ISSN 0354-8139
UDC 616-006

ARCHIVE OF ONCOLOGY

Founded 1993

Vol 17 Suppl 2
November 2009

Editor-in-Chief: Vladimir Baltić

http://www.onk.ns.ac.rs/Archive

Official Journal of the
ONCOLOGY INSTITUTE OF VOJVODINA
SREMSKA KAMENICA
SERBIA

Archive of Oncology publishes original articles describing clinical research on the cellular and molecular characterization, prevention, diagnosis, and therapy of human cancer. All submissions undergo peer review.

Founder, owner and publisher: Oncology Institute of Vojvodina, Institutski put 4, 21204 Sremska Kamenica, Serbia

By the decision No. Fi 81/07 issued by the Chamber of Commerce, Novi Sad, dated April 30, 2007, *Institute of Oncology Sremska Kamenica* was registered under the new name *Oncology Institute of Vojvodina*.

Archive of Oncology is covered by Biomedicina Serbica, Biomedicina Vojvodina, Biomedicina Oncologica, EMBASE/Excerpta Medica, ExtraMED, SCOPUS.

UDC 616-006
ISSN 0354-8139

DOI is assigned by Narodna biblioteka Srbije, Skerlićeva 1, 11000 Belgrade

Preparation for printing and printing:
Printing firm „Stojkov Štamparija d.o.o.“,
Stojkov Mihajlo, Laze Nančića 34-36, Novi Sad, Serbia

Circulation: 400

Novi Sad, 2009

Archive of Oncology is financed by the Oncology Institute of Vojvodina and partly by the Ministry of Science and Environmental Protection of the Republic of Serbia. The journal is registered by the Bureau for Intellectual Property of Serbia.

Archive of Oncology is published four times a year, in April, July, October and December.
Publication program in 2009: Volume 17 (four issues).

2009 subscription rates, Volume 17 (4 issues)*
Serbia: Individuals: Din. 3 240; Institutions: Din. 4 320
Europe: Individuals: EUR 40; Institutions: EUR 50
Elsewhere: Individuals: US$ 70; Institutions: US$ 100

* Before subscribing for the journal please contact the Editorial Office for getting an invoice.

CIP – Каталогизација у публикацији
Библиотека Матице српске, Нови Сад

616-006

ARCHIVE of Oncology / Supplement / editor in chief Vladimir Baltić. – Vol. 3, br. 1 (nov. 1995)– . – Sremska Kamenica: Institute of Oncology, 1995–. – 28 cm

Povremeno
ISSN 0354-8139

COBISS.SR-ID 45273858

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ARCHIVE OF ONCOLOGY
Vol 17 Suppl 2 November 2009

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KANCEROLOŠKA NEDELJA 2009.
Program za medicinske sestre

Petak, 13. 11. 2009.

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46th Annual Meeting of Oncology Section – Serbian Medical Association

Institute for Oncology and Radiology of Serbia, Belgrade (photo selected by Ljiljana Vučković Dekić)

OP 1

UDC: 616.348-006:616.351-006:615-085

Impact of new drugs and individualization of treatment approaches in metastatic colorectal cancer

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Key words: Colorectal Neoplasms; Neoplasm Metastasis; Antineoplastic Agents; Fluorouracil; Organoplatinum Compounds; Camptothecin; Treatment Outcome; Prognosis

Some important notices concerning colorectal cancer

Colorectal cancer is one of the most common human neoplasia. If diagnosed in its early stage this malignancy is curable with minimal morbidity and mortality. Unfortunately a significant proportion of patients present in advanced stage of the disease being either locally unresectable or metastatic. The colorectum can be divided in four different regions: ascending colon, transversal colon, descendent and sigmoid colon and the rectum.

From all of these regions metastases can occur either by lymphatic extension or by hematogenous spread or by implantation. In colon carcinoma the cancer cells metastasize through lymphatics along the major arteries, and the metastases reside in lymph nodes of the mesocolon. In rectal cancer there is a predictable course of lymphatic disease that reside at first in the perirectal lymph nodes at the level of primary tumor and afterwards involve the chain that accompany the superior hemorrhoidal veins. Discontinuous or skip metastases are less frequent.

Hematogenous spread occurs via the portal vein system. The first primary site of the hematogenous metastases is usually the liver. Skip metastases to the lungs without metastases in the liver are infrequent in colon cancer and proximal rectal cancer. Due to dual venous drainage, cancer of the distal rectum may spread either to the liver or directly to the lungs, bones, or central nervous system. The liver is the main site of the hematogenous metastatic disease and in about 40% of the autopsy studies liver is the only site involved.

Implantation metastases have been reported with tumor cells shed intraluminally but more often intraperitoneally from tumors involving and penetrating to the serosa. Distal rectal cancer rarely is the cause of peritoneal carcinosis.

Colorectal cancer with metastases in regional lymph nodes may be a curable disease when treated with surgery combined by adjuvant chemotherapy.

Colorectal cancer with a more disseminated abdominal lymphogenous spread or with intraperitoneal dissemination or which has metastatised hematogenicaly has not been considered as a curable disease. Nevertheless, patients with a limited number of liver metastases can be cured with surgery preceded or not by neoadjuvant chemotherapy.

The principal aim of chemotherapy in metastatic colorectal cancer

The principal aim of drug development in metastatic colorectal cancer is targeted to provide symptom relief, to increase the time to progression and to provide a prolonged survival, usually without intent of cure. In managing metastatic colorectal cancer patients we must individually decide whether our main aim is achievement of a response or disease control in general. Response is obviously the main target for patients that are considered for liver resection, and the advent of new drugs along with development of surgical techniques has increased the percentage of patients considered for liver surgery with a curative intent.

5-Fluorouracil: the old and classic drug

Until recently the only effective drug for colorectal cancer was 5-Fluorouracil (5-FU). Several trials have been performed in order to modulate its antitumor activity, since response rates with the single drug were rather low, although a limited percentage of long lasting disease control and long survivals were reported. The only apparently active potentiator of 5-FU activity remained Leucovorin. This was a small but important advance and the leucovorin-5-FU regimen in different dosages remained a standard approach to metastatic colorectal cancer. A further improvement was the introduction of continuous infusional 5-FU such as in so-called deGramont regimen; this regimen appeared to increase activity in comparison to bolus 5-FU administration and decreased toxicities. In fact the different 5-FU regimens were usually well tolerated although the main inconvenience was the infrequent but spectacular occurrence of non-hematological grade IV toxicities associated with bone marrow aplasia. This complication, at first poorly explained, proved to be the consequence of systemic diphosphopyridindexidrogenase (DPD) deficiency. Once resistance to 5-FU developed the only drug that remained for second line options was mitomycin C, a poorly effective and relatively toxic cytotoxic drug.

Changing aspect of colorectal cancer in the last decade

In the last decade the situation of metastatic colorectal cancer has dramatically changed with the advent of four new cytotoxic drugs, two peroral fluoropyrimidines (capecitabine and tegafur-uracil), oxaliplatin, and irinotecan. The addition of these new active drugs in addition to 5-FU gave additional options for combination chemotherapy and sequential treatments that resulted with a significant prolongation of disease control and survival in patients with metastatic colorectal cancer. Nevertheless even in a subcategory of patients treated with these new drugs the best response remained progressive disease. The game was therefore moved to the field of pharmacogenomics and pharmacogenetics. The problem became increasingly acute with the advent of additional two new drugs belonging to the so-called category of biologicals: cetuximab (Erbitux), a monoclonal antibody to the epidermal growth factor receptor (EGFR) and bevacizumab (Avastin), an antibody to VEGF; both drugs added an improvement to the overall efficacy of treatment of metastatic colorectal cancer but added a drastic increase in treatment cost. A question was therefore raised about defining the subcategory of patients who would benefit most from their use. So, the question of predictive markers of response to new drugs, both cytotoxics and biologicals, was raised and investigations were started to find best markers for predicting drug activity, drug toxicity, and drug resistance.

Capecitabine: the 5-FU prodrug

Capecitabine is a drug from the fluoropyrimidine family of compounds, belonging to the same group as 5-FU. In contrast to 5-FU, capecitabine does not have as native molecule cytotoxic properties. It shares the toxicity profile common to all fluoropyrimidines irrespective of their cytotoxic potential. This toxicity includes low-grade diarrhea, usually low-grade but occasionally troublesome palmo-plantar erythrodysesthesia (so-called hand and foot syndrome) and several other events with low clinical significance. Due to its prolonged administration in clinical practice, during which patients are for usually 14 days exposed to fluoropyrimidines it has additional side effects not usually observed with 5-FU which is usually administered for not more than 5 days successively. This includes interference with vitamin K metabolism and interference with vitamin K dependent factors of the prothrombin complex, and also hemolysis caused by alterations in red blood cell membrane (1). Capecitabine is administered peroraly. Its active principle is in fact 5-FU which is generated from capecitabine by thymidine phosphorylase (TP); this enzyme is present in small quantities in the intestinal wall, is present in insignificant quantities in normal cells, but may be hyperexpresed in cells of breast and colorectal cancers. Thus it is in fact a prodrug, with high bioavailability. When passing through the intestinal wall, a small quantity of 5-FU is generated, usually not enough to cause 5-FU related cytotoxic effects. In the normal cells and cells poor in Thymidine phosphorylase content the prodrug is not converted to its active principle. In cancer cells rich in thymidine phosphorylase the prodrug is metabolized to 5-FU which exerts its action only intracelulary. Capecitabine has an advantage over 5-FU in the fact that its toxicities are less DPD dependent. The result could be that it should be a drug of choice replacing 5-FU in patients with systemic DPD deficiency, since most of toxicities related to DPD deficiency would thus be avoided. However as capecitabine has to be converted to 5-FU in order to be active on cancer cells, and needs hyperexpresion of TP, cancers whose cells are poor in TP have limited possibility of intracellular 5-FU generation and capecitabine may prove poorly effective in such cases.

Oxaliplatin: a DACH platinum effective for colorectal cancer

Oxaliplatin belongs to the third generation of organoplatinum compounds used for treatment of human malignant disease. It belongs to the group of diaminocyclohexanoplatinums (DACH platinums) and is characterized by linkage of the platinum to the DACH ring. DACH ring confers to the cytotoxic drug several new properties. It is hydrophobic and thus the compound once infused into circulation achieves immediately a large distribution volume permitting wide contact with cancers cells. It is also lipophylic and thus passes readily through the cell membrane. Once fixed to DNA in the nucleus of cancer cells, the DACH ring presents a steric hindance to the action of DNA repair mechanisms. The drug makes part of different FolFOX regimens the most widely used being the FolFOX 4 regimen. It has a dose limiting toxicity, the cumulative neurotoxicity which asks for treatment arrest and which usually occurs after a cumulative dose of the drug of 800 mg/m2 has been reached. The intracellular fate of the drug is determined by enzymes of the gluthatione S-transferase superfamily and fast degradation of the drug may interact with its binding to DNA, resulting in poor activity of the drug.

CPT-11: a camptothecine active in colorectal cancer

The third new drug which proved to be a useful addition to the arsenal of drugs active for colorectal cancer is CPT-11 (or campto or irinothecan). It has no cross resistance to either 5-FU or Eloxatin. CPT-11 is in fact a pro drug and its active principle is designated as SN-38. SN-38 is responsible both for the anticancer activity and late toxicities of Irinothecan. SN-38 is the main intracellular metabolite of Irinothecan and its increased level in the plasma due either to individual variabilites or to deficient detoxation is associated to excessive toxicity pattern. SN-38 is inactivated and excreted through the process of glucuroconjugation. Drugs or metabolites that are also excreted by same mechanism tend to prolong the SN-38 half life in the plasma. So, for instance, patients with increased bilirubin levels (bilirubin is also excreted by glucuroconjugation) should not be treated with CPT-11 and the critical bilirubin level has been fixed at 25-50 mmol/L. The native CPT-11 molecule is responsible for early side effects such as early cholinergic diarrhea, as CPT-11 is a cholinergic stimulator; these side effects if excessive can be prevented by anticholinergic such as atropine. SN-38 is responsive for late side effects that are more troublesome and which include a wider range of events including secretory diarrhea and bone marrow toxicity. Degradation of SN-38 is dependent upon activity of different UDP-glucuronosyl transferases and their genetic polymorphisms may be involved both in activity and toxicity of the drug.

Molecular basis for rational use of antitumor drugs in metastatic colorectal cancer

We now know that the new drugs such as oxaliplatin and CPT-11 are more active in colorectal cancer than 5-FU in single drug setting either in relation to response rate and possibly survival benefit. But we also know that there are patients treated with 5-FU that achieve a long survival, in excess of 2 years. We also know that there are patients treated with either oxaliplatin or CPT-11 who do not achieve disease control with these two drugs and whose best response is progressive disease.

So, the question has arisen whether we can or can not predict efficacy of any of the three drugs by any means in order to individualize chemotherapy in a given patient, in order to achieve the optimal result.

Pharamacogenomics and pharmagonetics are starting to give us a clue concerning this particular topic.

Molecular basis for rational use of fluoropyrimidines

It appears that both tumor dihydropyrimidin dehidrogenase (DPD) and thymidine synthetase (TS) are good predictors for 5-FU activity. A significant increase in TS expression score was observed in 5-FU sensitive colorectal cancers compared to 5-FU resistant ones. Although the role of DPD expression in cancer 5-FU sensitivity remained somewhat controversial it now appears that patients with low DPD expression have longer disease free interval or longer disease control with 5-FU than patients with high DPD expression (2). DPD expression in normal cells is a significant factor determining 5-FU toxicities, patients with DPD deficiency in normal cells tending to exhibit life threatening toxicities when treated with 5-FU (3). However the DPD contend in normal and cancer cells in the same individual need not to be identical and there appears to be individuals with adequate DPD content in normal cells and low expression of DPD in cancer cells. By retrograde analysis it has been shown that patients with low tumor DPD and high tumor TS treated with 5-FU only can achieve survival of over 24 months.

The situation might not be identical with peroral fluoropyrimidines. Tegafur-Uracil shares apparently the same pattern with 5-FU concerning cancer cell levels of DPD and TS. Capecitabine could be presumed to be inferior to 5-FU in patients with low TP levels because TP is necessary for conversion of this pro drug into 5-FU that is its active principle. On the other hand, the S-1 compound (combination of tegafur-CDHP and potassium oxonate) is more active than 5-FU in cancers with a high DPD activity due the fact that CDHP is a potent inhibitor of DPD (4).

Thus it appears that, based on the tumor level of DPD, TP, and TS, we can make the choice between different fluoropyrimidines best suitable for a particular patient.

