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Aim: The aim of our retrospective study was to determine the influence of demographic and clinical characteristics of patients, initial stage of disease and tumor size on symptom period in children with malignant tumors.

Introduction: One of the main goals in pediatric oncology is timely diagnosis, cause it allows prompt and more effective treatment and significantly decreases the number of complications. The majority of children with malignant tumors have specific or non-specific symptoms certain time period before the diagnosis which can point towards malignant disease.

Methods: Our study included 296 children with malignant tumors, diagnosed and

treated between 2005 and 2016 in University Children's Hospital in Belgrade. Collected data included sociodemographic parameters, variety of symptoms and its duration, initial stage of disease and size of the tumor.

Results: The most frequent tumors were as follows: neuroblastoma, Hodgkin and non-Hodgkin lymphoma and kidney tumors. Non-Hodgkin lymphoma was diagnosed more frequently in boys, while Ewing sarcoma and primitive neuroectodermal tumors were seen mostly in girls. The majority was admitted at IV stage (30.1%) in opposite to 13.5% of patients in I stage. The average symptom interval was 87.7 days (median 46; SD = 164), from 5 to 2190 days. We have proven that following factors have significant effect on the extent of symptom interval: age ($p < 0.001$), type of tumor ($p < 0.05$), its localization ($p < 0.001$), specific symptoms ($p < 0.05$), and refferal from primary health care unit in comparison to secondary one ($p < 0.05$).

Conclusion: The results of our study give a new insight in symptom interval of children with malignant tumors in our country. More detailed comprehension of patients' characteristics, their diseases, healthcare system and their effect on symptom interval could significantly contribute to early diagnosis, as well as decreased number of complications at admission and during treatment.[1–6]

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PS069

Impact of prior malignancies on the outcome of colorectal cancer: Revisiting clinical trial eligibility criteria

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Aim: To study the impact of prior malignancies on the survival of subsequent CRC.

Introduction: Colorectal cancer (CRC) is the third most common cancer in the US.[1–3] Some studies have correlated a prior history of malignancy with an increased incidence of CRC. Patients with history of cancer are generally excluded in clinical trials. This practice, not only affects clinical trials accrual, but also limits the potential therapeutic options for this population. The rationale behind this exclusion is that a history of malignancy could potentially interfere with the study outcomes.[4] However, little is known about its real impact on survival of subsequent CRC.

Methods: We identified patients with CRC diagnosed between 1973 and 2008 using the National Cancer Institute's SEER database.[5,6] Outcomes of interest were overall survival and cause-specific survival of subsequent CRC in general, and specifically stage IV disease. Unadjusted Kaplan-Meier test and multivariable covariate-adjusted Cox models were used to assess the eligibility of enrollment of stage IV CRC patients in clinical trials.

Results: Overall, 550,325 patients with CRC were identified, of whom 31,663 patients had a prior malignancy. Both, history of prior non-leukemic malignancy and prior leukemia were associated with a worse overall survival (HR = 1.165 95% CI = 1.148–1.183, $P < 0.001$) and (HR = 1.825 95% CI = 1.691–1.970, $P < 0.001$), respectively. However, a history of any prior non-leukemic malignancy showed a favorable colorectal-specific survival (HR = .930 95% CI = .909–.952, $P < 0.001$). Analysis of stage IV CRC showed that a history of any prior non-leukemic malignancy was not associated with a significant difference in overall survival but having a history of leukemia showed a worse overall survival (HR = 1.535, 95% CI = 1.303–1.809, $P < 0.001$).

Conclusion: Clinical trials should take these results into consideration when including/excluding stage IV CRC patients with prior malignancies.

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PS071

Intervention of diabetes mellitus and metabolic risk factors in AMPK-PGC1α-SIRT3 pathway in the human corpus cavernosum

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Aim: This study aims to investigate the signaling pathway AMP-activated protein kinase (AMPK)-Peroxisome proliferator-activated receptor-gamma coactivator (PGC)1α-sirtuin (SIRT)3 in the human corpus cavernosum (HCC) between healthy individuals and those with cardiovascular disease risk factors (CVDRF).

