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Definition of IUGR in twins

Proposed definitions

- Discordance >20% - >25%
(O'Brien et al 1986, Erkkola et al 1985, Blickstein et al 2003)
- Discordance >25% is associated with an increased risk of neonatal mortality
(Tan et al 2005)

Definition of IUGR in twins

Discordance

- **Discordance ≠ IUGR**
 - both fetuses can be AGA, yet have a discordance >20-25%
- The rate of >25% discordance decreases as the total twin weight (weight of twin A + weight of twin B) increases
(Blickstein 1999)

Discordance and percentile

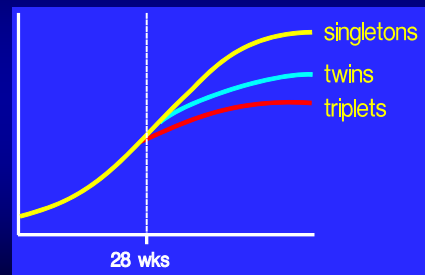
However:

- Selective MC-IUGR is only present in 50% of patients with 20% discordance
(O'Brien 1986)
- >25% discordance is only present in 67% of patients with Selective MC-IUGR and TTTS
(Quintero et al, 2007)

Definition of IUGR in twins

- IUGR should be defined solely on the diagnosis of an AC <2 SD (FW <10th percentile)

What growth chart should we use?



Differential diagnosis between TTTS and Selective MC-IUGR

TTTS

- ❑ Maximum vertical pocket >8, <2
- ❑ Estimated fetal weight discordance: 0-65%

Selective MC-IUGR

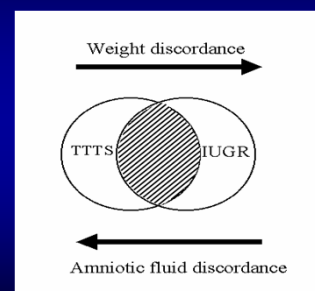
IUGR

- ❑ Maximum vertical pockets ≠ >8, <2
- ❑ Estimated fetal weight <10th ile

Discordance not used in the definition



Relationship between TTTS and Selective MC-IUGR



Classification of IUGR in twins

- ❑ Both twins IUGR
- ❑ Only one twin IUGR
 Selective IUGR = Selective MC-IUGR
- ❑ IUGR with TTTS

INCIDENCE

- Selective MC-IUGR occurs in 25% of all MC twins
- For comparison:
- twin-twin transfusion syndrome occurs in 5-15% of all MC twins

Gaziano EP, et al. J Matern Fetal Med 2000;9:89-96.

Pathophysiology

- Etiology of **Selective MC-IUGR**
- Natural history of **Selective MC-IUGR**

Etiology

- Placental insufficiency
- Placental territory
- Vascular anastomoses
- Nutritional factors

Placental insufficiency

- Impaired trophoblastic invasion supported by increased resistance in spiral arteries
- Unequal allocation of blastomeres in the first trimester
- Both twins may be affected but with different severity

Placental territory

May be responsible for:

- Severe discordance
- Selective MC-IUGR in twin gestations
- Postoperative IUFD of a single fetus after laser surgery.

Placental territory

Individual Placenta Territory

- The individual placental mass divided by the total placental mass
- Survival can occur with as little as 10% and 14% placental territory in non-TTTS and TTTS patients respectively laser
- Cases with unequal placental sharing have a 9.8 times greater likelihood of birth weight discordance, than cases with equal placental sharing

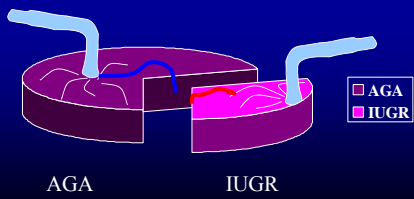
Vascular anastomoses

Two kinds of communications between two MC fetuses:

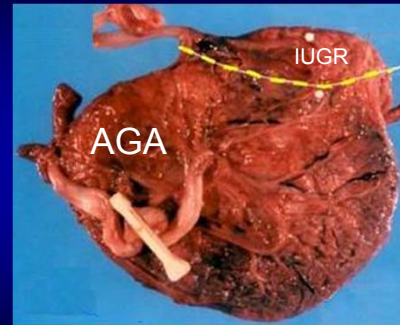
- **Deep (AV):** involve the sharing of one cotyledon by both twins
- **Superficial communications (AA and VV):** AA anastomoses consist of an arterial vessel at both ends.

