Introduction and objectives: Anoikis is a programmed cell death induced upon cell detachment from extracellular matrix. Anoikis resistance, is a critical mechanism in tumor metastasis. Studies in non-malignant and malignant cancer cell lines suggest that the expression of several molecules are altered in potentially metastatic cells, such as nitric oxide (NO). Cellular production of NO is catalyzed by nitric oxide synthase (NOS) enzyme and this reaction can be inhibited by L-N^G^-Nitroarginine methyl ester (L-NAME), a L-arginine analogues, which binds competitively to NOS, to attenuate the NO production. NO is accepted as an important player of cancer metastasis and is frequently found to be up-regulated in the tumor area. PI3K/AKT and Ras/Erk pathways are related to survival and cell proliferation, besides, also are directly related with eNOS regulation. While Akt/PKB active eNOS, MAP Kinase 1/2 (Erk 1/2) regulates eNOS activity through an as yet unclear phosphorylation process. This work aims to analyze the signaling pathways involved in the regulation of eNOS in endothelial cells resistant to anoikis (Adh-EC) and endothelial cells transfected with EJ-ras oncogene (EJ-ras EC).

Materials and Methods: NO Analyzer and Griess reaction were used to determine NO production; qPCR and Western Blot were used to analyze eNOS expression; Immunofluorescence was used to locate Akt and ERK in cells; Annexin V-FITC/PI staining was used to evaluate apoptosis rate. Cells were treated with L-NAME.

Results and Conclusions: Anoikis resistant and transfected endothelial cells shows an increase in NO production and eNOS expression, in relation to EC. Akt and ERK levels is increase after treatment with L-NAME in all cells linages. L-NAME treatment do not interfering in cell growth and apoptosis rate in Adh-EC and EJ-ras EC cells. These findings suggest that Akt and ERK are involved in regulation of eNOS in endothelial cells resistant to anoikis.

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Key words: Anoikis; endothelial nitric oxide synthase; signaling pathways.