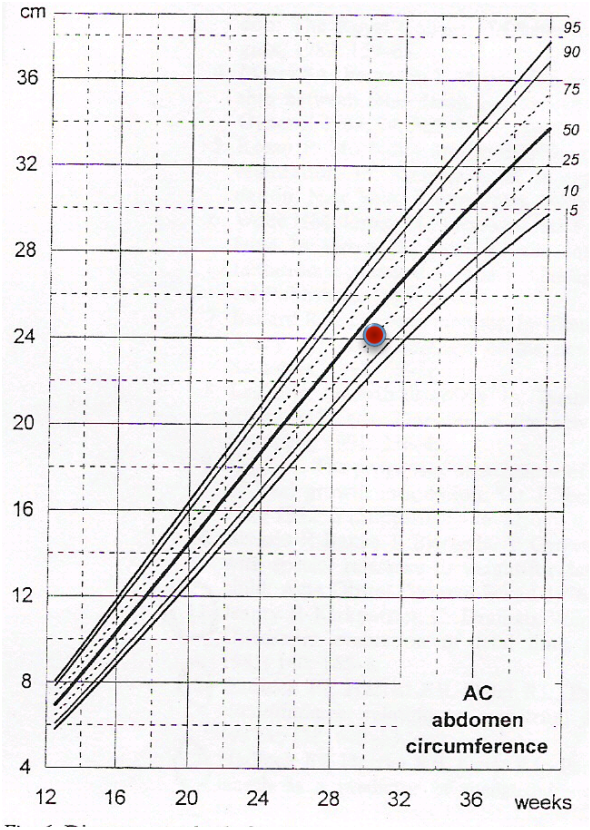
Dott.ssa Danila Morano

DIAGNOSI, MONITORAGGIO CLINICO E TIMING DEL PARTO DEL FETO IUGR

Come si definisce la crescita fetale?

Definizione statistica: dimensioni corporee (peso, lunghezza), per l'EG, inferiori ad un determinato "valore-soglia" (M-2DS,3°,5°, 10°C per l'EG) della popolazione di riferimento

Valutazione auxologica trasversale, prenatale basata su carte antropometriche fetali



Valutazione della crescita fetale

Aumentare la **sensibilità** della diagnosi di restrizione di crescita fetale

- principale fattore di rischio per mortalità fetale
- associazione con patologie dell'età adulta
- l'identificazione prenatale dei feti di basso peso alla nascita migliora gli outcome neonatali

Aumentare la **specificità** della diagnosi di restrizione di crescita fetale

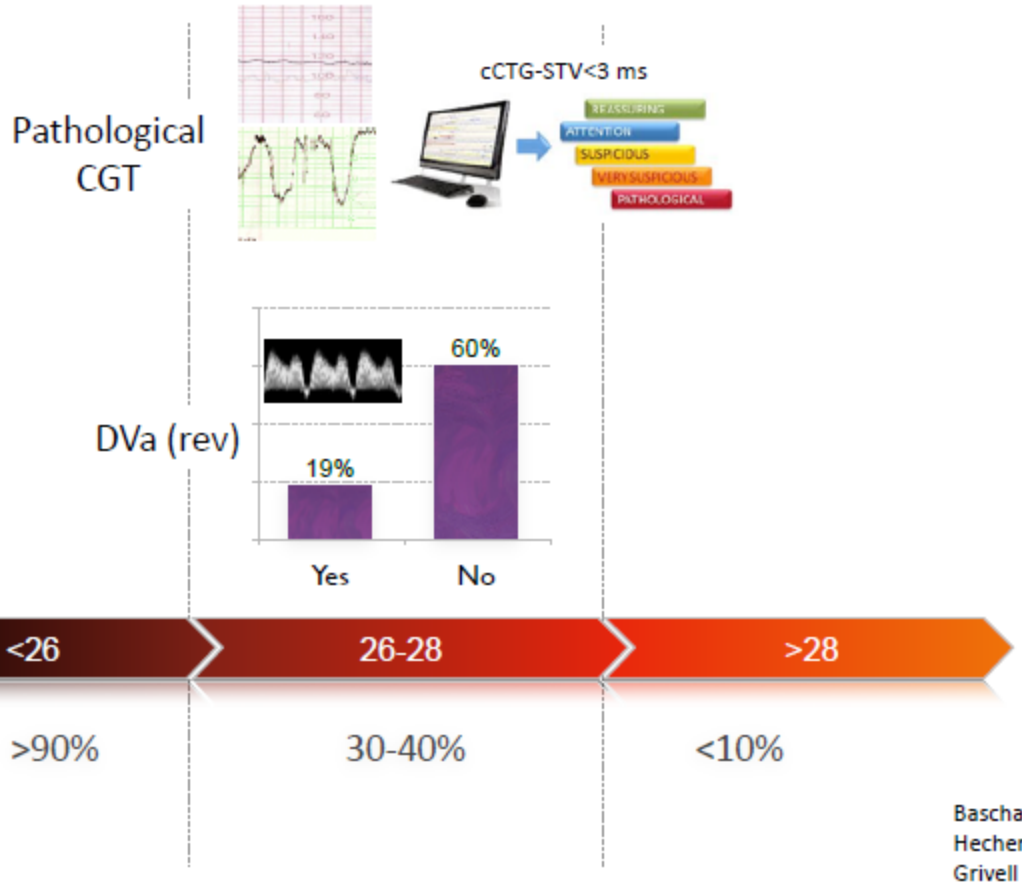
- aumenta il rischio di :
  - induzione del travaglio
  - taglio cesareo
  - parto pretermine iatrogeno

	Not identified as SGA (n=573)	Identified as SGA (n=681)	Adjusted OR
Adverse fetal outcome	67 (11.7)	34 (5.0)	4.1 (2.5-6.8)
Cerebral Damage	10 (1.7)	7 (1.0)	2.3 (0.8-6-6)
HIE moderate-severe	0	3	
Intracranial hemorrhage	4	2	
Cerebral palsy	2	2	
Mental retardation	4	1	
Severe fetal distress	34 (5.9)	12 (1.8)	4.5 (2.2-9.0)
Apgar score <4 at 5 min	11	4	
Neonatal convulsions	3	3	
Umbilical pH <7	21	7	
Fetal or infant death	32 (5.6)	17 (2.5)	4.2 (2.1-8.5)
Stillborn	20	6	
Intrapartum death	0	0	
Infant death	12	11	

Lindqvist PG. Ultrasound Obstet Gynecol 2005; 25: 258

BEING SMALL EARLY IN PREGNANCY IS A PROBLEM

PROBLEM #1: MORTALITY



Perinatal Mortality

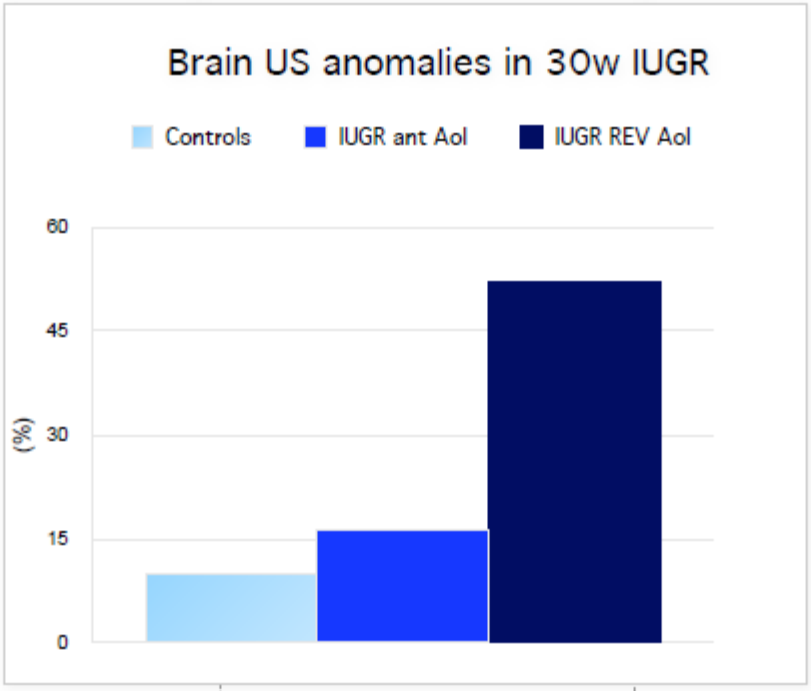
BCNATAL

www.medicinafetalbarcelona.org/

Baschat 2003
Hecher 2003
Grivell 2009
Cruz-Lemini 2012

Early-onset IUGR

PROBLEM #2: (NEUROLOGICAL) MORBIDITY

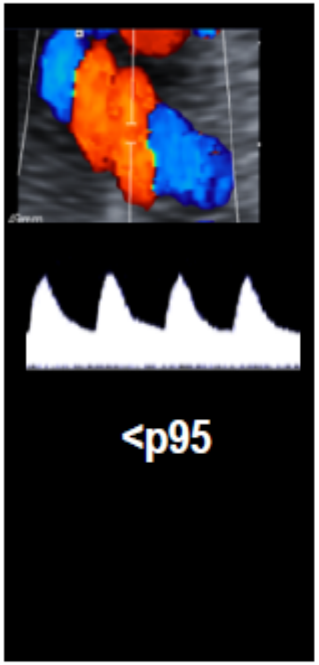


	<29	29-32	>32.0
Neurological Morbidity	>90%	30-40%	<10%

Fouron 2004
Del Rio 2008
Cruz-Martinez 2012

BEING SMALL LATE IS ALSO A PROBLEM

SGA



Significant increase in the risk of adverse perinatal outcome

Hershkovitz et al. Ultrasound Obstet Gynecol 2000

Severi et al. Ultrasound Obstet Gynecol 2002

Figueras et al . Eur J Obstet Gynecol Reprod Biol 2008

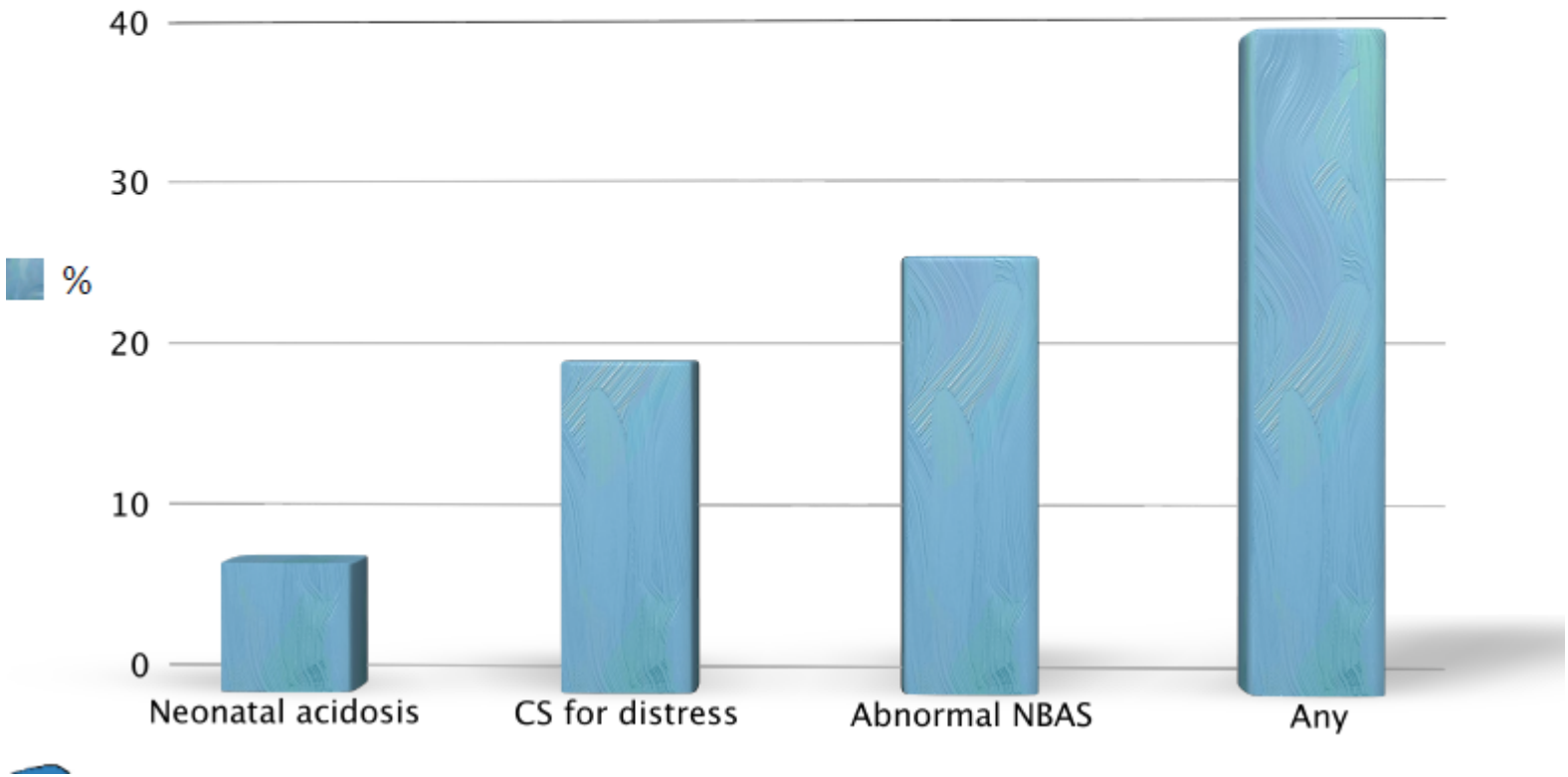
Significant increase in the risk of adverse neurodevelopment

