INAHTA Brief

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Title DNA Mismatch Repair Deficiency Tumour Testing for Patients With Colorectal Cancer: A Health Technology Assessment

Agency CADTH

Reference DNA mismatch repair deficiency tumour testing for patients with colorectal cancer: a health technology assessment. Ottawa: CADTH; 2016 Aug. (CADTH optimal use report; vol.5, no.3b).

Aim

Testing tumours for DNA mismatch repair deficiency (dMMR) has been identified as a practice that is potentially overused. There is uncertainty about who should have dMMR tumour testing, how well dMMR testing works, and its cost-effectiveness. To assist decision-makers considering the implementation of dMMR tumour testing, CADTH conducted a health technology assessment on the clinical utility, diagnostic accuracy, cost-effectiveness, and related patient perspectives and experiences of dMMR testing strategies. The ability of dMMR tumour test results to inform colorectal cancer prognosis or chemotherapy response was also evaluated.

Conclusions and results

Polymerase chain reaction-based and immuno-histochemistry (IHC)-based tumour tests have similar sensitivity and specificity for detecting dMMR. IHC-based testing is less expensive, however, and has the advantage of identifying which mismatch repair protein is affected, which can guide follow-up testing.

Universal testing of colorectal tumours for dMMR followed by reflex testing for MLH1 promoter hypermethylation can identify patients for germline sequencing and inform chemotherapy decisions, and it was found to be one of the cost-effective strategies. This testing strategy has the advantage of identifying more cases of Lynch syndrome and decreasing the potential for missed diagnoses of Lynch syndrome. Universal testing (rather than using criteria such as age or family history) also improves equity.

The review of patient experience literature suggests that most patients value knowing if their colorectal cancer is hereditary and the implications for their family members. The review also highlighted generally low levels of knowledge about genetic testing and a need for support throughout the testing process.

The ethics analysis indicated that all of these tests require a clear consent process, including an option for patients to decline testing. Education about the tumour tests should be available. Genetic counselling should be available for all patients considering germline testing so that they can understand their results and have support in making decisions about disclosing results to family members, and about future colorectal cancer screening.

Recommendations

Based on the CADTH HTA, the Health Technology Expert Review Panel, or HTERP, recommends universal dMMR tumour testing for patients with colorectal cancer, followed by reflex tumour testing for MLH1 promoter hypermethylation.

Methods

To evaluate the clinical validity and effectiveness of dMMR tumour testing for patients with colorectal cancer, a systematic review was conducted, including a review of the published literature on patient preferences and experiences. A cost-utility analysis was conducted to compare various interventions related to tumour dMMR testing in newly diagnosed colorectal cancer patients and the subsequent identification of Lynch syndrome among the relatives of probands. An analysis of ethical considerations regarding dMMR testing was also conducted. Based on the results of these analyses, a panel of experts developed recommendations for the adoption of dMMR testing.

Further research/reviews required

There is a lack of published research regarding the potential prognostic value of dMMR testing, and related patient perspectives and experiences. No relevant literature was uncovered for inclusion in our review, and therefore our analysis excludes discussion of this use of test results. Future research to explore the value that people living with colorectal cancer might place on using knowledge of their dMMR status to guide treatment decisions would be valuable.

Written by

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