11th Congress of Maternal Fetal Medicine and Perinatology Society of Turkey

Diagnosis and Management of the Early Growth Restricted Fetus

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Disclosures

No Relevant Financial Relationships

Objectives

At the end of this presentation the participant will be able to:

- Classify IUGR fetuses
- Describe the cardiovascular changes that occur in early IUGR fetuses
- Describe the management of IUGR fetuses

IUGR

15,000 papers

IUGR-Definition

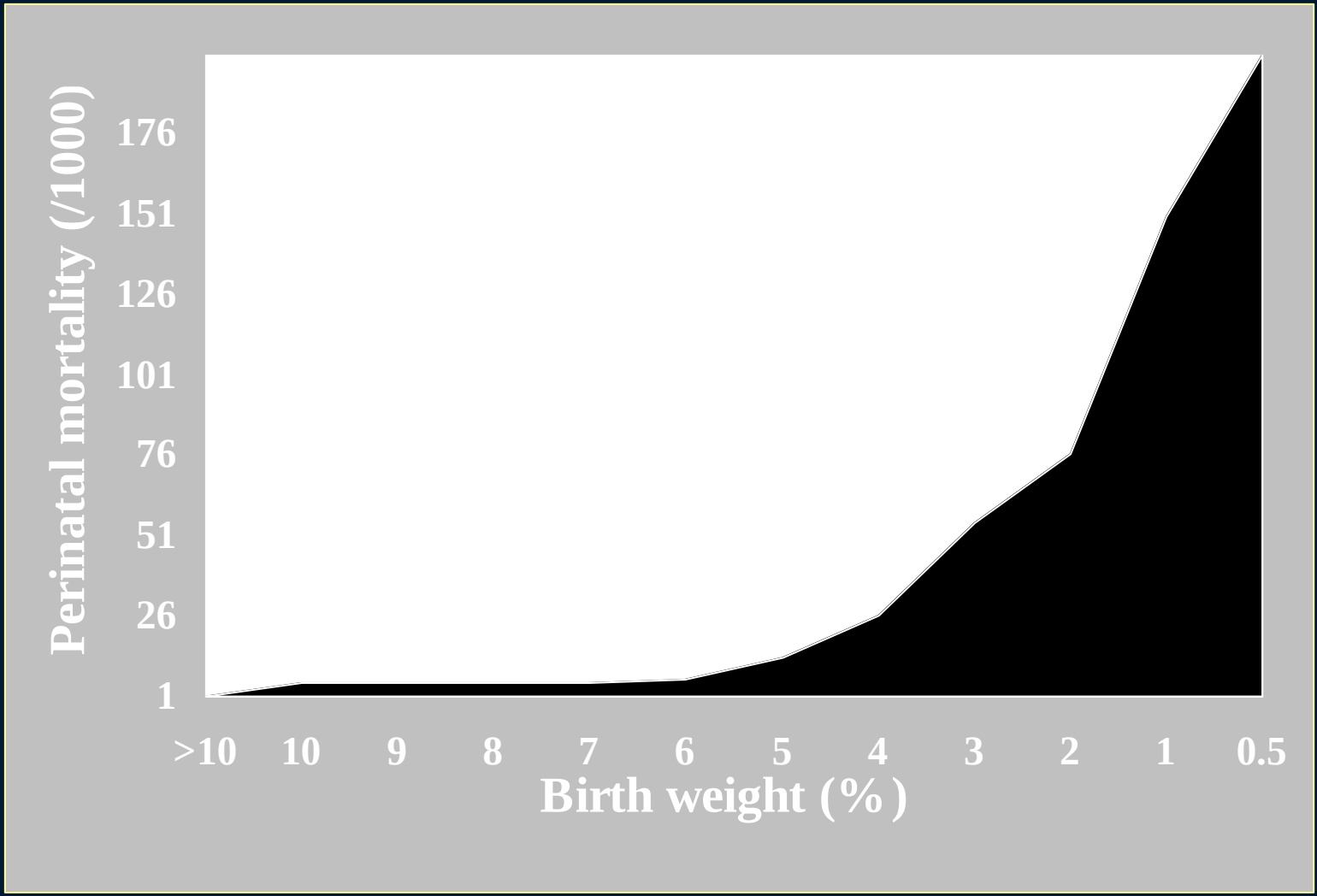
- Istanbul
- Memphis
- Rome

IUGR

Definitions:

- EFW < 10th percentile (USA)
- EFW < 5th percentile (USA)
- EFW < 3rd percentile (USA)
- EFW < 15th percentile (USA)
- EFW > 2 SD below mean (Europe)
- AC (10th → 2.5^{th} percentile (Europe)

Perinatal Mortality



Modified from Manning F. Fetal Medicine, 1995;7:307

EFW < 10th percentile

Normal

80%?

Pathologic

20%?

IUGR (abnl Doppler)

1) Gestational age
2) Causes
3) Vital weeks
4) Fetal Weight
5) When to use the umbilical artery Doppler?
6) When to use the MCA Doppler?
7) When to use the Ductus venosus Doppler?
8) Delivery Timing
9) Doppler changes in the “Early IUGR”
10) IUGR Protocol used in Memphis

#1
Gestational age

IUGR Classification

- Early (≤ 32 weeks)
- Late (> 32 weeks)

#2
Causes

Placental Insufficiency

"Umbrella that covers our ignorance in terms of etiology and pathogenesis of the utero-placental chronic dysfunction"

Assali, Eur J Obstet Gynecol Reprod Biol 1975;5:87-91

Placental Insufficiency

It is not the cause of IUGR but is rather the consequence of a disease process that often we do not understand

Comparison

IUGR	Pneumonia
Placental Insufficiency	Fever
??????????? ?????	Virus/Bacteria/Other

IUGR

Idiopathic and secondary to maternal or fetal conditions

Mari G and Hanif F COG 2007;50:497-509

IUGR Classification

- Idiopathic
- Chromosomal abnormalities
- Chronic Hypertension
- Preeclampsia
- Infections
- Diabetes
- Other

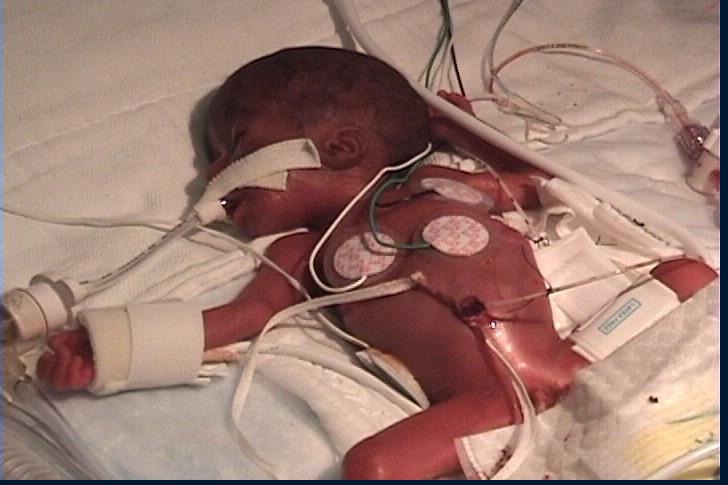
#3
Vital weeks

IUGR and Gestational Age at Delivery

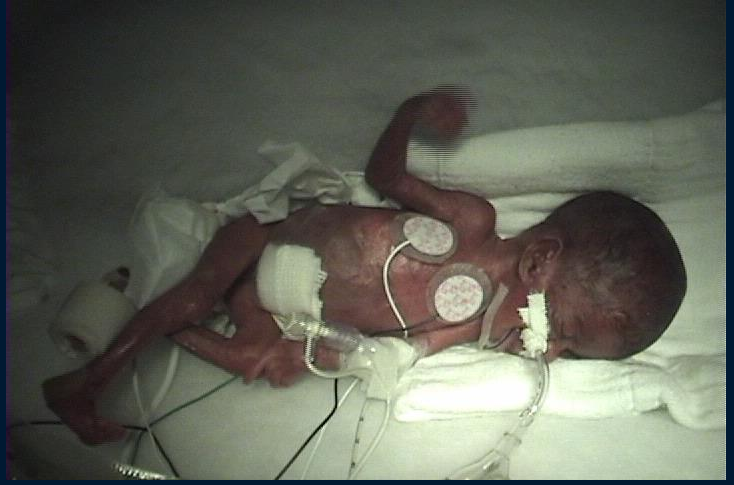
Between 25 and 29 weeks ("vital weeks"), for each week the IUGR fetus remains *in utero* the mortality decreases by 48%

