From hysteroscopy to laparoendoscopic surgery: what is the best surgical approach for symptomatic isthmocele? A systematic review and meta-analysis.

Related Articles

From hysteroscopy to laparoendoscopic surgery: what is the best surgical approach for symptomatic isthmocele? A systematic review and meta-analysis.
Arch Gynecol Obstet. 2020 Jan 27;:

Abstract
PURPOSE: To investigate the effectiveness and risks of different surgical therapies for isthmocele in symptomatic women with abnormal uterine bleeding, infertility, or for the prevention of obstetric complications, considering safety and surgical complications.
METHODS: PubMed/MEDLINE, Scopus, Embase, Science Direct, and Cochrane Library were systematically searched (n° CRD4201912035) for original articles on the surgical treatment of isthmocele published between 1950 and 2018. Data synthesis was completed using MedCalc 16.4.3. The body of evidence was assessed using the GRADE methodology.
RESULTS: We retrieved 33 publications: 28 focused on a single surgical technique, and five comparing different techniques. Meta-analysis showed an improvement of symptoms in 85.00% (75.05–92.76%) of women after hysteroscopic correction, 92.77% (85.53–97.64%) after laparoscopic/robotic correction, and 82.52% (67.53–93.57%) after vaginal correction. Hysteroscopic surgery was associated with the lowest risk of complications (0.76%, 0.20–1.66%).
CONCLUSIONS: We found adequate evidence supporting the use of surgery for the treatment of symptomatic isthmocele, as it was found to improve the bleeding symptoms in more than 80% of patients. Differently, we found a lack of evidence regarding the role of surgery with the purpose of improving fertility or reducing the risk of obstetric complications in women with asymmetric isthmocele. The hysteroscopic correction of isthmocele may be the safest and most effective strategy in those patients with adequate residual myometrial thickness overlying the isthmocele. Laparoscopic and vaginal surgeries may be the preferred options for patients with a thinner residual myometrium over the defect (PMID: 31989288 [PubMed — as supplied by publisher])


Abstract
Uterine leiomyoma is one of the most common gynaecologic benign tumours, but its genetic basis remains largely unknown. Six previous GWAS identified 33 genetic factors in total. Here, we performed a two-staged GWAS using 13,746 cases and 70,316 controls from the Japanese population, followed by a replication analysis using 3,483 cases and 4,795 controls. The analysis identified 9 significant loci, including a novel locus on 12q23.2 (rs17033114, P = 6.12 × 10–25 with an OR of 1.177 (1.141−1.213), LINC00485). Subgroup analysis indicated that 5 loci (3q26.2, 5p15.33, 10q24.33, 11p15.5, 13q14.11) exhibited a statistically significant effect among multiple leiomyomas, and 2 loci (3q26.2, 10q24.33) exhibited a significant effect among submucous leiomyomas. Pleiotropic analysis indicated that all 9 loci were associated with at least one proliferative disease, suggesting the role of these loci in the common neoplastic pathway. Furthermore, the risk T allele of rs2251795 (3q26.2) was associated with longer telomere length in both normal and tumour tissues. Our findings elucidated the significance of genetic factors in the pathogenesis of leiomyoma.
PMID: 31988393 [PubMed — in process]
Ado-trastuzumab emtansine (T-DM1) in patients with HER2-amplified tumors excluding breast and gastric/gastroesophageal junction (GEJ) adenocarcinomas: results from the NCI-MATCH trial (EAY131) subprotocol Q.

Abstract

BACKGROUND: The National Cancer Institute-Molecular Analysis for Therapy Choice (NCI-MATCH) is a national precision medicine study incorporating centralized genomic testing to direct refractory cancer patients to molecularly targeted treatment subprotocols. This treatment subprotocol was designed to screen for potential signals of efficacy of ado-trastuzumab emtansine (T-DM1) in HER2-amplified histologies other than breast and gastroesophageal tumors.

