Fetal Growth Restriction

Becky Liu and Asma Khalil

Contents

Electronic Supplementary Material The online version of this chapter (https://doi.org/10.1007/978-3-030-47652-6_13) contains supplementary material, which is available to authorized users. The videos can be accessed by scanning the related images with the SN More Media App.

A. Khalil et al. (eds.), *Twin and Higher-order Pregnancies*,
https://doi.org/10.1007/978-3-030-47652-6_13

Trailer

Fetal growth restriction (FGR) complicates 19.7% of monochorionic twins and 10.5% of dichorionic twins. It is associated with perinatal mortality, premature delivery, and neurological sequelae and death in the surviving co-twin. Twins show a different pattern of growth to singleton pregnancies; therefore, care should be taken to use twin-specific growth charts to avoid over-diagnosis and unnecessary intervention. To date, its diagnosis has shown inconsistencies amongst clinicians and researchers, but a recent consensus using the Delphi procedure has achieved uniform diagnostic criteria. Close surveillance should be undertaken using ultrasound, and referral to a tertiary unit with relevant expertise should be taken if required. Management of this condition can be difficult, as considerations must be made for the normally grown co-twin; therefore, decisions for delivery must not be made with haste. Risks and benefits of conservative management, prenatal intervention, and early delivery must be carefully assessed, and the parents sensitively counselled, in order to plan the course of action.

Definitions

Fetal growth restriction (FGR): a pathological restriction of the fetus in reaching its full genetic growth potential.

Selective fetal growth restriction (sFGR): in twin pregnancies, when FGR affects at least one twin.

Appropriate for gestational age (AGA): the fetus reaching its full genetic growth potential according to its gestational age.

Fetoscopic surgery: the insertion of a fetoscope into the amniotic sac in order to perform a prenatal intervention.

Selective reduction: the termination of one (or more) fetus(es) in a multiple pregnancy whilst continuing the pregnancy with a live fetus(es).

Intrauterine death (IUD): the death of a fetus in utero.

Preterm delivery: the delivery of babies prior to 37 weeks gestation

Learning Objectives

- To understand the definition of fetal growth restriction in multiple pregnancies.
- To understand the diagnosis and surveillance of these pregnancies
- To understand the risks and outcomes associated with these pregnancies
- To understand the management techniques and their associated complications

13.1 Introduction

Fetal growth restriction (FGR) is defined as a pathological restriction of the fetus in reaching its full genetic growth potential. Selective fetal growth restriction (sFGR) is when this occurs in one twin, while the other twin is appropriate for gestational age (AGA). It is associated with neurological comorbidities, intrauterine and perinatal death, which can in turn lead to preterm birth, and co-twin demise or neurological sequelae for the AGA twin [1, 2]. A higher rate of perinatal mortality is seen in MC than in DC twins (75:1000 vs. 33:1000, respectively), as well as higher neurological comorbidities [3, 4]. This difference may be due to monochorionic specific complications, such as twin-to-twin transfusion syndrome (TTTS) and the different etiology of sFGR [5–7].

In DC twin pregnancies, the normal growth trajectory is similar to that of singletons up to 30 weeks gestation and shows a relative reduction thereafter. In MC twins, the estimated fetal weight (EFW) centile is generally lower than DC twins and singletons throughout the gestations [8]. A discordance in EFW between the twins is significantly associated with perinatal loss [19]. In this chapter, we aim to identify the definitions and classifications for FGR, their outcomes and complications, their diagnosis, and management options.

13.1.1 Etiology

In DC twins, sFGR is typically caused by placental insufficiency of one of the placentas [4]. Conversely in MC twins, it is usually as a result of unequal distribution of blood flow and placental sharing due to placental anastomoses [6]. Pre-eclampsia is therefore more commonly seen in association with sFGR in DC than MC twin pregnancies [9]. Other causes can include discordant fetal anomalies, and intrauterine infections [10, 11]. So far, a link between pre-existing maternal risk factors and sFGR has not been clearly established, and the available literature presents controversial findings [25–29].

13.1.2 Diagnosis

Diagnostic Criteria

The diagnostic criteria for this condition have been inconsistent amongst clinicians and researchers. The International Society of Ultrasound in Obstetrics and Gynecology have recommended that for DC twins, EFW <10th centile for either twin should be used, and for MC twins, EFW <10th centile and an inter-twin weight discordance of >25% should be used to diagnose sFGR [10].

A recent consensus, using the Delphi procedure, aimed to achieve uniform diagnostic criteria and reporting parameters in sFGR twins. This concluded that an EFW <3rd centile alone for one twin should be used to diagnose sFGR. In DC twins, two of the three parameters – EFW <10th centile, EFW discordance of ≥25%, and umbilical artery pulsatility index (UA PI) >95th centile in the smaller twin can also be used for diagnosis. In MC twins, two of the four parameters – EFW <10th centile, AC <10th centile, EFW discordance of ≥25%, and UA PI >95th centile in the smaller twin – have been agreed for the diagnosis of sFGR [12] (Fig. 13.1).

Screening for sFGR

A discrepancy in crown rump length (CRL) in the first trimester screening has been shown to be associated with sFGR. A CRL discordance of ≥7% in the first trimester has a 92% sensitivity and 76% specificity in detecting sFGR [20]. A discordance at this early stage can be associated with other poor outcomes such as pregnancy loss and preterm delivery [11].

DC twins should have ultrasound assessments 4 weekly from 20 weeks, and MC twins 2 weekly from 16 weeks. Head circumference (HC), abdominal circumference (AC), and femur length (FL), as well as UA PI and mid-

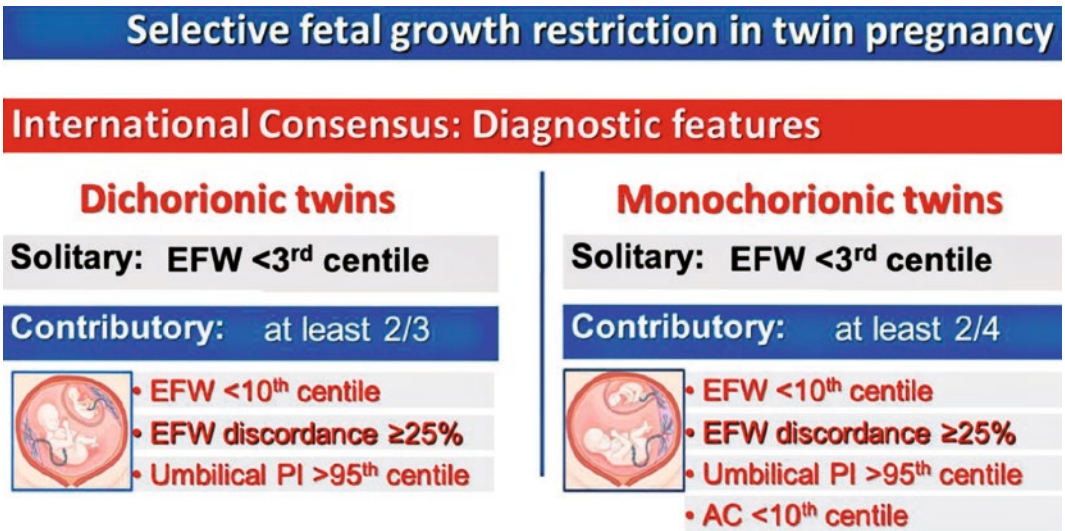

Fig. 13.1 Diagnostic criteria for sFGR as stratified by the recently published Delphi consensus (Khalil 2019) for both dichorionic and monochorionic twins [12]

dle cerebral artery pulsatility index (MCA PI), and peak systolic velocity (PSV) for MC twins, should be measured at each scan [10]. If the diagnostic criteria above are fulfilled, closer monitoring may be required depending on severity and clinician practice. Detailed ultrasound examinations should also be performed to exclude discordant fetal anomalies, and maternal serum serology taken to check for infection, as well as invasive prenatal testing considered in order to rule out genetic conditions [10]. Figures 13.2, 13.3, and 13.4 demonstrate ultrasound features of intertwin size discrepancy in HC and AC measurements.

