Appendicitis: Risk Stratification and Making Sense of Scoring Systems

Appendicitis remains the most common unscheduled abdominal surgery in pediatric patients and a high source of emergency practitioner malpractice cases. This course will review best practices in identifying appendicitis, and compare clinical decision rules including risk stratification schemes, and scoring systems used in emergency care of children.

OBJECTIVES

- Describe the commonly used clinical scores used for pediatric appendicitis and discuss their advantages and limitations
- Outline how the use of evidence-based strategies reduce radiation exposure, improve accuracy, and reduces cost

3/24/2015
2:45 PM-3:30 PM
Grand Ballroom
TU-7

DISCLOSURES:
(+ No significant financial relationships to disclose
Disclosures

★ The speaker has no financial interests in any product or device discussed.

★ The speaker has no conflict of interests to disclose.

★ This presentation will not involve discussion of unapproved or off-label medications or experimental or investigational use devices.
Objectives

- At the end of this session, participants will be able to:
  - Review an approach to the child with suspected appendicitis
  - Discuss the different scoring systems used to risk stratify patients presenting with acute abdominal pain for appendicitis
  - Evaluate the utility of scoring systems as a part of a pathway to manage patients presenting with acute abdominal pain

Validation of A Prediction Rule To Identify Children at Low Risk for Appendicitis

Anupam Kharbanda, Nanette Dudley, Lalit Bajaj, Michelle Stevenson, Manoj Mittal, Richard Bachur, Jonathan Bennett, Kelly Sinclair, Craig Huang, Charles Macias and Peter Dayan
Abdominal Pain in Children

* Common complaint
  * 3.5-5% of all visits to the ED
* Causes vary depending on the patient’s age
* “Extra-abdominal” causes
* Establishing diagnosis
  * Location of pain
  * Accompanying signs and symptoms

Acute Abdominal Pain in Children
Common Causes by Age - Medical

* Infants
  * Colic
  * Gastroesophageal reflux
  * Gastroenteritis
  * Milk protein allergy
  * Trauma
* Toddlers and Preschool Children
  * Gastroenteritis
  * Urinary tract infection
  * Constipation
  * Henoch – Schönlein purpura
  * Trauma
* School – aged Children
  * Gastroenteritis
  * Urinary tract infection
  * Constipation
  * Asthma
  * Group A streptococcal pharyngitis
  * Functional abdominal pain
  * Trauma
* Adolescents
  * Gastritis
  * Gastroenteritis
  * Gastroesophageal reflux disease
  * Constipation
  * Trauma
  * GU and Gyn disorders
Acute Abdominal Pain in Children
Surgical/Critical Causes by Age

* Infants
  * Malrotation, volvulus*
  * Intussusception
  * Enterocolitis (Hirschsprung)
  * Incarcerated/strangulated hernia (56% of cases in 1st year of life)
  * Trauma – non-accidental
  * ALCAPA

* Toddlers/Preschool Children
  * Intussusception
  * Appendicitis
  * Incarcerated/strangulated hernia
  * Intest. Obstruction
  * Peritonitis
  * Trauma
  * DKA
  * Myocarditis
  * Meningitis

* School – aged Children
  * Appendicitis
  * Megacolon (IBD)
  * Peritonitis
  * Hepatitis
  * Ingestion
  * Trauma
  * DKA

* Adolescents
  * Appendicitis
  * Ectopic pregnancy
  * PID
  * Biliary disease
  * Pancreatitis
  * IBD
  * Trauma
  * Diabetic ketoacidosis
  * Myocarditis
  * Ingestion

Case

* 10 year old boy with peri-umbilical abd. pain & anorexia for 4 hours

* T 36° CHR 77    RR 22    BP 114-70

* Uncomfortable

* Abdomen: soft; diffuse tenderness, mainly peri-umbilical; not tender in RLQ

* X-ray abd. c/w constipation ➔ fleet enema/miralax/home

* (RN note: Tender RLQ, guarding, pain on walking)
Case-cont.