METHODS: Eligible patients had HER2 amplification at a copy number (CN) >7 based on targeted next-generation sequencing (NGS) with a custom Oncomine AmpliSeq™ (ThermoFisher Scientific) panel. Patients with prior trastuzumab, pertuzumab or T-DM1 treatment were excluded. Patients received T-DM1 at 3.6 mg/kg i.v. every 3 weeks until toxicity or disease progression. Tumor assessments occurred every three cycles. The primary end point was centrally assessed objective response rate (ORR). Exploratory end points included correlating response with HER2 CN by NGS. The impact of co-occurring genomic alterations and PTEN loss by immunohistochemistry were also assessed.

RESULTS: Thirty-eight patients were enrolled and 36 included in efficacy analysis. Median prior therapies in the metastatic setting was 3 (range 0–9; unknown in one patient). Median HER2 CN was 17 (range 7–139). Partial responses were observed in two (5.6%) patients: one mucoepidermoid carcinoma of parotid gland and one parotid gland squamous cell cancer. Seventeen patients (47%) had stable disease including 8/10 (80%) with ovarian and uterine carcinomas, with median duration of 4.6 months. The 6-month progression-free survival rate was 23.6% [90% confidence interval 14.2% to 39.2%]. Common toxicities included fatigue, anemia, fever and thrombocytopenia with no new safety signals. There was a trend for tumor shrinkage with higher levels of gene CN as determined by the NGS assay.

CONCLUSION: T-DM1 was well tolerated. While this subprotocol did not meet the primary end point for ORR in this heavily pre-treated diverse patient population, clinical activity was seen in salivary gland tumors warranting further study in this tumor type in dedicated trials.

PMID: 31987089 [PubMed — in process]

Low-volume metastatic nodal disease in endometrial cancer.

Related Articles

Low-volume metastatic nodal disease in endometrial cancer.


Authors: Hambálek J, Maděrka M, Kolečková M, Pilka R

Abstract

AIM: To review contemporary knowledge of the low volume metastatic disease in patients with endometrial cancer.

TYPE OF STUDY: A literature review.

SETTINGS: Department of Obstetrics and Gynecology, University Hospital Olomouc; Department of Clinical and Molecular Pathology, University Hospital Olomouc.

INTRODUCTION: The presence of micrometastases or isolated tumor cells in the sentinel node detected by ultrastaging leads to the change of tumor stage. Low volume lymph node involvement represents up to 30% of the affected lymph nodes in patients with endometrial cancer. The enhanced sentinel lymph node investigation aims to more accurately determine the extent of illness from stage I to stage IIIC. Particularly important is the detection of low-volume metastatic nodal involvement in low-risk tumors, because compared with macrometastases, micrometastases may occur earlier in tumors with lower carcinologic aggressiveness.

CONCLUSION: Detection of low volume metastatic disease decreases the false negativity of nodal involvement and is helpful for adjuvant treatment planning.

PMID: 31948256 [PubMed — indexed for MEDLINE]

Histopathological and clinical features of molar pregnancy.

Related Articles

Histopathological and clinical features of molar pregnancy.

Ceska Gynekol. 2019;84(6):418–424

Authors: Heřman J, Rob L, Robová H, Drochýtek V, Hruda M, Pichlík T, Kujal P, Drozenová J

Abstract

OBJECTIVE: To analyse own set of molar pregnancies and to develop clinically relevant procedures.

TYPE OF STUDY: Review article with analysis of own data.

SETTINGS: Department of Pathology 3rd Faculty of Medicine,
INTRODUCTION: The study monitors the decrease of laboratory values of beta-subunit of hCG gonadotropin (beta-hCG) after evacuation of partial and complete hydatidiform moles in a set of 45 partial and 46 complete moles. Two case reports of invasive moles.

