Monochorionic Twin Gestations

CHORIO-ANGIO-PAGUS
(Placenta-Vascular-Conjoined)

Multiple births, United States: 1980-2014

December 28, 1981: Elizabeth Jordan Carr, America's first "test tube baby", was born.

First IVF baby born in the US

Birth rate (per 1,000 live births)

40
35
30
25
20
15

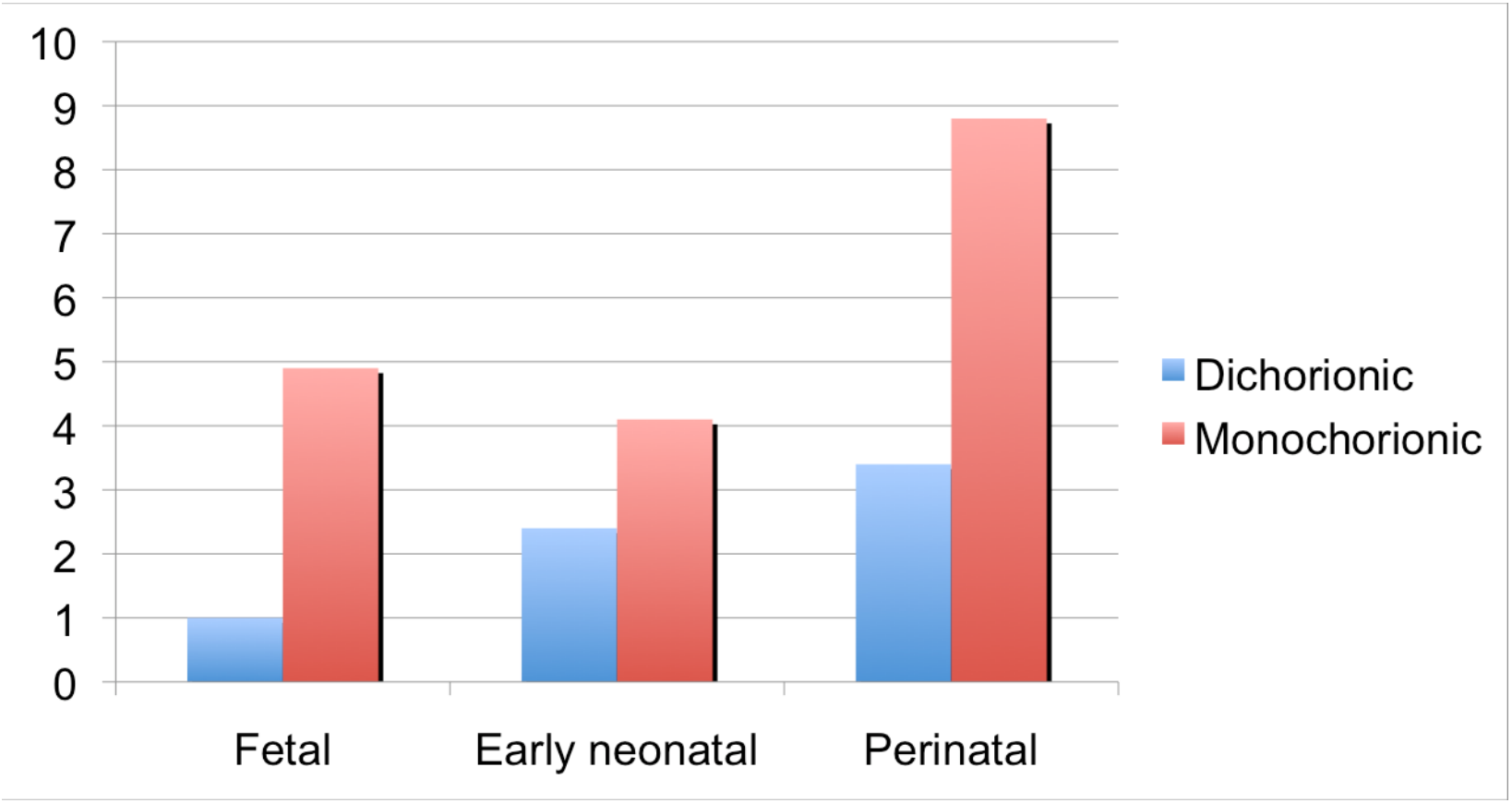
1980 1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014

Multiple Birth Rate
Twin Birth Rate

76% increase

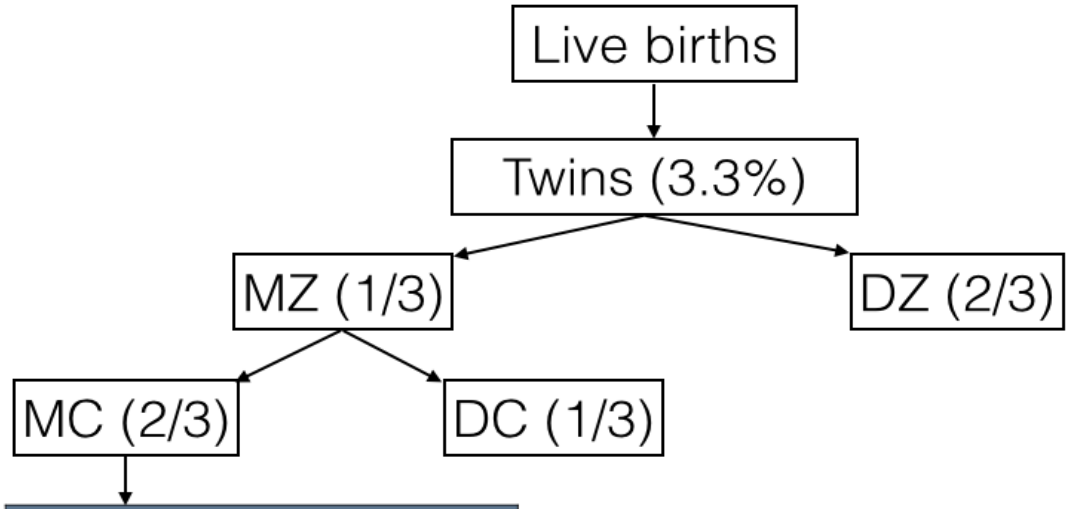
National Vital Statistics Reports, Vol. 64, No. 12, December 23, 2015

Mortality (%): dichorionic vs monochorionic



Loos R. et al. Twin Research 1998,1:167-175

Twins



Complications

- TTTS (10-15%)
- sFGR (10-19%)
- TAPS (3-5%)
- MA (1:1,650-1:93,734)
- TRAP (1:35,000)
- Conjoined
- Discordant anomalies