Etiology of Selective MC-IUGR

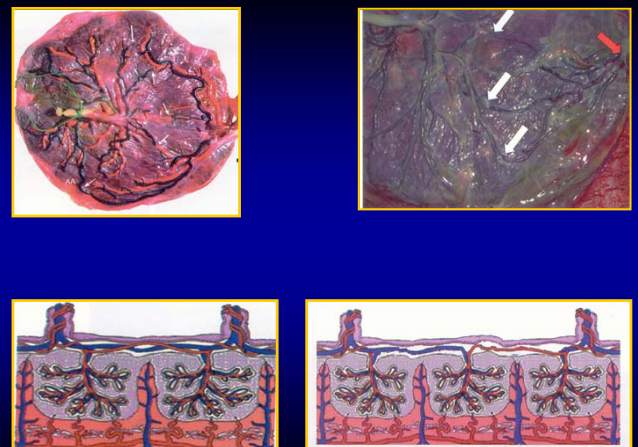
- Abnormal placental sharing
- Vascular anastomoses



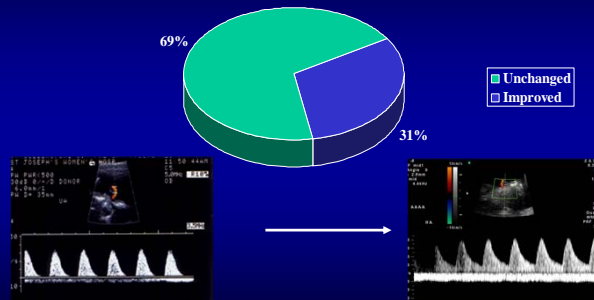
Abnormal placental sharing



Is there evidence that vascular anastomoses are related to **Selective MC-IUGR**?



Improvement in umbilical artery Doppler studies after laser for Selective MC-IUGR



Chang YL, Chmait R, Quintero R. ISUOG 2005

Catch-up growth

- Weight discordance decreases after laser therapy for twin-twin transfusion syndrome.

Chmait R, Chang YL, Bornick PW, Quintero RA, ISUOG 2005

Cord abnormalities

Velamentous cord insertion

- More common in
 - Selective MC-IUGR and TTTS than in appropriately grown MC twins
- the donor twin or in the Selective MC-IUGR twin, but not in the smaller of control twins

AA anastomoses

- Consist of an arterial vessel at both ends.
- Both twins pump blood towards opposite directions within this vessel.
- Depending on the pressure gradient between the two fetuses and the presence or absence of arterial branches, → AA anastomoses may behave as functional AV unidirectional communications

AA anastomoses

- Absence of superficial anastomoses has been correlated with the development of TTTS
- umbilical artery Doppler indices in a subset of Selective MC-IUGR twins improves following laser treatment Murakoshi et al 2003
- catch-up growth of Selective MC-IUGR fetuses which has been observed after laser Schmalt 2005

Nutritional Factors

Lack of transfer of nutrients probably not a cause in the development of Selective MC-IUGR.

- Fetal plasma leptin concentrations are 2-fold higher in the AGA than in the IUGR twin
- Fetal IGFBP-1 is high in the IUGR twin but not in the AGA twin or in concordant twin pairs.

Complications

Monochorionic (MC) pregnancies

- Perinatal mortality rate adjusted for age twice as high in MC twins but is the same in dichorionic twins and singletons (Hamilton 1998)
- **Can develop TTTS and Selective MC-IUGR.**

Selective MC-IUGR complications

- Increased morbidity/mortality secondary to:
 1. Iatrogenic premature delivery
 2. Fetal demise of the one twin

Iatrogenic premature delivery

- Affects almost 100% of MC twin pregnancies with Selective MC-IUGR
- Advised in order to avoid the consequences of the potential in utero demise of the Selective MC-IUGR twin

