The Challenges of Monochorionic Twin Pregnancies

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MATERNAL-FETAL MEDICINE
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Disclosures

- I have nothing to disclose.

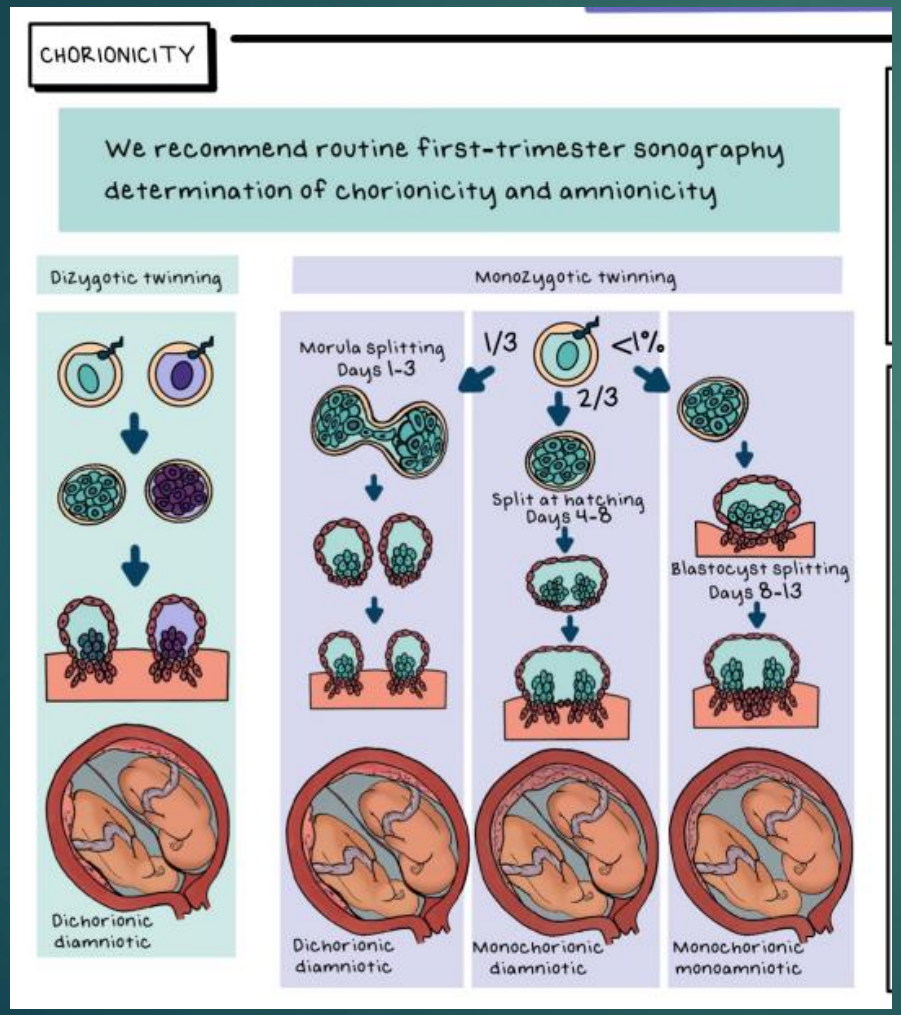
OBJECTIVES

- Review risks of monochorionic/diamniotic twin pregnancies
- Review of major monochorionic-diamniotic twin pregnancy pathologies
  - Diagnostic criteria
  - Pathophysiology
  - Cardiovascular changes
  - Management and clinical considerations

Twin Pregnancies: The Basics

- Increased risks of maternal and perinatal complications
  - Congenital abnormalities, preterm birth, hypertensive disorders of pregnancy, gestational diabetes, fetal growth restriction, still birth, neonatal death
- ~20% twin pregnancies are monochorionic
  - Diamniotic
  - Monoamniotic
- Increased risks associated with monochorionic pregnancies: **VASCULAR ANASTAMOSES**

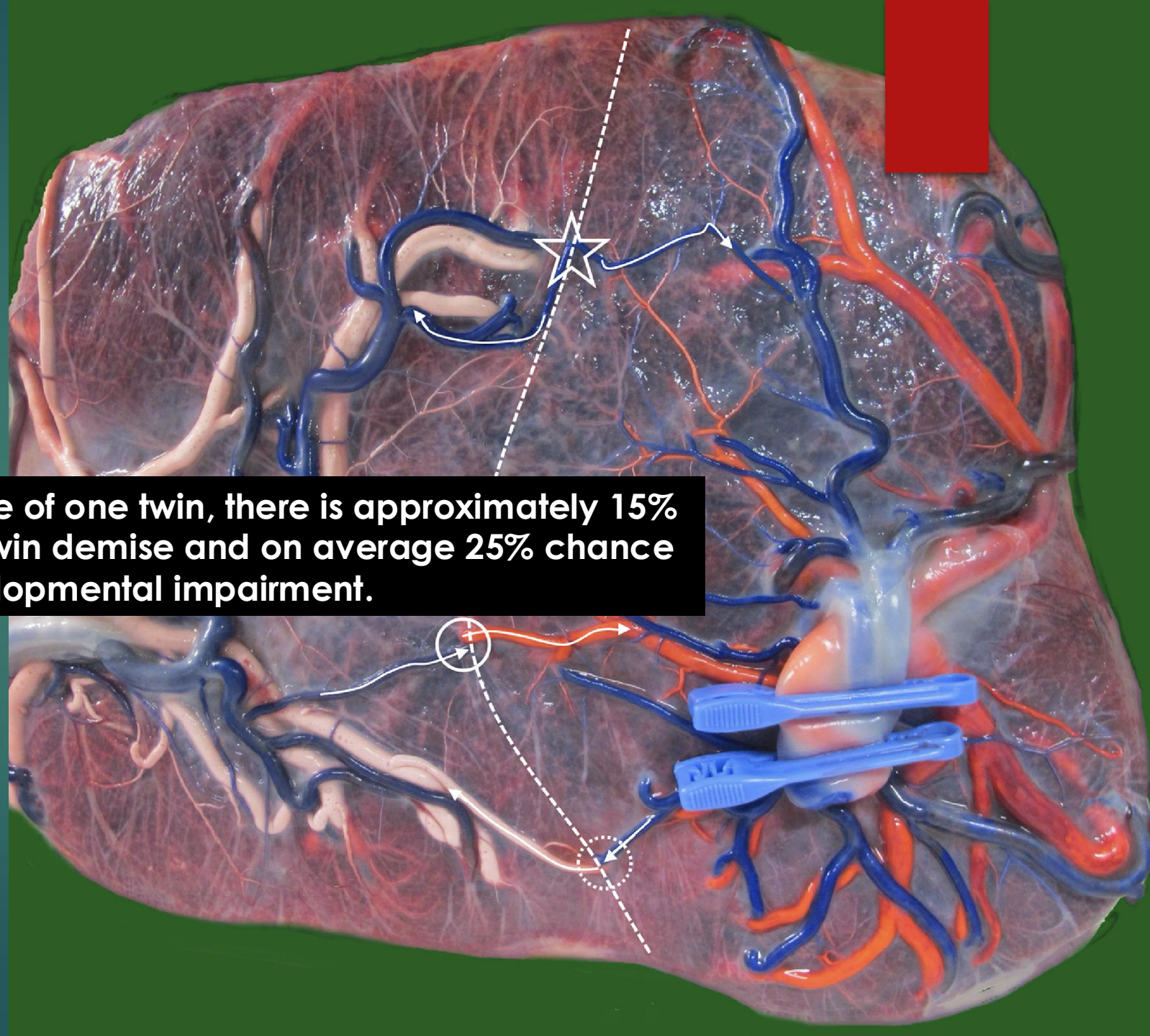
The Beginning



SMFM Consult Series #72

- Step one: Confirm dating using ACOG criteria
  - Compare earliest ultrasound with sure LMP
  - Use largest CRL
- Determine chorionicity best done 10-14 weeks gestation
  - T-sign
  - Lambda sign
- Determine risks to the pregnancy and schedule follow-up accordingly

Vascular Anastomoses: Why we care



With demise of one twin, there is approximately 15% risk of co-twin demise and on average 25% chance neurodevelopmental impairment.

