Clinical Consensus Statement:
Genetic Risk Assessment in Hereditary Kidney Cancer

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The need for genetic evaluation guidelines in renal cell carcinoma (RCC)

- **Background**
  - An estimated 5-8% of RCC have a hereditary component
  - Yet, limited guidelines exist for genetic risk assessment
  - Strict adherence to available guidelines would miss up to 35% of cases with hereditary component
  - **Objective**: To gauge current expert opinions on genetic risk assessment in suspected hereditary kidney cancer in a clinical consensus statement.

- **Methods**
  - Invited national experts to consensus meeting
  - Prior to meeting, questions and topics for discussion were generated by modified Delphi methodology
  - Questions solicited from invitees were curated by steering committee and presented using live polling at conference
  - 85% agreement considered consensus per NCCN criteria

- **Results**
  - 52 questions generated, separated into five subcategories
  - 30 statements reached consensus

### Specialty

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<th>Specialty</th>
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<td>Urology</td>
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<td>Medical oncology</td>
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<td>Genetic counselor</td>
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<td>Clinical geneticist</td>
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### Years in practice

| Average | 13.1 +/- 9.6 |

### How many patients do you recommend for kidney cancer genetic risk assessment annually?

| < 10 | 2 (8%) |
| 10-20 | 6 (23%) |
| 20-50 | 12 (46%) |
| > 50 | 6 (23%) |

### Do you order your own germline testing?

| Yes | 19 (73%) |
| No  | 7 (27%)  |

### How often have your parents had trouble with insurance reimbursement for genetic testing?

| 0%    | 4 (17%) |
| 0-20% | 9 (39%) |
| 20-50% | 8 (35%) |
| > 50% | 2 (9%)  |
Consensus statements for genetic risk assessment in RCC

• Who should undergo evaluation?
  • An individual with or without renal tumor(s) and syndromic manifestations associated with hereditary kidney cancer
  • An individual with or without renal tumor(s) with a first degree relative with syndromic manifestations associated with hereditary kidney cancer
  • An individual with or without renal tumor(s) with a first or second degree relative with documented germline mutation associated with RCC
  • An individual with a renal tumor and first degree or two second-degree (same lineage) relatives with RCC
  • An individual with bilateral or multifocal tumors (including AML) without syndromic manifestations
  • An individual with RCC of any of the following histologies: SDH, FH deficiency, hybrid chromo/oncocytoma

• What testing should be done?
  • Single gene test in an individual with a somatic alteration in an RCC-associated gene who undergoes germline testing
  • Multigene panel in an individual without suspicion of a classic syndrome but at least one risk factor for hereditary kidney cancer

• When should evaluation be initiated?
  • Prior to management, in an individual with a localized renal tumor <3cm and strong suspicion for hereditary syndrome
  • Genetic risk assessment should not be delayed in order to obtain a biopsy of a skin lesion which resembles those associated with hereditary syndromes in an individual with a renal tumor

• How should evaluation be performed?
  • Germline testing should not be performed in anyone without pre-test counseling
  • If germline testing is pursued without pre-test counseling, a kidney specific gene panel should be used
  • Physicians with expertise in hereditary kidney cancer may offer pre-test counseling
  • Telehealth/telegenetics visit with a licensed counselor is sufficient for evaluation of individuals suspected of having hereditary kidney cancer

• Which isolated extra-renal manifestations should prompt genetic evaluation?
  • Pheochromocytoma, paraganglioma, endolymphatic sac tumor, uveal melanoma, FH-deficient uterine fibroid