Establishing Universal Lynch Syndrome Screening in the Community

November 12, 2016

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THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER
Universal Tumor Screening for Lynch Syndrome: 
*The Ohio State Experience*

Lynch Syndrome Common and Preventable

Success of Citywide and Statewide Initiatives
Lynch Syndrome

Over 1.2 million individuals in the U.S. have Lynch Syndrome

Inherited condition that causes high risks for colorectal cancer, endometrial cancer and other cancers

Preventable cancers with early and more frequent screening

95% of affected individuals do not know they have Lynch Syndrome

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Genetic Features of Lynch Syndrome

- Genes belong to DNA mismatch repair (MMR) family
- Mutations in MMR genes lead to microsatellite instability (MSI)
  - Test is positive in 15% of colorectal and 24% of endometrial tumors
  - Sensitivity is 77-89% for Lynch Syndrome
- MMR proteins missing in tumor tissue making Immunohistochemical (IHC) staining useful
  - 1-2 proteins absent in 20% of colorectal and 25% of endometrial tumors
  - Sensitivity is 83% for Lynch Syndrome
- Immune therapy recently shown very effective in treating patients whose tumors have defective MMR

Universal Tumor Screening for Lynch Syndrome: *The Ohio State Experience*

Lynch Syndrome Common and Preventable

Success of Citywide and Statewide Initiatives
Feasibility of Screening for Lynch Syndrome Among Patients with Colorectal and Endometrial Cancer

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COLORECTAL CANCER
n=1566

MSI positive
n=188 (12%)

Immunohistochemistry
Methylation of MLH1 Promoter
Complete genetic testing

Pathogenic Mutation
n=44 (2.8%) with Lynch Syndrome

Citywide 1999-2008

ENDOMETRIAL CANCER
n=563

MSI positive
n=131 (23%)

Immunohistochemistry
Methylation of MLH1 Promoter
Complete genetic testing

Pathogenic Mutation
n=14 (2.5%)

with Lynch Syndrome

Hampel H et al. Cancer Res. 2007;67:9603
44 Colorectal Cancer Patients with Lynch Syndrome

- Age at diagnosis 51.4 (range 23-87)
- 50% diagnosed over age 50
- 25% did not meet either Amsterdam or Bethesda criteria
- Mutations
  - 20.5% MLH1
  - 13.6% MSH6
  - 52.3% MSH2
  - 13.6% PMS2

Hampel et al. NEJM 2005;352:1851-60
14 Endometrial Cancer Patients with Lynch Syndrome

- Age at diagnosis 51.4 (range 39-69)
- 65% diagnosed over age 50
- 65% did not meet either Amsterdam or Bethesda criteria
- Mutations
  - 14.3% MLH1
  - 64.3% MSH6
  - 21.4% MSH2
  - 0% PMS2

Hampel et al. NEJM 2005;352:1851-60
Cascade Testing: Follow mutation through Lynch Syndrome families

297 Relatives Tested
130 Positive

Average 6 relatives tested per family revealing 3 with Lynch Syndrome

Differentiators of Citywide Initiative
1. Free genetic counseling
2. Free genetic testing
3. Counseling provided locally
Universal Tumor Screening for Lynch Syndrome
Cost Effective and Recommended

- Incremental Cost Effectiveness Ratio = $31,391 per year of life saved
  - Experts agree that interventions with an Incremental Cost Effectiveness Ratio <$50,000 per year of life saved are cost effective

- Universal tumor screening for Lynch Syndrome is recommended by:
  - Evaluation of Genetic Applications in Practice & Prevention (CDC)
  - National Comprehensive Cancer Network
  - US Multi-society Task Force on colorectal cancer
  - Society for Gynecologic Oncology & American College of Obstetrics and Gynecology
  - Healthy People 2020 goal: Increase # of newly diagnosed colorectal patients screened for Lynch Syndrome at diagnosis

Slow Adoption of Universal Tumor Screening for Lynch Syndrome

Cancer Center Adoption Rates:

- **71%** NCI-Comprehensive Cancer Centers
- **36%** COS-accredited Community Hospital Comprehensive Cancer Programs
- **15%** Community Hospital Cancer Programs

80% of cancer patients are treated in community hospitals with lowest adoption rates