It is currently common practice to use standardised singleton growth charts to monitor growth in twins. But as the twin growth trajectory is known to be different to that of singletons [8], the usage of singleton growth

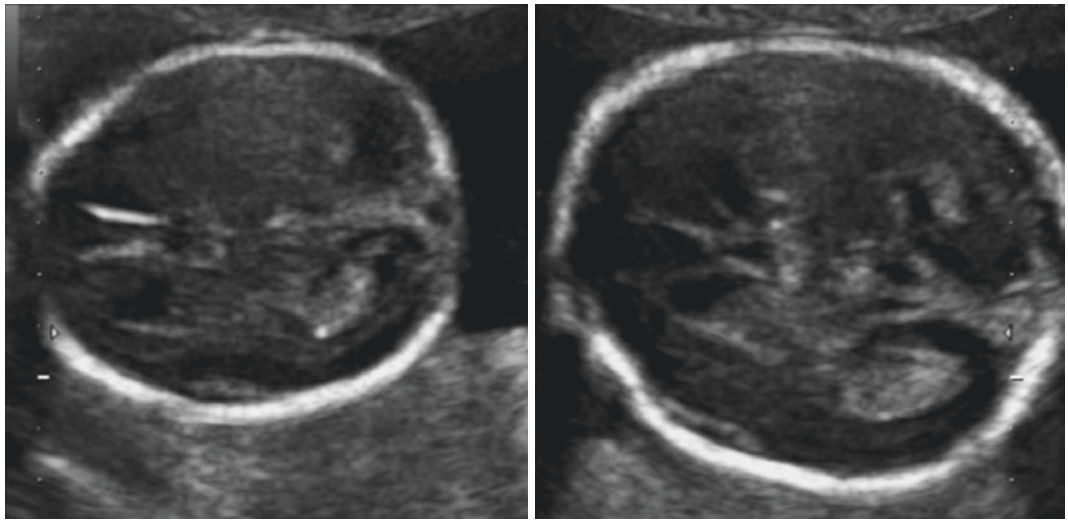

Fig. 13.2 2D ultrasound section of the head circumference, displaying a size discordance between twins

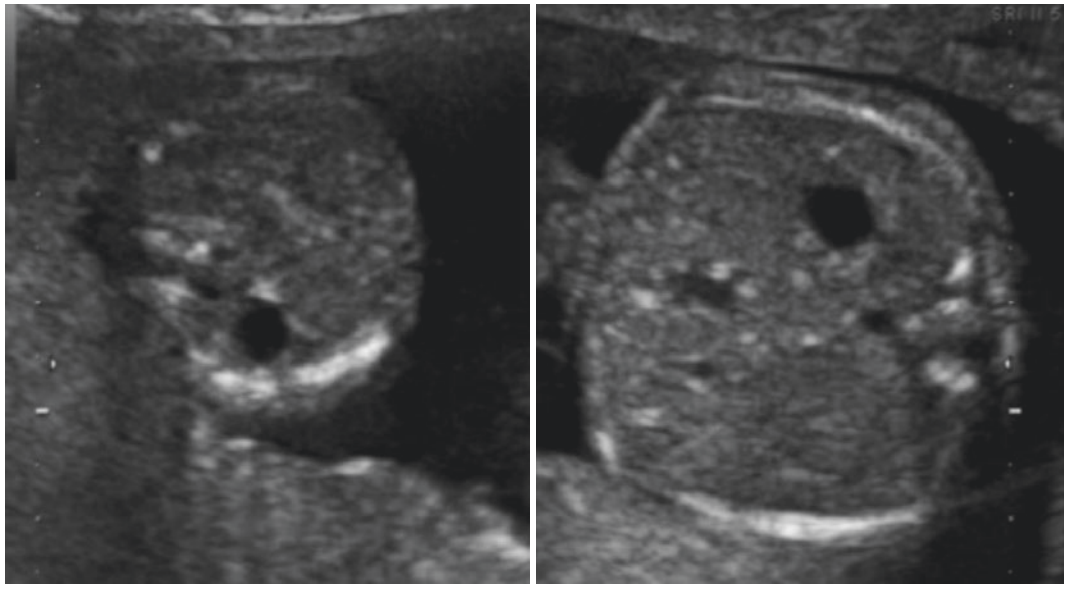

Fig. 13.3 2D ultrasound section of the abdominal circumference, displaying a size discordance between twins

charts can lead to over diagnosis of sFGR and unnecessary intervention. Twin-specific growth charts have now been formulated based on twin-specific growth ranges, derived through the analysis of a large cohort of twin pregnancies, which should be used to monitor growth in twin pregnancies [8].

An earlier study showed that in twins where fetuses were classified as FGR according to singleton charts, MC twins were twice as likely to suffer from perinatal death as singletons; however, the outcomes of DC twins were the same as singletons [31]. This may be the reason for the continued use of singleton growth charts in twins, as poor outcomes have been described for small MC twins according to these criteria.

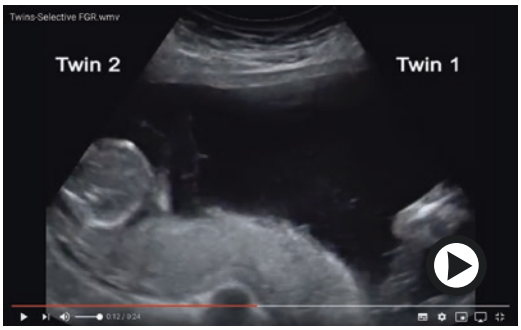

Fig. 13.4 (Twins-Selective FGR): Figure demonstrating the difference in size and amniotic fluid volumes in twins with selective fetal growth restriction (https://doi.org/10.1007/000-2tc)

Classification of sFGR in MC Twins

Gratacós et al. formulated a system to classify sFGR in MC twins. They found that direction and magnitude of blood flow through the different types of placental anastomoses specific to MC twins can give rise to different umbilical artery (UA) Doppler patterns, which in turn, can lead to different clinical evolution and outcomes [4, 13, 14, 18]. These are outlined in Table 13.1. Figure 13.5 displays the different UA Doppler patterns in the different types of sFGR, and Fig. 13.6 demonstrates the bidirectional flow in artery-to-artery anastomosis in type 3 sFGR.

