Roundtable Discussion 8

The ABC's of CHC: What's the use of Gynecologic Cytologic-Histologic Correlation

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There are no disclosures necessary.
The ABC’s of CHC

What’s the use of gynecologic cytologic-histologic correlation?

History

- Web site with comments
- CDC-CAP Gynecologic Cytopathology Quality Consensus Conference (GCQC2) June 4, 2011
- Final recommendations after consensus

Why do we do CHC?

- CLIA
  - § 493.1274(c)(2): Laboratory comparison of clinical information, when available, with cytologic reports and comparison of all gynecologic reports with a diagnosis of HSIL+ with the histopathology report, if available in the laboratory, and determination of the causes of any discrepancies
- CAP LAP
  - CYP.01900 Resolve “significant” discrepancies in addendum or QA
  - CYP.07530 Issue corrected report if discrepancies affect current patient care
  - CYP.07543 Review histology of HSIL+ Pap tests
  - CYP.07556 Attempt to obtain follow up if unavailable
  - CYP.07568 Correlate with available clinical information
Cytologic-Histologic Correlation

“This monitor should not be viewed as just an evaluation of the performance of the cytopathology laboratory. This is a true ‘system’ monitor. The statistics represent the performance of all personnel and processes in the system of obtaining, processing, and evaluating both cytology and biopsy specimens. Performance must be evaluated at each step of the process to identify improvement opportunities.”

Jones BA, Davey DD. Quality Management in Gynecologic Cytology Using Interlaboratory Comparison Arch Pathol Lab Med. 2000;124:672–681

What do we do?

• CHC ranked first in QA importance
  – 4.2 on a scale of 5
  – Multiheaded review
  – Retrospective review in current HSIL
• 94% actively monitor CHC
• 63.7% report CHC in QA reports
• 15% report corrective action

What Don’t We Do?

• No standard method of collecting data
• No uniform definition of “correlation”
• Glass slide review is not always performed
• No metric for interlaboratory comparison
CHC Consensus Statement 1:
When do you perform CHC?

- CHC may be performed in “real time”
  - Review Pap slides at time of histology
  - Impacts current patient care
  - Preferred for HSIL+ Pap and negative biopsy
- CHC may be performed retrospectively
  - After both reports are finalized
  - Ease of data collection/statistical analysis
- Both

CHC Consensus Statement 2:
What cases/material are reviewed?

- Minimum
  - HSIL + Pap tests and negative biopsies
- Glass slides of both specimens (if available)
- At 3-4 month interval (no more than 6 months)
- Method of reporting discrepancy
  - Biopsy report
  - QA document
  - Does not require release of QA information (generic comment)
- Real time review assumes that efforts are made to optimize the histology

What specimens and time frame?

- HSIL+ Pap Tests
  - Cervical biopsy within the following 6 months
    - Exclude ECC unless it demonstrates abnormality
  - LEEP, Cone and Hysterectomy
- HSIL+ Biopsies
  - Most abnormal Pap test in preceding 6 months
  - Exclude Pap test taken at time of biopsy*

Survey:
Standards: What do users want?

- 47% desire correlation standardization
  - What statistics to maintain
  - What to do when a discordance is discovered
  - What to recommend in a comment
- 35% unsure

CHC Consensus Statement 3:
Standardization of metrics and CHC process is desirable

What metric?

<table>
<thead>
<tr>
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</tr>
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Positive predictive value |
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Negative predictive value |
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**No biopsies**

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**Over represented**

**No biopsies**
CHC Consensus Statement 4: What Metric?

- Positive Predictive Value of a Positive Pap Test
- PPV Median: 83-88% (range: 71-94%)*

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* CAP Q-Track data, 2005-2010

Positive Predictive Value

- Laboratory as a whole
- 20 events for statistical validity
- Assumes biopsy is gold standard
  - True positive:
    - Both Pap and biopsy are both “positive”
  - False positive
    - “Positive” Pap
    - “Negative” biopsy
- Independent of disease prevalence
  - Enhances interlaboratory comparison

True Positive

- Any biopsy and Pap, in any combination:
  - LSIL/ CIN1/ HPV changes
  - HSIL/ CIN 2, 3/ CIS
  - SIL, indeterminate
  - AIS
  - Carcinoma (squamous, adenocarcinoma, NOS)
  - Other malignant diagnosis
- ASCUS, ASC-H, AGC are excluded
False Positive

