2019 Health Technology Reassessment Report

Safety and Effectiveness Assessment of DUPAN-II Test

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Summary (English)

□ Background

The Korean Health Insurance Review and Assessment Service (HIRA) sought the opinions of relevant academic societies/associations on changing the coverage status of the items listed in the no-coverage list to preliminary coverage before the introduction of the New Health Technology Assessment System. The HIRA requested the Korea National Evidence-based Healthcare Collaborating Agency (NECA) to assess the safety and effectiveness of those items for which feedback from the relevant academic societies/associations was "need for safety and effectiveness assessment." In this report, one of such items, the DUPAN-II (Duke pancreatic monoclonal antigen type 2) test, is assessed.

The Korean Society of Laboratory Medicine (KSLM) suggested the DUPAN-II test needed to be assessed. The KSCP expressed that the clinical demand was believed to be very low, and few articles had discussed its clinical effectiveness. Therefore, it would be necessary to perform a safety and effectiveness assessment. The number of cases in South Korea that have undergone the DUPAN-II test is estimated to be low and hence, it could be removed from the no-coverage list.

On the other hand, the Korean Medical Association (KMA) expressed that the said technology should remain on the no-coverage list because it is currently utilized, is an essential test for diagnosis, and it has been performed overseas when requested (2016).

□ Committee operation

To assess the clinical safety and effectiveness of DUPAN-II, a subcommittee of 6 members (2 gastroenterologists, 2 oncologists, and 2 clinical pathologists) held a total of 4 meetings within approximately 5 months from April 16 to August 30, 2019.

The members conducted a systematic review and participated in designing the study protocol, selecting keywords following the PICO search strategy, and

establishing selection and exclusion criteria. They also provided consultation as objective experts.

During the 3rd Health Technology Reassessment Committee meeting (November 8, 2019) of 2019, the results of the DUPAN-II test clinical safety and effectiveness assessment were finally reviewed and a recommendation grade was determined.

□ Purposes and Methods

The DUPAN-II test was listed as a healthcare service not covered by the national health insurance on May 1, 2001. The test is used for screening (or making differential diagnosis) patients with confirmed (or suspected) cancer in the digestive system (pancreatic, gallbladder, liver, and stomach cancers).

Details on the testing method of the said technology were not found in the service descriptions of the non-coverage items. Based on the review of relevant literature and the subcommittee discussion (August 7, 2019), however, the opinion was that, in practice, the test would generally be conducted on serum specimens using test kits and enzyme immunoassay (EIA) or radioimmunoassay (RIA).

In this study, the safety and effectiveness of the DUPAN-II test were assessed through a systematic review. In a subcommittee meeting (June 12, 2019), it was opined that it would be reasonable to examine recent data published in 2001 or thereafter because the DUPAN-II test was added to the list of health insurance benefit costs in the year 2001. In addition, a suggestion was made that evidence should also be obtained from additional data sources (clinical practice guidelines, systematic review articles, reviews, etc.). The safety and effectiveness assessment proceeded following the suggestions.

□ Results

I. Safety

Among the articles published in or after 2001, none investigated the use of the DUPAN-II test in screening or diagnosing (differential) patients with (suspected of) pancreatic/gallbladder/liver/stomach cancer. Thus it was not possible to find study findings relevant to the safety of the DUPAN-II test. Further, the findings on the safety of the test were not found in the additionally examined sources, such as clinical practice guidelines, systematic review articles, and reviews.

The subcommittee determined that there would be no safety issue in conducting the DUPAN-II test because in most cases the test would be performed ex vivo for serum specimens using EIA or RIA after blood is obtained from patients. However, there was an opinion that when the test is used for screening or diagnosis, caution should be exercised concerning the impact of false-positive or false-negative results.

II. Effectiveness

The use of the DUPAN-II test in screening or diagnosing patients with (or suspected of) pancreatic, gallbladder, liver, or stomach cancer was investigated. Thus, it was impossible to verify the findings relevant to the effectiveness of the DUPAN-II test.

In the additionally examined sources (such as clinical practice guidelines, systematic review articles, and review), findings on the use and effectiveness of the DUPAN-II test for screening, diagnosis, and follow-up of patients with (or suspected of) pancreatic, gallbladder, liver, or stomach cancer were not found. However, the review by Rhodes (1999) reported that the sensitivity (38–76%) and specificity (59–66%) of DUPAN-II were lower than those of CA19-9 (carbohydrate antigen 19-9 : sensitivity 68–94%, specificity 76–100%) and CEA (carcinoembryonic antigen : sensitivity 30-92%, specificity 58-95%). On the other hand, findings on the DUPAN-II test performed in gallbladder/liver/stomach cancer patients were not found in any of the additionally examined data.

The subcommittee expressed the opinion that the effectiveness of the DUPAN-II test is lower than that of tumor markers with identical or similar indications, and, therefore, the clinical need for this test would not be high.

□ Conclusion

Based on the assessment results, the DUPAN-II test subcommittee made the following suggestions.

It was determined that there was no safety issue associated with using the DUPAN-II test but its effectiveness is low for screening, diagnosis (differential), and follow-up in patients confirmed with (or suspected of) cancer in the digestive system (pancreatic, gallbladder, liver, and stomach cancers).

Based on the subcommittee's review, the Health Technology Reassessment Committee made the following assessment on the DUPAN-II test (November 8, 2019).

The Health Technology Reassessment Committee does not recommend the DUPAN-II test for screening, diagnosis, or follow-up for cancer in the digestive system (pancreatic, gallbladder, liver, and stomach cancers) (Grade of recommendation - II). The rationales for the recommendation are as follows.

Articles reporting on the clinical safety of the DUPAN-II test were not found. However, it was determined that safety would not be an issue with the test because it is conducted ex vivo in most cases, after blood is taken from patients, on serum specimens using EIA or RIA.

Studies published in or after 2001 that examined the use of the DUPAN-II test for screening, diagnosis, and follow-up for pancreatic cancer were not found. It was reported that the DUPAN-II test showed lower sensitivity and specificity than the CA-19-9 and CEA when used as a pancreatic tumor marker test (Rhodes 1999).

	Sensitivity	Specificity
DUPAN-II	38-76%	59-66%
CA-19-9	68-94%	76-100%
CEA	30-92%	58-95%

No studies published in or after 2001 on the use of the DUPAN-II test for screening, diagnosis, and follow-up for gallbladder, liver, or stomach cancers were found.

Based on the review results, the Health Technology Reassessment Committee concluded that the DUPAN-II test should not be recommended (grade of recommendation - II) for screening, (differential) diagnosis, and follow-up for cancers of the digestive system (pancreatic, gallbladder, liver, and stomach cancers).