Mari G et al. J Ultrasound Med 2007; 26:555-59

#4
Fetal weight



25+5 weeks
360 grams



DOL# 1

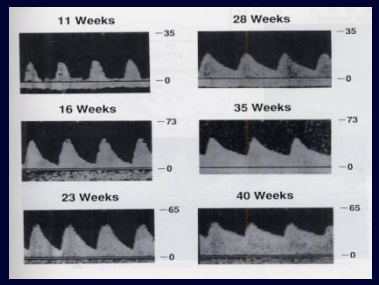
DOL# 7

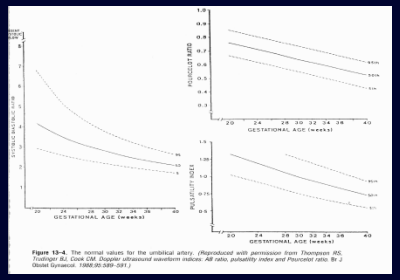
Two years later

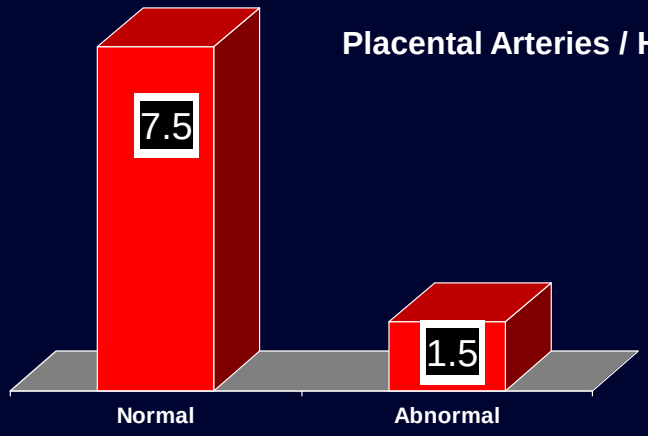
Doppler in IUGR

Umbilical artery
Middle cerebral artery
Ductus venosus

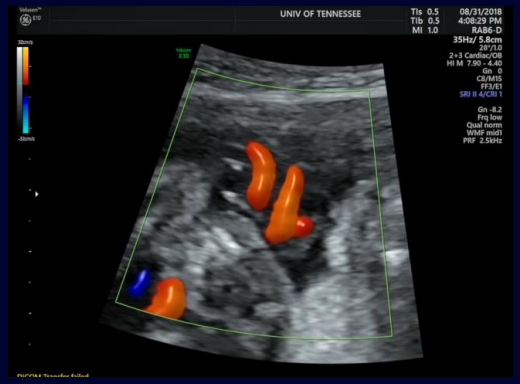
Umbilical Artery

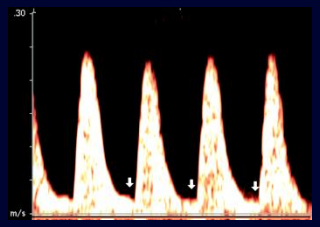




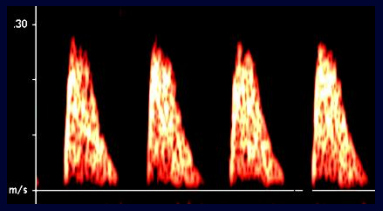


Giles WB, et al. Br J Obstet Gynecol 1985;92:31

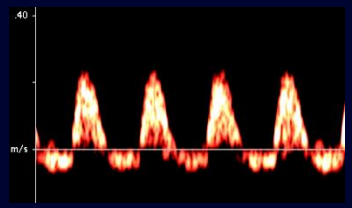




A



B



C

In cases of high placental vascular resistance (see IUGR), the umbilical artery diastole decreases (A), it becomes absent (B), and in the most severe cases, there is reversed flow (C)

#5
When to use the umbilical artery Doppler?

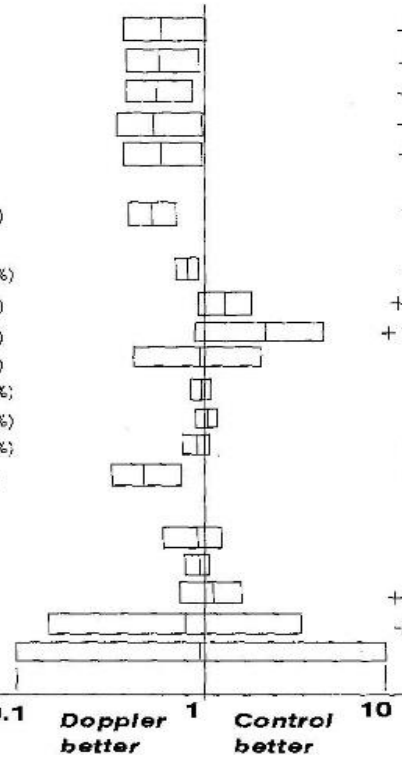
Do we need to use the UA Doppler as a screening test for IUGR?

- **Randomized and quasi-randomized studies (Doppler vs no Doppler in normal pregnancies)**
- **Five trials (14,624 women)**
- **There is no conclusive evidence that the use of routine UA Doppler, or combination of UA and uterine artery Doppler in low-risk or unselected populations benefits either mother or baby**

Alfirevic Z. et al. Cochrane Database Sys Rev. 2015

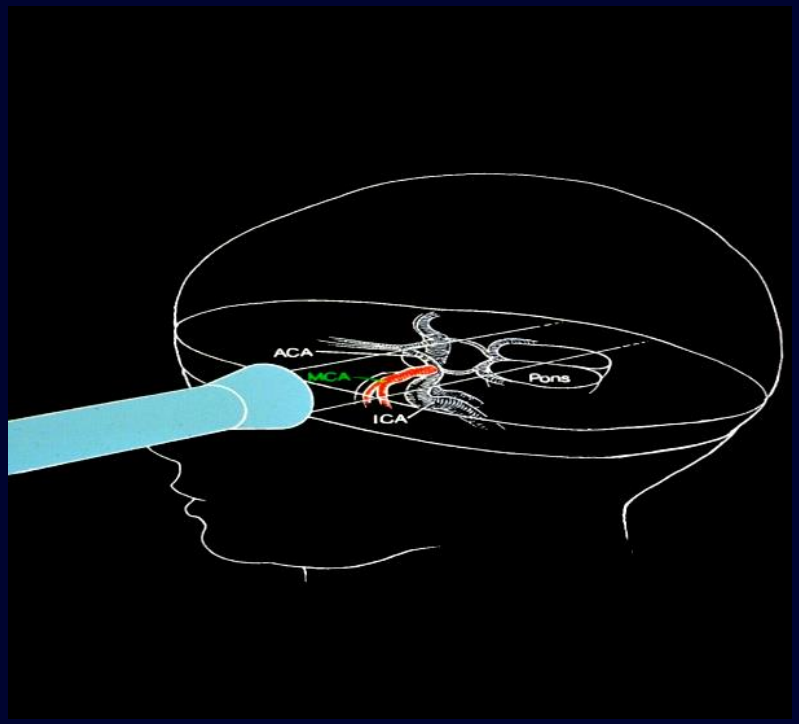
Do we need to use the UA Doppler in high risk pregnancies?

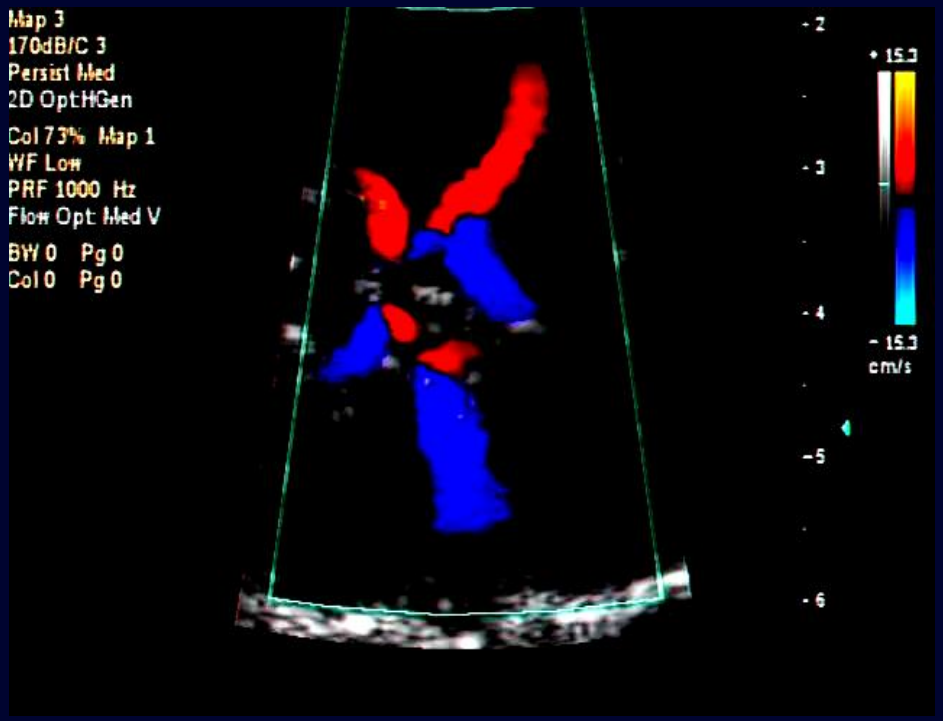
Outcome (Number of trials)	Number of deaths: Doppler	Number of deaths: Control	Odds ratio and 95% confidence interval	Change in Odds ratio (95% confidence interval)	Heterogeneity
Mortality					
Stillbirths (12)	24/3687 (0.6%)	39/3787 (1.0%)		-37% (-62% to+3%)	p=0.47
Neonatal deaths (12)	35/3684 (0.9%)	57/3751 (1.5%)		-38% (-59% to-7%)	p=0.46
All deaths-normally formed (12)	44/3687 (1.2%)	75/3787 (2.0%)		-41% (-59% to-15%)	p=0.64
Stillbirths-normally formed (12)	18/3687 (0.5%)	33/3787 (0.9%)		-44% (-68% to-3%)	p=0.67
Neonatal deaths-normally formed(12)	25/3684 (0.7%)	42/3751 (1.1%)		-39% (-62% to-1%)	p=0.87
Antenatal outcome					
Admission to hospital (3)	200/556 (35.8%)	262/547 (47.9%)		-44% (-57% to-28%)	p=0.2
Delivery					
Induction of labour (9)	620/2778 (29.5%)	978/2847 (34.3%)		-20% (-28% to-10%)	p=0.14
Delivery <37 weeks (2)	68/578 (11.7%)	51/571 (8.9%)		+36% (-7% to-98%)	p=0.63
Delivery <34 weeks (1)	12/241 (5.0%)	5/235 (2.1%)		+128%(-13% to+501%)	
Instrumental delivery (2)	11/322 (3.4%)	11/316 (3.5%)		-2% (-58% to+130%)	p=0.62
Caesarean sections (8)	660/2867 (23.8%)	677/2794 (24.2%)		-4% (-15% to+9%)	p=0.5
Elective Caesarean section (10)	395/3216 (12.3%)	392/3306 (11.9%)		+4% (-11% to+21%)	p=0.22
Emergency Ceasarean section (7)	336/2605 (12.9%)	378/2667 (14.2%)		-11% (-24% to+4%)	p=0.08
Caesarean for fetal distress (3)	28/558 (5.0%)	55/547 (10%)		-52% (-69% to-24%)	p=0.41
Neonatal outcome					
Low Apgar score at 5 min (8)	75/3008 (2.5%)	84/3115 (2.7%)		-7% (-32% to+27%)	p=0.07
Admission to neonatal unit (9)	475/3096 (15.3%)	509/3190 (15.9%)		-6% (-19% to+8%)	p=0.82
Ventilatory support (4)	51/949 (5.4%)	47/972 (4.8%)		+14% (-25% to+74%)	p=0.14
Intracranial haemorrhage (4)	3/982 (0.3%)	4/1011 (0.4%)		-23% (-82% to+241%)	p=0.2
Necrotising enterocolitis (1)	1/108 (0.9%)	1/104 (0.9%)		-4% (-96% to+1550%)	



