Sudden Cardiac Death: The Molecular Autopsy

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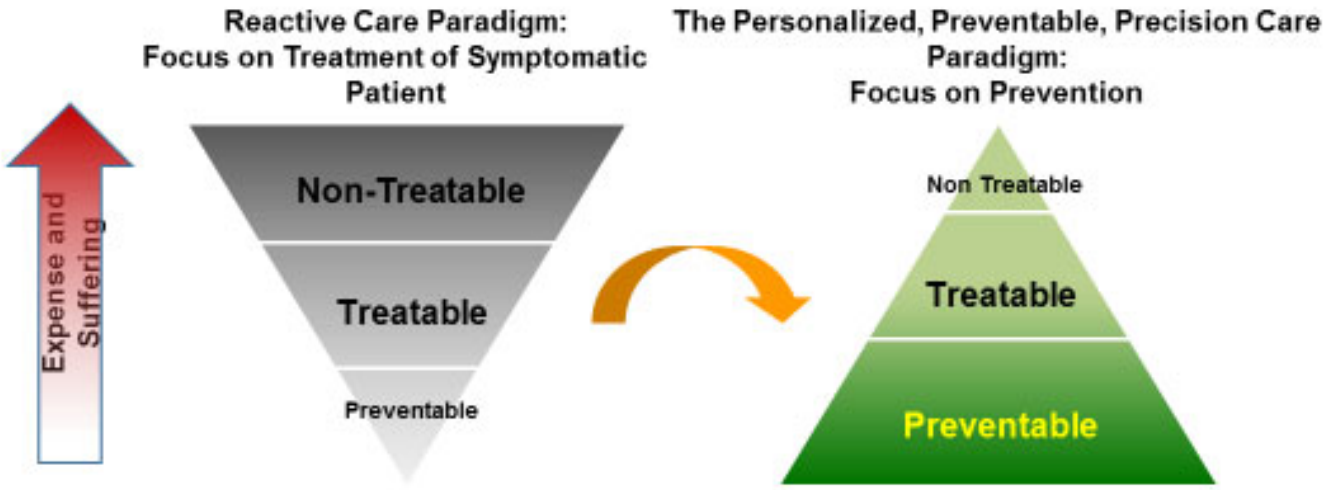
Objectives

- Describe the role of the “molecular autopsy” in a sudden cardiac death victim
- Describe the process of obtaining a molecular autopsy
- Understand benefits and limitations of the molecular autopsy

Precision medicine

There is rapidly accumulating evidence that genetic variants contribute to both rare and common disorders. Gene-based treatments are beginning to show promise for reducing catastrophic complications of disease and help reduce morbidity and mortality.



Slide adapted from GMI

The molecular autopsy

- Obtaining a source of DNA for evaluation of a possible genetic cause of sudden cardiac death
- Selection of the best testing option based on the clinical scenario/ differential
- Sequencing and deletion/ duplication studies of genes associated with SCD
  - Almost always performed at outside labs
  - Genes tested varies from lab to lab
  - Updated regularly based on new discoveries

The molecular autopsy

- What is needed?
  - Consent from family
  - Genetic counseling
  - Purple top EDTA tube- preferably 5 mL or more
    - blood spot card, frozen sample tissue sample of heart, liver, or spleen
    - additional blood for banking if available

Consent and genetic counseling

- Not all families desire genetic information
  - Secondary findings
- Complexity of testing
  - Return of results and communication to at risk family members
  - Interpretation of variants of undetermined clinical significance
  - Cost
- Provides the family an understanding of the process, benefits and limitations

Testing outcomes

- “pathogenic”
- “likely pathogenic”
- “variant of unknown significance”
- “likely benign”
- “benign”

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Testing options and limitations in 2020

- Many labs offer “cardiac gene panels”
  - Inpatient testing, not directly reimbursed
  - Cost ranges from $1,500-3,200
    - Unlikely to change medical management of the patient
- Sponsored genetic testing
  - Up to 150 genes, no charge
- Exome/ genome sequencing
  - Proband only $1200
- Clinical banking of DNA
  - $169

Practical application

- Do what is right for the patient and family
  - Ethics consult
- Assess the phenotype
  - Collaboration with cardiology, intensivists, medical examiners, primary care, pathologists
  - Family assessment
- Genetic testing in the most cost effective manner
- Family/ patient/ physician team communication
- Follow up

Resources

- Genetic services available at most major medical centers
- Find a genetic counselor
  - www.nsgc.org
- rmoran@metrohealth.org
- Labs offering sponsored testing
  - Invitae- www.invitae.com
- Labs offering testing for sudden cardiac arrest
  - NCBI, Genetic testing registry
    - https://www.ncbi.nlm.nih.gov/gtr/