Hereditary Cancer in Clinical Practice 2008; 6(2) pp. 84-87

DNA testing for variants conferring low or moderate increase in the risk of cancer

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1. DNA test based on analysis of 3020insC in *NOD2* gene

3020insC in the *NOD2* gene increases the risk of:
- breast cancer DCIS below age 50 about 5-fold – this mutation is detected in 8% of all breast cancer cases,
- colorectal cancer approximately 2-fold above age 60 – this mutation is present in 15% of all colorectal cancer cases,
- lung cancer about 2-fold – this mutation is present in 12% of all lung cancer cases,
- ovarian cancer about 1.5-fold – this mutation is present in 11% of all ovarian cancer cases [1, 2].

Surveillance for carriers of 3020insC in *NOD2* gene recommended as an option:

Recommendations for women:
- breast self-examination,
- breast examination by doctor from age 20, 1 × 6 months,
- breast USG from age 20, 1 × year,
- mammography from age 35, 1 × year, alternately with breast USG,
- intravaginal USG from age 45, 1 × year,
- colonoscopy or barium enema age 60, every 5 years or more often in case of intestinal abnormalities,
- smoking forbidden, diet richer in fruits and vegetables.

Recommendations for men:
- colonoscopy or barium enema age 60, every 5 years or more often in case of any intestinal abnormalities,
- smoking forbidden, diet richer in fruits and vegetables.

2. DNA test based on analysis of 1100delC, IVS2+1G>A, del5395, I157T mutations in *CHEK2* gene

CHEK2 protein truncating mutations (1100delC, IVS2+1G>A, del5395) increase the risk of:
- breast cancer about 2.4-fold – these mutations are present in about 2.5% of all breast cancer cases,
- prostate cancer about 2.3-fold – these mutations are present in about 2.5% of all prostate cancer cases and about 5% of familial prostate cancer cases; the risk is increased about 5-fold if prostate cancer is present in at least one first degree relative,
- papillary thyroid cancer – about 5-fold – these mutations are present in about 4% of all papillary thyroid cancer cases [3-5].

Missense mutation I157T in the *CHEK2* gene increases the risk of:
- breast cancer (more commonly lobular subtype) about 1.5-fold – this mutation is present in about 7% of all breast cancer cases,
- prostate cancer about 1.6-fold – this mutation is present in about 8% of all prostate cancer cases and about 12% of familial prostate cancer cases; the risk is increased about 3-fold if prostate cancer is present in at least one first degree relative,
- papillary thyroid cancer – about 2-fold – this mutation is present in about 9% of all papillary thyroid cancer cases,
- kidney cancer – about 2-fold – this mutation is present in about 10% of all kidney cancer cases,
- colorectal cancer – about 2-fold – this mutation is present in about 10% of colorectal cancer cases [2-4],
- ovarian cancer of low-grade about 2-fold – this mutation is present in about 10% of ovarian cancer cases G1; and ovarian epithelial tumours of borderline malignancy about 2.5-fold – this mutation is present in about 11.5% of ovarian cancer cases of borderline malignancy [6].

Surveillance for carriers of protein truncating mutations of *CHEK2* (1100delC, IVS2+1G>A, del5395) recommended as an option:

Recommendations for women:
- breast self-examination,
- breast examination by doctor from age 25, 1 × 6 months,
- breast USG from age 25, 1 × year,
- mammography from age 35, 1 × year, alternately with breast USG,
- thyroid USG from age 20, 1 × year.

Recommendations for men:
- digital rectal examination of prostate, PSA from age 50, 1 × year,
- consideration of saturation biopsy of prostate after age 60 – in case of a positive family history of prostate cancer in a first degree relative.

Surveillance for carriers of *CHEK2* I157T missense mutation recommended as an option:

Recommendations for women:
- breast self-examination,
- breast examination by doctor from age 40, 1 × 6 months,
- breast USG from age 40, 1 × year,
- MRI or mammography from age 40, 1 × year, alternately with breast USG,
- intravaginal USG from age 25, 1 × year,
- abdominal USG from age 40, 1 × year,
- colonoscopy or barium enema from age 60, every 5 years or more often in case of intestinal abnormalities,
- thyroid USG from age 20, 1 × year.

Recommendations for men:
- abdominal USG from age 40, 1 × year,
- colonoscopy or barium enema from age 60, every 5 years or more often in case of intestinal abnormalities,
- digital rectal examination of prostate, PSA from age 50, 1 × year,
- consideration of saturation biopsy of prostate after age 60 – in case of a positive family history of prostate cancer in a first degree relative.