Single Fetal Demise In Twin Gestation

Incidence

- Variable
- 5-25 %
- Higher in certain subsets of MC gestations

Single Fetal Demise In Twin Gestation

- In Selective MC-IUGR pregnancies intrauterine fetal demise (IUFD) was 14% when the Selective MC-IUGR twin had normal Dopplers and 20% with AREDV
Gratacos 2004
- IUFD rate 4.6% in MC pregnancies with simple discordance vs. 26.3% in Selective MC-IUGR with AREDV of the smaller twin
Huber 2006

Consequences of single fetal death in MC gestations

- Demise of the second twin up to 25% of the cases
- Neuromorbidity of the second twin

Mechanism

➤ Older theory

Thromboplastic material from the dead fetus enters the co-twin's circulation via patent placental vascular anastomoses causing DIC with subsequent fetal and maternal morbidity and mortality.

Mechanism

Recent data

➤ Exsanguination of the surviving twin into the demised fetus results in acute hypotension of the survivor

➤ Serial fetal hemoglobin measurements obtained by cordocentesis in surviving MC twins showed anemia

Okamura 1994

➤ Perimortem fetofetal hemorrhage observed during fetoscopy with a plethoric IUFD twin and a pale surviving twin

Quintero 2002

Neuromorbidity

➤ Cerebral palsy, intraventricular hemorrhage (IVH) grade III and IV, periventricular leukomalacia.

➤ Incidence ranges from 0 to 60%.

➤ Antenatal detection possible with ultrasound/MRI.

Natural history of Selective MC-IUGR

➤ Demise of the IUGR twin: 2-26%

➤ Co-demise of the AGA twin: 9-40%

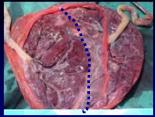
➤ Neurological damage to surviving co-twin: 18%

*Burke MS. Single fetal demise in twin gestation. Clin Obstet Gynecol. 1990;33:69-78.

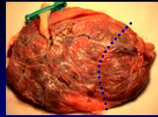
*Lin JJ, et al. Infants of twin pregnancies with one twin demise in the uterus. Taiwan Erh Ko I Hsueh Hui Tsa Chih. 1999;40:92-6.

*Petersen IR, et al. Multiple pregnancies with single intrauterine demise. Acta Obstet Gynecol Scand. 1999;78:202-6.

*Fuji L, Gordon H. Twin pregnancy complicated by single intrauterine death. Br J Obstet Gynaecol. 1990;97:511-6.

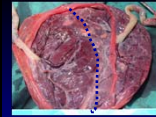


Selective IUGR

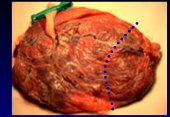


- Discordance: $(A-B) \times 100/A$
- Definition: $< 10\%$ EFW

One parameter which best reflects the differences in intrauterine growth restriction (IUGR) in MC with respect to singletons or dichorionic twins is **umbilical artery (UA) Doppler flow**.



Selective IUGR



In MC fetuses with IUGR, UA Doppler flow may show one of three main waveform patterns, as defined by the characteristics of diastolic flow:

- Positive diastolic flow **TYPE-1**
- **persistently absent/reversed** **TYPE-2**
- **intermittently absent/reversed** **TYPE-3**

a cyclical pattern and unique to MC twins resulting from the presence of transmitted waveforms from the larger into the smaller twin's cord due to the existence of **placental large artery-to-artery(AA) anastomoses**.

Selective MC-IUGR

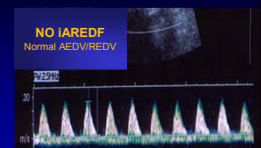
TYPE-1

- Positive diastolic flow :

Fetuses with positive UA diastolic flow are generally considered to have a benign prognosis, although there are no prospective studies addressing the outcome of this subgroup.

Gratacos E, Lewi L, Carreras E, Becker J, Higuera T, Deprest J, Cabero L. Ultrasound Obstet Gynecol 2004; 23: 456-460
Huber A, Diehl W, Zalusig L, Bregenzler T, Hackelbauer BJ, Hecher K. Ultrasound Obstet Gynecol 2006; 27: 46-52.