RESULTS: In cases of partial hydatidiform moles there was complete regression of beta-hCG in all cases, 89% regressed in six weeks, none of the women showed no subsequent elevation after reaching negativity. In cases of complete hydatidiform moles the decrease was less gradual, the negativity after six weeks was confirmed in 78%, three complete moles became malignant.

CONCLUSION: The decrease of beta-hCG after molar pregnancy termination is variable. Even if in cases of complete hydatidiform moles the risk of malignization after reaching negativity is low, beta-hCG checks are recommended at monthly intervals for 6 months. Correct diagnosis of complete mole and its differentiation from partial mole can be achieved using immunohistochemistry — p57 antibody.

PMID: 31948249 [PubMed — indexed for MEDLINE]

Coix lacryma-jobi var. ma-yuen Stapf sprout extract induces cell cycle arrest and apoptosis in human cervical carcinoma cells.

Related Articles

Coix lacryma-jobi var. ma-yuen Stapf sprout extract induces cell cycle arrest and apoptosis in human cervical carcinoma cells.


Authors: Son ES, Kim SH, Kim YO, Lee YE, Kyung SY, Jeong SH, Kim YJ, Park JW

Abstract

BACKGROUND: Cervical cancer is the second-leading cause of cancer-related mortality in females. Coix lacryma-jobi L. var. ma-yuen (Rom.Caill.) Stapf ex Hook. f. is the most widely recognized medicinal herb for its remedial effects against inflammation, endocrine system dysfunctions, warts, chapped skin, rheumatism, and neuralgia and is also a nourishing food.

METHODS: To investigate the activity of Coix lacryma-jobi sprout extract (CLSE) on cell proliferation in human cervical cancer HeLa cells, we conducted a Cell Counting Kit-8 (CCK-8) assay. Flow-cytometric analysis and western blot analysis were performed to verify the effect of CLSE on the regulation of the cell cycle and apoptosis in HeLa cells.

RESULTS: We observed that CLSE significantly inhibited cell proliferation. Furthermore, CLSE dose-dependently promoted cell cycle arrest at the sub-G1/S phase in HeLa cells, as detected by bromodeoxyuridine (BrdU) staining. The cell-cycle-arrest effects of CLSE in HeLa cells were associated with downregulation of cyclin D1 and cyclin-dependent kinases (CDKs) 2, 4, and 6. Moreover, CLSE induced apoptosis, as determined by flow-cytometric analysis and nuclear DNA fragmentation with Annexin V/propidium iodide (PI) and 4′6-diamidino-2-phenylindole (DAPI) staining. Induction of apoptosis by CLSE was involved in inhibition of the antiapoptotic protein B-cell lymphoma 2 (Bcl-2) and upregulation of the apoptotic proteins p53, cleaved poly (ADP-ribose) polymerase (PARP), cleaved caspase-3, and cleaved caspase-8. Finally, we observed that CLSE inactivated the phosphoinositide 3-kinase (PI3K) and protein kinase B (AKT) pathways.

CONCLUSIONS: CLSE causes cell cycle arrest and apoptotic cell death through inactivation of the PI3K/AKT pathway in HeLa cells, suggesting it is a viable therapeutic agent for cervical cancer owing to its anticancer effects.

PMID: 31729992 [PubMed — indexed for MEDLINE]

Estimating the public health impact of a national guideline on cervical cancer screening: an audit study of a program in Campinas, Brazil.

Related Articles

Estimating the public health impact of a national guideline on cervical cancer screening: an audit study of a program in Campinas, Brazil.


Authors: Vale DB, Menin TL, Bragança JF, Teixeira JC, Cavalcante LA, Zeferino LC

Abstract

BACKGROUND: A Brazilian guideline on cervical cancer screening was released in 2011. The objective was to verify changes in screening indicators around this period.

METHODS: An audit study which sample was all screening tests performed by the public health system of Campinas city from 2010 to 2016. Variables were absolute tests numbers, excess tests, intervals and results, by age. For trend analysis was used Cochran-Armitage × 2 and linear regression.