Lewi L

Monochorionic diamniotic twin pregnancies

American Journal of Obstetrics & Gynecology MFM, 2021; 4

Antepartum Surveillance Strategies

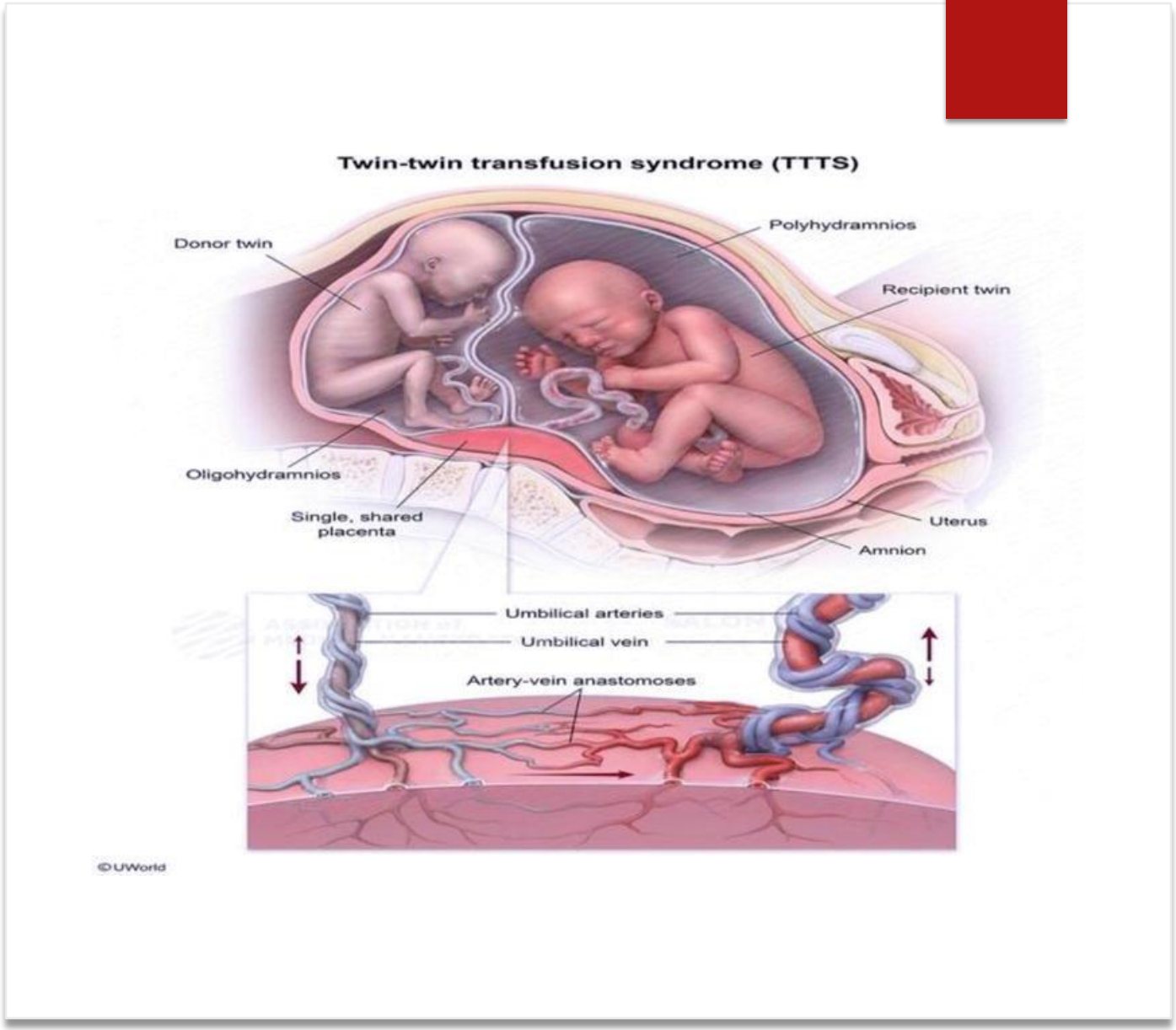
- Fluid, bladders, stomachs for **TTTS** screening
- MCA Doppler studies for **TAPS** screening
- Serial growth ultrasounds for **selective FGR**
- Umbilical artery Doppler studies to aid in staging/typing

Monitoring and Surveillance

- ☐ Serial ultrasound exam starting at 16 weeks of gestation
  - Every 2 weeks for assessment of amniotic fluid deepest vertical pocket and bladder filling
  - Consider umbilical artery and middle cerebral artery Doppler evaluation with routine surveillance depending on local resources and patient access to care
  - Every 4 weeks for evaluation of fetal growth
- ☐ Detailed fetal anatomy survey at 18 to 22 weeks of gestation (or earlier if technically feasible).
- ☐ Fetal echocardiogram at 18 to 22 weeks of gestation
- ☐ Antenatal fetal surveillance (nonstress test or biophysical profile), weekly starting at 32 0/7 weeks for uncomplicated MC/DA twins, individualized in consultation with maternal-fetal medicine specialist for complicated MC/DA twins.
- ☐ Prophylactic cerclage and prophylactic progesterone are not recommended.

Twin to Twin Transfusion (TTTS)

- ~15% of monochorionic twin pregnancies
- Will have a presence of at least 1 ateriovenous anastomosis
- Pathology is not as simple as net transfer of red blood cells (no hemoglobin discrepancy)
- Complex physiology with endocrine systems likely contributing



TTTS Staging

TABLE 1
Quintero staging of twin-twin transfusion syndrome[22]

Stage	Ultrasound assessment	Criteria
I	Amniotic fluid	Maximal vertical pocket <2 cm in donor sac and maximal vertical pocket >8 cm in recipient sac
II	Fetal bladder	Nonvisualization of fetal bladder in donor twin over 60 minutes of observation
III	Doppler studies	Absent or reversed umbilical artery end-diastolic velocity, reversed ductus venosus a-wave flow, pulsatile umbilical vein flow
IV	Fetal ascites or hydrops	Ascites or hydrops in 1 or both twins
V	Fetal cardiac activity	Fetal demise in 1 or both twins

Society for Maternal-Fetal Medicine. Twin-twin transfusion syndrome and twin anemia-polycythemia sequence. Am J Obstet Gynecol 2024.

Table 1. Cincinnati staging system for twin–twin transfusion syndrome

Stage	Donor	Recipient	Recipient cardiomyopathy
I	Oligohydramnios (DVP < 2 cm)	Polyhydramnios (DVP > 8 cm)	No
II	Absent bladder	Bladder seen	No
III	Abnormal Doppler	Abnormal Doppler	Possible
IIIa	± Abnormal Doppler	± Abnormal Doppler	Mild
IIIb	± Abnormal Doppler	± Abnormal Doppler	Moderate
IIIc	± Abnormal Doppler	± Abnormal Doppler	Severe
IV	Hydrops	Hydrops	
V	Death	Death	

DVP, deepest vertical pocket.

Table 2. Grading of severity of recipient-twin cardiomyopathy in twin–twin transfusion syndrome

Variable	Cardiomyopathy grade		
	Mild	Moderate	Severe
AVVR	Mild	Moderate	Severe
RV/LV hypertrophy	Mild	Moderate	Severe
MPI	> +2 *Z*-score	≥ +3 *Z*-score	≥ +4 *Z*-score
Left MPI	> 0.43, < 0.48	≥ 0.48, < 0.53	≥ 0.53
Right MPI	> 0.48, < 0.56	≥ 0.56, < 0.64	≥ 0.64

Mean MPI in normal fetuses in our institution: right MPI, 0.32 ± 0.08; left MPI, 0.33 ± 0.05. AVVR, atrioventricular valve regurgitation; MPI, myocardial performance index; RV/LV, right ventricular/left ventricular.