Order	Prevalence
Twins	1:80
Monozygotic	4-5:1,000
Triplets	1:8,000

Placental for Mono Di: TTTS/TAPS/SIUGR

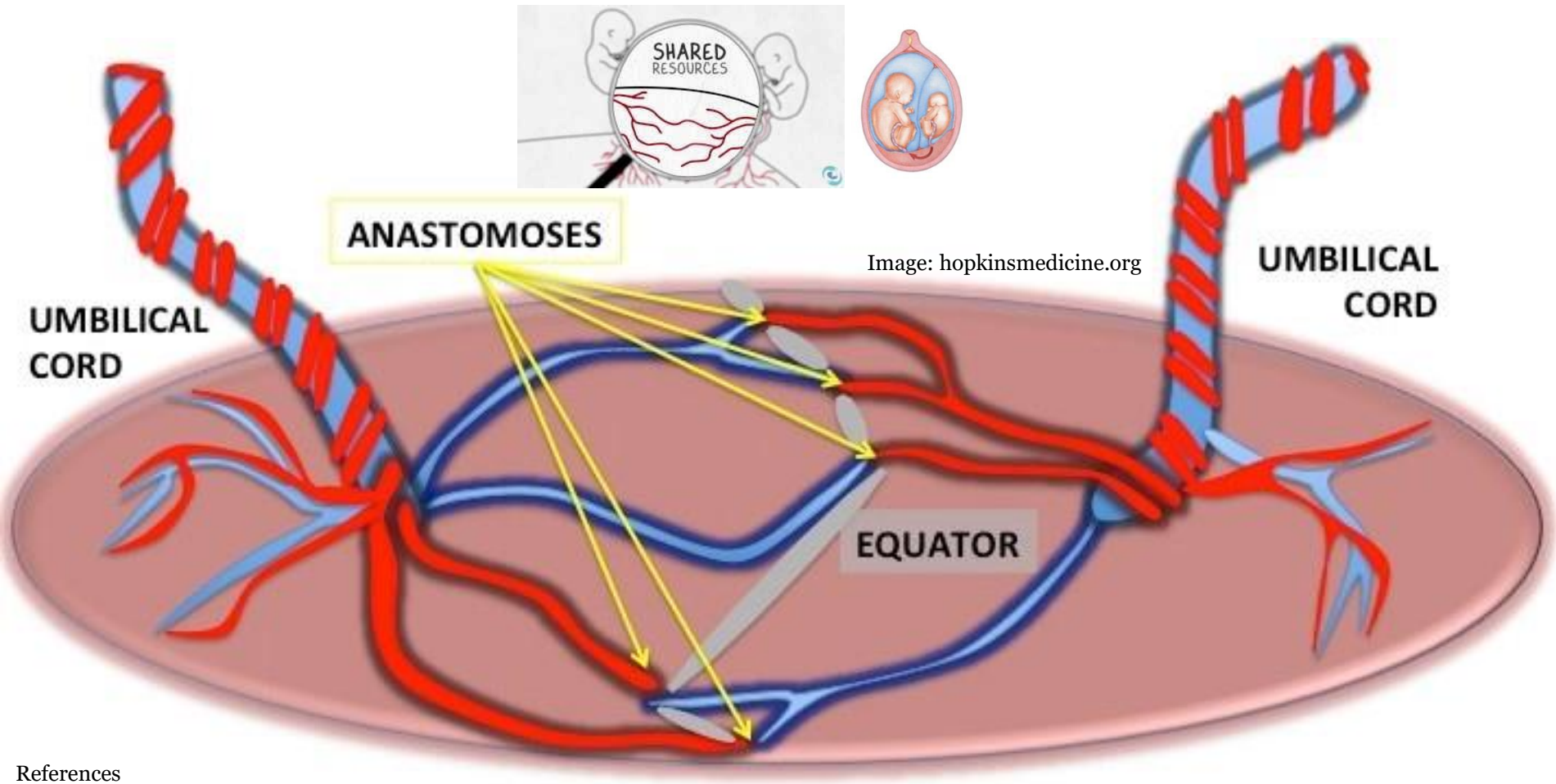
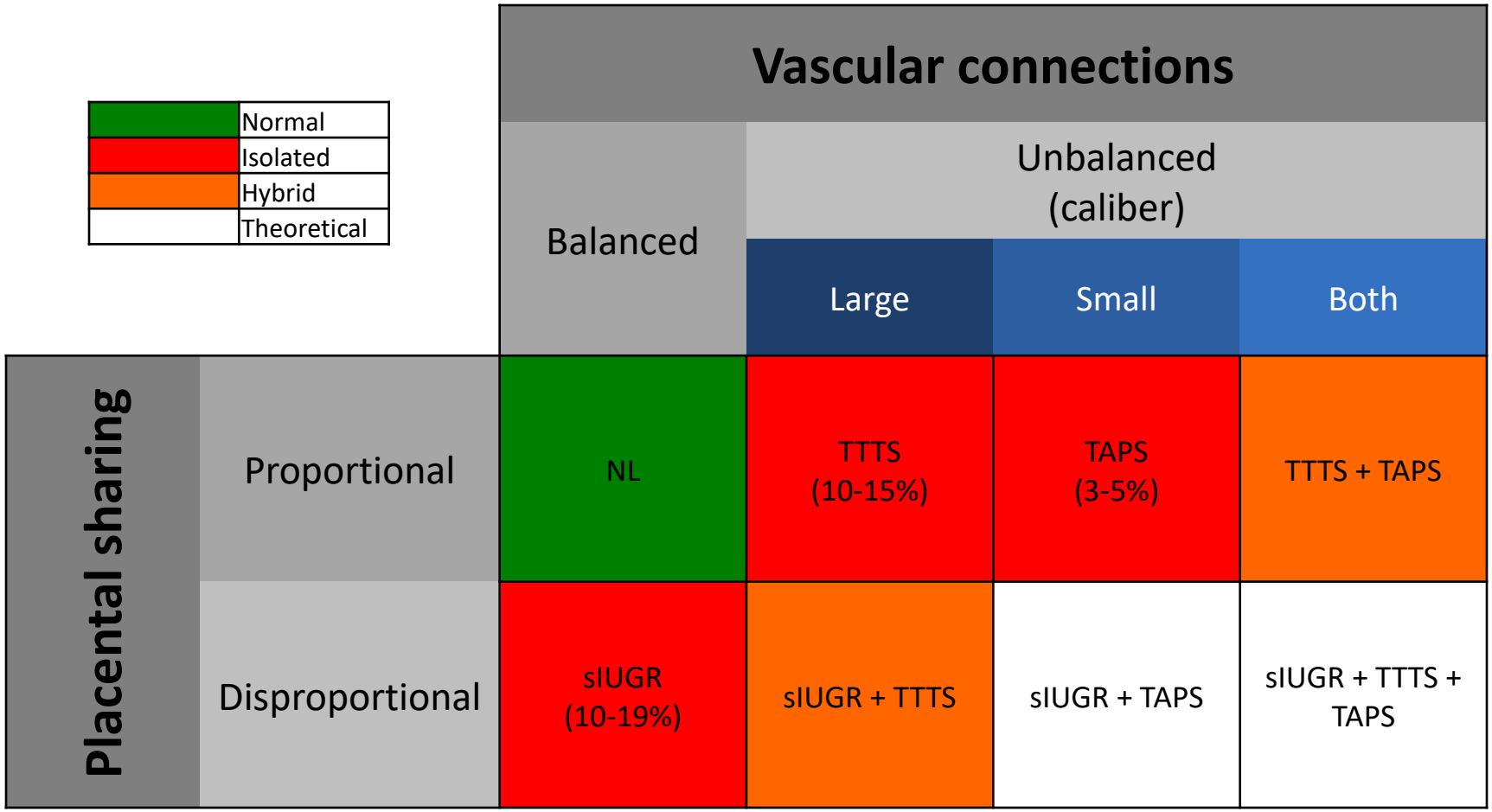


Image: hopkinsmedicine.org

References
- Denbow ML et al: Placental angioarchitecture in monochorionic twin pregnancies: relationship to fetal growth, fetofetal transfusion syndrome, and pregnancy outcome. AJOG 2000;182:417-426
- Gratacos E et al: A systematic approach to the differential diagnosis and management of the complications of monochorionic twin pregnancies. Fetal Diagnosis and Therapy 2012;32:145-155

Complications: placenta (chorioangiopagus)

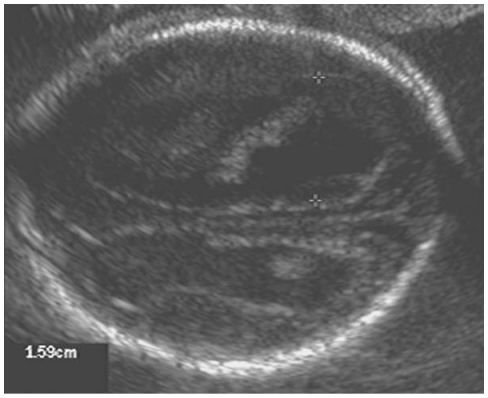


NL normal, **TTTS** twin twin transfusion syndrome, **TAPS** twin anemia polycythemia sequence, **sIUGR** selective in utero growth restriction

Main Concern: demise of co-twin

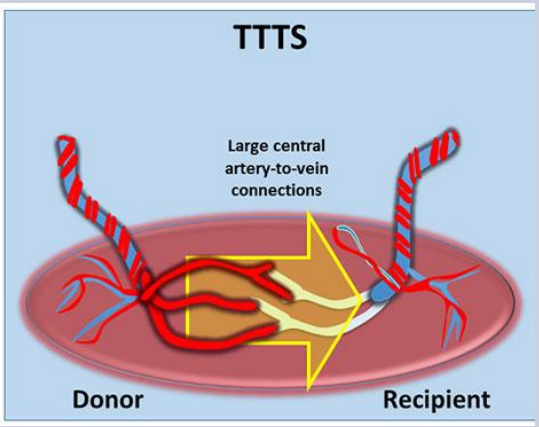
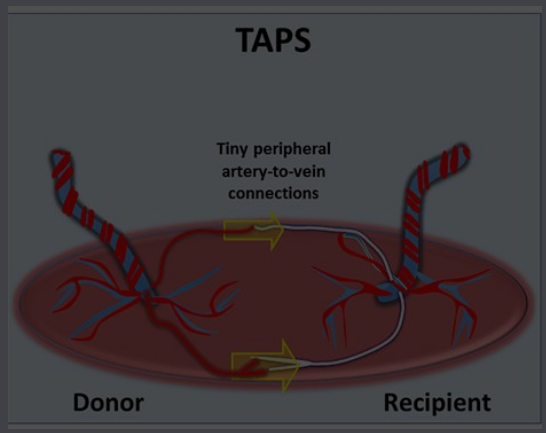
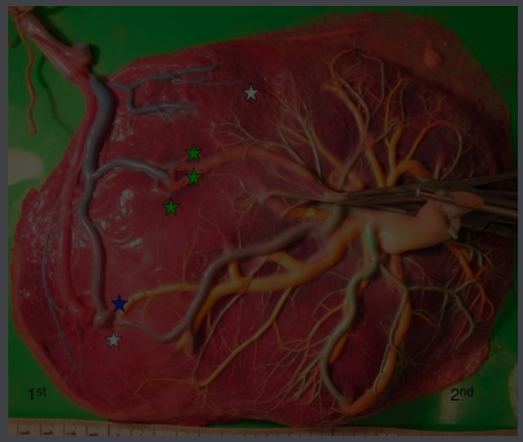
- MRI abnormalities in the surviving fetus
- Retrospective observational study at UCSF
- 21 monochorionic twins no intervention (RFA or Laser)

- Mean GA at demise: 19 6/7 wks (12 4/7-26 5/7 wks)
- Interval to MRI: 4 3/7 wks (0-12 1/7 wks)
- 41% were associated with TTTS
- Abnormal findings in 7 cases (33%):
  - Polymicrogyria
  - Germinolytic cysts
  - Intracranial hemorrhage
  - Ventriculomegaly
  - Delayed sulcation
- Majority had a normal ultrasound



Jelin et al. Am J Obstet Gynecol. 2008; 199:398.e1-5.

TTTS

TTTS	TAPS	SIUGR
10%[1] Large AV/VA discordant flow via anastomses[2]	3-5%[1] Tiny vessel anastomoses (<1mm diam[1])	10-15%[1,2] Discrepancy in placental territory
		

Images from hopkinsmedicine.org

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2. Gratacos E et al: A systematic approach to the differential diagnosis, management of the complications of monochorionic twin pregnancies. Fetal Diagnosis and Therapy 2012;32:145-155
3. Bennasar et al: "Selective intrauterine growth restriction in monochorionic diamniotic twin pregnancies" 2017 Seminars in Fetal & Neonatal Medicine

TTTS: Evaluation – Quintero Staging

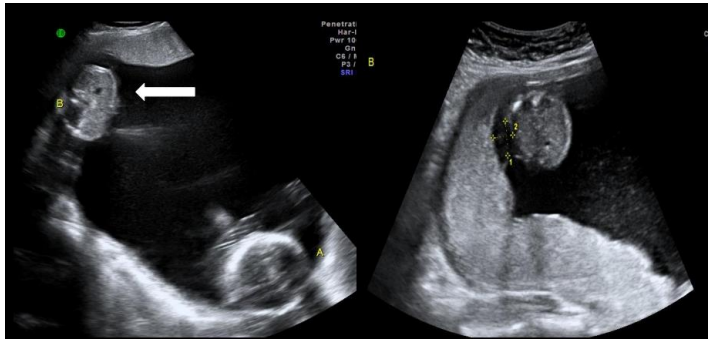
Box 1. Staging for Twin–Twin Transfusion Syndrome

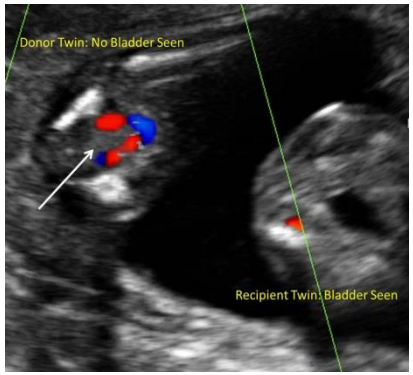
Stage 1	Monochorionic–diamniotic gestation with oligohydramnios (MVP less than 2 cm) and polyhydramnios (MVP greater than 8 cm)
Stage 2	Absent (empty) bladder in donor
Stage 3	Abnormal Doppler ultrasonography findings*
Stage 4	Hydrops
Stage 5	Death of one or both twins

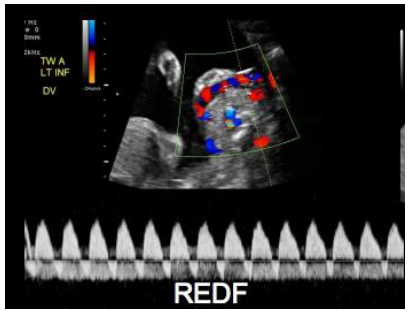
Abbreviation: MVP, maximum vertical pocket.