RESULTS: Were carried out 62,925 tests in 2010 and 43,523 tests in 2016, a tendency at a reduction (P = 0.001). Excess tests were higher than 50% over the years, with a tendency at a reduction (P CONCLUSION: The proportion of cervical cancer screening tests performed out of the recommendation showed a significant reduction in the period. This indicates a tendency to align cervical cancer screening in Campinas with the standards recommended.

PMID: 31703661 [PubMed — indexed for MEDLINE]
Long-term predictors of residual or recurrent cervical intraepithelial neoplasia 2–3 after treatment with a large loop excision of the transformation zone: a retrospective study.

Related Articles

Long-term predictors of residual or recurrent cervical intraepithelial neoplasia 2–3 after treatment with a large loop excision of the transformation zone: a retrospective study.

BJOG. 2020 02;127(3):377–387

Authors: Fernández-Montolí ME, Tous S, Medina G, Castellarnau M, García-Tejedor A, de Sanjosé S

Abstract

OBJECTIVE: To assess the long-term risk factors predicting residual/recurrent cervical intraepithelial neoplasia (CIN 2–3) and time to recurrence after large loop excision of the transformation zone (LLETZ).

DESIGN: Retrospective study.

SETTING: Colposcopy clinic.


METHODS: Age, margins, and high-risk human papillomavirus (HR-HPV) were estimated using Cox proportional hazard and unconditional logistic regression models. The cumulative probability of treatment failure was estimated by Kaplan-Meier analysis.

MAIN OUTCOME MEASURE: Histologically confirmed CIN 2–3, HR-HPV, margins, age.

RESULTS: CIN 2–3 was associated with HR-HPV (HR = 30.5, 95% confidence interval [CI] = 3.80−246.20), age >35 years (HR = 5.53, 95% CI = 1.22−25.13), and margins (HR = 7.31, 95% CI = 1.60−33.44). HR-HPV showed a sensitivity of 88.8% and a specificity of 80%. Ecto+ /endocervical+ (16.7%), uncertain (19.4%) and ecto– /endocervical+ margins (9.1%) showed a higher risk of recurrence (odds ratio [OR] = 13.20, 95% CI = 1.02−170.96; OR = 15.84, 95% CI = 3.02−83.01; and OR = 6.60, 95% CI = 0.88−49.53, respectively). Women with involved margins and/or who were HR-HPV positive had more treatment failure than those who were HR-HPV negative or had clear margins (P-log-rank  5 years. Three themes emerged; inadequate cervical cancer knowledge, willingness and strategies for support, and shared versus autonomous decision making for screening. Social structure with emphasis on male leadership could be leveraged in cervical cancer screening promotion for SSAI women.

PMID: 31084466 [PubMed — indexed for MEDLINE]


Related Articles


J Virol. 2019 04 15;93(8):