Villa, C.R., Habli, M., Votava-Smith, J.K., Cnota, J.F., Lim, F.-.-Y., Divanovic, A.A., Wang, Y. and Michelfelder, E.C. (2014), Assessment of fetal cardiomyopathy in early-stage twin–twin transfusion syndrome: comparison between commonly reported cardiovascular assessment scores. Ultrasound Obstet Gynecol, 43: 646-651. https://doi.org/10.1002/uog.13231

Recipient Cardiac Dysfunction in TTTS: Highlights

- ✓ Up to 70% recipient fetuses have some evidence of cardiac compromise at time of diagnosis of TTTS
- ✓ ~50%: cardiomegaly due to increased myocardial thickness (rather than ventricular dilation)
- ✓ Can see increase in cardiac output of recipient (aligns with volume overload)
- ✓ Diastolic function worse than systolic function

TEI INDEX

- Changes in MPI often seen in pregnancies not yet meeting TTTS criteria (but often will)
- Diastolic dysfunction usually more compromised than systolic= increased MPI
- Cannot be used for upstaging without other TTTS criteria

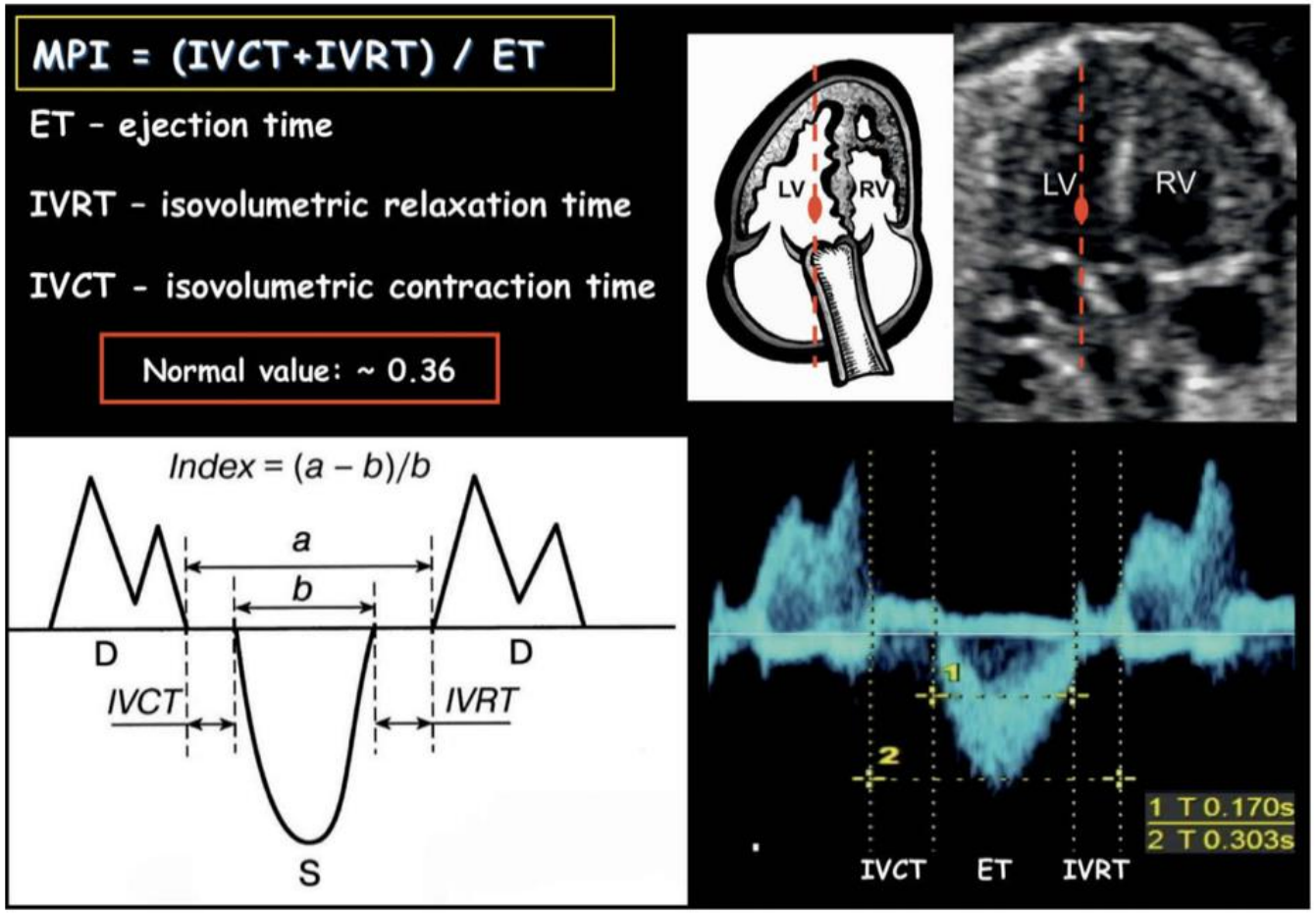
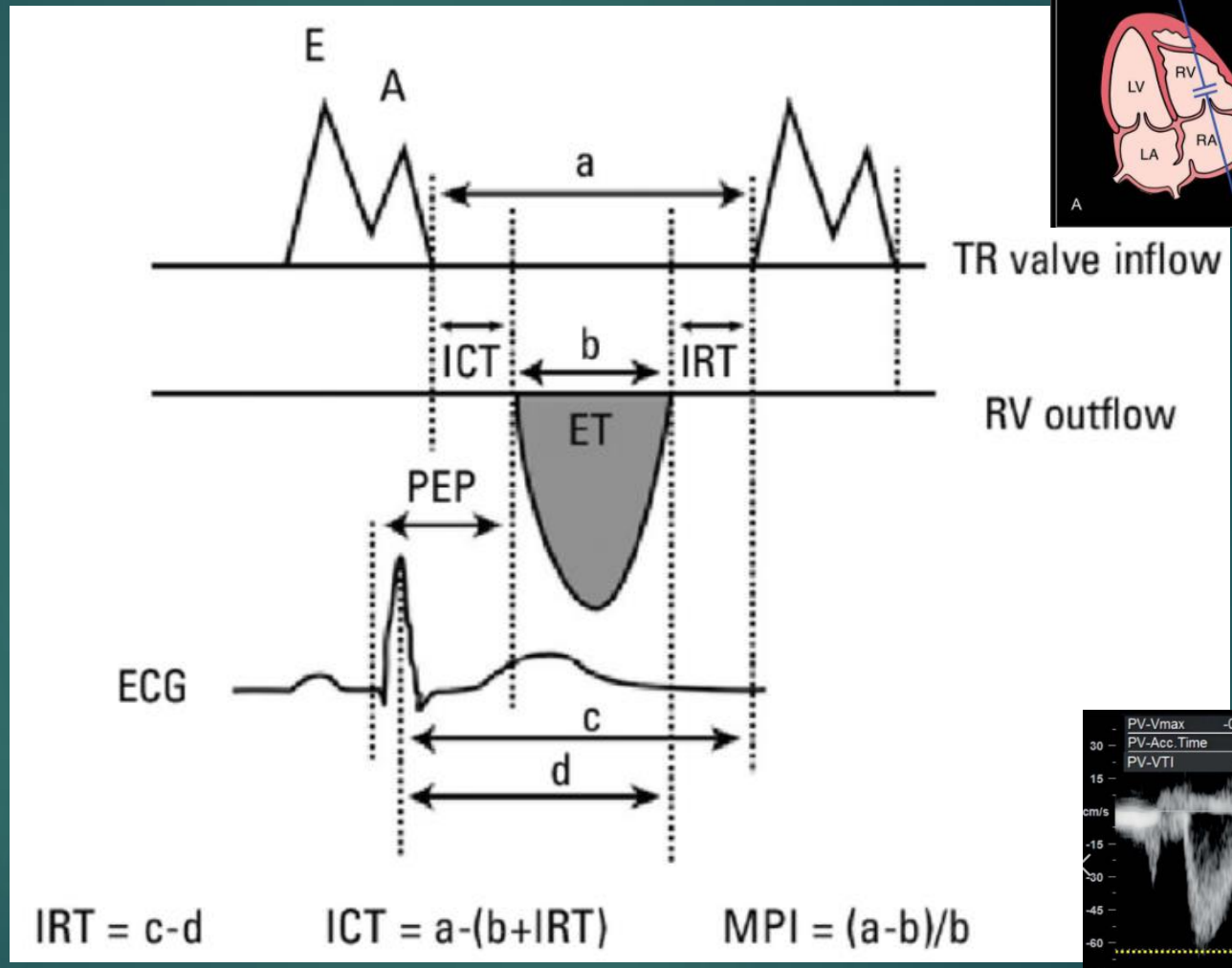
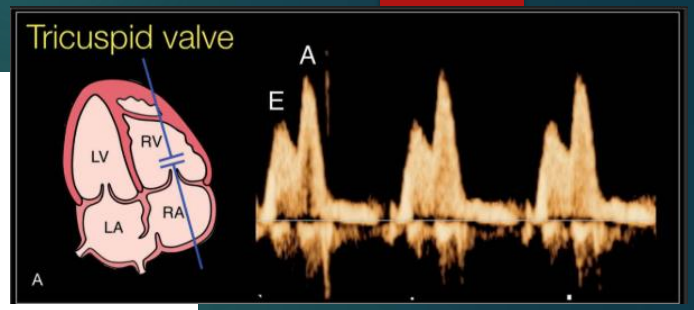
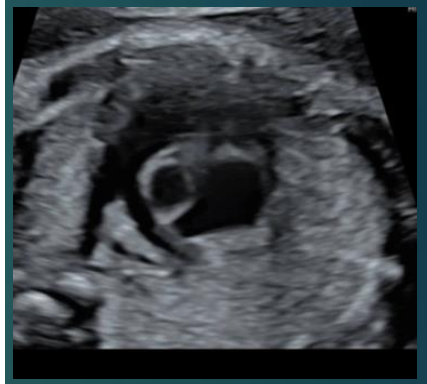