*Defined as the presence of one or more of the following: umbilical artery absent or reversed diastolic flow; ductus venosus absent or reversed diastolic flow; or umbilical vein pulsatile flow.

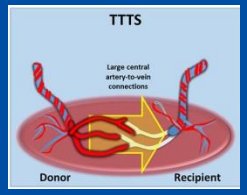
Data from Quintero RA, Morales WJ, Allen MH, et al. Staging of twin-twin transfusion syndrome. J Perinatol 1999;19:550–5.







TTTS: Diagnosis



Diagnostic Criteria of TTTS

1. Confirmed MC pregnancy
2. MVP:
    1. Poly in recipient: MVP ≥ 8cm*
    2. Oligo in donor: MVP < 2cm
3. Discordant fetal bladders
    1. Markedly large in recipient
    2. V small / nonvisible in donor (for most of examination)

* The cutoff above 20 weeks is still a subject of debate. A cutoff of ≥10 cm beyond 20 weeks has been used in randomized trials and is commonly used by European groups, while a unique cutoff of 8 cm is more commonly used in the United States. Both cutoffs are considered to be acceptable for the diagnosis.

Gratacos Ortiz Martinez Fetal Diagn Ther 2012

Letters to the Editor

Modified diagnostic criteria for twin-to-twin transfusion syndrome prior to 18 weeks' gestation: time to change?

Table 1 Modified diagnostic criteria of twin-to-twin transfusion syndrome in monochorionic diamniotic twin pregnancy

Gestational age	*Criteria for diagnosis*
< 18 weeks	Oligohydramnios in donor sac: DVP ≤ 2 cm Polyhydramnios in recipient sac: DVP ≥ 6 cm
18–20 weeks	Oligohydramnios in donor sac: DVP ≤ 2 cm Polyhydramnios in recipient sac: DVP ≥ 8 cm
> 20 weeks	Oligohydramnios in donor sac: DVP ≤ 2 cm Polyhydramnios in recipient sac: DVP ≥ 10 cm

DVP, amniotic fluid deepest vertical pocket.

Letter to the Editor, A. Khalil Ultrasound Obstet Gynecol: Modified diagnostic criteria of TTTS based on GA and 90 % 97.5%ile MVPs. A Khalil 2017

MVP maximum vertical pocket

Twin-Twin Transfusion Syndrome (TTTS)

- Complicates 10 to 15 % of MC twins
- Less than 0.1 percent of all live births
- Approximately 16 % of perinatal deaths in twins
- Mortality rate > 80 % in severe cases

TTTS: Management

Box 1. Staging for Twin–Twin Transfusion Syndrome

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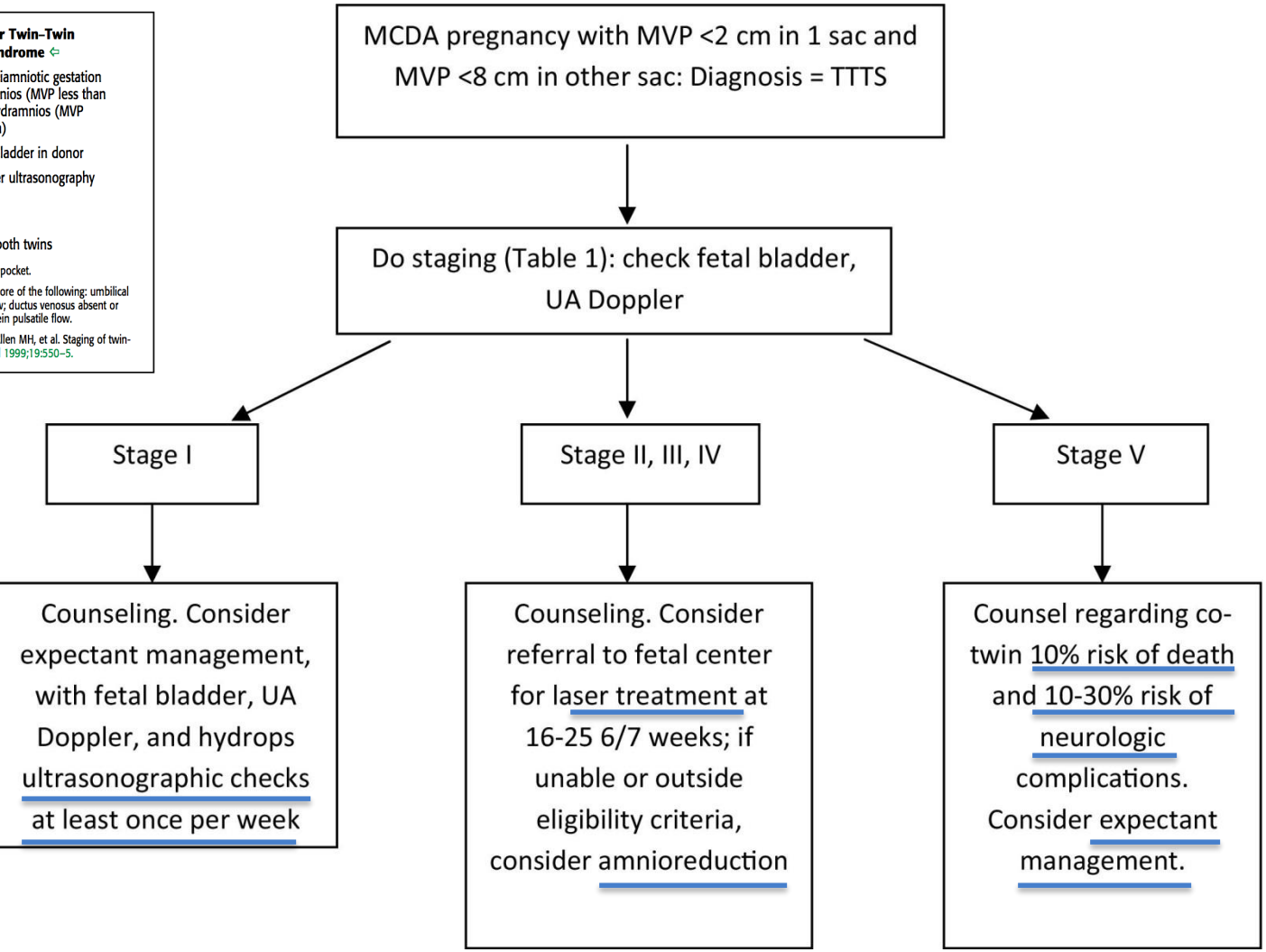
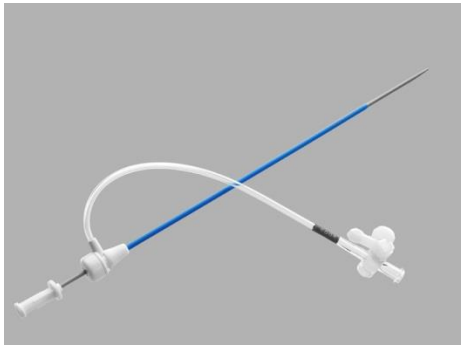


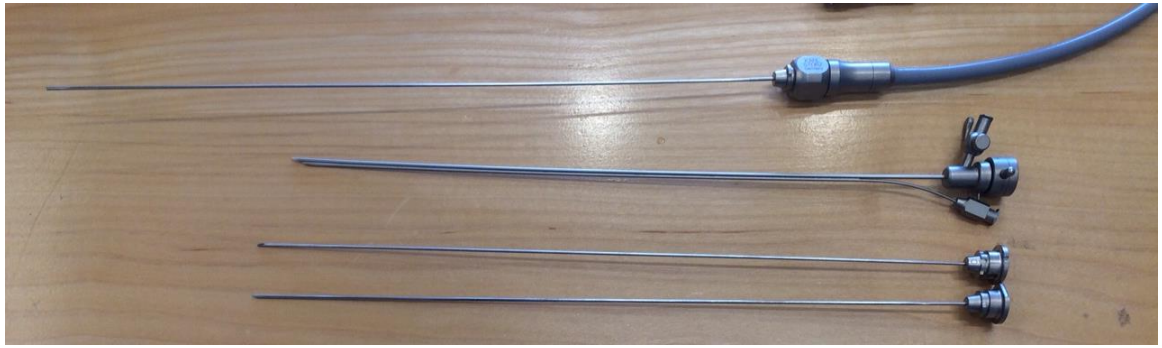
American Journal of Obstetrics & Gynecology 2013 208, 3-18DOI: (10.1016/j.ajog.2012.10.880)

Management opptions

- Expectant
- Termination
  - Total
  - Selective
- Septostomy
- Amnioreduction
- Selective Laser Photo Coagulation