Alfirevic Z. and Neilson JP. Am K Obstet Gynecol 1995;172:1379
Alfirevic Z., et al. Cochrane Database Syst Rev 2013

Circle of Willis

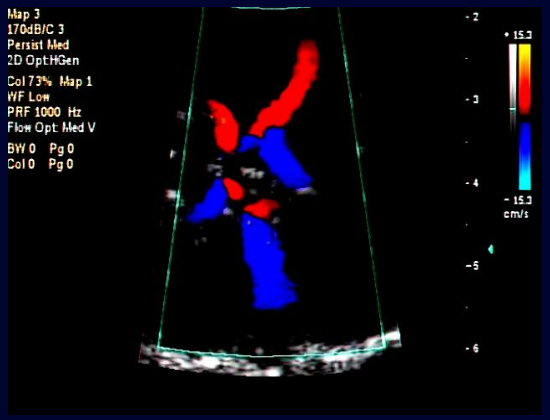


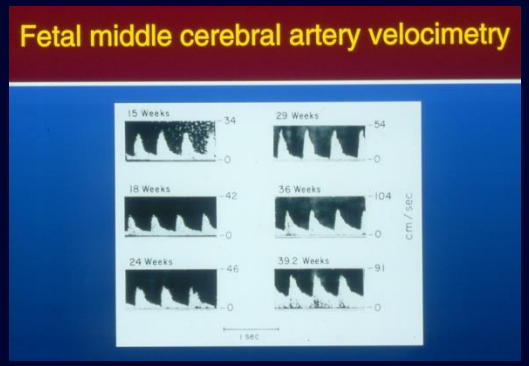


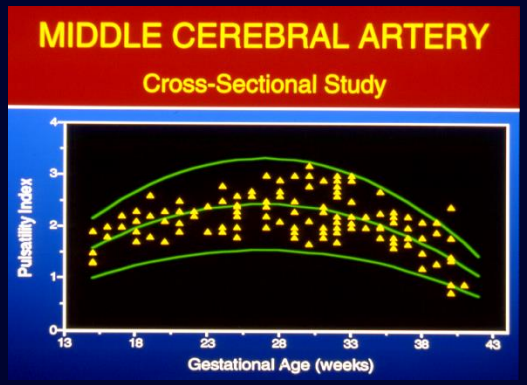
The most studied artery of the Circle of Willis is the middle cerebral artery (MCA)

Am J Obstet Gynecol 1989;160:698

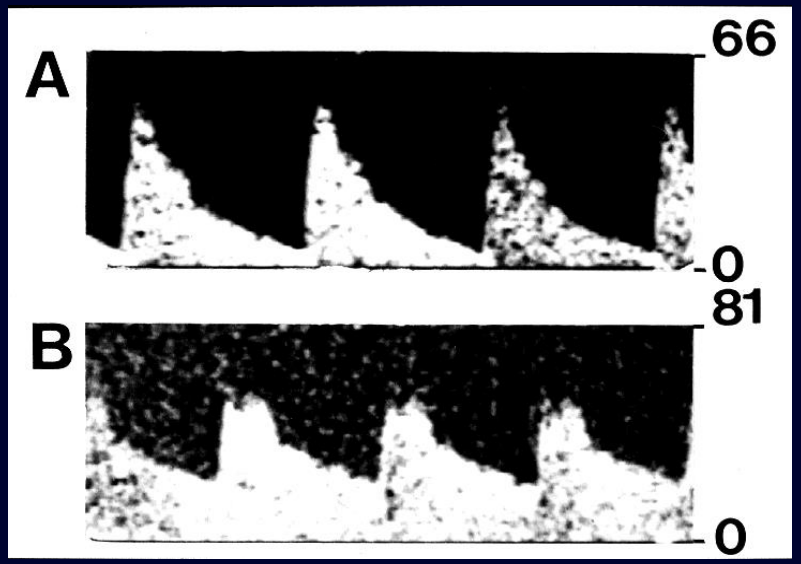
Middle Cerebral Artery







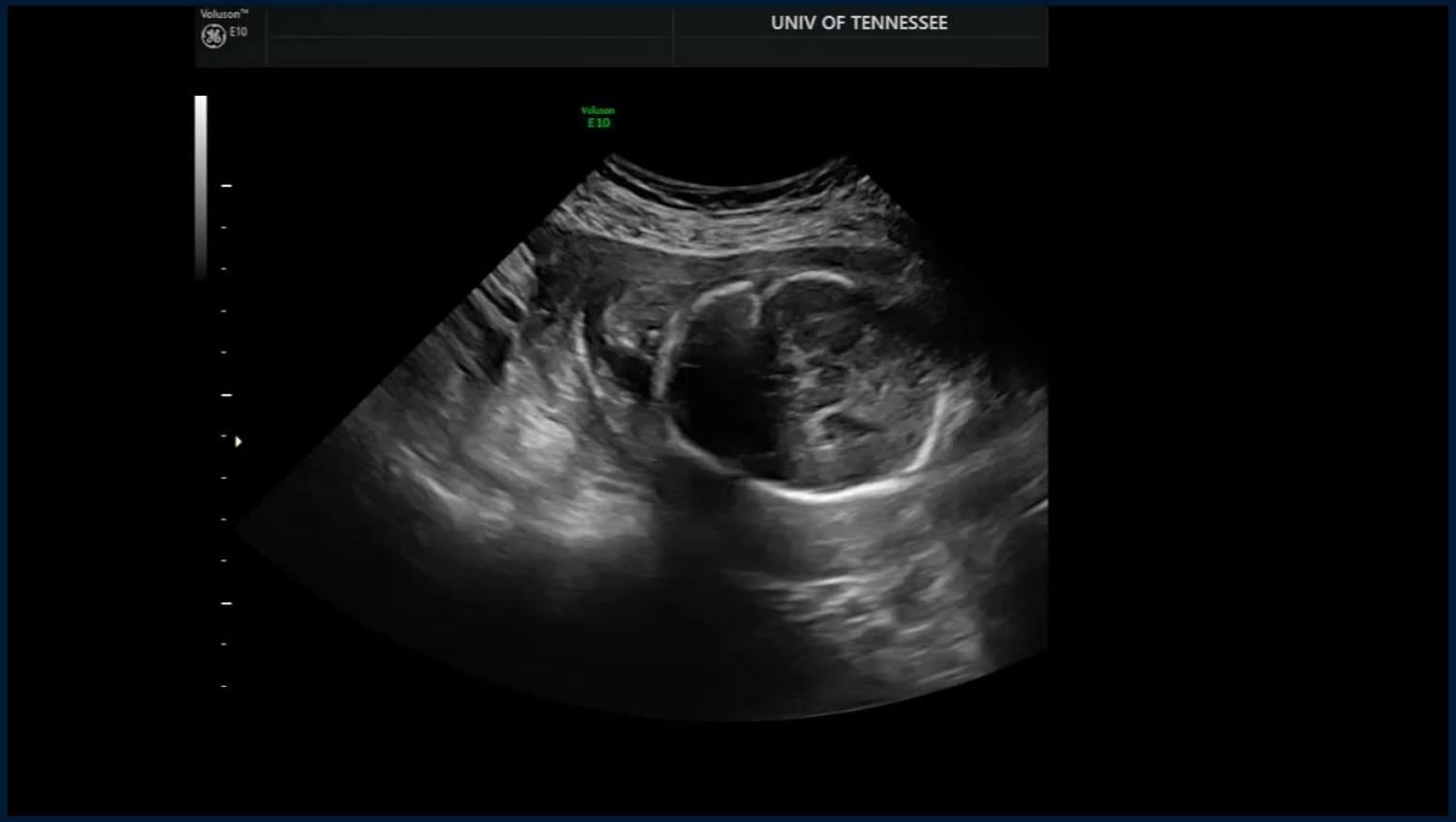
24 Weeks' Gestation



A = Normal
B = "Brain sparing Effect"

