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Comparison of Predictive Models PREMM$_{1,2}$, MMRpro and Wijnen for Mutation Detection Associated With Lynch Syndrome in MLH1 and MSH2 Genes

C. Guillen-Ponce[1], M.J. Molina-Garrido[2], M. Goicoechea[3], D. Salas[3], A. Carrato[1]. [1]*Hospital Ramón y Cajal, Medical Oncology, Madrid, Spain;* [2]*Hospital Virgen de la Luz, Medical Oncology, Cuenca, Spain;* [3]*Direccion de Salud Publica, Oficina del Plan del Cancer, Valencia, Spain*

Background: Lynch syndrome is the most common inherited cause of colorectal cancer, and is due to germline mutations in mismatch repair (MMR) genes. Most mutations occur in genes MLH1 and MSH2. Currently, clinical and molecular criteria are used for selecting individuals with Lynch syndrome. Several predictive computer models have been development to predict the probability of being a carrier of a mutation in the MMR genes.
Material and Methods: Between 2005–2008, 124 MLH1 (64) and MSH2 (60) analyses in patients with suspected Lynch syndrome were performed. Retrospectively, all patients were applied the predictive models PREMM$_{1,2}$, MMRpro and Wijnen's model. The predictive ability of each model was assessed using the area under the receiver operating curve (AUC). Sensitivity and specificity at different cutoffs were compared for different models.
Results: Pathogenic MMR gene mutations were detected in 20 (16.13%); 6 of MLH1 gene and 14 of MLH2 gene. PREMM$_{1,2}$ had better predictive ability to detect between mutation carriers and noncarriers (AUC 0.698 [95% CI, 0.576 to 0.82]), which MMRpro model (AUC 0.631 [95% CI, 0.502 to 0.76]) ($z = 16.75$, $p < 0.05$). Also, both models were superior to the Wijnen's model (AUC 0.533 [95% CI, 0.386 to 0.679]) ($z = 10.89$ versus MMRpro, $z = 12.69$, $p < 0.05$). From 6% cutoff, PREMM$_{1,2}$ discriminated between individuals carrying germline mutation in the MLH1 and/or MSH2 ($p = 0.028$), for this cutoff point, its sensitivity was 90%, while specificity of 35.82%. The cutoff of PREMM$_{1,2}$ 20% had a sensitivity of 71.64% and specificity of 45%, negative predictive value 81.35% and 32.14% positive predictive value.
Conclusions: The model PREMM$_{1,2}$ has better discriminative power of germline mutation in MLH1 and MSH2 genes that MMRpro models and Wijnen, although its sensitivity and specificity for different cutoff points were low.

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Urological Leaks After Pelvic Exenterations Comparing Formation of Colonic and Ileal Conduits

S. Teixera[1], F.T.J. Ferenschild[2], L. Rodwell[3], J.D. Harrison[3], J.M. Young[3], A. Vasilaris[4], D. Eisinger[4], P. Lee[5], C. Byrne[5], M.J. Solomon[3]. [1]*Erasmus Medical Center Rotterdam, Surgical Oncology, Rotterdam, The Netherlands;* [2]*UMCN St. Radboud Nijmegen, Surgical Oncology, Nijmegen, The Netherlands;* [3]*Surgical Outcome Research Centre (SOuRCe) University of Sydney NSW Australia, SOuRCe, Sydney, Australia;* [4]*Department of Urology Royal Prince Alfred Hospital Sydney Australia, Urology, Sydney, Australia;* [5]*Department of Colorectal Surgery Royal Prince Alfred Hospital Sydney Australia, Colorectal Surgery, Sydney, Australia*

Objective: Assess risk factors for urinary leakage of a newely formed urinary conduit after a pelvic exenteration.
Summary Background Data: Pelvic exenterations are a potentially curative treatment for locaaly advanced pelvic cancer. After the creation of an ileal or colonic conduit there is a high risk of urinary leaks. We expect multiple factors would be of influence.
Materials and Methods: Analysis conducted from prospectively collected data of patients who underwent a Pelvic Exenteration with conduit formation for advanced pelvic cancer, in the period from December 1995 until December 2010.
Results: Of 232 patients undergoing pelvic exenteration, 74 (32%) had an ileal (64%) or a colonic (36%) conduit formed. Patients were aged between 14 and 91 years and 74% were male. Twelve (16%) patients developed a leak in total, of which 9 within the first month. The factors significantly associated with a urine leak were involved surgical margins, the magnitude of the exenteration and a current cardiovascular medical history. The 30 day leak rate for colonic conduits was 4% (1/27) compared with 17% (8/47) for an ileal conduit. Survival was not significantly differnt between the patients with or without a leak. The median survival time was however significantly longer for patients without a leak ($P = 0.04$).
Conclusions: Urine leaks after conduit formation in association with exenterations are quite common. Cardiovascular risk facors, positive surgical margins and the magnitude of pelvic exenterations but not radiotherapy were associated with leaks. Colonic conduits had a slightly lower leak rate than ilal conduits.