Introduction: SIRT3 is a mitochondrial NAD+-dependent-protein-deacetylase involved in the regulation of cellular metabolism.[1,2] As a key factor in AMPK and PGC1-α activation in stress, the decrease in SIRT3 expression or activity is associated with diverse pathologies and aging. Actually, SIRT3 expression was found decreased in HCC of aged individuals with CVDRF.[3] CVDRF such as diabetes mellitus (DM), dyslipidemia, hypertension and obesity strongly associate to endothelial dysfunction, which early manifests as erectile dysfunction (ED).[4]

Methods: HCC's samples from individuals aged 40-60 years, submitted to programmed urological surgeries at Hospital São João-Porto, were divided in three groups (n = 4): (1)-controls without ED or CVDRF; (2)-DM patients; and (3)-patients with three or more CVDRF including DM. Dual immunolabelling of SIRT3 and superoxide dismutase (SOD)2 with alpha-actin was carried out. As well, levels of SIRT1, SIRT3, SOD2, PGC1α, NADPH oxidase (Nox)1, phospho-AMPK and AMPK were assessed by Western-blotting(WB).

Results: We observed SIRT3 and SOD2 expression in α-actin-labelled fusiform muscle cells in all groups. The semi-quantification by WB demonstrated a significant decrease in SOD2 expression in group 3 relatively to controls, as well as, an increased tendency of Nox1 and PGC1α and a decreasing trend in phospho-AMPK in groups 2 and 3. No differences in SIRT1 and SIRT3 were observed among groups.

Conclusion: This study suggests that CVRF including DM increase oxidative stress in HCC owning to a decrease in SOD2 expression and concomitant increment in Nox1. Further studies with an increased number of HCC samples will be necessary to elucidate the role of the AMPK-PGC1α-SIRT3 signaling pathway in the response to oxidative damage.[5]

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PS075

Examination of antiproliferative effects of the horseradish extracts

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Aim: The aim of the study was to investigate in vitro the antiproliferative effects of the horseradish juice and pulp using different solvents for the extraction.

Introduction: Horseradish (*Armoracia rusticana*, Brassicaceae) is a perennial herbal plant, which is widely used in human nutrition, as well as in a traditional medicine. Horseradish is a rich source of bioactive compounds such as isothiocyanates, that have proved to be significant antitumor agents.

Methods: Samples were prepared by the Kupchak extraction method, and the antiproliferative effects of the horseradish juice and pulp extracts were examined on the human tumor cell line MDA-MB-231 (ER–, human breast adenocarcinoma). Cell growth was determined by measuring the total protein by colorimetric sulforhodamine B assay. The obtained results (expressed as mean ± SD) were analyzed by Tukey HSD test and the differences were considered statistically significant at $p < 0.05$.

Results: According to the IC50 parameter (the concentration that inhibited the cell growth by 50%), as an important indicator of the antiproliferative effects, the most pronounced antitumor activity was observed for chloroform juice extract (IC50 = 5.52 ± 1.47 μg/ml). In addition, highly potent was chloroform pulp extract (IC50 = 19.44 ± 3.82 μg/ml), as well as the dichloromethane juice (IC50 = 26.50 ± 4.15 μg/ml) and pulp (IC50 = 26, 01 ± 2.45 μg/ml) extracts. On the other hand, significantly lower in vitro antitumor effect was noticed for the butanol pulp extract (IC50 = 114.52 ± 0.28 μg/ml). IC50 vales for butanol juice extract, as well as water juice and pulp extracts were higher than 500 μg/ml.

Conclusion: The obtained results suggest that *A. rusticana* is as a significant source of antitumor agents, especially liposoluble isothiocyanates and as such, it should be recommended for further use in a human nutrition and prevention of cancer.

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PS080

Contribution of the determination of numeric value of adc map in early detection of prostate cancer

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Aim: To define the range of ADC values for the absence of malignant disease, as well as to determine the threshold of ADC values for suspected prostate cancer.