- Next day: patient recalled because of radiology read of appendicolith
- Headache, Vomiting; lethargic
- T 39° C HR 110 RR23 BP102/47
- Sick looking; abdomen diffusely tender - max. RLQ, guarding
- WBC: 3.1; ANC 2,542; CRP 2.9; lactate: 7.1
- **Diagnosis:** Perforated appendicitis with septic shock

Appendicitis Epidemiology

- Commonest surgical emergency in children
- Increases with age till adolescence
- Missed appy 2nd commonest diagnosis in PEM malpractice claims

O’Shea JS. PEC 1988
Selbst SM. PEC 2005
Locations of Appendix

- Right Lower Quadrant (85%)
- Pelvic/Retrocecal
- Retroileal
- Left Lower Quadrant

Can we improve our diagnostic accuracy for appendicitis?
Zero Sum Myth

Missed appy (1-10%)
Perforation 18-35%
Negative Appendectomy 1-20%
Current State Of Outcome Matrices For Appendicitis

- Prospective multi-center study
- Time period: 2009-2010
- N = 2,625
- Missed appendicitis: <1%
- Perforation: 27%
- Negative appendectomy rate: 8.5%

Kharbanda A. Arch Pediatr 2012

Perforation

- Higher morbidity & mortality than non-ruptured appendicitis
- Associated with tubal infertility in girls
  - Case Control Study
  - 279 with tubal infertility & 957 controls
  - Unruptured AP - no increased risk
  - Ruptured AP - relative risk 4.8

Mueller BA. NEJM 1986
Perforation

* Associated with:
  * Low socioeconomic status, medicaid
  * African-American, Hispanic
  * Limited English proficiency
  * Centers with fewer number of cases
  * Younger children
  * Obesity
  * Longer duration of abdominal pain
  * Retro-cecal appendix

Smink DS. Pediatrics 2005
Levas MN. Jped 2014

Perforation Sub-sample

Test for trend: OR=1.65, 95% CI (1.50, 1.82)

Should we scan them all?

Bayes’ theorem

<table>
<thead>
<tr>
<th>Pre-test probability (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Post-test probability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>94</td>
<td>95</td>
<td>93</td>
</tr>
<tr>
<td>5</td>
<td>94</td>
<td>95</td>
<td>50</td>
</tr>
<tr>
<td>80</td>
<td>94</td>
<td>95</td>
<td>98.7</td>
</tr>
</tbody>
</table>

Diagnosis

☆ Concordance / preponderance of evidence
☆ History ➔ Examination ➔ Labs ➔ Imaging
### Pertinent symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>3.4 (2.4-4.8)</td>
</tr>
<tr>
<td>RLQ pain</td>
<td>1.2 (1-1.5)</td>
</tr>
<tr>
<td>Mid-abd. Pain migrating to RLQ</td>
<td>2.5 (1.9-3-1)</td>
</tr>
<tr>
<td>Nausea, vomiting</td>
<td>1.19 (1.05–1.35)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>1.42 (1.25–1.61)</td>
</tr>
</tbody>
</table>

Bundy DG. JAMA 2007  
Santillanes G. Acad Emerg Med 2012

### Pertinent exam findings

<table>
<thead>
<tr>
<th>Sign</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>RLQ tenderness</td>
<td>1.3 (1.1-1.4)</td>
</tr>
<tr>
<td>Rebound tenderness</td>
<td>3.0 (2.3-3.9)</td>
</tr>
<tr>
<td>Guarding</td>
<td>2.0 (1.4-3.9)</td>
</tr>
<tr>
<td>Diffuse peritonitis</td>
<td>25 (1.4-414)</td>
</tr>
<tr>
<td>Pain with jumping</td>
<td>2.0 (1.7-2.4)</td>
</tr>
<tr>
<td>Rectal tenderness</td>
<td>2.3 (1.3-3.1)</td>
</tr>
<tr>
<td>Psoas sign</td>
<td>2.3</td>
</tr>
<tr>
<td>Obturator sign</td>
<td>2.2 (1.4-3.4)</td>
</tr>
<tr>
<td>Rovsing sign</td>
<td>1.9 (1.3-2.8)</td>
</tr>
</tbody>
</table>

Bundy DG. JAMA 2007
Duration of Abdominal Pain

<table>
<thead>
<tr>
<th>Duration of Symptoms (Hrs)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 hours</td>
<td>29</td>
</tr>
<tr>
<td>12-23 hours</td>
<td>33</td>
</tr>
<tr>
<td>24-35 hours</td>
<td>18</td>
</tr>
<tr>
<td>36-47 hours</td>
<td>9</td>
</tr>
<tr>
<td>48-71 hours</td>
<td>10</td>
</tr>
</tbody>
</table>

CHOP QI data

ANC and CRP in Appendicitis-
Duration of Symptoms

<table>
<thead>
<tr>
<th>Duration of Symptoms (Hrs)</th>
<th>ANC</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 hrs</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>13-24 hrs</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>25-48 hrs</td>
<td>13.5</td>
<td>5.3</td>
</tr>
<tr>
<td>&gt; 48 hrs</td>
<td>17.3</td>
<td>9</td>
</tr>
</tbody>
</table>

CHOP QI data
ANC Scatter Plot

ANC result for patients with positive appendicitis
(n = 80)

CRP Scatter Plot

CRP result for patients with positive appendicitis
(n = 78)
## Useful CDR

<table>
<thead>
<tr>
<th>Groupings</th>
<th>Zones</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk</td>
<td>Below test threshold</td>
<td>Discharge home</td>
</tr>
<tr>
<td>Moderate-risk</td>
<td>Between test and treatment thresholds</td>
<td>Imaging</td>
</tr>
<tr>
<td>High-risk</td>
<td>Above treatment threshold</td>
<td>Appendectomy</td>
</tr>
</tbody>
</table>

Pauker SG & Kassirer JP. NEJM 1980

## The Alvarado (MANTRELS) Score & The Pediatric Appendicitis Score (PAS)

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>Alvarado Score</th>
<th>PAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migration of Pain</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anorexia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tender RLQ</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Rebound pain</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Elevated temp &gt; 37.3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Leucocytosis (&gt; 10,000)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Shift to left (Neut. &gt; 75%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cough/percussion/hopping cause pain in RLQ</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

Alavarado A. Ann Emerg Med 1986
Samuel M. J Pediatr Surg 2002
Systematic Review

* Inclusion criteria: Prospective cohort studies to determine accuracy of Alvarado score and PAS in children
  * 11 studies
* Calculated summary likelihood ratios for low-, moderate-, and high-risk groups, using all possible cutoffs
* Pre-test probability of appendicitis in pediatric studies: 33%


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Clinical Application Of Optimum Test & Treatment Thresholds

<table>
<thead>
<tr>
<th>Score</th>
<th>Points</th>
<th>LR</th>
<th>Pretest Probability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Alvarado</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>&lt; 4</td>
<td>0.02 (0-0.4)</td>
<td>0.2</td>
</tr>
<tr>
<td>Low risk</td>
<td>&lt; 5</td>
<td>0.04 (0-0.4)</td>
<td>0.4</td>
</tr>
<tr>
<td>High risk</td>
<td>≥ 7</td>
<td>4.2 (3.3-5.3)</td>
<td>32</td>
</tr>
<tr>
<td>High risk</td>
<td>≥ 9</td>
<td>8.5 (5.6-12.8)</td>
<td>48</td>
</tr>
<tr>
<td><strong>PAS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>&lt; 4</td>
<td>0.13 (0.04-0.4)</td>
<td>1.4</td>
</tr>
<tr>
<td>High risk</td>
<td>≥ 8</td>
<td>8.1 (4.1-15.9)</td>
<td>47.3</td>
</tr>
</tbody>
</table>

Limitations

- Clinical judgement may provide similar performance
- Diverse group of studies from various geographic areas
- Wide CI around LR
- History and exam features have variable reproducibility
- Duration of abd. Pain before presentation not presented
- 8 elements in the score-burdensome
- Consider the “risk” that the physician and family are willing to accept

Physician Gestalt

- Considering that the prevalence of appendicitis in our cohort selected for labs/imaging was 39%:
  - Pre-test probability = 10%
  - Test: Physician gestalt
  - Post-test probability: 39%
  - LR⁺ of physician gestalt: 5.8
- Experienced clinicians more often rely on clinical gestalt rather than formal scoring systems

Bundy DG. JAMA 2007
Automation of scoring

- To evaluate a natural language processing and machine-learning based automated method
  - By analyzing the content of the electronic health record
  - To risk stratify 2,100 children presenting with abdominal pain using PAS
- The automated appendicitis risk categorization showed comparable performance to physician chart reviewers as measured by their inter-annotator agreement

Deleger L. J Am Med Inform Assoc. 2013

CDR To Identify Patients At Low Risk For Appendicitis

- ANC < 6750
- No nausea and
- No max tenderness in RLQ

- NPV 98%; LR⁻ 0.06 (Derivation sample)
- NPV 92%; LR⁻ 0.13; Post-test prob. 7.6% (Validation study)*

Kharbanda AB. Pediatrics 2005
*Kharbanda A. Arch Ped Adol Med 2012
So, what else can we do?