Eixarch et al. Ultrasound Obstet Gynecol 2008

Severi et al. Ultrasound Obstet Gynecol 2002

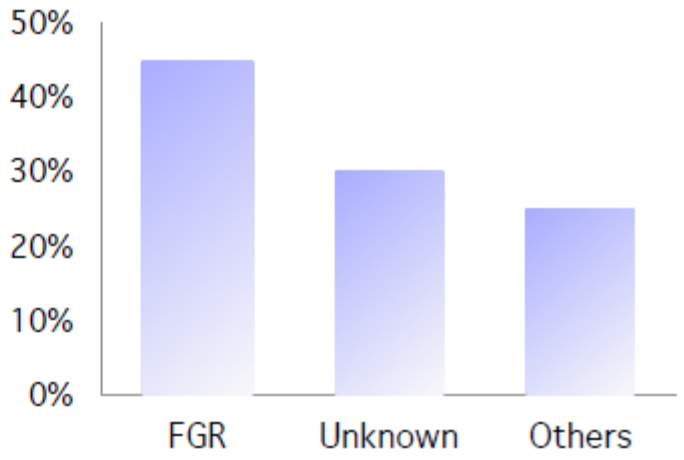
Figueras et al . Eur J Obstet Gynecol Reprod Biol 2008

SGA: proportion of perinatal adverse outcomes in 376 consecutive cases



fetal iD

IMPACT OF NON-DETECTED IUGR ON LATE FETAL MORTALITY
Barcelona
2005-2010

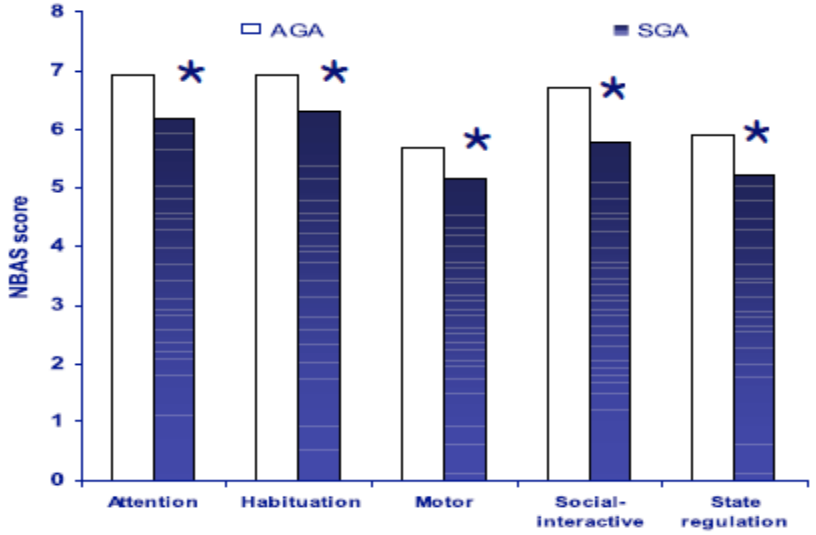


Classification of stillbirth by relevant condition at birth (ReCoDe): population-based cohort study
Gardosi et al. BMJ 2005 and 2013

IUGR as relevant condition identified in 43-60%

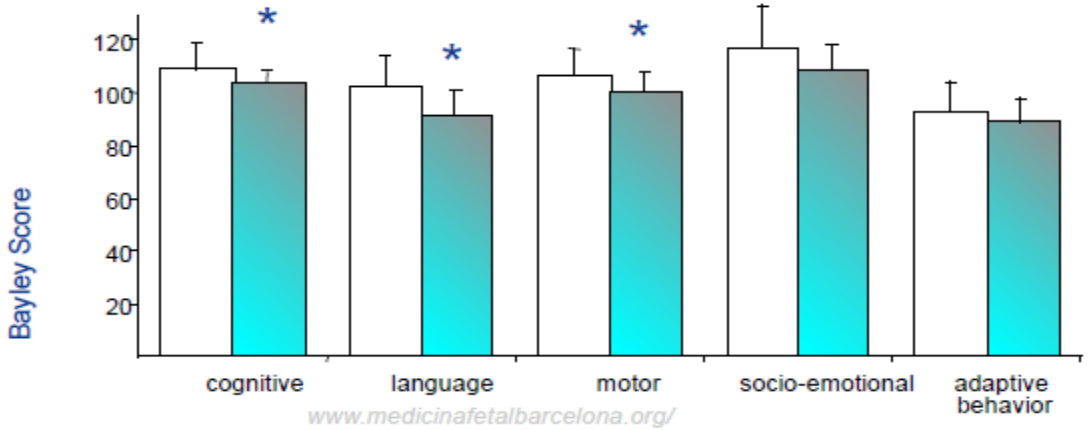
Overall stillbirth rate (/ 1000 births) 4.2, but only 2.4 in non-SGA pregnancies, increasing to
9.7 with antenatally detected IUGR and 19.8 in not detected IUGR.

Neurobehavioral performance of term SGA newborns



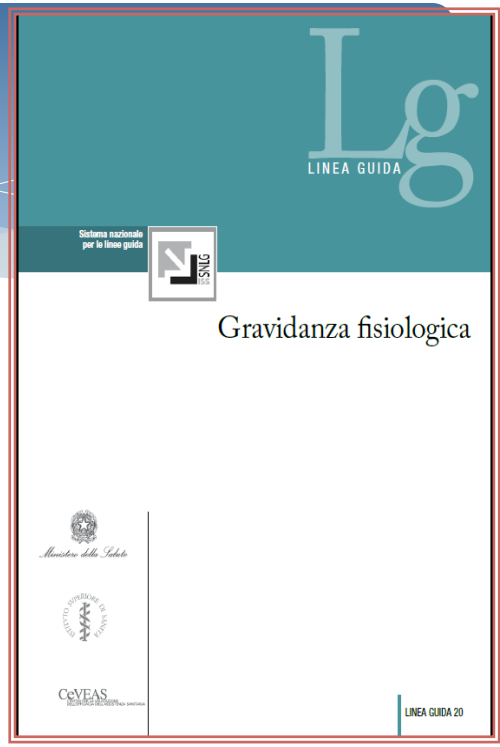
N=120
SGA vs
100 AGA

** p <0.05*
Adjusted for GA, maternal age, socioeconomic status and smoking



Satchev, 2012
Geva 2008
Figueras 2008
Eixarch 2010

Misurazione della lunghezza sinfisi-fondo
Sensibilità 27% - 80%



The Investigation and Management of the Small–for–Gestational–Age Fetus

Green–top Guideline No. 31

2nd Edition | February 2013 | Minor revisions – January 2014

SOGC CLINICAL PRACTICE GUIDELINE

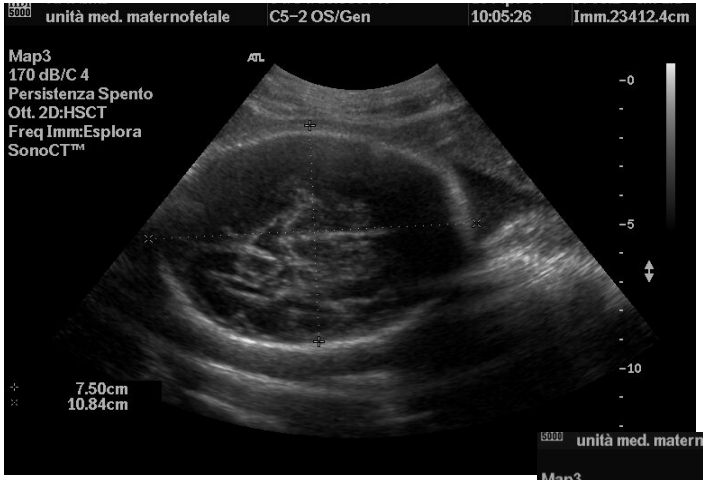
No. 295, August 2013

Valutazione della crescita fetale: il ruolo dell'ecografia ostetrica

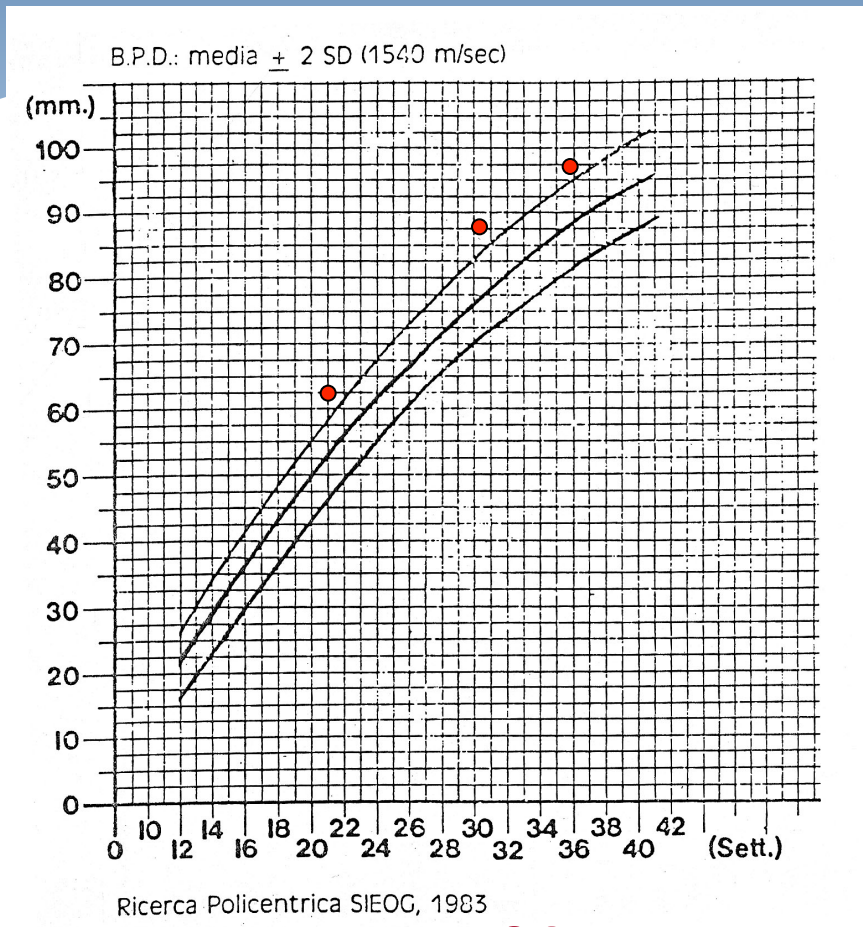
1. Corretta misurazione parametri biometrici
2. Confronto con valori di riferimento e curve di crescita
3. Corretta datazione della gravidanza