Molecular basis for rational use of oxaliplatin

Members of the glutathione S-transferase (GST) superfamily are important in cellular defense mechanisms. These enzymes attach reduced glutathione to electrophilic groups in a wide variety of toxic compounds, including chemotherapeutic agents. Certain polymorphisms in GSTs are associated with changes in enzyme activity, sensitivity to chemotherapy, and overall patients' survival (5). There are three subclasses of GSTs, designated as P-1, T-1, and M-1. The GST P-1 has been shown to be associated with slower or faster inactivation of oxaliplatin in cancer cells and thus directly related to its activity concerning disease control. There are three variants of GST P-1 differing in only one amino acid residue in the position 105. These three variants determine three phenotypes: the homozygous isoleucine/isoleucine phenotype, the homozygous valine/valine phenotype, and the heterozygous isoleucine/valine phenotype. This genetic polymorphism has been found to have a profound influence on disease control and survival in patients treated with oxaliplatin.

In a retrospective study conducted on patients progressing on 5-FU and subsequently treated with oxaliplatin the impact of genetic polymorphism of GST P-1 on the survival was analyzed. Patients homozygous for the isoleucine/isoleucine phenotype had a median survival of 7.9 months, while those homozygous of the valine/valine phenotype had a median survival of 24.9 months. The heterozygous patients, i.e. those of the isoleucine/valine phenotype had a median survival which was intermediary i.e. 13.3 months.

Thus determination of the GST P-1 might have a crucial impact on choice of patients likely to respond to oxaliplatin and to exclude from this treatment the ones that should have no benefit from it.

Molecular basis for rationale use of CPT-11

Although the results are still preliminary there appears to be a relationship between UDP-glucuronosyltransferase (UGT) and activity and toxicity of CPT-11 (6).

The impact of the polymorphism of two members of this family, UGT1-A7 and UGT1-A9 was analyzed in relation to activity and toxicity. Low enzyme activity of the UGT1-A7 genotypes (UGT1-A7 2/2 and UGT1-A7 3/3) was associated with antitumor response and lack of severe gastrointestinal toxicity. In the UGT1-A9 family the UGT1-A9-118 genotype was significantly associated with reduced toxicity and increased response. UGT1-A1 and UGT1-A6 do not appear any impact on activity. However patients who are either homozygous or heterozygous for UGT1-A1- 28 appear to have a significant risk of toxicity by CPT-11.

It appears that determination of UGT1-A7 and UGT1-A9 polymorphism might predict at least toxicity to CPT-11 and perhaps enable us to select patients likely to have a good probability of response to CPT-11 without significant toxicities related to SN-38 (7).

The good and bad prognosis patient with metastatic colorectal cancer

It is perhaps too early to speculate about the prognostic significance of molecular markers in predicting outcome of patients with metastatic colorectal cancer.

Perhaps, it is not.

We could conceive that a patient whose tumor has a high TS content, low DPD content, who is homozygous for the valine/valine phenotype of the GST P-1 and with low enzyme activity of the UGT1-A7 should be a good prognosis patient: its median survival on 5-FU could be over 24 months, on oxaliplatin again over 24 months and this patient would have a good chance of having a therapeutic response to CPT-11 without excessive toxicity.

On the other hand a patient whose tumor has a low TS content and a high DPD content, who is homozygous for the isoleucine/isoleucine phenotype would have a poor chance of response to 5-FU and shall be probably resistant to oxaliplatin. If this patient is in addition homozygous to UGT1-A1- 28 he would have a significant risk for severe toxicity on CPT-11. This patient would be a classic poor prognosis patient even with the most recent drugs.

The biologicals in treatment of colorectal cancer

At the moment there appears to be at least three different targets that could be attacked by available biologicals: the intracellular part of the EGFR, prone to attack by small molecule tyrosine kinase inhibitors; the extracellular part of EGFR that can be blocked by monoclonal antibodies; and the tumor released vascular endothelial growth factor (VEGF) that is critical for the development of specific tumor blood vessels.

Two small molecular weight molecules with selective tyrosine kinase inhibition properties directed to EGFR are available on the market: ZD1839 (Iressa) and OSI-774 (Tarceva). These drugs are orally administered and are reported to induce tumor stabilization in previously treated patients with metastatic colorectal cancer. Addition of these two drugs either to Oxaliplatin or CPT-11 does not appear to increase the specific toxicity of these cytotoxic agents. Unfortunately neither it does add to their activity (8).

A recent advance is represented by bevacizumab (Avastin), a monoclonal antibody against VEGF that has own promising pre clinical and clinical activity in metastatic colorectal cancer, especially in combination with cytotoxic drugs. Addition of bevacizumab to the CPT-11 + 5-FU/LV regimen in previously untreated patients with metastatic colorectal cancer has prolonged survival from 15.6 months (patients treated with CPT-11 + 5-FU/LV only) to 20.3 months. The response rate was also positively affected as well as duration of response in responders, and the drug found its way to neoadjuvant combinations for borderline respectable metastatic liver disease.

Another recent advance is represented by cetuximab (Erbitux), a monoclonal antibody that binds to the extracellular part of EGFR, thus blocking its activity. In combination with CPT-11 a proportion of heavily pretreated patients displayed response or stabilization thus adding a third or fourth treatment line in colorectal cancer. Its activity in first line treatment is under investigation but the results in a defined subpopulation of patients are very promising. Its activity is highly dependent on several molecular markers.

Markers predicting activity of biological agents

At the moment there are no validated biomarkers to predict the efficacy of Bevacizumab in colorectal cancer. In breast cancer there are data that point to the possibility that VEGF genetic variations may be linked to improved survival of patients with breast cancer treated with Bevacizumab and chemotherapy. Patients with genetic variations VEGF-2578 AA and VEGF-1154 A showed better overall survival than those with alternative genotypes (9). Unfortunately no such relation has been proved for colorectal cancer.

Circulating endothelial cell monitoring in metastatic colorectal cancer patients treated with first line bevacizumab based combinations has been studied in at least one randomized phase II study in order to establish a possible relation to response. The results indicate that the base line and end-of-cycle 1 circulating endothelial cell levels may predict tumor control in patients with metastatic colorectal cancer starting Bevacizumab- including chemotherapy (10). However, results require further validation and at the moment circulating endothelial cell level should not be used as a predicting factor in clinical practice.

The predictors of activity for cetuximab are far better known. Their use in clinical practice is mandatory. The EGFR membrane density has been shown to be irrelevant to decision whether to apply Cetuximab or not. Moreover even tumors that appear to be EGFR negative with available techniques have the potential to respond to Cetuximab in both first line and salvage setting. The interpretation of this finding may be that binding of the drug to even minimal amount of EGFR, undetectable with available techniques, may have impact on cancer cell survival.

The situation with K-Ras and BRAF markers are clearer. Both molecular factors are involved more or less directly in the EGF signaling pathway. In the presence of wild type K-Ras and BRAF blocking EGFR directly interferes with the pathway. If either of them is mutated the signaling pathway bypasses the usual sequence and blockade of EGFR is ineffective, and in consequence, the effect of cetuximab is wiped out.

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OP 2

UDC: 616.351-006:615-085:615.849.1

Chemoradiation with capecitabine and mitomycin c in preoperative treatment of locally advanced rectal cancer

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Key words: Rectal Neoplasms; Treatment Outcome; Preoperative Care; Combined Modality Therapy; Colorectal Surgery; Radiotherapy, Adjuvant; Chemotherapy, Adjuvant; Mitomycin; Antineoplastic Combined Chemotherapy Protocols

Background

In recent years, several reports of preoperative chemoradiation in respectable locally advanced rectal cancer have been published. These reports showed an interesting rate of negative pathologic specimens (9%-29%), an increased proportion of sphincter-saving surgical procedures (up to 66- 85% of patients) and low incidence of acute toxicity (2- 19%) (1,2). The rationale for combining cytotoxic agents and radiotherapy is based on ability of some drugs to act as enhancer of radiotherapy (2).

The purpose of this study was to evaluate toxicity and treatment results of preoperative capecitabine plus mitomycin C and radiation therapy in patients with locally advanced rectal cancer.

Material and methods

From October 2006 to April 2008, an open-label, nonrandomized, phase II study was conducted in the Institute for Oncology and Radiology of Serbia. The primary endpoint of this study was to evaluate the pathological complete response (pCR). Secondary endpoints were clinical response and toxicity.

Inclusion criteria were: minimum age of patients 18 years, histological confirmed, locally advanced stage II (T3/ T4, N0, M0) and stage III (T3 /T4, N1/2, M0) rectal adenocarcinoma of up to 16 cm from the anocutaneous line; no pretreatment except formation of an artificial anus (e.g. due to immanent intestinal obstruction); ECOG (Eastern Cooperative Oncology Group) status ≤ 2; sufficient bone marrow, liver and, renal function.

Patients were assessed at baseline by digital rectal examination, total colonoscopy with biopsy of the rectal tumor and determination of the distance between the lower edge of the tumor and the anocutaneous line, pelvic NMR, abdominal CT, transrectal ultrasonography, chest X ray.

Preoperative radiochemotherapy was started in the same day. Capecitabine 825 mg/m^2/d p.o., on days 1-35, splitting the total daily dose into 2 separate dose; mitomycin C: 7 mg/m^2 IV, on days I and 29 as a two-hour infusion in 500 ml glucose 5%.

Radiotherapy began on day 1 of chemotherapy after administration of mitomycin C; it is performed conventional at a daily dose of 1.8 Gy, at the reference point according to ICRU 50/62 once per day and five times per week, in 25 fractions over a period of 5 weeks, until a total reference dose of 45 Gy was reached. Radiotherapy was delivered with high-energy photons (15, 18 MeV) on linear accelerators.

Five to six weeks after preoperative treatment, before surgery, restaging was performed. Treatment response was evaluated after 5-6 weeks after radiochemotherapy completion according to the RECIST criteria (3). NCI-CTC criteria were used for toxicity grading (4).

Dependent of tumor stages determined by histopathology, after surgery, patients received adjuvant therapy according to hospital routine practice.

After operation, standardized histopathological examination was done with assessment of tumor regression in accordance with a tumor regression grading method established by Dworak (5): grade 0: no regression; grade 1: minimal regression; dominant tumor mass with obvious fibrosis and vasculopathy; grade 2: moderate regression; fibrotic changes dominate with few tumors cell nests easily to locate; grade 3: good regression; very few isolated tumor cells that are hard to find under the microscope, in predominantly fibrotic tissues and pools of mucus. Grade 4: complete regression: no tumor cells, only fibrotic tissue. Responses were thus defined as complete (grade 4), major (grades 3 and 2), or minor (grade 1).

Follow-up procedures were performed every 3 months within the first 2 years and every 6 months in years 3-5.

Results

The study included 49 patients. The median follow-up was 18 months (range 6- 29 months). All 49 enrolled patients were analyzed for clinical response, histopathological response, toxicity, overall survival, and disease-free survival. The median age was 52 years, with the baseline ECOG status 0 or 1. The T3 stage at diagnosis was in 34 (69.4%) patients and T4 in 15 (30.6%) patients. Positive lymph nodes were diagnosed in 28 (57.1%) patients. In all patients tumor was localized in distal (36 patients) and middle third part (13 patients) of rectum.

Confirmed objective clinical tumor response was seen in 40 (82%) patients (95%CI 0.69-0.90) calculated on an intention-to-treat basis. Complete response was noticed in 10 (20.4%) patients, partial

response in 30 (61, 2 %) patients and stabile disease in 9 (18, 4%) patients. No patient showed disease progression.

After evaluation on chemoradiotherapy, all patients underwent surgery. R0 resection was performed in 46 patients (93.9%) and R1 in 3 patients (6.1%).

Histopathological complete response was seen in 8 (16%, 95%CI 0.09-0.29) patients, major response was noticed in 24 (49%) patients and minor response in 14 (29%) patients. Histopathological response was not seen in 3 (6%) patients. Out of 49 patients, who underwent surgery, 24 patients (49%) had positive lymph nodes (20 patients had pN1 and 4 patients had pN2).

Tumor regression grade was assessed in all patients. Tumor regression rate are presented in Table 1.

Table 1. Incidence of tumor regression rate determined by histopathology

Mitomiycin C/Capecitabine/Radiotherapy		
	No. of cases N=49	%
Grade 4	8	16.3
Grade 3	6	12.2
Grade 2	18	36.7
Grade 1	14	28.7
Grade 0	3	6.1

Tumor downstaging was noticed in 26 (53.1%) patients.

Almost all patients received >90% of planned dose intensity for both drugs (capecitabine 92%, rang 69-108; mitomycin C 94%, range 54-105). Out of 49 patients, toxicity grades 1-4 were diagnosed in 35 (71.4%) patients. Radiotherapy was temporarily interrupted in one patient due to diarrhea grade 3 for 7 days and all patients completed radiotherapy. Chemotherapy was definitely stopped in 2 (4.1%) patients. Hematological toxicity was noticed in 14 (28.6%) patients, and nonhematological in 33 (67.3%) patients. The most common non-hematological side effects were dermatitis noticed in 29 (59.2%) patients and diarrhea in 15 (30.6%) patients. One-year disease-free survival was 93.3%, and two-year disease-free survival was 82%. One-year survival was 97.7%. Overall, 5 of 49 patients relapsed.

Discussion

Searching through literature (Medline), we did not find published clinical study that investigated preoperative radiotherapy combined with capecitabine and mitomycin C. There are some studies which investigated combinations of 5-FU and mitomycin C in preoperative settings combined with radiotherapy. Our results showed that preoperative radiotherapy with capecitabine/mitomycin had clinical tumor response rate of 82%, pCR of 16%, and downstaging rate of 53 %, with very acceptable treatment tolerance.

In FUMIR study (6), 83 patients were treated with mitomycin C, 10 mg/m2 day 1, plus 24h continuous infusion IV 5-FU 1000mg/m2 days 1-4, and concurrent radiotherapy with tumor dose of 37.8 Gy, conventionally fractionated 1.8 Gy per day, 5 times per week. Almost all patients, 98%, had T3 tumors. Response rate was 77% and pCR 8%. Tumor downstaging was reported in 57% of patients. Hematological toxicity grade 3/4 was noticed in 12% of patients. Treatment was temporarily interrupted in 11% due to acute complications. One of recent studies which investigated combination of 5-FU and mitomycin C in neoadjuvant settings was published by Chau and coauthors (7) 36 patients received protracted venous infusion 5-FU (300mg/m2/day for 12 weeks) with mitomycin (7 mg/m2/day IV bolus every 6 weeks) and beginning on week 13, 5-FU was reduced to 200 mg/m2/day and combined with concomitant radiotherapy with 50.4 Gy. Postoperatively, patients received 12 weeks of mitomycin and 5-FU at the same preoperative doses. There was no grade 3 and 4 hematological toxicity. Nine patients (25%) had grade 3 and 4 nonhematological toxicity such as diarrhea, stomatitis, infection, and hand-foot syndrome. Response rate was 81%. Pathological CR was find in one patient, 25 patients (74%) had down-staging of their primary tumor on histological examination. Preoperative radiotherapy with capecitabine/mitomycin in our study showed higher pCR rate and favorable toxicity profile (especially hematological toxicity) in comparison to results obtain in studies that combined preoperative radiotherapy with 5-FU/mitomycin.