Am J Obstet Gynecol 1992;166:1262

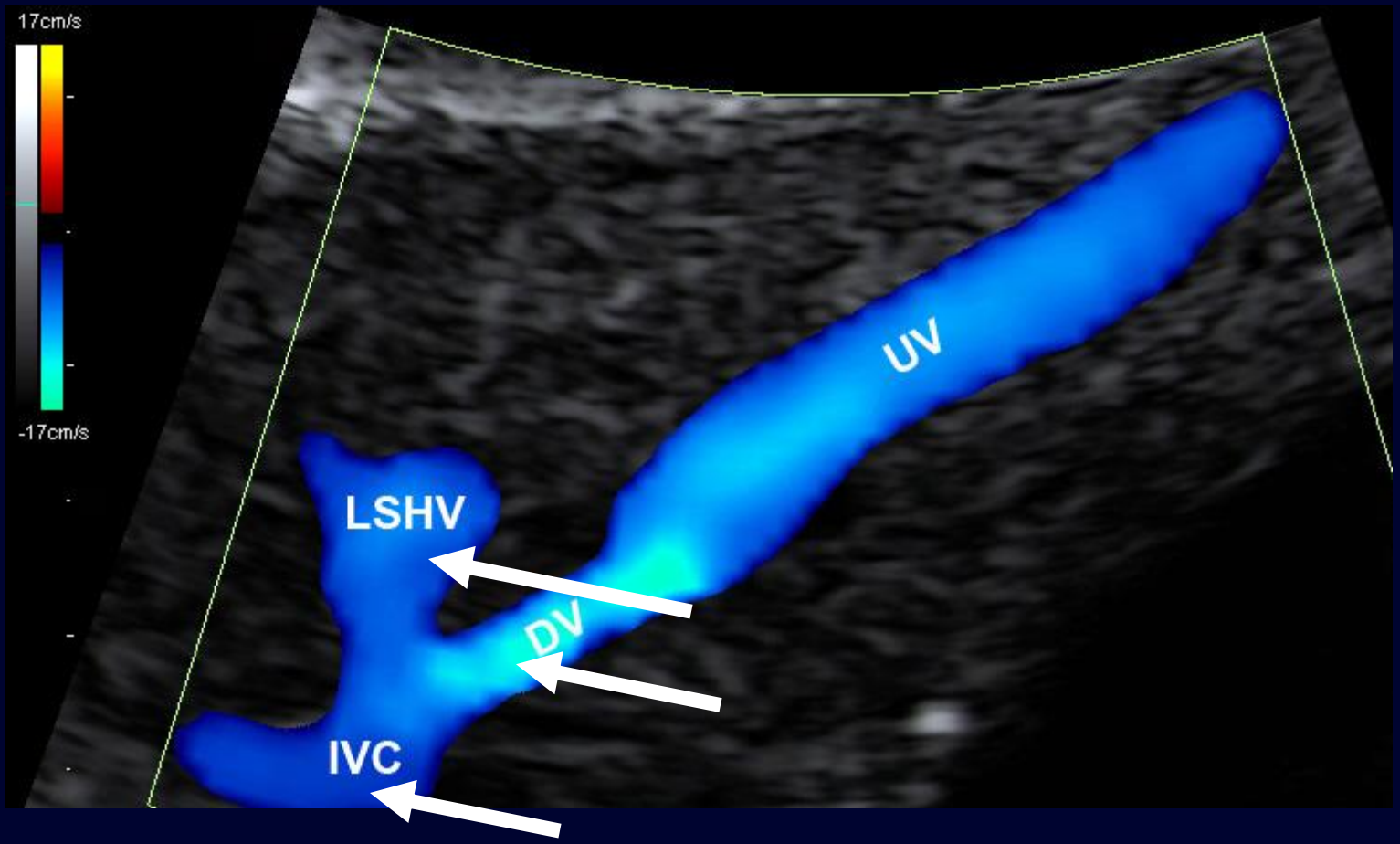
MCA

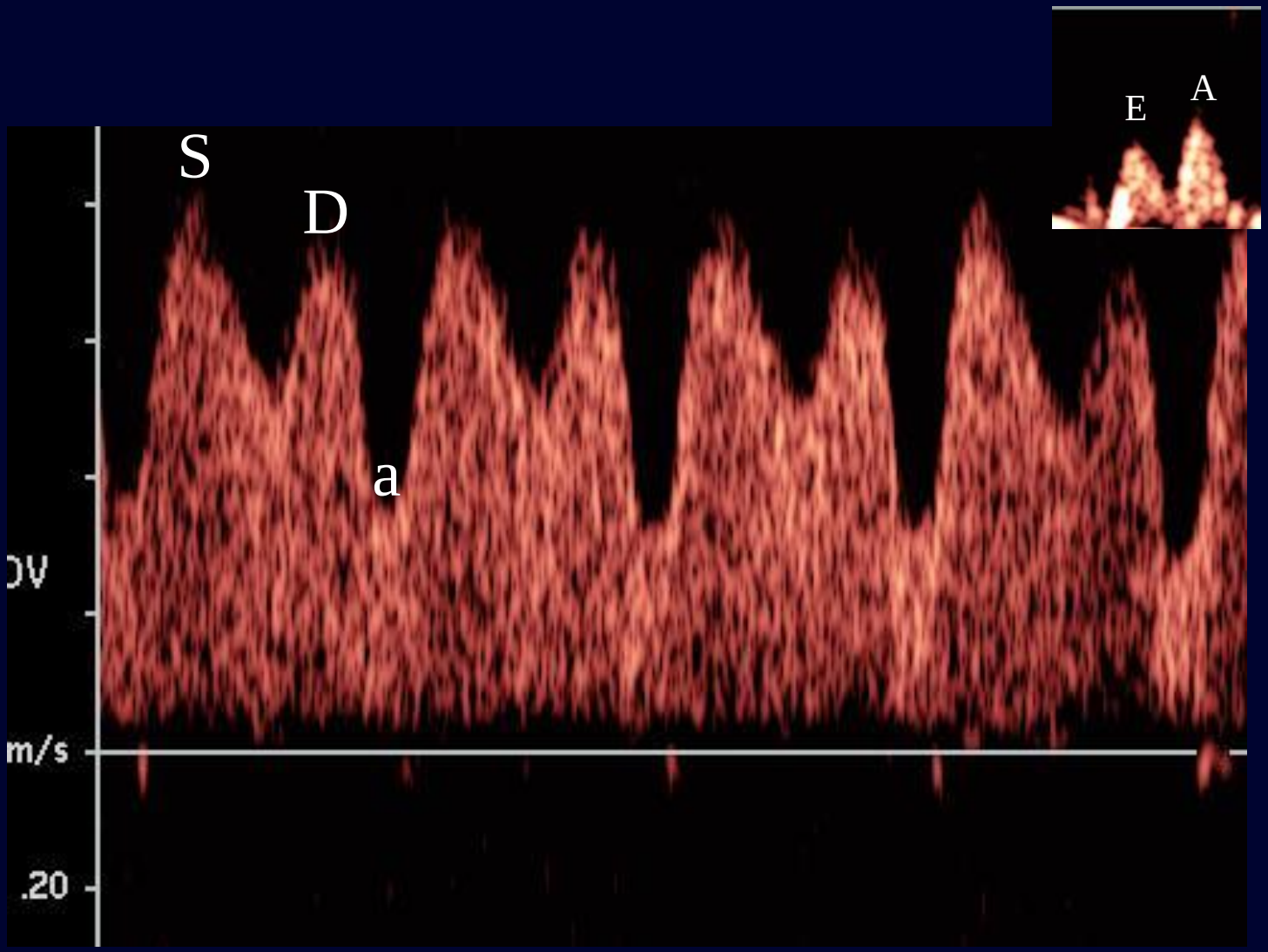


#6
When to use the MCA Doppler?

Do we need to use the MCA Doppler or the MCA/UA in IUGR?

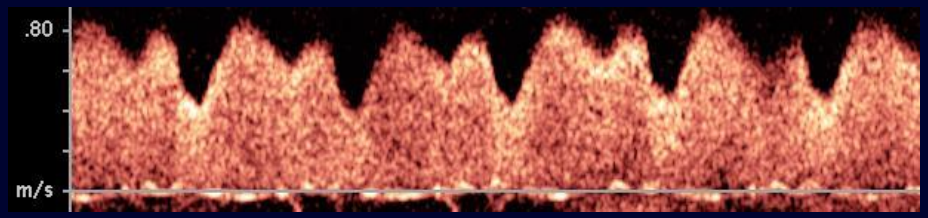
- It has not to be used as a screening test
- There is no data that shows that the MCA/UA ratio is better than the MCA PI in IUGR
- It can be used with the umbilical artery Doppler in fetuses suspected to be IUGR