Valutazione della crescita fetale

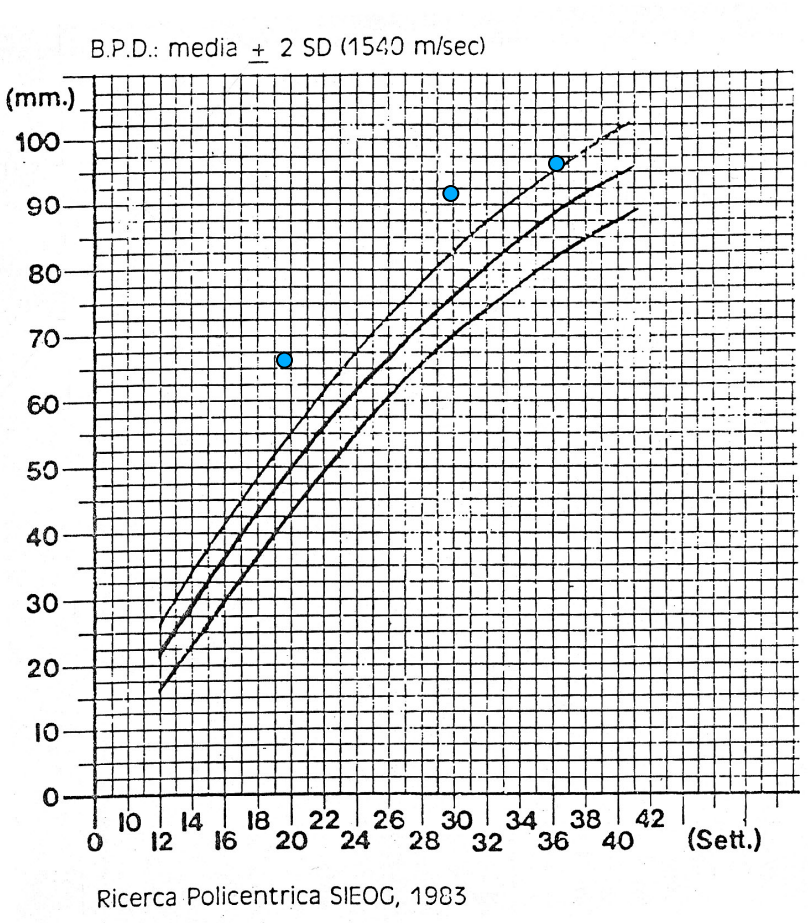
1. Corretta misurazione parametri biometrici



Valutazione della crescita fetale



Low profile



Late flattening

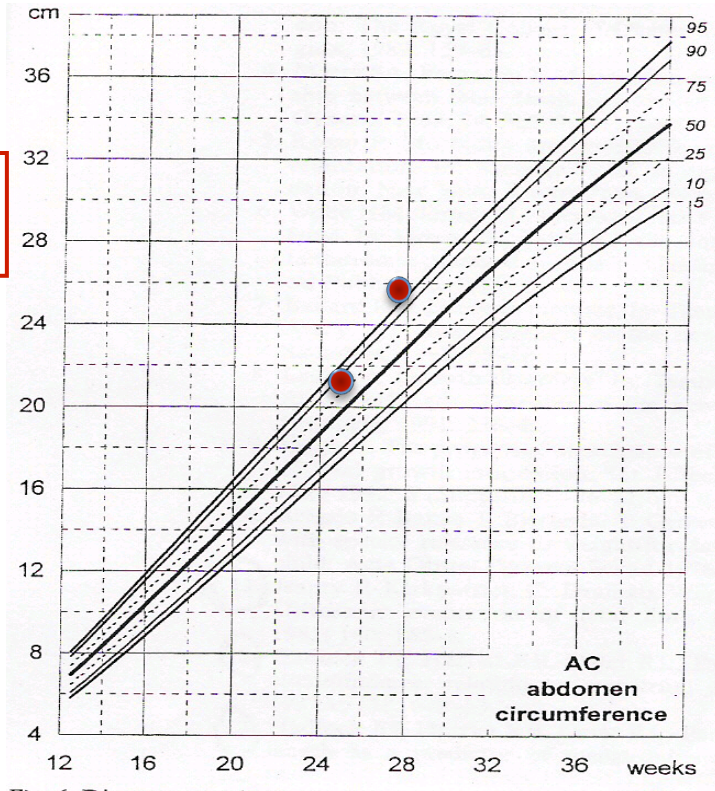
Campbell et al. Lancet, ii: 1002, 1971

Valutazione della crescita fetale

2.Confronto con valori di riferimento e curve di crescita

Confronto tra crescita individuale e crescita normale

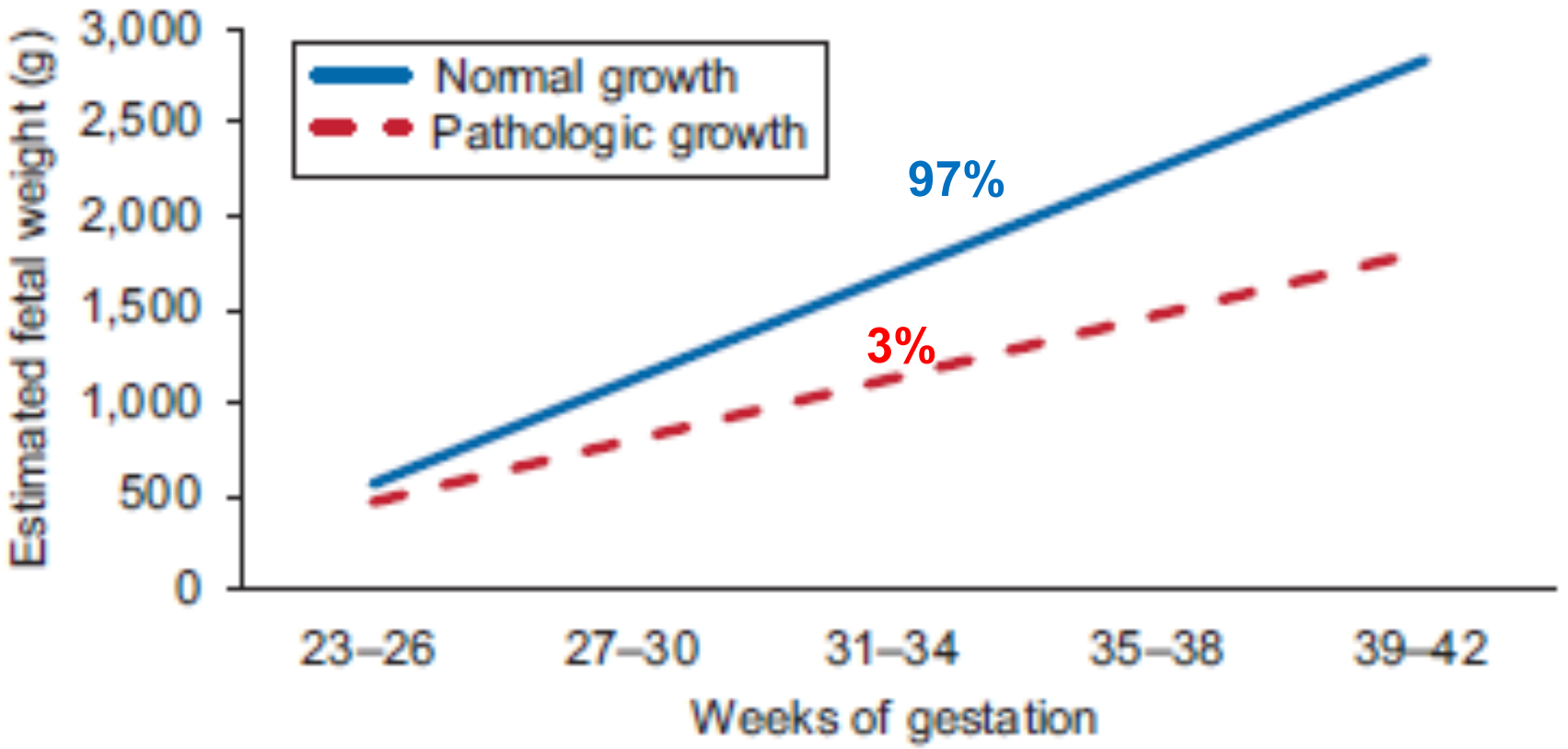
la crescita è una velocità!



The Role of Growth Trajectories in Classifying Fetal Growth Restriction

Barker E. Obstet Gynecol 2013

Perinatal complications			
Composite adverse neonatal outcomes	45.9% (20, 37)	3.8% (41, 1,079)	21.52* (10.50–44.10)
NICU admission	89.2% (33, 37)	25.9% (279, 1,079)	23.67* (8.31–67.40)
Gestational age at delivery (wk)	32.02±3.42 (n=37)	38.02±2.74 (n=1,079)	0.672* (0.62–0.73)



Quali curve di crescita?
Standard vs. Reference vs. Customizzate

* ***Standard:***
  valori di riferimento della popolazione sana ossia con crescita ottimale
* ***Reference:***
  valori di riferimento della popolazione generale ossia crescita osservata (possibile sottostima di FGR)
* ***Curve customizzate***

Correzione per variabili indipendenti che influiscono sulla crescita?

→ gruppo etnico
→ predisposizione genetica
→ sesso
→ parità
→ fattori ambientali (es. altitudine)

Gestation Network

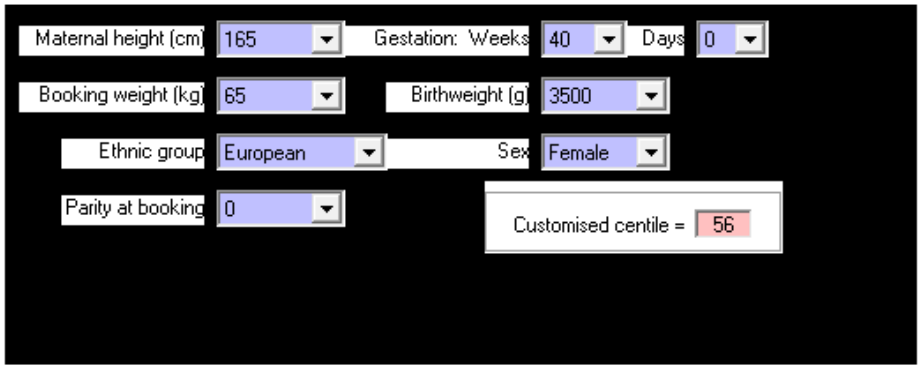
GROW Customised Centiles - Online Calculator - United Kingdom

Click below to use the individual centile calculator.

The current version is v5.16 dated October 2011

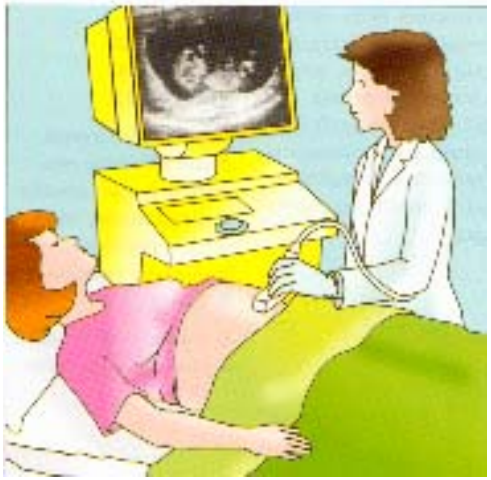
To generate a customised birthweight centile, you need to enter a value in each of the eight fields. The centile is calculated automatically

Please note:
If you have a large set of centiles to calculate, you should use the bulk centile calculator.



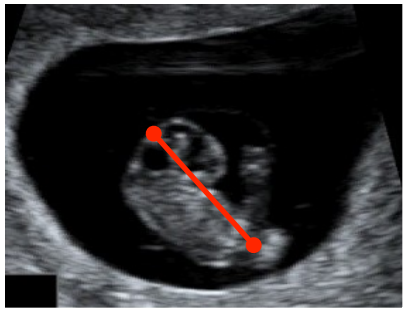
Valutazione della crescita fetale

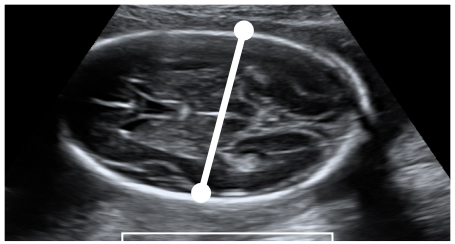
3. Corretta datazione della gravidanza



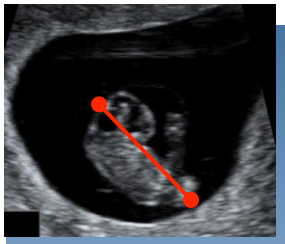
- ✓ CRL fino a 65 mm e BPD fino 23 mm (12 settimane +5 gg) sono equivalenti
- ✓ BPD > 23 mm è più accurato di CRL

CRL

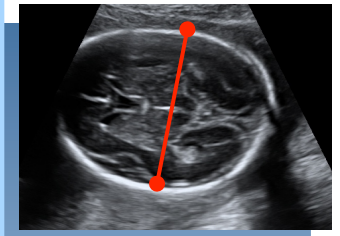




BPD



Datazione della gravidanza



QUALI VARIABILI BIOMETRICHE?

SIEOG

Il **CRL** misurato tra 7 e 11 settimane ha una accuratezza di ± 3-4 giorni nel 95% dei casi.

Il **BPD** misurato fra 12 e 16 settimane (più di 21 mm) ha un'accuratezza di ± 3-4 giorni nel 95% dei casi.