These phase I/II studies, including our study, suggest higher pCR compared with 5-FU based chemoradiotherapy alone. However, some studies have shown that increased pCR leads an increase in acute toxicity, and data on long-term toxicity are not yet available (8,9). Phase III trials are necessary to determine whether these novel combination regimens, including capecitabine/mitomycin regimen, offer an advantage compared with 5-FU based combined modality protocols. Regarding these different possibilities and combinations of cytotoxic drugs, the future challenge in the treatment of advanced rectal cancer is to identify and select patients for the appropriate treatments according to predictive and prognostic molecular markers and further investigations with monoclonal antibodies.

Conclusion

Preoperative chemoradiation with capecitabine and mitomycin C appeared to be effective treatment combination with safety application and low toxicity. Further phase III studies are necessary.

Acknowledgements: This study was supported by a grant from the Ministry of Science and Environmental Protection of Serbia (Project No. 145059).

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OP 3

UDC: 616.348-006:616-089.8:615.38

News in treatment of peritoneal carcinomatosis from colon cancer by cytoreductive surgery and hyperthermic perioperative intraperitoneal chemotherapy

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Key words: Colorectal Neoplasms; Chemotherapy, Cancer, Regional Perfusion; Hyperthermia, Induced; Peritoneal Neoplasms; Carcinoma; Intraoperative Period; Combined Modality Therapy; Surgery

Peritoneal involvement in colorectal cancer occurs in approximately 30% of patients. Approximately 8% of patients are diagnosed with synchronous peritoneal dissemination at the time of primary colorectal surgery and 25% of patients have recurrence confined to the peritoneal cavity (1).

Systemic chemotherapy treatment alone is no longer appropriate for patients with limited peritoneal dissemination from a primary or recurrent colon cancer. The surgical management of peritoneal surface malignancies of colonic origin with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) has been clearly defined and continues to improve.

Better surgical techniques that include peritonectomy procedures, standardized methods to deliver intraoperative hyperthermic intraperitoneal chemotherapy and better patient selection criteria, have resulted in a significant improvement in survival and in morbidity and mortality of the surgical management of this particular group of stage IV colon cancer patients.

Sugarbaker and colleagues (1990) proposed cytoreductive surgery and perioperative intraperitoneal chemotherapy as a definitive treatment for peritoneal dissemination from appendiceal neoplasms and diffuse malignant peritoneal mesothelioma (2-4). Better surgical techniques that include peritonectomy procedures, standardized methods to deliver intraoperative hyperthermic intraperitoneal chemotherapy and better patient selection criteria, along with the strong treatment rationale and superior results when compared to historical controls, have lead to the establishment of numerous treatment centers in the United States and Europe. Over the last decade, an increasing number of international treatment centers have published their prospective results using cytoreductive surgery and HIPEC in the management of peritoneal surface malignancies of colorectal origin. In 2003, the Dutch group conducted a randomized controlled trial comparing systemic chemotherapy with cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy and this trial clearly demonstrated the superiority in survival of the combined treatment group (5). In 2004, a multi-institutional registry study from 28 international treatment centers showed that the median survival was 19 months and 3-year survival was 39% after cytoreductive surgery and HIPEC for 506 patients with colorectal peritoneal carcinomatosis (6).[1]

An analysis of evidence indicates improvement of survival and potential for cure in patients with low volume metastatic adenocarcinoma of colonic origin limited to the peritoneal cavity using cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC). However, as pointed out by Yan et al in a recent systematic review of the quality of evidence in 14 rigorously selected series, there were 2 randomized controlled trials, one randomized comparative study, and 11 observational studies without control groups, including one multi-institutional study (7). In addition, the indications for, the technique of HIPEC, the drugs used and the degree of heat, vary among physicians using these methods of treatment.

Preoperative evaluation

Long-term survival can only be achieved by cytoreductive surgery and HIPEC when a complete cytoreduction is accomplished. Proper patient selection remains a crucially important aspect in the treatment of patients with peritoneal dissemination from colorectal cancer. Review of the data in multiple series shows that those patients that have an incomplete removal of their peritoneal dissemination have a median survival of about 6 months and therefore these patients do not benefit from a surgical procedure (8,9).

Once a patient has been diagnosed with colorectal cancer with peritoneal involvement, the work-up usually includes a complete colonoscopy as well as a CT scan of the chest, abdomen, and pelvis with maximum oral and intravenous contrast to evaluate the extent of peritoneal dissemination. A PET scan can be considered if there is any question of extra-abdominal disease. Review of two published series trying to address the diagnostic accuracy of the CT scan as an imaging modality can be summarized by stating that the detection of peritoneal carcinomatosis by CT scan is only moderately useful and that it has severe limitations in detecting small peritoneal implants, especially in the small intestine. In addition, CT scan was considered of limited value in selecting colorectal patients with peritoneal carcinomatosis, who will not benefit from cytoreductive surgery with HIPEC (10,11).

The role of abdominal laparoscopy in the pre-treatment evaluation of peritoneal carcinomatosis

Garofalo et al. achieved full laparoscopic Peritoneal Cancer Index assessment in 96/97 cases, while only 2/96 cases were under staged. There was a good correlation between the open successive surgery data and the laparoscopic Peritoneal Cancer Index. There was no mortality and no neoplastic colonization at the trocar port site. Patients with massive involvement of their small bowel or mesentery by staging laparoscopy should be considered not amenable for peritonectomy. They considered laparoscopy a useful tool in peritoneal surface malignancies. It allows direct visualization even of small cancer nodules and provides a reliable assessment of the feasibility of peritonectomy (12).

A group of French investigators also evaluated the role of explorative laparoscopy to evaluate candidates for complete resection of peritoneal carcinomatosis combined with hyperthermic intraperitoneal chemotherapy (HIPEC). Eleven patients planned to undergo a cytoreductive surgery + HIPEC underwent an explorative laparoscopy. Laparoscopic evaluation was successful in all 11 patients (13). The conclusion was that laparoscopic scoring of peritoneal carcinomatosis is accurate to assess the complete resectability of peritoneal carcinomatosis in patients for which there is inadequate or contradictory information concerning disease extent.

Variables associated with the increased chances of having a complete cytoreduction

Complete cytoreduction means that no macroscopic residual disease was left after the operative procedure. The following are clinical and radiographic variables that are usually associated with the increased chances of achieving a complete removal of an entire tumor greater than 2.5 mm:

(1) ECOG performance status two or less;
(2) No evidence of extra-abdominal disease;
(3) Up to three small, resectable parenchymal hepatic metastases;
(4) No evidence of biliary obstruction;
(5) No evidence of ureteral obstruction;
(6) No evidence of intestinal obstruction at more than one site;
(7) Small bowel involvement: no evidence of gross disease in the mesentery with several segmental sites of partial obstruction;
(8) Small volume disease in the gastro-hepatic ligament (14).

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

Cytoreductive surgery will include peritonectomy procedures in order to remove all visible tumors. If a complete cytoreduction, CC-0/CC-1, by the completion of cytoreduction score or a R0/R1 by the R scoring system is achieved, then the patients will undergo hyperthermic intraperitoneal chemotherapy (HIPEC) with mitomycin C (15– 35 mg/m^2) with a target intraperitoneal temperature of 39–42^{0}C for 60–120 min. Whether an open or closed method for the chemotherapeutic perfusion is used, and whether or not early post-operative intraperitoneal chemotherapy (EPIC) with 5 days of 5-FU is used, will be the surgeon's preference. In those patients with symptomatic ascites in whom an adequate cytoreduction could not be achieved, HIPEC could be performed at the discretion of the surgeon with the intention of palliating the intractable ascites. Although mitomycin C is the most commonly used drug, oxaliplatin is being used more frequently with very promising results.

Survival

There are two prospective randomized controlled trials (RCT), one non-randomized comparative study and numerous observational studies regarding clinical an oncological outcome of patients with peritoneal carcinomatosis arising from CRC. Verwaal et al. reported a disease- specific survival of 22.2 months after additional CRS and HIPEC vs. 12.6 months after standard systemic treatment with 5-FU and leucovorin (8,15).[8,2] In patients with complete macroscopic cytoreduction (CCR-0/1), median survival was 48 months and 5-year survival rate was 45%, respectively. The second RCT was closed after inclusion of only 35 patients during a 4-year accrual period. The 2-year survival rates were 60% in both arms (16).[3] In the comparative study published by Mahteme et al., the median survival in the HIPEC group was 32 months vs. 14 months in the control group. 5-year survival rates were 28% and 5% respectively (17). In the observational studies, the overall median survival ranged from 15 to 32 months and from 28 to 60 months after complete macroscopic cytoreduction (CCR0-1), respectively (18).

Conclusion

The current evidences suggest that cytoreductive surgery combined with perioperative intraperitoneal chemotherapy is associated with an improved survival, as compared with systemic chemotherapy for peritoneal carcinomatosis from colorectal carcinoma.

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OP 4

UDC: 616.329-006:615.849.1:615.38

Preoperative chemoradiotherapy in esophageal cancer

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The results of treatment modalities in esophageal cancer remain inconclusive. We report preliminary results of our study with combined treatment. This prospective, multicentric, single-arm phase II study is a part of the Ministry of Science Project No 145059. The primary objectives are evaluation of histopathological tumor regression (TRG), clinical response rate and toxicity. Secondary objectives are resectability rate, disease-free survival and overall survival. From September 2006 to August 2009, 56 patients with squamous cell esophageal cancer were enrolled. All of them received chemoradiotherapy with cisplatin plus infusion high-dose 5-FU/LV in 4 cycles every 14 days, and a total reference irradiation dose up to 50.4 Gy. After the clinical assessment, medically operable and fit patients underwent surgery. Up to now, 52 patients are evaluated (median age 56 years, 8 female and 44 male patients). All patients had T3 (46%) and T4 (54%) tumor stage (clinical stage II: 11 patients, stage III: 41 patients). Total reference irradiation dose was applied in all patients. Twenty-nine patients received all 4 cycles of chemotherapy. In 23 patients, chemotherapy was interrupted due to high-grade toxicity. During the treatment, most common toxicity was hematological (grade 3 and 4 noted in 14 patients). Non-hematological toxicity included dermatitis, dysphagia, nausea, vomiting, diarrhea and cardiotoxicity and it was mostly low grade (I-II). There were no treatment related deaths. Clinical response rate was 48% (CR: 3 patients, PR: 22 patients, SD: 17 patients, PD: 10 patients. Radical operation was performed in 17 patients (15 had R0 and 2 had R1 resection). Histopathological complete tumor regression (TRG 1) was noted in 6 patients, partial tumor regression (TRG 2) in 3, (TRG 3) in 4 patients, and minimal tumor regression (TRG 4) in 4 patients. Four patients died in postoperative course. The median observation time was 7 months. Up to now, 41 patients died. Average survival time for the whole group was 9.75 months (operated patients 12.6 months, and not operated 7 months). Eleven patients are still alive (9 had surgery after chemoraditherapy and 7 of them are in complete remission). According to these results, it may be expected that multimodal treatment of locally advanced squamous cell carcinoma of the esophagus improves local control and possibly even survival.

Keywords: Esophageal Neoplasms; Carcinoma, Squamous Cell; Combined Modality Therapy; Antineoplastic Agents; Drug Therapy; Radiotherapy

OP 5

UDC: 616.33-006:616-089.8:616.428

The importance of surgery for gastric carcinoma

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Gastric cancer remains a major cause of cancer death despite a significant decrease in its incidence, particularly in areas out of Eastern countries. Surgery remains the only potentially curative therapeutic option, yet the overall results from surgery alone remain poor. Surgical therapy is effective in small, early-stage malignancies as a technique to locoregional control of the disease. Lymphatic spread through the numerous lymphatic vessels is common in gastric cancer. Radical D2 lymph node dissection improves survival in patients with early lymphatic spread. Locoregional recurrence remains a significant problem in up to 30% of all patients, but more extensive lymphadenectomy is believed to remove a number of these sites of relapse. The lymphatics to the lesser and greater curvature are usually removed, while the celiac, porta hepatis, subpyloric, gastroduodenal, splenic, supra-pancreatic, retro-pancreatico-duodenal, peri-esophageal, superior mesenteric, and periaortic lymph nodes are at risk. At times, these lymph nodes may contain metastatic cancer when the perigastric nodes do not. Minimally one third of all patients with gastric cancer present with disease that is amenable to surgical resection for cure. The proportion of potentially resectable gastric malignancies has increased lately because of earlier diagnosis, improved surgical techniques, and enhanced perioperative care. Adjuvant therapies have not demonstrably altered patient survival after resection in gastric cancer, yet much can be learned from a review of adjuvant trials. No standard adjuvant therapy has been shown to improve survival after surgical resection of gastric adenocarcinoma, and future studies should be based on the data that have been accumulated to date.

Key words: Stomach Neoplasms; Digestive System Surgical Procedures; Gastrectomy; Lymph Node Excision; Reconstructive Surgical Procedures

OP 6

UDC: 616.37-006:616-089.8

Surgery for pancreatic cancer

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Ductal adenocarcinoma accounts for the majority of all pancreatic neoplasms (80%-90%). It is one of the most aggressive tumors with incidence in the USA and the Western countries of 10-11 per 100 000 people and an overall 5-year survival rate of less than 5%. Approximately two-thirds of all ductal adenocaricnoma arise in the pancreatic head, neck or uncinate process. The remaining one-third is found within the body or tail or diffusely throughout the gland. Pancreatic cancer is characterized by retroperitoneal and perineural infiltration, angio-invasion, early formation of local and distant metastasis, high rates of local relapse after resection and resistance to most of the available treatment regimens. There are three steps in the diagnosis of pancreatic carcinoma before deciding on the treatment approach. The first step is to detect the tumor. The next is to differentiate pancreatic adenocarcinoma from other pancreatic lesions. Finally, imaging should be able to permit staging of the tumor. In nearly 50% of cases, a diagnosis is made in a stage of illness in which metastases are present and 80% percent are inoperable (unresectable). The standard operation for tumors of pancreatic head is cephalic pancreaticoduodenectomy, whereas tumors of the body or tail can be resected using a distal pancreatectomy. Total pancreatectomy is generally reserved for newly selected situations in which cancer involves most of the gland. The authors analyzed the resectability rate, treatment, morbidity, mortality, and follow up in 265 patients (161 men and 104 women) with pancreatic cancer treated and monitored at the University Medical Center “Bezanijska kosa” from January 2000 to December 2008. Radical (potentially curative) procedure was performed in 73 patients and palliative procedures in case of 182 patients. In the group of patients that underwent potential curative resection, there were 44 cephalic duodenopancreatectomies, (classical Whipple-26, PPPD-18) 8 total duodenopancreatectomies, 18 distal, 2 central, 1 near total pancreatectomy. Portal vein (PV) resection was performed in 2 pts and lateral PV excision in 3 pts. The operative treatment of pancreatic head cancer in the group of patients that underwent palliative procedures, in most cases (138 patients), involved biliary enteric bypassing (hepaticojejunostomy) and prophylactic or therapeutic GEA as a standard procedure. Operative mortality in radically treated was 6 pts (8.2%). In the group of patients that were subjected to palliative procedures, mortality was 12 pts (6.7%). The most common postoperative complications in patients with resection procedures were the following: pancreatic fistula, erosive bleeding, atonia and gastric emptying disorders, biliary fistula and residual intra-abdominal abscess. Patients who undergo resection have the best change for long-term survival. Patients with unresectable or incurable disease, found during exploration, are generally considered to be the best treated with surgical palliation. The most common symptoms that require palliation in patients with pancreatic cancer are obstructive jaundice, gastric outlet obstruction and pain. To palliate obstructive jaundice, a biliary bypass (hepaticojejunostomy) should be performed. In addition to the biliary bypass, gastrojejunostomy should be performed routinely to prevent gastric outlet obstruction due to tumor ingrowth or compression of the duodenum. Initial severe pain treatment can be analgesic, but when the disease progresses this will not be sufficient in many cases. A neurolytic plexus coeliac block can be performed percutaneously.