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Neoadjuvant Capecitabine-based Chemoradiotherapy in Resectable Rectal Cancer

L. López[1], J. Medina[1], D. Palomares[2], S. Alonso[1], B. Martinez[1], J.I. Chacon[1], L. Diaz[1], N. Cordero[1], M.A. Cruz[1], F. Molina[2]. [1]*H. Virgen de la Salud, Oncology, Toledo, Spain;* [2]*H. Virgen de la Salud, Surgery, Toledo, Spain*

Background: Preoperative 5-FU based chemoradiotherapy (CRT) improves local tumour control in resectable rectal cancer. Capecitabine (CAP), an oral fluoropyrimidine, is converted to active 5-FU in tumour cells. CAP has shown to be as effective and well tolerated as 5-FU iv in the adjuvant and metastatic colorectal cancer. Previous studies in rectal cancer have shown that CAP replace 5-FU in this setting. The aim of this retrospective analysis was to evaluate the effectiveness and safety of preoperative capecitabine-based CRT in patients with resectable rectal cancer.
Methods: From February 2004 to May 2010, patients with resectable rectal cancer, age$\geqslant$18, ECOG$\leqslant$2, adequate haematologic, renal and hepatic functions were included in this analysis. Neoadjuvant chemotherapy was CAP (825 mg/m^2/12h, 5 day/w, oral) with RT (50.4 Gy) for a median of 6 weeks. Surgery was performed a median of 6 weeks after RT. Survival curves were estimated by Kaplan–Meier method.
Results: Sixty one patients, 70.7% men and 29.31% women with a median age of 67 (45−82), ECOG 0−1, with locoregional 47.5% uT3N$_X$, 26.2% uT3N$_+$, 10% uT4N$_X$, 11.5% uT4N$_+$ and well-moderately differentiated G1−2(90%) tumours. Performed surgeries were Abdominoperineal amputations (78%) and low anterior resections (21%). Only 7 patients (12.5%) had CAP reductions. Fifty-two patients (85%) did not have any adverse event grade 3−4 treatment-related. Adverse event consisted of diarrhea and anemia (2 patients each), skin toxicity (1 patient), mucositis and medullar aplasia with DPD deficiency subsequently confirmed (1 patient). After resection, pathological stages were pT0N0 (10.5%), pT1N0 (3.5%), pT2N0 (23%), pT2N1−2 (5.2%), pT3N0 (30%), pT3N1−2 (24.5%), Pt4N0 (3.5%), histological tumour grades were G1 23% (13 pts), G2 62% (35 pts), G3 3% (2 pts), and tumour regression TRG1−2 (15%), TRG3−4 (50%). After surgery, 98% of the pts received adjuvant treatment. At 4-year follow-up there were 8 deaths, being survival from diagnosis to death 85.4% (95% CI, 73.0–92.4) with 3 progressions, and survival from diagnosis to progression 94.5% (95% CI, 84.0–98.2).
Conclusions: Efficacy and tolerance of Neoadjuvant capecitabine-based chemoradiotherapy in patients with well-moderately differentiated locoregional rectal cancer is similar to concurrent RT+5-FU as previous studies had suggested. Long-term follow-up demonstrated high rates of survival from diagnosis, with few disease progressions.

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Colorectal Cancer Resectable Liver Metastases Patient 5-year Survival After Preoperative Transarterial Chemoembolization With Oxaliplatin Followed by Liver Resection

I. Rebeko[1], V. Zharkov[2], V. Kokhnyuk[3], V. Dudarev[4], V. Akinfeyev[4], D. Dorosh[2]. [1]*N.N. Alexandrov National Cancer Centre of Belarus, Abdominal Oncological Department, Minsk, Belarus;* [2]*N.N. Alexandrov National Cancer Centre of Belarus, Thoracic Oncological Department, Minsk, Belarus;* [3]*N.N. Alexandrov National Cancer Centre of Belarus, Deputy Director, Minsk, Belarus;* [4]*N.N. Alexandrov National Cancer Centre of Belarus, Radiological Department, Minsk, Belarus*

Background: Liver resection (LR) is a standard treatment option in resectable colorectal cancer (CRC) liver metastases patients. Perioperative chemotherapy has allowed to raise reccurence-free survival by 9% but role of neoadjuvant therapy hasn't been learned yet.
Material and Methods: Prospective nonrandomized trial, including 66 synchronous and metachronous CRC resectable liver metastases patients, has been completed. Resectability criteria were removal of all metastases with reservation of more than 30% liver parenchyma; portal vein, more than 2 hepatic vein and inferior cava invasion absence. LR has been performed in group 1 ($n = 40$, average age-59 years old, 25 men, 15 women). Transarterial chemoembolization (TACE) with 50–100 mg oxaliplatin, followed by LR in 4−6 weeks, has been carried out in group 2 ($n = 10$, 58, 2/8). TACE with 30−50 mg doxorubicin, followed by LR in 4−6 weeks, has been conducted in group 3 ($n = 16$, 56, 8/8).
Results: Median and 5-year recurrence-free survival (RFS) have amounted to 13.1 months and 22.3$\pm$6.6% in group 1; 36.9 months and 40.0$\pm$15.0% in group2; 13.8 months and 5.9$\pm$5.7% in group 3, respectively ($p = 0.015$). RFS was hgher in group 2 versus group 1 ($p = 0.033$) and group 3 ($p = 0.003$). Median and 5-year survival (OS) have amounted to 32.8 months and 30.3$\pm$7.4% in group 1, median hasn't been obtained and 5-year survival has amounted to 58.3$\pm$16.1% in group 2, 31.1 months