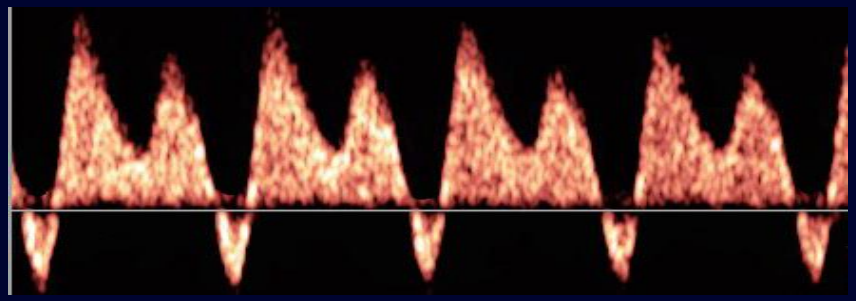

17cm/s
-17cm/s
UV
LSHV
DV
IVC

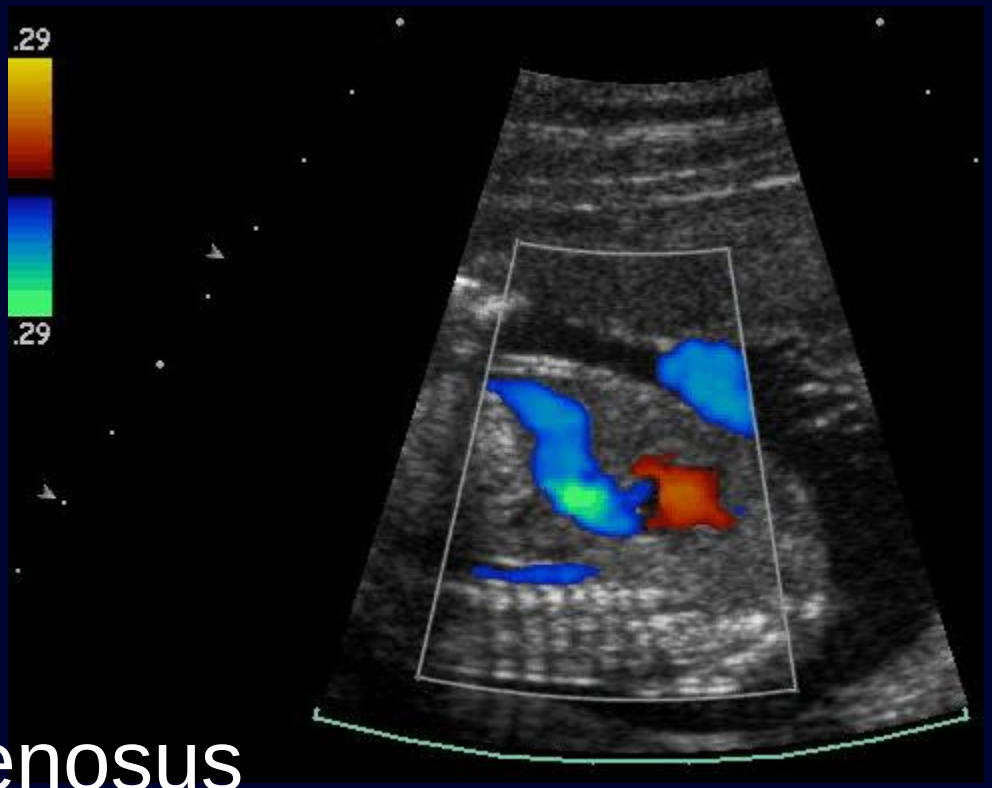


$$PIV = \frac{S - a}{Tmax}$$

Hemodynamically, these phases (S, D, a) reflect the rapid chronologic change in pressure gradients between the umbilical vein and the right atrium.

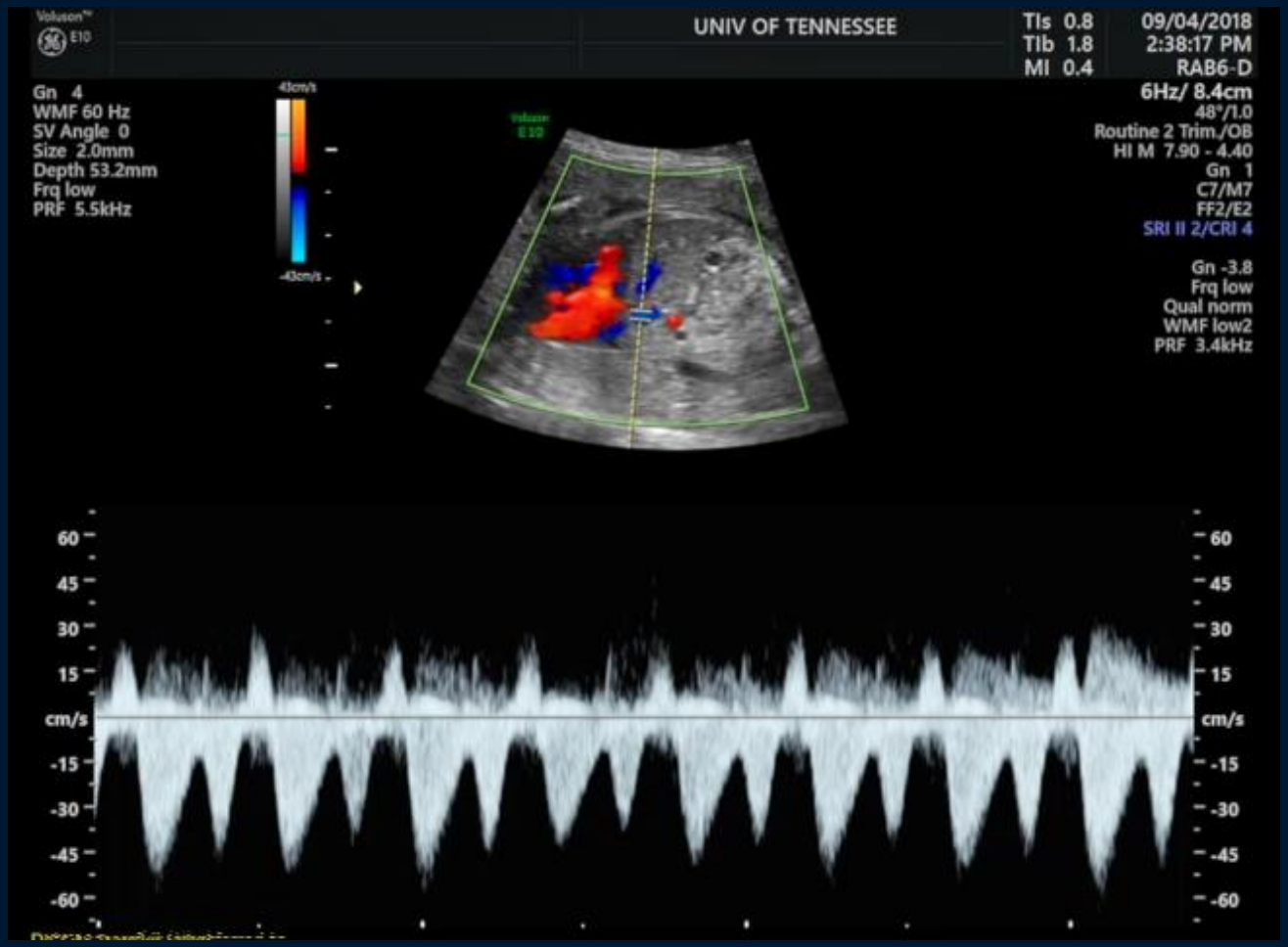






Ductus Venosus

Ductus venosus



#7
When to use the Ductus venosus Doppler?

Do we need to use the DV Doppler in IUGR?

- **It provides information on the severity of IUGR**
- **A randomized trial on the use of Doppler of the DV for timing IUGR delivery was not conclusive**
- **It has not to be used for timing the delivery of IUGR fetuses**

#8
Delivery Timing

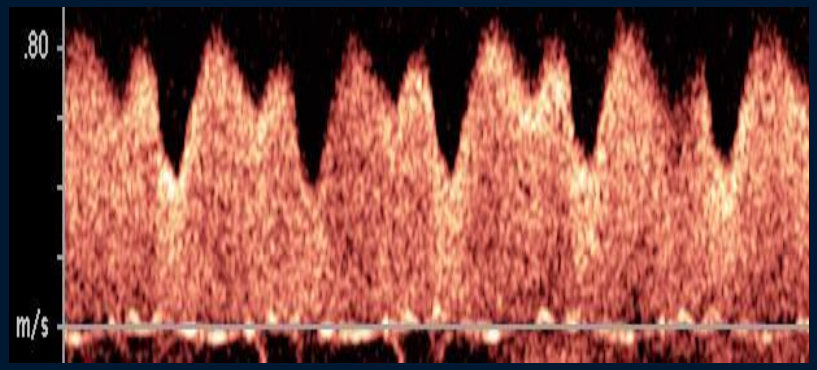
IUGR Delivery?

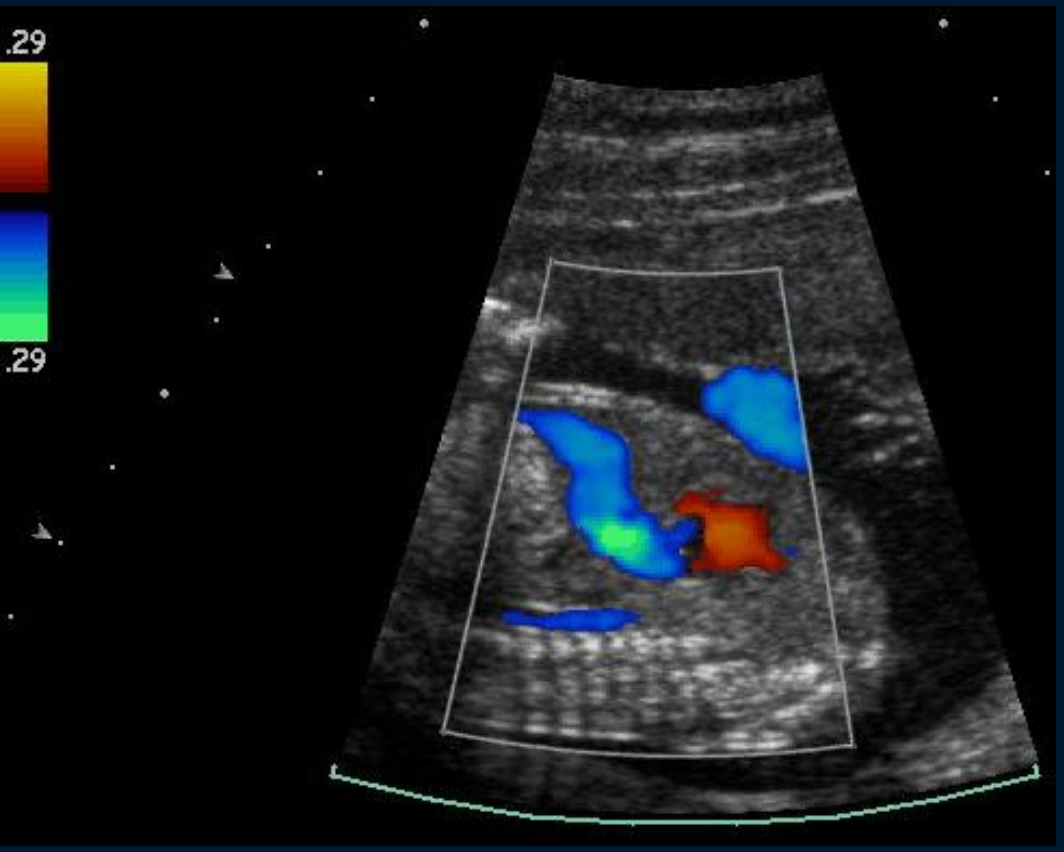
- GRIT (24-36 weeks)
- DIGITAT (>36 weeks)
- PORTO (24-36.6)
- TRUFFLE (26-32 weeks)