Key words: Pancreatic Neoplasms; Diagnosis, Differential; Adenocarcinoma; Surgery; Treatment Outcome

OP 7

UDC: 616.37-006:615.015.2:341.18

Pancreatic cancer - adjuvant chemotherapy

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Pancreatic cancer is highly fatal cancer with >95% mortality rate. Resection is associated with improved survival, with 5-year survival rate of 0.4%-4%. Options of adjuvant therapy for pancreatic cancer (chemoradiotherapy or chemotherapy alone) are controversial. European Study Group for Pancreatic Cancer (ESPAC1) study was designed to answer the roles of adjuvant chemoradiation and adjuvant chemotherapy in 289 patients. Final results showed no survival benefit in chemoradiation arm. However, chemotherapy only arm achieved significant benefit in median survival (20.1 months vs. 15.5 months). Meta-analysis of 5 randomized trials (total 686 patients/550 deaths) was designed to investigate the role of adjuvant chemotherapy based on 5FU. These trials showed a significant trend in favor of chemotherapy with 29% and 46% reduction in the risk of death with chemotherapy. (HR indicated a 25% significant reduction in the risk of death with chemotherapy). The overall benefit for chemotherapy was shown by patients' median survival of 19 months in the group with chemotherapy and 13.5 months in the group without chemotherapy. The 2-and 5-year survival rates were estimated at 38% and 19% in the group with chemotherapy and 28% and 12% in the group without chemotherapy. Charité Onkologie (CONKO-001) study compared the benefit of adjuvant gemcitabine therapy with no postoperative anticancer therapy. Median overall survival was 22.1 months in the gemcitabine group and 20.2 months in the control group. In the qualified analysis, the overall survival advantage for gemcitabine was significant (24.2 months vs. 20.5 months in the control group). In the patient subgroups a significant difference in median overall survival in favor of adjuvant gemcitabine was observed for R0 patients, T3-4 patients, and for N negative patients. The CONKO-001 data, which were reanalyzed in March 2008, showed a significant difference in overall survival between the gemcitabine and surgery-only groups after long-term observation (5-year survival rate, 21.0% vs. 9.0%). ESPAC-3 (v2) was designed to compare 5-fluorouracil plus leucovorin and gemcitabine alone in adjuvant treatment of 1088 patients with resected pancreatic cancer. There was no statistically significant difference in survival between adjuvant fluorouracil plus leucovorin group and adjuvant gemcitabine group (median overall survival, 23.0 vs. 23.6 months). This study suggests that, although there was no significant difference in survival of patients in both study groups, gemcitabine may be suitable for clinical use as adjuvant therapy because the rate of serious adverse events was significantly lower than that in patients treated with fluorouracil plus leucovorin (7.5 vs. 14%).

Key words: Pancreatic Neoplasms; Chemotherapy, Adjuvant; Antineoplastic Combined Chemotherapy Protocols; Treatment Outcome

OP 8

UDC: 616.37-006:615.38:615.015.2

Systemic chemotherapy for advanced pancreatic cancer

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In Europe, cancer of the pancreas is the 10th most frequent cancer, accounting for some 2.6% of cancer in both sexes, and the eighth leading cause of cancer-related death with 65 000 deaths each year. The overall incidence of pancreatic cancer is approximately 8-10 cases per 100,000 persons per year. Incidence of pancreatic cancer in males has been slowly dropping over the past 2 decades, while the incidence in females has increased slightly. Histologically there are three types of pancreatic cancer. Infiltrating ductal adenocarcinomas account for 90% of pancreatic neoplasms, the remaining 10% being represented by acinar cell carcinoma. In patients with advanced and unresectable disease treatment with gemcitabine may be a reasonable choice. A phase III trial of gemcitabine versus 5-FU (well-tested older drug) as first-line therapy in patients with advanced or metastatic adenocarcinoma of the pancreas reported a significant improvement in survival among patients treated with gemcitabine. The use of a combination of gemcitabine with other cytotoxic agents (5FU, irinotecan, cisplatin, oxaliplatin, and docetaxel), is not supported by an advantage in survival. Recent clinical trials have not shown that combining gemcitabine and capecitabine produces any change in clinical response or quality of life. Another therapeutic possibility is a combination of gemcitabine and erlotinib (targeted therapy in the form of epidermal growth factor receptor antagonists), recently approved by FDA and EMEA on the basis of a randomized trial from the NCI of Canada. A preliminary report of a phase III trial (CAN-NCIC-PA3) comparing gemcitabine alone versus the combination of gemcitabine and erlotinib (100 mg/day) in patients with advanced or metastatic pancreatic carcinomas showed that erlotinib modestly prolonged survival when combined with gemcitabine alone (1-year survival was 18% with gemcitabine as compared with 2% with 5-FU, $P = .003$). However, the very modest survival gain (about 2 weeks), the high economic costs of the treatment and having in mind that this combination is with no small amount of patient toxicity question the role of this combination in metastatic pancreatic cancer. At the moment there is no evidence supporting the use of either cetuximab or bevacizumab in the overall setting of pancreatic cancer. There is no standard chemotherapy for patients who have progressed in first-line treatment. Capecitabine alone or capecitabine plus erlotinib may provide second-line therapy benefit in patients refractory to gemcitabine. The low objective response rate and lack of survival benefit with current chemotherapy indicates that clinical trials are still appropriate treatment option for the patients with pancreatic cancer. The signature molecular defects initially identified in pancreatic cancer, KRAS mutation, and epidermal growth factor receptor (EGFR) expression were the basis of initial trials of targeted agents. More recently recognized defects such as CDKN2A, TP53, and SMAD4/DPC4, hedgehog signaling PI3 kinase provide a platform for further development and investigation of drugs.

Key words: Pancreatic Neoplasms; Adenocarcinoma; Antineoplastic Agents; Antineoplastic Combined Chemotherapy Protocols

OP 9

UDC: 616.348-006:616.351-006:616.071:615-085

KRAS: A new predictive biomarker in the treatment of metastatic colorectal cancer

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A selective approach for the first-line treatment of metastatic colorectal cancer (mCRC) is more effective than non-selective treatment options. Personalized treatment, in which only those patients most likely to benefit receive a particular therapy, is possible if good biomarker can be found. Several molecular markers have been recently investigated as potential predictors of response to the epidermal growth factor receptor (EGFR) inhibitors. Currently, the only validated biomarker predictive of anti EGFR therapy is mutational status of KRAS oncogene, which is situated downstream in the EGFR signaling pathway. Up to 65% of colorectal cancers express the KRAS wild type (WT) gene. Recent published studies with cetuximab in combination with standard chemotherapy in first line treatment of mCRC have showed improved outcome with cetuximab in KRAS WT patients. In CRYSTAL study, addition of cetuximab to FOLFIRI in first-line treatment of KRAS WT mCRC patients improved response rate (39.7% vs.57.3%, $p<0.0001$), progression free survival (8.4 vs. 9.9 months, $p=0.0012$) and overall survival (20.0 vs. 23.5 months, $p=0.0094$). Furthermore, addition of cetuximab to FOLFOX regimen in same setting was investigated in OPUS study. Improvement is registered in response rate (34% vs. 57.3%, $p=0.0027$), PFS (7.2 vs. 8.3months, $p=0.0064$) and OS (18.5 vs. 22.8 months, $p=0.385$). National Comprehensive Cancer Network recommended determination of KRAS gene status of either the primary tumor or the site of metastasis in the pre-treatment work-up for all patients diagnosed with mCRC. Testing for KRAS status is therefore essential for ensuring appropriate patient selection for treatment in first-line mCRC.

Key words: Colorectal Neoplasms; Neoplasm Metastasis; Tumor Markers, Biological; Genes, ras; Receptor, Epidermal Growth Factor; Antineoplastic Agents

OP 10

UDC: 616-006:615-085:504.06

Education of cancer patients as a psychosocial support

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In the Institute for Oncology and Radiology of Serbia, cancer patients' specific education is an integral part of oncology treatment. The essence of cancer patients' education is in providing information and knowledge about cancer and anticancer treatments and giving psychosocial support. The aims of cancer patients' education are to demystify facts about cancer, to explain possibilities of contemporary treatment, to reduce emotional tension, to accomplish social participation, and to improve quality of life. Faculty for cancer patients' education includes multiprofessional and interdisciplinary team. Cancer patients' education is organized with individual and groups approaches. In our ten years long practice, the assessment of readiness and needs for education showed that the most of our patients needed more knowledge about nutrition, alternative and complementary cancer treatment. They required more knowledge about coping strategies, inter-family relationships in such situation, and supportive resources in society. They wanted to know more about their own active participation in the process of adaptation in the new situation created by cancer. Our results about influences of cancer patients' education on their life aspects confirmed that better understanding, knowledge, and skills in arrangement treatment goals, and creating plans for future achieved during education, have important positive impact on quality of life. Cancer patients' education has outstanding contribution in establishing self-management approach in which patients assume responsibility for their behavior, for changing their environment, and for planning their future.

Key words: Medical Oncology; Patient Education as Topic; Health Knowledge, Attitudes, Practice; Social Support; Adaptation, Psychological; Quality of Life

OP 11

UDC: 616-006:159.938.363.6:616.071

Psychological reactions of cancer patients: Thoughts, feelings, behavior, and body reactions of patients faced with diagnosis of cancer*

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The diagnosis of cancer usually creates a distress or crisis that requires adaptation to catastrophic information. Negative psychological states - stress, anxiety, and depression - are frequently associated with the diagnosis and treatment of cancer. At the initial phase of the disease, a certain amount of emotional distress is a normal reaction against the stressor, since the cancer experience is a negative life event requiring an enormous effort from patients and their families in order to adapt to the multiple challenges posed by the disease. The aim of this study was to assess the impact of cancer diagnosis on several psychological dimensions, thoughts, feelings, body sensations, and behavior of cancer patients when they faced the new situation. The investigation was conducted at the Institute for Oncology and Radiology of Serbia, Belgrade within European educational program (EEP) *Learning to live with cancer*. As a member of multidisciplinary team, the psychologist gave two lectures: *Cancer as personal and family distress and crisis, and (dis)functional mechanisms of reactions* and *Coping strategies*. Eighty cancer patients were enrolled. At the beginning of lectures, we asked patients to describe (anonymously) their common thoughts, feelings, behavior, and body sensations, in the first six weeks when they faced the fact that they were affected by cancer. The great majority of our patients experienced deny (65% of patients), reexamination (60%), and 40% of patients had dark thoughts (suicidal ideation). Only 20% of patients had positive thoughts about selves and self-encouraging, and 15% thought about ways how to increase the quality of life. The common feelings quoted by most (90%) patients were depression and disappointment, while fear, hopelessness, and emptiness were mentioned by 85% of patients; 70% patients reported sadness, while 65% of patients quoted angry and anxiety; 50% of patients quoted despair, and 30% quoted guilt and shame. Only twelve patients reported self-compassion. Nervousness and irritability as common behavior was mentioned by 90% of patients. Fifty-two patients quoted insomnia, 30% mentioned hypoactivity and passiveness, while 16 patients quoted hyperactivity. Eight patients mentioned acting-out behavior, while twenty-eight patients quoted muscles tension as most common body sensation. Dizziness, tremor, and sweat quoted 20% of patients, while only twelve patients quoted vomiting. The diagnosis of cancer and cancer treatment can cause distress, emotional turmoil, and different psychosocial disorders. Considering different psychological reactions of cancer patients can be helpful for organizing adequate psycho-educational and psychosocial support and psychotherapy for cancer patients and their families.

* The results of this research will be published in Journal of BUON, 2010.

Key words: Neoplasms; Diagnosis; Medical Oncology; Psychology, Medical; Psychological Phenomena and Processes; Adaptation, Psychological

OP 12

UDC: 616-006:616-052:371.64:504.06(497.11 Serbia)"2007"

Mission of the Patient Support Workgroup

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Patient Support Workgroup was established in the Institute for Oncology and Radiology of Serbia in early 2007. It is made up of patient representatives, representatives from the Patient Association, and experts from the Institute itself.

The Workgroup has been established to further activities aimed at supporting Oncology patients and to improve communication between patients and health workers. These activities include:

- Providing adequate information about malignant diseases, diagnostics, up to date treatments, rehabilitation, and palliative care;
- Organizing meetings in behalf of patient associations and individuals so as to point out current problems, exchange patient experiences and interests;
- Developing an action plan for strengthening roles of patients in society;
- Making contacts and strengthening connections between representatives of patient associations, doctors, and other experts who aspire to improve all forms of oncology treatment.

The Workgroup reaches these goals through organizing popular educational lectures, creative workshops, through working in small groups, selecting and preparing educational materials, and through cooperation with patient associations in the country and abroad, which are concerned with education, support and representation of interests of persons inflicted with malignant diseases.

Main mission of the Workgroup is improving the quality of life of ailing individuals.