Recent research has looked into the natural history, outcomes according to gestation of onset, and the different diagnostic criteria of sFGR in both MC and DC twins. In MC twins, it was found that early sFGR was slightly more common than late sFGR, with

Table 13.1 Definition, placental anastomoses, perinatal outcomes and overall survival according to Gratacós classification of selective fetal growth restriction (sFGR) in monochorionic (MC) twins [4, 14, 15, 19]

	Type 1	Type 2	Type 3
Definition	Positive UA EDF	Persistent absent or reversed UA EDF	Intermittent absent or reversed UA EDF
Placental anastomoses	Similar to uncomplicated cases	Reduced number large AA anastomoses	Large number of large AA anastomoses (90%), leading to unstable blood sharing and acute TTTS or sudden IUD
Deterioration	Up to 26%	Up to 90%	10.8%
Unexpected IUD	2.6% in small and large twins, 3% double IUD, 2% small twin IUD	0% in small and large twins, 13% double IUD, 10% small twin IUD	15.4% in small twin and 6.2% in large twin, 0% double IUD, and 8% small twin IUD
Overall survival	82–97%	51–58%	77–80%

UA umbilical artery, *EDF* end-diastolic flow, *AA* arterio-arterial, *IUD* intrauterine death, *TTTS* twin-to-twin transfusion syndrome

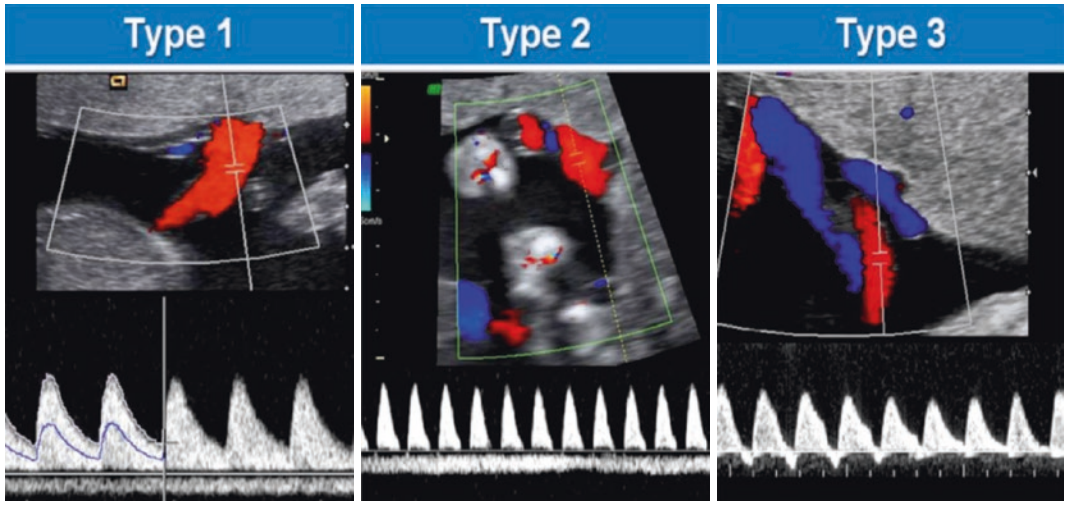

Fig. 13.5 Gratacós classification of selective fetal growth restriction in monochorionic twins. Type 1 displays persistently positive end-diastolic flow in umbilical artery Doppler flow. In type 2, this is persistently absent (or reversed). Type 3 consists of cyclical or intermittently absent or reversed end-diastolic flow

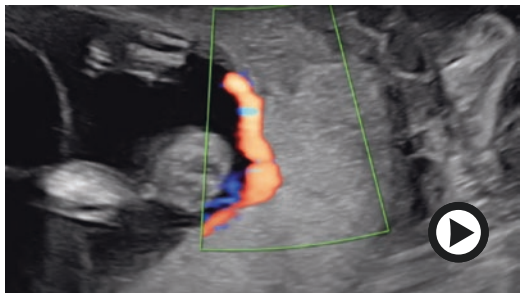

Fig. 13.6 (Clip AA sFGR III): Figure demonstrating the bidirectional flow in artery-to-artery anastomosis in type 2 selective fetal growth restriction (https://doi.org/10.1007/000-2td)

worse outcomes [30]. Figure 13.7 demonstrates the incidence of different types of sFGR in early and late sFGR according to Gratacós classification in MC twins. It seems important to mention that large series on unselected monochorionic twin pregnancies are largely missing. The figures in the tables are largely based on retrospective cohort series from tertiary referral centres, so that there may be a selection bias towards more severe cases. In this study, it was found that the different diagnostic criteria gave a varying incidence of sFGR, thereby supporting the use of the standardised international diagnostic criteria.

Superimposed TTTS can be associated with MC twins complicated with sFGR, which may be secondary to the transfusion imbalance that contributed to TTTS. The incidence of this or its correlation with the gestational age at onset of sFGR has previously not been described in the literature. The recent study by Curado et al. found that superimposed TTTS is more prevalent in early sFGR (27%) vs. late sFGR (6%), and that it co-existed in 13% of type I sFGR, 60% of type II sFGR, and none of type III sFGR [30] (as shown in Fig. 13.8).

13.1.3 Management

sFGR in Dichorionic Twins

As the etiology for FGR is the same in DC twins as that of singletons, with separate placentation, the current recommendation is to manage these pregnancies as growth-restricted singletons [10, 11]. Ultrasound to assess growth and Doppler indices should be performed at least twice weekly, or more frequently, depending on the severity [10]. Assessments should be similar to that of singleton pregnancies, where the deterioration of umbilical artery (UA), middle cerebral artery (MCA), and ductus venosus (DV) Dopplers should be monitored carefully. Recent evidence has suggested that the time of deterioration and disease progression in DC twins

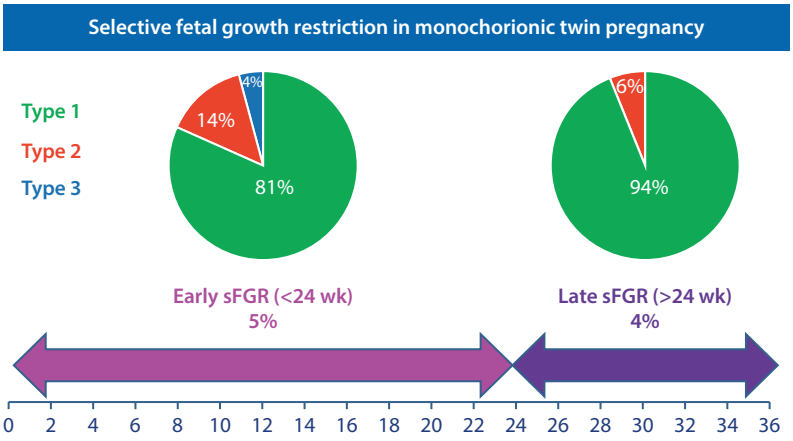

Fig. 13.7 Pie charts demonstrating the incidence of the different types of sFGR according to Gratacós classification in early and late sFGR in monochorionic twins [30]

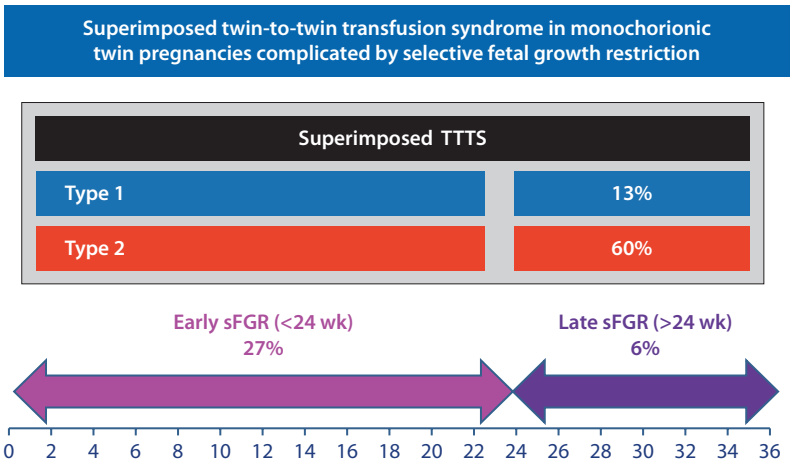

Fig. 13.8 Incidence of superimposed twin-to-transfusion syndrome (TTTS) in different types of sFGR and its prevalence in early and late sFGR in monochorionic twins

may be longer than that of singletons, perhaps due to a delay in delivery to allow more time for growth in the AGA twin [15].

Selective fetocide has a limited role in DC twins, due to the increased risk of preterm labour. A few cases have been reported for its use in severe preterm pre-eclampsia [16]. However, conservative management can lead to intrauterine demise of the sFGR twin, which can in turn lead to preterm delivery in 54%, as well as a 2% risk of neurological damage, and 3% of death in the surviving co-twin [17]. Early delivery may give rise to complications due to prematurity for both the AGA and the FGR twins. Generally, delivery is not recommended prior to 32–34 weeks' gestation. Therefore, these pregnancies require careful monitoring, and the decision for delivery should be made on a risk-benefit assessment for each twin and thorough counselling [10].

▪ sFGR in Monochorionic Twins

Management of MC twin pregnancies can vary according to the Gratacós classification. Ultrasound assessment should be performed to monitor growth two weekly, and to monitor Doppler indices at least weekly [10]. Deterioration of the UA, MCA, and DV Dopplers should be checked to assess disease progression.

Type I sFGR generally has a good prognosis; however, with progression rates reported up to 26% [18], they should continue to receive regular monitoring. Delivery can often take place at 34–36 weeks [4]. Type II sFGR has the worst prognosis, with progression rates up to 90% [13], with an intact survival rate of 33% for both twins [14]. Type III sFGR has a lower rate of progression, but due to the large AA anastomoses, the risk of sudden IUD is higher [13].

In MC twins, single twin demise of the sFGR twin can have drastic consequences for the co-twin, due to the shared placental circulation, it can result in hypoperfusion of the brain and other organs. It has been reported that the surviving co-twin has a 15% risk of IUD, a 26% of neurological morbidity, and a 68% risk of preterm delivery [17]. Therefore, prenatal intervention in the form of fetoscopic surgery are more likely required in sFGR types II and III due to their poor prognosis [4, 11]. According to the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guideline, selective fetal reduction might be considered if there is a significant risk of single twin demise before 26 weeks [10]. After 26 weeks, however, the risk of prematurity is lower; therefore, delivery after this gestation can be considered if significant deterioration is evident [4].

Recent systematic reviews and meta-analyses of retrospective cohort studies have shown that Type I sFGR have an optimal outcome with conservative management, and that Type II is associated with a higher rate of perinatal morbidity and mortality than Type I, but not significantly different to Type III. Abnormal postnatal brain imaging was more prevalent in Types II and III sFGR, and overall adverse composite outcomes were similar in Types II and III sFGR, and lower in Type I [32]. Selective laser photocoagulation of connecting vessels for Types II and III sFGR revealed a higher mortality, and lower neurological morbidity rate than conservative management. In groups who compared the outcomes of selective reduction with laser treatment, a lower incidence of IUD was found in the larger twin following selective reduction [33]. Figures 13.9, 13.10, 13.11, 13.12, and 13.13 demonstrate the outcomes following cord occlusion, laser, and expectant managements of MC twins with different types of sFGR. It seems important to mention that the optimal management of sFGR type II-III remains largely uncertain as no randomised control trials exist and retrospective cohort studies are prone to several forms of bias.

Fetoscopic Surgery for sFGR in Monochorionic Twins

Selective laser photocoagulation of connecting vessels (SLPCV) is a procedure commonly used for TTTS. Even though these connecting vessels are not the cause for sFGR, coagula-

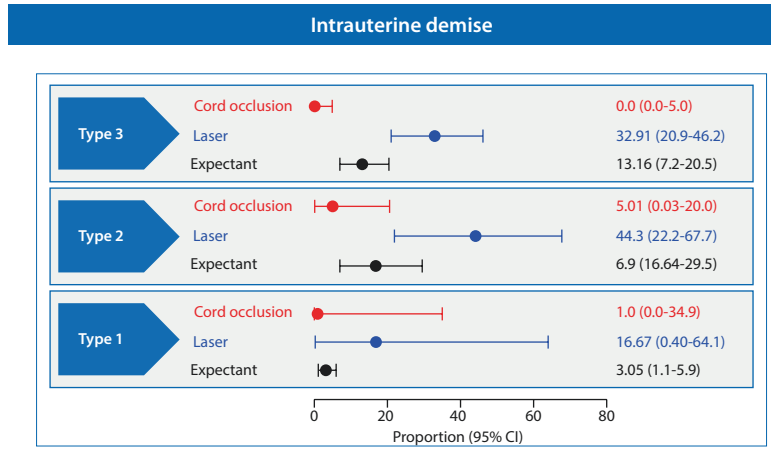

Fig. 13.9 Demonstration of the proportion of intrauterine demise following cord occlusion (in non-reduced larger twin), laser, and expectant management of MC twins with types 1, 2, and 3 sFGR [33]

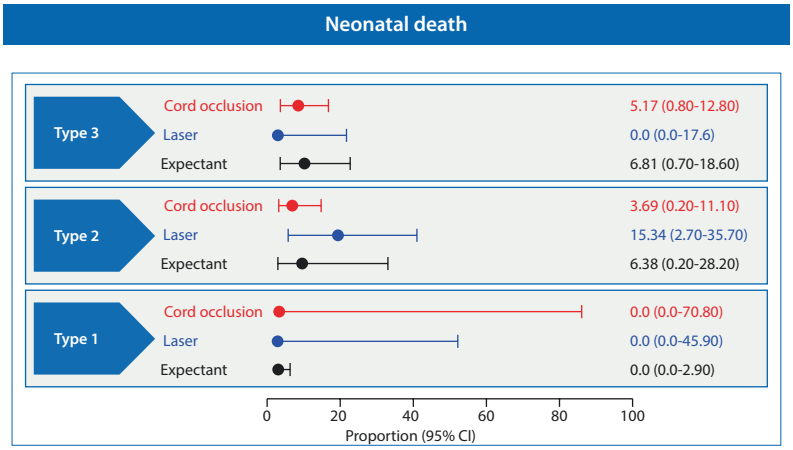

Fig. 13.10 Demonstration of the proportion of neonatal death following cord occlusion (in non-reduced larger twin), laser, and expectant management of MC twins with types 1, 2, and 3 sFGR [33]