Fetoscopy: instruments





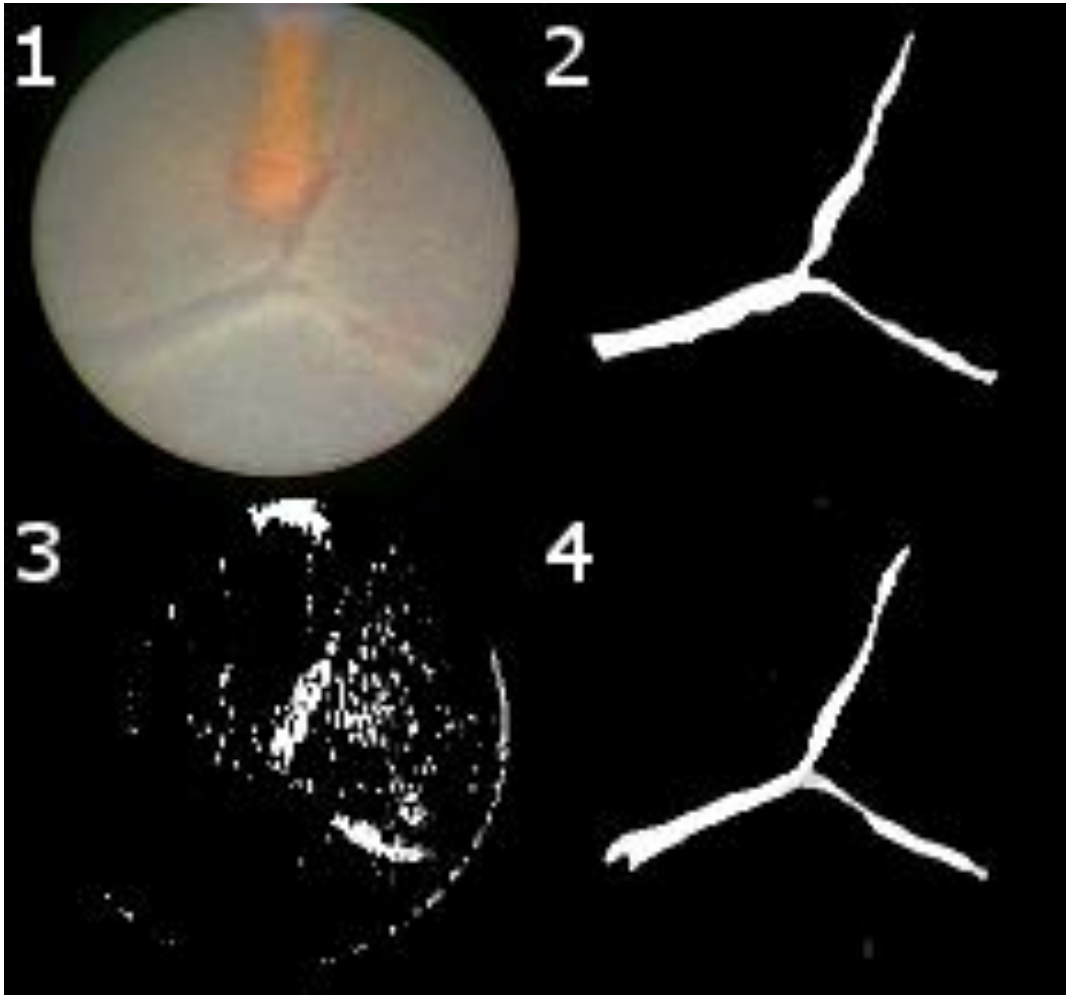
Fetoscopy

Yale Fetal Care Center

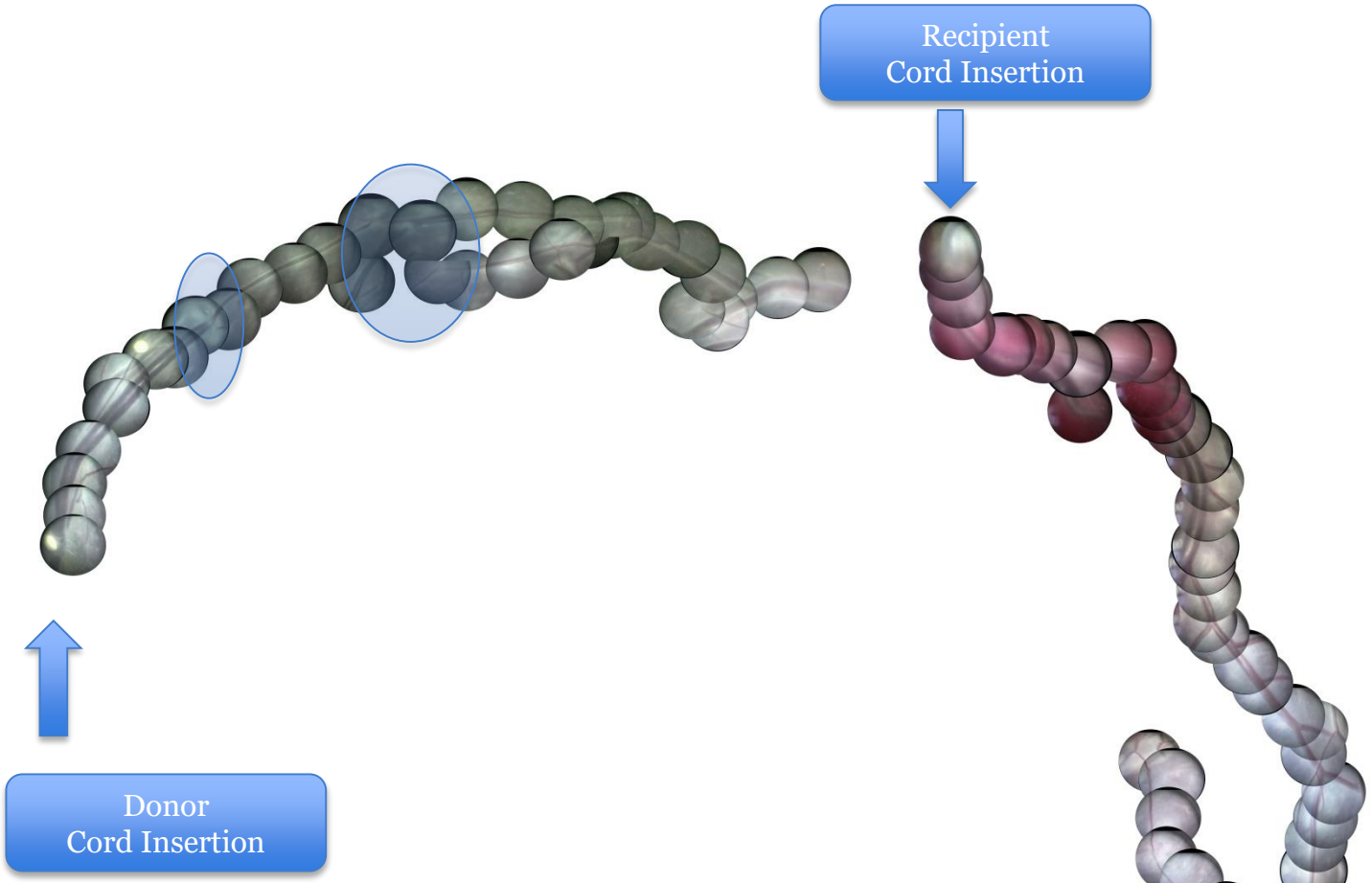
Virtual Placenta

Virtual Placenta

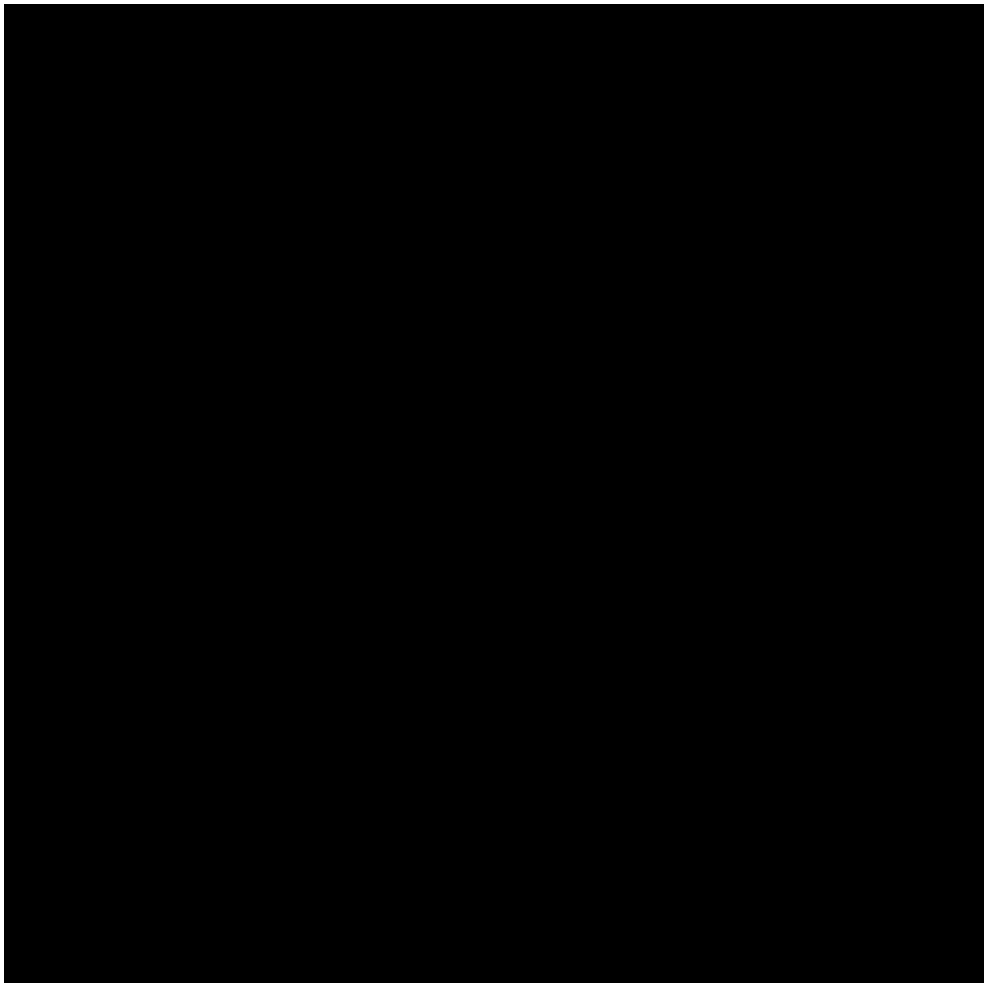
Virtual Placenta



Virtual Vascular Mapping

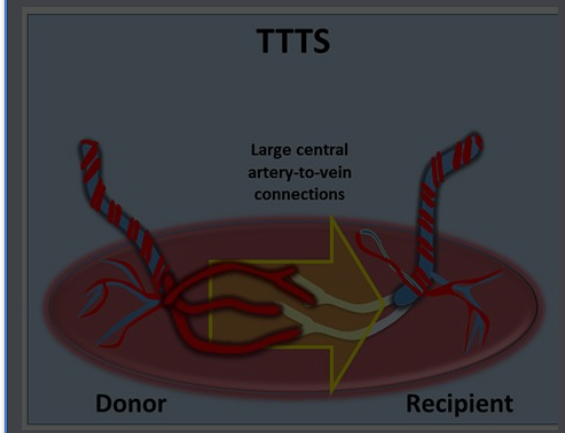
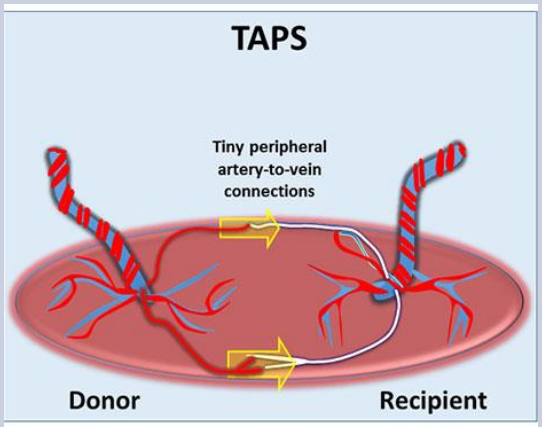
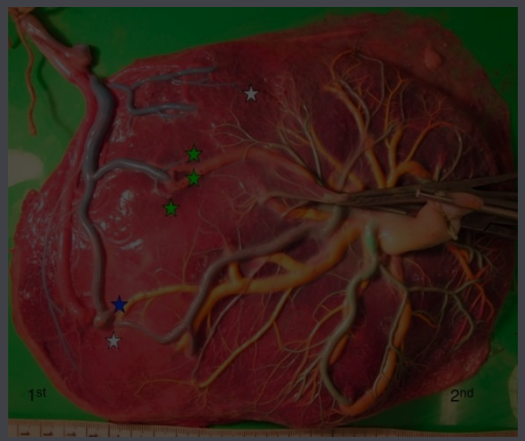


