Sonographic Evaluation of Early Pregnancy Loss

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Disclosures
Relevant Financial Relationships: None

Learning Objectives
After completing this presentation, the learner will:

Objective 1: understand the limitations of the hCG “discriminatory level”
Objective 2: know the sonographic criteria for definite pregnancy failure and probable pregnancy failure in early pregnancy
Objective 3: know the sonographic findings that, in the presence of an embryonic heartbeat, indicate a high risk of impending pregnancy loss

Introduction
• 10-25% of all clinically recognized pregnancies end in pregnancy failure (“miscarriage”)
• Ultrasound is the primary method for diagnosing pregnancy failure, using criteria for definite, probable, and impending pregnancy failure
• Sonographic criteria for definite pregnancy failure should be set to virtually eliminate false positives, in order to avoid interventions that could eliminate or damage a normal intrauterine pregnancy

Lecture Outline
• Normal U/S findings in early pregnancy
  • Early pregnancy loss: terminology, incidence, general principles
  • Early pregnancy loss: sonographic diagnosis
    – Scenario 1: Ultrasound demonstrates no intrauterine or ectopic pregnancy in a woman with positive pregnancy test
    – Can a single hCG value (“discriminatory level”) exclude a viable IUP?
    – Scenario 2: Ultrasound demonstrates an intrauterine gestational sac; no cardiac activity is seen (with or without a visible embryo)
    – What findings indicate definite pregnancy failure?
    – Scenario 3: Ultrasound demonstrates an intrauterine pregnancy with cardiac activity
    – What findings suggest impending pregnancy failure?
Normal Sonographic Findings in Early Pregnancy

<table>
<thead>
<tr>
<th>Gestational Age (weeks)</th>
<th>Normal Sonographic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>Gestational sac</td>
</tr>
<tr>
<td>5.5</td>
<td>Yolk sac</td>
</tr>
<tr>
<td>6.0</td>
<td>Embryo with heartbeat</td>
</tr>
<tr>
<td>6.5</td>
<td>Amnion around embryo</td>
</tr>
<tr>
<td>7.0</td>
<td>Amnion around embryo</td>
</tr>
</tbody>
</table>

- **5.0 Weeks**: No Visible Contents ("nonspecific" saclike structure)
- **5.5 Weeks**: Yolk Sac
- **6.0 Weeks**: Embryo with Heartbeat
- **7.0 Weeks**: Amnion around embryo

U/S of Early Pregnancy Loss

- **Terminology**
  - *Miscarriage*: Spontaneous loss of an intrauterine pregnancy prior to 20 weeks of gestation
  - *Early pregnancy failure*: Often used to describe spontaneous loss of an intrauterine pregnancy in the first trimester
  - Other terms:
    - spontaneous abortion
    - blighted ovum

- **Incidence**
  - 10-25% of all clinically recognized pregnancies end in miscarriage
  - Highest rate of miscarriage is at ≤6 weeks of gestation, then progressively declines

- Chromosomal anomalies are thought to be the most common cause of miscarriage

Society of Radiologists in Ultrasound Consensus Conference on Early 1st Trimester Sonography: Guidelines for Diagnosing Miscarriage and Excluding a Viable Intrauterine Pregnancy

Baltimore, MD October 23-24, 2012
Society of Radiologists in Ultrasound
Consensus Conference on Early 1st Δ Sonography:
Guidelines for Diagnosing Miscarriage and
Excluding a Viable Intrauterine Pregnancy

Moderator: Peter Doubilet

- Beryl Benacerraf
- Carol Benson
- Rusty Brown
- Roy Filly
- Ted Lyona
- Dolores Pretorius

- OB/Gyn
- Tom Bourne
- Steven Goldstein
- Misty Porter
- Ilan Timor

- Emergency Medicine
- Michael Blaivas
- Chris Fox
- John Kendall

Doubilet

Diagnostic Criteria for Nonviable Pregnancy
Early in the First Trimester

Peter M. Doubilet, M.D., Ph.D., Carol B. Benson, M.D.,
Tom Bourne, M.B., B.S., Ph.D., and Michael Blaivas, M.D., for the Society of
Radiologists in Ultrasound Multispecialty Consensus Panel on Early First Trimester
Diagnosis of Miscarriage and Exclusion of a Viable Intrauterine Pregnancy*