Ultrasound Obstet Gynecol 2008; 31: 388–396
Published online 17 March 2008 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.5225

New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study

B. O. VERBURG*†‡, E. A. P. STEEGERS‡, M. DE RIDDER†, R. J. M. SNIJDERS*, E. SMITH*, A. HOFMAN†, H. A. MOLL§, V. W. V. JADDOE*† and J. C. M. WITTEMAN†

**The Generation R Study Group and Departments of †Epidemiology and Biostatistics, ‡Obstetrics and Gynecology and §Pediatrics, Erasmus Medical Center, Sophia Children's Hospital, University Medical Center Rotterdam, Rotterdam, The Netherlands*

Table 3 Crown–rump length (CRL) in relation to gestational age

	Gestational age (weeks + days)		
CRL (mm)	*5th centile*	*Median*	*95th centile*
5	5 + 6	6 + 2	6 + 6
10	7 + 0	7 + 4	8 + 1
15	7 + 5	8 + 2	9 + 0
20	8 + 2	9 + 0	9 + 5
25	8 + 6	9 + 4	10 + 2
30	9 + 2	10 + 0	10 + 6
35	9 + 5	10 + 3	11 + 2
40	10 + 1	10 + 6	11 + 5
45	10 + 3	11 + 2	12 + 1
50	10 + 6	11 + 5	12 + 4
55	11 + 1	12 + 0	13 + 0
60	11 + 3	12 + 3	13 + 3
65	11 + 6	12 + 5	13 + 5
70	12 + 1	13 + 0	14 + 0
75	12 + 3	13 + 3	14 + 3
80	12 + 5	13 + 5	14 + 5
85	13 + 0	14 + 0	15 + 1
90	13 + 2	14 + 2	15 + 3
95	13 + 4	14 + 4	15 + 5
100	13 + 6	15 + 0	16 + 1

Table 4 Biparietal diameter (BPD) (outer–outer) in relation to gestational age

	Gestational age (weeks + days)		
BPD outer–outer (mm)	*5th centile*	*Median*	*95th centile*
10	8 + 4	9 + 1	9 + 5
15	10 + 0	10 + 5	11 + 3
20	11 + 2	12 + 1	13 + 0
25	12 + 4	13 + 3	14 + 3
30	13 + 5	14 + 5	15 + 6
35	15 + 0	16 + 1	17 + 2
40	16 + 2	17 + 3	18 + 5
45	17 + 4	18 + 6	20 + 2
50	19 + 0	20 + 2	21 + 5
55	20 + 2	21 + 6	23 + 3
60	21 + 5	23 + 2	25 + 0
65	23 + 2	24 + 0	26 + 5
70	24 + 6	26 + 4	28 + 4
75	26 + 3	28 + 2	30 + 3
80	28 + 1	30 + 1	32 + 2
85	29 + 6	32 + 0	34 + 2
90	31 + 5	34 + 0	36 + 3
95	33 + 4	36 + 0	38 + 5
100	35 + 5	38 + 2	41 + 0
105	37 + 5	40 + 3	43 + 3
110	40 + 0	42 + 6	45 + 6

Quindi ….in caso di riscontro di restrizione di crescita fetale alla valutazione ecografica:

1) Verificare corrispondenza tra biometria ed EG anamnestica ad ogni ecografia
2) Se EG e valutazione biometrica non corrispondono:
   valutare tutti fattori che possono aver influenzato la crescita fetale
3) Datare la gravidanza sulla base dell'ecografia eseguita più precocemente, e comunque entro la prima metà della gravidanza
4) Tenere sempre in considerazione la datazione ecografica una volta effettuata.
5) Di fronte a una discrepanza tra biometria ed EG:
   verificare sempre se è stata eseguita una corretta datazione utilizzando tutti gli elementi disponibili

SMALL FOR GESTATIONAL AGE (SGA)

Definition:Estimated Fetal Weight (EFW) or Abdominal Circumference < 10° centile

SGA

HETEROGENEOUS POPULATION

- **constitutional**
- **malform/infections**
- **twins**
- **abnormal placental function (IUGR)**

Todros et al. Early Human Development 1996; 45:1

SGA vs IUGR

The definition of small-for-gestational age for a fetus in utero is an estimated fetal weight that measures < 10th percentile on ultrasound. This diagnosis does not necessarily imply pathologic growth abnormalities, and may simply describe a fetus at the lower end of the normal range. *SOGC, 2013*

Intrauterine growth restriction refers to a fetus with an estimated fetal weight < 10th percentile on ultrasound that, because of a pathologic process, has not attained its biologically determined growth potential. *RCOG, 2013*

SGA vs IUGR

The main goal in FGR is identification

Small fetus (EFW<p10) must be divided in:

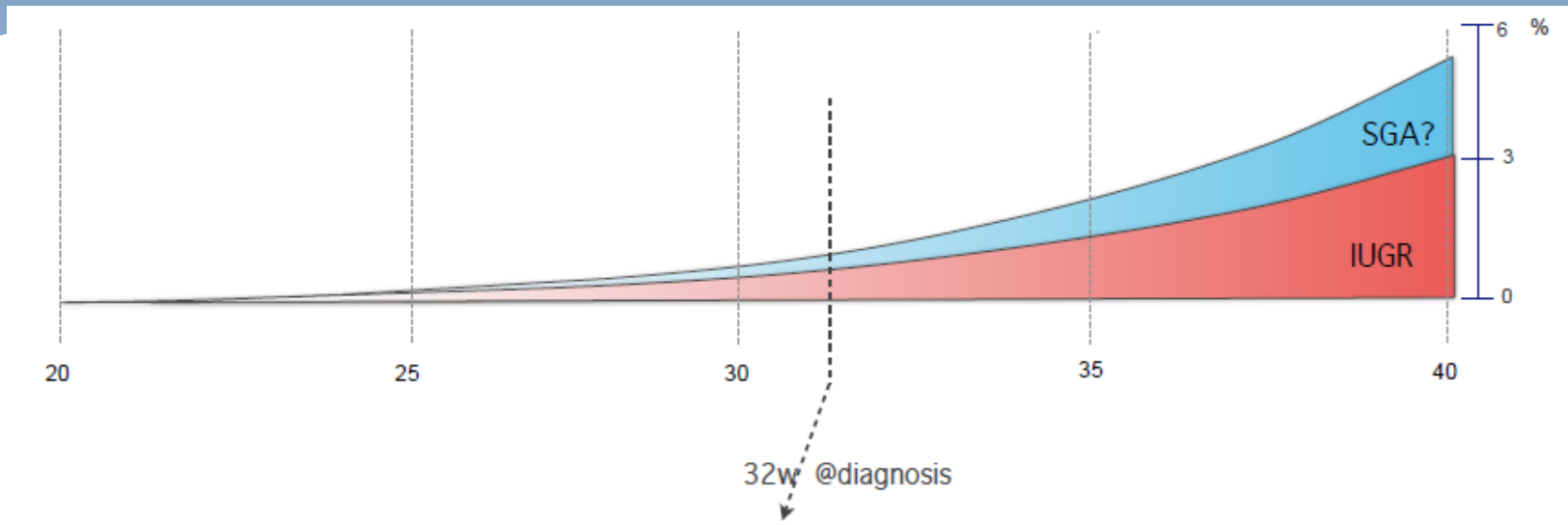
FGR (placenta, poor perinatal and long-term outcome)

SGA (we don't know, perinatal outcome N, poor long term)

Early and late-onset FGR (GA 32s) represent two distinct phenotypes of the same disease

Clinically, a single stage-based protocol allows optimizing decisions in all cases

EARLY AND LATE IUGR



EARLY IUGR (1%)	**LATE IUGR** (5-7%)
PROBLEM: MANAGEMENT	PROBLEM: DIAGNOSIS
Placental disease: high (UA+, PE high)	Placental disease: low (UA-, PE low)
Hypoxia ++: systemic CV adaptation	Hypoxia +/-: central CV adaptation
Tolerance to hypoxia. Natural history	Low tolerance: no natural history
High mortality and morbidity	Low mortality but poor long outcome.

DIAGNOSI DI IUGR

COLLOQUIO INFORMATIVO CON LA COPPIA: cause, rischi materni (Preeclampsia) e fetali (mortalita', morbidita' neurologica, sviluppo neurocognitivo, distress respiratorio) , monitoraggio, prognosi

- ecocardiografia fetale
- esami infettivologici
- cariotipo

DIAGNOSI DI IUGR

MONITORAGGIO FETALE
E
TIMING DEL PARTO

SGA vs IUGR

Exclude primary fetal defect

Exclude extrinsic cause

ISOLATED FETAL SMALLNESS = POORER PROGNOSIS

Perinatal *and* Long-term Outcomes

Poor perinatal outcome + IUFD
(Doppler) Signs of adaptation

IUGR

Placental insufficiency

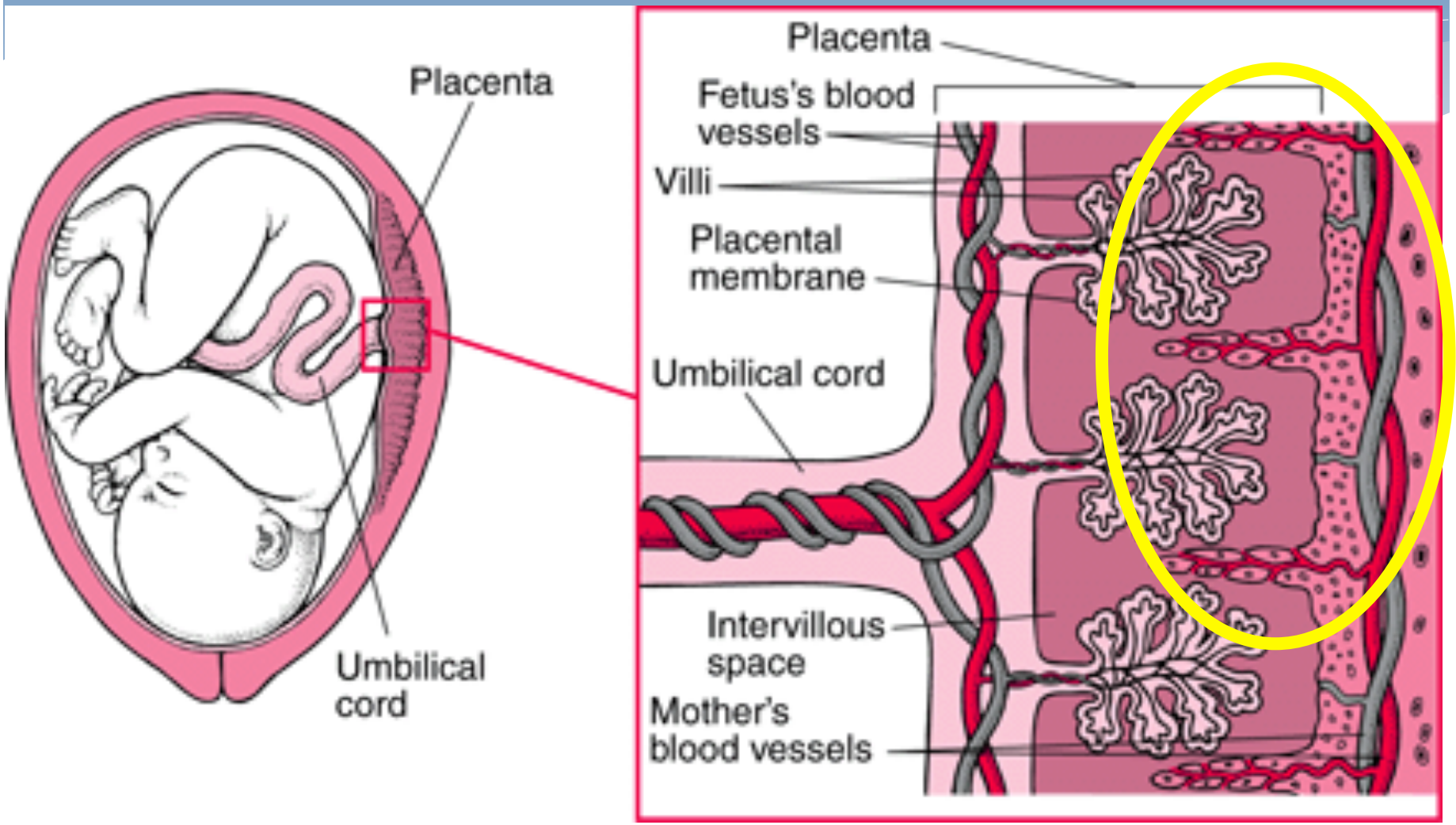
Perinatal outcome normal - No IUFD
NO signs of adaptation