Key words: Medical Oncology; Communication; Professional-Patients relations; Health Education; Social Support; Quality of Life

PP 13

UDC: 616.988.6:616.711-006:615-085

Treatment results of Ewing's sarcoma of the vertebrae

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Ewing's sarcomas of the vertebrae are rare tumors. Treatment is multidisciplinary: surgery, radiotherapy, and chemotherapy. From 2000 to 2007, 7 patients with primary tumors of vertebrae were treated. No one patient had tumor of the cervical vertebrae. Five patients had tumors of thoracic and 2 had tumor of lumbar vertebrae. The median age at diagnosis was 13 years (range, 12 to 18 yrs.). Six patients were boys, 1 patient was girl. No one had metastases at diagnosis. Surgery was performed in 5 patients. Complete surgical excision was done in 2 and maximal tumor reduction in 3 patients. Biopsy alone was done in 2 patients. After surgery, all patients received chemotherapy: EICESS 92 (EVAIA chemotherapy regimen) was given to 4 patients and 3 patients received Euro Ewing 99. Radiotherapy was performed in 6 patients: after 2 cycles of chemotherapy in 2 patients and after 3 cycles in 4 patients. Median dose 5040 cGy (range: 5018-5400 cGy) in conventional fractionation. Daily fractionation was from 180 to 193 cGy. The mean follow-up was 41 months (range: 4 to 104 months). Overall survival (OS) rate was 71.42%. One patient progressed and died after complete treatment, another one died during chemotherapy but before radiotherapy. In our series of Ewing's sarcoma of the vertebrae, good surgery initially, early definitive radiotherapy and aggressive multimodal therapy (surgery/radiotherapy/chemotherapy) may be effective in disease control and survival.

Key words: Sarcoma, Ewing`s; Spinal Neoplasms; Treatment Outcome; Combined Modality Therapy

PP 14

UDC: 618.19-006:615.015.2:616-079.4

Differentially - diagnostic dilemmas of skin changes caused by cytostatics: A case report

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Skin changes caused by cytostatics are usually manifested by erythema. Xeloda, oral fluoropyrimidine, which commonly causes hand-foot syndrome, can also cause lupus-like syndrome. A 44-old patient was diagnosed with locally progressive breast cancer. Treatment started with neoadjuvant chemotherapy according to FAC protocol. After down staging, radical left mastectomy with dissection of axilla was performed. Afterwards, the treatment continued by administrating taxane and carboplatin. Soon after, metastases in liver were verified and carboplatin was replaced by trastuzumab because it was HER2 positive carcinoma. After eight chemotherapy cycles, partial regression was accomplished and taxane was replaced by Xeloda. After first cycle, multiform rash appeared on the skin of the torso and arms and in the shape of a butterfly on the face, together with the changes on the lip and oral mucosa. In the meantime, patient was exposed to sunlight. Differential diagnostics included systemic lupus erythematosus (SLE), lupus-like syndrome, Stevens-Johnson syndrome, Lyell syndrome, and others. The doses of Xeloda had been reduced by 30%. Antinuclear antibodies were positive, C4 decreased. Skin biopsy and histopathologic findings indicated the polymorphic eruption of light. Specific symptomatic treatment was administered together with corticosteroids, followed by regression of the skin changes. One year after the original skin eruption, darker pigmentation persisted on the skin of face, hands, and torso. SLE is chronic autoimmune disease manifested by skin changes, enanthema, arthritis, changes of serosa, anemia, leucopenia, false-positive test results for lues and positive antinuclear antibodies. Lupus-like syndrome is caused by many medications and out of cytostatics most often by Xeloda and taxanes. It is mainly manifested by skin changes, but specific antibodies were not found. It is associated with anemia and thrombocytopenia, and it disappears once the medications are stopped. Even with all the clinical symptoms, histopathologic findings, findings of different antibodies, it is often impossible to clearly differentiate etiology of skin changes during cytostatics administration. Cytostatic effects enhanced by exposure to sunlight could have induced exacerbation of SLE in this patient's case, although lupus – like syndrome cannot be completely excluded, either.

Key words: Breast Neoplasms; Neoadjuvant Therapy; Cytostatic Agents; Skin Manifestations; Diagnosis, Differential

PP 15

UDC: 617.735:2-446:616-089.8:615.849.1

Multidisciplinary treatment of bilateral retinoblastoma – 10 years experience

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Treatment of children with bilateral retinoblastoma is multidisciplinary. From1999 to 2009 we treated 31 patients (7 female and 3 male patients) with high-risk retinoblastoma. We had 10 patients with bilateral retinoblastoma; median age at the time of diagnosis was 14.5 months (range: 2 to 31 months. Tumor invasion into the optic nerve was present in 3 (30%) patients. Leptomeningeal dissemination was not diagnosed in treated children. Bone marrow was also not affected in followed patients. Enucleation of one eye was performed in 5 patients and enucleation of both eyes in 2 patients. Local radiotherapy was applied in 3 patients and 7 patients received focal treatment modalities (cryotherapy, thermotherapy). All patients received systemic chemotherapy (protocol consists of carboplatin, etoposide, and vincristine). During the 12-108 months follow-up period (median follow up 48 moths) overall survival rate was 80%; 2 patients died. Sixty percent of all cases preserved useful one eye vision. Multidisciplinary treatment is essential in children with bilateral retinoblastoma. Delay of diagnosis and infiltration of the optic nerve had a negative impact on survival. Seven patients required enucleation of one or both eyes at some stage, but 60% of patients preserved useful one eye vision. Aggressive chemotherapy treatment with focal treatment modalities (cryotherapy, thermotherapy) can result in avoiding of radiotherapy.

Key words: Retinoblastoma; Child; Combined Modality Therapy; Antineoplastic Combined Chemotherapy Protocols; Cryotherapy; Hyperthermia, Induced; Radiotherapy; Surgery

PP 16

UDC: 616.36-006:616.071

Focal hepatic lesions and hepatocellular carcinoma

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The number of new cancer cases increases every year worldwide. About 10.9 million new cancer cases and 6.7 million cancer deaths occur worldwide every year. Cancer of unknown primary site (CUP) occurs in 6% of all cancers. Hepatocellular cancer (HCC) is one of the most frequent cancers with five-year relative survival less than 10%. Over 80% of the total liver cases occur in developing countries. Rates are higher in men than in women (ratio 4:1). The aim of this study was to prove frequency of primary HCC in patients with initial ECHO ultrasound or CT discovered metastatic lesions in the liver without known primary site of tumor. This paper presents 60 patients hospitalized in Clinic of Oncology, Clinical Centre Banja Luka. Detailed history of disease was taken and clinical examination (laboratory analyses, hepatitis markers, tumor markers, ECHO examination, CT scan) was done for all patients. In addition, fine needle aspiration was performed in some of them. Disease was confirmed micromorphologically in 51 (85%) patients. Primary HCC (χ^2=9.40 p<0.01) was found in 14 (27%) patients (13 men and 1 woman, average age 63 [range: 48-74 years]); 28% patients had previously cirrhosis; 43% patients were alcohol consumers. HBsAg positivism was found in 33.3% of patients, HBV antibodies were proved in 28.6%, and HCV antibodies were confirmed in 14% of patients. Extrahepatic primary process was found in 26 (51%) patients and CRC was found in 70% of all studied patients. Hepatocellular cancer was proved in 27% of examined patients. Colorectal cancer is the most frequent tumor in patients with secondary deposits in the liver (70%).

Key words: Carcinoma, Hepatocellular; Liver Neoplasms; Neoplasm Metastasis; Liver Diseases; Diagnosis

PP 17

UDC: 618.19-006:616-052:504.06

Patient's personal narrative

Jasmina Lukić

Belgrade, Serbia

My name is Jasmina Lukic (53). Four years ago, I had first surgery of breast cancer and two years later, I had the second surgery. On my road to recovery, I went through several different and specific therapies at the Institute for Oncology and Radiology in Belgrade. Today, I feel healthy and satisfied primarily because I was able to overcome the pernicious disease and I learned how to maintain my recovered health. During the illness and the treatment, I had great family support by my two sons, mother, and my husband. In addition, my doctors who treated me and my friends supported me too. Breast cancer is a stressful life event and shock to both patients and their families. When I realized how serious was my disease I decided that I must accept reality as it is and I decided to be healthy again. I explained my diagnosis to my beloved ones clearly not allowing them to fear. It was important for them to have patience and understanding for supporting me in my struggle to recovery. It was the first moment of good communication with my family and later with all of my friends. I surrounded myself with positive things. I did the things I enjoyed as long as I enjoyed them. I relaxed, read novels, and minimized watching TV. I spend my free time with my family and my friends, walking, talking, and laughing. However, as usually happens, difficult moments come, and then all of them were there to give me their positive attitude, not letting bad mood to continue. Doctors and team form counseling department always were there to clarify every dilemma. My mother's supporting words , comfort and understanding, great patience and attention of my family, help at home from my husband and sons, my kids' smiles and their success in school, big heart and a little surprise and concerns of my friends, were support to me on my road to recovery.

Key words: Breast Neoplasms; Patients; Narration; Social Support; Family; Quality of Life

PP 18

UDC: 616-006:316.246:504.06

The social support net

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A human being is a psychological and social being so the importance of psychosocial support in stress situation is quite understandable. Numerous clinical and epidemiological researches showed that the level in which the sick person has the support and feels the presence of the support is important factor in his/her adapting to the illness as well as in keeping the life quality. That is the reason that professional staff should check the level of existing support given to a patient. Our aim was to identify when there is a lack of it and in that case to recommend some additional resources and information referring to the way of its obtaining. The aim of this study was to inform the participants with the resources of psychosocial support in our circumstances, verified by the results of survey, done in 2006 with the oncologic patients. The survey results showed that the family is the main resource of psychosocial support for 38% of examinees; 22% of them recognize the support in professional staff of the Health Care System; 35% of examinees have the support of Support Associations, while 5% of examinees are without any kind of support. The family means the resource of not only a practical support but also the most intensive social affective base that obtains trust and the sense of belonging. The examinees expected the informative support to be provided by professional staff from social institutions, and instrumental one by NG sector. Relying only on family is unsuitable; most frequent unwelcome occurrences are chronic fatigue syndrome, changing of family roles and economic pressure on family. The best results are achieved by combination of support by family members but also by the others who do not belong to family system. Not less important are also emotional, informative and practical support so it is of a crucial importance to recognize the kind of social support that is suitable for the current status of a patient and his/her family.

Key words: Medical Oncology; Social Support; Family; Quality of Life; Adaptation, Psychological

PP 19

UDC: 611.71:612.83-006:615-085:615.849.1:006.31.8

Extracranial metastases from medulloblastoma in children

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Extracranial metastases by hematogenous spread from primary intracranial neoplasms occur rarely. The most common site of metastases is bones (more than 80%) and the other common sites are bone marrow, lymph nodes, liver, and lung. From 1990 to 2008, 122 patients with intracranial medulloblastoma were treated in the Institute for Oncology and Radiology of Serbia. We reported three cases (10- and 14-years old boys, and 16-years old girl) of extracranial metastases from medulloblastoma. In primary treatment after adequate staging (CHANG staging system – T3 M1, T3 M0 and T3 M0), all patients were treated with standard therapy strategy. After surgery (subtotal/total extirpation) and craniospinal irradiation (55 Gy to the area of the primary tumor, 35 Gy whole brain and spine), they received six cycles of chemotherapy (CCNU, vincristine). In the first patient, after follow up period of 7 months, bone (calvarium, vertebra, ribs, humerus, femur) and bone marrow metastases were developed. The second patient, after 36 months of follow-up period, developed bone metastases (distal femurs). Third patient after 24 months of follow-up period developed bone metastases (left humerus, left scapula, left and right femur, costae IV). Histopathological diagnosis was confirmed by biopsy. In all patients, levels of alkaline phosphatase and lactate dehydrogenase were elevated. In secondary treatment first two patients received ten cycles of chemotherapy (CDDP: 20 mg/m^2 days 1-5; VP16: 60 mg/m^2 days 1-5) while the second patient had local radiotherapy of bone metastases with 36 Gy. After initial partial response with loss of pain, both patients died within one-year time due to dissemination of disease. In the third patient, 16 years old girl, secondary treatment included five cycles of secondary chemotherapy (carboplatin, etoposide, vincristine) and palliative irradiation of left shoulder and proximal part of the left humerus and right and left hip and proximal part of both femurs with TD 36 Gy. Because of the progression of disease (tibia and fibula bilateral, metastases in both breasts, in supraclavicular and left axilla lymph nodes), tertiary treatment included four cycles of chemotherapy (doxorubicin, CDDP, actinomycin D, vincristine) and palliative radiotherapy (left knee, left axilla, and supraclavicular region left, costae IV). Aggressive multimodal therapy with controlled pain slowed down the natural course of disease, so she lived another 18 months after relapse of disease. A greater understanding of the pathogenesis of the systemic metastases may be valuable in designing of future, more aggressive multimodal therapy.

Key words: Medulloblastoma; Child; Neoplasm Metastasis; Bone and Bones; Combined Modality Therapy; Radiotherapy; Antineoplastic Combined Chemotherapy Protocols

PP 20

UDC: 616.33-006:615.849.1:615.015.2

Postoperative radiochemotherapy in gastric cancer

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Based on results of the INT0116 study, adjuvant radiochemotherapy has become the standard treatment after complete resection of gastric adenocarcinoma. In this study, we evaluated the results of postoperative radiochemotherapy of patients with resected, high-risk, gastric cancer. Since January of 2006, 22 patients with resected gastric cancer were treated with adjuvant radiochemotherapy at our Institute. Sex distribution was as follows: 15 male and 7 females; mean age was 54 years (range: 40-65 yrs). Types of surgically treatment were: total gastrectomy (18 pts), subtotal gastrectomy (4 patients.); with: Ro resection (12 patients), R1 (5 patients) and Rx (4 patients). Adenocarcinoma of the stomach was histopathologically proven in 22 patients (grade I: 1, grade II: 4, grade III: 8, grade IV: 3, and unspecified grade: 6 patients). According to UICC staging system, 3 patients were in pathological stage II, 6 patients in IIIA, 3patients in IIIB, and 10 patients in IVA stage. The adjuvant treatment consisted of adjuvant chemotherapy with 5FULV followed by radiotherapy with concomitant 5FULV, and then two more courses of adjuvant chemotherapy with 5FULV. Radiation dose of 45 Gy was delivered in 25 fractions at 1.8 Gy per fraction, five days per week over five weeks to the tumor bed, anastomoses and stumps, and regional lymphatics. Radiation was delivered using Linear accelerator with 6-18MV photons. In majority of cases, we used conventional technique: parallel-opposed AP-PA, 3 or 4 field arrangements. We started to use a conformal technique of radiation delivery, on October 2008. Toxicity, during radiochemotherapy course was as follows: dermatitis grade 1 in 1 patient, leucopenia grade 2 in 2 patients, neutropenia grade 2 in 2 patients, anemia in 1 pt, grade 2 in 2 patients, grade 3 in 1 pt, nausea grade 1 in 3 patients, grade 2 in 4 patients, vomiting grade 2 in 2 patients and diarrhea grade 2 in 3 patients. After the end of radiochemotherapy, complete clinical response was achieved in 17 patients, and progression of disease had 4 patients (peritoneal metastases 1 pt, liver metastases 1 pt, lenticular metastases 1 pt, and local progression 1 pt). After the end of radiotherapy, patients were followed up from 1 to 44 months (median 9 months). During follow up, progression of disease occurred in another 6 patients with mean period to progression of 5.2 months (range: 1-12 m): local relapse in 1 pt, liver metastases in 1 pt, lung metastases in 1 pt, bone metastases in 1pt, ovarian metastatic cancer in 1pt, regional lymph nodes metastases in 1 pt. Mean overall survival time was 12 months (1-44 months). Postoperative radiochemoherapy should be considered for all patients at high risk for recurrence of gastric cancer who have been done curative resection.

