FETAL THERAPY
REALITIES AND PROSPECTS

Eduard Gratacós
www.fetalmedicinebarcelona.org
Fetal Medicine & Therapy

- recent development
- high tech
- multidisciplinarity
- fetal surgery
- referral activity
- increasing importance
- high legal pressure
Evolution of social demands in Fetal Medicine & Therapy: the fetus as a patient

perception fetus as a person

capacity Dx & Tx

society of information

DEMANDS

www.fetalmedicinebarcelona.org/
| 1 | Diagnosis | Primary level |
Levels in Fetal Medicine 
integration in public health

1 Diagnosis

Primary level
Levels in Fetal Medicine integration in public health

<table>
<thead>
<tr>
<th>1</th>
<th>Diagnosis</th>
<th>Primary level</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Advanced studies</td>
<td>Tertiary Hospital (1 in 300,000)</td>
</tr>
<tr>
<td></td>
<td>US-guided fetal therapy</td>
<td></td>
</tr>
</tbody>
</table>

www.fetalmedicinebarcelona.org/
Levels in Fetal Medicine integration in public health

<table>
<thead>
<tr>
<th>Level</th>
<th>Service</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diagnosis</td>
<td>Primary level</td>
</tr>
<tr>
<td>2</td>
<td>Advanced studies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>US-guided fetal therapy</td>
<td>Tertiary Hospital (1 in 300,000)</td>
</tr>
<tr>
<td>3</td>
<td>Endoscopic therapy &amp; Fetal Surgery</td>
<td>Fetal surgery Center (1 in 15-20 million)</td>
</tr>
</tbody>
</table>
Levels in Fetal Medicine
integration in public health

Pregnancies

100 %

Public Health System

Complexity
Multidisciplinarity
Levels in Fetal Medicine integration in public health

Pregnancies

100 %

Public Health System

Advanced Fetal Medicine

Tertiary Center

5 %

Complexity Multidisciplinarity

www.fetalmedicinebarcelona.org/
Levels in Fetal Medicine integration in public health

Pregnancies

100 %

Advanced Fetal Medicine
Tertiary Center

Fetal surgery center
National or transnational level

Public Health System

Complexity
Multidisciplinarity

0.2%
(1 in >1,000)

5 %
FETAL SURGERY ≈ FETOSCOPY

- fetus ≠ smaller neonate
- uterus and mother not operable
FETAL SURGERY ≈ FETOSCOPY

• fetus ≠ smaller neonate

• uterus and mother not operable
FETAL THERAPY MUST BE NICE FOR PATIENTS NOT FOR DOCTORS ("PIONEERS TIME" IS OVER)
FETAL THERAPY MUST BE NICE FOR PATIENTS NOT FOR DOCTORS ("PIONEERS TIME" IS OVER)
FETAL THERAPY MUST BE NICE FOR PATIENTS NOT FOR DOCTORS ("PIONEERS TIME" IS OVER)
FETAL THERAPY MUST BE NICE FOR PATIENTS NOT FOR DOCTORS ("PIONEERS TIME" IS OVER)
FETAL THERAPY MUST BE NICE FOR PATIENTS NOT FOR DOCTORS ( "PIONEERS TIME" IS OVER)
FETAL THERAPY
common indications and procedures

- FETAL ANEMIA
- MONOCHORIONIC TWINS
- LUNG DEFECTS AND MASSES
- URINARY TRACT OBSTRUCTION
- FETAL TUMORS
- SPINA BIFIDA

www.fetalmedicinebarcelona.org/
FETAL THERAPY
common indications and procedures

- FETAL ANEMIA
- MONOCHORIONIC TWINS
- LUNG DEFECTS AND MASSES
- URINARY TRACT OBSTRUCTION
- FETAL TUMORS
- SPINA BIFIDA

www.fetalmedicinebarcelona.org/
COMPLICATIONS OF MONOCHORIONIC PREGNANCY

Chronic unbalanced transfusion
- Twin-twin transfusion syndrome (TTTS)
- Twin anemia polycytemia syndrome (TAPS)