Selective MC-IUGR



TYPE-2

- Persistently absent/reversed :

Fetuses with **persistently** absent or reversed end-diastolic flow (AREDF) in the UA have been reported to have a high risk of hypoxic deterioration and consequently intrauterine demise

Gratacos E, Lewi L, Carreras E, Becker J, Higuera T, Deprest J, Cabero L. Ultrasound Obstet Gynecol 2004; 23: 456-460
Huber A, Diehl W, Zalusig L, Bregenzler T, Hackelbauer BJ, Hecher K. Ultrasound Obstet Gynecol 2006; 27: 46-52.

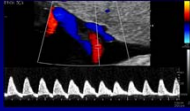
Selective MC-IUGR

TYPE-3

intermittently absent/reversed :

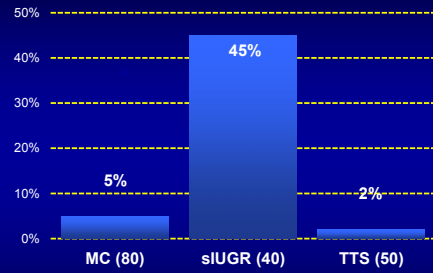
Fetuses with intermittent absent or reversed end-diastolic flow (iAREDF) normally show an atypical clinical evolution

- with an increased risk of sudden death of the IUGR twin
- increased rate of parenchymal brain damage in the normally grown twin.

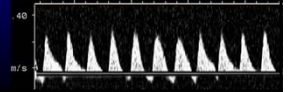


Gratacos E, Lewi L, Carreras E, Becker J, Higuera T, Deprest J, Cabero L. Ultrasound Obstet Gynecol 2004; 23: 456-460
Huber A, Diehl W, Zikulinig L, Bregenzer T, Hackeloeer BJ, Hecher K. Ultrasound Obstet Gynecol 2006; 27: 49-52.

Incidence of intermittent diastolic flow in MC pregnancies



*p < .0001

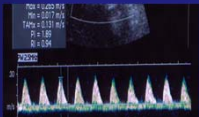


E. Gratacos, L. Lewi, E. Carreras, J. Becker, T. Higuera, J. Deprest. UOG 2004

Selective MC-IUGR (growth discordance >25 %)

To treat or not to treat?

no iAREDF (n=38) ("normal" AEDV/REDV)



expectant

n= 33

EG 31

IUFD 1/33

LM 6%

delivery 30w

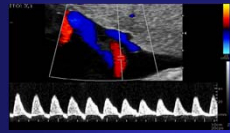
n=28

EG 31

IUFD 14 % (4)

LM 19% (3)

iAREDF (n=44)



laser*

n=16

EG 33

IUFD 62 % (10)

LM 6 % (4)

cord occl.

n=5

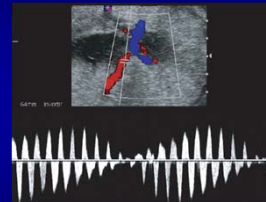
EG 35

IUFD 0/6

LM 0%

Gratacos E, Deprest J et al.

The large placental arterioarterial anastomoses bidirectional and periodic pattern resulting from the collision of the two systolic waveforms.

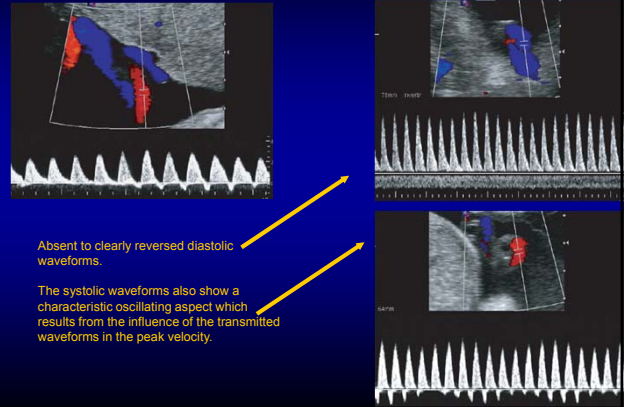


Taylor MJ, Denbow ML, Tanawattanacharoen S, Gannon C, Cox PM, Fisk NM. Hum Reprod 2000; 15: 1632-1636.

Selective IUGR

- The management protocol considered the option of cord occlusion in the smaller twin if severe fetal deterioration was observed before 28 weeks

Typical image of iAREDF with cycles showing absent and/or reversed flow.