Virtual Placenta – ver 2.0



- P. Sadda. Data Driven Treatment Response Assessment and Preterm,
- Perinatal, and Paediatric Image Analysis, 2018, pp. 128 – 137.
- P. Sadda. Laparoscopic, Endoscopic and Robotic Surgery, vol. 1, no. 2, pp. 27
- – 32, Sep. 2018.
- P. Sadda. International Journal of Computer Assisted Radiology and
- Surgery (In Revision).

TAPS

TTTS	TAPS	SIUGR
10%[1] Large AV/VA discordant flow via anastomses[2]	3-5%[1] Tiny vessel anastomoses (<1mm diam[1])	10-15%[1,2] Discrepancy in placental territory
		

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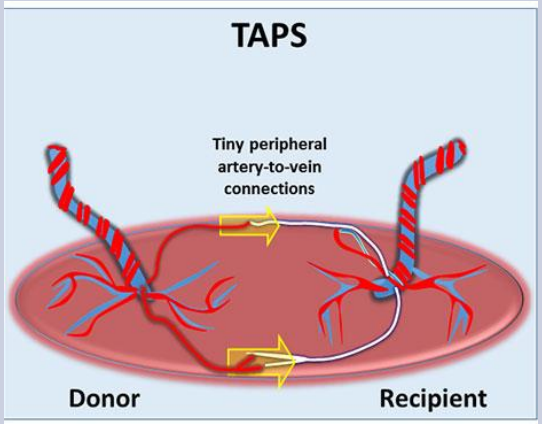
TAPS

TAPS

3-5%[1]
Tiny vessel anastomoses
(<1mm interface[1])



- Chronic slow and unbalanced transfusion
- Donor: anemia
- Recipient: polycythemia
- Lack of amniotic fluid imbalance
  - No MVP diff
  - No bladder diff
- Any time during pregnancy
- Spontaneous more likely after 26 wks

Incomplete separation of anastomoses with Laser Coag[1]

- Recurrent TTTS (14%)
- Development of TAPS (13%)

Note: Solomonization[2]

- Recurrent TTTS (1%)
- Development of TAPS (3%)

1. Robyr R et al: Prevalence and management of late fetal complications following successful selective laser coagulation of chorionic plate anastomoses in twin-to-twin transfusion syndrome. AJOB 2006;194:796-803
2. Slaghekke, Lopriore et al. Fetoscopic laser coagulation of the vascular equator versus selective coagulation for twin-to-twin transfusion syndrome: an open-label randomized controlled trial. Lancet 2014.

Staging: prenatal

Stage	Description
I	MCA-PSV: >1.5 MoM AND <1.0 MoM, No fetal compromise.
II	MCA-PSV >1.7 MoM AND <0.8 MoM, No fetal compromise
III	Stage 1 or 2 and cardiac compromise of donor, defined as critically abnormal Doppler flow*.
IV	Hydrops of donor.
V	IUFD of one or both fetuses preceded by TAPS.

*Absent or reversed end-diastolic flow in umbilical artery, pulsatile flow in the umbilical vein or increased pulsatility index or absent or reversed flow in A-wave of ductus venosus. **MCA-PSV** middle cerebral artery peak systolic velocity, **MoM** multiples of median, **IUFD,** intrauterine fetal death.

Slaghekke F. et al. Fetal Diagn Ther 2010;27:181-190.

Staging: prenatal (new proposal)

Stage	Description
I	Delta PSV >0.5 MoM AND No fetal compromise.
II	Delta-PSV >0.7 MoM AND No fetal compromise
III	Stage 1 or 2 and cardiac compromise of donor, defined as critically abnormal Doppler flow*.
IV	Hydrops of donor.
V	IUFD of one or both fetuses preceded by TAPS.

Sensitivity=83% (95% CI, 67-93%), specificity=100% (95% CI, 92-100%), PPV=100% (95% CI, 88-100%), NPV=88% (95% CI, 77-94%), PLR not calculated, NLR 0.17

*Absent or reversed end-diastolic flow in umbilical artery, pulsatile flow in the umbilical vein or increased pulsatility index or absent or reversed flow in A-wave of ductus venosus. **MCA-PSV** middle cerebral artery peak systolic velocity, **MoM** multiples of median, **IUFD,** intrauterine fetal death.

Tollenaar SAL. Ultrasound Obstet Gynecol. 2018 Aug 20. doi: 10.1002/uog.20096. [Epub ahead of print]

TAPS evaluation for management

- Optimal prenatal treatment not established
- Options:
  - Expectant
  - Selective feticide (<24 wks)
  - Delivery
  - Intrauterine transfusion for the anemic fetus
    - Risk: skin necrosis, further transfusion from donor to recipient
  - Fetoscopic laser photocoagulation [1,2]
  - Partial exchange transfusion for the polycthemic fetus [3]

1. Weingertner A.S. et al. Ultrasound in Obstetrics & Gynecology 2010;35:490-494
2. Lopriore E. et al. Am J Obstet Gynecol 2009;201:66e1-66e4
3. Genova L. et al. Fetal Diagnosis and Therapy 2013;34:121-126

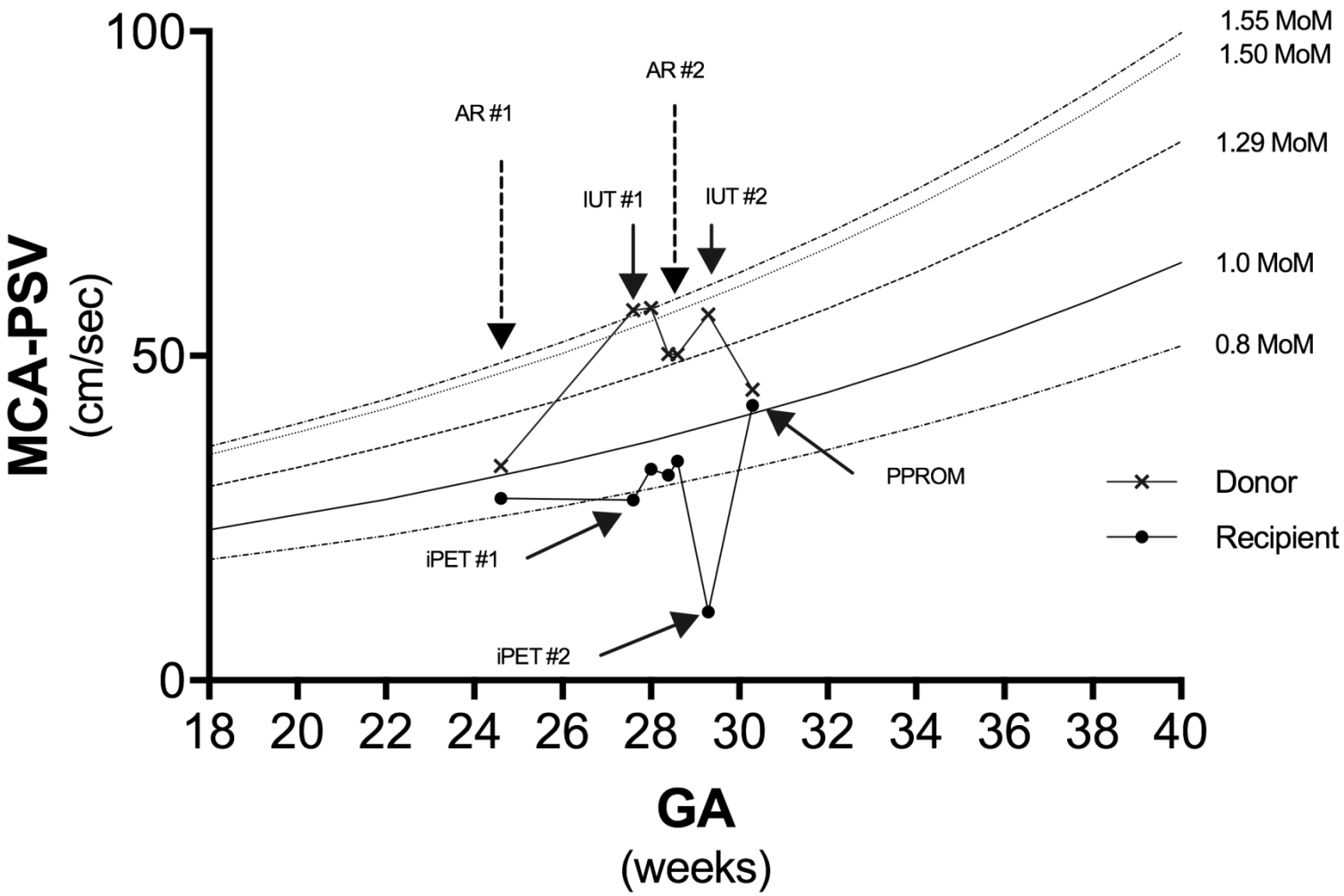
Yale Fetal Care Center

#	GA_Dx	Stage	Mode Conception	Other	iPET	Complication	GA_Del	Indication
1	26.1	IV	Spontaneous		1	Incomplete	27.1	Worsening
2	27.6	II	IVF	Stage 1 TTTS	2	Amniostomy	30.4	PPROM
3	24.6	II	IVF		2	-	36.4	PTL