Biomarkers

- Procalcitonin\(^1\)
- Urine leucine-rich α-2 glycoprotein (LRG)
  - Enriched in diseased appendix\(^2\)
- Plasma S100A8/A9
  - A calcium binding protein secreted in inflammatory conditions\(^3\)
- Plasma cytokines and RNA gene expression\(^4\)

Gavela T. PEC 2012\(^1\)
Kentsis A. Annals Emerg Med 2010, 2012\(^2\)
Bealer JF. Acad Emerg Med 2010\(^3\)
Muenzer JT. PEC 2010\(^4\)
# Test Characteristics of US in the Diagnosis Of Appendicitis

<table>
<thead>
<tr>
<th>Test Characteristic</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>72 (67-77)</td>
</tr>
<tr>
<td>Specificity</td>
<td>97 (95-98)</td>
</tr>
<tr>
<td>PPV</td>
<td>92 (88-95)</td>
</tr>
<tr>
<td>NPV</td>
<td>88 (85-90)</td>
</tr>
<tr>
<td>LR⁺ (Weighted for prevalence)</td>
<td>12.4 (8-19.1)</td>
</tr>
<tr>
<td>LR⁻ (Weighted for prevalence)</td>
<td>0.14 (0.12-0.17)</td>
</tr>
</tbody>
</table>

Mittal MK et al. Acad Emerg Med July 2013

# Results

Restricting the analysis - appendix specifically classified as normal or abnormal (469 cases [49%]):

- NPV 98% (94-99)
- PPV 92% (88-95)

Mittal MK et al. Acad Emerg Med July 2013
Sensitivity and specificity of US to detect appendicitis

Sensitivity test for trend: OR=1.39, 95% CI (1.14, 1.71)

CT

- **CT with IV contrast** suitable for most cases
- **Sensitivity:** ≥ 93%; **specificity:** ≥ 92%
- Invasive, higher cost
- Ionizing radiation related cancer risk

Kharbanda A. *Radiology* 2007
Howell JM. *Ann Emerg Med* 2010

### Sensitivity and specificity of CT to detect appendicitis

![Sensitivity and specificity graph](image)

Low-dose CT

- **Setting:** Single-center
- **Subjects:** 891, age 15-44 yrs. with suspected appy
- **Study type:** Randomized, low-dose (effective radiation dose 2 mSv) or standard-dose (8mSv)
- **IV contrast in all**
- **Results:**
  - Sens: 94.5 vs. 95; Spec: 93.3 vs. 93.8
  - Similar neg. appy rate (3.5 vs. 3.2)
  - Similar perf. rate (27 vs. 23)

Kim K. NEJM 2012

Expedited MRI

- **Setting:** Single-center, 208 children, age 3-17 years, with suspected appendicitis
- **Methods:** Expedited 4-sequence protocol; no contrast; no sedation
- **Results:**
  - Sens: 98%; spec 97%; PPV 89%; NPV 99%
  - MRI time: median 12 min.
  - Time to report (after MRI done): median 46 min
- **Recent study:** Equally good for those with < 24 hrs vs. > 24 hrs of abdominal pain

Moore MM. Pediatr Radiol 2012
Koning JL. Abdom Imaging. 2014
Evaluation of A Clinical Practice Guideline

★ Aims of guideline:
★ Risk stratification
★ Staged imaging: US followed by CT if needed
★ Early surgical involvement in high-risk cases

★ Setting: Prospective, single-center, 475 children

Santillanes G. Acad Emerg Med 2012
Evaluation of A Clinical Practice Guideline

Results:

- Appendicitis over-all in 41%
- 58% managed without CT scan
- 37% of those with appendectomy had no imaging
- Patient-related outcomes:
  - Negative appendectomy rate: 1%
  - Missed appendicitis: 2%
  - Perforation rate: 18%

Santillanes G. Acad Emerg Med 2012
Take-home Points

* Develop a Clinical pathway
* Use clinical evaluation, intuition, gestalt (± WBC, ANC, CRP) to risk-stratify patients
* Imaging for equivocal patients
* US as 1st line imaging modality if available
* If US does not identify appendix, and clinical concern persists, consider continued observation, surgical consult &/or CT with IV contrast
* Emerging modalities: Other biomarkers, low-dose CT, expedited MRI

Thanks
References


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