

Expression of circulating microRNA-141 and mRNA of PTEN (Phosphatase and Tensin Homolog) in blood plasma of ovarian tumor and epithelial ovarian cancer patient

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ABSTRACT

Epithelial Ovarian Cancer (EOC) is the most lethal gynecological malignancies among woman. This disease is most frequently diagnosed at advanced stage due to the lack of specific symptoms and effective screening methods. Therefore, an adequate biomarker for early detection is required and might improve patient survival. MicroRNA is a small, non-coding RNA that regulates gene expression in post-transcriptional level. Several studies have shown the ability to detect microRNA in blood circulation, so microRNA might be used as a minimally invasive biomarker for EOC. microRNA-141 (miR-141) plays a major role in EOC by regulating the expression of several tumor suppressor gene. Previous studies have confirmed that miR-141 regulates PTEN gene directly by interacting with 3'UTR sequence of PTEN mRNA, and upregulation of miR-141 caused downregulation of PTEN expression in vivo. PTEN is an important tumor suppressor gene and its inactivation was found in various human cancers. PTEN is a protein with lipid phosphatase activity that negatively regulate PI3K-AKT signaling pathway, thus playing a important role in various cellular process such as proliferation, growth, cell survival, EMT, cell motility, and angiogenesis. Despite various studies have found that PTEN mRNA and protein expression is significantly downregulated

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in EOC tissue, little is known about the expression of PTEN mRNA in blood circulation of EOC patient, especially in Yogyakarta population.

The aims of this study isare to measure and investigate the correlation of miR-141 and mRNA PTEN expression in plasma of ovarian tumor patient and EOC patient. This cross-sectional study was performed using 50 samples, 25 blood plasma of ovarian tumor and 25 blood plasma of EOC were collected. Total RNA was isolated and reverse transcribed to obtain cDNA. The expression of miR-141 and mRNA PTEN were measured by quantitative real-time polymerase chain reaction assay (qPCR). The $2^{(-\Delta\Delta cq)}$ method was used to calculate relative quantification of miR-141 and mRNA PTEN using miR-16 as reference gene for microRNA and beta-actin mRNA as reference genes for PTEN mRNA.

Expression of miR-141 was significantly elevated in blood plasma of epithelial ovarian cancer patient compared to the ovarian tumor ($p=0.001$, fold change=7.59). Expression of PTEN mRNA was significantly downregulated in blood plasma of epithelial ovarian cancer patient compared to the ovarian tumor ($p=0.001$, fold change=11.63). There was a significant negative correlation between miR-141 expression and mRNA PTEN expression in blood plasma of epithelial ovarian cancer patient ($p=0.033$; $r=-0.428$).

MiR-141 and mRNA PTEN were expressed in blood plasma of ovarian tumor and epithelial ovarian cancer patient. There was a negative correlation between miR-141 and mRNA PTEN expression in blood plasma of epithelial ovarian cancer patient.

Keywords: Epithelial ovarian cancer, circulating microRNA, miR-141, PTEN mRNA