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228 FACTORS ASSOCIATED WITH LYMPHEDEMA AFTER TREATMENT FOR UTERINE CERVICAL NEOPLASMS: A SYSTEMATIC REVIEW

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Objectives Realize a systematic literature review of studies that identified factors associated with lymphedema after treatment for uterine cervical neoplasms.

Methods A systematic review of the literature was performed according to the PRISMA guidelines. Eligible studies were identified through the databases Medline (via PubMed), LILACS, Scopus and Web of Science. For the search, we used descriptors, keywords and synonyms for: uterine cervical neoplasms, lymphedema and outcomes of interest (incidence, prevalence, frequency, occurrence, morbidity, risk factors and prognosis). We included cross-sectional, retrospective or prospective cohort studies, or case-control studies, published in the English, Portuguese or Spanish languages, with frequency data and risk factors for lymphedema after uterine cervical neoplasms treatment.

Results Fifteen studies were included in the review. The risk factors for lymphedema included adjuvant radiotherapy, removal of circumflex iliac lymph nodes, retroperitoneal closure, open surgical procedure, cellulitis, post-surgery lymphocytes, BMI $\geq$ 25 kg/m^2, pelvic and para-aortic lymphadenectomy.

Conclusions The different delineations and methodologies employed by the authors make it difficult to compare them and may interfere with the frequency and risk factors associated with lymphedema. There is no consensus on the best method used in the diagnosis of lymphedema and the risk factors are mainly associated with cancer treatment and obesity.

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229 GENETIC HETEROGENEITY OF OVARIAN SEX CORD-STROMAL TUMORS

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Objectives Sertoli-Leydig and granulosa cell tumors are sex cord-stromal tumors of the ovary that primarily impact young women. Adult-type granulosa cell tumors (aGCTs) are characterized by pathognomonic somatic *FOXL2* mutations, whilst 30–60% of Sertoli-Leydig cell tumors (SLCTs) harbor *DICER1* mutations. A comprehensive assessment of the repertoire of genomic alterations of sex cord-stromal tumors has yet to be performed.

Methods Primary SLCTs (n=2), juvenile (j)GCTs (n=2) and a primary and matched mixed SLCT/aGCT recurrence (n=2) were subjected to whole-exome sequencing. Somatic mutations and copy number alterations were defined using state-of-the-art bioinformatics algorithms.

Results Ovarian sex cord-stromal tumors displayed a low mutational burden, with a median of 22 (range 13–82) somatic mutations. Mutational analysis revealed the presence of a *DICER1* p.R293lfs*4 frameshift mutation in the pure SLCT. A *FOXL2* p.C134W hotpot mutation was identified in the primary and recurrent mixed SLCT/aGCT; in addition, *LAMA5*, *ZNF837*, and *HCFC1* missense mutations and an *UBR2* splice-site mutation were present only in the mixed recurrence but absent in the primary mixed SLCT/aGCT. Neither of the two jGCTs harbored *FOXL2* or *DICER1* mutations, and none of the identified somatic mutations and copy number alterations were shared between the two jGCTs. jGCT1 harbored *GATA4* p.L281M/Q missense mutations and copy number gains of chromosomes 4 and 8, whereas jGCT2 displayed *a TOPAZ1* p.K335R missense mutation and chromosome 12 and 18 gains.

Conclusions Sex cord-stromal tumors are a genetically heterogeneous group of rare ovarian neoplasms. Larger studies to assess whether jGCTs harbor recurrent genetic/epigenetic alterations are warranted.

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230 REFERRAL PATTERNS AND UPTAKE OF RISK REDUCING SURGERY FOR NON-BRCA GENES ASSOCIATED WITH INCREASED RISK OF EPITHELIAL OVARIAN CANCER

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Objectives To identify referral patterns and uptake of risk reducing surgery (RRS) in patients with non-*BRCA* genes associated with an increased risk of epithelial ovarian cancer.

Methods A chart review of patients with mutations in *MLH1, MSH2, EPCAM, MSH6, PMS2, RAD51C/D, BRIP1* was conducted from 2015–2018. Patients with *BRCA1/2* and variants of uncertain significance were excluded; *MSH6 and PMS2* were included (though recent change to insufficient evidence). Primary outcomes of interest were referral to a gynecologic oncologist and the uptake of RRS.

Results Of 78 patients, 18 had undergone surgical management for treatment of cancer prior to genetic testing and were excluded. The majority of the patients (41 of 60, 68%) with non-*BRCA* actionable mutations were associated with Lynch Syndrome (LS). Of these patients, 23 of 60 (56%) were seen by gynecologic oncologists. Twenty of 41 (49%) underwent RRS. Excluding the *MSH6* and *PMS2* patients, 9 of 21 (43%) of patients with LS underwent RRS.

Among patients with the non-*BRCA* and non-LS associated genes (*RAD51C, RAD51D, BRIP1*) the most common reason for testing was family history of cancer (10 of 19). Fifteen of 19 were referred to a gynecologic oncologist; all patients with *BRIP1* mutation were referred, while 70% of those with *RAD51/D* were referred. Among this subset of patients, 9/19 (47%) patients underwent RRS; the remaining patients were screened with surveillance ultrasounds and/or CA-125.

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