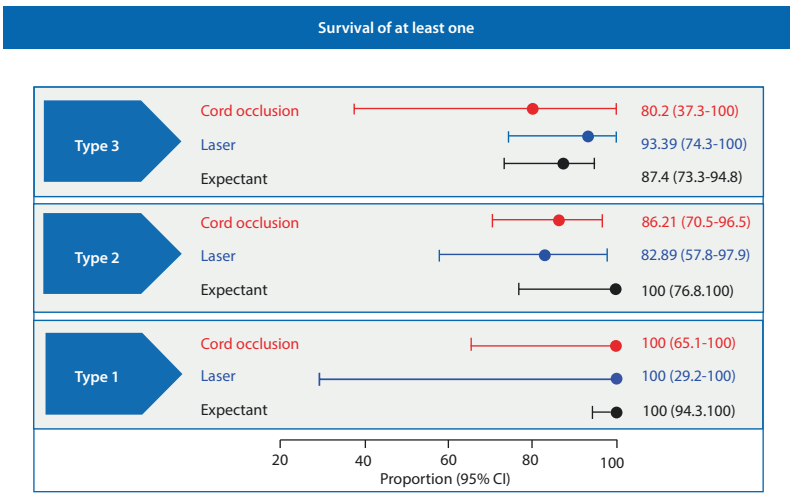

Fig. 13.11 Demonstration of the proportion of survival of at least one twin following cord occlusion (in non-reduced larger twin), laser, and expectant management of MC twins with types 1, 2, and 3 sFGR [33]

tion of these vessels allows separation of the circulations (dichorionisation), allowing protection of the AGA twin in case of co-twin IUD, and may hasten the IUD of the FGR twin, as the protective blood flow from the AGA twin is separated. This technique has an overall survival rate of 53%, and a 72% survival rate of at least one twin. The survival rate of the AGA twin is 68–74% following SLPCV, and the smaller twin 30–39% [21]. This technique is more challenging to perform than for TTTS, due to the normal amniotic fluid volume in the AGA twin (absence of polyhydramnios) [4, 11].

Selective reduction is performed when there is a high risk of single twin demise in the FGR twin prior to 26 weeks. By stopping the blood flow into the FGR twin, it prevents consequences of co-twin demise and neurological sequelae for the AGA twin. Techniques used can include bipolar or laser cord coagulation (Fig. 13.14), radiofrequency ablation (RFA), or interstitial laser coagulation in earlier gestations. This gives a survival rate of 87–93% for the AGA twin, which is higher than that following SLPCV, but given the demise of the FGR twin, the overall survival rate is lower at 44–47% [22–24]. Therefore,

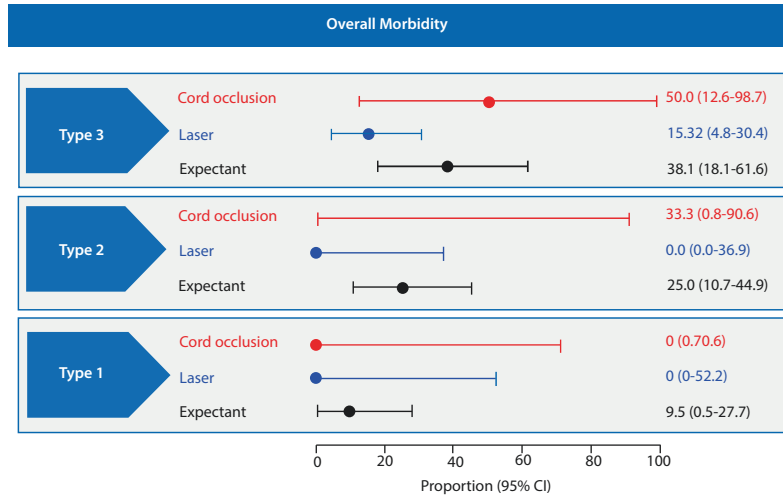

Fig. 13.12 Demonstration of the proportion of the overall neonatal morbidity following cord occlusion (non-reduced larger twin), laser, and expectant management of MC twins with types 1, 2, and 3 sFGR [33]

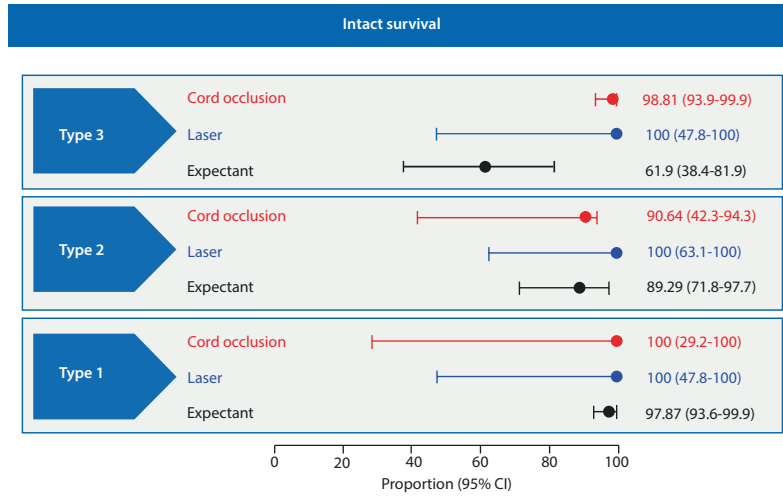

Fig. 13.13 Demonstration of the proportion of intact survival following cord occlusion (non-reduced larger twin), laser, and expectant management of MC twins with types 1, 2, and 3 sFGR [33]

this technique gives a higher survival rate for the AGA twin, but SLPCV allows for possible survival of the FGR twin.

Fetoscopic surgery carries a risk of preterm labour, preterm prelabour rupture of membranes, iatrogenic monoamnionicity, and chorioamnionitis. Therefore, consideration should be taken if fetal deterioration is seen after 26 weeks, to balance the risks and benefits of fetoscopic surgery versus preterm delivery.

13.1.4 Triplet Pregnancies

Limited literature is available for FGR in triplet pregnancies. Attempts have been made to

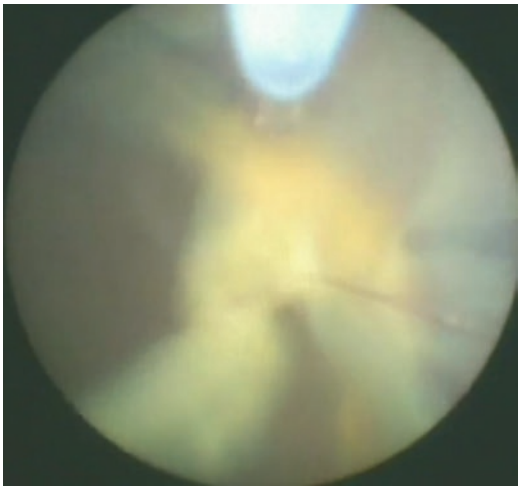

Fig. 13.14 Fetoscopic laser cord occlusion at the site of placental cord insertion, for selective reduction of a twin with severe selective fetal growth restriction

establish normal growth patterns and weight centiles of triplets [34, 35], but currently, singleton growth charts are still being used antenatally to monitor fetal growth. One study found that the incidence of FGR was 13.3% in DC triplets, and 12.3% in trichorionic (TC) triplets [36], whilst an earlier study found this to be as high as 61.8% [37] (defined as birth weight <10th centile). Other observational studies have reported on the incidence of low birthweights in triplets (12.7% TC triplets and 17.4% DC triplets <1000 g, 43% of both groups <1500 g), but this was not adjusted to the gestational age at delivery [38].