U/S of Early Pregnancy Loss
Key Principle

- Criteria for pregnancy failure should be set to:
  - eliminate false positives
  - apply to a broad range of U/S facilities that
    meet at least minimum quality criteria, not
    solely to experts in early OB U/S

U/S of Early Pregnancy Loss
Three Scenarios*

- Normal U/S findings in early pregnancy
- Early pregnancy loss: terminology,
  incidence, general principles
- Early pregnancy loss: sonographic
  diagnosis

U/S Finding | Key Questions
---|---
No IUP seen | Can a single hCG value (“discriminatory level”) exclude viable IUP?
IUP, no heartbeat (± embryo) | What findings indicate definite pregnancy failure?
What findings are suspicious for pregnancy failure?
IUP with heartbeat | What findings suggest impending pregnancy failure?

* all with @hCG and normal adnexa
U/S of Early Pregnancy Loss
Three Scenarios*

- No IUP seen (PUL)
- IUP, no heartbeat (± embryo)
- IUP with heartbeat

* all with βhCG and normal adnexa

U/S Finding | Key Questions
---|---
No IUP seen | Can a single hCG value ("discriminatory level") exclude viable IUP?
IUP, no heartbeat (± embryo) | What findings indicate definite pregnancy failure? What findings are suspicious for pregnancy failure?
IUP with heartbeat | What findings suggest impending pregnancy failure?

hCG "Discriminatory Level"

- Concept Originated by Kadar in 1981
- Definition
  - hCG level at which normal IUP is consistently seen
- Improved U/S Technology → ↓ Discrim Level
  - 1981: 6500 mIU/ml
  - 1985: 3600 mIU/ml
  - 1990 & beyond (TV U/S): 1000-2000 mIU/ml

hCG "Discriminatory Level" Rationale

hCG > 2000 mIU/ml & US: No intrauterine fluid collection
→ Can't have normal IUP

DDx: Failed IUP Ectopic

hCG "Discriminatory Level" Proposed Management Algorithms

- hCG > discriminatory level & no IUP seen
  - IM MTX for presumed ectopic pregnancy
- hCG > discriminatory level & no IUP seen
  - D&C
  - Treat for ectopic pregnancy if no chorionic villi

hCG "Discriminatory Level" Reality

hCG = 4336 mIU/ml
No visible gestational sac
1 month later

Normal 9½ week IUP
Normal term baby
**hCG “Discriminatory Level” Reality**

- hCG = 2217 mIU/ml
- No visible gestational sac
- No IUP seen
- 6 days later
- Normal 5½ week twin IUP
- Normal term twins

**hCG ⇔ Pregnancy of Unknown Location (PUL)**

- hCG levels in normal IUPs, abnormal IUPs, and ectopic pregnancies have considerable overlap
- If U/S shows no evidence of intrauterine or ectopic pregnancy, don’t intervene based on a single hCG measurement
- Get at least one F/U U/S & hCG, in order to avoid:
  - damaging a potentially normal IUP
  - giving MTX to a woman with failed IUP

**U/S of Early Pregnancy Loss Three Scenarios**

- No IUP seen (PUL)
- IUP, no heartbeat (∓ embryo)
- IUP with heartbeat

**Diagnosis of Pregnancy Failure Criteria**

- Non-visualization of a heartbeat by a certain embryonic size
  - Crown-rump length (CRL) without heartbeat
- Non-visualization of an embryo by a certain gestational sac size
  - Mean sac diameter (MSD) without embryo
- Non-visualization of an embryo by a certain point in time
  - No embryo seen after a time interval since 1st scan
Diagnosis of Pregnancy Failure
Criteria: Up to ~2012

• Non-visualization of a heartbeat by a certain embryonic size
  – Crown-rump length ≥ 5 mm without heartbeat
• Non-visualization of an embryo by a certain gestational sac size
  – Mean sac diameter ≥ 16 mm without embryo
• Non-visualization of an embryo by a certain point in time
  – Not well established

Crown-Rump Length

 따른 점은 다음과 같습니다.

• Heartbeat is usually seen as soon as the embryo is visible
  – Crown-rump length = 1.7 mm

At what CRL is the heartbeat always seen in a normal pregnancy?