3. DNA test based on analysis of 657del5 mutation in *NBS1* gene

Mutation 657del5 in the *NBS1* gene increases the risk of:
- breast cancer about 2-fold – this mutation is present in about 1% of all breast cancer cases,
- prostate cancer about 4-fold – this mutation is present in about 3% of all prostate cancer cases and about 9% of familial prostate cancer cases; the risk is increased about 15-fold if prostate cancer is present in at least one first degree relative [7].

Surveillance for carriers of *NBS1* 657del5 mutation recommended as an option:

Recommendations for women:
- breast self-examination,
- breast examination by doctor from age 30, 1 × 6 months,
- breast USG from age 30, 1 × year,
- mammography from age 30, 1 × year, alternately with breast USG.

Recommendations for men:
- digital rectal examination of prostate, PSA from age 50, 1 × year,
- consideration of saturation biopsy of prostate after age 60 – in case of a positive family history of prostate cancer in a first degree relative.

4. DNA test based on analysis of A148T variant of *CDKN2A* (p16) gene

A148T in the *CDKN2A* gene increases the risk of:
- malignant melanoma – about 2-fold – this mutation is present in about 7% of all melanoma cases,
- breast cancer (more commonly DCIS) about 1.5-fold – this mutation is present in about 5% of all breast cancer cases,
- colorectal cancer – about 1.5-fold – this mutation is present in about 5% of all colorectal cancer cases,
- lung cancer – about 2-fold – this mutation is present in about 7% of all lung cancer cases [8-10].

Surveillance for carriers of *CDKN2A* A148T mutation recommended as an option:

Recommendations for women:
- breast self-examination,
- breast examination by doctor from age 20, 1 × 6 months,
- breast USG from age 20, 1 × year,
- mammography from age 35, 1 × year, alternately with breast USG,
- colonoscopy or barium enema from age 60, every 5 years or more often in case of intestinal abnormalities,
- smoking forbidden, diet rich in fruits and vegetables,
- the use of high sun protection factor sunscreens (30 or more), avoidance of physical trauma of nevi,

- in cases with moles showing clinical signs of malignant transformation (increase of size, red hue, bleeding, pruritus) immediate consultation by dermatologist or oncologist.

Recommendations for men:
- colonoscopy or barium enema from age 60, every 5 years or more often in case of intestinal abnormalities,
- smoking forbidden, diet rich in fruits and vegetables,
- the use of high sun protection factor sunscreens (30 or more), avoidance of physical trauma of nevi,
- in cases with moles showing clinical signs of malignant transformation (increase of size, red hue, bleeding, pruritus) immediate consultation by dermatologist or oncologist.

5. DNA test based on analysis of variants C142G, G355T, G4326C of *CYP1B1* gene

Homozygous carriers of variants C142G, G355T, G4326C (homozygotes GTC) of the *CYP1B1* gene are at 2-fold increased risk of breast cancer. This genotype is present in about 12% of breast cancer cases [11].

Surveillance recommended as an option for women with homozygous GTC genotype in *CYP1B1* gene:
- breast self-examination,
- breast examination by doctor from age 25, 1 × 6 months,
- breast USG from age 25, 1 × year,
- MRI or mammography from age 25-30, 1 × year, alternately with breast USG.

6. DNA test based on analysis of C5972T variant of *BRCA2* gene

C5972T variant in the *BRCA2* gene increases the risk of breast cancer with DCIS below age 50 about 3-fold; homozygous carriers of this variant (homozygotes TT) are at about 5-fold increased risk of breast cancer below age 50; this variant is present in about 6% of breast cancer cases below age 50 [12].

Surveillance recommended as an option for carriers of *C5972T* variant:
- breast self-examination,
- breast examination by doctor from age 25, 1 × 6 months,
- breast USG from age 25, 1 × year,
- mammography from age 35, 1 × year, alternately with breast USG.

7. DNA test based on analysis of C61G and 4153delA mutations in *BRCA1* gene in men

C61G and 4153delA mutations in the *BRCA1* gene increase the risk of prostate cancer about 3.6-fold – these mutations are present in about 0.4% of all prostate cancer cases; the risk is increased about 12-fold if prostate cancer is present in at least one first degree relative [13].

Surveillance recommended as an option for men with C61G or 4153delA mutation:
- digital rectal examination of prostate, PSA from age 50, 1 × year,
- consideration of saturation biopsy of prostate after age 60 – in case of a positive family history of prostate cancer in a first degree relative.

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