DNA TEST (COLOTECT) – DETECTION OF THE PRECANCEROUS STAGE OF COLORECTAL CANCER INDEPENDENTLY OF THE APPEARANCE OF BLOOD IN THE STOOL

DNA TEST (COLOTECT) – DETEKCIA PREDRAKOVINOVÉHO ŠTÁDIA KOLOREKTÁLNEHO KARCINÓMU NEZÁVISLE OD VÝSKYTU KRVI V STOLICI

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Abstract
Colorectal cancer is an oncological disease that can be avoided practically one hundred percent with the help of preventive measures. If colorectal cancer is caught in the early stages, its curability is 90%. Despite significant preventive activities, up to 25% of colorectal cancer patients still arrive late at the hospital. Recently, it appears that a new preventive screening method DNA test (Colotect) could change this adversity. Diagnosis can also be made from stool taken at home, and the test reveals already preclinical stages of colorectal cancer development *(Ref. 10). Text in PDF www.lekarsky.herba.sk.*
KEYWORDS: colorectal cancer, blood in the stool, colonoscopy, DNA test, Colotect, prevention, screening.

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Abstrakt
Kolorektálny karcinóm je onkologické ochorenie, ktorému sa môžeme pomocou preventívnych opatrení prakticky stopercentne sa vyhnúť. Ak sa rakovina hrubého čreva a konečníka zachytí v počiatočných štádiách, jej liečiteľnosť je 90 %. Napriek významným preventívnym aktivitám stále prichádza až 25% pacientov s kolorektálnym karcinómom do nemocnice neskoro. V poslednom čase sa ukazuje, že nová preventívna skríningová metóda DNA test (Colotect) by mohla tento nepriaznivý stav zmeniť. Diagnostiku možno robiť aj zo stolice odobranej doma a test odhaľuje už predklinické štádiá rozvoja kolorektálneho karcinómu *(lit. 10). Text v PDF www.lekarsky.herba.sk.*
KĽÚČOVÉ SLOVÁ: kolorektálny karcinóm, krv v stolici, kolonoskopia, DNA test, Colotect, prevencia, skríning.
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DNA stool testing, also known as stool DNA testing, is a noninvasive screening method for colorectal cancer. This test looks for certain DNA mutations and other molecular markers in a sample of stool that may indicate the presence of cancer or precancerous polyps in the colon or rectum (1-4).

The most well-known stool DNA test is the Cologuard® test, which checks for genetic mutations associated with colorectal cancer as well as for hidden blood in the stool, which can be a sign of cancer. It's designed for use in individuals who are at average risk for colorectal cancer: those without a personal history of colorectal cancer, polyps, familial adenomatous polyposis, or inflammatory bowel disease (Crohn's disease or ulcerative colitis), and without a family history of colorectal cancers or syndromes that increase the risk significantly.

This test is attractive for people looking for a noninvasive screening option, but it's important to note that it is not a replacement for traditional screening methods like colonoscopy in certain cases, especially for those at high risk. While DNA stool testing can detect many

cancers, it may not catch all of them, and a negative test result does not guarantee that a person is cancer-free. Any positive test result from a stool DNA test needs to be followed up with a colonoscopy to visually inspect the colon and rectum and, if necessary, remove any suspicious growths for biopsy (2-6).

The frequency of testing recommended for stool DNA testing is usually once every three years if the initial test is negative, but recommendations can vary based on individual risk factors and guidelines from healthcare providers.

Stool DNA tests, such as the Cologuard® test, look for specific DNA mutations in cells shed by colorectal tumors or precancerous polyps into the stool. These mutations are in genes that are often altered in colorectal cancers. The test also checks for the presence of blood in the stool, another potential indicator of colorectal cancer.

The specific mutations targeted can vary between tests, but generally, they include alterations in genes associated with colorectal cancer, such as (6-8):

1. APC - Mutations in the APC gene are common in colorectal cancer and are often seen in the early stages of cancer development.
2. KRAS - Mutations in the KRAS gene are involved in about 40% of colorectal cancer cases and are associated with cancer progression and resistance to certain therapies.
3. BRAF - Mutations in the BRAF gene, particularly the V600E mutation, are found in a subset of colorectal cancers and can influence prognosis and treatment response.
4. PIK3CA - Mutations in the PIK3CA gene can also be involved in colorectal cancer, playing a role in the pathway that controls cell growth and survival.

The stool DNA test also looks for abnormalities in the DNA itself that are indicative of cancer, such as:

- **Microsatellite instability (MSI):** MSI is a condition of genetic hypermutability (predisposition to mutation) that results from impaired DNA mismatch repair. MSI is a hallmark of a type of colorectal cancer associated with the hereditary nonpolyposis colorectal cancer (HNPCC) syndrome but is also found in sporadic cancers.
- **Alterations in the methylation patterns** of certain genes: DNA methylation is a process that can control gene expression, and changes in the normal methylation pattern can lead to cancer. For example, hypermethylation of the promoter region of the MLH1 gene, which is involved in DNA repair, can lead to its silencing and contribute to cancer development.