Crown-Rump Length

Cutoff value above which cardiac activity is consistently visible on TV U/S in a normal pregnancy

• Early studies
  – Levi 1990: 4 mm
  – Goldstein 1992: 4 mm
  – Brown 1990: 5 mm
  – Pennell 1991: 5 mm
• 5 mm became the generally accepted cutoff

Crown-Rump Length

Concerns With the Early Data

– Small study populations → 95% confidence range of specificity = 0.90-1.0
– Several cases of embryos with CRL of 5-6 mm and no cardiac activity that subsequently proved to be normal have been reported (Abdallah 2011; Hamilton 2011)
– Interobserver variability of CRL measurement has been found to be ±15% (Pexsters 2011)
  • One practitioner’s 6 mm CRL may be 15% higher, or 6.9 mm, when measured by others

Crown-Rump Length

• CRL ≥ 7 mm & no heartbeat: definitive for failed pregnancy
• CRL < 7 mm & no heartbeat: suspicious for failed pregnancy

SRU Consensus Panel

Definite Pregnancy Failure

3 mm & no heartbeat

Suspicious for Pregnancy Failure

7 mm & no heartbeat
Mean Sac Diameter

Cutoff value above which an embryo is consistently visible on TV U/S in a normal pregnancy

• Early studies
  – Levi 1988: 16 mm
  – Tongsong 1994: 17 mm
• 16 mm became the generally accepted cutoff

Mean Sac Diameter

• Concerns With the Early Data
  – Small study populations ⇒ 95% confidence range of specificity = 0.88-1.0
  – Several cases of embryos with MSD of 17-21 mm and no cardiac activity that subsequently proved to be normal have been reported (Abdallah 2011; Rowling 1997)
  – Interobserver variability of MSD measurement has been found to be ± 19% (Pexsters 2011)
    ▪ One practitioner’s 21 mm MSD may be 19% higher, or 25.0 mm, when measured by others

Mean Sac Diameter

• MSD ≥ 25 mm & no embryo: definitive for failed pregnancy
• MSD 16-24 mm & no embryo: suspicious for failed pregnancy

Mean Sac Diameter

Definite Pregnancy Failure

Scan 1

Gestational sac without YS

≥ 2 weeks

No embryo

Scan 2

Gestational sac with YS

≥ 11 days

No embryo

No embryo >6 weeks after LMP*

* suspicious for pregnancy failure

Definite Pregnancy Failure

Scan 1

Gestational sac without YS

≥ 2 weeks

No embryo

Definite Pregnancy Failure

Scan 2

Gestational sac without YS

≥ 15 days

No embryo
Time-Based Criteria
**Definite Pregnancy Failure**

- Gestational sac with YS
- ≥ 11 days
- No embryo

Time-Based Criteria
**Suspicious for Pregnancy Failure**

- Gestational sac without YS
- 7-13 days
- No embryo

Time-Based Criteria
**Suspicious for Pregnancy Failure**

- Gestational sac with YS
- 7-10 days
- No embryo

Time-Based Criteria
**Suspicious for Pregnancy Failure**

- LMP
- 6.4 weeks
- No embryo

Other Criteria Suspicious for Pregnancy Failure

- “Empty amnion”
  - Amnion adjacent to yolk sac, no embryo
- Large yolk sac (>6-7 mm)

“Empty Amnion” Suspicious for Pregnancy Failure

- Embryo normally appears earlier than amnion
  - Embryo at 6 weeks, amnion at 7 weeks
- Identification of the amnion with no visible embryo is abnormal
**Failed Intrauterine Pregnancy (Miscarriage) Diagnostic Criteria**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definite Pregnancy Failure</th>
<th>Suspicious for Failure (F/U in 7-10 Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRL</td>
<td>≥7 mm and no heartbeat</td>
<td>&lt;7 mm and no heartbeat</td>
</tr>
<tr>
<td>MSD</td>
<td>≥25 mm and no embryo</td>
<td>16-24 mm and no embryo</td>
</tr>
<tr>
<td>Time</td>
<td>Absence of embryo ≥22 weeks after a scan that showed a gestational sac without yolk sac</td>
<td>Absence of embryo 7-13 days after a scan that showed a gestational sac without yolk sac</td>
</tr>
<tr>
<td>Other</td>
<td>Empty amnion</td>
<td>Enlarged yolk sac (&gt;6-7 mm)</td>
</tr>
</tbody>
</table>

**U/S of Early Pregnancy Loss Three Scenarios**

1. **No IUP seen**
   - Can a single hCG value ("discriminatory level") exclude viable IUP?

2. **IUP, no heartbeat (± embryo)**
   - What findings indicate definite pregnancy failure?
   - What findings are suspicious for pregnancy failure?