- Pap Test demonstrating an epithelial cell abnormality (excluding ASC-US/ASC-H/AGC)
  - Minimum is HSIL+
  - Laboratory can determine categories
- Biopsy not demonstrating
  - LSIL/ CIN1/ HPV changes
  - HSIL/ CIN 2, 3/ CIS
  - SIL, indeterminate
  - AIS
  - Carcinoma (squamous, adenocarcinoma, NOS )
  - Other malignant diagnosis

False Positive

- Review of the cytology and biopsy
  - Pap may be “correct” upon review
    - Remains a false “positive” for PPV
  - Pap may be “incorrect” upon review
    - Is false positive
  - Surgical biopsy may be “incorrect”
    - Pap remains false positive
- May monitor interpretive or sampling discordances for education and process improvement

Standardization Recommendations

1. Where possible, only one final result per patient (one pair)
2. Original interpretations used for “positive” or “negative” correlation statistics rather than the review interpretation
3. Exclude ASC-US, ASC-H, AGC and “equivocal” biopsy results
4. Maintain laboratory statistics—a minimum of 20 events required for statistical significance
5. Difficult to collect sufficient number of events to monitor for individuals unless in high-volume laboratories
High PPV?

• Not a measure of a “good laboratory”
• May only report most obvious lesions in both specimens.
• May not recognize subtle lesions
• Actions
  – Compare with overall laboratory/ individual abnormal rates (lower than benchmarks?)
  – Rescreen error rates (higher than benchmarks?)

Low PPV?

• Investigate diagnostic accuracy and intradepartmental variability
  – Group consensus slide review
  – Outlier individuals associated with discordance
    • Correlate with other monitors:
      • ASC:SIL ratio
      • Rescreen variances
      • Diagnostic category rates
  – Investigate biopsy quality
  – Investigate colposcopic quality

CHC Consensus Statement 5:
What to do with discordant pairs?

• Notify health care provider of confirmed negative biopsy and HSIL+ Pap test
• Notify health care provider of negative biopsy and reclassified Pap test when the original Pap was HSIL+ and the review interpretation is NILM
• Optimizes patient care
  – Discordant pairs should be followed
    • 45% of “false positive” Pap tests will discover SIL
  – Minimizes emphasis of biopsy
  – Decreases unnecessary
• Histological report, cytological report, QA document
CHC Consensus Statement 6:
• Laboratories should attempt to obtain correlation biopsy information for all patients with a HSIL or cancer Pap test.
  – Ask for follow up information
  – Notify provider if no follow up received
    • Laboratory defined time
    • 6 months
  – Must have a procedure and documentation

CHC Consensus Statement 7:
• Microscopic review of all slides from discordant Pap/biopsy pairs is desirable.
  – Define other discordant pairs
  – Define additional non-correlation metrics
  – Review all available slides
  – Document review

CHC Consensus Statement 8: CHC should be a multilayered approach
• Develop QA programs based upon
  – Available resources
  – Potential problems
• Multilayered approach
• Tailored to laboratory size, issues and practice
• Additional QA monitors may be
  – Interval
    • Target specific pairs for a pre-defined period
    • Acquire a “snapshot” of laboratory performance for that indicator
  – Continuous
    • Desirable for laboratories with high personnel turnover, disruptive environments, or mitigating variables outside of the laboratory’s control
Consensus Statement 1: CH correlation may be performed “real time”, retrospectively or both. “Real time” preferentially impacts immediate patient care and is strongly preferred for a HSIL Pap test/ negative biopsy.

1.1 Should pathologists inform the caregiver if s/he cannot perform “real time” correlation for HSIL Pap/ negative biopsy?

1.2 The ASCCP provides guidelines for appropriate follow-up of a negative biopsy, HSIL+ Pap test. Should this recommended follow-up be part of the biopsy report?

Consensus Statement 2: At a minimum, review all available slides for HSIL Pap-negative biopsy discrepancies, in the shortest interval possible (preferably within 3-4 months but no greater than 6 months).

2.1 Some patients (such as pregnant patients) may not be biopsied within a 6-month window from the time of the Pap test. What other alternatives are there for following up on those patients if this guideline is implemented?

2.2 For laboratories that perform ONLY Pap interpretation or ONLY biopsy interpretation, is it sufficient to perform only a “paper” correlation? Does this provide useful information that can be used to improve quality?