SGA

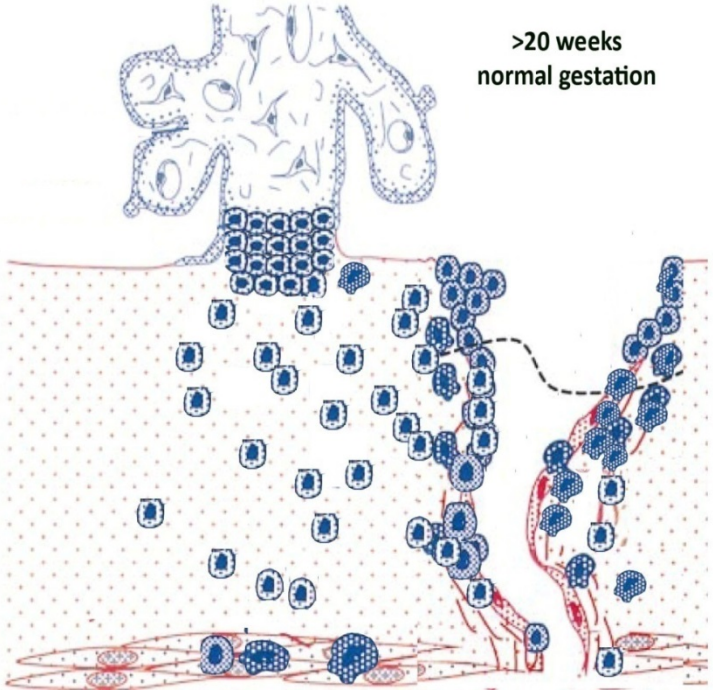
Unknown (constitutional + others)

FGR vs. SGA: DIFFERENT MANAGEMENT

Interazione feto-placenta



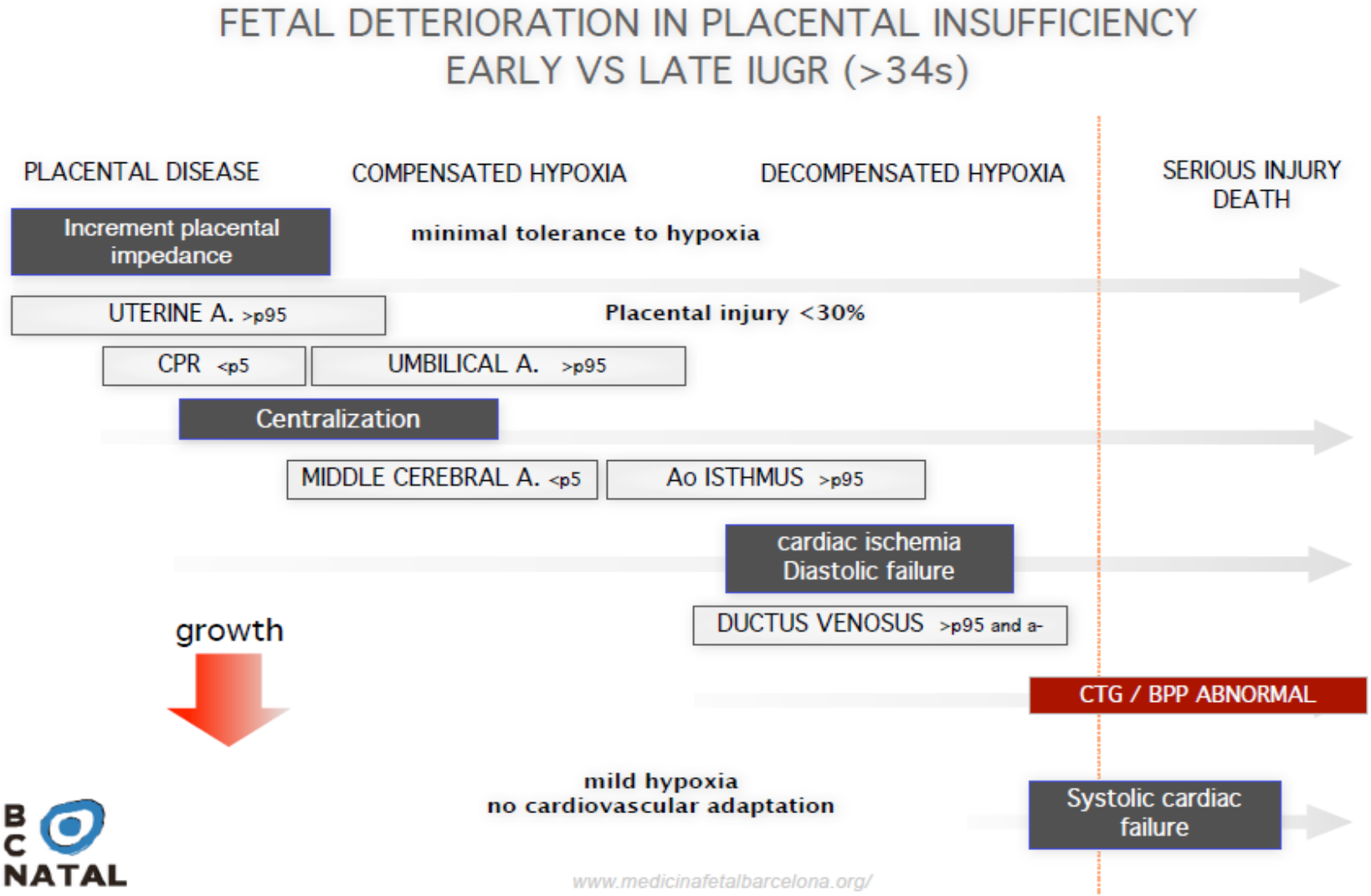
Interazione feto-placenta



The extravillous trophoblast cells invade into the uterine wall as far as the first third of the myometrium and its associated spiral arteries, where they disrupt the endothelium and the smooth muscle layer and replace the vascular wall.
This results in the conversion of the narrow calibre arteries into distended utero placental arteries, thereby increasing blood flow to the placenta and allowing an adequate supply of oxygen and nutrients to the growing fetus.

