Oncology Update

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I have no conflict of interest with the material in this presentation. I have no financial relationships to disclose.





- CancerSEEK blood test that can detect 8 different cancers
- Low level smoking and cancer risk
- Updated ACS colorectal cancer screening guidelines
- Cardiovascular morbidity in older adults with colorectal cancer

Important!!

• This blood test is not yet approved for general use

 HOWEVER...it's received a lot of airplay and your patients may ask you about it

eneral use and your

• What is it?

- Multianalyte blood test
- Can detect eight cancer types through circulating tumorrelated proteins and mutations in cell-free DNA
- Five cancer types have no screening test: ovary, liver, gastric, pancreatic, esophagus
 - May help screen populations at high-risk

ing tumor-N Ny, liver, gastric,

How helpful is it? Positive in 70% of patients with the eight cancer types Sensitivity 69-98% for the "no screening test" cancers Specificity >99%





- Looks pretty sweet...what's the problem?
 - Positive results may be <u>stage</u>
 <u>dependent</u>
 - The test needed must detect at an early stage to be helpful!



Bottom line…

- Looks promising
- More work into diagnosis at early stage...prior to clinically evident would be helpful!
- Cost for high risk patients acceptable: \$500 (2016) average colonoscopy cost - \$3,081)

- "How low can you go?"
 - Risk rate for smoking-related illnesses related to exposure
 - Theoretically, less exposure should lower risk
 - Is there a threshold where risk is no greater than non-smoking population?



- Association of Long-term, Low-Intensity Smoking With All-Cause and Cause-Specific Mortality in the National Institutes of Health–AARP Diet and Health Study (Choi, MI, et al.; JAMA Intern Med. 2017;177(1):87-95)
 - Over 290,000 adults in National Institutes of Health–AARP Diet and Health Study aged 59 to 82 years
 - Initial query 1995-1996
 - Follow-up query 2004-2005, participants scanned until death or 12/31/2011, whichever came first
 - All-cause and cause-specific mortality among current, former, and never smokers



■>30		
	40	
	30	Relative mortality
	20	rate
	10	
	0	

(Choi, MI, et al.; JAMA Intern Med. 2017;177(1):87-95)



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- Conclusions
 - Participants who smoke <1 or 1-10 cigarettes per day over their lifetime are at a substantially higher risk of premature mortality from a broad spectrum of smoking-related causes of death than never smokers
 - Former smokers of <1 or 1-10 cigarettes per day had higher mortality rates relative to non-smokers, but lower risk than those who continued to smoke at those levels

(Choi, MI, et al.; JAMA Intern Med. 2017;177(1):87-95)

 Strengths Large sample size Prospective Longitudinal

Weaknesses

intensity smokers

 Retrospective of smoking use

I cigarette/day broad

Modest number of low-

"How low can you go?"
Your best bet...zero!



- Background
 - Fourth most common cancer in American adults
 - \bullet >140,000 cases this year
 - Second leading cause of cancer-related death; highest incidence and mortality rate in blacks, American Indians and Eskimos

- Background
 - Trends in incidence and mortality in the >55 age group have been trending downward over the last 20 years...most of the trend due to screening
 - Incidence in the <55 age group increased 51% over the last 20 years...this group isn't screened as well
 - CRC Deaths 2010-2014 age 50-54: 7.6% of total
 - CRC Deaths 2010-2014 age 45-49: 5.1% of total

Wolf AWD, et al.; online access: https://onlinelibrary.wiley.com/doi/abs/10.3322/caac.2 1457

 Concept—improving screening rates in the <55 age group may lead to better detection, removal of precursor lesions, better outcomes



- How do we screen?
 - Stool based tests
 - Highly sensitive fecal immunochemical test (FIT) every year
 - Highly sensitive guaiac-based fecal occult blood test (gFOBT) every year
 - Multi-targeted stool DNA test (MTsDNA) every 3 years



Wolf AWD, et al.; online access: https://onlinelibrary.wiley.com/doi/abs/10.3322/caac.21457

