2022-RA-1369-ESGO TRICIN: A PHASE II TRIAL ON THE EFFICACY OF TOPICAL TRICHLOROACETIC ACID IN PATIENTS WITH CERVICAL INTRAEPITHELIAL NEOPLASIA

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Introduction/Background Data on non-surgical treatment approaching cervical intraepithelial neoplasia (CIN) are scarce. Retrospective analysis suggest high efficacy of topical treatment with trichloroacetic acid (TCA). This study set out to investigate the efficacy of a single application of 85% TCA in the treatment of CIN I/II.

Methodology In this prospective phase II trial patients with CIN I/II were treated a single time with 85% TCA. After three and six months colposcopic, histologic and HPV evaluation was performed. The primary endpoint was treatment efficacy defined as complete histologic remission six months after treatment. The secondary endpoint was HPV clearance six months after treatment. Rates of histologic regression and remission and type specific HPV clearance three and six months after treatment are described.

Results A total of 102 patients with a median age of 26.6 (19.3–50.0) were included into this trial. Complete histologic remission rates were 75.5% (66.0 – 83.5%) and 78.4% (69.2 – 86.0%) three and six months after TCA treatment, respectively. The observed complete histologic remission rate is significantly higher than an expected spontaneous remission rate of 55% ($p<0.001$). Clearance rates of HPV 16, 18 and other high risk types were 76.5%, 91.7%, 68.7% after six months, respectively. Side effects of TCA were mild and lasted usually less than 30 minutes.

Conclusion This is the first prospective trial reporting high histologic complete remission rates in patients with CIN I/II after a single 85% TCA treatment. In the future, TCA may represent an effective and feasible non-surgical treatment approach for CIN.

2022-RA-1373-ESGO 'HSA-MIR-124 & EPB41L3 DNA METHYLATION ANALYSIS IN LIQUID-BASED CYTOLOGY FOR CERVICAL CANCER SCREENING: A PRELIMINARY DATA IN NORTHERN GREEK POPULATION.'

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Introduction/Background Cervical cancer is the second most common cancer in women worldwide and is caused by a persistent infection with high-risk types of the human papillomavirus (hrHPV). The development of cervical squamous cell carcinomas occurs via well-recognizable premalignant precursor lesions (cervical intraepithelial neoplasia (CIN), graded 1–3), whereas less is known about the different precursor stages preceding cervical adenocarcinomas . Epigenetic mechanisms, including DNA methylation, can influence gene activity without changing the DNA sequence. DNA methylation is a stable, heritable, covalent modification to DNA, occurring mainly at CpG dinucleotides, but is also found at non-CpG sites. Methylation is associated with normal developmental processes, as well as the changes that are observable during oncogenesis and other pathological processes, such as gene silencing of tumor suppressor or DNA repair genes.

Methodology Cervical scrapings were obtained from from cervical cancer patients, 50 referred with an abnormal cervical smear (30 with high-grade cervical intraepithelial neoplasia (CIN2+), 5 with squamous cell carcinoma and 15 without CIN). All scrapings were analyzed by liquid based cytology (LBC) histologicaly confirmed, hr-HPV detection and DNA methylation analysis for detection (EPB41L3 and hsa-miR-124) using quantitative methylation-specific PCR(qMSP).

Results In CIN2+ patients methylation analysis was positive in hsa-miR-124 (19,5%) and EPB41L3 (25%), in SCCs patients hsa-miR-124 (91%) and EPB41L3 (93%). None of the normal samples scored positive for hsa-miR-124 or EPB41L3.

Conclusion This study shows that methylation of hsa-miR-124 and EPB41L3 is a frequent and functionally relevant event in cervical carcinogenesis. The high positivity rates in CIN2+ and carcinomas emphasize us that methylation is not directly related to the presence of of hrHPV. Our pilot study suggest that detection of cervical neoplasia by DNA methylation analysis either or not in combination with other promising methylation markers can improve future cervical screening strategies based on primary hrHPVtesting or triage in cervical pathology.

2022-RA-1377-ESGO ROBOTIC ANTERIOR PELVIC EXENTERATION: SAFE AND FEASIBLE?

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Introduction/Background With nearly 570,000 new cases/year and 310,000 deaths/year, cervical cancer is the second most frequent cancer in women and the third leading cause of cancer-related deaths in females. The transition of pelvic exenteration from a palliative procedure to a potentially curative one in patients with advanced pelvic cancer has been established. With improving surgical technology and increasing surgical experience, exenteration is a logical extension of current robotical practice. So far, there have been various single case reports in literature of robotic anterior exenteration being done for cervical cancer. The prime indication for pelvic exenteration is recurrent cervical cancer after full radiation.

Methodology We present a review in which we included articles concerning the anterior robotic exenteration and the feasibility and outcomes of this procedure. We will also present a case of 61 years old patient that was diagnosed with squamous cell cervical carcinoma FIGO stage IVA with radio chemotherapy treatment and that underwent robotic anterior exenteration.

Results Robotic pelvic oncosurgery is no longer a novelty. We performed a robotic total hysterectomy with bilateral salpingo-oophorectomy with extended parametric resection, bilateral pelvic lymphadenectomy and radical cystectomy with Bricker ileal conduit diversion in our case. The goal of exenterative surgery should always be resection of the

tumor with tumor free margins. The procedure is feasible robotically and if combined with intracorporeal urinary diversion, the overall morbidity and hospitalization can be decreased considerably. Since follow-up of our patient is 10 months, it is too early to discuss survival. Nevertheless, the patient is disease free after 10 months. There were no complications in our case.