In TC triplets, sFGR can be managed in a similar fashion to DC twins. In DC or MC triplets, sFGR in one or more of the monochorionic fetuses can be difficult to manage. Small case series have reported the use of cord occlusion and SLPCV in triplets, where the outcomes were similar to those reported in twin pregnancies (83% survival, 13% long-term comorbidities) [39], but these were not performed for sFGR. Another case series reported the use of SLPCV as a treatment for both sFGR and TTTS in DC and MC triplets. It was found that the overall survival rate was significantly less in DC triplets who underwent SLPCV specifically for sFGR (52.4%) compared to those who received the treatment for TTTS (72.7%) [40].

13.1.5 Conclusion

The management of sFGR poses a clinical conundrum. Conservative management can lead to single twin demise and complications to the surviving co-twin, fetoscopic surgery is associated with a higher mortality of the smaller twin, and early delivery can also expose the AGA twin to significant complications as a result of prematurity. The increased risk of perinatal mortality associated with sFGR requires close monitoring of the condition, whereas over-diagnosis may be minimised using twin-specific growth charts and the most recent diagnostic criteria as proposed by the Delphi consensus. Referral to a tertiary Fetal Medicine centre with adequate levels of expertise is recommended, and patients should be thoroughly counselled regarding the risks and benefits of different management strategies and their outcomes.

13.1.6 Review Questions

1. What is the difference in the etiology of selective fetal growth restriction in monochorionic and dichorionic twins?
2. What is the benefit of designing a uniform diagnostic criterion for selective fetal growth restriction using the Delphi consensus?
3. Describe the differences in umbilical artery end-diastolic flow in the classification of sFGR in monochorionic twins.
4. What is the possible reason that singleton charts are still routinely being used to monitor the growth of twins?
5. What are the options for management in sFGR in monochorionic twins, and what are the differences in outcomes?
6. What are the complications of Type II sFGR in monochorionic twins?

13.1.7 Multiple-Choice Questions

1. What is the incidence of selective fetal growth restriction in dichorionic twins?
   (a) 5.5%
   (b) 10.5%
   (c) 15.5%
   (d) 20.5%
   (e) It depends on the diagnostic criteria used

Answer: (e)

2. Which of the following criteia is not included the diagnosis of selective fetal growth restriction in dichorionic twins?
   (a) Uterine artery PI >95th centile
   (b) Estimated fetal weight <10th centile
   (c) Intertwin estimated fetal weight discordance >25%
   (d) Umbilical artery PI >95th centile

Answer: (a)

3. Which umbilical artery Doppler finding suggests Type III selective fetal growth restriction?
   (a) Persistent absent end-diastolic flow
   (b) Positive end-diastolic flow
   (c) Intermittently reversed end-diastolic flow
   (d) Persistent reversed end-diastolic flow

Answer: (c)

4. What is likely the most optimal management in Type I selective fetal growth restriction?
   (a) Conservative
   (b) Selective laser photocoagulation of connecting vessels
   (c) Selective fetocide
   (d) Early delivery

Answer: (a)

5. What is the favourable outcome following selective fetocide compared to selective laser photocoagulation of connecting vessels in treatment of Types II and III fetal growth restriction?
   (a) Reduced neurological comorbidities this does not follow from the text/ figures
   (b) Reduced risk of twin to twin transfusion syndrome
   (c) Reduced stillbirth in co-twin
   (d) Reduced preterm delivery (I would say this is the correct answer 36 weeks vs 32 weeks)

Answer: (d)

6. What is the rate of preterm delivery following the death of one twin in a dichorionic pregnancy?
   (a) 34%
   (b) 44%
   (c) 54%
   (d) 64%

Answer: (c)

7. What is the main concerning risk in Type III selective fetal growth restriction?
   (a) Increased neurological comorbidity (not entirely wrong)
   (b) Increased risk of sudden intrauterine death
   (c) Increased risk of twin to twin transfusion syndrome
   (d) Increased risk of disease progression

Answer: (b)

Patient Testimonials

Stijn and Ruben, Fetal Growth Restriction from a Parent's Perspective

Our little boys, Stijn and Ruben, identical monochorionic twins, were born at 28 weeks and 4 days into the pregnancy. They are now plucky little 5-year-olds. However, my pregnancy and the first year of their life did not proceed in line with what we are usually told or read. Pregnancy diabetes, a difference in growth between the two babies, an emergency caesarean section, premature birth, operations, etc., led to an emotional, fearful period raising many questions.

During the first 2 months, everything went well and I encountered no problems. It all started on a night in January when I suffered blood loss. An ultrasound scan revealed that the babies were growing at a different rate and there was doubt as to whether my pregnancy could continue. Because I was being monitored at a fairly small hospital, I was referred to UZ Leuven, which has a team that specialises in monochorionic twins.

My pregnancy was associated with several risks, including twin-to-twin transfusion syndrome between 16 and 26 weeks of pregnancy, discordant growth, or a disorder in one of the babies. It soon became clear after the first examination that it was a case of growth discordance. To monitor the babies as closely as possible and avoid any potential risk, I was monitored with a weekly ultrasound scan. These were always quite worrying moments. Would both hearts still be beating? Would more problems be detected? It makes your pregnancy an emotional and stressful roller coaster. Other women can enjoy their pregnancy and hope it isn't over too soon, but I kept wishing to be another week ahead.

As my pregnancy progressed, we received some more bad news. The brain of the smallest baby wasn't developing as it should. Again, we were given extensive information and were kept up to date. The brain volume was measured at regular intervals and a final estimate would be made at 23 weeks. Would we continue with the pregnancy? Would we decide to keep one baby or give up altogether? Aware that there were quite a few risks, my (mother) heart told me that we would fight this together and not give up. From that moment on, I wanted to name my babies. The biggest baby became Ruben and the smallest one Stijn. This was particularly important to me, because I was safe in the knowledge that our boys had a name, even if something went wrong.

You continue to hope and wait with trepidation. Despite everything and the fact that Stijn's brain was not developing at the same rate, the outlook was still relatively good. When I was 23 weeks pregnant, an assessment was made and fortunately, Stijn's brain had developed satisfactorily to continue the pregnancy.

It became clear that I would be admitted for observation at 28 weeks and have a caesarean section at 32 weeks. Whilst I was in hospital, I was connected to the monitor three times a day. I needed regular glucose tests because of my pregnancy diabetes and had to stick to quite a strict diet.

Sunday 22 May 2011, the fourth day of admission, things suddenly changed apace. The morning graph on the monitor clearly showed there was a problem with Stijn as his heartbeat increased from 80 to 200. There was no other option but to perform a caesarean as soon as possible. Ruben weighed 1.550 kg and Stijn 670 g.

