52 Top Ten Advances in Gastrointestinal Pathology 2011

David Lewin MD

2011 Annual Meeting – Las Vegas, NV

AMERICAN SOCIETY FOR CLINICAL PATHOLOGY
33 W. Monroe, Ste. 1600
Chicago, IL 60603
This valuable summary session will review the top ten abstracts/articles from recent clinical meetings and journals. Many of the most important advances in gastrointestinal pathology are presented at clinical meetings and within clinically oriented journals and often missed by pathologists. Pathology related advances from Digestive Disease Week (DDW) and the American Society for Clinical Oncology (ASCO) meetings will be reviewed. The focus will be on practical pathology topics with specific emphasis on molecular pathology and endoscopic imaging techniques.

- New advances coming in gastrointestinal pathology.
- Gain an understanding of the importance of non-pathology venues for advances in GI pathology.

FACULTY:

David Lewin MD

Practicing Pathologists
Surgical Pathology
Surgical Pathology (GI, GU, Etc.)
1.0 CME/CMLE Credit

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Top 10 Advances in GI Pathology

David Lewin MD
Medical University of South Carolina

Overview

• Top Articles/presentations in the following areas
  – Imaging (3)
  – Molecular (2)
  – Therapeutics (3)
  – Surgical pathology (2)
Most Significant GI Advances are **not** Presented at Pathology Meetings or Journals

- **Digestive Disease Week**
  - Combined meeting of AGA, AASLD, ASGE, SIAT
  - 15,000+ attendees
  - 450 posters
  - 140 (searching for pathology)

- **ASCO**
  - 30,000+ attendees
  - 21,000 abstracts
  - 970 GI

- **USCAP**
  - 1960 posters
  - 137 GI posters
  - 94 Liver and Pancreas posters

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**Impact Factor**
- NEJM: 53.48
- Gastroenterology: 12.03
- Hepatology: 10.885
- Gut: 10.61
- J. Hepatology: 7.4
- Am J. Hepatology: 6.882
- Am J Pathology: 5.224
- AJSP: 4.106

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**#10 to #8**

- Imaging abstracts
- Toward a “Optical Biopsy”
- Threats to pathology
Narrow Band Imaging

- Short wavelength, narrow-bandwidth “blue light”
  - Provided at a push of the button on scope
- Enhances mucosal detail and vascular structures
  - Allows assessment of microvascular density
    - Increased angiogenesis appears darker

Barrett Esophagus
Results

| Table A: Performance characteristics of the NSW classifier for rectal polyps and colorectal adenomas detected during colonoscopy. |  
|---|---|---|---|---|
| Feature | Accuracy | Sensitivity | Specificity | PPV | NPV |
| Color | 68% | 84% | 51% | 51% |
| Size | 65% | 80% | 38% | 38% |
| Surface | 61% | 86% | 31% | 31% |
| Table B: Performance characteristics of the NSW classifier with pathological information. |  
|---|---|---|---|---|
| Feature | Accuracy | Sensitivity | Specificity | PPV | NPV |
| Color | 68% | 84% | 51% | 51% |
| Size | 65% | 80% | 38% | 38% |
| Surface | 61% | 86% | 31% | 31% |

Optical diagnosis of small colorectal polyps at routine colonoscopy (Detect InSpect Characterise Resect and Discard; DISCARD trial): a prospective cohort study

MUSC Health
Results

<table>
<thead>
<tr>
<th>Polyps ≤ 3 mm (N) (%)</th>
<th>Polyps &gt; 3 mm (N) (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>386</td>
<td>67</td>
</tr>
<tr>
<td>Optical diagnosis</td>
<td>271 (70%)</td>
<td>62 (94%)</td>
</tr>
<tr>
<td>Polyp size</td>
<td>37 (95%)</td>
<td>6 (90%)</td>
</tr>
<tr>
<td>Ulcers</td>
<td>14 (41%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Correct optical diagnosis</td>
<td>244 (75%)</td>
<td>41 (68%)</td>
</tr>
<tr>
<td>Biopsyopsy</td>
<td>89 (25%)</td>
<td>22 (32%)</td>
</tr>
<tr>
<td>Accuracy of length</td>
<td>90%</td>
<td>90%</td>
</tr>
</tbody>
</table>

*Yates’ exact test

Table 3: Differences in diagnosis according to polypt size only (p-value with optical and histological diagnosis)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, diagnosis</td>
<td></td>
</tr>
<tr>
<td>No, diagnosis</td>
<td></td>
</tr>
</tbody>
</table>

Comparison of Probe-Based Confocal Laser Endomicroscopy With Virtual Chromendoscopy for Classification of Colon Polyps

10/10/2011
Hyperplastic Polyp

Adenoma

Results

| Table 1: Comparison of histological and histopathological features of hyperplastic polyps and adenomas

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hyperplastic Polyp</th>
<th>Adenoma</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Intra-luminal</td>
<td>Intra-luminal</td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>Consistency</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>Surface Elevation</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>Gross Appearance</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
</tr>
</tbody>
</table>