Ultrasound Obstet Gynecol 2007; 30: 28–34

A classification system for selective intrauterine growth restriction in monozygotic pregnancies according to umbilical artery Doppler flow in the smaller twin
E. GRATACOS[†], L. LEWIS, B. MUÑOZ[†], R. ACOSTA-ROJAS[†], E. HERNANDEZ-ANDRADE[†], J. M. MARTINEZ[†], E. CARRERAS[†] and J. DEPREST[‡]

Table 1 Pregnancy course and perinatal outcome according to umbilical artery Doppler classification

Parameter	Normal (n = 76)	Type I (n = 39)	Type II (n = 30)	Type III (n = 65)
GA at diagnosis (weeks, mean (range))	—	23 (16–27)	20 (16–25)	22 (16–26)
GA at delivery (weeks, mean (range))	35.5 (30–38)	35.4 (16–38)	30.7 (27–40)*	31.6 (23–39)*
Birth weight (g, mean (range))	—	—	—	—
Larger twin	2439 (1450–3530)	2385 (1200–3350)	1468 (760–2900)*	1713 (930–3450)*
Smaller twin	2187 (1260–3233)	1688 (800–2400)	787 (390–1360)*	1017 (450–2130)*
Fetal weight discordance (%), mean (range)	10 (1–22)	29 (25–37)*	38 (25–58)*	36 (25–64)*
In-utero deterioration of IUGR fetus (n (%))	—	0/39 (0)	27/30 (90.0)†	7/65 (10.8)
Unexpected IUFD (n (%))	—	—	—	4/65 (6.2)
Larger twin	—	1/39 (2.6)	0/30 (0)	10/65 (15.4)‡
Smaller twin	—	1/39 (2.6)	0/30 (0)	—
Intraventricular hemorrhage (n (%))	—	—	—	—
Larger twin	—	0/38 (0)	1/30 (3.3)	2/61 (3.3)
Smaller twin	—	0/38 (0)	3/21 (14.3)‡	3/50 (6.0)
Parenchymal brain damage (n (%))	—	—	—	—
Larger twin	—	0/38 (0)	1/30 (3.3)	12/61 (19.7)‡
Smaller twin	—	0/38 (0)	3/21 (14.3)‡	1/50 (2.0)

*P < 0.0001 vs. uncomplicated and Type I; †P < 0.0001 vs. Type I and Type III; ‡P < 0.05 vs. Type I; §P < 0.05 vs. Type I and Type II. GA, gestational age; IUFD, intrauterine fetal death; IUGR, intrauterine growth restriction.

Selective MC-IUGR

- Fetal deterioration in Type II MC twins (persistent AREFD) could be predicted in most cases by close fetal monitoring, allowing timely cord occlusion or elective delivery. Elective laser coagulation of the placental anastomoses for cases defined as Type II in this study has been proposed as an alternative to cord occlusion.
- MC twins presenting with iAREDF, and defined as Type III in this study, have a distinct condition among Selective MC-IUGR MC twins.
- MC twins presenting with iAREDF are characterized by an atypical clinical evolution of the IUGR twin, which normally fails to show Doppler signs suggesting fetal deterioration, as would be expected for fetuses with similar degrees of growth restriction.

Selective MC-IUGR

- Selective intrauterine growth retardation (IUGR) occurs in approximately 10% of monozygotic twins. IUGR in monozygotic twins typically affects only one of the fetuses (selective IUGR, Selective MC-IUGR).
- The definition of Selective MC-IUGR as follows: one twin measures less than the 10th percentile for the given gestational age;
- the Selective MC-IUGR twin has persistent absent or reversed flow in the umbilical artery.
- Note that amniotic fluid discordance plays no role in the diagnosis of this condition.
- Selective MC-IUGR appears to be a distinct condition from TTTS, albeit there may be significant overlap. It is believed that Selective MC-IUGR develops because of unequal placental share, with the Selective MC-IUGR fetus utilizing a minority portion of the common placenta. In addition, preliminary data from Chang
- Chang YL, Chmait RH, Bornick PW, et al. The role of laser surgery in dissecting the etiology of absent or reverse end-diastolic velocity in the umbilical artery of the donor twin in twin-twin transfusion syndrome. Am J Obstet Gynecol 2006; 195:470-483 have shown that placental vascular anastomoses may also play a causative role in a subset of Selective MC-IUGR patients.