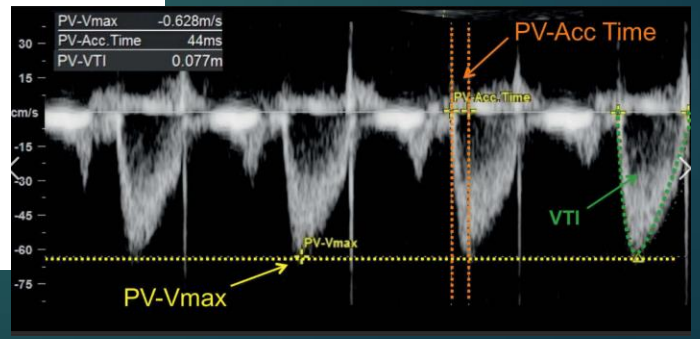
Image: OBGYN Key

Right Ventricular MPI : Same measurements but 2 views needed









Slide adapted from Laura Vricella, MD

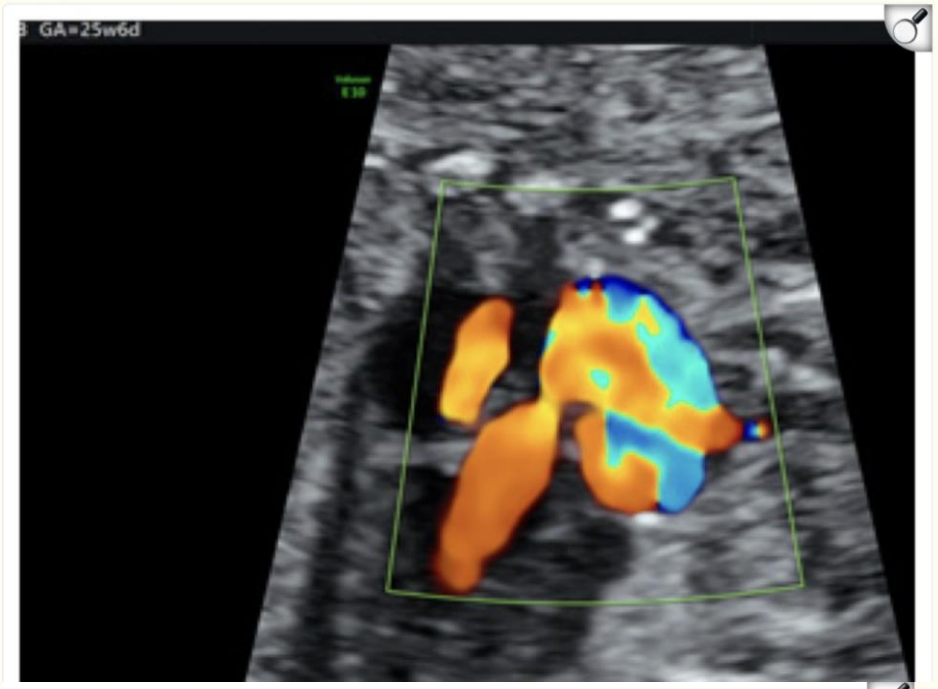
Role of MPI in multiple disease states

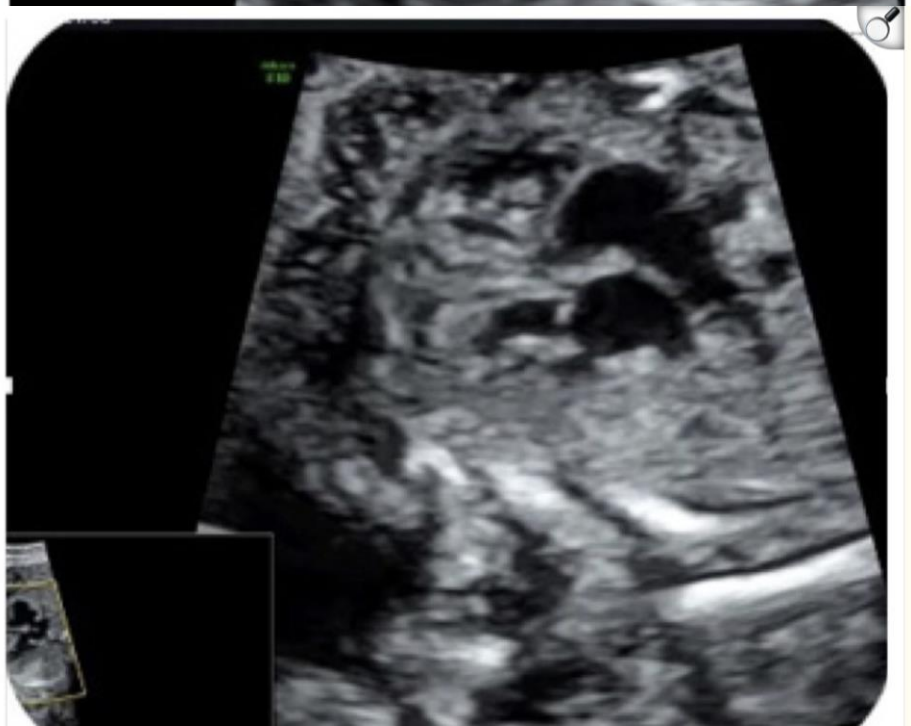
Condition	MPI Range	Clinical Significance	Recommended Action	
Normal fetus	0.35–0.45	Normal function	Routine monitoring	[1]
Borderline	0.46–0.50	Possible mild dysfunction	Enhanced surveillance	[1]
TTTS recipients	>0.55	Dysfunction likely	Specialist referral	[2]
Severe FGR	>0.55	Early compromise	Consider delivery	[3]
Maternal diabetes	0.48-0.60	Subclinical dysfunction	Glycaemic optimization	[4]
Preeclampsia	>0.60	Combined dysfunction	Multidisciplinary care	[5]
Any condition	>0.65	Severe dysfunction	Immediate assessment	[1]

1. Hernandez-Andrade et al., 2005. https://doi.org/10.1002/uog.1959
2. Michelfelder et al., 2007. https://doi.org/10.1002/uog.5188
3. Cruz-Martinez et al., 2011. https://doi.org/10.1097/AOG.0b013e3182097a13
4. Al-Biltagi et al., 2013. https://doi.org/10.1007/s00246-012-0501-2
5. Godfrey et al., 2012. https://doi.org/10.1002/uog.10066

Functional Pulmonary Atresia in the Recipient

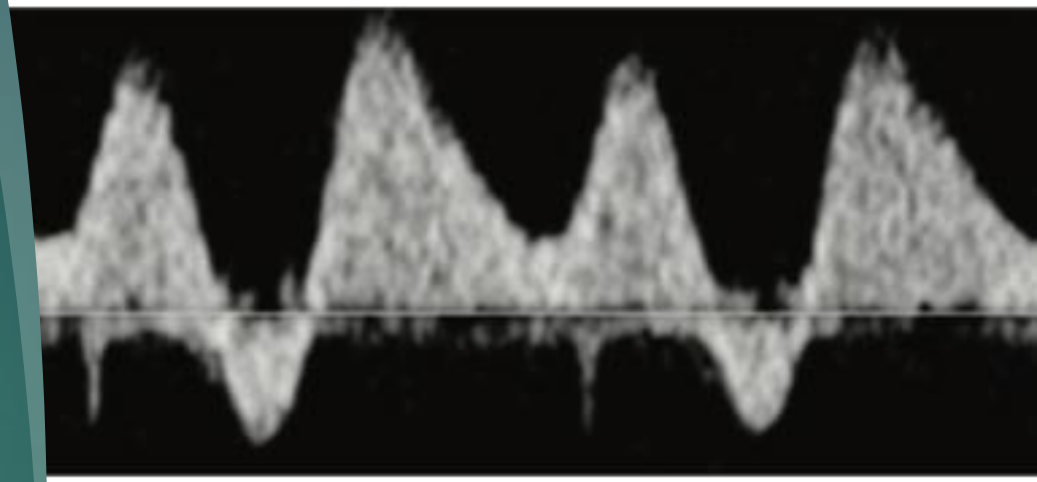
- Worsening ventricular hypertrophy and systolic dysfunction can lead to narrowing and stenosis of pulmonary valve
- Up to 90% can resolve post-laser therapy





