Diagnostic Challenges in Dermatology: over-diagnosis

Robert A. Swerlick, MD
Alicia Leziman Stonecipher Professor and Chairman
Emory University School of Medicine

Disclaimer

- I have no financial conflicts associated with this presentation other than I recognize it is likely financially disadvantageous to me to hold this set of beliefs

Educational Goals

- Present a counter-intuitive argument suggesting that melanoma may be over-diagnosed and patients may derive little or no benefit from programs put in place to screen for, and detect early melanoma in asymptomatic populations
- Call into question the ability of 150 year old diagnostic tool to function as the gold standard of diagnosis
What is overdiagnosis?

- “Over-diagnosis happens when people get a diagnosis they don’t need. It can happen when people without symptoms are diagnosed and then treated for a disease that won’t actually cause them any symptoms, and it can happen for people whose symptoms or life experiences are given a diagnostic label which brings them more harm than good.”

- http://www.preventingoverdiagnosis.net/?page_id=1176

Over-diagnosis

- Treatment of risk states in asymptomatic patient populations not likely to benefit from intervention
  - Cancer – Breast, Prostate, Melanoma, Thyroid
  - Osteoporosis
  - Mental health disorders – Manic/Dep, Autism, ADHD
Many cancer screening efforts have been a major disappointments

Hypothesis

• Much of the increased incidence of cancer discovered in asymptomatic people by screening, can be explained by a diagnostic and surveillance artifact.
Hypothesis

- The source of this diagnostic artifact in melanoma diagnosis is the inability of conventional histology to give reproducible, verifiable, and truly predictive information about the biologic potential of relatively common pigmented lesions.

Thin melanomas

- Our fears of melanoma are based upon a basic premise, based on a simple prediction:
  - Thin lesions, if left alone, will almost invariably result in development aggressive and biologically relevant melanoma which will kill the host.
  - Look's remotely like (taxonomic assessment) = behaves like?
  - Is the taxonomic tool useful as predictive tool?
"Extraordinary claims require extraordinary evidence".
Carl Sagan

- We make these predictions based upon a 150 year old technology first developed by Virchow.
- Just how good is this diagnostic (predictive) test?
- How well does it measure up to other tests?
- Does it represent extraordinary evidence?

Assessment of the Utility of a Diagnostic Test

- Reproducibility – how does it operate in different hands?
- Definition of Sensitivity and Specificity
  – Context specific?
- Verification by a Gold Standard
  – Ability to predict biologic behavior
- How does conventional histological exam of pigmented lesions measure up?

Reproducibility

- Can we get the same results repeatedly with the same or different operators?
  – 8 expert dermatopathologists, 37 typical melanomas or nevi that shared features with melanoma
  – Unanimous agreement in 30%, single discordant in 32%
  – One expert called 21 malignant and 16 benign, while another called 10 malignant, 16 benign
- How do we know who is right?
Anatomic Pathology and Bayesian Analysis

- All diagnostic tests have operating characteristics – specificities and sensitivities
- What is the sensitivity and specificity of anatomic pathology in regards to melanoma Dx?
  - Do these operating characteristics change when the contexts of application change?

Have the Criteria for the Dx of Melanoma Changed Over Time?
(van der Esch et al, Int J Ca 47:483, 1991)

- The average thickness of melanoma has decreased markedly over time:
  - 1930 - No lesions less than 0.75 mm and less than 4% less than 1.5 mm
  - 1990 - over 50% less than 0.75 mm and in some limited series, percentage of lesions less than 0.75 mm over 70%
- Criteria may not have changed but the context has

Cancer Diagnosis vs Predicting the Weather

- What will be the high temperature in Washington, DC on July 15th, 2011?
- Analyze data e.g. - previous highs on given date, standard deviation, examine recent and long-term trends...
- An educated guess can be made but all the variables cannot be defined.
- The day will arrive and prove the prediction right or wrong
Predictions in Daily Life

- Stock Market - How high will the stock market be on January 1, 2020?
- Horoscopes - Will you become rich and famous?
  - These predictions have one thing in common. Whether the prediction is right or wrong can be defined.
  - Is this true of the prediction implied by a diagnosis of “early” cancer?

Melanoma as a taxonomic assessment

- 1930’s assessment
  - Clinical presentation - pigmented nodule
  - DDx - Hemangioma, melanoma, SCCA
  - Dx - melanoma = very likely death
- At this time the Pathologist functioned as taxonomist of advanced lesions where the outcomes were very binary and the outcomes were known relatively quickly

Melanoma as a Prediction

- 2000’s prediction
  - Clinical presentation - small pigmented macule
  - DDx - nevus vs. dysplastic nevus vs. melanoma
  - melanoma = ???
  - Now, the Pathologist functions as an assessor of risk
  - What is the actual risk of death associated with a 2 mm lesion called a thin melanoma by a pathologist?
- What if we come to the conclusion that Pathologists are using a tool not capable of guiding them in any sort of clinically meaningful way?
Early predictive tools –
Oracle bones of ancient China

• Interested parties would submit questions to deities regarding important issues such as the weather, crop planting, military endeavors, and topics. These questions were then carved onto a bone or shell in oracle bone script using a sharp tool followed by the application of intense heat until the bone or shell cracked.

• The diviner would then interpret the pattern of cracks and write the prognostication upon the piece as well.

• This practice went on for centuries and was highly valued for its predictive capabilities. Archaeologists have unearthed virtual mountains of oracle bones.

• Lesson: it is hard to know when your predictive tools may be less useful than you might believe.

In general, how do we assess risk?

• What can we learn from other contexts where we must deal with dangerousness?

Who was dangerous?
Barry Marshal 1995 Nobel Prize for Medicine

Theodore Bundy – Notorious Serial murderer

Who is dangerous?
• Missed diagnosis – Is the diagnosis only obvious because of hindsight?
• Over diagnosis – Almost impossible to identify in a single person but obvious when looking back at diagnostic patterns in retrospect
• Diagnosis v. Risk assessment – those who make predictions should know they often will be wrong.

What do we tell patients?
• Public health agenda vs. personal health agendas?
• What information should we be sharing with the public?
  – How to frame the numbers?
  – What do the numbers mean?
  – How much confidence do we have in our interventions?
What if we need to terrify 10,000, 100,000, or 1 million to save one life?