Gastroenterology Volume 153 Number 4 October 2017

Association Between Natural Killer Cell Activity and Colorectal Cancer in High-Risk Subjects Undergoing Colonoscopy

Gilles Jobin[1,2], Roberto Rodriguez-Suarez[3], and Katia Betito[3]

[1]Department of Medicine, University of Montréal, Montréal, QC, Canada; [2]Division of Gastroenterology, Maisonneuve-Rosemont Hospital, Montréal, QC; and [3]ATGen Canada, Laval, QC, Canada

Background

Low natural killer cell activity (NKA) has been linked to an increased risk of cancer, such as reported in colorectal cancer (CRC) patients. There is a need of additional screening tests for CRC that may be helpful in the triage of those patients at higher risk of finding cancer at colonoscopy

Methods

Study design: This was an open-label, prospective, cross-sectional study performed in Montreal, QC, Canada, from October 2014 through January 2016. From 1081 high-risk subjects (over the age of 40) that were enrolled, blood samples were collected on the same day they were screened for CRC by colonoscopy. Statistical analysis was performed on the 872 evaluable subjects

Test methods: ELISAs were performed to quantify interferon gamma secretion by subjects' NK cells upon *in vitro* whole blood stimulation with cytokines

Results

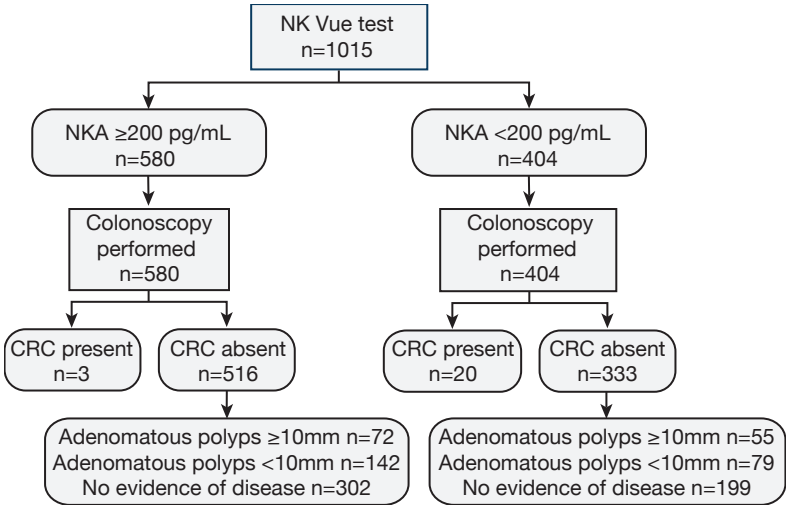
A significant difference in NKA between the 23 subjects with pathology-confirmed CRC and the 849 subjects without CRC was observed. NKA test identified subjects with CRC with 87.0% sensitivity, 60.7% specificity, a positive predictive value of 5.7%, and a negative predictive value of 99.4%. The odds ratio for detection of CRC in subjects with low NKA vs those with higher NKA was 10.3 (95% CI, 3.03–34.9)

Clinical Importance

In a high-risk population, measuring NKA through a simple blood test may provide a way to assess risk of CRC and may supplement existing screening strategies, such as the FIT test

STUDY DESIGN

Open-label, prospective, observational cross-sectional clinical performance study of the *in vitro* diagnostic device NK Vue



OBJECTIVES

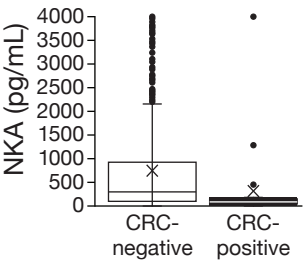
- To determine if there is a difference in NKA in subjects with cancer-negative colonoscopies versus those with pathologically confirmed colorectal cancer
- To determine the performance of NK Vue for the detection of colorectal cancer

METHODS

- 1 mL of blood was drawn from subjects prior to the colonoscopy
- Measurement of NKA using the NK Vue assay
- Pathological verification of histology samples
- Patient classification as follows: No evidence of disease, adenomatous polyps <10 mm, adenomatous polyps ≥10 mm, or CRC positive

NK VUE TEST PERFORMANCE

Comparison of NKA between subjects with pathologically confirmed CRC and those negative for CRC



Wilcoxon Mann-Whitney, p= .0002

NK Vue test performance (n=872)	CRC
NKA ≥ 200 pg/mL (%) (n)	0.6 (3)
NKA < 200 pg/mL (%) (n)	5.7 (20)
Sensitivity (%)	87.0
Specificity (%)	60.8
Positive predictive value (%)	5.7
Negative predictive value (%)	99.4
Odds ratio	10.3

NK Vue and FIT test performance (exploratory analysis) (n=170)

Test Results	Odds Ratio
NKA < 200 pg/mL	12.7
NKA < 200 pg/mL + FIT positive	41.3

SUMMARY

In a high risk population it was observed that:

- NKA is significantly lower in CRC subjects than in non-CRC subjects
- NK Vue has a high sensitivity (87%) and negative predictive value (99.4%) for CRC
- Subjects with NKA above 200 pg/mL have a very small chance (0.6%) of having CRC.
- Subjects with NKA below 200 pg/mL have an odds ratio of 10.3 for CRC i.e. those with low NKA are 10 times more likely to have CRC
- Subjects with low NKA and positive FIT test have an odds ratio of 41.3 for CRC. i.e. they were even more at risk of having CRC detected during colonoscopy

CONCLUSION

This study indicates a potential use of the NKA test in patients as a risk assessment tool for CRC in a high-risk population. This approach may potentially be used to stratify subjects on colonoscopy waiting lists and may also help to better manage resources

Follow-up studies in both high-risk and average-risk populations are needed to confirm the performance of the NKA test for CRC, either alone or in combination with existing fecal tests used for CRC screening

REFERENCE

Association Between Natural Killer Cell Activity and Colorectal Cancer in High-Risk Subjects Undergoing Colonoscopy

Jobin G, Rodriguez-Suarez R, Betito K.

Gastroenterology. 2017 Oct;153(4):980-987. doi: 10.1053/j.gastro.2017.06.009. Epub 2017 Jun 15.

Summary provided by NKMax Canada