GA gestational age, **Dx** diagnosis, **IVF** in vitro fertilization, **TTTS** twin twin transfusion syndrome, **PET** partial exchange transfusion, **Del** delivery, **PPROM** preterm premature rupture of membranes, **PTL** preterm labor

Bahtiyar MO. Fetal Diagnosis and Therapy. 2018. doi: 10.1159/000486198

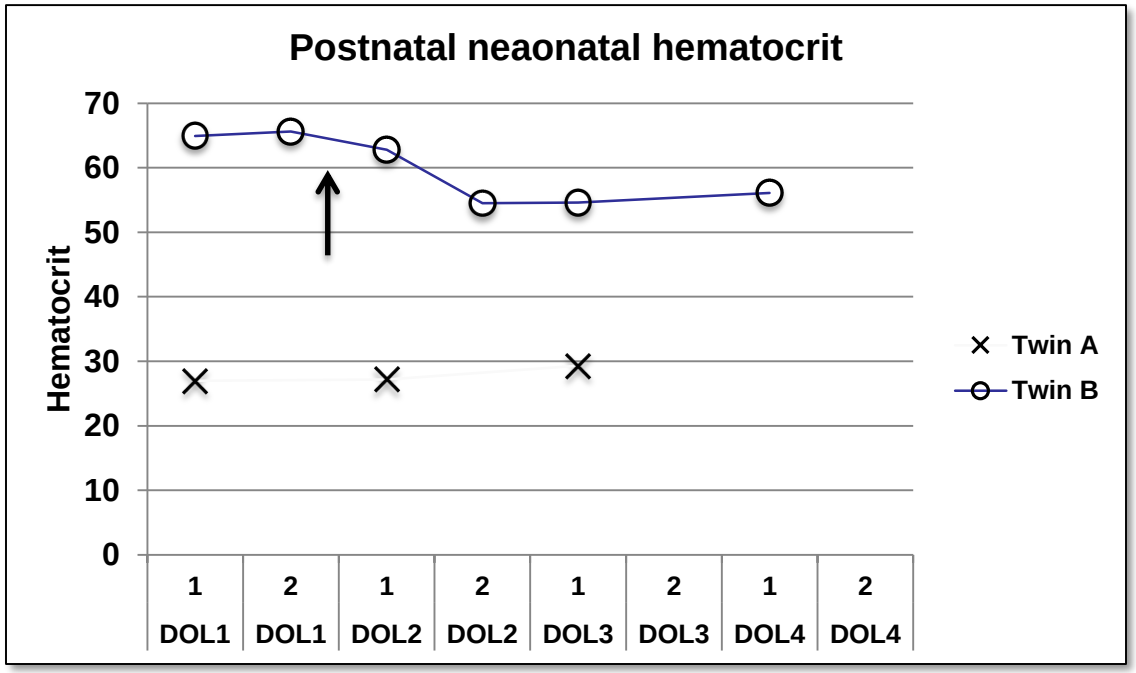
Partial Exchange Transfusion



Prenatal Course

Procedure	GA (wks)	Stage	Opening Hct (hemoglobin)	IVT or PET	Closing Hct
Transfusion 1	27 5/7	2			
Twin A			21%	50 cc PRBC	39%
Twin B			63%	18 cc 0.9% NaCl	60.3%
Transfusion 2	29 5/7	1			
Twin A			24%	40 cc PRBC	37%
Twin B			62.8%	18 cc 0.9% NaCl*	59.7%
Post natal	30 3/7 §	1			
Twin A			27.2% (9.8 mg/dL)	Observation	
Twin B			62.8% (20.3 mg/dL)	Partial exchange x1	

Neonates


Postnatal neaonatal hematocrit
Hematocrit
70
60
50
40
30
20
10
0
1 DOL1
2 DOL1
1 DOL2
2 DOL2
1 DOL3
2 DOL3
1 DOL4
2 DOL4
Twin A
Twin B

Outcome: postnatal

#	Neonate	Outcome
1	A	A/W
	P	Death
2	A	A/W
	P	A/W
3	A	A/W
	P	A/W

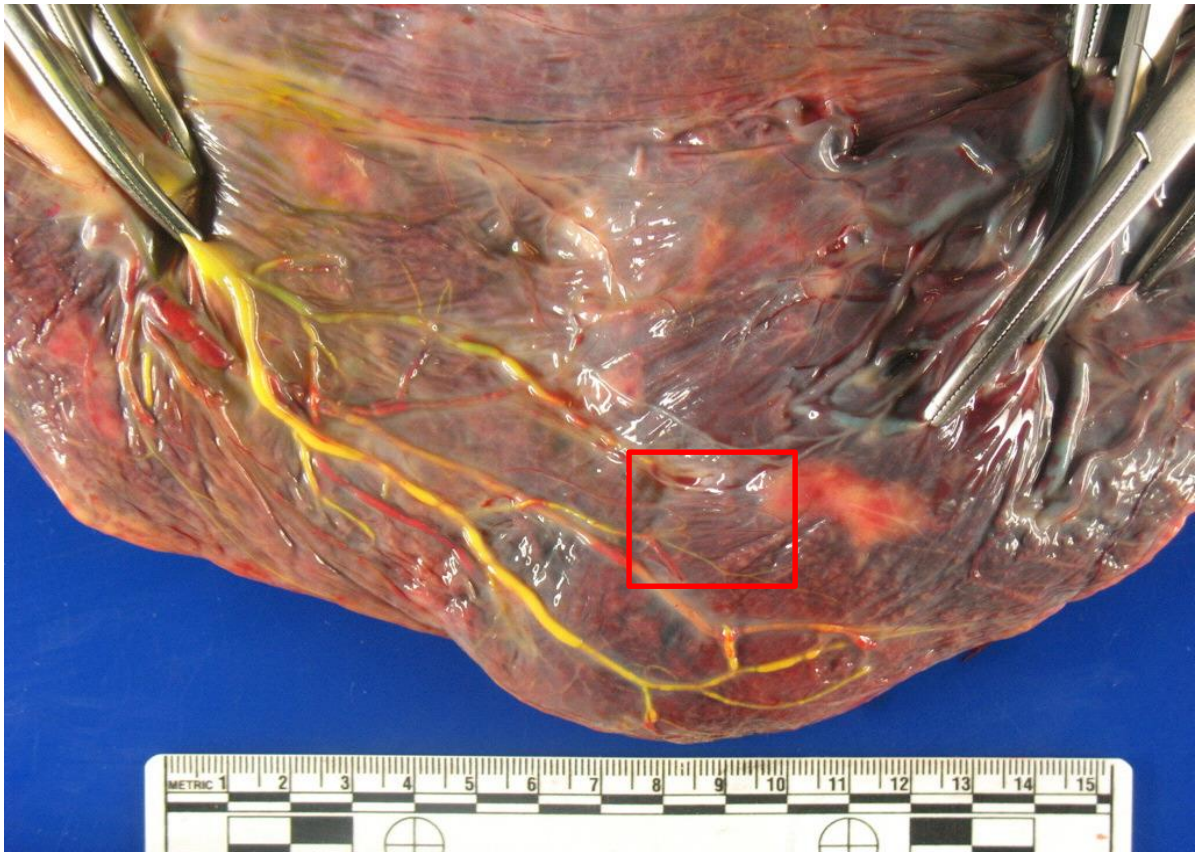
A anemic fetus, **P** polycythemic fetus, **A/W** alive and well

Postnatal

Postnatal intracranial imaging*	
Twin	Head US
A	Normal
B	Normal. Multiple choroid plexus cysts

Placental pathology: Superficial fetal vascular anastomoses are demonstrated using dye infusion studies and appear to involve **two small-caliber vessels with a 0.1 cm diameter**. Deep anastomosis are not demonstrated after perfusion of numerous vessels of both of twin A and B.

Placenta



Gross image of monochorionic diamniotic placenta in Case 2. Dye studies confirm the presence of small caliber vascular anastomoses (red box) between the circulations of the twins. Ruler below in centimeters. Image courtesy of Dr. R. Morotti, MD (Yale School of Medicine, Department of Pathology).

SIUGR

TTTS	TAPS	SIUGR
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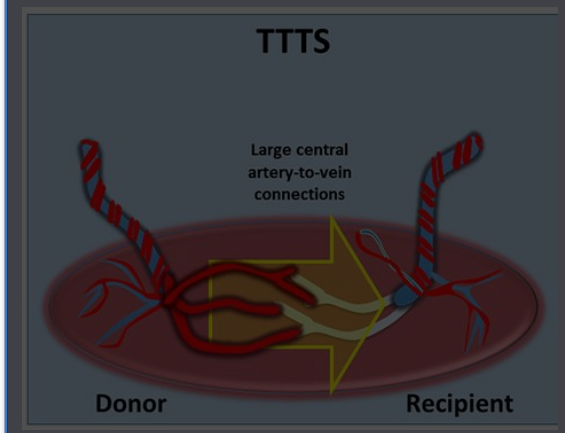	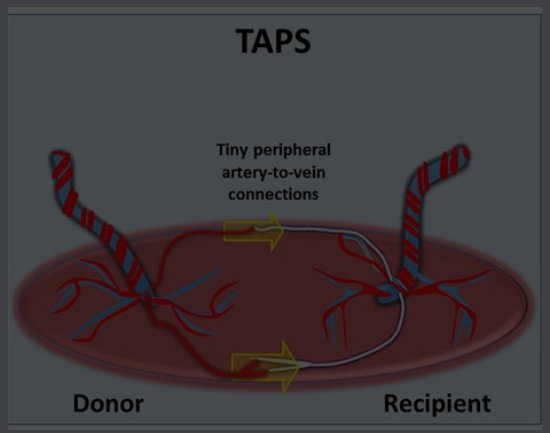	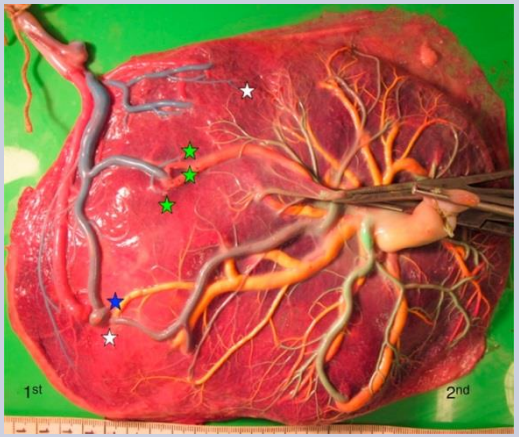