Selective MC-IUGR

- Expectant management of patients with Selective MC-IUGR is associated with a variable likelihood of spontaneous demise of the Selective MC-IUGR twin, which may result in concomitant demise or severe neurological handicap of the appropriately grown (AGA) twin. These complications occur from exsanguination of the AGA twin into the demised Selective MC-IUGR twin through the placental vascular communications.
- The overall survival rate in this subgroup was 60%. The neurological injury rate was not described.
 - Huber A, Diehl W, Zikulnig L, et al. Perinatal outcome in monozygotic twin pregnancies complicated by amniotic fluid discordance without severe twin-twin transfusion syndrome. Ultrasound Obstet Gynecol 2006; 27:48-52.
- The survival rate of the Selective MC-IUGR twin was 59%. The rate of short-term neurological complications (including periventricular leukomalacia, intraventricular hemorrhage, and ventriculomegaly) was 14% of neurological injury in the expectantly managed group versus 0% in the laser group.
 - Quintero RA, Bornick PW, Morales WJ, Allen MH. Selective photocoagulation of communicating vessels in the treatment of monozygotic twins with selective growth retardation. Am J Obstet Gynecol 2001; 185:689-696.

Management of Selective MC-IUGR

- Expectant management. Early delivery
- Termination of pregnancy
- Umbilical-cord occlusion
- ? Selective laser photocoagulation of communicating vessels

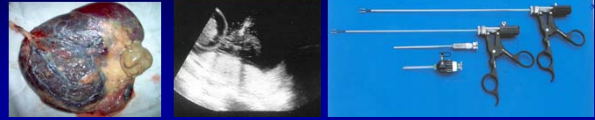
Expectant management

- Allows natural history
- Likelihood of an adverse outcome
 - Co-demise
 - Neurological damage
 - Total adverse outcome: 18-30%
- **Almost always will result in iatrogenic preterm delivery**

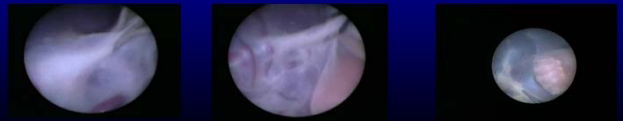
Umbilical-cord occlusion Techniques

- Bipolar electrocoagulation
- Laser photocoagulation of the umbilical cord

Cord occlusion at 16-28 wks



	N	Success	Survival	Delivery <32 wks
Endoscopic laser	6	67%	100%	33%
Cord ligation	24	79%	54%	62%
Bipolar coagulation	32	100%	81%	23%



Laser for Selective MC-IUGR Special considerations

- Lack of polyhydramnios
- Different types of anastomoses
- Different location of the anastomoses

Complications of MZs

- Increased malformation rate
- High order multiples
- Increased placental vascular anomalies

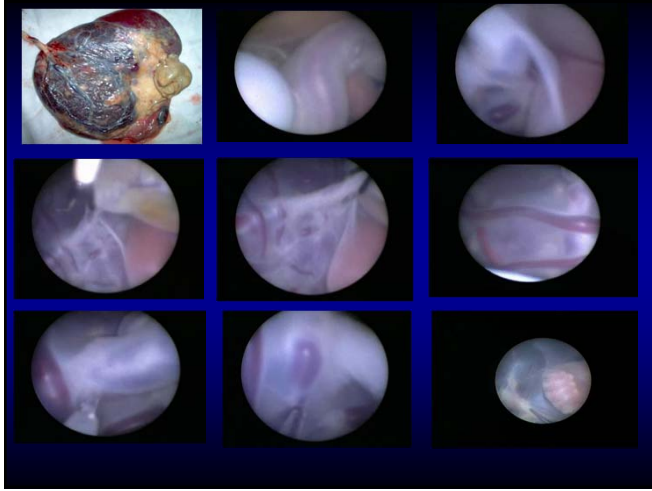
TTTS

TRAP sequence

Selective MC-IUGR

Single twin death

Conjoined twins



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