GS = Gold standard
Simplified = compared to histology
Modified = Neoplastic = adenoma + all polyps greater than 1 cm
# 7 and 6

- Molecular
  - KRAS and HER2/neu
- Opportunities for pathology

**Phase 3 trial: Cetuximab combined with Irinotecan in first-line therapy for metastatic colorectal cancer (CRYSAL)**
- FOLFIRI (Irinotecan, fluorouracil, leucovorin)
- Cetuximab (Erbitux): Immunoglobulin G1 monoclonal antibody against epidermal growth factor receptor (EGFR)
- Subgroup analysis for KRAS mutational status
  - 540 patients (of 1200 from initial study)
    - 64% wild-type KRAS
    - KRAS mutations in codons 12 and 13 via PCR
Bottom Line

- For tumor response: Significant benefit in KRAS wild type tumors (p=0.3)
- No significant benefit for progression free survival (p=0.7) or overall survival (p=0.44)
• Trastuzumab: monoclonal antibody against human epidermal growth factor receptor 2 (HER2 or ERBB2)
• 594 pts randomized to standard chemo (capecitabine or fluorouracil + cisplatin) vs standard chemo + iv trastuzumab
• HER2 + by 3+ immunohistochemistry or FISH + – 22% (810 of 3665 cancers)
# 5 to 3

- Endoscopic Therapy
  - Endoscopic resections
    - Specimens we will receive
  - Radiofrequency Ablation
    - Treatment and alteration of specimens may receive
  - NOTES (natural orifice translumenal endoscopic surgery)
    - Future?

## ESMD V EMR

Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection

Arakaki Sato, Masatoshi Hidano, Takeshi Masuda, Shiono Takahara, Horiuchi Tomonori, Sato Yosuke, M wanting, Y. Yano, Hozumi Shoichi, Takahiro Fujii

## Methods/ Results

- 145 colorectal tumors treated by ESMD
- 228 treated by EMR
- ESMD
  - Longer procedure time (108 vs 29 min)
  - Higher en bloc resection rate (84% v 33%)
  - Larger resection specimens (37 vs 28 mm)
  - 2 recurrences (2%) vs 33 (14%) with EMR
  - Perforation rate (6%) vs 1.3% with EMR
- 31-34% Adenomas, 66-69% Carcinomas (sm1)
  - sm1 = no invasion deeper than 1,000 um from muscularis mucosa
Methods

- Use of HALO (BARRX Medical)
- 191 eligible for review by central pathology
  - 22 did not meet entry criteria
    - 6 upgraded to cancer, 14 downgraded (indef or no dys), 2 neg for IM
- 169 met pathology criteria (LGD or HGD)
- 127 randomized (64 LGD, 63 HGD)
  - 2:1 RF vs sham
Implications

• A treatment modality for low grade and high grade dysplasia in BE
• Subsquamous intestinal metaplasia
  – 5.1% after RF
    • Still need screening endoscopy post RF with biopsy of the previous BE segment

NOTES (Natural Orifice Translumenal Endoscopic Surgery)

• First described in a survival porcine model in 2000 at DDW.
• 429 human NOTES case have been published to date
  – 316 transvaginal, 113 transgastric
    • Most with laparoscopic assistance
• DDW 2011
  – 26 abstracts presented

Abstract Topics DDW 2011

• Navigation (9 studies)
  – Visualization of peritoneal cavity and mediastinum
• Closure (5 studies)
  – Endoscopic closure of access to the peritoneal cavity
• Complications (2 studies)
• Tolerance (2 studies)
• Development of therapeutic interventions
  – Cholecystectomy, appendectomy, adhesiolysis, tubal ligation, oophorectomy, gastroenterostomy
    • Ultimate indication has not been found
Top 2

• Changes in pathology nomenclature and grading
• Neuroendocrine tumors of the gastrointestinal tract
Neuroendocrine Tumors

- Histology:
  - Well or Poorly Differentiated
  - Mitotic Count (per 10 HPF)
    - G1 = 2
    - G2 = 2-20
    - G3 = >20
- Immunohistochemistry:
  - Expression of neuroendocrine markers (chromogranin or synaptophysin)
  - Proliferative activity via Ki-67
    - G1 = <2%
    - G2 = 2-20%
    - G3 = >20%
- Stage

Pancreatic endocrine tumors: improved TNM staging and histopathological grading permit a clinically efficient prognostic stratification of patients

Aldo Stanga1,2, William Merluzzi5, Paolo Gaggiolo3, Stefano Biglioli6, Letizia Veronesi3, Fabio Gervasio2, Fabio Pichini2, Paolo Pietranda1, Gianluca del Fante3 and Massimo Falcone4
1Department of Oncology, University of Verona, Italy; 2ARCNET Center for Applied Research on Cancers, Verona, Italy; 3Department of Medicine and Public Health, University of Verona, Verona, Italy; 4Department of Surgery and Gastroenterological Sciences, University of Verona, Verona, Italy and 5Department of Digestive and Liver Diseases, A School of Medicine, University ‘La Sapienza’, Rome, Italy
Summary

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Top 10 advances in Gastrointestinal Pathology: References:


