

# High expression levels of circulating miRNA-618 and miRNA-203a-3p are associated with prolonged survival in patients with metastatic colon cancer

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## OBJECTIVES

Circulating microRNAs (miRNAs) are promising non-invasive biomarkers for colorectal cancer (CRC). The aim of the present study was to evaluate the role of five circulating miRNAs – miRNA-618, miRNA-26a-1, miRNA-15b-5p, miRNA-200c, miRNA-203a-3p which are involved in key cell signal processes in tumors such as proliferation, migration, and apoptosis. These miRNAs are thoroughly investigated in tumor tissue, but little is known regarding their levels of expression in the blood of patients with CRC.

## RESULTS

The circulating miRNA-618, miRNA-26a-1, miRNA-15b-5p, miRNA-200c, and miRNA-203a-3p were significantly overexpressed in CRC patients in comparison with healthy volunteers.

## METHODS

97 patients with colorectal metastatic disease before starting the chemotherapy and 80 healthy volunteers were investigated. miRNAs were isolated from serum samples by commercial kit. cDNA was generated from each sample by reverse transcription. All miRNA data were analyzed by normalization with constitutively expressed endogenous control U6. qPCR was performed and the relative expression of each miRNAs was calculated by using  $2^{-\Delta\Delta C_t}$  method.

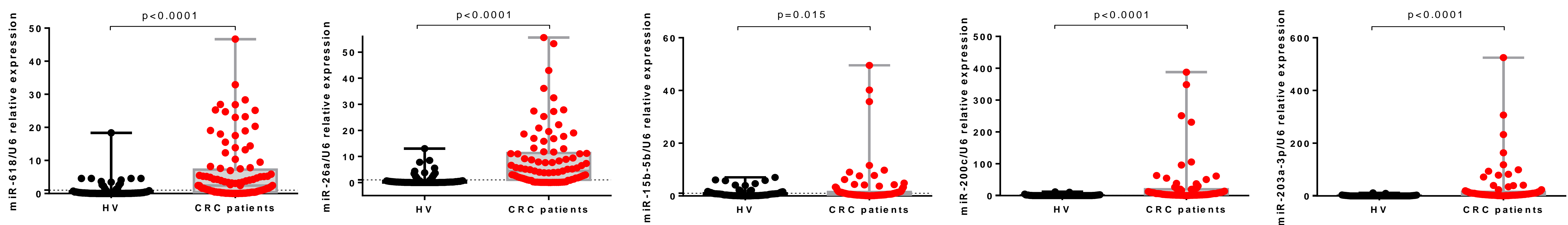


Fig 1. Relative expression of miRNA-618, miRNA-26a-1, miRNA-15b-5p, miRNA-200c, and miRNA-203a-3p in sera. miRNA expression was measured using qPCR in sera from healthy volunteers (HV, n=80) and CRC patients (n=97). U6 RNA was used as an internal control.

Patients with low levels of **miRNA-618** had significantly shorter mean overall survival (OS) of **14 months** (95% CI, 8.63-19.37) as compared to those with high expression - **21 months** (95% CI, 14.36-27.64). According to multivariate Cox proportional analysis low level of **miRNA-618** expressions were also associated with a shorter OS, HR=2.02 (95% CI, 1.24-3.29; p=0.005).

Patients with low levels of **miRNA-203a-3p** had a significantly shorter mean OS of **14 months** (95% CI, 8.81-19,19) as compared to those with high expression **20 months** (95% CI, 17.05-22.95). According to multivariate Cox proportional analysis low level of **miRNA-203a-3p** expressions were also associated with a shorter OS, HR=1.77 (95% CI, 1.08-2.91; p=0.025).

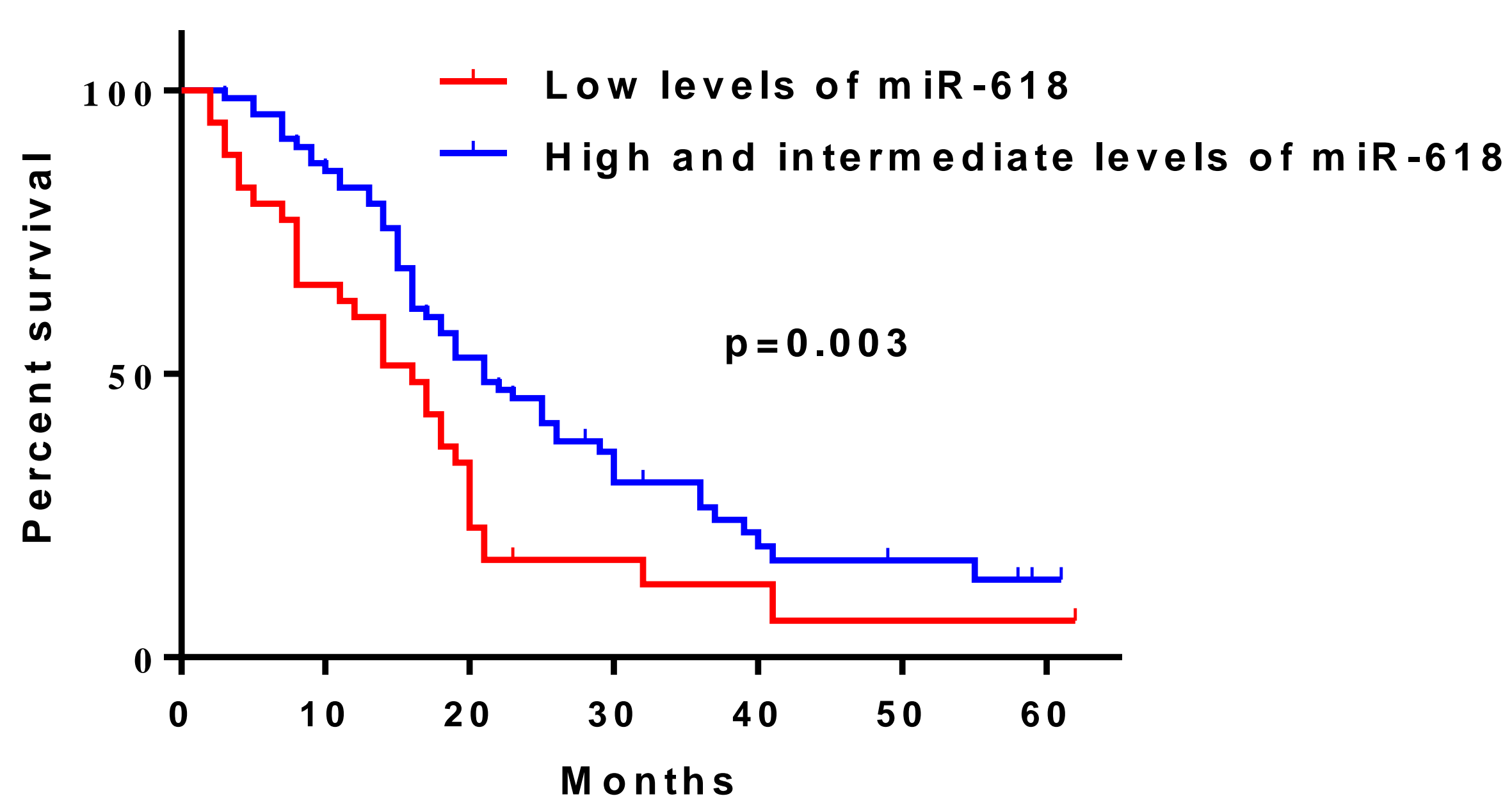


Fig 2. The Kaplan–Meier estimate of overall survival analysis on the basis of miR-618 expression in sera from 97 CRC patients.

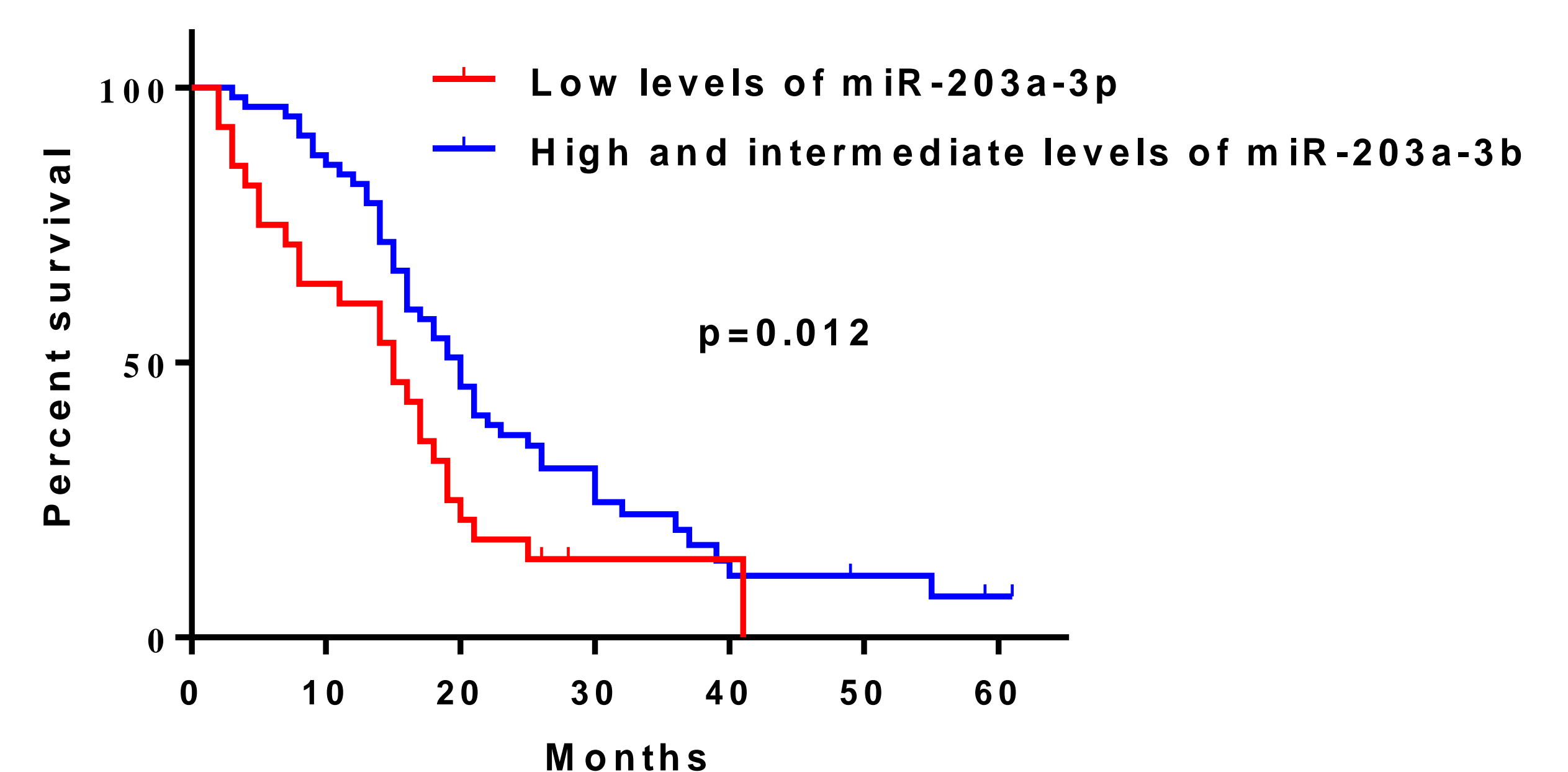


Fig 3. The Kaplan–Meier estimate of overall survival analysis on the basis of miR-203a-3p expression in sera from 97 CRC patients.

## CONCLUSIONS

It is known that overexpression of miR-618 and miRNA-203a-3p inhibited proliferation, migration, invasion and promoted apoptosis in CRC tumor tissues. There are they are significantly downregulated and are associated with poor survival in CRC patients. Our data suggest that investigation of expression levels of these two miRNAs in sera could be useful non-invasive prognostic biomarkers in CRC patients.

## Funding

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