Key words: Stomach Neoplasms; Gastrectomy; Postoperative Period; Radiotherapy, Adjuvant; Chemotherapy, Adjuvant

PP 21

UDC: 616.351-006:615.849.1:615.015.2

The role of preoperative radiotherapy in the treatment of locally advanced rectal cancer: A case report

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Preoperative radiochemotherapy is accepted as standard treatment option for locally advanced rectal cancer. The purpose of this report was to show our experiences with preoperative radiotherapy for locally advanced rectal cancer at our Institute. In presented case, the initial treatment was radiotherapy followed by surgery and chemotherapy. A 47-year old female patient started oncology treatment in May 2008, after biopsy of suspected tumor mass in rectal region. Histopathological finding was adenocarcinoma well differentiated HG1 NG2. CT scan of abdomen and lower pelvis showed oval, intraluminal, inhomogenous mass (4 cm) with infiltration of posterior vaginal wall. Physicians' consulting decision was to start with preoperative radiotherapy (RT) as initial treatment, beginning in June 2008. It was conducted on LINAC 6-Mev, with tumor dose 50 Gy in 22 fractions using isocentric technique. The end of RT treatment was in July 2008. The operation was performed in September 2008 (abdominoperineal resection Miles and hysterectomy with bilateral adnexetomy). Postoperative histopathological finding was infiltrating adenocarcinoma of the rectum HG2 NG2 with rectovaginal fistula. The status of lymph nodes was unknown. Further treatment option was systematic chemotherapy, and cycle I capecitabine (Xeloda) started in November 2008. After completion of eight chemotherapy cycles, the patient was in stable condition without any sign of illness progression. The physicians' consulting decision was to finish specific oncology treatment. Further, follow up in regular intervals. On the first control exam, three months later multi-sliced CT of abdomen and lower pelvis showed no focal lesion in liver, no enlarged nodes in retroperitoneum, insignificant small lymph nodes in inguinal. Bone scintigraphy shows no pathological findings. Values of tumor markers were normalized. Radiologic examination of lungs showed no secondary deposits. Patient was in stable overall condition. This case confirms that preoperative radiotherapy with or without chemotherapy appears to be well-tolerated and effective initial treatment of locally advanced rectal cancer.

Key words: Rectal Neoplasms; Radiotherapy; Preoperative Care; Radiotherapy, Adjuvant

PP 22

UDC: 618.19-006:616.71-006:615-085

Breast cancer: Is a skeleton scintigraphy a method of choice in evaluation of bone metastatic spread?

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Breast cancer is the most common malignancy in women, accounting for 32% of all cancers. The most common sites of distant breast metastasis are the lungs, liver, and bone. Assessment of disease extent in skeleton is bone scintigraphy (BS), which should be performed as a screening of the entire skeleton, and radiography or CT (Computed Tomography) should additionally examine suspicious lesions. BS remains a method of choice in the evaluation of the entire skeletal system, providing, among other data, the insight into the metabolic activity in the bones. BS is rather sensitive (over 90%), revealing the presence of bone metastases even 6-12 months before they could be seen on a conventional bone radiogram. The investigation was aimed at evaluating the diagnostic value of the skeleton scintigraphy in defining the breast cancer spread. The primary examined group included 103 patients with a verified breast cancer, differing in histological types, who received no therapy prior to bone scintigraphy. The statistic analysis of the obtained data was performed by the t-test, non-parametric analysis with subsequent testing of the difference significance and multi-parametric correlation analysis. The diagnostic efficiency of the test was evaluated by the methods induced from the Bays' theorem. Bone metastases were registered in 40 patients of examined group. Pathologic finding includes solitary focal lesions and multiple lesions. Solitary bone metastases were registered in 13 patients, while multiple bone lesions were found in 27 of the patients. Solitary bone metastases were found in the thoracic and lumbar spine, shoulder bones, the sacroiliac joint, long bones, and skull, while multiple metastases were most frequently localized in the endpoints of the femur, thoracic vertebrae, ribs, pelvis, and in the skull and scapula. By the addition of all metastases, the ribs are most often affected (22.92%), then femur (20.83%) and vertebrae (19.44%). Long bone metastases were registered at 35 sites – in end points 85.71% and in the marrow 14.28%. Considering the particular bones, metastases appeared in the endpoints of femur 7 times, diaphysis 1 time, as well as in the end-points of the tibia. Regarding the humerus, its end-points were involved once and diaphysis twice. Analyzing the entire examined group, bone metastases are registered in 39.6% of the patients; of them, 9.17% have metastases at the same other localizations. Other patients (30.43%) constituted the group with a limited disease until BS was performed, which, giving positive findings, completely changed the selected therapy procedure. This seems to be a crucial data, pointing to the relevance of BS performed at the moment of establishing the diagnosis. Based on the Bays' theorem and the obtained data, a high sensitivity of the method has been calculated, accompanied with a slightly lower specificity, which speak in favor of BS as a method of choice for assessment of the skeleton system involvement by malignancy. Bone scintigraphy is a highly sensitive, specific, and accurate method and takes important place in assessment of disease extent, changing completely the therapeutic approach in asymptomatic patients.

Key words: Breast Neoplasms; Neoplasm Metastasis; Bone and Bones; Radionuclide Imaging; Sensitivity and Specificity

PP 23

UDC: 616.348-006:616.351-006:616-036.22(497.115 Kosovo and Metohija)

Pathomorphological and epidemiological characteristics of colorectal carcinomas in the population of Serbian municipalities of Kosovo and Metohija

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Colorectal carcinoma is known to be one of the most frequent tumors in the European and North American population. The overall incidence of the disease may vary between 30 and 55 cases per 100000 people. Our country is placed into the group of those involving a high risk, having an average incidence of over 30 cases per 100 000 inhabitants. Colorectal carcinoma occurs at a similar frequency in both genders, with an average patient age of 60 years. The aim was to analyze epidemiological, clinical, and morphological characteristics of colorectal carcinoma, along with both histological and clinical staging of the disease. The retrospective analysis was performed on biopsy samples acquired at the Institute between 2004 and 2008. During the stated period, 31 cases of colorectal carcinoma have been diagnosed. The gender structure was as follows - there have been 15 cases detected in male patients (48.39%), and 16 cases in the female group (51.61%). The average age of the patients was found to be 64.29 years (minimum age - 26 years, maximum age - 79 years). The carcinoma was most frequently located in the rectosigmoid junction (64.52%). In the vast majority of cases (96.77%), the infiltrative-stenosing form was macroscopically recognized. The average size of the tumor was 6.37cm (minimum size - 2cm, maximum size - 14cm). Rectal bleeding and meteorism were stated as the main symptoms in 41.94% of cases diagnosed, and those lasted for an average of 6 months. The detected colorectal carcinomas are histologically classified as adenocarcinomas, and most of them are grade II carcinomas. In 41.94% of cases, an invasion of lymph and blood vessels was involved, as well as a perineural invasion. The disease's stages were determined according to the Astler-Coller method. Stage B (51.61%) and stage C (32.26%) were the ones with the highest frequency rate. While stage B carcinomas were more frequently diagnosed in female patients, stage C was usually associated with male gender. Colorectal carcinoma is nearly equally distributed between both genders, occurring at an average age of 64.29 years, and is typically located at the rectosigmoid junction, usually being detected in stage B.

Key words: Colorectal Neoplasms; Epidemiology; Serbia

PP 24

UDC: 616.33-006:616-076:616.98:615-085

Gastric MALT lymphoma: A case report

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We present a case of successful treatment MALT lymphoma in 22-year old man. The patient was admitted to hospital with a pain in epigastrium accompanied with heartburn. For clinical diagnosis of the patient, gastroscopy was performed, which showed malignant alteration. With histopathological analysis of changed mucosa, low-grade gastric MALT lymphoma with presence of *Helicobacter pylor*i was diagnosed. CT of thorax, abdomen, and pelvis did not show pathological enlargement of lymph nodes. Ultrasonography of the neck, axillae, and inguina did not show pathological enlargement lymph nodes. Biochemical analyses of serum were within reference ranges. Biopsy of hipbone did not show pathological infiltration of bone marrow with lymphoma cells. The phase of disease has been determined as IE. We have treated the patient with eradication therapy for *Helicobacter pylori*: clarithromycin, amoxicillin, and proton pump inhibitor. After three months of eradication therapy, a complete remission was achieved.

Key words: Stomach Neoplasms; Lymphoma, B-cell, Marginal Zone; Helicobacter Pylori; Drug Therapy

23rd Annual Meeting of Oncology Nurses – Technicians of Republic of Serbia

Institute for Oncology and Radiology of Serbia, Belgrade (photo selected by Ljiljana Vučković Dekić)

OP 25

UDC: 616.3-006:616-036.22(497.11 Serbia)

Epidemiology of malignant illnesses within gastrointestinal tract

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There are more than 30 million people worldwide suffering from cancer nowadays. The number of people with newly discovered cancer with different locations rises every year, and now is at level of about 12 million people per year. It is estimated that the number of newly discovered cases in 2020 will be approximately 20 million. Malignant illnesses are one of the most frequent causes of death worldwide, and gastrointestinal tract is the third most frequent locations of malignant tumors. The tumors of colon, stomach, pancreas, liver, and esophagus are the most frequent, whereas tumors of gall bladder and small intestine are less frequent. The objective of the paper is presentation of epidemiological characteristics of malignant illnesses within gastrointestinal tract and their importance in Serbia. The method implied the analysis of the epidemiological situation with malignant illnesses within gastrointestinal tract, according to the data on incidence and death rate due to those illnesses. Malignant illnesses within gastrointestinal tract are at the third place in Serbia, with incidence of about 6800 persons per year. Considering locations, the most frequent are colon tumors (58%), followed by stomach tumors (20%), pancreas tumors (13%), and liver tumors (9.5%). Incidence rates in Serbia are among lower European rates, but they increase constantly. Most of the patients are detected in later phase, when treatment is less successful. For some locations, there are good measures for primary prevention (such as for liver cancer), whereas secondary prevention, like early detection and screening (in case of colon cancer, for instance), is more important for other locations. Colon cancer is one of the most important solid tumors. The reason for this is not only its incidence (about 4000 persons in Serbia per year), but also the possibility of healing, which is greater than for all other solid tumors within gastrointestinal tract taken together. Analysis of epidemiological situation, with application of proper primary and secondary prevention measures and adequate treatment of malignant illnesses within gastrointestinal tract, are the prerequisite for decreasing the incidence and mortality due to those illnesses.

Key words: Digestive System Neoplasms; Epidemiology; Serbia

OP 26

UDC: 616.351:616-072:614.253.5

Medical nurses within the endoscopic team during diagnosis and patient's treatment with post-irradiation proctitis

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Proctitis is an inflammatory process of the inner layer of the rectal wall. It occurs because of radiotherapy in 75% of patients with malignant diseases: prostate, ovary, uterine cervix, uterine corpus, and rectum. A diagnostic endoscopic procedure (rectoscopy and flexible sigmoidoscopy) presents a diagnostic method for patients with post-irradiation proctitis. For now, there are no standardized treatment protocols, and the result of therapy is often unpredictable. The aim of this paper was to point out the important role of the nurse in performing endoscopic methods in diagnosis and treatment of patients with post-irradiation proctitis. The role of nurses is to give all the needed information to the patient, to make psycho-physical preparation, preparation for rectoscopy and flexible sigmoidoscopy apparatus, to assist during a recto-sigmoidoscopy, to send a biopsy sample to histopathological analysis and to take care of the patient after the intervention. The nurse has a very responsible role in that diagnostic – endoscopic team caring about patients during their treatment with post-irradiation complications of radiotherapy. Endoscopy is a „gold standard" in diagnosis, therapy evaluation, and treatment of patients with post-irradiation proctitis.

Key words: Nurse`s Role; Sigmoidoscopy; Proctoscopy; Radiation Injuries; Proctitis

OP 27

UDC: 616.329-006:615.38:615-085.1:341.18

Unwanted effects during the combined chemoradiotherapy at patients with cancer of esophagus – health care

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Cancer of esophagus is a relatively rare disease. The most common causes are genetic predisposition and chronic irritation of esophageal mucosis. The main symptoms of this disease are difficult swallowing, loss of appetite, loss in body weight, pain behind sternum, hoarseness, and cough. The diagnosis is made with different diagnostic procedures, such as esophagographic examination, esophagoscopic examination with biopsy, and CT of thoracic cage. In case of cancer, which cannot be operated, the best treatment is a combined chemoradiotherapy, and after that, chirurgic treatment is performed. A combined chemoradiotherapy can cause hematological and non-hematological unwanted effects.

Our aim was to show the importance of prompt recognizing and treating acute unwanted effects, in health care of patients with cancer of esophagus, during the chemoradiotherapy.

In the period from August 2006 to September 2009, in IORS Belgrade, 52 patients of different age with esophagus cancer were treated with chemoradiotherapy. Chemoradiotherapy was carried out simultaneously. Cisplatin was applied at days 1, 15, 30, 5FU and leucovorin at days 1, 12, 15, 16, 30, and 31. Radiotherapy began at day 3 of chemotherapy with TD 50 Gy in 28 fractions. Unwanted effects during the treatment were: dysphagia – 38 patients, anemia – 38 patients, leukopenia – 25 patients, thrombocitopenia – 12 patients, nausea-11 patients, pain – 9 patients , febrile neutropenia – 7 patients, stomatitis – 4 patients , thrombosis of profound veins – 4 patients , vomiting – 1 patient, diarrhea – 1 patient. Nurses should promptly recognize the unwanted effects of therapy and make some interventions to improve the quality of life of patients with esophagus cancer.