The adrenaline that pumped through my body at the time has awoken a sense of determination in me since the birth of Ruben and Stijn that I was unaware I possessed. Once again, you are confronted with fear about how everything will progress, what the babies' chances are, etc. We were told during the pregnancy that the babies would have to spend some time in the neonatal care unit. Due to the emergency caesarean, my husband and I did not have time to visit this department beforehand, but being a nurse myself, I knew more or less what to expect, e.g. monitors, alarms, drips, etc. Nevertheless, I was now a mother and that initial confrontation was quite difficult and emotional.

The first few days were quite challenging. You miss your babies, your emotions are all over the place, you wonder why on earth you had to give birth so prematurely. Aspects that you cannot control yourself and that make you feel powerless. It subsequently became clear that Stijn had been saved before he was born thanks to the twin-to-twin transfusion with Ruben. Without Ruben, Stijn would only have weighed 100 g. That was quite sobering news, we were incredibly lucky.

We received excellent support at the neonatal care unit. We were allowed to see our babies whenever we wanted to. Despite everything that happened, the time went relatively quickly. Ruben and Stijn's condition varied from day to day, small steps forward and sometimes a step backward. New worries and fears presented themselves time and again. Five days after the birth we were told that Stijn suffered from narrowing of the aorta, which was operable but not before he weighed 2.5 kg. A decision was made to insert a temporary stent as soon as he weighed 1 kg. Before that, he was put on medication. After a while, Stijn suffered a pulmonary haemorrhage, but once again he fought his way through. Ruben developed relatively well until they found blood in his stools due to an intestinal infection, which almost resulted in him having a perforated bowel. Fortunately, swift action avoided this. Stijn received a temporary stent on 20th June. It was a particularly high-risk operation with a 50% chance of success, but our little fighter once again pulled through.

Ruben was allowed to come home on 30th July. We obviously had mixed feelings. On the one hand, we were very pleased, but on the other hand, we were sad because we had to leave our other baby behind. Stijn continued to improve but still had to be put in isolation twice when a bacterium was found in his stools. His stent had to be dilated on 6th September. But then … finally!!!! Stijn was allowed to leave hospital on 15th September. My husband and I went to collect him, together with Ruben, a very emotional moment. I had waited so long for this, but finally my family was united! Stijn's operation to treat the narrowing of the aorta went well. Both boys are thriving. During the first 3 years, they were particularly vulnerable and more prone to becoming sick. Now, however, things have much improved.

Because of everything I went through during my pregnancy and the problems affecting Ruben and Stijn after the birth, I have learnt to put things into perspective in life. It was definitely not easy but looking around me, I realised that some people face even greater challenges. We were lucky because our boys were real fighters. It isn't always easy, but despite everything you must not lose faith and continue to hope and believe that it will turn out alright in the end. I always continued to put my faith in Stijn and Ruben and when I see how far they have come, I can only be incredibly happy and more than anything infinitely grateful.

References

1. D'Antonio F, Odibo AO, Prefumo F, Khalil A, Buca D, Flacco ME, Liberati M, Manzoli L, Acharya G. Weight discordance and perinatal mortality in twin pregnancy: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018;52(1):11–23.
2. Hillman SC, Morris RK, Kilby MD. Co-twin prognosis after single fetal death: a systematic review and meta-analysis. Obstet Gynecol. 2011;118:928–40.
3. Glinianaia SV, Obeysekera MA, Sturgiss S, Bell R. Stillbirth and neonatal mortality in monochorionic and dichorionic twins: a population-based study. Hum Reprod RCOG, London. 2011;26(9):2549–57.
4. Townsend R, Khalil A. Twin pregnancy complicated by selective growth restriction. Curr Opin Obstet Gynecol. 2016;28(6):485–91.
5. Lewi L, Gucciardo L, van Mieghem T, de Koninck P, Beck V, Medek H, Van Schoubroeck D, Devlieger R, De Catte L, Deprest J. Monochorionic diamniotic twin pregnancies: natural history and risk stratification. Fetal Diagn Ther. 2010;27:121–33.
6. Valsky DV, Eixarch E, Martinez JM, Crispi F, Gratacós E. Selective intrauterine growth restriction in monochorionic twins: pathophysiology, diagnostic approach and management dilemmas. Semin Fetal Neonatal Med. 2010;15:342–8.
7. Inklaar MJ, van Klink JM, Stolk TT, van Zwet EW, Oepkes D, Lopriore E. Cerebral injury in monochorionic twins with selective intrauterine growth restriction: a systematic review. Prenat Diagn. 2014;34:205–13.
8. Stirrup OT, Khalil A, D'Antonio F, Thilaganathan B. Fetal growth reference ranges in twin pregnancy: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. Ultrasound Obstet Gynecol. 2015;45(3):301–7.
9. Wu D, Huang L, He Z, et al. Pre-eclampsia in twin pregnancies: association with selective intrauterine growth restriction. J Matern Fetal Neonatal Med. 2016;29:1967–71.
10. ISUOG. Practice guidelines: the role of ultrasound in twin pregnancy. Ultrasound Obstet Gynecol. 2016;47:247–63.
11. Townsend R, Khalil A. Fetal growth restriction in twins. Best Pract Res Clin Obstet Gynaecol. 2018;49:79–88.
12. Khalil A, Beune I, Hecher K, Wynia K, Ganzevoort W, Reed K, Lewi L, Oepkes D, Gratacós E, Thilaganathan B, Gordijn SJ. Consensus definition and essential reporting parameters of selective fetal growth restriction in twin pregnancy: a Delphi procedure. Ultrasound Obstet Gynecol. 2019;53:47–54.
13. Gratacós E, Lewi L, Munoz M, Acosta-Rojas R, Hernandez-Andrade E, Martinez JM, Carreras E, Deprest J. A classification system for selective intrauterine growth restriction in monochorionic pregnancies according to umbilical artery Doppler flow in the smaller twin. Ultrasound Obstet Gynecol. 2007;30:28–34.
14. Ishii K, Murakoshi T, Takahashi Y, et al. Perinatal outcome of monochorionic twins with selective intrauterine growth restriction and different types of umbilical artery Doppler under expectant management. Fetal Diagn Ther. 2009;26:157–61.
15. Vanlieferinghen S, Anselem O, Le RC, Shen Y, Marcellin L, Goffinet F. Prognostic value of umbilical and cerebral Doppler in fetal growth restriction: comparison of dichorionic twins and singletons. PLoS One. 2015;10(4):e0123067.
16. Audibert F, Salomon LJ, Castaigne-Meary V, et al. Selective termination of a twin pregnancy as a treatment of severe preeclampsia. BJOG. 2003;110:68–9.
17. Hillman SC, Morris RK, Kilby MD. Co-twin prognosis after single fetal death: a systematic review and meta-analysis. Obstet Gynecol. 2011;118:928–40.
18. Rustico MA, Consonni D, Lanna M, et al. Selective intrauterine growth restriction in monochorionic twins: changing patterns in umbilical artery Doppler flow and outcomes. Ultrasound Obstet Gynecol. 2017;49(3):387–93.
19. D'Antonio F, Khalil A, Dias T, Thilaganathan B. Southwest Thames Obstetric Research Collaborative (STORK). Weight discordance and perinatal mortality in twins: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. Ultrasound Obstet Gynecol. 2013;41:643–8.
20. Memmo A, Dias T, Mahsud-Dornan S, Papageorghiou AT, Bhide A, Thilaganathan B. Prediction of selective fetal growth restriction and twin-to-twin transfusion syndrome in monochorionic twins. BJOG. 2012;119(4):417–21.
21. Peeva G, Bower S, Orosz L, Chaveeva P, Akolekar R, Nicolaides KH. Endoscopic placental laser coagulation for monochorionic diamniotic twins with type II selective fetal growth restriction. Fetal Diagn Ther. 2015;38(2):86–93.
22. Bebbington MW, Danzer E, Moldenhauer J, Khalek N, Johnson MP. Radiofrequency ablation vs bipolar umbilical cord coagulation in the management of complicated monochorionic pregnancies. Ultrasound Obstet Gynecol. 2012;40(3):319–24.
23. Chalouhi GE, Marangoni MA, Quibel T, Deloison B, Benzina N, Essaoui M, et al. Active management of selective intrauterine growth restriction with abnormal Doppler in monochorionic diamniotic twin pregnancies diagnosed in the second trimester of pregnancy. Prenat Diagn. 2013;33(2):109–15.
24. Parra-Cordero M, Bennasar M, Martínez JM, Eixarch E, Torres X, Gratacós E. Cord occlusion