Beamer et al, JCO 2012;30(10):1058-63
Statewide 2012-2017

Supported by Pelotonia
$ 4.5 Million

Research Project

1

Universal Screening for Lynch Syndrome

Albert de la Chapelle
Heather Hampel
Richard Goldberg
Wendy Frankel

2

Adherence to Colorectal Cancer Screening

Electra Paskett

3

Molecular Epidemiology of Colorectal Cancer

Peter Shields

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Building the Network

- Met with stakeholders in person
- Track record of success with citywide project
  - Testimonials from collaborators ensuring that we had not stolen patients
- Neutral branding – OCCPI has its own logo that is not related to Ohio State
- Patients stay local
  - Samples come to Ohio State for testing but patients stay local
  - For those with a mutation, genetic counseling provided by a local genetic counselor, telephone genetic counselor or we provided it at their location
- Reimbursement for expenses
  - Sites reimbursed for the costs of accrual on a per patient basis (including pathology costs)

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Statewide Coverage

50 participating hospitals

Patients enrolled in all 88 counties
Statewide Coverage

50 participating hospitals

Patients enrolled in all 88 counties

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Results

MSI and/or IHC testing

+  
Defective Mismatch Repair
385 (15.3%)  
-  
MLH1 promoter methylation

-  
Defective Mismatch Repair
Without MLH1 Methylation
142 (36.8% of dMMR)  
+  
Defective Mismatch Repair
With MLH1 Methylation
243* (63.1%)
*2 with germline methylation  

Eligible for Genetic Testing
142  
-  
Coloseq

-  
Unexplained
46  
+  
Coloseq Tumor  

Lynch Syndrome = 90
Other = 10
96 patients* (3.8%)  
-  
Genetic Counseling
Cascade Test Family  

Eligible for Genetic Testing
924  
-  
MyRisk

Lynch Syndrome = 4
Other = 64
65 patients* (2.6%)  
+  
DONE

Proficient Mismatch Repair
2125 (84.7%)  
Clinical Criteria
1. Dx <50  
2. First Degree Relative with CRC or EC  
3. >1 CRC or EC

CrC Patients with Testing Complete
2510  

* some patients fit into >1 category
some patients have > 1 gene mutation
Results

EC Patients with Testing Complete
284

MSI and/or IHC testing

+ 

Defective Mismatch Repair
76 (26.8%)

MLH1 promoter methylation

Defective Mismatch Repair
Without MLH1 Methylation
16 (21% of dMMR)

Proficient Mismatch Repair
208 (73.2%)

Done

Eligible for Genetic Testing
16

Coloseq

- 

Unexplained
7

Coloseq Tumor

Lynch Syndrome = 9
Other = 0
9 patients (3.2%)

Genetic Counseling
Cascade Test Family

Double somatic MMR Mutations=7

* some patients fit into >1 category
some patients have > 1 gene mutation
Universal Screening for Lynch Syndrome

Results

Genetic Counseling
Cascade Test Family

417 Relatives Tested

134 Positive
- Receive intensive surveillance and prevention
- Children are at risk

253 Negative
- Receive general population screening
- Children are not at risk
Cancer Moonshot Blue Ribbon Panel

Recommendation…

A call for a “nationwide demonstration project to systematically screen all people diagnosed with colorectal and endometrial cancer for Lynch Syndrome.”

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Potential Impact

- 134,500 new cases of CRC in the US in 2016
- 4,035 have Lynch syndrome (3%)
- 12,105 of their relatives have LS (~3 per proband)
- 60,050 new cases of EC in the US in 2015
- 1,800 have Lynch syndrome (3%)
- 3,600 of their relatives have LS (~2 per proband)
- Total of 21,540 individuals who could be diagnosed with LS this year with universal screening
First patient diagnosed with Lynch syndrome in OCCPI
First patient diagnosed with Lynch syndrome in OCCPI
First patient diagnosed with Lynch syndrome in OCCPI
Conclusions

- 1 out of every 26 CRC patients has LS
- 1 out of every 31 EC patients has LS
- Family history criteria will miss 25% of CRC patients with LS and 65% of EC patients with LS
- Lives can be saved by diagnosing LS early
- Universal Screening for LS among all newly diagnosed CRC patients
  - Is feasible
  - Is recommended
  - Is cost-effective
A CANCER-FREE WORLD BEGINS HERE