## Major Radiodiagnostic Imaging in Pregnancy and the Risk of Childhood Malignancy: A Population-Based Cohort Study in Ontario

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### Editors' Summary - Background

- **childhood cancer**
  - ≤ 14 years old
  - a major cause of death
  - genetic predisposition: 10%
  - most childhood cancer remains unknown
  - exposure to ionizing radiation in pregnancy?

### Why Was This Study Done?

- CT and radionuclide imaging expose the fetus to considerably higher doses of radiation than plain radiographs.
- Many pregnant women could be exposed to major radiodiagnostic tests in emergency situations.
- 50% of pregnancies are unplanned and unaware.
  - determine the risk of cancer to those exposed

### What Did the Researchers Do and Find?

- Retrospective population-based cohort study
- 1,835,517 maternal-child pairs in April 1, 1992 to March 31, 2008 in Ontario, Canada
- major radiodiagnostic test performed on the mother up to one day before her delivery date
- weighed ≥ 2,500 g, ≥ 37 wk gestation, survived for at least 30 days
  - The findings would remain applicable to most pregnancies

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### Alvarado Score

<table>
<thead>
<tr>
<th>Adult</th>
<th>Child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migratory RLQ pain</td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Nausea with vomiting</td>
<td></td>
</tr>
<tr>
<td>RLQ Tenderness</td>
<td></td>
</tr>
<tr>
<td>Rebound Tenderness</td>
<td></td>
</tr>
<tr>
<td>BT ≥ 38°C</td>
<td></td>
</tr>
<tr>
<td>WBC &gt; 10,000</td>
<td>2</td>
</tr>
<tr>
<td>Left shift of Neutrophil &gt; 75%</td>
<td>1</td>
</tr>
<tr>
<td>Total Points</td>
<td>10</td>
</tr>
</tbody>
</table>

### Left Shift of WBC

- ≤ 2: rule out appendicitis
- ≥ 7: rule in appendicitis

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Risk of childhood malignancy in the offspring of women exposed to major radiodiagnostic testing in pregnancy compared to unexposed women.

<table>
<thead>
<tr>
<th>Major Radiodiagnostic Test Exposure In Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed (n=3,350)(3760)</td>
</tr>
<tr>
<td>n events (%)</td>
</tr>
<tr>
<td>4 (0.12)</td>
</tr>
</tbody>
</table>

- Prevalence: 4/3350 = 0.07%
- Hazard ratio

What Do These Findings Mean?
- The absolute risk appears to be low, while the relative risk is not materially higher than that of unexposed controls.
- The possibility that fetal exposure to CT or radionuclide imaging is carcinogenic cannot be excluded. (95%CI 0.25-1.8)
- Suggestion:
  - beta hCG testing
  - lead apron shielding
  - non-radiation-emitting imaging should be considered first (MRI and ultrasonography)
  - brief counseling

Take home messages
- The anatomic and physiologic alterations associated with pregnancy.
- The differential diagnosis of right-sided pain in pregnancy is broad
  - ligamentous laxity
  - hemorrhagic corpus luteum cyst
  - renal colic
  - ovarian torsion
  - degenerating fibroid
- Difficulty in diagnosis of appendicitis may result in delayed treatment and complications from delayed diagnosis of appendicitis.

Background
- Limitations of Ultrasonography:
  - Graded compression US may not be feasible owing to the size of the enlarged gravid uterus, particularly in the 3rd trimester
  - normal appendix is visualized in 13%--50% of patients who are not pregnant
  - Negative predictive value of a nonvisualized appendix is, at best, 90%
- Computed tomography (CT) has high radiation dose.
Purpose

To retrospectively assess the diagnostic performance of magnetic resonance (MR) imaging in pregnant patients suspected of having acute appendicitis.

Materials and Methods

Retrospective

Patients

- March 1999 and April 2004
- 51 pregnant patients in Beth Israel Deaconess Medical Center
- Mean patient age was 28.3 years (age range, 15–37 years)
- Mean gestational age was 19.8 weeks (range, 4–38 weeks)

Imaging Protocol

- Patients received an oral contrast material
- Half-Fourier single-shot fast spin-echo
- T1-weighted, T2-weighted images
- Time-of-flight T2*-weighted gradient-echo images
- Transverse/coronal/sagittal planes

Initial interpretations

- Negative: < 6 mm in diameter and/or it was filled with oral contrast material, air, or both.
- Positive: > 7 mm in diameter
- Inconclusive: 6–7 mm in diameter (periappendiceal fat stranding, abscess were used to make the diagnosis)

Retrospective Review:

- Three radiologists reviewed MRI after 3 months.