3. **IUP with heartbeat**
   - What findings suggest impending pregnancy failure?

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*all with @hCG and normal adnexa*
### Embryonic Heart Rate (6-7 Weeks) Relationship to 1st Δ Survival Rate

<table>
<thead>
<tr>
<th>Heart Rate (bpm)</th>
<th>GA ≤ 6.2 Weeks (CRL ≤ 4 mm)</th>
<th>GA 6.3-7 Weeks (CRL 5-9 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;80 0%</td>
<td>36%</td>
<td>0%</td>
</tr>
<tr>
<td>80-89 68%</td>
<td>89%</td>
<td>57%</td>
</tr>
<tr>
<td>90-99</td>
<td></td>
<td>82%</td>
</tr>
<tr>
<td>≥ 100</td>
<td></td>
<td>93%</td>
</tr>
</tbody>
</table>

$1^{st} \Delta$ Survival Rate (%)

### Early Heart Rate Classification

<table>
<thead>
<tr>
<th>Classification</th>
<th>≤6.2 Wks CRL ≤ 4 mm</th>
<th>6.3-7.0 Wks CRL 5-9 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow</td>
<td>&lt;90 bpm</td>
<td>&lt;110 bpm</td>
</tr>
<tr>
<td>Borderline</td>
<td>90-99 bpm</td>
<td>110-119 bpm</td>
</tr>
<tr>
<td>Normal</td>
<td>≥100 bpm</td>
<td>≥120 bpm</td>
</tr>
</tbody>
</table>

### Slow Embryonic Heart Rate Suspicious for Impending Pregnancy Failure

Demise 5 days later

Demise 1 week later

### Irregular Embryonic Heart Rate Suspicious for Impending Pregnancy Failure

demise on follow-up scan 3 weeks later

### Subchorionic Hematoma in Conjunction with Heartbeat Clinical Significance

- Subchorionic hematomas have been classified as small, medium, large based on:
  - Subjective assessment
  - Fraction of gestational sac surrounded by hematoma
  - Estimated volume of hematoma
Most studies of subchorionic hematoma in the presence of an embryonic heartbeat find that:

- Large SCH carries an elevated risk of subsequent pregnancy failure
  - likelihood of failure is ~20-40%
- Small-moderate SCH carries little-no added risk of subsequent pregnancy failure

**Clinical Significance**

- Large Subchorionic Hematoma in Conjunction with Heartbeat
  - Suspicious for Impending Pregnancy Failure

- Small Subchorionic Hematoma in Conjunction with Heartbeat
  - Little-No Risk

- Small Gestational Sac Size in Conjunction with Heartbeat
  - Suspicious for Impending Pregnancy Failure

- Small sac size in relation to the embryo can be diagnosed by:
  - Quantitative criterion: MSD-CRL < 5 mm*
  - Subjective assessment

- 16 early 1st Δ pregnancies with normal embryonic heart rates and small sac size →15 (94%) ended in pregnancy loss*

* Bromley 1991
Small Gestional Sac Size in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

“Expanded Amnion” in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

- Amnion normally appears at 6.5-7 weeks (CRL 6-10 mm)
- Identification of the amnion with CRL ≤ 5 mm carries an elevated risk of subsequent pregnancy failure

“Expanded Amnion” in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

1 week later

Enlarged Yolk Sac in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

- “Enlarged Yolk Sac in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

7 weeks

Demise 1 month later (9.5 week size)

Sliding Sac in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

- Sliding Sac in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

6 weeks

No gestational sac 6 days later
Conclusions

- Criteria for definite pregnancy failure include:
  - Crown rump length ≥7 mm and no heartbeat
  - Mean sac diameter ≥25 mm and no embryo
  - Absence of embryo ≥2 weeks after a scan that showed a gestational sac without yolk sac
  - Absence of embryo ≥11 days after a scan that showed a gestational sac with yolk sac

- When U/S demonstrates an embryo with heartbeat, signs of impending pregnancy failure include:
  - Slow or irregular embryonic heartbeat
  - Large subchorionic hematoma
  - Small gestational sac size in relation to embryo
  - Expanded amnion
  - Large yolk sac (> 6-7 mm)
  - Sliding gestational sac

Key References

Doubilet PM, Benson CB. Further evidence against the reliability of the hCG discriminatory level. J Ultrasound Med 2011; 30: 1637-1642


Doubilet