Discordant placental territories
- Selective IUGR

Discordant Malformation

Unidirectional acute transfusion
- Single fetal demise
- Sustained bradichardia in one fetus

High risk
Chronic unbalanced transfusion

- Twin–twin transfusion syndrome (TTTS)
- Twin anemia polycytemia syndrome (TAPS)

- Poly (>8cm) + oligohydramnios (<2cm)
- Very discordant bladders

J Perinat Med 2013
Chronic unbalanced transfusion

- Twin–twin transfusion syndrome (TTTS)
- Twin anemia polycytemia syndrome (TAPS)

- Poly (>8cm) + oligohydramnios (<2cm)
- Very discordant bladders

J Perinat Med 2013
TTTS: laser therapy

Laser = best treatment option
NEJM 2004

Current survival of at least one fetus in 80-85%
J Perinat Med 2013
TTTS: laser therapy

Laser = best treatment option
NEJM 2004

Current survival of at least one fetus in 80-85%
J Perinat Med 2013
FETAL THERAPY
common indications and procedures

- MONOCHORIONIC TWINS
- URINARY TRACT OBSTRUCTION
- FETAL TUMORS
- SPINA BIFIDA
- FETAL ANEMIA
- LUNG DEFECTS AND MASSES

www.fetalmedicinebarcelona.org/
Percutaneous Feto-Endoscopic Tracheal Occlusion
Deprest J, Gratacos E, Nicolaides K. UOG 04

- increase airways pressure
- accelerated growth
- first case: oct 01
- currently >500

TOTAL RCT international trial ongoing
Percutaneous Feto-Endoscopic Tracheal Occlusion

Deprest J, Gratacos E, Nicolaides K. UOG 04

- increase airways pressure
- accelerated growth
- first case: oct 01
- currently >500

TOTAL RCT international trial ongoing
LUNG DEFECTS

CCAM: prognosis & natural history

CCAM & hydrops

MORTALITY 100%

(Winteres et al. JCU 1997)
(Kitano et al. W.B. Saunders, 1999)

MAIN FACTOR: SIZE

Maternal mirror syndrome (placental hídrops)

www.fetalmedicinebarcelona.org/
LUNG DEFECTS

Lung Mass + hydrops = fetal therapy
LUNG DEFECTS

Pleural effusion + hydrops = fetal therapy

Nicolaides K, 1990
Smith RP, UOG 05
Murabayashi, Fet Dx Ther06
LUNG DEFECTS

Pleural effusion + hydrops = fetal therapy

Nicolaides K, 1990
Smith RP, UOG 05
Murabayashi, Fet Dx Ther06
LUNG DEFECTS

Bronchial atresia
LUNG DEFECTS

Bronchial atresia

Martinez et al. Fetal Diagn Ther 2013
LUNG DEFECTS

Bronchial atresia

Martinez et al. Fetal Diagn Ther 2013
FETAL THERAPY

common indications and procedures

- FETAL ANEMIA
- MONOCHORIONIC TWINS
- LUNG DEFECTS AND MASSES
- URINARY TRACT OBSTRUCTION
- FETAL TUMORS
- SPINA BIFIDA

www.fetalmedicinebarcelona.org/
Lower Urinary Tract Obstruction

Urethral Posterior Valves

- Often associated other nephro-urologic anomalies
- At best 50% intact survival

Shunt (PLUTO, Lancet 2013)
No apparent benefit (N=31)

Fetoscopy with valve ablation
Intact survival 45-50%
Ruano et al. n=11
Martinez et al. n=14
LUTO
Obstructive ureterocele
LUTO
Obstructive ureterocele

www.fetalmedicinebarcelona.org/
FETAL THERAPY

common indications and procedures

- FETAL ANEMIA
- MONOCHORIONIC TWINS
- LUNG DEFECTS AND MASSES
- URINARY TRACT OBSTRUCTION
- FETAL TUMORS
- SPINA BIFIDA

www.fetalmedicinebarcelona.org/
MRI anatomical evaluation of fetal tumors
FETAL THERAPY
common indications and procedures