in monochorionic twins with early selective intrauterine growth restriction and abnormal umbilical artery doppler: a consecutive series of 90 cases. Fetal Diagn Ther. 2016;39(3):186–91.
25. Vasario E, Borgarello V, Bossotti C, Libanori E, Biolcati M, Arduino S, Spinelli R, Delle Piane L, Revelli A, Todros T. IVF twins have similar obstetric and neonatal outcome as spontaneously conceived twins: a prospective follow-up study. Reprod Biomed Online. 2010;21(3):422–8.
26. Geisler ME, O'Mahony A, Meaney S, Waterstone JJ, O'Donoghue K. Obstetric and perinatal 254 outcomes of twin pregnancies conceived following IVF/ICSI treatment compared with 255 spontaneously conceived twin pregnancies. Eur J Obstet Gynecol Reprod Biol. 2014;78-83(256):181.
27. Moini A, Shiva M, Arabipoor A, Hosseini R, Chehrazi M, Sadeghi M. Obstetric and neonatal outcomes of twin pregnancies conceived by assisted reproductive technology compared with twin pregnancies conceived spontaneously: a prospective follow-up study. Eur J Obstet Gynecol Reprod Biol. 2012;165(1):29–32.
28. Qin JB, Wang H, Sheng X, Xie Q, Gao S. Assisted reproductive technology and risk of adverse obstetric outcomes in dichorionic twin pregnancies: a systematic review and meta-analysis. Fertil Steril. 2016;105(5):1180–92.
29. Gerber RS, Fields JC, Barberio AL, Bodenlos K, Fox NS. Outcomes of twin pregnancies in women 45 years of age or older. Obstet Gynecol. 2017;129(5):827–30.
30. Curado J, Sileo F, Bhide A, Thilaganathan B, Khalil A. Early and late selective fetal growth restriction in monochorionic diamniotic twin pregnancies: natural history and diagnostic criteria. Ultrasound Obstet Gynecol. 2019; https://doi.org/10.1002/uog.20849. [Epub ahead of print]
31. Hamilton E, Platt R, Morin L, Usher R, Kramer M. How small is too small in a twin pregnancy? Am J Obstet Gynecol. 1998;179:682–5.
32. Buca D, Pagani G, Rizzo G, Familiari A, Flacco ME, Manzoli L, Liberati M, Fanfani F, Scambia G, D'Antonio F. Outcome of monochorionic twin pregnancy with selective intrauterine growth restriction according to umbilical artery Doppler flow pattern of smaller twin: a systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2017;50(5):559–68.
33. Townsend R, D'Antonio F, Sileo FG, Kumbay H, Thilaganathan B, Khalil A. Perinatal outcome of monochorionic twin pregnancy complicated by selective fetal growth restriction according to management: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2019;53(1):36–46.
34. Min SJ, Luke B, Min L, Misiunas R, Nugent C, Van de Ven C, Martin D, Gonzalez-Quintero VH, Eardley S, Witter FR, Mauldin JG, Newman RB. Birth weight references for triplets. Am J Obstet Gynecol. 2004;191(3):809–14.
35. Vora NL, Ruthazer R, House M, Chelmow D. Triplet ultrasound growth parameters. Obstet Gynecol. 2006;107(3):694–700.
36. Spencer J, Ingardia C, Nold C, Borgida A, Herson V, Egan J. Perinatal and neonatal outcomes of triplet gestations based on placental chorionicity. Am J Perinatol. 2009;26(08):587–90.
37. Boulot P, Hedon B, Pelliccia G, Sarda P, Montoya F, Mares P, Humeau C, Arnal F, Laffargue F, Viala JL. Favourable outcome in 33 triplet pregnancies managed between 1985-1990. Eur J Obstet Gynecol Reprod Bio. 1992;43(2):123–9.
38. Simões T, Queiros A, Gonçalves MR, Periquito I, Silva P, Blickstein I. Perinatal outcome of dichorionic-triamniotic as compared to trichorionic triplets. J Perinat Med. 2016;44(8):875–9.
39. Schoubroeck D, Lewi L, Ryan G, Carreras E, Jani J, Higueras T, Deprest J, Gratacos E. Fetoscopic surgery in triplet pregnancies: a multicenter case series. Am J Obstet Gynecol. 2004;191(5):1529–32.
40. Peeva G, Chaveeva P, Gil Guevara E, Akolekar R, Nicolaides KH. Endoscopic placental laser coagulation in dichorionic and monochorionic triplet pregnancies. Fetal Diagn Ther. 2016;40:174–80.

Key Reading

Gratacós E, Lewi L, Munoz M, Acosta-Rojas R, Hernandez-Andrade E, Martinez JM, Carreras E, Deprest J. A classification system for selective intrauterine growth restriction in monochorionic pregnancies according to umbilical artery Doppler flow in the smaller twin. Ultrasound Obstet Gynecol. 2007;30:28–34.

ISUOG. Practice guidelines: the role of ultrasound in twin pregnancy. Ultrasound Obstet Gynecol. 2016;47:247–63.

Khalil A, Beune I, Hecher K, Wynia K, Ganzevoort W, Reed K, Lewi L, Oepkes D, Gratacós E, Thilaganathan B, Gordijn SJ. Consensus definition and essential reporting parameters of selective fetal growth restriction in twin pregnancy: a Delphi procedure. Ultrasound Obstet Gynecol. 2019;53:47–54.

Townsend R, Khalil A. Twin pregnancy complicated by selective growth restriction. Curr Opin Obstet Gynecol. 2016;28(6):485–91.

Townsend R, Khalil A. Fetal growth restriction in twins. Best Pract Res Clin Obstet Gynaecol. 2018;49:79–88.