Role of Dopplers in the Recipient Fetus

- Ductous venosus can act as a reflection of pressure-volume changes in the fetal heart
- Advanced changes in blood flow/impaired cardiac function can reflect in the DV first by decreased pulsatility and ultimately, reversal of the a-wave
  - Can be a poor prognostic marker, correlated with developing hydrops
- Pulsatile umbilical vein can also be seen



(a)

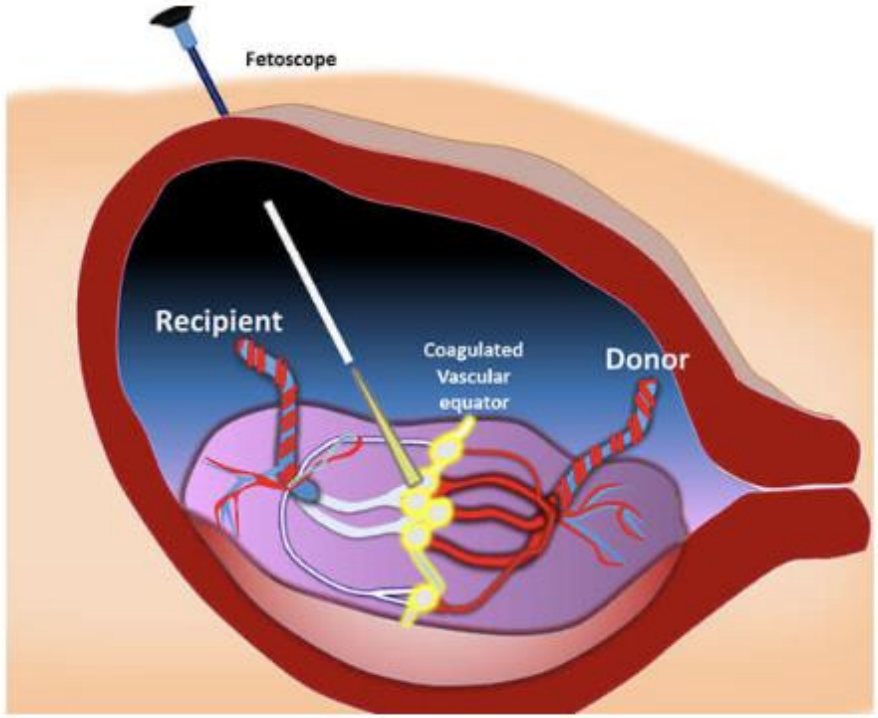
(b)

Donor Cardiac Considerations

- Cardiac findings are generally secondary to significant uteroplacental insufficiency
  - Abnormal DV waveform, tricuspid regurgitation, umbilical vein pulsations
- Constantly decreased blood flow can lead to more permanent vascular changes
  - Increased collagen synthesis
  - Smooth muscle hypertrophy
  - Vascular medial hypertrophy

Treatment options

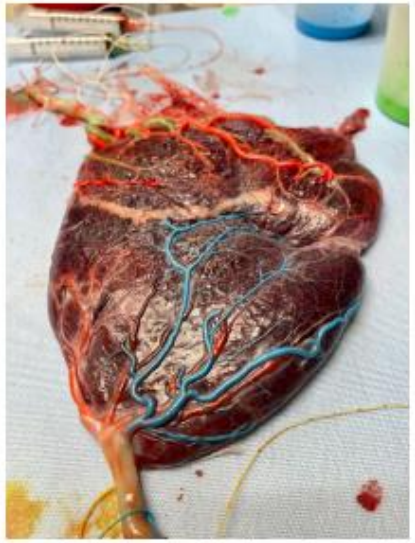
- Fetoscopic laser surgery: photocoagulation of intertwin placental anastomoses, functionally aiming to "dichorionize" placental circulation
  - Dual survivors >50-70%
  - 1 survivor 20-30%
  - No survivors 10-20%
- Laser for ≥ Stage 2 with consideration on Stage 1 under certain circumstances 16-26 weeks
- Therapeutic Amnioreduction: symptomatic relief butalso can improve hemodynamics
  - Can be used when laser intervention is not feasible



https://www.hopkinsmedicine.org/gynecology-obstetrics/specialty-areas/fetal-therapy/fetal-interventions-procedures/fetoscopic-laser-surgery

Fetoscopic Laser Photocoagulation

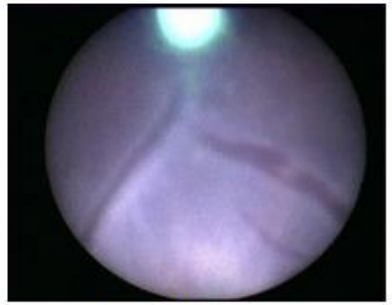
FIGURE 13
Placental dye study of a monochorionic-diamniotic twin placenta following laser photocoagulation with adjunct Solomon equatorial dichorionization



A horizontal hypoechoic line extending from edge to edge acros placental surface is observed, representing photocoagulation acros intertwin vascular equator. Colored dye has been injected into each t umbilical vessels, and no dye is observed to communicate betweer placental territories.
[Image courtesy E. Bergh, MD].

Society for Maternal-Fetal Medicine. Twin-twin transfusion syndrome and twin a polycythemia sequence. Am J Obstet Gynecol 2024.

FIGURE 12
Fetoscopic view of a single arteriovenous anastomosis



A thick-walled artery (left) containing relatively deoxygenated (visibly darker) blood is observed to communicate with a thinner-walled vein (right) containing relatively oxygenated blood immediately before laser photo-coagulation. The tip of the laser fiber is in view at 12 o'clock.
[Image courtesy R. Miller, MD].

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Fetoscopic laser therapy completed, now what?

- Ongoing risks to fetuses to monitor:
  - Post-laser TAPS
  - Recurrent TTTS
  - Obstetrical Complications
  - Failure to improve primary process
- **TWIN ROLES CAN REVERSE!**
  - Donor can become recipient/polycythemic
  - Recipient can become donor/anemic
- Realistic Expectations
  - Donor bladder may not return for weeks
  - DV (recipient) and UA Doppler studies (donor) commonly improve by day 5 but can be longer
  - Improvement on fetal echocardiogram gradual, full recovery can take months
  - Donor can have worse hemodynamic state initially (ex: right heart overload)

Fetal cardiac function in recipient twins undergoing fetoscopic laser ablation of placental anastomoses for Stage IV twin–twin transfusion syndrome

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- Retrospective study of 34 Stage IV cases of TTTS (hydrops) undergoing fetoscopic laser
- 15 ultimately met criteria with pre- and post-fetal echo
- All had abnormal pre-operative fetal echocardiogram
- Follow-up fetal echo at median of 26 days post-laser showed significant improvement in cardiac function but wasn't completely resolved in time period
- Functional pulmonary atresia resolved in all surviving fetuses

TABLE 2
Prenatal staging of twin anemia-polycythemia sequence[85,95]

Stage	Criteria	Intertwin criteria
1	MCA-PSV >1.5 MoM in donor and MCA-PSV <1.0 MoM in recipient	Δ MCA-PSV >0.5 MoM without cardiac compromise of donor[a]
2	MCA-PSV >1.7 MoM in donor and MCA-PSV <0.8 MoM in recipient	
3	Stage 1 or 2 with cardiac compromise of donor[a]	
4	Ascites or hydrops of donor	
5	Single or double fetal demise	

MCA-PSV, middle cerebral artery Doppler peak systolic velocity; *MoM*, multiples of the median.

Adapted from Slaghekke et al,[85] 2010 and Tollenaar et al,[95] 2019.

[a] Cardiac compromise defined as absent or reversed end-diastolic flow in umbilical artery, pulsatile flow in umbilical vein, or reversed a-wave in the ductus venosus.