Placenta (2000), **21, Supplement A, Trophoblast Research, 14, S25–S30**

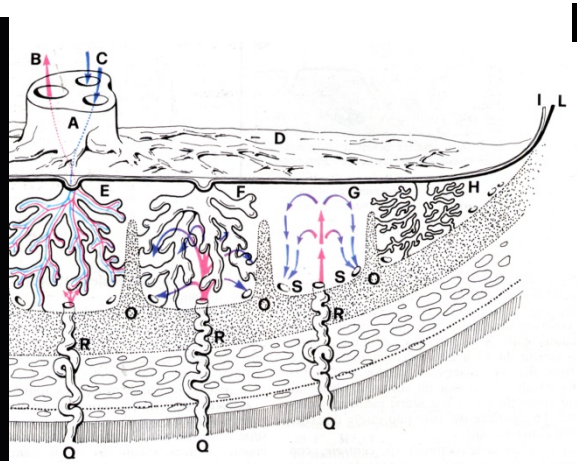
IUGR MONITORAGGIO CLINICO

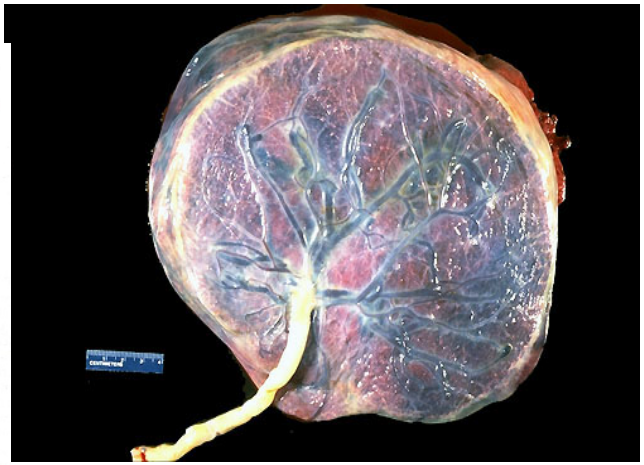


DOPPLER

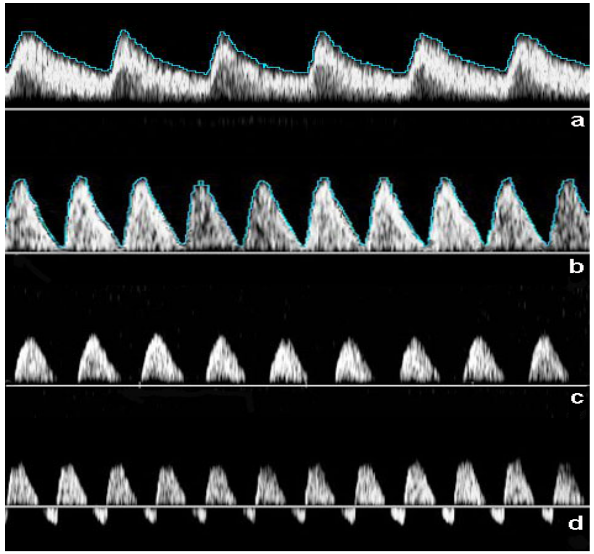
ABNORMAL DOPPLER =IUGR

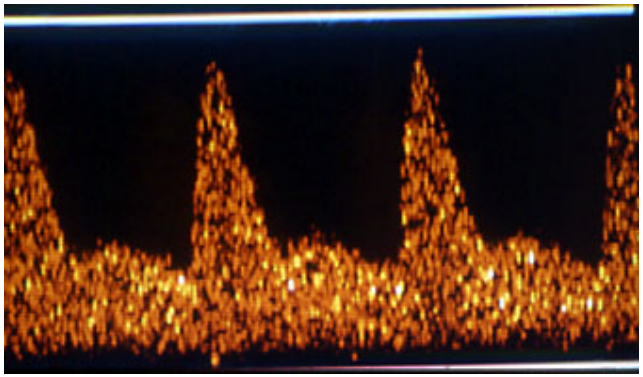
NORMAL DOPPLER= CONSTITUTIONAL SGA





umbilical



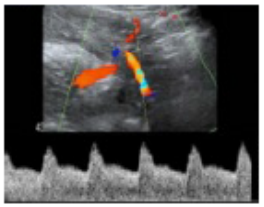


uterine

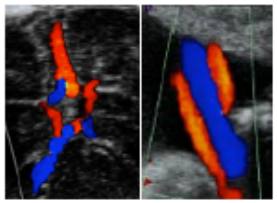
SGA vs IUGR

FGR = EFW <p10 + any of

UtA
>p95

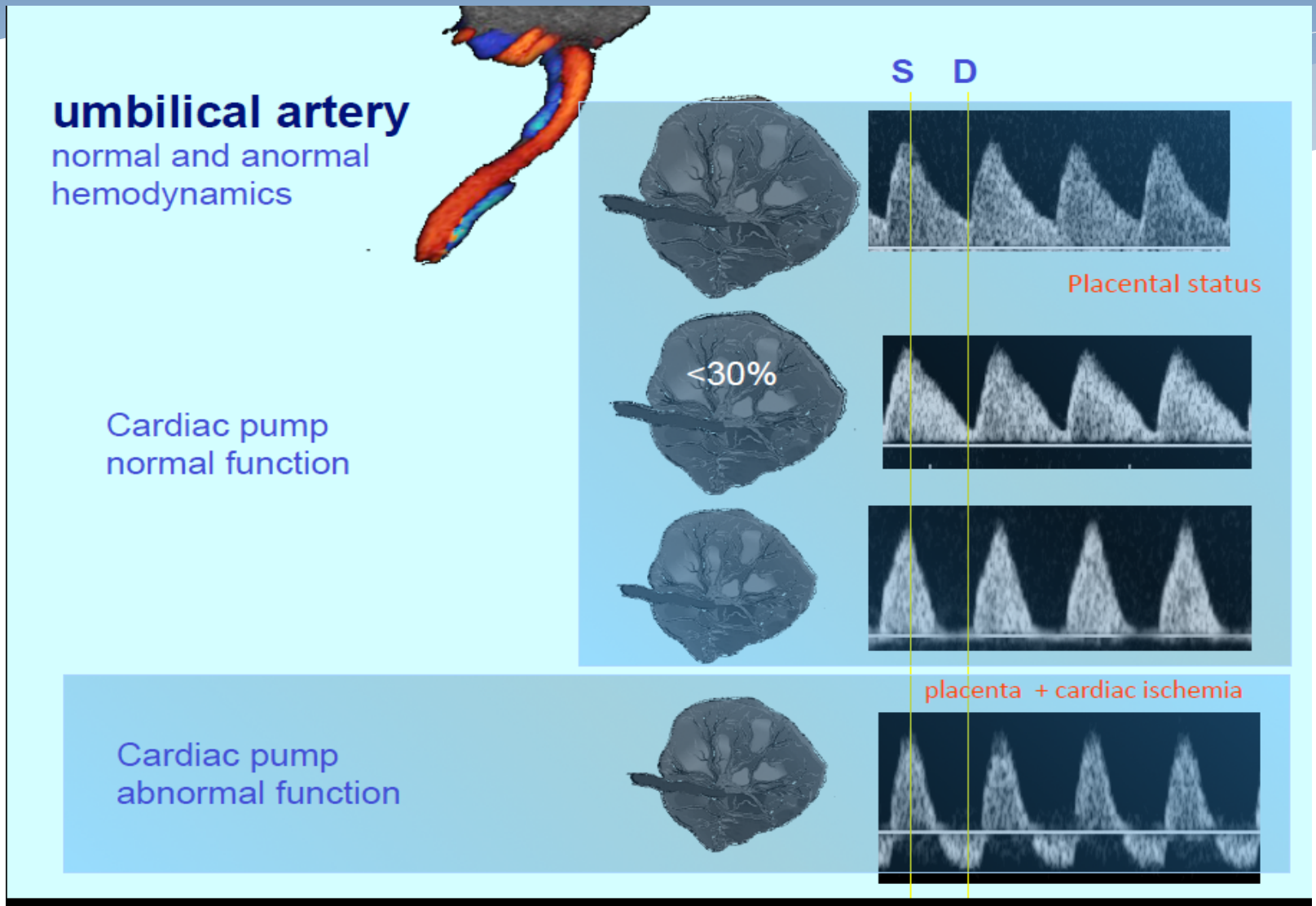


CPR
<p5



EFW CENTILE <3

DOPPLERVELOCIMETRIA ARTERIE OMBELICALI

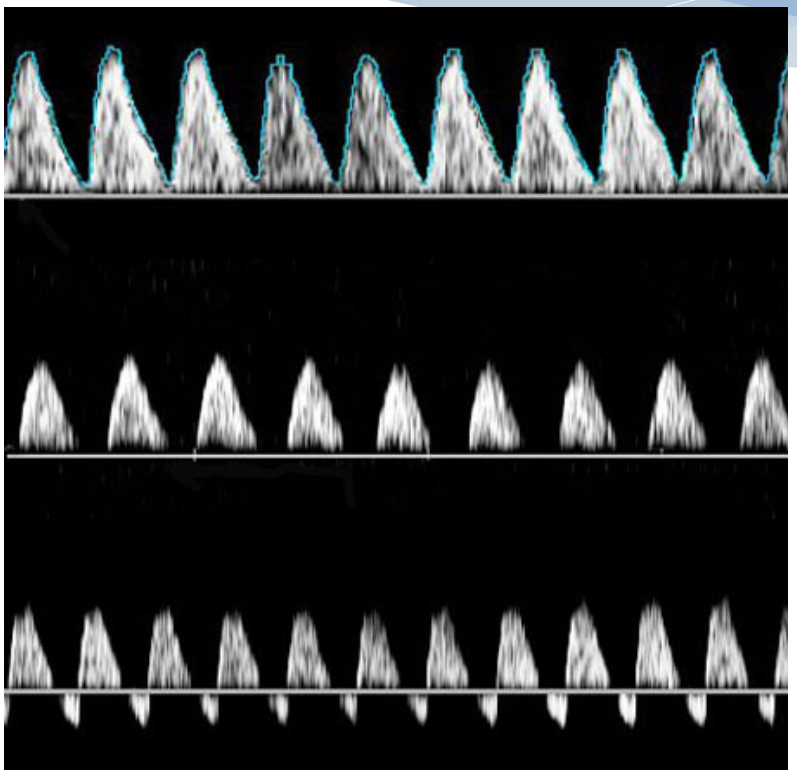


DOPPLERVELOCIMETRIA ARTERIE OMBELICALI

↑ resistenze placentari

↓ flusso telediastolico

↓ PI



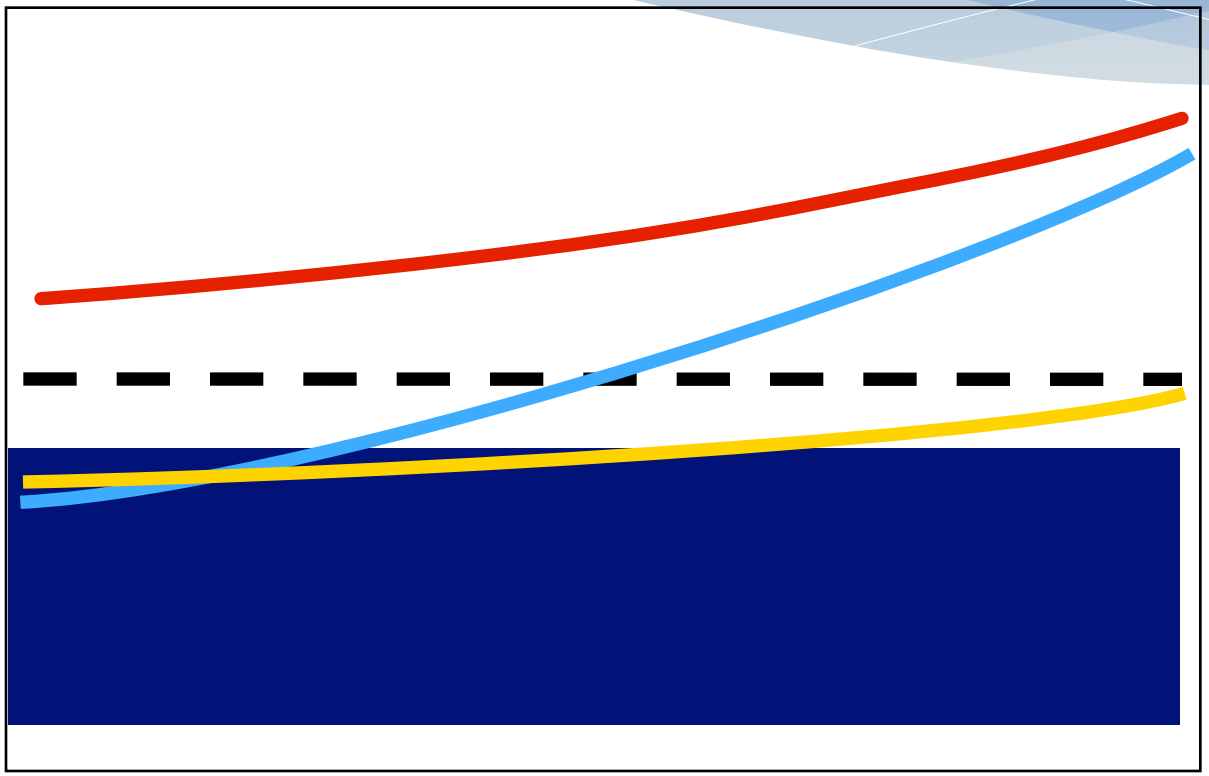
PED

AED

AED

La Dopplervelocimetria delle arterie ombelicali ha sensibilità e specificità elevate nell'individuare i feti che andranno incontro ad esiti sfavorevoli

Regressione Lineare del PI dell'Arteria Ombelicale: Tre Pattern di Progressione



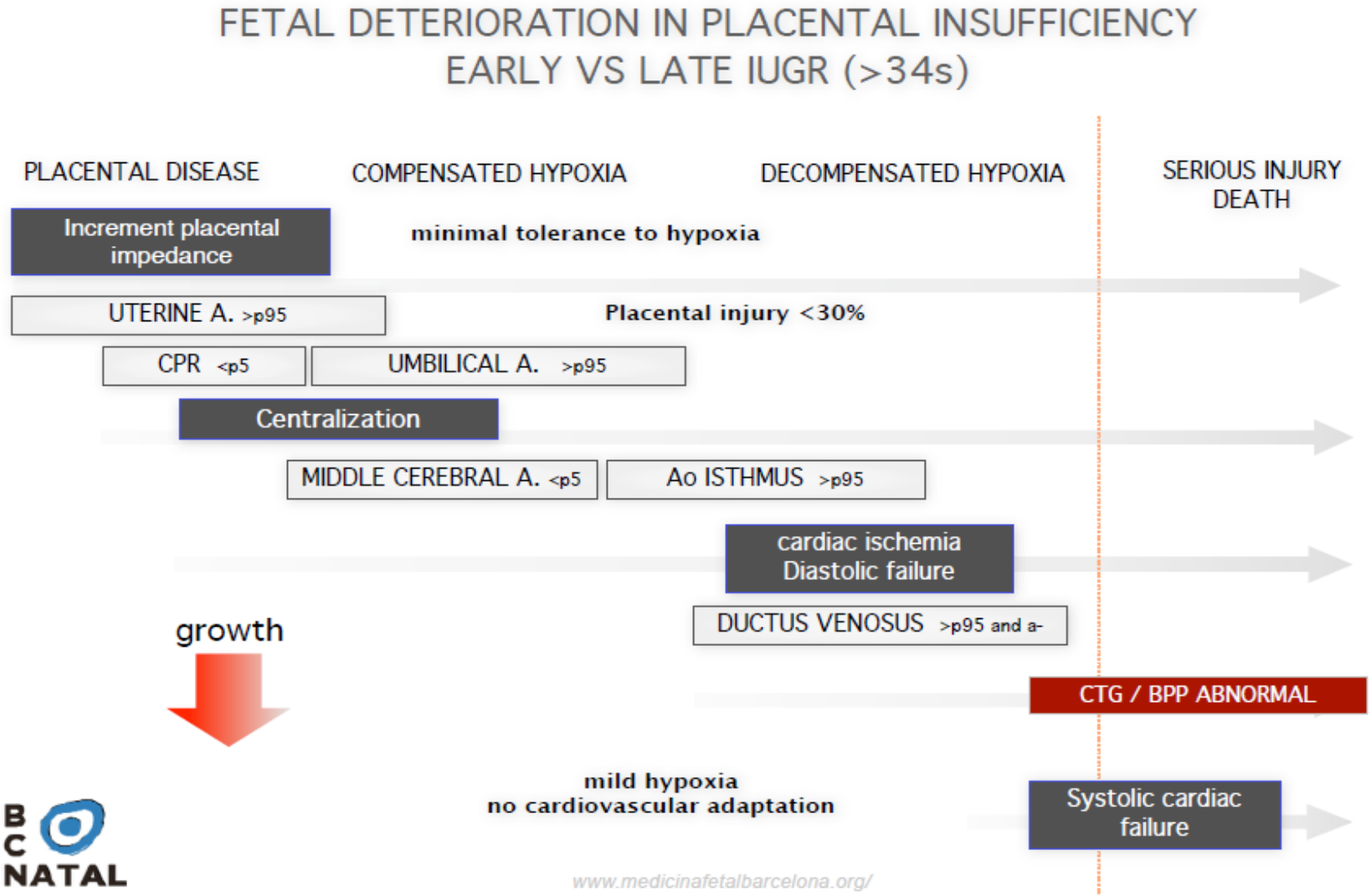
Turan OM et al. Ultrasound Obstet Gynecol 2008;32:160-7.

ODDS RATIOS PER MORTALITÀ PERINATALE ED EMORRAGIA CEREBRALE CORRETTA PER ETÀ

	PED	AED	RED
Mortalità perinatale	**1.0**	**4.0**	**10.0**
Emorragia cerebrale	**1.0**	**2.6**	**5.0**

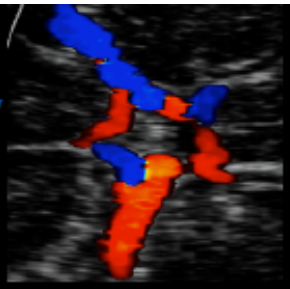
Karsdorp VHM et al. Lancet, 1994; 344: 1664