• How do we screen? • Visual (structural) exam Colonoscopy every 10 years CT colonography (virtual) colonoscopy) every 5 years Flexible sigmoidoscopy (FSIG) every 5 years



- Adults aged 45 and older with an average risk...
 - Regular screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability
 - All positive results on non-colonoscopy screening tests should be followed up with timely colonoscopy

- Adults aged 45 and older with an average risk...
 - The recommendation to begin screening at age 45 is a *qualified* recommendation
 - The recommendation for regular screening in adults aged 50 and older is a strong recommendation

- Average-risk adults in good health with a life expectancy of greater than 10 yrs continue CRC screening through the age of 75 yrs (qualified recommendation)
- ACS recommends that clinicians individualize CRC screening decisions for individuals aged 76 through 85 yrs based on patient preferences, life expectancy, health status, and prior screening history (qualified recommendation)
- The ACS recommends that clinicians discourage individuals over age 85 yrs from continuing CRC screening (qualified recommendation)

Wolf AWD, et al.; online access: https://onlinelibrary.wiley.com/doi/abs/10.3322/caac.21457

- Burdens of screening
 - Overdiagnosis
 - Cost
 - Screening test cost varies widely
 - Out-of-pocket expense varies widely

• Assume screening costs of \$250 per person, the direct cost to prevent 900 CRC deaths annually would be \$5.5 billion, or about \$6.1 million per death averted (Bretthauer M, et al.; Ann Intern Med (2018) 10 July)

- What does a "qualified recommendation" mean? Clear benefit exists
 - Uncertainty exists whether benefit outweighs harms
- What do I do?
 - Discuss screening average risk patients who are 45 years old
 - Educate patients on benefits/burdens of screening so they can make informed choice



Kenzik KM, et al.; J Clin Oncol 36:609-616; 2018

- Growing number of CRC survivors > 65 years of age
- Systemic treatment utilizes fluorinated pyrimidines (5-FU or capecitabine), both of which can induce angina; acute MI rarely reported
- No historic data on long-term CV disease
- Is there an increased risk to patients who have received these agents for developing CV disease?

New-Onset Cardiovascular Morbidity in Older Adults With Stage I to III Colorectal Cancer

Kenzik KM, et al.; J Clin Oncol 36:609-616; 2018

- SEER database queried for individuals >65 years with Stage I to III colon or rectal cancer diagnosed between January 1, 2000 and December 31, 2011
- Medicare claims captured until death or December 31, 2013.
- Total: 72,408 patients with cancer (56,077 colon, 16,331 rectal)
- 72,408 age and demographic-matched Medicare recipients served as the control group

- 10 year cumulative incidence of CV morbidity 71% for cancer patients vs 28% for controls (p < 0.001)
- Incidence of CHF 54.5% for cancer patients vs 18% for controls (p<0.001)
- CRC diagnosis shortened timed to CHF diagnosis by 58% (4.19-fold increased risk for CHF)



- 10 year cumulative incidence of CVD 57% in cancer patients vs 22% in controls (p<0.001)
- CRC diagnosis shortened time to developing CVD by 57.4% (3-fold increased risk for CVD)



Predictors for CV morbidity • CHF: African ancestry, radiation therapy • CVD: African ancestry, radiation therapy

 Customary predictors were also important



Medication-related propensity • CHF

• Less than 2 years: capecitabine 3.65 fold increased risk

• 2 or more years: capecitabine 1.57 fold increased risk



- Medication-related propensity CVD
 - Less than 2 years: capecitabine use lowered risk by 37%
 - 2 or more years: capecitabine use lowered risk by 23%



Kenzik KM, et al.; J Clin Oncol 36:609-616; 2018

- Conclusions...
 - Older patients with CRC are at increased risk for CHF and CVD
 - Other risk factors (DM, HTN, etc) interact with chemotherapy to increase risk of CV morbidity
 - We need to keep increased risk in mind in CRC survivors who have received chemotherapy



Concluding Remarks

 State-of-the-art molecular screening coming of age, but much work has yet to be done

There is no such thing as a "light" smoker • Emerging role for CRC screening prior to age 50 Chemotherapy for CRC increases risk of CV morbidity



Questions?