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Twin Anemia Polycythemia Sequence (TAPS)

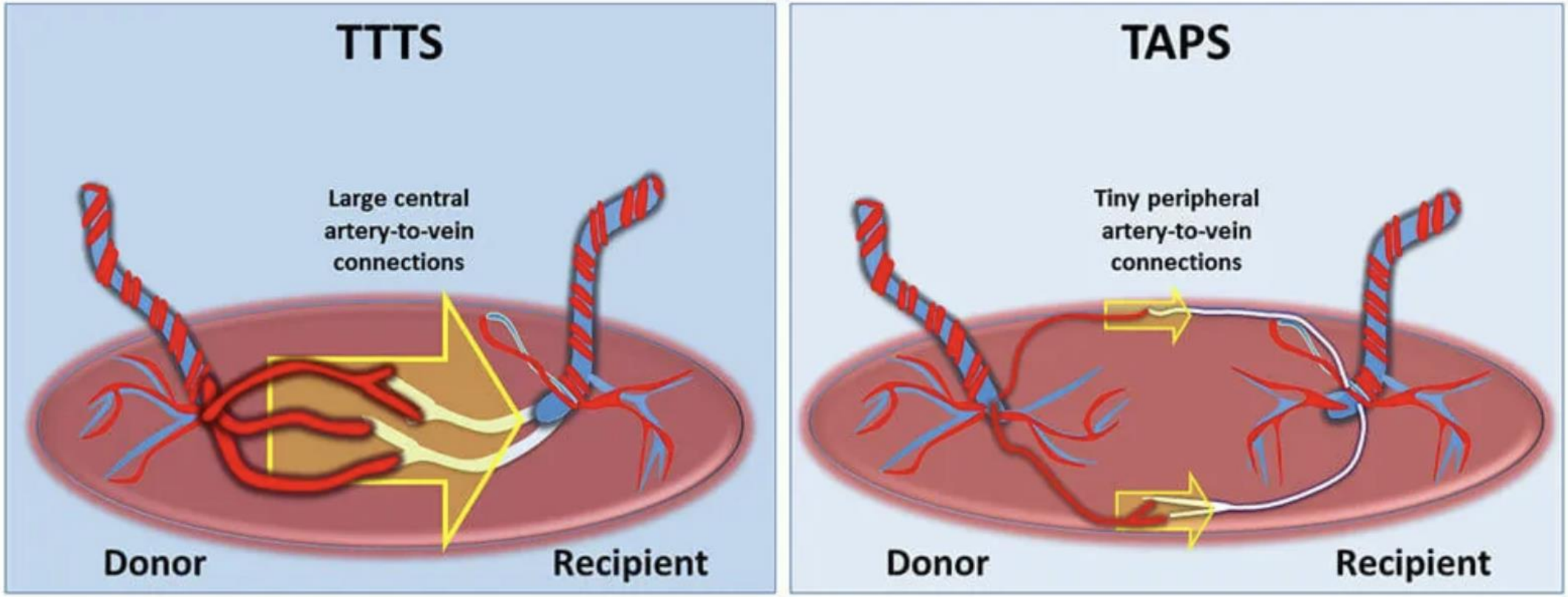


Image: TTTS Foundation

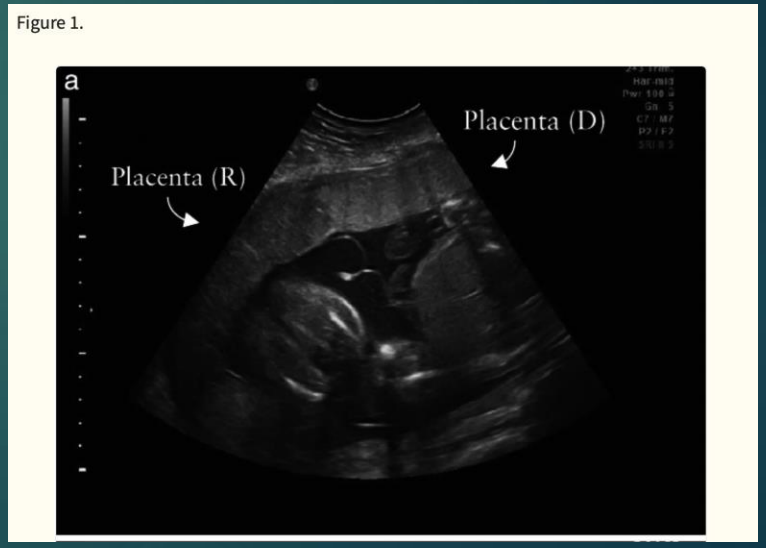
Possible Associated Ultrasound Findings

Anemic Twin

- **Cardiomegaly, hyperdynamic state**
- **Hydrops fetalis**
- Thicker, hyperechogenic placenta portion

Polycythemic Twin

- "Starry sky appearnce" of liver:
  - Diminished echogenicity of liver parenchyma
  - Increased brightness of portal venule walls
- Thin, more translucent placenta



Prevalence of placental dichotomy, fetal cardiomegaly and starry-sky liver in twin anemia–polycythemia sequence

L S A Tollenaar [1,✉], E Lopriore [2], J M Middeldorp [1], F J C M Klumper [1], M C Haak [1], D Oepkes [1], F Slaghekke [1]

- Retrospective study in the Netherlands looking at 91 pregnancies complicated by TAPS between 2006-2019
- Prevalence of 3 ultrasound markers:
  - Placental dichotomy
  - Cardiomegaly (anemic twin)
  - "Starry-sky" appearance of liver (polycythemic twin)

Prevalence of placental dichotomy, fetal cardiomegaly and starry-sky liver in twin anemia–polycythemia sequence

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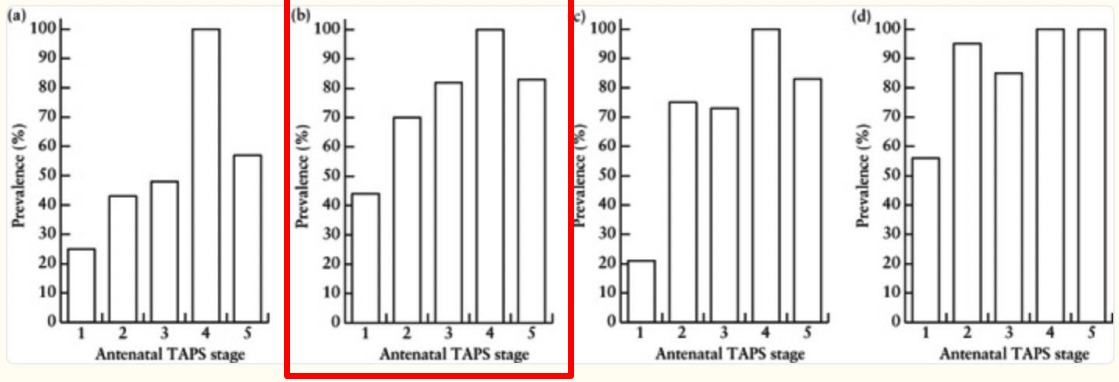
Results:

Figure 2.



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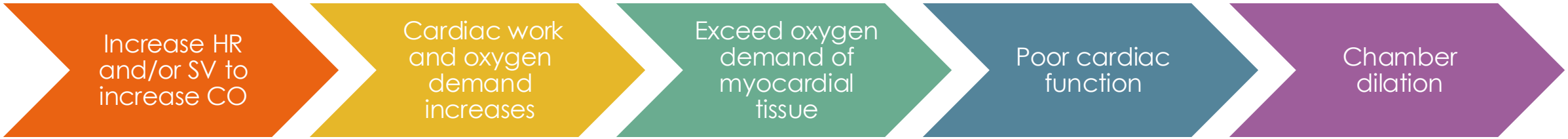
Prevalence of placental dichotomy (a), cardiomegaly in donor twin (b), starry-sky liver in recipient twin (c) and at least one of these ultrasound markers (d) in 91 pregnancies with twin anemia–polycythemia sequence (TAPS), according to antenatal TAPS stage. In total, 16 cases were Stage 1, 40 were Stage 2, 27 were Stage 3, two were Stage 4 and six were Stage 5.

- Cardiomegaly: Most frequently observed ultrasound finding
- 70% of the TAPS pregnancies had cardiomegaly
- More than 40% Stage 1 TAPS showed cardiac remodeling in response to the anemic environment