IUGR MONITORAGGIO CLINICO



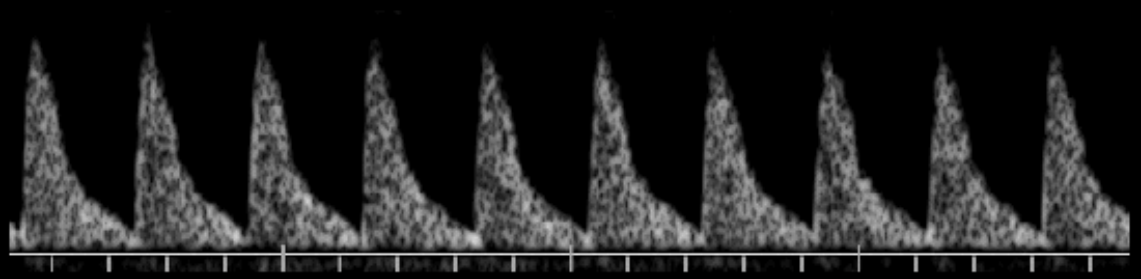
middle cerebral artery

normal and abnormal hemodynamics

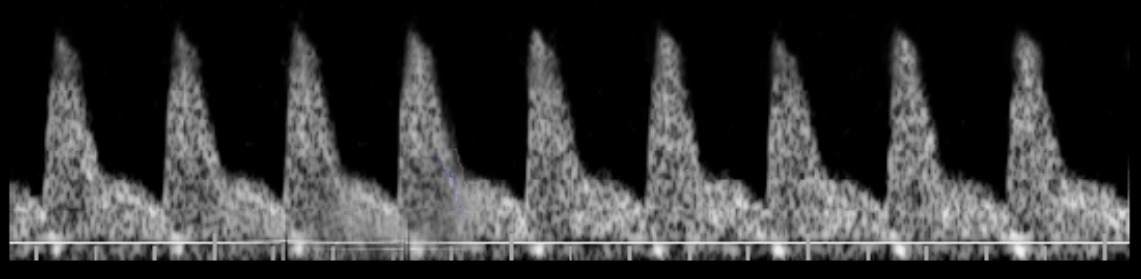


Normal oxygenation

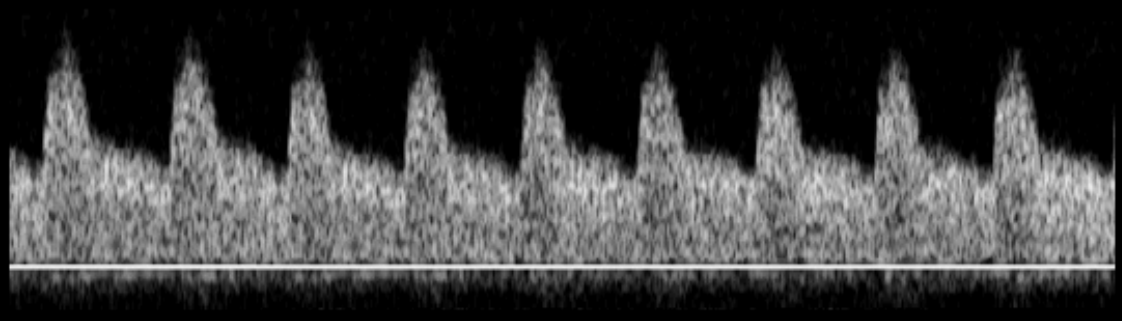
[normal waveform]



[mild vasodilation]



[marked vasodilation]

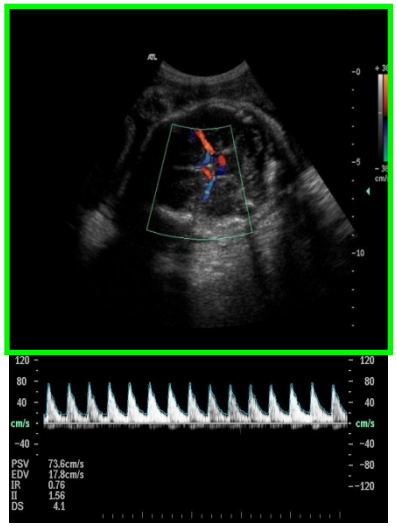


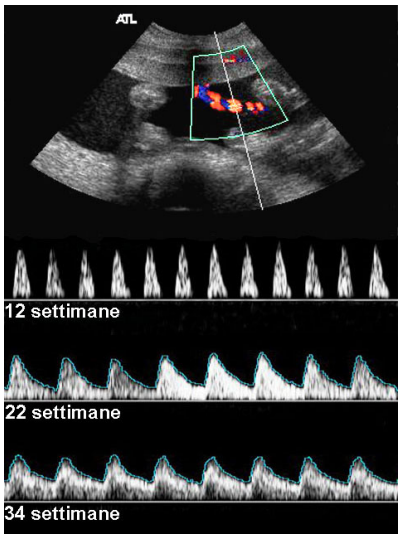
hypoxia

CEREBRO-PLACENTAL RATIO

Reflects hypoxia induced redistribution of blood flows

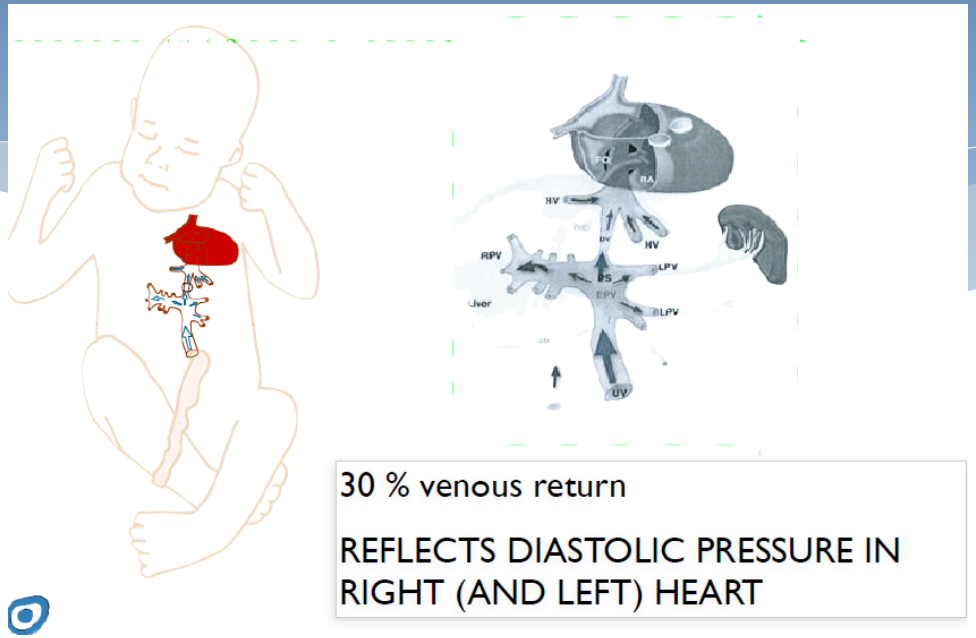
May be more sensitive to hypoxia than its individual components





Gramellini D, 1992
Hershkovitz R, 2000
Roza S, 2008
Figueras F, 2014

Il Dotto Venoso

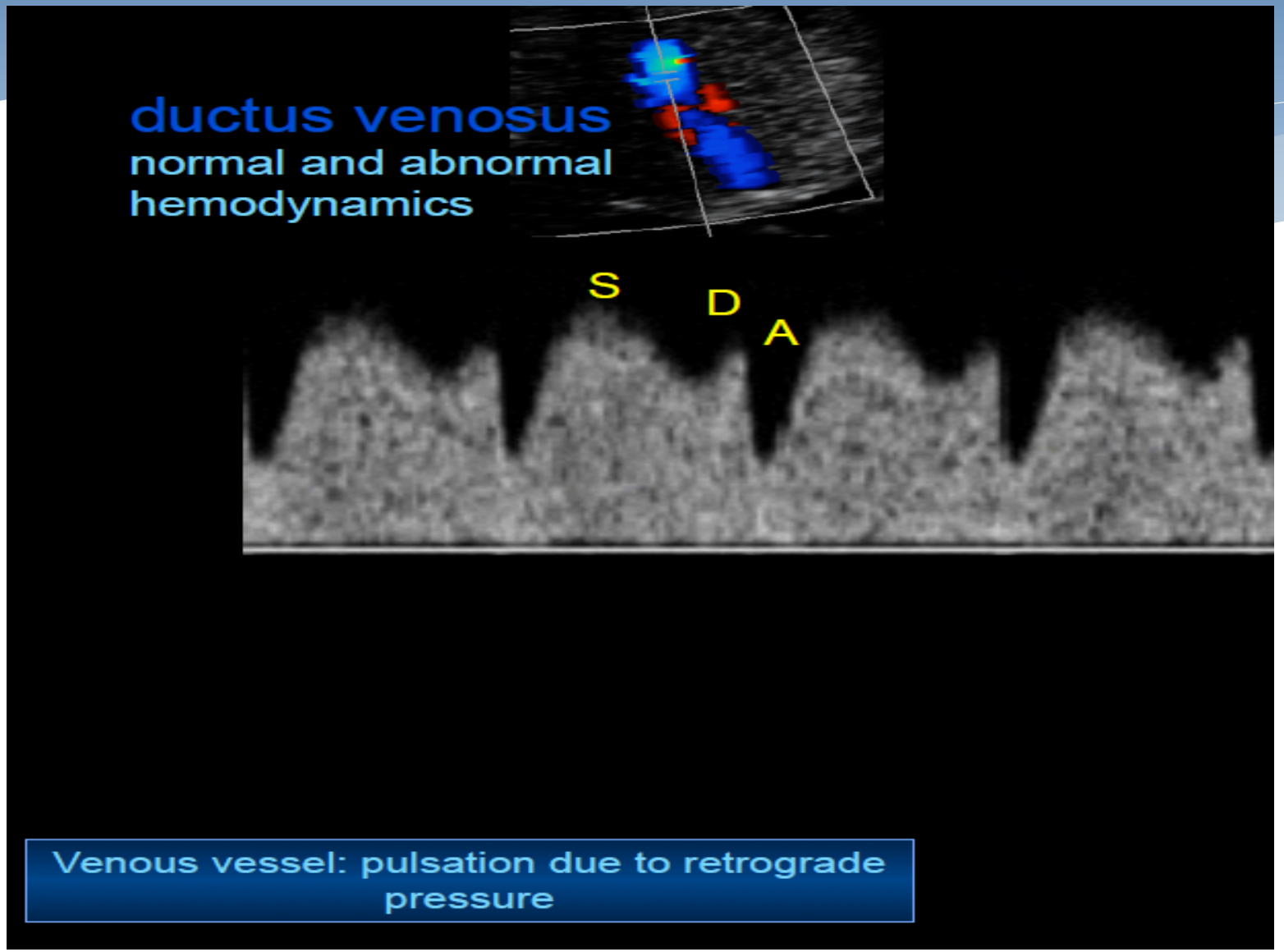


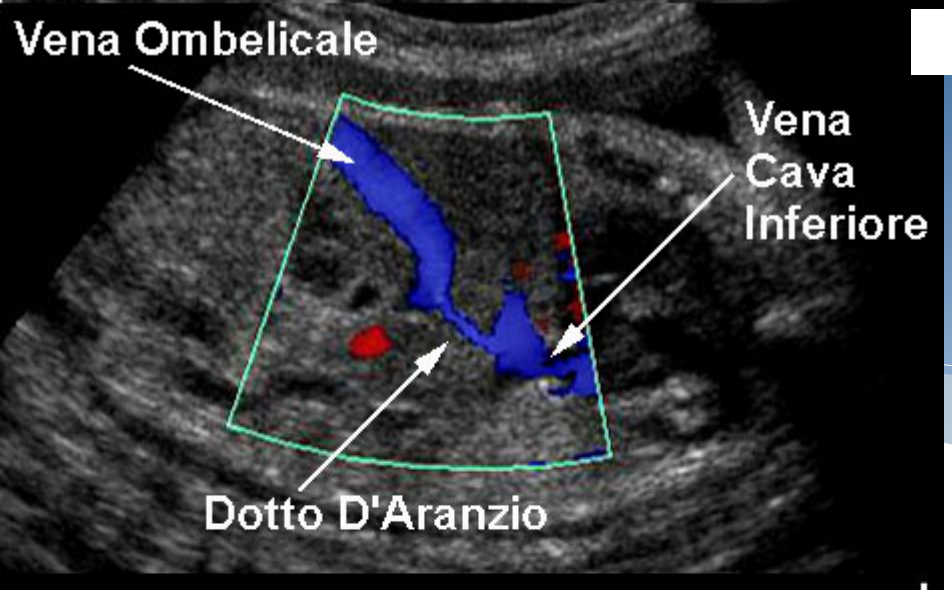
30 % venous return

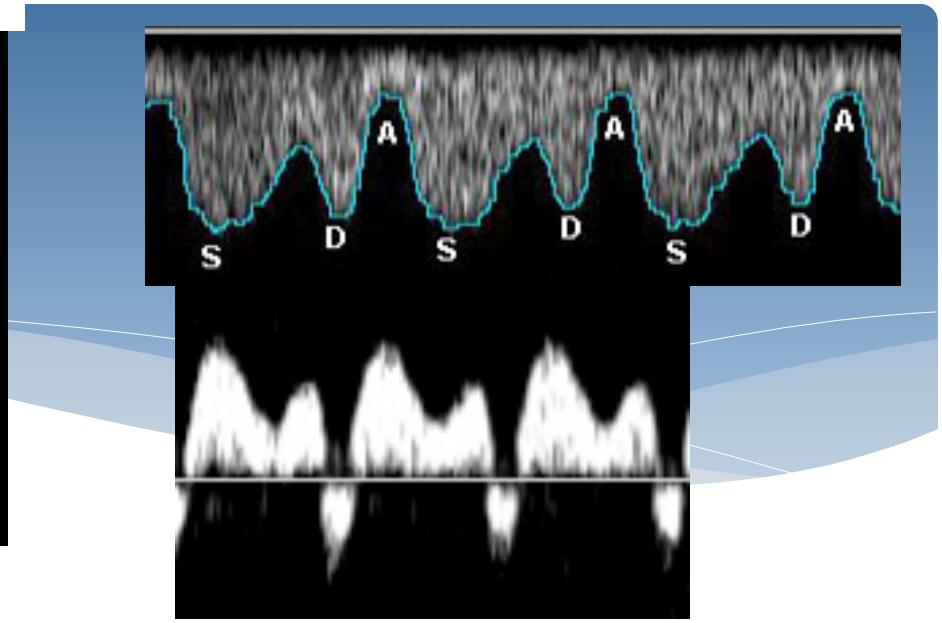
REFLECTS DIASTOLIC PRESSURE IN RIGHT (AND LEFT) HEART

The ductus venosus (DV) connects the intra-abdominal portion of the umbilical vein to the left portion of the inferior vena cava just below the diaphragm. The vessel is identified by visualizing this connection by 2D imaging either in a midsagittal longitudinal plane of the fetal trunk or in an oblique transverse plane through the upper abdomen.