Trial of Umbilical and Fetal FLow In Europe

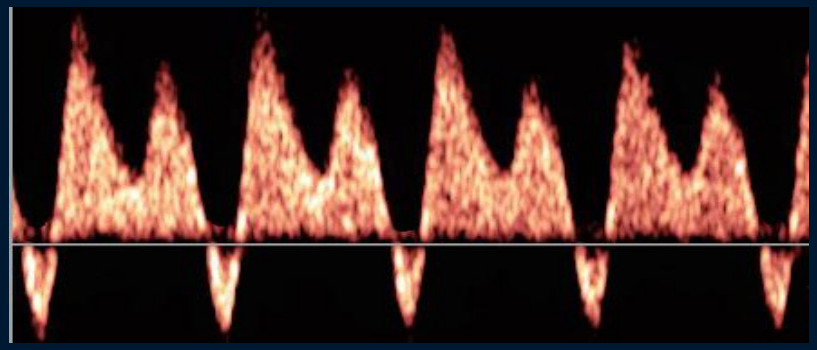
IUGR: AC <10th% + abnl UAPI

26-32 weeks' gestation





- CTG (abnormal STV)
- DV (abnormal PI)
- DV (ARF a wave)



TRUFFLE Trial

Primary Outcome

- Primary outcome:
  - Survival w/o cerebral palsy or neurosensory impairment
  - Bayley III developmental score of less than 85, at 2 years of age

Lees et al. Lancet, 2015; 385:2162-72

TRUFFLE Trial
Results

- Liveborn: 491 (98%)
- Discharged home: 463 (92%)
- No. neonatal morbidity: 345 (69%)
- Fetuses alive at 2 years: 461 (92%)
- Follow-up at 2 years: 402 (80%)
- Bayley III cognitive test: 356 (70%)

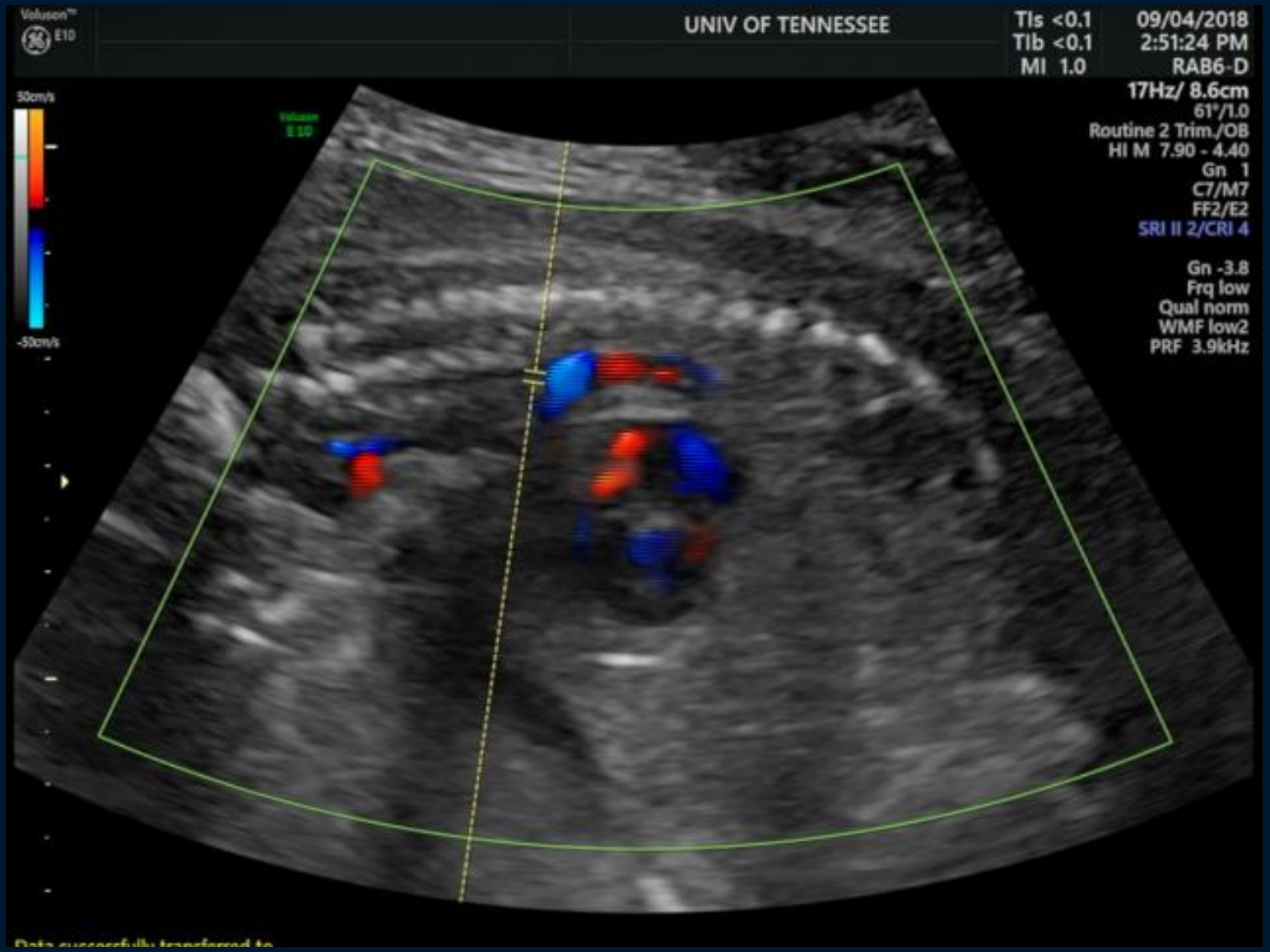
No difference in short-term outcomes between the 3 groups

No difference in neurodevelopment impairment between the 3 groups (however, less frequent in DV-ARF group)