High Output Cardiomyopathy

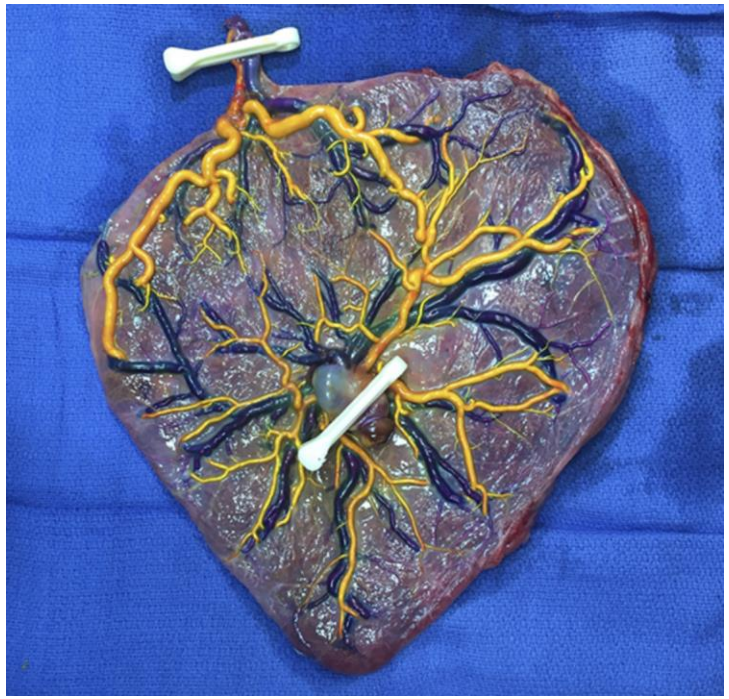


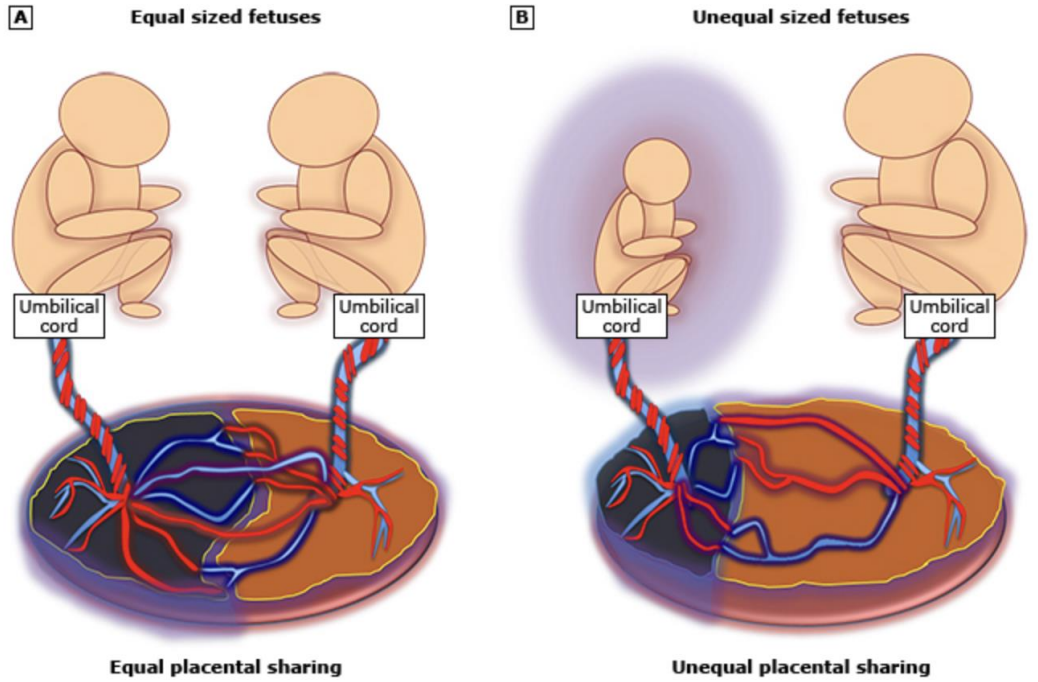
Management of TAPS

- Severe mid-trimester TAPS at least stage 2: Consider fetoscopic laser therapy
  - Might be more technically challenging
- Consider intrauterine transfusion, intraperitoneal transfusion +/- intraperitoneal blood transfusion where laser therapy is inadvisable
- Consideration for delivery based on gestational age

Selective Fetal Growth Restriction (sFGR)

- Fetal weight for one twin < 10% and EFW discrepancy between fetuses is at least 25%
- Etiology: unequal placental sharing with different placental anastomoses
- Classification system for prognosticating:
  - Type 1: Forward Flow in UA Dopplers
  - Type 2: Persistent absent or persistent reversal of end diastolic flow (EDF) in the UA Doppler
  - Type 3: Intermittent absent/reversed EDF in UA Dopplers with characteristic appearance





UpToDate

Pathophysiology of selective FGR: Unequal placental sharing

SFGR Dopplers: improving accuracy

- The vessel wall filter, variously called 'low-velocity reject', 'wall-motion filter' or 'high-pass filter', is used to eliminate noise resulting from the movement of the vessel walls. According to convention, it should be set as low as possible ($\leq 50–60$ Hz), in order to eliminate the low-frequency noise from peripheral blood vessels. When using a higher threshold for the filter, a gap between the Doppler line and the Doppler signals can be seen. This can create the spurious effect of absent EDV (see Figure 4b).

Guidelines for results you can trust

- Wall motion filter should be set lower (< 50-60 Hz) to eliminate low-frequency noise from peripheral blood vessels

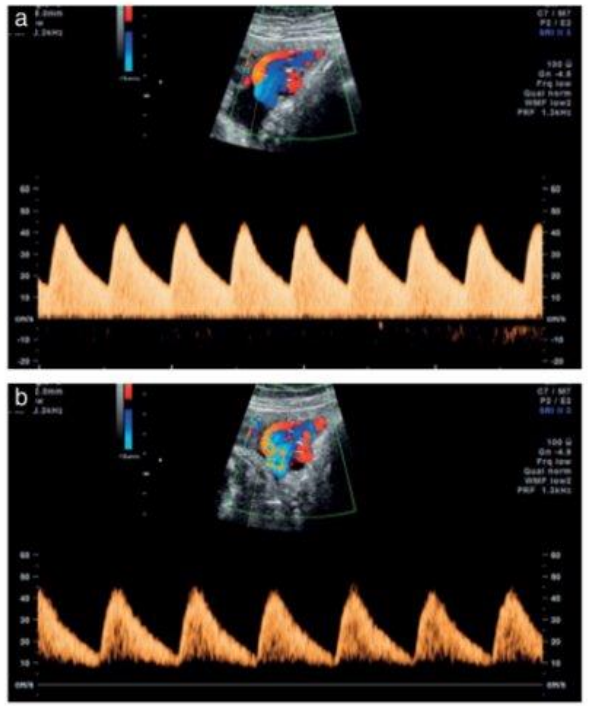


Figure 4 (a) Umbilical artery velocity waveform recorded with a low vessel wall filter setting showing normal flow and (b) a recording with apparently very low diastolic flow and absent flow signals at baseline, due to use of incorrect vessel wall filter, which is set too high, thereby concealing the low velocities along the zero line.