Il Dotto Venoso



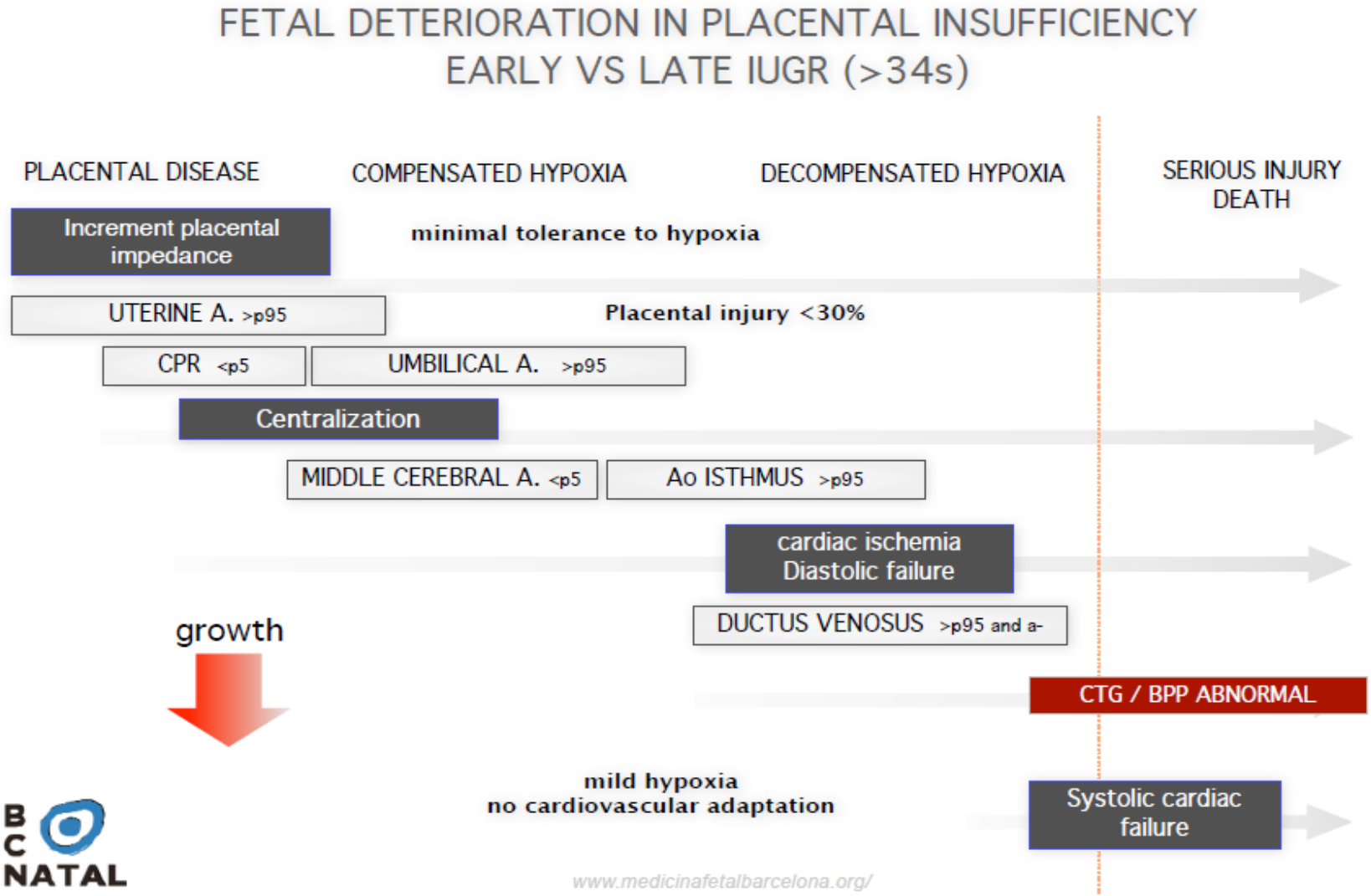




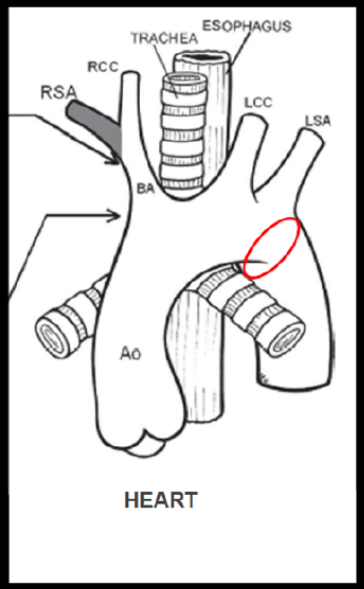
Il Doppler del Dotto Venoso è un fattore predittivo di acidosi

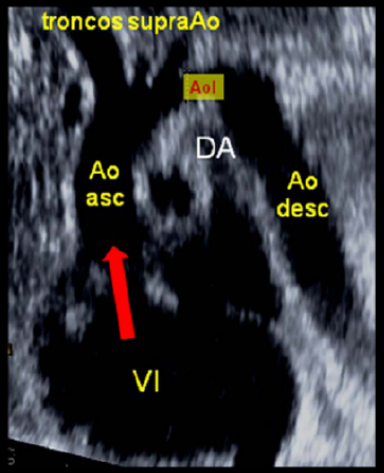
Ruolo nel timing del parto nello IUGR

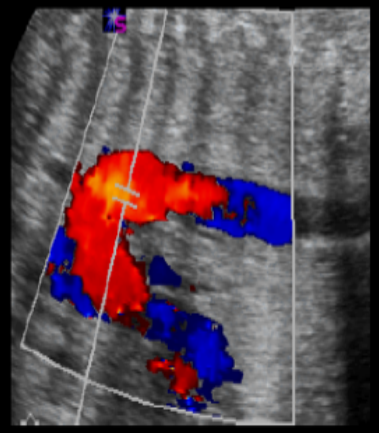
IUGR MONITORAGGIO CLINICO

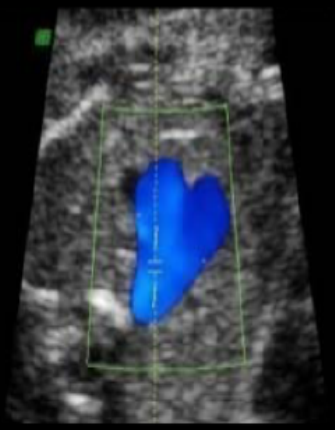


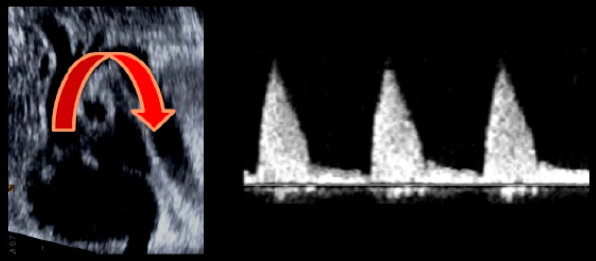
Istmo aortico

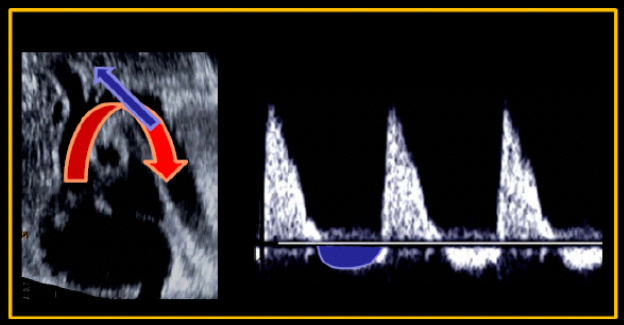


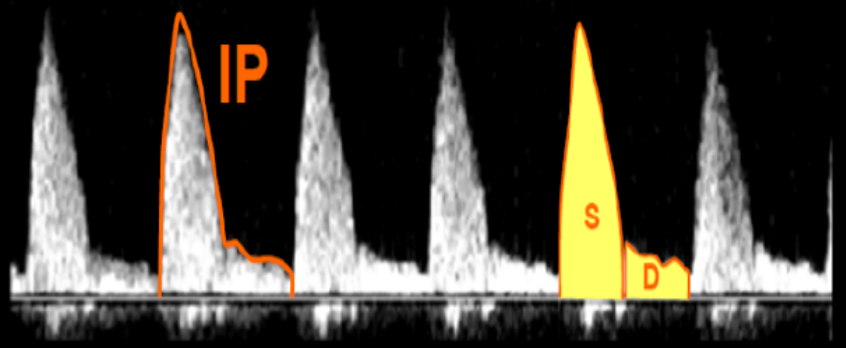












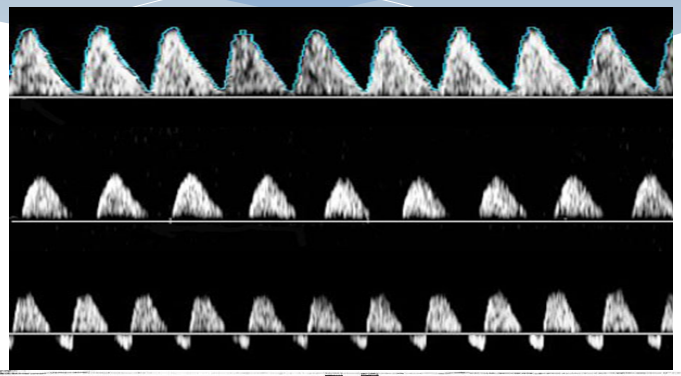
IFI

$$\frac{\text{VTI sístole + VTI diástole}}{\text{VTI sístole}}$$

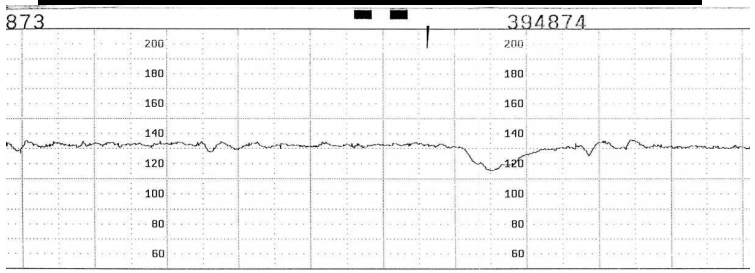
Fouron AJOG 2001, Del Río UOG 2006

Sorveglianza Fetale

Doppler

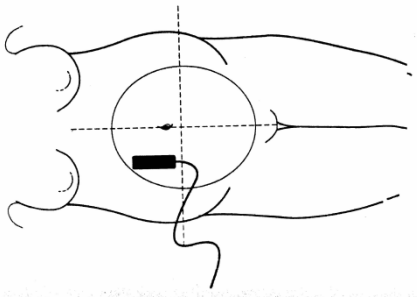


CTG



STV **< 3.5 msec a 26-29 sett**
< 4 msec a 29-32 sett

Liquido Amniotico



PROFILASSI ANTI-RDS NEGLI IUGR: SI'

Modifica gli esiti a lungo termine degli esposti

- inficia la crescita post-natale, ma…
- riduce in modo significativo la sopravvivenza senza

Amiya et al 2014
(review di studi osservazionali)

WHO recommendations on interventions to improve preterm birth outcomes

PROFILASSI CON MGSO4 NEGLI IUGR: SI'

Riduce in modo significativo l'incidenza di handicap motorio e di paralisi cerebrale.
DOSAGGIO: megli schemi di somministrazione che prevedono dose di attacco + dose di mantenimento. L'unica ad aver dato risultati significativi: 6g in 20-30 min + 2g/h per 12 ore.

Doyle et al 2009
(Cochrane database of systematic review)