Abstract

TMPO2 was previously suggested to be an oncogenic long noncoding RNA which is excessively expressed in cervical cancer cells and inhibits E-cadherin gene expression by recruiting transcription repressor EZH2 to the gene promoter. So far, the function and regulation of TMPO2 in cervical cancer remain largely unknown. Herein, we found that TMPO2 expression was correlated with human papillomavirus 16/18 (HPV16/18) E6 and E7 in cervical cancer cell lines CaSki and HeLa. Tumor suppressor p53, which is targeted for degradation by HPV16/18, was demonstrated to associate with two p53 response elements in the TMPO2 promoter to repress the transcription of the TMPO2 gene. Reciprocally, ectopic expression of TMPO2 was demonstrated to sequester tumor repressor microRNAs (miRNAs) miR-375 and miR-139 which target HPV16/18 E6/E7 mRNA and resulted in an upregulation of HPV16/18 E6/E7 genes. Thereby, HPV16/18 E6/E7 and the long noncoding RNA (lncRNA) TMPO2 form a positive feedback loop to mutually derepress gene expression in cervical cancer cells. Moreover, results of RNA sequencing and cell cycle analysis showed that knockdown of TMPO2 impaired the expression of cell cycle genes, induced cell cycle arrest, and inhibited HeLa cell proliferation. Together, our results indicate that TMPO2 and HPV16/18 E6/E7 mutually strengthen their expression in cervical cancer cells to enhance tumorigenic activities.IMPORTANCE Human papillomaviruses 16 and 18 (HPV16/18) are the main causative agents of cervical cancer. Viral proteins HPV16/18 E6 and E7 are constitutively expressed in cancer cells to maintain oncogenic phenotypes. Accumulating evidences suggest that HPVs are correlated with the deregulation of long noncoding RNAs (lncRNAs) in cervical cancer, although the mechanism was unexplored in most cases. TMPO2 is a newly identified lncRNA excessively expressed in cervical cancer. However, the mechanism for the upregulation of TMPO2 in cervical cancer cells remains largely unknown and its relationship with HPVs is still elusive. The significance of our research is in revealing the mutual upregulation of HPV16/18 E6/E7 and TMPO2 with the molecular mechanisms explored. This study will expand our understandings of the oncogenic activities of human papillomaviruses and lncRNAs.

PMID: 30728257 [PubMed — indexed for MEDLINE]
Class II PI3Ks α and β Are Required for Rho-Dependent Uterine Smooth Muscle Contraction and Parturition in Mice.

Abstract
Class II phosphoinositide 3-kinases (PI3Ks), PI3K-C2α and PI3K-C2β, are highly homologous and distinct from class I and class III PI3Ks in catalytic products and domain structures. In contrast to class I and class III PI3Ks, physiological roles of PI3K-C2α and PI3K-C2β are not fully understood. Because we previously demonstrated that PI3K-C2α is involved in vascular smooth muscle contraction, we studied the phenotypes of smooth muscle-specific knockout (KO) mice of PI3K-C2α and PI3K-C2β. The pup numbers born from single PI3K-C2α-KO and single PI3K-C2β-KO mothers were similar to those of control mothers, but those from double KO (DKO) mothers were smaller compared with control mice. However, the number of intrauterine fetuses in pregnant DKO mothers was similar to that in control mice. Both spontaneous and oxytocin-induced contraction of isolated uterine smooth muscle (USM) strips was diminished in DKO mice but not in either of the single KO mice, compared with control mice. Furthermore, contraction of USM of DKO mice was less sensitive to a Rho kinase inhibitor. Mechanistically, the extent of oxytocin-induced myosin light chain phosphorylation was greatly reduced in USM from DKO mice compared with control mice. The oxytocin-induced rise in the intracellular Ca2+ concentration in USM was similar in DKO and control mice. However, Rho activation in the intracellular compartment was substantially attenuated in DKO mice compared with control mice, as evaluated by fluorescence resonance energy transfer imaging technique. These data indicate that both PI3K-C2α and PI3K-C2β are required for normal USM contraction and parturition mainly through their involvement in Rho activation.

PMID: 30476019 [PubMed — indexed for MEDLINE]

Cohort Profile: the Million Women Study.

Abstract
To critically appraise factors influencing human papillomavirus (HPV) vaccination among immigrant parents in the United States, a comprehensive search of electronic databases and reference lists was conducted. The findings from 22 articles were ordered based on a socioecological model. About 30% of children initiated and 14% completed a three-dose series. Correlates of HPV vaccine initiation rates included lack of information, concerns about vaccine safety and promiscuity, providers’ recommendations, school mandates, financial issues, immigration laws, and living in disadvantaged neighborhoods. Upstream initiatives embracing cultural descriptors could facilitate HPV vaccination, reducing HPV-related disparities in cancer among immigrants in the US.

PMID: 29161198 [PubMed — indexed for MEDLINE]