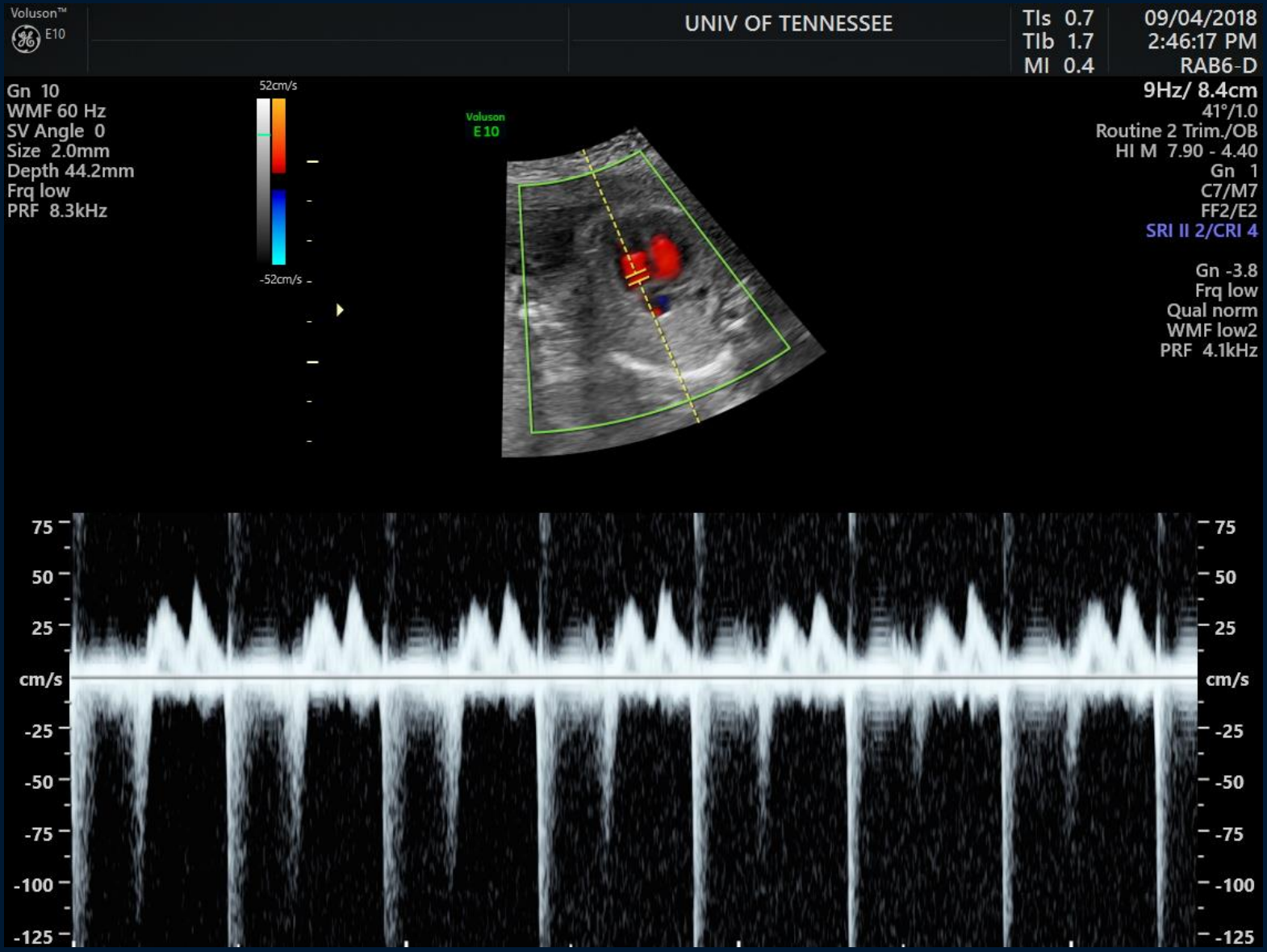
Lancet, 2015; 385:2162-72

#9
Doppler changes in the Idiopathic IUGR at < 30 weeks

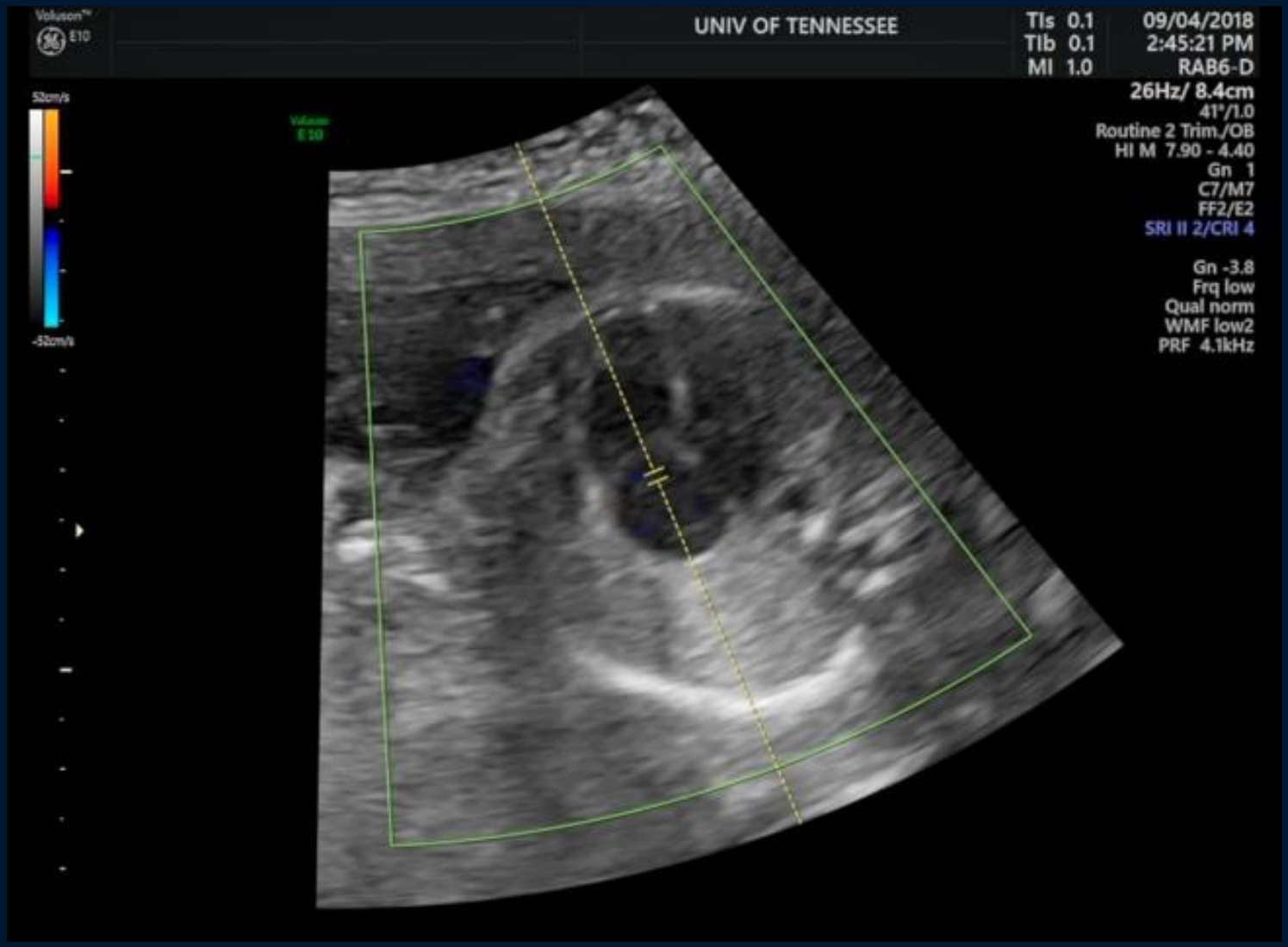
Aortic isthmus

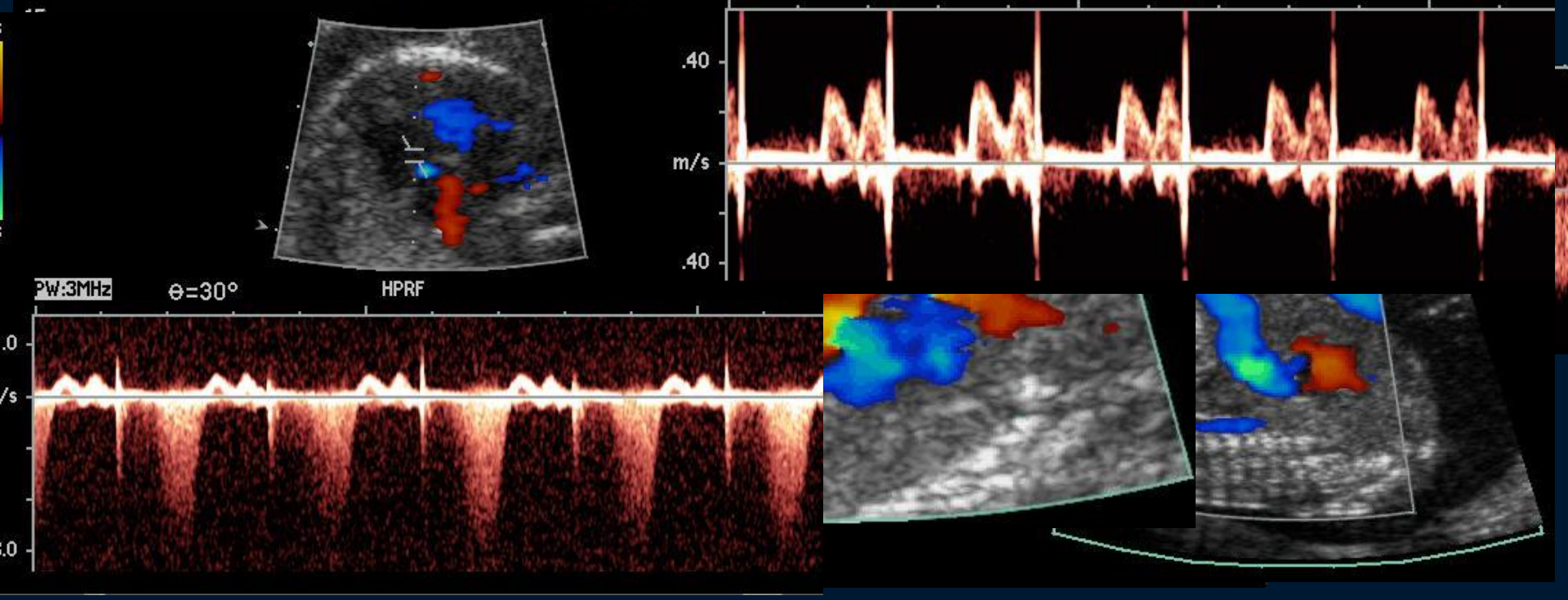


Tricuspid regurgitation

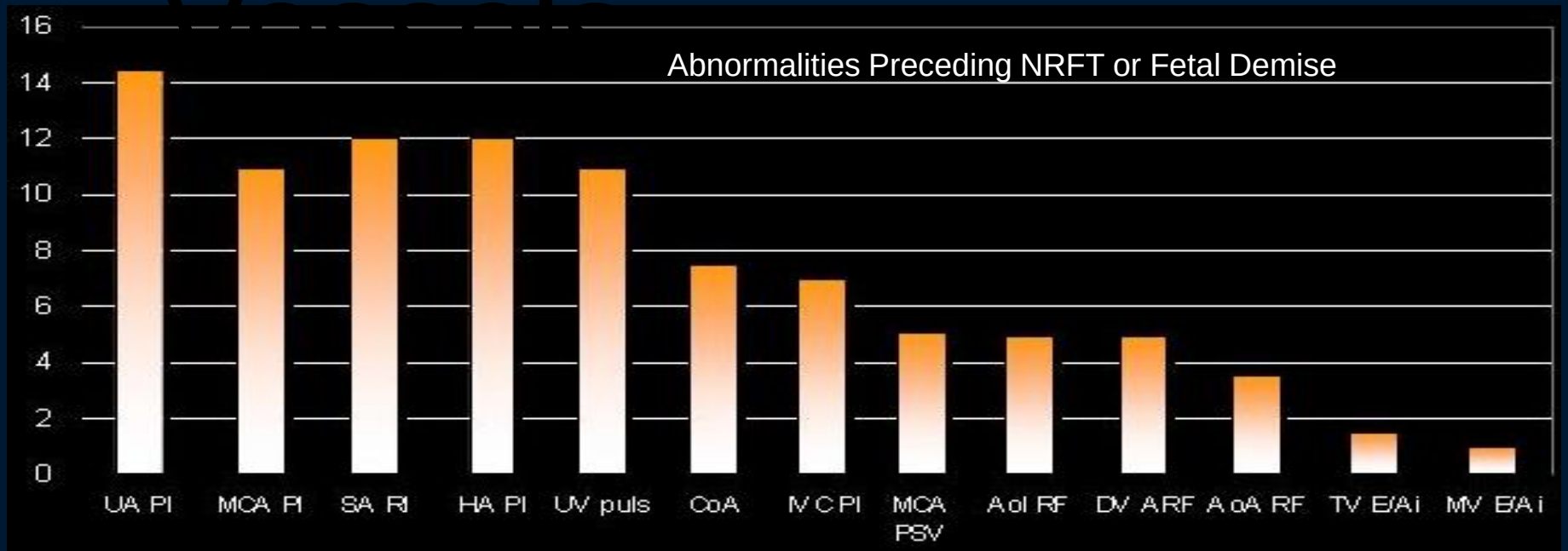


Tricuspid regurgitation




.40
m/s
.40
PW:3MHz
θ=30°
HPRF

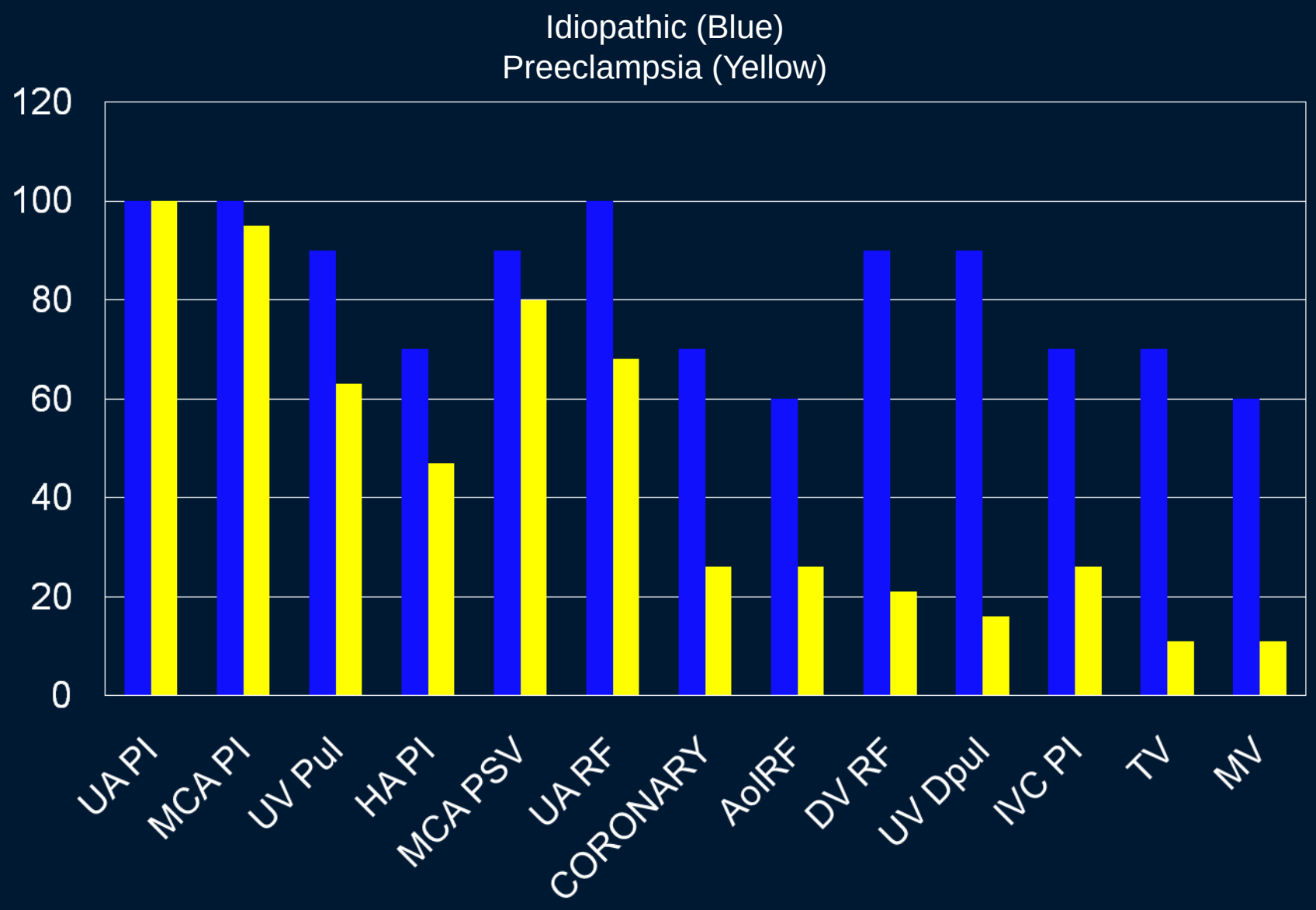
Vessels


Abnormalities Preceding NRFT or Fetal Demise
16
14
12
10
8
6
4
2
0
UA PI
MCA PI
SA RI
HA PI
UV puls
CoA
IVC PI
MCA PSV
Aol RF
DV ARF
AoA RF
TV E/Ai
MV E/Ai

Doppler changes in IUGR in pregnancies with and without preeclampsia

Pren Diagn 2008 28:377-83

Percent Parameters Abnormal in the Two Groups



Pren Diagn 2008 28:377-83

IUGR (EFW < 10th percentile) Staging

Stage I IUGR:	Normal UA-MCA
Stage II IUGR:	Abnormal UA-MCA PI
Stage III IUGR:	UA-AREDV
Stage IV IUGR:	DV-AREDV

AFI =	Normal (N)
	Abnormal (A)

#10
IUGR Protocol used in Memphis

EFW or AC <10th %

Dopplers (UA, MCA, DV, Ut artery)

Normal Dopplers

AFI > 5

Stage 1-N

INITIAL follow up in 1 w

IG + Dopplers every 2 weeks

From 30-35.6 weeks:
(Once a week surveillance)

Alternate BPP + Doppler + IG one week versus NST+AFI the alternate week

From 36-38.6 weeks:
(Twice a week surveillance)

Monday- NST

Thursday- BPP (with NST only if concerns on US) + Dopplers + IG (Q 2 weeks)

Delivery at 39 weeks or at 37 weeks if IG <200 g.

AFI < 5

Stage 1-A

To L&D triage: r/o ROM and transition to 23H observation

Give steroids

From diagnosis:
(Once a week surveillance)
Thursday- BPP (with NST only if concerns on US) + Dopplers + IG (Q 2 weeks)

From 28 weeks-onwards:
(Twice a week surveillance)
Monday- NST
