Introduction to Personalized Cancer Care

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Learning Objectives

• Know the value of individualized prognostication in personalized cancer care
• Identify current limitations in individualized prognostication approaches
• Recognize the need for quality indicators for prognostication algorithms
• Visualize future directions in personalized cancer care
“Personalized Cancer Care”

• The challenge we face in cancer care:
  – Each patient is unique.
  – Each cancer is unique.
  – Each care environment is unique.

• For decision-making and patient management on a truly “individual” level we need to incorporate data about each of the above plus:
  – Costs
  – Patient choice
  – Ethical, legal (right to die; right to try), other

This is a big data and AI challenge - subject for tomorrow
A Starting Point: Personalized Prognosis

- Prognosis is the basis of cancer management strategy
- Prognosis is “an expert prediction of outcome based on an accurate diagnosis, knowledge of the natural history of the disease, the disease’s response to treatment, and the progression of the disease in the patient in question”

- Bailey, Concise Dictionary of Medical-Legal Terms
Prognosis in Oncology: Why Is It Important?

• Patients need to know.
  – How bad is it? What are my chances? How long do I have?
  – Will the treatment cure me?
  – For me, is it worth going through treatment?

• Physicians need to know.
  – What is the right treatment and appropriate management for this particular patient with this particular cancer?
  – Am I over- or under-treating this patient?

• Scientists need to know.
  – Are “like” patients being compared?
  – Is therapy altering outcome?
  – Are we making progress against cancer (are outcomes changing)?
Prediction is very difficult, especially if it's about the future.

(Niels Bohr)
A Short History of Prognostication

- **Mantic prognosis**: foretelling the outcome of illness based on omens and magic
  - An ancient practice traced back to the beginning of recorded history
- **Semiotic prognosis**: foretelling the outcome of illness based on clinical findings
  - Traces back to Sumerian civilization (2000 BC)
  - Reached height of sophistication with Hippocrates (400 BC)
  - Relied on complexes of symptoms and signs (still true today)
  - Resembled modern medicine: clinical observation and pattern recognition
  - Differed from modern medicine: inferred directly from signs and symptoms without going through the process of diagnosis (in ancient medicine, there was no theory of disease, per se)
Current Prognostication

**Estimation of a future event**: Prediction of survival after Dx and Rx

- Risk of dying of the disease
- Likelihood of surviving the disease
- Often expressed in terms of a specific timeframe based on prior observation (data)
- Relies primarily on population data or clinical trials data
- Other end-points: disease-free survival, cancer-specific survival
- **Always** an estimate and always depends on high-quality, accurate data
Determining Prognosis

• Medical prediction is typically based on **statistical averages** from **population data** relating to all patients with comparable disease features

  – For any GIVEN patient, the prediction is most often imprecise.

  – Complete resection is curative for 80% of stage II colon cancer patients; individual patients want to know if they are one of the 80% or not!

  – More individualized prognosis depends on mathematical calculation based on validated prognostic factors present in any given patient.
A Starting Point: Individualized Prognostication

- Anatomic stage is the strongest prognostic factor for solid tumors
  - Based on accurate diagnosis (per staging rules)
  - Codifies the progression of the cancer in the patient
  - Codifies known responses to treatment
What Information TNM Does Provide

- Site of primary cancer
- Extent of cancer present in the body
  - Additional anatomic detail: lymphatic, venous and/or neural invasion
- How data assessed: clinically vs. pathologically
- When assessed: before or after neoadjuvant therapy
  - Status after surgical therapy (R status: 0,1,2)
What Information TNM Does Not Provide

- Information about the cancer
  - Type of cancer
  - Grade of the cancer
  - Syndromic or sporadic
  - Molecular characteristics of the cancer
  - Radiologic characteristics of the cancer

- Information about the patient
  - Age, gender, co-morbidities, performance status

- Information about the care environment
  - Accreditation, experience/volume, specialized facilities
8th Edition AJCC Cancer Staging Manual Moves Ahead

