Polycystic Kidney Disease Genetics and Screening

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Outline

- Inheritance and Genetics of PKD
- Diagnosis of PKD
- Imaging
- Genetic Testing
  - Pros and Cons
ADPKD - Introduction

- Characterised bilateral renal cysts.
- May arise in other organs eg. the liver.
- Associated with intracranial aneurysms (10%).
- Typically adult onset: 2-5% of patients present in childhood.
Introduction

Autosomal dominant polycystic kidney disease (ADPKD) affects between one in 400 and one in 1,000.

Accounts for 4–5% of patients who require renal transplantation or dialysis.

Caused by mutations in either PKD1 or PKD2.

Mutations in PKD1 account for ~85% of cases and cause more severe disease.
Genetics of PKD

- PKD1 (16p13.3)
- PKD2 (4q21)
Autosomal dominant inheritance

- Often affected individuals in multiple generations.
- Both males and females are affected.
- Recurrence risk up to 50% (1 in 2).
- It shows variable expression.
- Not under our control.
- Exception: new mutations (5%).
What is screening?

Screening refers to the regular use of certain examinations in people who do not have any symptoms but who are at risk of developing a condition.

Screening permits early detection and treatment of complications.

Appropriate counselling prior to screening, including a discussion of the possible impact on insurability and employability.
Screening for Polycystic Kidney Disease

The initial evaluation of at-risk relatives should be imaging of the kidneys.
Kidney Imaging

- Reliable for the diagnosis of ADPKD in older individuals.

- A negative ultrasound does not exclude ADPKD with certainty in an at-risk individual younger than age 30 years.

Criteria:

- The presence of three or more (unilateral or bilateral) renal cysts in an individual aged 15-39 years

- The presence of two or more cysts in each kidney in an individual aged 40-59 years
Why not just do genetic testing?

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td>Specific</td>
<td>Not 100% sensitive</td>
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<tr>
<td></td>
<td>Long time</td>
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<td></td>
<td>Expensive</td>
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<td>Pre-symptomatic</td>
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Specific

- When a definite diagnosis is required in young individuals without a family history.
PKD1: £1794

PKD2: £594

The presence of at least one family member who developed ESRD at or before age 55 years is highly predictive of PKD1.

The presence of at least one family member with ESRD at or over age 70 years is highly predictive of PKD2.
Not 100%.....

- definite mutation: 65
- non-definite: 26
- None: 9
Types of genetic testing

- Diagnostic
- Pre-symptomatic
Pre-symptomatic Testing

Testing a healthy individual for a disease causing mutation that is known to occur in the family
## Pre-symptomatic Genetic Testing

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<td>Enable kidney donation</td>
<td>Anxiety</td>
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<tr>
<td>Enable family planning</td>
<td>Variability</td>
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Genetic Counselling

Determine the facts:
- Diagnosis, inheritance patterns, prognosis, natural history, treatment and recurrence of risk.

Transmitting the information:
- To those requesting it in a sensitive, culturally appropriate, understandable way.

It is non-directive.
Pre-symptomatic Testing

Screening of asymptomatic children is not currently advocated for adult onset conditions
Pre-implantation Genetic Diagnosis

- IVF & Genetic Testing
- 20% success rate
- Ethical issues
- Funding required
1. If I have a genetic test will I be able to get insurance?

The results of a predictive genetic test will not currently affect your ability to take out any type of insurance other than life insurance over £500,000.

For all types of life and health insurance, whether or not you get cover, and the terms you are offered, will depend on:

- Your health and medical history (including any diagnostic genetic test results)
- Your family history
- Your lifestyle – for example, whether you smoke and your occupation
The future.....

- Better treatment
- Better testing
- Cheaper testing
Conclusions

- Screening for PKD is by ultrasound
- There are pros and cons of genetic testing
- There are specific instances where genetic testing is very helpful