Thursday- BPP (with NST only if concerns on US) + Dopplers + IG (Q 2 weeks)

Delivery at 37 weeks

UA PI >95th % or MCA PI <5th %

AFI > 5

Stage 2-N

From diagnosis:
(Once a week surveillance)
Thursday- BPP (with NST only if concerns on US) + Dopplers + IG (Q 2 weeks)

Beginning at 30 weeks:
(Twice a week surveillance)
Monday- NST
Thursday- BPP (with NST only if concerns on US) + Dopplers + IG (Q 2 weeks)

Delivery at 37 weeks

AFI <5

Stage 2-A

Hospital admission

Give steroids

Consult MFM

NST AM, BPP noon, and NST PM

Dopplers twice/week in MedPlex

IG (Q 2 weeks)

Delivery at 34-37 weeks

Absent/Reversed A-REDF UA

Stage 3

Hospital admission

Give steroids

Consult MFM

NST AM, BPP noon, and NST PM

Dopplers twice/week in MedPlex

IG (Q 2 weeks)

Delivery at 32 weeks for REDV or at 34 weeks for AEDV or anytime *after, pending MFM* consultation for non-reassuring NST or BPP 4/8 on 2 occasions 4 hours apart.

Absent/Reversed A-R a wave DV

Stage 4

Hospital admission

Give steroids

Consult MFM

NST AM, BPP noon, and NST PM

Dopplers twice/week in MedPlex

IG (Q 2 weeks)

Delivery at 30-32 weeks or anytime *after, pending MFM* consultation for non-reassuring NST or BPP 4/8 on 2 occasions 4 hours apart.

EFW: Estimated Fetal Weight, AC: Abdominal circumference, UA: umbilical artery, MCA: middle cerebral artery, DV: ductus venosus, ut A: uterine artery, AFI: amniotic fluid index, PI: pulsatility index, IG: interval growth, BPP: biophysical profile, NST: non stress test, AEDF: absent end diastolic flow, REDF: reversed end diastolic flow, L & D: labor and delivery

Conclusion

- No standard in the diagnosis and management of the IUGR fetus
- Specialized centers
- Protocol vs. individualized care