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**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 ≥ 25 kg/m², 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 employed in the diagnosis of lymphedema and the risk factors are mainly associated with cancer treatment and obesity.

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**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 (jGCTs) (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. Mutation analysis revealed the presence of a DICER1 p.R293His* frameshift mutation in the pure SLCT. A FOXL2 p.C134W hotspot 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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**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.