

group ($p < 0.01$). Bcl-2 expression in the study group was significantly decreased compared with the control group ($p < 0.01$). p53 showed no significant differences between the two groups ($p = 0.791$). There were statistically significant differences in fistula failure between the study group and control group (26.7% versus 6.7%, $p = 0.038$). The association we have found between previously punctured veins and apoptosis indicates the role that venipuncture may play in the development of apoptosis. Patients with increased apoptosis showed an increased fistula failure, which is of importance for the improvement of the AVF procedure itself.

Keywords: native vein wall; arteriovenous fistula; hemodialysis; apoptosis; fistula failure.

THE ASSOCIATION OF *BIRC5* GENE POLYMORPHISM AND SURVIVIN EXPRESSION IN DIFFERENT TUMORS TYPES

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Survivin, encoded by *BIRC5* gene, belongs to the family of inhibitors of apoptosis (IAP) proteins. Survivin is an essential chromosomal passenger protein required for mitotic progression. It is also an inhibitor of apoptosis and can prevent caspase-mediated cell death. It is usually expressed in embryonic tissues and homozygous survivin deletion results in early embryonic death, showing its essential role in cell development, differentiation and homeostasis. In healthy organisms it is not expressed in differentiated tissues, while its expression is markedly increased in most cancers (including bladder cancer, lung cancer, breast cancer, stomach, esophagus, liver, ovarian cancers and hematological cancers).

In tumors its presence correlates with increased resistance to chemo- and radiotherapy, as well as worse survival rate. Although its expression is usually confined to G2-phase and mitosis, survivin is in cancer often expressed throughout the cell cycle.

At least 5 different splice variants of the survivin gene have been reported in humans so far (wild type, 2 α , 2B, 3B and deltaEx3). All survivin protein isoforms arising from the splice variants share the same N-terminus region, but differ in the carboxyl end. The transcript expression levels of various survivin isoforms have been significantly associated with clinico-pathologic characteristics in several cancers.

Several *BIRC5* polymorphisms in promoter and 3'UTR regions were studied in various types of cancer, and were found to be correlated with susceptibility (gastric, bladder and hepatocellular), survival (colorectal and breast) or age of onset (ovarian cancer).

In this study we investigated the role of *BIRC5* polymorphisms and survivin gene expression in several types of cancer. 74 normal samples, 48 oral and oropharyngeal squamous cell carcinoma (SCC) samples, 35 breast cancer (BC) samples and 40 ovarian carcinoma (OC) samples were typed for *BIRC5* polymorphisms using high resolution melting analysis and Sanger sequencing. For samples with available tumor tissues, either fresh frozen (48 SCC samples and 23 OC samples) or paraffin embedded (26 BC samples), survivin expression was measured with qPCR or immunohistochemistry. For OC samples, levels of different survivin isoforms were also determined.

19 polymorphisms were found, 7 were found in promoter region, 1 in 5'UTR, 4 in coding region and 7 in 3'UTR. 10 polymorphisms were found in all 4 groups, 5 in 3 groups, 1 in 2 groups and 3 in only 1 group of samples. Two of the polymorphisms that were found only in one sample each have not previously been reported. Both, one in exon 2B (c.221+1199G>A), and second, in 3'UTR (c.9349G>C) were found in SCC samples.

47 SCC samples showed survivin mRNA expression. 24 BC samples showed protein survivin expression. All 23 OC samples expressed wild type survivin, but isoform expression varied greatly. The highest expression of all splice variants was of survivin 2 α , then wild type survivin, followed by survivin deltaEx3 and survivin 3B. The lowest expression was of the splice variant survivin 2B, which was expressed in only 16 of 23 samples analyzed. All splice variants had higher expression in ovarian cancer compared to healthy Fallopian tube tissue.

Keywords: surviving; *BIRC 5*; squamous cell carcinoma; ovarian cancer; breast cancer.