Consensus Statement 3: Standardization of metrics and CH correlation process is desirable and allows for interlaboratory comparison.

3.1 If most laboratories adopted a standardized process for CHC, would your laboratory maintain current statistical measures in addition to the standard?

3.2 What portions of the CHC process should be standardized?

Consensus Statement 4: PPV of a positive Pap test is the preferred standard CH correlation metric.

For Pap tests, \[ PPV = \frac{TP}{TP + FP} \]

- True Positive = “positive” pair
- False Positive = “positive” Pap test but “negative” biopsy

Positive = any combination of LSIL, CIN1, HSIL, CIN2, CIN3, AIS, SCCA, ADCA, or malignant neoplasm

PPV median = 83-88%; range 71-94% (CAP Q-Track data, 2005-2010)

4.1 What are the disadvantages and advantages of calculating the PPV?

4.2 Is this the only CHC metric that laboratories should standardize?
**Consensus Statement 5:** Pathologists must have a method of notifying the caregiver, in a timely manner, of a Pap test review when microscopic review confirms a negative biopsy and a HSIL/AIS/cancer Pap test OR when the biopsy is negative and review of a HSIL/AIS/cancer Pap is re-interpreted as NILM.

5.1 What would notification look like and how would you document it?

5.2 If notification involved a comment in the biopsy report, what information should be conveyed and how should it be worded?

5.3 What is your opinion of the following statements?

A. “Cervical biopsies may not correlate with Pap tests, most commonly because of sampling errors. Almost half of the patients with unconfirmed HSIL are subsequently found to have cervical intraepithelial neoplasia.”

B. “Patients with HSIL Pap tests and negative cervical biopsies occur because of sampling or interpretive causes. The Pap test has been reviewed and confirmed as HSIL; the biopsy is reviewed and is confirmed as negative. If colposcopy was suspicious for abnormality, further biopsies may be necessary since CIN may be found in subsequent biopsies.”

C. “CIN 2-3 may be found despite a negative Pap test. False negative Pap tests occur because of sampling (failure to obtain the abnormal slides at the time of the Pap test), rare abnormal cells on the original Pap test, or misinterpretation of abnormal cells. The Pap test and this cervical biopsy have been reviewed and the discordance is confirmed.”

D. “The patient’s previous Pap test (give number here) interpreted as (give previous interpretation of Pap here) is reviewed concurrently with this biopsy. **The Pap test and tissue are concordant.**”

E. “The patient’s previous Pap test (give number here) interpreted as (give previous interpretation of Pap here) is reviewed concurrently. The Pap test and tissue do not correlate. This is likely the result of **tissue sampling variance.**”

F. “The patient’s previous Pap test (give number here) interpreted as (give previous interpretation of Pap here) is reviewed concurrently. The Pap test and tissue do not correlate. This may be a sampling variance or may be due to a lesion that has since regressed. **Note: Most low-grade lesions are transient and hence regress spontaneously.**”

G. “The patient’s previous Pap test (give number here) interpreted as (give previous interpretation of Pap here) is reviewed concurrently. The Pap test and tissue do not correlate. This is felt to be due to a **cytology sampling variance.** The lesion seen on the biopsy is not represented in the cytology specimen.”
H. “The patient’s previous Pap test (give number here) interpreted as (give previous interpretation of Pap here) is reviewed concurrently. The Pap test and tissue do not correlate. This is felt to be due to a cytology interpretive variance.”

I. “The previous Pap test (give number here) is reviewed in conjunction with this case. The results are recorded in a quality assurance document and (the caregiver) has been notified of any significant discordant results.”

Consensus Statement 6: Laboratories should attempt to obtain correlation biopsy information for all patients with a HSIL Pap test (HSIL follow-up).

6.1 How much effort should pathologists make to obtain biopsy follow-up information?

Consensus Statement 7: Microscopic review of all slides from non-correlating (discordant) Pap/biopsy pairs is desirable.

7.1 If laboratories cannot obtain slides for microscopic review, what is the next step?

7.2 Is it difficult to collect the data for CHC from the biopsy report when Pap test review is concurrent with biopsy sign-out?

Consensus Statement 8: CH correlation benefits from a “multilayered” approach designed by the laboratory as part of its quality plan.

8.1 What is your opinion of this statement?