Conclusion Robot assisted anterior pelvectomy with anterior vaginal wall preservation is a feasible and mini-invasive technique. Our results have demonstrated the feasibility and oncological safety of performing anterior exenteration robotically in advanced pelvic cancer patients with acceptable morbidity.

2022-RA-1383-ESGO HIGH VISCERAL FAT PERCENTAGE IS LINKED TO UPREGULATED INFLAMMATORY TUMOUR SIGNALLING AND PREDICTS POOR OUTCOME IN UTERINE CERVICAL CANCER

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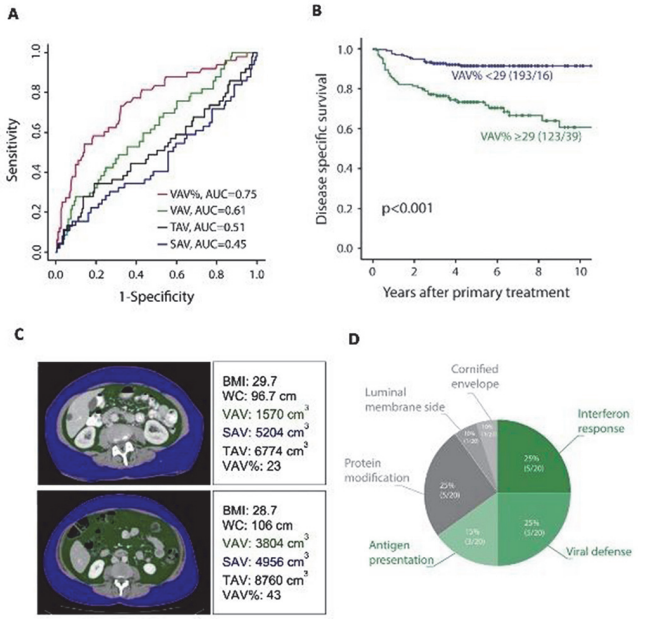
Introduction/Background The aim of this study was to explore abdominal fat distribution markers from computed tomography (CT) in relation to clinicopathologic characteristics and patient outcome in uterine cervical cancer (CC). By unravelling possible links between fat distribution profiles and altered tumour signalling pathways, potential molecular targets for treatment based on body composition profiles may be identified, which may enable more individualized treatment strategies in CC.

Methodology The study included 316 CC patients diagnosed during 2004–2017 who had pre-treatment abdominal CT scans. CT images were analysed to quantify total abdominal fat volume (TAV), subcutaneous abdominal fat volume (SAV), visceral abdominal fat volume (VAV), visceral fat percentage (VAV% = VAV/TAV x100), liver density (LD) and waist circumference (WC). CT morphometric markers were explored in relation to clinicopathologic characteristics and disease-specific survival (DSS), and to gene expression profiles (L1000 mRNA) in a subset of 108 patients.

Results High TAV, VAV and VAV% and low LD were all associated with high (≥44 years) patient age (p≤0.017) and high International Federation of Gynaecology and Obstetrics (FIGO) (2018) stage (p≤0.01). High VAV% was the only CT marker predicting high-grade histology (p=0.028), large tumour size (p=0.016) and poor DSS (HR 1.06, p<0.001). VAV% was strongly positively correlated with age (r=0.68, p<0.001) and VAV (r=0.65, p<0.001). Patients with high VAV% had CC tumours with enrichment of gene sets (false discovery rate [FDR] <5%) related to inflammatory signalling with 65% (13/20) of the top ranked Gene Ontology gene sets related to interferon signalling, viral- or immune response.



Abstract 2022-RA-1383-ESGO Figure 1 High visceral fat percentage is linked to upregulated inflammatory tumour signalling and predicts poor outcome in uterine cervical cancer. (A) Time-dependent receiver operating characteristic (tdROC) curves for predicting disease-specific survival (DSS) at 5 years after diagnosis based on visceral abdominal fat percentage (VAV%), visceral abdominal fat volume (VAV), total abdominal fat volume (TAV) and subcutaneous abdominal fat volume (SAV). VAV% yielded significantly higher AUC (0.75) than the other morphometric makers (P<0.001 for all). B) Kaplan-Meier plot depicting significantly reduced DSS in patients with VAV%≥29 compared with patients with VAV%<29 (p<0.001). C) Abdominal compared lomography (CT) scans with segmentation of visceral and subcutaneous fat compartments carcinoma, international federation of gynaecology and obstetrics (FIGO) (2018) stage III. Patient I, aged 61 yrs, who had low VAV% (23%) received primary radiation therapy and subsequent chemotherapy with cisplatin. She developed pelvic metastases and died from cervical cancer 14 months after primary treatment. D) Gene set enrichment analysis (GSEA) revealed that patients with VAV%>29 had tumours exhibiting upregulated signalling pathways for gene sets involved in inflammatory signalling and immune response (shown in green)

Conclusion High VAV% is associated with high-risk clinical features and predicts reduced disease-specific survival in CC patients. CC patients with high VAV% have tumours with upregulated genes involved in inflammatory signalling, suggesting that the metabolic environment induced by visceral adiposity influences the regulatory signalling pathways relevant for tumour progression in CC.

2022-RA-1385-ESGO TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY VERSUS LAPAROSCOPIC-ASSISTED VAGINAL RADICAL HYSTERECTOMY FOR THE TREATMENT OF EARLY-STAGE CERVICAL CANCER

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