Key words: Esophageal Neoplasms; Radiotherapy; Antineoplastic Combined Chemotherapy Protocols; Drug Therapy+adverse effects

OP 28

UDC: 616.33-006:612.39:614.253.5

Enteral nutrition via nutritive tubes after total gastrectomy in patients with gastric carcinoma

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Enteral nutrition (EN) is a term used to comprise all forms of food intake, including oral way or nutritional tubes placed on different levels of gastrointestinal tract (GIT). EN via feeding tubes is applied in patients unable to eat or when per oral way is contraindicated. In patients with total gastrectomy due to gastric cancer, continuity of GIT is provided with esophageal-jejunal anastomosis. Traditionally, in these patients oral feeding is contraindicated until full bowel motility is achieved. Nutritional support is provided by parenteral way and fasting can last even 10 or more days. Recently, the intraoperative placement of nutritional naso-jejunal tubes under the anastomosis has provided EN on a first postoperative day. Early EN, by individually calculated requirement, significantly improves recovery of patients at high risk due to natural intestinal absorption via GIT. Also, it diminishes parenteral requirements and shortens hospitalization in surgical intensive care (SIC) unit. The aim of this study was to present specificity of nursing interventions in application and maintenance of naso-jejunal tubes after total gastrectomy due to gastric cancer. After total gastrectomy and positioning of naso-jejunal tubes, patients were admitted to SIC unit. Type, volume, and flow speed of nutritional formula was calculated by anesthesiologist. Nursing interventions in appliance of EN are: tube position checking, check the transience of tube by flushing sterile normal saline, preparation of nutritional solution, connection to enteric pump, adjustment of flow speed, tube flushing after application of per oral medicaments, continuing monitoring, and recording. Nausea, vomiting, diarrhea, constipation, reflux, pulmonary aspiration, and hypoglycemia are most common side effects and complications of EN *via* feeding tubes. We have analyzed the specificity of nursing interventions considering medical care process, recognition, and recording of side effects and complications of EN. EN *via* feeding tubes in early postoperative course after total gastrectomy made significant improvement in fast recovery of patients with gastric cancer. Choice of nutrition formula and its adequate appliance are prerequisite of fast rehabilitation and forehand adjuvant oncology treatment. Specificities of nursing interventions are regarded to continuing monitoring of other parameters of surgical patients care and therefore require well trained and experienced team.

Key words: Enteral Nutrition; Stomach Neoplasms; Gastrectomy; Nursing; Nurse`s Role

OP 29

UDC: 616.34-008.3:371.64:316.6

Preparing the patient for life with stoma

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The aim of education of stoma patients is to help them understand the feelings for upcoming surgical procedure that includes stoma formation. The process of adjusting the patient for life with stoma is time consuming. It is essential to build up patient's self-confidence and to include him/her in everyday activities as soon as possible. The preparation of patients for life with stoma has two segments: psychological preparation and rehabilitation. Psychological preparation begins even before operation and continues in the period of rehabilitation. First of all, patient should be informed on current health status and about forthcoming surgical procedures. It's also very important to inform family members on these details, in order for them to provide necessary help and support to the patient. Rehabilitation is divided in two segments: (a) psychological and (b) physical. Psychological rehabilitation is started by stoma therapist as soon as patient returns from operating theatre. Physical rehabilitation is commenced when we are certain that the patient is ready to learn the skills needed for his independent life and to confront with future life with stoma.

Key words: Patient Eduction as Topic; Surgical Stomas; Adaptation, Psychological; Activities of Daily Living

OP 30

UDC: 616.348-006:614.253.5:371.64

Education of patients with colostomy

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Colostomy, or an artificially created anus, represents an artificial opening on some part of intestine for evacuation of fecal masses and gases with no willing control by patients or sphincter mechanism participation. Depending on the period of their use colostomies can be temporary or permanent. Adaptation of patients to life with colostomy is not easy and fast process. Beside the doctor and therapist important part of the team is the nurse both in education and care of patients with colostomy. Based on hospital registry of Institute of Oncology and Radiology of Serbia, in Belgrade the number of newly registered patients with colorectal carcinoma during the last year was 485 patients (10% of all patients), from which 43 underwent surgical procedure-colostomy.
Our aim was to present standardized nurse interventions in education of patients with colostomy. Documentation used: Protocol of health care of Institute of Oncology and Radiology in Belgrade and nurse documentation. Through application of standardized nurse activities, involving education and care of patients with colostomy, their adaptations to new conditions of life is faster and less traumatic.

Key words: Colostomy; Nursing; Patient Education as Topic; Nurse`s Role; Reference Standards

OP 31

UDC: 616.348-006:616.351-006:614.44:577.21

Importance of KRAS gene mutations detection in patients with metastatic colorectal carcinoma

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Screening for the KRAS mutations, necessary prior Erbitux treatment of patients with metastatic colorectal carcinoma (mCRC), have been performed at Institute for oncology and radiology of Serbia for more than one year and half. KRAS plays a key role in the EGFR signaling pathway, frequently altered in tumor cells. Mutations in the KRAS oncogene are frequently found in human cancers; 30-40% of patients diagnosed with metastatic colorectal cancer harbor mutations in the KRAS gene. The presence of these mutations correlates with a lack of response to certain EGFR inhibitor therapies such as Erbitux. Our aim was detection of KRAS gene mutations in patients with mCRC, before introduction of Erbitux. DNA extraction was done from paraffin embedded tissue, using DNA FFPE Tissue kit. KRAS gene mutations were detected by ARMS-Scorpions Real-Time PCR. This method is highly sensitive, detects seven KRAS mutations in codons 12 and 13, and can detect 1% of mutant in a background of wild type (wt) genomic DNA. Detection of the mutations was performed in 184 patients with mCRC; 68 (37%) patents were harboring KRAS gene mutations. Patients with wild type (wt) were subjected to Erbitux treatment. Number of patients with mCRC, having KRAS gene mutations, is the same in our population as reported elsewhere. The development of personalized medicine and such kind of molecular-diagnostic tests is of the highest importance for the patient, making possible to achieve the best medical outcome with a minor side effects.

Key words: Colorectal Neoplasms; Neoplasm Metastasis; Genes, ras; Antineoplastic Agents; Receptor, Epidermal Growth Factor; Antibodies, Monoclonal; Polymerase Chain Reaction

PP 32

UDC: 612.323.5:616-089.8:614.243.5

Duties of an operating room nurse during the total gastrectomy procedures

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Total gastrectomy is a procedure, which implies complete removal of stomach. The continuity of gastrointestinal tract is maintained by the primary esophagojejunal anastomosis. The duties of the operating room nurses, as members of a surgical team, are standardized and require a high level of professionalism with the absolute care of keeping aseptic environment. Our aim was to present the activities of the operating room nurse during the total gastrectomy procedure. The activities of the operating room nurse include proper handling of surgical instruments during the surgical procedure, which adds up to the smoothness of the procedure. Following the strict procedures and fulfilling all the duties of the operating room nurse, minimizes the chances of making a mistake during the procedure, which leads to higher level of safety for the patients.

Key words: Gastrectomy; Surgical Procedures, Operative; Nurse`s Role

PP 33

UDC: 616-006:616-089.168:614.253.5

Activities of the operative room nurse during the total pelvic exenteresis

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Total pelvic exenteresis (TPE) is a surgical procedure, which considers removal of all visceral pelvic organs, distal ends of all three tracts: genital, urinary and digestive, with the corresponding parts of perineum. It was developed as the only onco-specific procedure in malignancies that have not responded to the chemo- and radiotherapy. Our aim was to present the activities of the operative room (OR) nurse during the TPE. Activities of the OR nurse include: acceptance of patients to the OR; positioning of patients in Trendelenburg position; various procedures of the OR nurse during the operative procedure. The activities of the OR nurse during such an extensive surgical procedure are tremendously important. By maintaining high standards and all measures of aseptic work, patient's safety is lifted to higher standards leading to successful surgical procedure.

Key words: Pelvic Exenteration; Surgical Procedures, Operative; Patient Care Team; Nurse`s Role

OP 34

UDC: 613.97:316.772.4:316.6

Conceptual model of communication in palliative care

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Communications are rather seen as an undividable factor of the whole social, economic, and cultural context, than as some separate system or field. With its global character, throughout implementation of integrated models, theories, skills and procedures, it pervades all activities and serves like a transmitter of cultural values with a main and deciding role in founding better communication in social structures. A good communication has vital significance for managing a successful healthcare and health therapies. Communicational skills or communicational competence is a speaker's skill to use his vocabulary in diverse and flexible way, adjusting it to communicational and social needs one faces throughout the life." (*Berruto, 1994*). The purpose is to emphasize the significance and peculiarity of the communication in palliative care through theoretical and analytic approach: analytical – synthetic method, abstractive method, and modeling method. Presented model is *Projected conceptual and interactive communicational model (Kekus D, 2009)*, which encompasses dimensions of summary and relationships throughout the following elements: process, outcome and expectations. Projected conceptual interactive communicational model is specially presented. It is combined with a model of interpersonal communication, which contains six elements: individually situational context, aim, interfering processes, response, feedback, and perception. A great significance of individual and situational process stands out, referring to personal characteristics of a communicator and to description of the situational surroundings, which gives a contextual background of the communication. The actual interaction between people leads to changes in one's knowledge, believes, attitudes and behavior (which is the base for any educational activity and supporting intervention in healthcare). During the development of a new conceptual model in both health and palliative care – the process begins with the research of the consumers' needs, with precise definitions and specifications of consumers' requirements, which is the system of functional questionnaires helping us to better satisfy all consumers' needs. It is presented through the phases where each one influences the upcoming one. The following issues are being transferred from the suggested conceptual model into the process of communication: previous experience, expectations, and the organization, which influences the patients' votes for the expectations vs. realization. The outcome vote presents new assumptions in the continuity of the health care. "Communication" as a health sector, unfortunately, does not exist in our health system as category, but for sure takes part in the quality of given health care, at least in the quantities in which it offers some benefits to the patients making them consider it important. Exact measuring of the feelings and satisfaction of patients during their visits to the physician, the time spent in hospital, medical procedure, home care and the whole experience with medical care, is a big challenge and opens further discussions and various questions.

Key words: Communciation; Palliative Care; Models, Psychological; Professional-Patient Relations; Interpersonal Relations; Needs Assessment; Consumer Satisfaction

OP 35

UDC: 616-006:616-032.882:614.253.5

Hospice philosophy

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„Why to be afraid of death, while we are here – the death is non-existent, and when it comes – we are gone"- Socrates

Crucial crossroads of every man is necessarily burdened by the thought of the inevitable death. People always, in a new way, ask numerous and significant questions related to moral postulates and spiritual values. A man's resistance to awareness of inevitability and the finality of the biological death has lasted and dominated since the time of rationalism and the abstract rationalization. Thus, through millennia, a mystic salvation exit from the unacceptable situation has been created. Every cured patient adds something to our sense of self-respect. Unfortunately, that is not the case with a patient that is dying. Dealing with death creates serious discomfort in many people. This statement is substantiated by the fact that there is not enough expert literature on the subject of death or dying, which points out the difficulties and the necessity of elaboration of this topic. Death is a natural and necessary mechanism of individual discontinuity within the continuum of regeneration. Our attitude towards a dying person is, primarily, a moral and civilizational matter, through which, the level of collective and individual consciousness and culture is mirrored. The patients in their terminal phase deserve support and necessary care in the last days of their lives. The number of hospices is getting bigger every day in the developed countries. Experiences of the modern society are increasingly getting present in our country and are becoming the reality. One of the imposing imperatives of the process of the ongoing transition is the adequate care and support to dying persons. A primary goal of presentation of hospices in our surroundings stresses the necessity of development of our awareness on the needs of the hospice. A maximal professional competence, extreme responsibility, highly developed awareness on seriousness and complexity of such a task, as well as moral quality, is the basic postulates for establishment of the hospice philosophy in our region.

Key words: Neoplasms; Terminal Care; Hospice Care

OP 36

UDC: 616.831-006:616-089.8:615.849.1:614.253.5

Health care of the patients on central nervous system palliative radio-therapy treatment

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About 40% of intracranial neoplasms are metastases often developed from tumors of the lungs, breast cancer, renal cancer, colon cancer, and melanoma. Intracranial neoplasms are diagnosed by computerized axial tomography (CAT) or magnetic resonance imaging (MRI) examination of endocranium. Their clinical manifestation is neurological and rarely psychical. Headache, nausea, vomiting, confusion, and lethargy appear due to increased intracranial pressure. Treatment option is surgery followed by radiotherapy, or radiotherapy alone. In our study we used health care files and medical records. We separate health care diagnosis and collaborative problems and the role of the nurse in symptom identification and specific intervention practicing in order to improve the quality of life for the patients on central nervous system palliative treatment. Changed cerebral tissue perfusion, selfcare deficit, changed thinking process, anxiety, emotional tension, injury possibility, conscious disorder, epilepsy stroke - all these symptoms should be avoid or mitigated.

Key words: Brain Neoplasms; Neoplasm Metastasis; Diagnosis; Nurse`s Role; Surgery; Radiotherapy; Palliative Care

OP 37

UDC: 616-006:612.39:371.64:614.253.5

Educating patients and families about proper nutrition for nausea and vomiting as side effects of chemotherapy-nursing interventions

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Nausea and vomiting are among the most unpleasant side effect of chemotherapy. Nausea and vomiting after chemotherapy may be acute and delayed. Acute occurs in the first 24 hours during chemotherapy, while delayed is the one that occurs after 24 hours of completed chemotherapy. Sometimes when patients expect to feel worse, they begin to experience symptoms before treatment and it is called anticipatory nausea and vomiting. Regardless of the use of premedication containing antinauseants, side effects occur because patients feel different intensity of symptoms. By giving tips on proper nutrition the nurse can help patients to prevent and reduce unpleasant adverse effects of chemotherapy. EONS recommendations also give advice what to avoid in preventing unwanted effects. The aim of this paper was to present recommendations on proper nutrition for nausea and vomiting as adverse effects of chemotherapy. Inadequate nutrition may aggravate nausea and vomiting after chemotherapy. The role of nurses is reflected in the education of cancer patients and their families about adequate nutrition. Thus patients feel better, have no fear of chemotherapy and the treatment is more successful.

Key words: Antineoplastic Agents; Nausea; Vomiting; Nutrition; Food; Patient Education as Topic; Nurse`s Role

PP 38

UDC: 616-006:616-052:616-051:504.06

Nursing in palliative care: What is the role of a nurse in a hospice team?

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The nurse's role in palliative care is to promote the quality of life for the patients and their family members during the course of the patient's illness. The place of nurses in a palliative care setting is alongside the patients and their families wherever that may be. Nurses who have undergone specific training and education in this field are the most valuable and effective members within the palliative care team. They can achieve their goals in two ways, either directly or indirectly. Direct role: assessment of a patient's symptoms and needs, solving the problems in accordance to the assessment and being present whenever nursing care is needed. This implies the best quality of nursing care, administration of prescribed drugs for symptom control as well as control of side effects and psychological support for patients and their families. Indirect role: education of other health care professionals, volunteers and patients and their family members. Having a nurse who has good knowledge and skills contributes greatly to the challenges faced by the patients and their family at the most difficult time. A nurse helps their patients to live with dignity in their last days, which is the main goal of palliative care.