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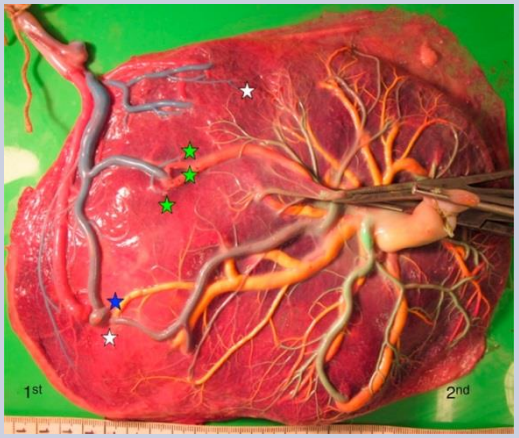
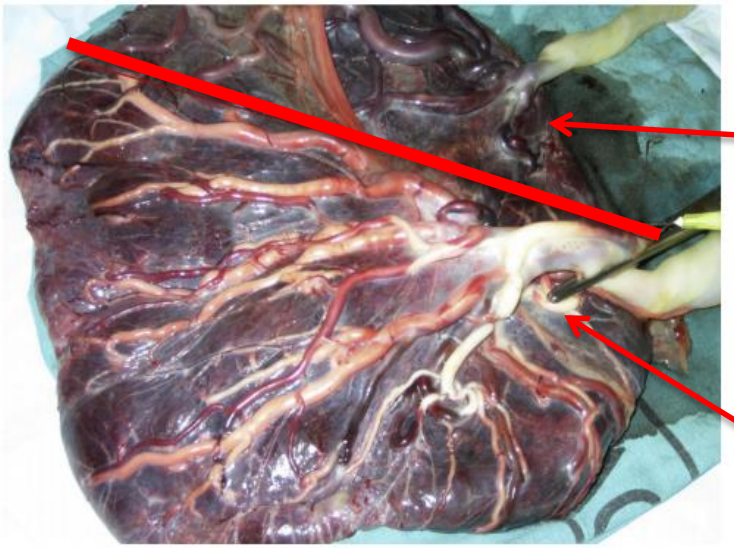
SIUGR

SIUGR

10-15%[1,2]
Discrepancy in placental territory





- Inadequate sharing of placental territory
- Anastomoses allowing for feto-fetal exchange may be protective

Risks:

1. Demise of small fetus (A)
   → concomitant death in larger fetus (B) 15-20% d/t feto-fetal transfusion s/p A demise
2. Neurologic impairment of B even with both born alive

Bennasar et al. Seminars in Fetal & Neonatal Medicine 2017: Selective intrauterine growth restriction in monochorionic diamniotic twin pregnancies

sIUGR

- Prevalence based on various diagnostic criteria
  - EFW < 10th percentile: 10-15%
  - Fetal weight discordance, ≥25%: 11-19%
  - Fetal abdominal circumference:

- sFGR diagnosis at Yale MFM Service:
  - At least one twin's EFW<10% percentile AND/OR growth discordance ≥25% in EFW.

Gratacos et al. Fetal Diagn Ther 2012;32:145-155.
Gratacos et al. Ultrasound Obstet Gynecol 2007; 30: 28-34.

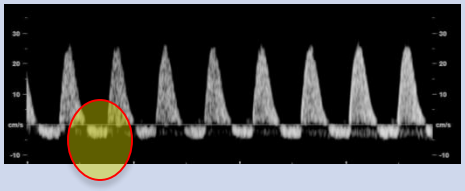
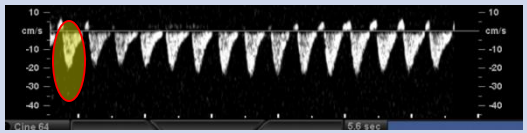
Discordant Growth, >20%

	Non-discordant (n=57)	Discordant (n=16)	P
GA at delivery	34.6 wk	32.4 wk	0.06
IVF	10.5%	6.7%	0.6
NT			
Large	1.5 mm	1.6 mm	0.2
Small	1.4 mm	1.8 mm	0.4
MSAFP	2.24 MoM	2.17 MoM	0.8
TTTS	12.3%	37.5%	0.02
AEDF/REDF	1.8%	31.3%	0.009
NICU Admit			0.01
Marg/velament			0.03
Placenta			N.S.
Small	40%	40%	
Large	60%	60%	

Zuckerwise et. J. Perinat. 2015; 35:387-89

SIUGR Evaluation: UA Doppler

- **Umbilical artery doppler of IUGR twin** provides the best clinical sign to identify sIUGR
- Wave form is combination of placental insufficiency and intertwin vascular connections
- Flow characteristics usually **remain unchanged** from very early in pregnancy to delivery[1]
- Stratification into types based on types of **diastolic flow:**

	Type I	Type II	Type III
UA diastolic flow	**Present** Milder discordance in territories Sufficient inter-twin flow 	Persistently absent/reverse **(AREDF)** Territory discordance = large Number + diam of anastomoses very small 	Intermittently Absent/Reverse **(iAREDF)** Territory discordance: largest Large AA anastomses: compensatory 
	Intrauterine mortality 2-4% Expectant mgmt R/o Type II U/S, dopplers qwk Delivery: 34-36wk	70-90%: fetal deterioration by 30wks (UA not useful here) 37% survival in smaller twin 55% survival in larger twin Doppler, BPP, FH qwk Cord occlusion, laser	Risk of unpredictable demise in smaller fetus, neuro dz in larger Qwk (UA Doppler doesn't show decomp) Deliver 32-34 wks ?Cord occlusion, laser

Bennasar M, et al. Seminars in Fetal & Neonatal Medicine (2017)
Gratacos et al. Ultrasounds in Obstet Gynec 2009

SIUGR: Eval tree

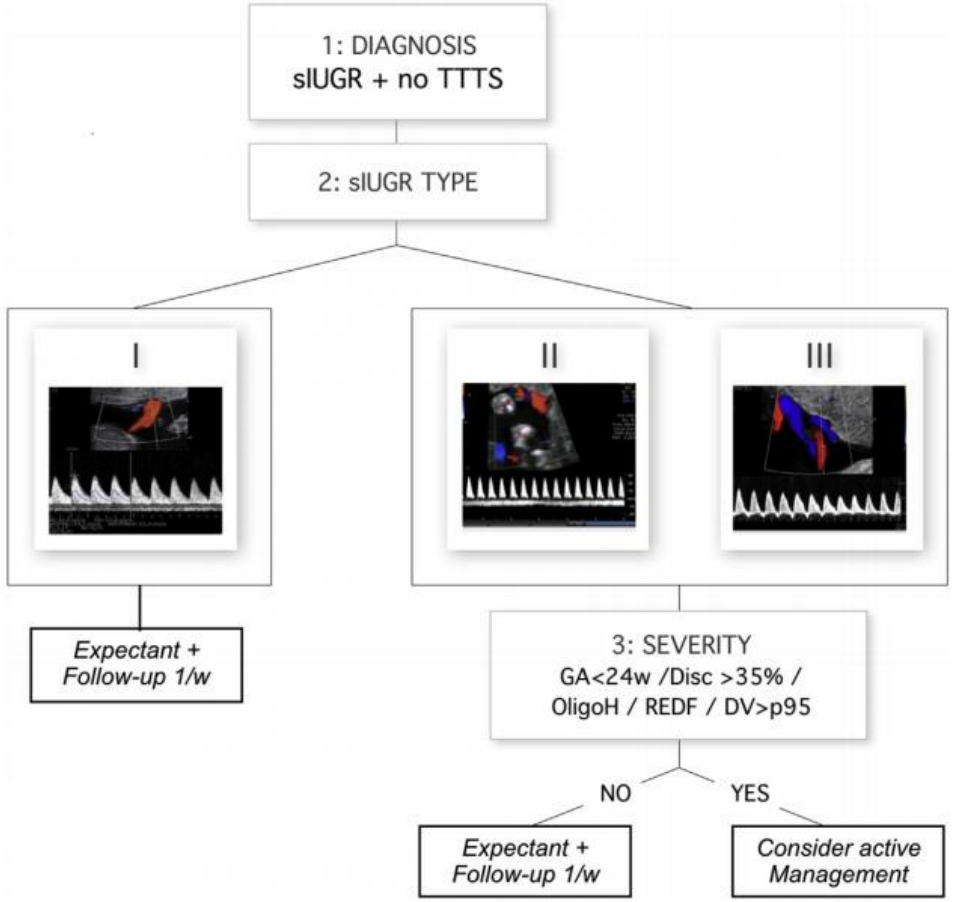


Fig. 7. Severity algorithm for patient counseling in monochorionic twins complicated with selective intrauterine growth restriction (sIUGR). TTTS, twin–twin transfusion syndrome; GA, gestational age; Disc, intertwin fetal weight discordance; OligoH, oligohydramnios; REDF, reverse end-diastolic flow in the UA Doppler; DV > p95, ductus venosus pulsatility index above 95th centile.

Bennasar M, et al., "Selective intrauterine growth restriction in monochorionic diamniotic twin pregnancies" Seminars in Fetal & Neonatal Medicine (2017), http://dx.doi.org/10.1016/j.siny.2017.05.001

Outcome: Expectant Management

PARAMETER	Normal	Type 1	Type 2	Type 3
In-utero deterioration	0%	0%	90%	10.8%
IUFD (over all)				
Large			22.2%	0%
Small			29.6%	15.4%
Unexpected IUFD				
Large	-	2.6%	0%	6.2%
Small	-	2.6%	0%	15.4%
IVH				
Large	-	0%	3.3%	3.3%
Small	-	0%	14.3%	6.0%
Parenchymal brain damage				
Large	-	0%	3.3%	19.7%
Small	-	0%	14.3%	2.0%

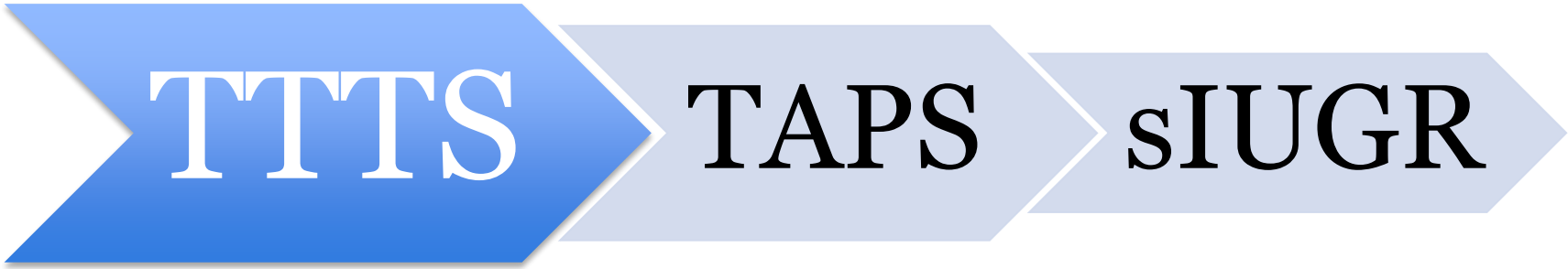
Gratacos et al. Fetal Diagn Ther 2012;32:145-155.
Gratacos et al. Ultrasound Obstetgynecol 2007; 30: 28-34.