isuog.org GUIDELINES

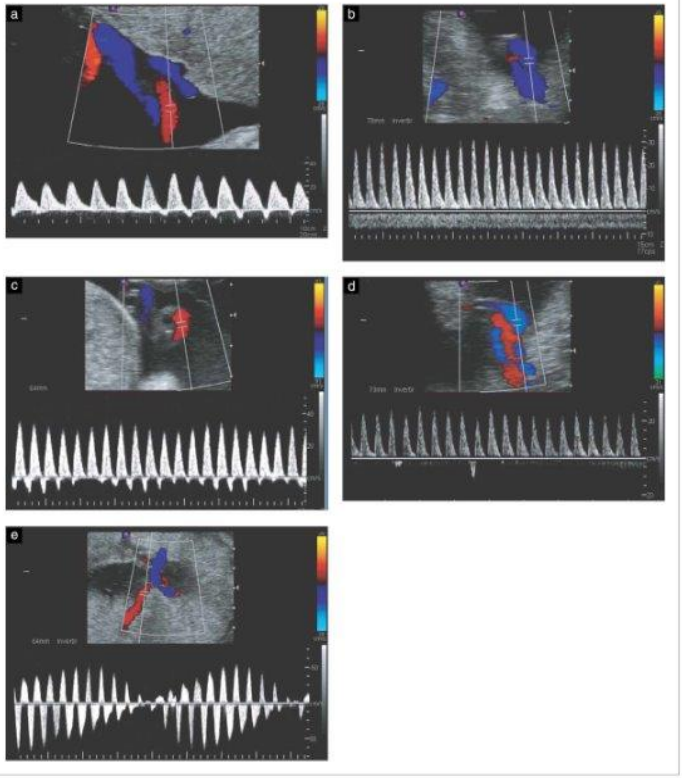


Figure 1 Open in figure viewer | PowerPoint

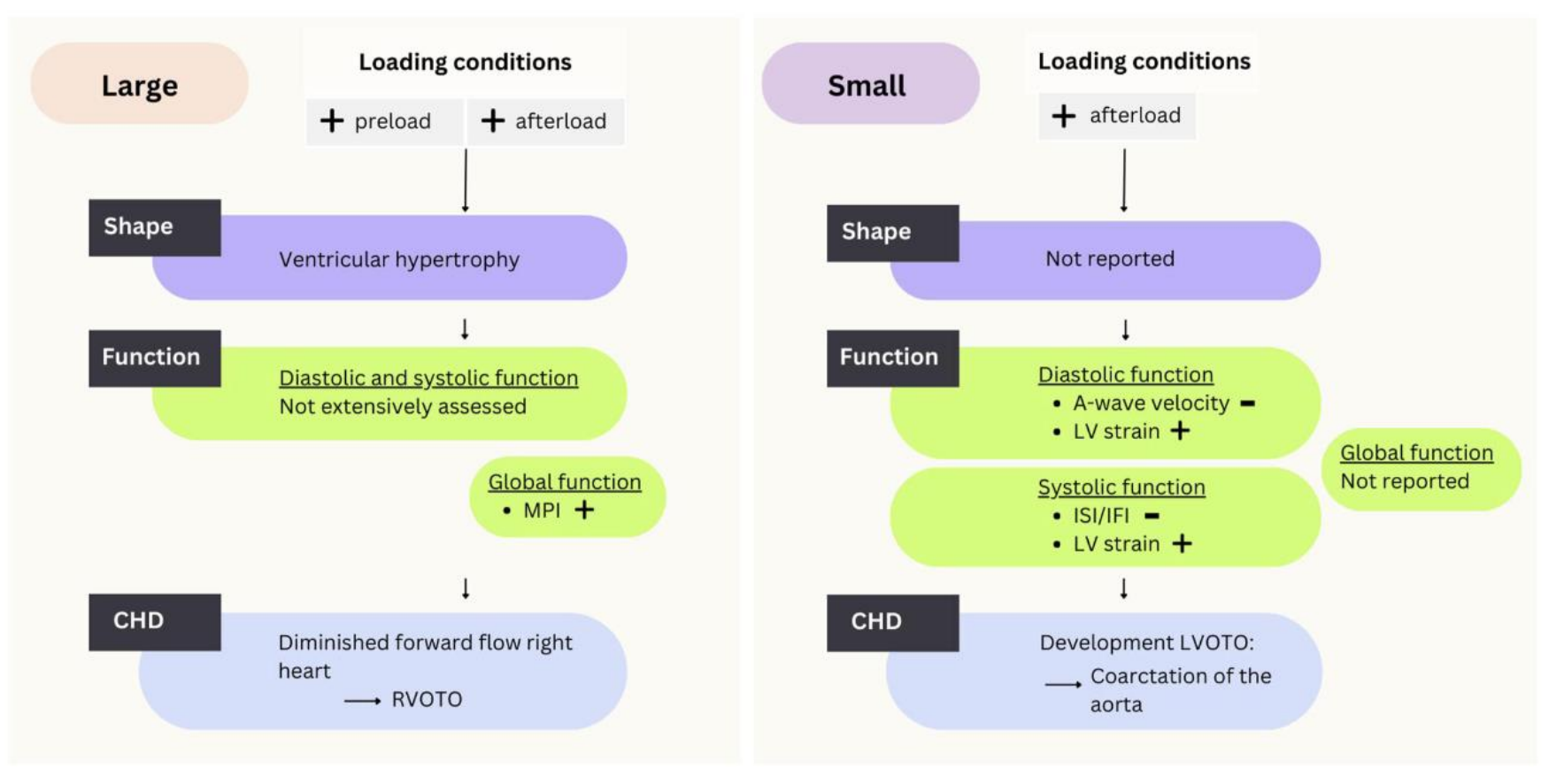
Different umbilical artery Doppler waveforms in monochorionic fetuses with selective intrauterine growth restriction and intermittent absent or reversed end-diastolic flow (iAREDF). (a) Typical image of iAREDF with cycles showing absent and/or reversed flow. (b,c) Using the fastest sweep speed allows better appreciation of the cyclical nature of the changes, as present in most cases, which may range from (b) absent to (c) clearly reversed diastolic waveforms. The systolic waveforms also show a characteristic oscillating aspect which results from the influence of the transmitted waveforms in the peak velocity. (d) In a proportion of cases, the intermittent appearance of absent or reversed waveforms is not cyclical and follows a more irregular pattern, occasionally appearing irregularly over periods of minutes rather than seconds. (e) The large placental arterioarterial anastomoses causing this Doppler phenomenon can virtually always be found and insonated26, showing the characteristic bidirectional and periodic pattern resulting from the collision of the two systolic waveforms.

Type 3 sFGR Examples

Management of sFGR

- Select cases of Type 2/3: offer Fetoscopic laser photocoagulation
- Cord occlusion (usually RFA) offered for Type 2-3
- Expectant management: prolonged hospitalization and frequent ultrasound/surveillance assessments
- Delivery considerations based on gestational age

Cardiac Implications with sFGR



Noll ATR, Gijtenbeek M, Verweij EJTJ, Lewi L, Herling L, Haak MC. Cardiac adaptation and malformation in twin-twin transfusion syndrome and selective fetal growth restriction: A systematic review. Prenat Diagn. 2024 Jun;44(6-7):832-845. doi: 10.1002/pd.6575. Epub 2024 Apr 21. PMID: 38643403.

Neonatal Considerations

Neonatal Outcome in Twin-to-Twin Transfusion Syndrome *Not* Treated with Fetoscopic Laser Surgery

Published online by Cambridge University Press: **30 May 2022**

Elina A. Lopriore, Femke Slaghekke, E. Joanne Verweij, Monique C. Haak, Annemieke J. M. Middeldorp and Enrico Lopriore

Show author details

- Retrospective study 2002-2021 out of Leiden University Medical Center looking at TTTS twins
- NOT treated with laser:
  - High rate of adverse neonatal outcome (30%)
  - NEC (11%)
  - Severe cerebral injury (14%)
  - Hypotension (24%)

	Non-laser group ($n = 88$)	Laser group ($n = 176$)	p value
Neonatal death — n (%)	**9 (10%)**	**9 (5%)**	.120
Donor	3 (7%)	6 (7%)	1.000
Recipient	6 (14%)	3 (3%)	.059
Severe cerebral injury — n (%)	**12 (14%)**	**9 (5%)**	.016
Donor	4 (9%)	5 (6%)	.480
Recipient	8 (18%)	4 (5%)	.020
Patent ductus arteriosus — n (%)	**10 (11%)**	**7 (4%)**	.021
Donor	5 (11%)	3 (3%)	.116
Recipient	5 (11%)	4 (5%)	.159
RVOTO — n (%)	**1 (1%)**	**1 (1%)**	1.000
Donor	0 (0%)	0 (0%)	–
Recipient	1 (2%)	1 (1%)	1.000
PPHN — n (%)	**8 (9%)**	**17 (10%)**	.882
Donor	5 (11%)	9 (10%)	1.000
Recipient	3 (7%)	8 (9%)	.751
Hypotension — n (%)	**21 (24%)**	**17 (10%)**	.002
Donor	11 (25%)	9 (10%)	.026
Recipient	10 (23%)	8 (9%)	.031
Anemia at birth — n (%)	**13 (15%)**	**10 (6%)**	.014
Donor	11 (25%)	6 (7%)	.003
Recipient	2 (5%)	4 (5%)	1.000
Polycythemia at birth — n (%)	**9 (10%)**	**3 (2%)**	.003
Donor	0 (0%)	2 (2%)	.314
Recipient	9 (21%)	1 (1%)	<.001
Necrotizing enterocolitis — n (%)	**10 (11%)**	**3 (2%)**	.001
Donor	6 (14%)	2 (2%)	.017
Recipient	4 (9%)	1 (1%)	.042
Respiratory distress syndrome — n (%)	**44 (50%)**	**68 (39%)**	.078
Donor	20 (46%)	33 (38%)	.379
Recipient	24 (55%)	35 (40%)	.108
Renal failure — n (%)	**7 (8%)**	**1 (1%)**	.002
Donor	5 (11%)	1 (1%)	.016
Recipient	2 (5%)	0 (0%)	.109
Adverse neonatal outcome — n (%)	**26 (30%)**	**19 (11%)**	<.001
Donor	11 (25%)	11 (13%)	.069
Recipient	15 (34%)	8 (9%)	0.001

Future Directions

- Continue research to better understand the pathophysiology of these monochorionic twin pregnancies
  - Aid in diagnosis, management, and prognostication
- Improve our fetal therapy options and techniques
  - How can we improve fetal and neonatal outcomes?
- Standardize the role of fetal echocardiography in protocols and how it can alter clinical management

Important Considerations

- Can be overlap or movement between the diagnoses of TTTS, TAPS, and selective fetal growth restriction
  - Important to continue full assessments throughout pregnancy
  - Difficult to accurately predict prognosis
  - Underlying etiologies are not completely understood
- Evaluation does not stop after fetal intervention
  - Continued follow-up with full assessment is necessary given that a different pathology may develop, or the primary one may persist
- Multidisciplinary efforts and collaboration among OB, MFM, Neonatology, Pediatric Cardiology are crucial to management of these high risk pregnancies

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Questions?