Key words: Palliative Care; Patient Care Team; Nurse`s Role; Patients; Quality of Life

PP 39

UDC: 616-052:005.57:504.06

Bringing back a smile to our patients

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High quality palliative care involves good symptom control, psychosocial care, and spiritual support for patients and their families. This can only be achieved through effective communication between a palliative care nurse on one side and patients and their families on the other as well as among the other members of the multiprofessional palliative care team. Communication is an exchange of information, ideas, thoughts, and feelings. Communication objectives are: collecting valid information, establishing a good relationship with patients and their families, and forming an agreement considering a patient's further treatment. For successful communication, it is absolutely necessary for the nurse to be properly trained and educated in communicative skills, capable of following relevant guidelines and has an ability to recognize other signs and signals within communication. Being able to successfully understand physical, psychological and spiritual problems is when actually start to give real help in symptom control and improve the wellbeing of a patient with terminal disease. This is the only way we can bring a smile back to our patients` faces and give them the opportunity to make the most of the time they have left with their families in the best possible way.

Key words: Palliative Care; Communication; Professional-Patient Relations; Quality of Life

OP 40

UDC: 611.91:611.93:616-006:615-085:615.849.1

Side effects of chemoradiotherapy plus cetuximab in patients with advanced head neck squamous cell carcinoma – health care

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Head and neck squamous cell carcinomas (SCCHN) are frequent tumors and account for around 500000 new cases per year. Seventy percent of the patients present with advanced stages require heavy and combined therapy. Induction chemotherapy and concomitant chemoradiotherapy plus cetuximab use sequentially provided optimal benefit for patients. The incidence of distant metastases is reduced and the radiotherapy efficacy is amplified. Treatment with concomitant chemoradiotherapy plus cetuximab improves locoregional control increasing the common toxic effect. At the Institute of Oncology and Radiology in Belgrade, in the period from January 2008 to June 2009, 32 patients with SCCHN were treated with concomitant chemoradiotherapy plus cetuximab. A planned treatment consisted of a loading dose of Cetuximab (400 mg/m^2) one week prior radiotherapy and then weekly (250 mg/m^2) with or without CDDP (40 mg/m^2), with radiotherapy 70Gy in 35 daily fractions. Patients were divided in two groups. Group I: patients treated with concomitant chemoradiotherapy plus cetuximab. Group II: patients treated with concomitant radiotherapy plus cetuximab. The most frequent side effects were: skin toxicity (group I 86%, group II 90%), mucositis (group I 100%, group II 100%), anemia (group I 54.5%, group II 10%), leukopenia with neutropenia (group I 27.9%), thrombocytopenia (group II 9.1%), diarrhea (group I 4.5%, group II 20%), febrile states (group I 36%), metabolic disorder: hypo Mg (group I 59%, group II 50%), hypo K (group I 36%, group II 30%), hypo Ca (group I 18%, group II 10%), hypo proteinemia (group I 45%, group II 30%), hypoalbuminemia (group I 27%, group II 50%). Cetuximab in treatment with concomitant radiotherapy increases the common toxic effect within the radiation portals. In combination with CDDP the frequency of severe neutropenia may be increased and thus may lead to a higher rate infections complication. Nurses should be familiar with these side effects and specific treatment of unwanted side effects – all aimed to improve the quality of life of such patients.

Key words: Head and Neck Neoplasms; Carcinoma, Squamous Cell; Combined Modality Therapy; Antineoplastic Agents; Drug Therapy; Radiotherapy; Antibodies, Monoclonal

OP 41

UDC: 618.19-006:618.2:615-085

Chemotherapy of breast cancer in pregnancy

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Chemotherapy is a choice-therapy for many cancers. For accurate use of cytostatics, it is important to understand the normal cell cycle, changes in cell cycle that bring to malignant transformation, and system of cytostatics that "kill" the tumor cells. Knowing the mechanisms of action and aim of the therapy are the key-elements of multiagent treatment. In multiagent regimens, different cytostatics have a different ways in blocking or changing cell cycle (for example anthracyclin-based and taxane-based regimens). Toxicity is also diverse. The aim of the paper was to present the treatment of two pregnant women receiving chemotherapy for breast cancer in Daily Hospital in IORS, during 2009. Use of chemotherapy in pregnancy, especially in first trimester, has been shown as very toxic and it can lead to many congenital and genetic disorders. Oocites can be damaged as well, so the next pregnancies can have a lethal result. Second and third trimesters are more comfortable for the use of cytostatics because the organogenesis is completed (presented at *Sixth Breast Cancer Congress*). However, the use of chemotherapy in pregnancy has to be carried out very carefully, not just because of patient but because of the fetus as well (detail genetic screening should be performed in children born after chemotherapy).

Key words: Breast Neoplasms; Pregnancy; Antineoplastic Agents; Drug Therapy

OP 42

UDC: 616-089.1:616-005.7:615.8

The role of physical therapy in prevention and treatment of postoperative thromboembolism

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Thromboembolic complications (TEC) are common in postoperative course. The most frequently are manifested as deep venous thrombosis and pulmonary embolism. Pulmonary embolism occurs 7 to10 days or later after surgery. It is strongly correlated with patient's immobility in the bed and suggests the importance of early mobilization, vessels damage, and coagulopathy. Risk factors for TEC are genetic (hereditary) and acquired. Acquired risk factors are age over 65 years, vein damage, heart insufficiency, obesity, sepsis, malignant diseases (7%), immobility, major abdominal and pelvic surgery, length of operation (longer than 6 hours brings twofold the risk), operative and other trauma, cardio-vascular insult (CVI). The aim of this study is to present postoperative TEC and to point out the role of physical therapy in both prevention and treatment. Early mobilization of patients in bed and verticalization in intensive care units significantly diminishes the risk of thromboembolism. Mechanical methods in high-risk patients are efficient if applied together with anti thrombotic prophylactics aiming to decrease venous stasis and improve circulation. Mechanical methods comprise appliance of elastic socks or bandages before, during, and after surgery until full patient's mobility is achieved. Active exercises for peripheral circulation in bed, early sit up, and walking of patients are mandatory. Timely and enhanced physical therapy in early postoperative rehabilitation in surgical patients significantly prevents postoperative thromboembolic complications. In addition, it improves overall performance status and faster recovery of patients and shortens hospital stay and costs.

Key words: Postoperative Complications; Thromboembolism; Pulmonary Embolism; Physical Therapy Modalities

PP 43

UDC: 616-006:616-001.47:615-085

Modern treatment of ulcerating tumors in cancer patients

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Complications in terms of infections that lead to ulcerating tumors are very common cause of morbidity and mortality in oncology patients. We examined whether the use of modern means of swathing of ulcerating tumors prevent infection spreading, reduce bleeding, and the costs of treatment. The study presents three ulcerating tumors changes that were treated with hydrocolloidal linings with silver ion during several weeks; they have antimicrobial effects and contain sodium carboxymethylcellulose that is highly adaptable and blotting. All patients treated with hydrocolloidal linings had changes in various locations: neck, inguinum, left breast. All wounds were infected. Following bacteria were isolated: *Enterococus*, *Pseudomonas, Esherichia coli.* After approximately two weeks of swabbing, there was a decrease in exudation, bleeding, and tumor size in a patient who had a tumor on a neck. This caused less pain and stress that tumor brings during the swathing period. Swabbing was performed every other day. The average price of a traditional treatment method is more expensive and requires the engagement of medical staff twice a day. Use of hydrocolloidal lining is cheaper and requires changing once in every other day. This also avoids bleeding because damaged blood vessels can cause greater complications. The use of this new swabbing method in oncology patients reduces the risk of further complications and the possible occurrence of intrahospital infections that is inevitable in oncology.

Key words: Neoplasms; Wounds Infection; Colloids; Bandages, Hydrocolloid; Treatment Outcome

PP 44

UDC: 618.14-006:616-089.8:614.253.5

Radical abdominal trachelectomy - health care in post surgical period

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Radical abdominal trachelectomy is a new procedure in treating operable cervical cancer. It is applied in young persons, when preserving reproductive ability is the goal. The role of a nurse, as a team member in period after the surgery is out of most importance for quicker rehabilitation of these patients. Our aim was to show standardized activities of a nurse - technician after the procedure of radical abdominal trachelectomy. In our work we used: data from history of diseases, protocol of health care of the Institute for Oncology and Radiology of Serbia, nurses' documentation. Radical abdominal trachelectomy is a choice surgery in young patients with operable cervical cancer, because life quality and reproductive capability are preserved. Nurse, as a team member, by applying standardized activities in great deal contributes to successfulness of treatment and complete rehabilitation of patients.

Key words: Uterine Cervical Neoplasms; Gynecologic Surgical Procedures; Nurse`s Role; Nursing; Quality of Health Care; Reference Standards

2009

NOVEMBER

1-4 6th International Guidelines International Network Conference
Lisbon , Portugal
E-mail: office@g-i-n.net
Websute: http://www.g-i-n.net
Tel: +49 30 4005 2501, Fax: +49 30 4005 2555

5-7 5th International Congress on Myeloproliferative Disorders and Myelodysplastic Syndromes
New York, USA
E-mail: meetings@imedex.com
Website: http://www.imedex.com/calendars/oncology.asp
Tel: +1 770 751 7332, Fax: +1 770 751 7334

8-11 3rd International Cancer Control Congress
Lake Como, Italy
E-mail: iccc2009@meet-ics.com
Website: http://www.cancercontrol2009.com
Tel: +1 604 681 2153, Fax: +1 604 681 1049

11-14 Cancer in Africa. 7th AORTIC International Cancer Conference
Dar Es Salaam, Tanzania
E-mail: info@aortic2009.org
Tel: +27 21 689 5359, Fax: +27 21 689-5350

12-14 Advanced Practice Nursing Conference
Tampa, USA
E-mail: customer.service@ons.org
Website: http://www.ons.org
Tel: +1 412 859 6100, Fax: +1-412-859-6162

13-15 10th Oncology Nursing Society Institutes of Learning
Tampa, USA
E-mail: customer.service@ons.org
Website: http://www.ons.org
Tel: +1 412 859 6100, Fax: +1-412-859-6162

27-29 Embracing excellence in prostate, bladder and kidney cancer. 2nd multi-disciplinary meeting on urological cancers
Barcelona, Spain
E- mail: emuc-meeting2009@congressconsultants.com
Website: http://www.emucbarcelona2009.org
Tel: +31 26 389 1751, Fax: +31 ^26 389 1752

29- Dec 4 95th RSNA Scientific Assembly and Annual Meeting
Chicago, USA
E-mail: reginfo@rsna.org
Tel: +1 630 571 7879, Fax: +1 630 571 7837

DECEMBER

5-8 2009 American Society of Haematology annual meeting
New Orleans, USA
E-mail: ash@hematology.org
Website: http://www.hematology.org/calendar.cfm

Tel: +1 202 776 0544, Fax: +1 202 776 0545

5-9 49th ASCB Annual Meeting
San Diego, USA
E-mail: ascbinfo@ascb.org
Tel: +1 301 347 9300, Fax: +1 301 347 9310

10-13 32nd San Antonio Breast Cancer Sympsoium
San Antonio, USA
E-mail: Rmarkow@ctrc.net
Website: http://www.sabcs.org
Tel: +1 210 450 5912, Fax: +1 210 450-5009

2010

FEBRUARY

2-5 ICACT: 21st International Congress on Anti-Cancer Treatment
Paris, France
E-mail: infos@im-events.com
Website: http://www.icact.com
Tel: +33 1 47 43 22 28, Fax: +33 1 47 43 22 26

6-7 2nd Asian Breast Cancer Congress
Bangalore, India
E-mail: abcc2010@gmail.com
Website: http://www.abcc2010.com
Tel: +91 98 80914343

18-21 7th American Psychosocial Oncology Society Annual Conference
New Orleans, USA
E-mail: info@apos-society.org
Website: http://www.apos-society.org
Tel: +1 434 293 5350

MARCH

3-5 St Jude-Viva Forum in Paediatric Oncology
Singapore, Singapore
E-mail: Mee_Cheng_TENG1@nuh.com.sg
Website: http://www.viva.sg/stjude/
Tel: +65 6772 5466, Fax: +65 677 5433

7-11 16th International Conference on Cancer Nursing
Atlanta, USA
E-mail: info@isncc.org
Website: http://www.isncc.org/conference
Tel: +1 604 630 5516, Fax: +1 604 874 4378

15-18 5th Latin American Congress for Palliative Care
Buenos Aires, Argentina
E-mail: alcp.cmonti@gmail.com
Website: http://vcongresoalcp.org/pagina-de-inicio
Tel: +54 3461 433351, Fax: +54 3461 433351

18-20 6th International Conference Clinical Cancer Prevention 2010
St. Gallen, Switzerland
E-mail: info@oncoconferences.ch
Website: http://www.oncoconferences.ch
Tel: +41 71 243 0032, Fax: +41 71 245 6805

23-27 7th European Breast Cancer Conference
Barcelona, Spain
E-mail: nicola@ecco-org.eu
Website: http://www.ecco-org.eu/Conferences-and-Events/EBCC-7/page.aspx/840

APRIL

15-17 7th EONS Spring Convention
The Hague, Netherlands
E-mail: nicola@ecco-org.eu
Website: http://www.ecco-org.eu/Conferences-and-Events/EONS-7/page.aspx/645

29 Apr - 3 May 34th ONS Annual Congress 2010
San Antonio, USA
E-mail: gpeeks@ons.org
Tel: +1 412 859 6301, Fax: +1 412 859 6167
Website: http://www.ons.org

MAY

14-15 5th Baltic Congress of Oncology
Riga, Latvia
E-mail: aivars.stengrevics@aslimnica.lv
Tel: +371 29 485649, Fax: +371 6 539160
Website: http://www.5BCO-2010-Riga.info

25-29 12th IPOS World Congress of Psycho-Oncology
Quebec City, Canada
E-mail: info@ipos-society.org
Tel: +1 434.293.5350, Fax: +1 434 977 1856
Website: http://www.ipos-society.org

JUNE

5-9 57th Society of Nuclear Medicine Annual Meeting
Salt Lake City, USA
E-mail: MeetingInfo@snm.org
Tel: +1 703 708 9000 ext. 1229,
Fax: +1 703 708 9274

15-19 4th World Congress of International Federation of Head & Neck Oncologic Societies
Seoul, South Korea
E-mail: ifhnos2010@meci.co.kr
Tel: +82 2 2082 2300, Fax: +82 2 2082 2314
Website: http://www.ifhnos2010.org

26-30 21st Meeting of the European Association for Cancer Research
Oslo, Norway
E-mail: nicola@ecco-org.eu:
Website: http://www.ecco-org.eu/Conferences-and-Events/EACR-21/page.aspx/1105

30 June-3 July 12th World Congress on Gastrointestinal Cancer
Barcelona, Spain
E-mail: meetings@imedex.com
Tel: +1 678-242-0906, Fax: +1 678-2420920
Website: http://www.imedex.com

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Altman DG. Statistic in medical jornals: some reacent trends. *Statistic Med.* 2000;19:3275-89.
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Dissertations and thesis
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