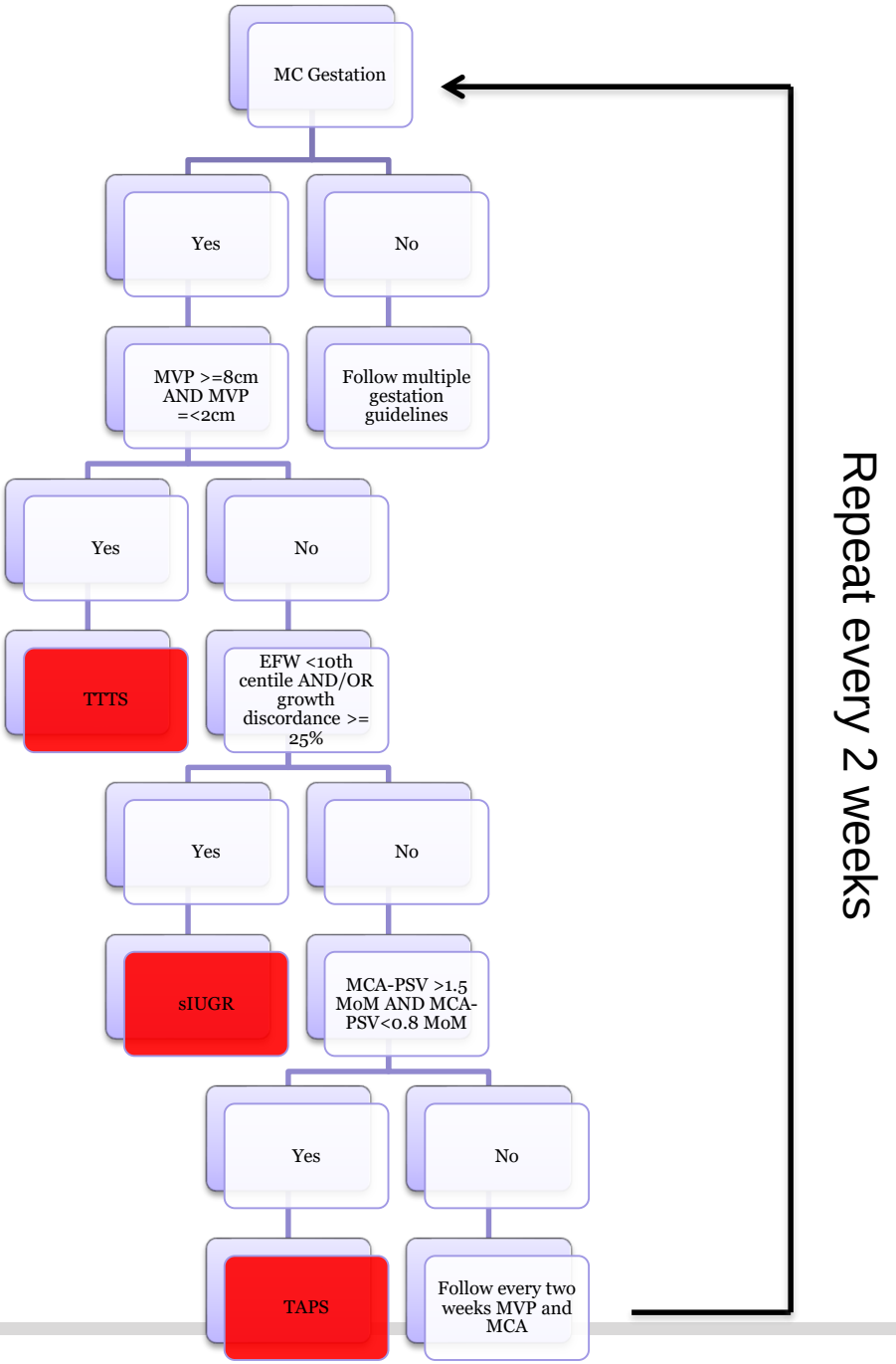
Placental for Mono Di: TTTS/TAPS/SIUGR

	Pathophys	Dx / AssessTool	Management
TTTS 10%	Large vessel anastomosis within placenta shunting high pressure donor to low pressure recipient	UA Doppler Quintero staging MVP 15-28 wks [2]	- Fetoscopic laser - Serial Amnioreduc - Selective feticide - Expectant - Delivery
TAPS 3-5%	Chronic slow transfusion via small vessel (<1mm diam) anastomosis, absence of fluid discord (13% s/p fetoscopic laser for TTTS)	MCA Doppler MVP 29-36 wks [2]	(No gold standard) Same as above - intrauterine transfusion +/- partial exchange transfusion
SIUGR 10-15%	Inadequate sharing of placental territory Protective: anastomoses	(No dx consensus) - UA Doppler (Type I-III) - EFW - Growth discord	Cord occlusion Laser therapy Expectant Delivery

1 Denbow ML et al: Placental angioarchitecture in monochorionic twin pregnancies: relationship to fetal growth, fetofetal transfusion syndrome, and pregnancy outcome. AJOG 2000;182:417-426
2 Gratacos E et al: A systematic approach to the differential diagnosis and management of the complications of monochorionic twin pregnancies. Fetal Diagnosis and Therapy 2012;32:145-155

Treatment priority




MC Gestation
Yes
No
MVP >=8cm AND MVP =<2cm
Follow multiple gestation guidelines
Yes
No
TTTS
EFW <10th centile AND/OR growth discordance >= 25%
Yes
No
sIUGR
MCA-PSV >1.5 MoM AND MCA-PSV<0.8 MoM
Yes
No
TAPS
Follow every two weeks MVP and MCA
Repeat every 2 weeks

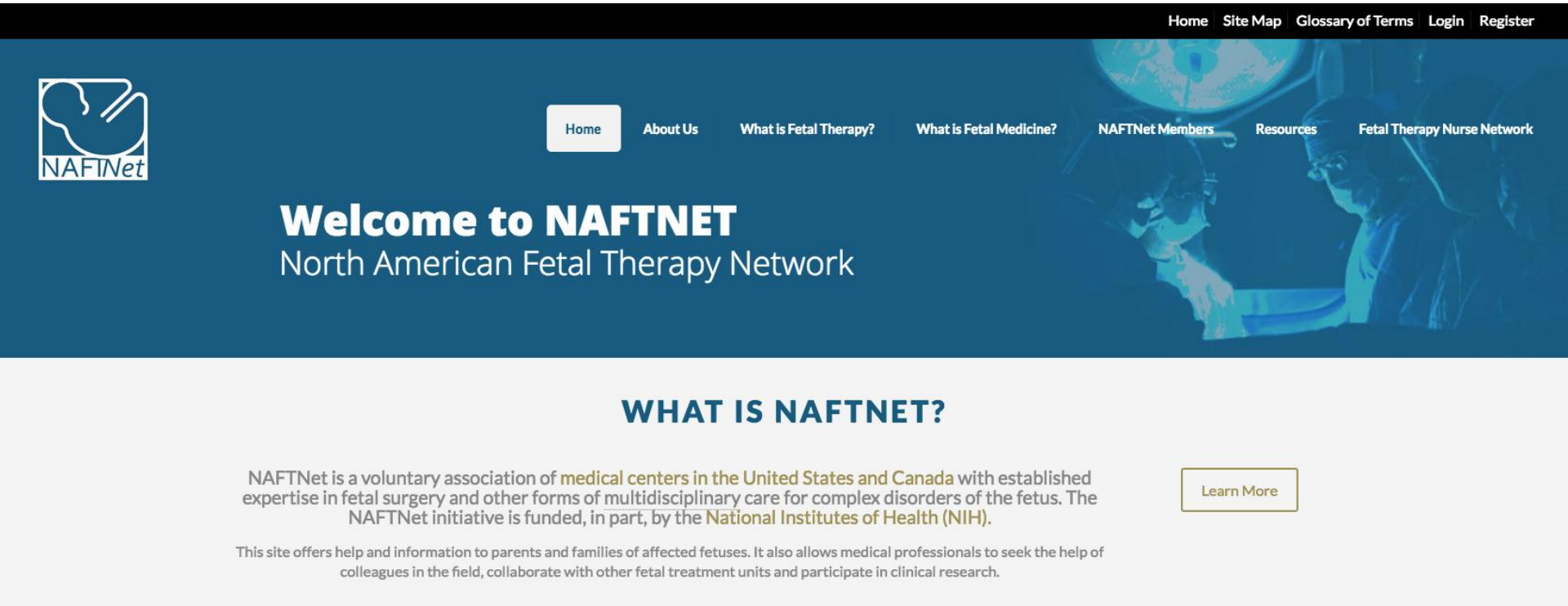
Routine Prenatal US Follow Up

12-14 wks determine chorionicity
11-14 wks 1st trimester screening
15-16 wks start serial assessments every 2 weeks
Minimum documentation: MVP, bladder status, MCA-PSV*
Patient education: rapidly increasing abdominal size and premature contractions
18-20 wks Level-II US
18-32 wks Serial cervical length assessments, every 2 to 4 weeks
20-22 wks Fetal echocardiogram
18-delivery Serial growth ultrasounds, every 2 to 4 weeks
Delivery Per standards, uncomplicated

MFM Referral for:
- Discordant amniotic fluid
- Discordant growth
- Suspected complication

North American Fetal Therapy Network (NAFT*Net*)

http://www.naftnet.org



Thank you