

PURPOSE / OBJECTIVES

Crohn's Disease (CD) and Ulcerative Colitis (UC) are the result of a dysfunctional activation of both the acquired and innate systems in the gut. While their exact pathophysiology still needs to be fully uncovered, several lines of investigation have shown the importance of the innate immune system in inflammatory bowel disease (IBD). Previous studies in patients with IBD and colorectal cancer (CRC) showed a decreased number of peripheral natural killer (NK) cells and/or defective NK cell activity (NKA). Our aim was to measure NKA using a simple, new *in vitro* diagnostic device (NK Vue, ATGen/NKMAX) in the whole blood of IBD and CRC patients so that the test may eventually be used as a diagnostic tool to help prioritize colonoscopy.

MATERIAL & METHODS

In the present pilot study, whole blood was collected from subjects with newly diagnosed CD or UC with active disease or CRC within an hour after colonoscopy. Seventy patients were recruited (17 patients with CRC, 19 patients with CD, 12 patients with UC, and 22 age and sex-matched control patients). NKA was measured as the amount of interferon-gamma (the biomarker) released in plasma, and after visual assessment for active CD, UC or for CRC (confirmed subsequently by pathology). An NKA result was considered low at levels below 200 pg/mL, based on previously published results.

RESULTS

Median NKA in patients with CRC [196 pg/mL (IQR 31.0, 925.0)] was statistically lower than that of controls [763.0 (IQR 258.3, 1000); $p=0.03$]. The odds ratio (OR) for discriminating a CRC patient from a control using the NKA test was 4.86 (95%CI 1.22, 20.66; $p=0.045$) at the optimal cut-off of 260 pg/mL and 5.06 (95%CI 1.16, 17.61; $p=0.039$) at a cut-off of 200 pg/mL. Median NKA in CD patients (117 pg/mL; IQR 31.0, 248.0) was statistically lower than that of controls ($p=0.0012$). The OR for discriminating a CD patient from a control using the NKA test was 18.21 (95%CI 3.30, 88.81; $p=0.0003$) at the optimal cut-off of 411 pg/mL and 9.75 (95%CI 2.34, 33.60; $p=0.002$) at a cut-off of 200 pg/mL. For UC patients, the median NKA was not different from controls and the test was not able to distinguish a UC patient from a control patient.

- Decreased NKA (natural killer activity) is correlated with IBD activity and colon cancer.
- NK Vue is a diagnostic device which measures NKA in a sample of whole blood.
- This pilot study shows a significant difference in NKA in CRC and CD but not in UC patients compared to matched control patients after endoscopy findings.
- The use of NKA testing may help to assess the risk of CD or CRC prior to colonoscopy.

RESULTS

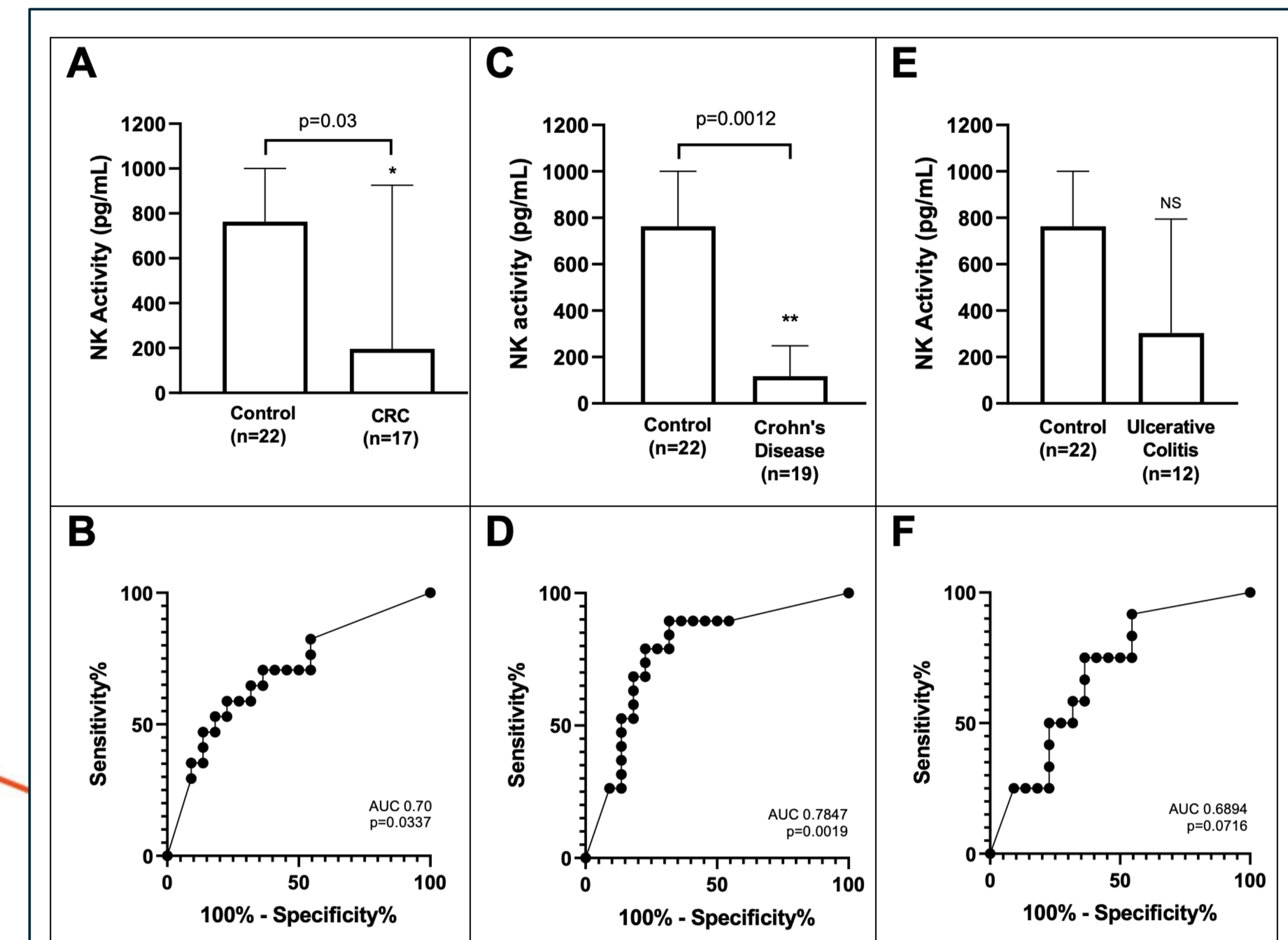


Figure 1: NK cell activity and ROC curves in Colorectal Cancer (CRC), Crohn's Disease (CD) and Ulcerative Colitis (UC) compared to colonoscopy-negative control subjects. A) Median NKA (pg/mL) with IQR shown for CRC patients compared to controls. B) ROC curve for CRC patients. C) Median NKA (pg/mL) with IQR shown for CD patients compared to controls. D) ROC curve for CD patients. E) Median NKA (pg/mL) with IQR shown for UC patients compared to controls. F) ROC curve for UC patients.

SUMMARY / CONCLUSION

NKA was found to be significantly reduced in CRC and active CD patients, compared to controls. NKA in active UC patients did not show a significant variation compared to controls. This information strengthens the notion that CD and UC, although they are both inflammatory conditions, rely on two different immunopathology mechanisms. The use of NKA testing may help to assess the risk of CD or CRC prior to colonoscopy.