently absent/reversed end-diastolic flow (iAREDF) in the UA Doppler waveform. iAREDF is defined as the presence of alternating phases, usually following a cyclic pattern during ultrasound examination, of positive with absent/reversed diastolic flow in the UA. iAREDF represents a sign unique to MC twins and it is caused by the existence of at least one large placental AA anastomosis. It is associated with an unpredictable evolution, a higher risk of fetal demise of the FGR fetus and/or neurologic injury in one or both twins.

Clinical features:

- Apparently benign clinical evolution. In most cases, the small fetus does normally not present any sign of Doppler deterioration (MCA or DV, since the UA is not useful by definition), even in severely small fetuses.

- High risk of fetal death of the FGR fetus (15-20%), which occurs unexpectedly despite normal Dopplers in previous ultrasound examinations.
- High risk of neurologic injury, mainly but not only, in the AGA twin (15-20%, particularly periventricular leukomalacia), which occurs irrespectively of whether both fetuses survive.

Other accompanying findings:

- Cardiomegaly and/or hypertrophy in the AGA fetus (up to 25%), suggesting cardiac overload in the AGA fetus. It normally indicates large EFW discordance, but it has not been documented to be associated with poorer prognosis.
- Hydropic signs (usually subcutaneous edema and/or ascites) can be very rarely found and suggests a previous recent acute twin-to-twin transfusion accident.

Management: Management of type III sFGR is challenging due to the unpredictable clinical course. Management options are the same as described for in sFGR type II. In the presence of severity criteria (Table 3) fetal therapy can be discussed as an option with parents (see Algorithm 2).

Criteria for Delivery (see Algorithm 1):

In cases with expectant management, delivery will be by elective caesarean section.

- No severity criteria (Table 3): 33-34 weeks.
- In cases with severity criteria, delivery at 32 weeks.
- In certain situations, delivery can be considered from 30 weeks:
  - Extreme degrees of estimated fetal weight discordance.
  - Prominent cyclic changes in the UA diastolic flow with pronounced reverse flow peaks.
  - Signs of moderate-to-severe cardiac dysfunction in the AGA fetus.
  - Fetal hydrops.
- If absent or reverse atrial flow in the DV, consider delivery at any time.

In case of active management, the same criteria as in type II sFGR apply (see above).

Table 3. Severity criteria in type II and III sFGR.

- Early diagnosis: < 24 weeks
- Fetal weight discordance ≥ 35%.
- Oligohydramnios
- REDF in UA
- DV-PI > 95th percentile

MANAGEMENT OF MC TWINS COMPLICATED BY FETAL DEMISE OF ONE TWIN

Intrauterine fetal death (IUFD) in MC twins poses particular risks to the co-twin due to acute feto-fetal transfusion/exsanguination into the circulation of the dying fetus through the placental anastomosis:

- Concomitant fetal demise (15-20%)
- Neurological injury (15-20%).

Although there is not conclusive evidence, clinical experience suggests that the risks for the co-twin are higher when the event occurs in the second half of gestation.

Neurological damage occurs during the process prior to or just after fetal death. Within hours the circulation of the IUFD fetus collapses, so that there is no longer risk of further transfusion/exsanguination.

The diagnosis of fetal death is virtually always made after the acute transfusion event. (*) The approach is:

- Doppler (UA, MCA and DV Doppler) and CTG (if >30 weeks) evaluation.
- Assessment of fetal anemia (MCA peak systolic velocity (PSV)) in the surviving fetus. If severe fetal anemia is suspected (MCA-PSV >1.5 MoMs), cordocentesis and eventual intrauterine transfusion in the surviving fetus can be considered, particularly if there is reasonable evidence that fetal death occurred very recently. There is not solid evidence about the protective effect of transfusion to reduce the risk of neurological injury. Therefore, the possibility of transfusion could be considered but should be discussed in detail with parents.

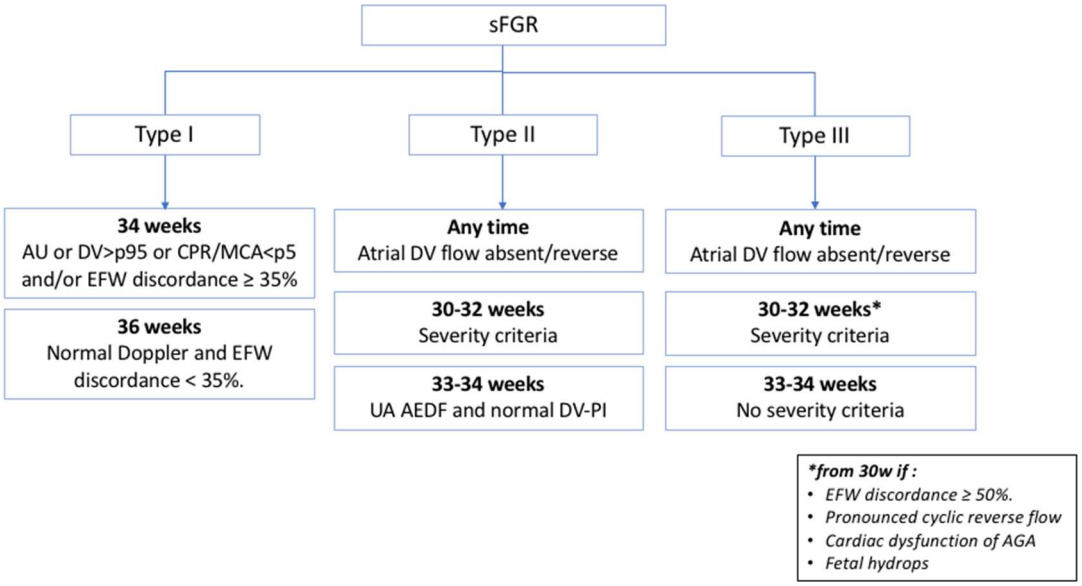
(*) In the rare event of detecting a situation suggesting impending fetal death of one MC twin (severe non-transient bradycardia with Doppler abnormalities), active management could be considered, consisting in cord occlusion of the perimortem fetus, together with cordocentesis and intrauterine transfusion (if fetal anemia is confirmed) in the surviving fetus.

Pregnancy follow-up:

- Weekly monitoring with active search of signs suggesting hypoxic-ischemic injury
- Neurosonography 4-6 weeks after the diagnosis
- Neurosonography and fetal brain MRI at 32 weeks.

Delivery is recommended at 34-36 weeks. The mode of delivery will depend on the obstetric conditions and previous history.

Algorithm 1. Criteria for elective delivery in sFGR MC twins.



Algorithm 2. Management options in MC-sFGR types II and III with severity criteria.