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Prognostic significance of pathologically detected extramural venous invasion (EMVI) in rectal carcinoma

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Background: Rectal carcinoma (RC), a common malignancy of the gastrointestinal tract, remains a great clinical challenge due to the increased risk of local and/or systemic recurrence. The mechanism of primary tumor progression and dissemination may be the crucial prognostic factor. Direct vascular spread, especially venous invasion, has been previously recognized and validated as an important predictor of adverse prognosis. Extramural venous invasion (EMVI) is characterized by the presence of tumor cells within veins outside the bowel wall and is strongly associated with poor survival, increased risk of local recurrence, systemic recurrence, and death. The aim of this study is to examine the prognostic value of pathologically detected EMVI and its relationship with other available clinicopathological parameters of patients with RC. **Patients and Methods:** This retrospective study included 100 untreated and non-metastatic RC patients (50 EMVI+ and 50 EMVI-) who underwent curative resection between January 2016 and June 2018 and were followed for the next five years (median follow-up of 71.1 months). The presence of EMVI was assessed on standard hematoxylin and eosin-stained histolological sections of postoperative tumor specimens samples, confirmed by a consultant pathologist in arbitrary cases, and in accordance with validated College of American Pathologist (CAP) guidelines. **Results:** The presence of EMVI within a selected cohort of RC patients significantly associated with female gender (p=0.039), T4 stage (p=<0.001), N2 stage (p=<0.001), less number (n≤3) of involved lymph nodes (p=<0.001), excessive lymphatic infiltration (p=0.044), presence of perineural invasion (p=0.002), positive circumferential margin (CRM) (p=0.003), and TNMIII stage (p=<0.001). In addition, within EMVI+ patients, metastases, dominantly in the liver (13/19, 68%), and death outcomes were more frequent events (p=0.013 and p=0.032, respectively), while survival analyses revealed that EMVI+ patients had significantly shorter overall survival (OS, p=0.035) and disease-free survival (DFS, p=0.030). **Conclusion**: Obtained results strongly suggest that the EMVI type of vascular invasion, considered independently of classical stage parameters and separately from lymphatic invasion, has the potential to be a reliable predictor of the course and outcome of the disease, which should be confirmed on a larger cohort of patients with RC.
Keywords: Extramural Venous Invasion (EMVI), Predictive Medicine, Rectal Cancer

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Genomic instability as a prognostic marker in malignant brain cancer

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Introduction: Glioblastoma and Astrocytoma are diffuse malignant brain tumors and characterized as the most aggressive and invasive brain cancers. Glioblastoma IDH wild-type is a primary brain tumour that develops de novo, and Astrocytoma IDH mutant is a secondary tumour which arises by progression from lower tumour grades. They are characterized by poor survival, resistance to therapy and poor prognosis which develops as a consequence of genomic instability. Genomic instability also contributes to tumour heterogeneity and provides the genomic diversity necessary for selection. **Materials and methods:** 31 patients with Glioblastoma IDH wild-type and Astrocytoma IDH mutant, grade 3 and 4, were analysed for the presence of genomic instability using AP-PCR, DNA profiling method. Comparing DNA profiles between tumour tissue and normal tissue (blood) of the same patient, we detected qualitative and quantitative changes. Qualitative changes are detected as the presence and absence of bands and are the manifestation of microsatellite instability (MIN). Quantitative changes are the representation of chromosomal instability (CIN) and are detected as differences in the intensity of bands. Survival analyses were performed using Kaplan & Maier test for survival data in relation to different histological tumour type and genomic instability. Statistical differences were considered significant for p≤ 0,05. **Results:** Patients with Glioblastoma IDH wild-type have significantly shorter survival compared to other histological types (p=0,025). For each histological type that we analysed and each type of instability,

MIN, CIN and total genomic instability, two groups of patients were made – those with high and low instability. Patients with Glioblastoma IDH wild-type that have low total genomic instability have significantly shorter survival (p=0,045) compared to other analysed types of brain cancer. Patients with Astrocytoma IDH mutant grade 4 who have high total genomic instability and high CIN have significantly shorter survival (p=0,018, p=0,007 respectfully). **Conclusion:** Patients with Glioblastoma IDH wild-type have shorter survival which makes this tumour the most aggressive and malignat of all analysed tumours. Our results show that low genomic instability in Glioblastoma IDH wild-type and high genomic instability lead by high CIN in Astrocytoma IDH mutant, gradus 4 contribute to shorter survival, which makes genomic instability a potential good prognostic marker.
Keywords: Astrocytoma,DNA profiling, genomic instability, Glioblastoma, survival

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Head and neck cancer: single- and two-stage reconstruction

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Background: In head and neck oncology, surgical treatment frequently results in microvascular reconstruction. Oncologic resection followed by immediate reconstruction is often associated with prolonged working and surgical duration, challenging a surgeon's concentration level and potentially worsening patient outcome. To improve the surgeon's performance and to reduce risk of potential complications, we implemented a two-stage procedure in patients with head and neck cancer. This study critically analyzed the surgical outcomes, organizational benefits, and investigated job satisfaction among affected health care professionals. **Patients and methods:** A retrospective data analysis of patients who had undergone microvascular reconstruction after oncologic head and neck surgery between 2010 and 2021 included 33 patients (n = 33). Twenty patients underwent single-stage reconstruction (group 1, n = 20) and 13 patients underwent two-stage reconstruction (group 2, n = 13) with 12.2 (± 7.4) days between surgeries. **Results:** The mean surgical duration, and mean start and end time of the reconstructive surgery component differed significantly (p = 0.002). The mean total complication rate (p = 0.58) did not differ significantly, although a trend toward higher demands for blood products was observed in group 1. There was no significant difference in five-year survival (p = 0.28). A questionnaire on subjective work performance was answered by the affected health care professionals (n = 34) and it revealed that 88% preferred long surgeries to be scheduled first and that 97% work most efficiently in the morning. **Conclusions:** Two-stage reconstruction is a suitable option in selected head and neck cancer patients offering the possibility of optimizing preoperative planning and organization. This may result in regular working hours, reduced surgeon fatigue, and improved job satisfaction without compromising patient outcomes or survival.
Keywords: head and neck cancer, head and neck reconstruction, mitigation strategies, patient safety, staged reconstruction, surgeon fatigue

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Simultaneous *EGFR* L858R and T790M mutations in treatment-naïve metastatic lung adenocarcinoma: a case study and therapeutic implications

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Background: The use of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) is now standard of care in the first-line treatment of patients with advanced adenocarcinoma of the lung who harbor *EGFR* mutations. Patients with the L858R mutation are candidates for first-generation (gefitinib, erlotinib) and second-generation (afatinib) EGFR-TKIs. While the introduction of EGFR-TKIs undoubtedly improves treatment outcomes for patients with *EGFR*-mutated lung adenocarcinoma, a large proportion of patients eventually develop resistance. The most common mechanism of acquired resistance is the occurrence of the T790M mutation in exon 20 of the *EGFR* gene. It has been shown that the T790M mutation can also occur as a primary mutation in patients who have not received EGFR-TKI therapy. This case study presents a rare case in which a patient was diagnosed with concurrent L858R and T790M mutation at the time of diagnosis. **Material and Methods:** This study presents a case of a non-smoking female patient diagnosed with stage IV lung adenocarcinoma at the age of 71 years. DNA isolation was performed from formalin-