These genetic and epigenetic changes can be detected in DNA that is shed from the cancer or polyp into the stool, providing a non-invasive method to screen for colorectal cancer. However, it's important to note that while these markers can indicate the presence of cancer, they are not definitive proof of cancer, and positive results require follow-up with diagnostic procedures like a colonoscopy.

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DNA stool testing is available as a screening method for colorectal cancer. In many countries, including the United States, stool DNA testing is approved by regulatory agencies such as the Food and Drug Administration (FDA) for use as a non-invasive screening option for average-risk adults. The Cologuard® test, for instance, is approved for use in adults aged 45 and older who are at average risk for colorectal cancer. This includes individuals without a personal history of colorectal cancer, adenomas, familial adenomatous polyposis, a confirmed family history of hereditary colorectal cancer syndromes, or a personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease) (8-10).

Stool DNA testing is considered a convenient option for colorectal cancer screening because it can be done at home without the need for bowel preparation or dietary restrictions that are necessary for other forms of screening like colonoscopy or sigmoidoscopy. After receiving a test kit from a healthcare provider, a person collects a stool sample using the provided materials and sends it to a lab for analysis.

While stool DNA testing offers a non-invasive screening alternative, it is generally recommended less frequently than other tests-every three years if the results are negative. It is important to note that a positive result from a stool DNA test does not diagnose colorectal cancer but indicates the need for further examination, typically by colonoscopy.

Healthcare professionals can help determine which screening method is most appropriate based on individual risk factors, preferences, and the availability of tests. It's crucial for individuals to discuss their options with their healthcare provider to decide on the best screening strategy for their specific situation.

The specificity and sensitivity of stool DNA testing, particularly for widely used tests like Cologuard®, are key factors in understanding its effectiveness as a colorectal cancer screening tool. Sensitivity refers to the test's ability to correctly identify individuals who have the disease (true positive rate), while specificity refers to its ability to correctly identify individuals who do not have the disease (true negative rate).

Cologuard® Test Performance Metrics

Sensitivity: The sensitivity of the Cologuard® test for detecting colorectal cancer is reported to be about 92-94%. This means that the test correctly identifies 92-94% of individuals who actually have colorectal cancer.

Specificity: The specificity of the Cologuard® test for detecting colorectal cancer is around 87%. This means

that the test correctly identifies 87% of individuals who do not have colorectal cancer, implying that 13% of the test results might incorrectly indicate the presence of cancer in healthy individuals (false positives).

Sensitivity for Advanced Precancerous Lesions

The sensitivity of the Cologuard® test for detecting advanced precancerous lesions is lower than its sensitivity for detecting colorectal cancer. It is reported to be around 42%. This reflects the inherent challenge of detecting precancerous conditions compared to cancerous lesions, as the latter shed more DNA and are thus easier to detect.

Considerations

- The relatively high sensitivity for colorectal cancer makes stool DNA testing a valuable screening tool, especially for individuals at average risk of the disease who are seeking non-invasive testing options.
- However, the specificity indicates that there is a risk of false positives, which can lead to unnecessary anxiety and additional diagnostic procedures like colonoscopy to confirm the results.
- The lower sensitivity for advanced precancerous lesions suggests that while stool DNA tests are useful for cancer detection, they may not be as effective in identifying individuals with precancerous conditions who could benefit from early interventions to prevent cancer development.

Conclusion

Stool DNA testing, including the Cologuard® test, represents a significant advancement in non-invasive colorectal cancer screening. Its sensitivity and specificity make it a practical option for many individuals, particularly those at average risk of colorectal cancer. Nonetheless, it's essential for individuals to consult with healthcare providers to understand the implications of test results and to choose the most appropriate screening method based on their risk factors, personal preferences, and medical history.

Stool DNA testing, like Cologuard®, is not directly used in the surgical management or during surgery for colorectal cancer. Its primary role is in the non-invasive screening for colorectal cancer and advanced precancerous polyps in individuals who are at average risk for the disease. The main utility of stool DNA tests is to identify individuals who may have colorectal cancer or precancerous conditions so that they can undergo further diagnostic evaluation, typically through a colonoscopy.

In the context of surgery and the management of colorectal cancer, stool DNA testing does not have a direct application. Surgical decisions, planning, and management rely on other diagnostic tools and procedures, including:

1. **Colonoscopy:** Provides a visual examination of the interior of the colon and rectum and allows for the biopsy of any suspicious areas.
2. **Imaging Studies**: Techniques such as CT scans, MRI, and PET scans help in staging the cancer, determining its spread (metastasis), and planning surgical or other treatments.
3. **Blood Tests**: Certain markers, such as carcinoembryonic antigen (CEA), can be monitored over time to assess treatment response and for surveillance after treatment.

Once colorectal cancer is diagnosed, the role of surgery is to remove the cancerous tissue, possibly along with nearby lymph nodes. The specifics of the surgery depend on the cancer's location, stage, and other factors. Stool DNA testing does not influence these surgical decisions directly. However, by facilitating early detection of colorectal cancer, stool DNA tests can indirectly impact surgical outcomes by identifying cancers at earlier, potentially more treatable stages.

After treatment, including surgery, stool DNA testing is not typically used for monitoring or surveillance. Instead, follow-up usually involves a combination of colonoscopy, imaging studies, and blood tests, depending on individual risk factors and the specifics of the cancer treated.*

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