5-point scale: (by Time-of-flight images)

- 1 not identified
- 2 less than half identified
- 3 approximately half identified
- 4 more than half identified
- 5 well visualized in its entirety.

Periappendiceal fat stranding, phlegmon, abscess, oral contrast material in the cecum

Additional findings

T2WI (Time-of-flight gradient-echo Image)

Blooming effect
Materials and Methods

- Statistical analysis:
  - Initial interpretations for accuracy
  - median and Fisher exact tests
  - Spearman correlation coefficient

Results

~Under MRI~

- Negative: 44
- Positive: 4 (under US: 2)
- Inconclusive: 3 (considered false-positive)
- Sensitivity: 100%  
  Prevalence: 22/23290
- Specificity: 93.6%

prevalence-adjusted
- positive predictive values: 1.4%
- negative predictive values: 100%
- Accuracy: 94% (48/51)

Inconclusive (7 mm)

T2WI

Coronal single-shot fast SE image (fat-saturated)

Sagittal single-shot fast SE image

Periappendical inflammation

Edematous, thickened wall
Retrospective Review

- Visualization of the appendix was achieved more often in patients with contrast material in the cecum than in those without. ($P=0.67$)
- There was a trend toward better visualization of the appendix with an earlier gestational age. ($P=0.1$)
- Of the 47 patients without acute appendicitis, MR imaging showed a normal appendix in 39 (83%).
- Appendix was well visualized in its entirety (spot) in 29 patients.

**Table 2**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients</th>
<th>Gestational Age (wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated right gonadal vein</td>
<td>11</td>
<td>20.3 ± 7.07</td>
</tr>
<tr>
<td>Right hydrosalpinx</td>
<td>6</td>
<td>24.4 ± 5.67</td>
</tr>
<tr>
<td>Mild</td>
<td>12</td>
<td>21.6 ± 6.37</td>
</tr>
<tr>
<td>Moderate</td>
<td>10</td>
<td>30.6 ± 5.87</td>
</tr>
<tr>
<td>Serous</td>
<td>3</td>
<td>15.3 ± 4.67</td>
</tr>
<tr>
<td>Degenerated fibroids</td>
<td>6</td>
<td>15.3 ± 4.67</td>
</tr>
<tr>
<td>Diverticulitis diverticulitis</td>
<td>5</td>
<td>27</td>
</tr>
<tr>
<td>Ileal intussusception</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Uterine fundus relaxation with vs in the urinary bladder</td>
<td>1</td>
<td>31</td>
</tr>
<tr>
<td>Sonographic liver fat</td>
<td>11</td>
<td>17.2 ± 6.7</td>
</tr>
<tr>
<td>Rightmost corpus luteus cyst</td>
<td>2</td>
<td>14 ± 5.4</td>
</tr>
</tbody>
</table>

* Four patients had no hydrosalpinx. Hydrosalpinx was not in four patients, neither in two, and unsure in one.
* Data are means ± standard deviations.
* A reported corpus luteus cyst was diagnosed on the basis of findings of a hemorrhagic cyst, fluid in the pelvis, and clinical presentation.

Discussion

- Negative predictive value of 100% → exclude appendicitis in pregnant patients
- Safety (no known deleterious effects)
- High rate of visualization
  - blooming effect caused by air and/or oral contrast
  - T2*-weighted time-of-flight images can help identify small blood vessels
  - T2-weighted images shows obstructed fluid-filled appendix

Limitation

- Not all pregnant patients with abdominopelvic pain underwent imaging
- Radiologist who covered the service attending the initial interpretations.
- The number of patients with acute appendicitis in our series is small.
- There was no pathologic confirmation in one of the cases.
- The change in interpretation of inconclusive studies made a false-positive result.
Conclusion

- MR imaging is an excellent modality for excluding acute appendicitis in pregnant women.
- MR imaging eliminates unnecessary radiation from CT.
- MR imaging offer an alternative diagnosis in pregnant women with right-sided abdominal pain.
- More studies with larger series of patients are needed to establish.

Take home messages

- MRI 提供了準確、非侵入性且無放射劑量問題的檢查。
- 對於懷疑有急性膿瘍的懷孕婦女，使其接受 MRI 檢查，來排除其罹病可能性，可減少沒必要的手術。
- 知道如何利用 blooming effect、periappendiceal fat stranding、phlegmon 來判讀 acute appendicitis 在 MRI 上的表現。