• Defines prognostic stage groups: finer degree of prognostication
• Incorporates non-anatomical information about the tumor
• Still based on a mathematical bin model that sorts patients into “bins”
• System defined as “classification” system

Classifiers group patients into ordered risk strata with probability estimate cut-points
Classifiers group patients into ordered risk strata with probability estimate cut-points

**Useful**
- Helpful way to differentiate degrees of prognosis: good to bad

**Limited**
- Limited by the number of categories that are manageable
  - Breast cancer bins escalated from 32 bins to 768 bins in 8th Edition
- Limited by the inherent variability of prognosis of patients in a given risk class
- Limited by the complexity of combining information from multiple predictors to form discrete ordered categories in a transparent manner
Calculators in Personalized Cancer Care

• Prognostication tools are risk calculators with individualized probability estimates
  – Algorithm-based computational integration of a variety of patient-specific data elements
  – No practical limit to number or types of prognostic factors
  – Calculate outcome estimates for an individual patient
  – Inherently more “personalized”

• The cancer community has generated hundreds of these
Calculators in Personalized Cancer Care

- Systematic review of scientific and non-peer reviewed literature (from 1996) on prediction tools in colorectal, breast, prostate, lung cancers and melanoma

- Variation in:
  - Degree of evidence supporting each tool
  - Mode of presentation/calculation
  - Use of prognostic factors
  - Target population
  - Outcome

- Published tool reviews: melanoma, lung, and colon
AJCC Precision Medicine Core

- **PMC comprised of**
  - Biostatisticians
  - Prediction Tool Developers
  - Data scientists
  - Epidemiologists
  - Disease experts

- **For 8\textsuperscript{th} Edition**
  - Developed and published evaluation criteria for tool quality
  - Evaluated existing predictive tools and algorithms for quality
  - Endorsed high-quality tools for the 8\textsuperscript{th} edition of the *AJCC Cancer Staging Manual*
  - Provided full disclosure of assessments - available online
Rule for Tools: AJCC Inclusion Criteria

- Overall or disease-specific survival must be the outcome predicted
- A clinically relevant question must be addressed
- The relevant predictors or a justification for omitting a relevant predictor must be included
- Included patients must be well-described along with the inclusion/exclusion criteria for them
- State of the art internal validation or truly external validation must be performed
- Time zero must be well-defined
- All predictors must be known at time zero and defined well enough for someone else to use
- Sufficient detail must be available to implement the model
- A measure of discrimination must have been reported
- Calibration in the small must be assessed (from the external validation data set) and provided
- The model developed in a timeframe and practice setting c/w contemporary practice
- All initial treatment(s), if any, must be clearly delineated, as well as frequency/timing
- Development and/or validation of the model must appear as a peer-reviewed journal article
Exclusion:

- A substantial proportion of patients had essentially no follow-up
- No information on number of missing values in validation data set
- The number of events in the validation data set is small
PMC Contributions to 8th Edition

- Number of prognostication tools evaluated by the PMC:
  - 27 for breast cancer
  - 37 for colorectal cancer
  - 16 for prostate cancer
  - 27 for lung cancer
  - 7 for melanoma
  - 4 for head and neck cancer
  - 4 for soft tissue sarcoma
  - 19 for selected hematologic malignancies

- The number that were endorsed:
  - 2 for colon
  - 4 for head and neck
  - 2 for prostate
  - 2 for breast
  - 1 for soft tissue sarcoma (GIST)
  - 0 for melanoma
  - 0 for lung
Going Forward

- Continue to evaluate new tools in reviewed sites
- Put evaluations and recommendations online
- Publish assessments of breast and prostate prognostication tools
- Encourage development of high-quality tools by the community
- Encourage development of tools for ALL patients at all stages of disease
- Build new AJCC tools collaboratively with partners and Expert Panels
Big Picture

- Harness big data, artificial intelligence, and machine learning to create truly individualized prognostication, management and treatment
  - Subject of tomorrow’s opening session
- Dedicate ourselves to quality on all fronts:
  - Quality data
  - Quality tools
  - Quality education
  - Quality research
- Above all, quality care for cancer patients
Thank You!

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