- FETAL ANEMIA
- MONOCHORIONIC TWINS
- LUNG DEFECTS AND MASSES
- URINARY TRACT OBSTRUCTION
- FETAL TUMORS
- SPINA BIFIDA
Fetal surgery for spina bifida (NEJM 11)

• Deambulation 20% vs 40% in treated
• Need Shunt 85% vs 35%
• Maternal-fetal complications > 50%
Fetal surgery for spina bifida (NEJM 11)

- Deambulation 20% vs 40% in treated
- Need Shunt 85% vs 35%
- Maternal-fetal complications > 50%
CHALLENGES

• Improve education
• Offer fetal therapy of 2013 not of 1993
• Improve instrumentation to reduce invasiveness + complications
Fetal Medicine Unit

www.fetalmedicinebarcelona.org/
FETAL MEDICINE DOES NOT EXIST WITHOUT DETECTION

THE CRITICAL ROLE OF IMPROVING EDUCATION

FETAL MEDICINE UNIT

Ultrasound Unit

Ultrasound Unit

Ultrasound Unit

Fetal Medicine Unit

www.fetalmedicinebarcelona.org
FETAL MEDICINE DOES NOT EXIST WITHOUT DETECTION

IMPROVING EDUCATION

Fetal Medicine Unit

www.fetalmedicinebarcelona.org
FETAL MEDICINE DOES NOT EXIST WITHOUT DETECTION

IMPROVING EDUCATION
The problem of regulating a low-volume + high-complexity activity

Spain and influence area n=250-300 / year
The problem of regulating a low-volume + high-complexity activity

Spain and influence area n=250-300 / year
The problem of regulating a low-volume + high-complexity activity

Spain and influence area n=250-300 / year
The problem of regulating a low-volume + high-complexity activity

Spain and influence area n=250-300 / year

• excellence, not distance is a problem
• ideal scenario:
  • minimal politics
  • “market” regulation
  • accreditation and national registry
Challenges of fetal medicine and therapy
Improving selection and reducing invasiveness

Instruments

(Quantitative) Imaging

www.fetalmedicinebarcelona.org/
FETAL LUNG MATURITY PROBLEMS AFFECT NEARLY 10% LARGEST CAUSE OF PERINATAL MORBIDITY PRE- AND NEAR

Testing to be Performed on amniotic fluid

- 32-38\( \frac{6}{7} \) weeks of gestation

### NEONATAL RESPIRATORY MORBIDITY

<table>
<thead>
<tr>
<th>Weeks gestation at birth</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;28</td>
<td>60-80</td>
</tr>
<tr>
<td>32-36</td>
<td>15-30</td>
</tr>
<tr>
<td>&gt;37</td>
<td>5</td>
</tr>
<tr>
<td>Term</td>
<td>Rare</td>
</tr>
</tbody>
</table>

~20,000 newborns/year (US)

www.fetalmedicinebarcelona.org/
FETAL LUNG MATURITY PROBLEMS AFFECT NEARLY 10% LARGEST CAUSE OF PERINATAL MORBIDITY PRE- AND NEAR (ACOG 2008)
FETAL LUNG MATURITY PROBLEMS AFFECT NEARLY 10% LARGEST CAUSE OF PERINATAL MORBIDITY PRE- AND NEAR (ACOG 2008)
FETAL LUNG MATURITY PROBLEMS AFFECT NEARLY 10% LARGEST CAUSE OF PERINATAL MORBIDITY PRE- AND NEAR (ACOG 2008)
FETAL LUNG MATURITY PROBLEMS AFFECT NEARLY 10% LARGEST CAUSE OF PERINATAL MORBIDITY PRE- AND NEAR (ACOG 2008)

FETAL LUNG MATURITY BY US TEXTURE ANALYSIS: MULTICENTER INTERNATIONAL STUDY

N=950 (expected >1,500)
FETAL THERAPY
REALITIES AND PROSPECTS

Eduard Gratacós
www.fetalmedicinebarcelona.org