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Recent research on cesarean section and on the health burden of cancer Investigación reciente sobre la cesárea y sobre el problema de la incidencia del cáncer

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CESAREAN SECTION

Cesarean section is the most commonly performed surgical procedure in the United States, with nearly 1.3 million cases performed each year. After rising for several decades, the cesarean rate has plateaued at approximately 32% of all deliveries⁽¹⁾. In Peru, the rate has continued increasing from 22.9% in 2011 to 34.8% in 2017⁽²⁾. The rate is higher in social security hospitals and much more in private hospitals.

Cesarean delivery is the single most important risk factor for maternal postpartum infection⁽³⁾. Already in 1993, a Peruvian collaborative study found the rate of cesarean sections in 19.3%, most of them with medical indication of previous cesarean section, with 21% of complications consisting in fever, 6% wound infection and 3% endometritis⁽⁴⁾. Several large studies evaluating antibiotic prophylaxis administered after cord clamping versus at the time of skin incision, however, found a reduced incidence of infectious morbidity when antibiotics were given within the 60 minutes preceding the skin incision. In 2011, The American College of Obstetricians and Gynecologists (ACOG) recommended pre-incision antibiotic administration as routine practice⁽⁵⁾.

A recent article published in Contemporary OB/GYN has a table related to evidence-based cesarean delivery guidelines in consideration of avoiding maternal postpartum infection. We think its analysis is worth to consider.

Evidence-based cesarean delivery guidelines⁽⁶⁾

- Prep abdomen with chlorhexidine-alcohol^(7,8). Consider vaginal preparation with antiseptic agents as well^(9,10)
- Administer cefazolin prior to skin incision for scheduled cesareans. Consider adding azithromycin for patients in labor or with ruptured membranes
- Limit sharp dissection by using a Joel-Cohen entry
- Avoid routine creation of a bladder flap
- Perform uterine extension bluntly, in a cephalad-caudal fashion
- Deliver the placenta spontaneously
- For vaginal birth after cesarean section candidates, perform a double-layer closure. A single-layer, non-locking suture also can be considered
- Avoid routine peritoneal closure or use of an adhesion barrier
- Close the subcutaneous tissue if it is > 2 cm
- Use subcuticular suture for skin closure.

Approaches to limit intervention during labor and birth

Data suggest that in women with normally progressing labor and no evidence of fetal compromise, routine amniotomy is not necessary.



The widespread use of continuous electronic fetal heart-rate monitoring has not improved outcomes when used for women with low-risk pregnancies. Multiple nonpharmacologic and pharmacologic techniques can be used to help women cope with labor pain. Women in spontaneously progressing labor may not require routine continuous infusion of intravenous fluids. For most women, no one position needs to be mandated nor proscribed. Nulliparous women who have an epidural and no indication for expeditious delivery may be offered a period of rest for 1–2 hours before initiating pushing efforts⁽¹¹⁾.

Planned vaginal delivery for twin pregnancies with a cephalic first twin at or after 32 weeks of gestation has been associated with low composite neonatal mortality and morbidity. Moreover, planned cesarean compared with planned vaginal delivery before 37 weeks of gestation might be associated with increased composite neonatal mortality and morbidity⁽¹²⁾.

FEMALE CANCER

United States Preventive Services Task Force recommendations on screening for cervical cancer⁽¹³⁾

- The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years (A recommendation).
- The USPSTF recommends screening every 3 years with cervical cytology alone, every 5 years with hrHPV testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting) in women aged 30 to 65 years (A recommendation).
- The USPSTF recommends against screening for cervical cancer in women younger than 21 years (D recommendation).
- The USPSTF recommends against screening for cervical cancer in women older than 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer (D recommendation).
- The USPSTF recommends against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion or cervical cancer (D recommendation).

BREAST CANCER

The association between increasing body mass index and risk of breast cancer is unique in cancer epidemiology in that a crossover effect exists, with risk reduction before and risk increase

after menopause. Data was obtained from 758 592 premenopausal women from 19 prospective cohorts from ages 18 through 54 years, median follow-up 9.3 years, with 13 082 incident cases of breast cancer. Increased adiposity was associated with a reduced risk of premenopausal breast cancer at a greater magnitude than previously shown and across the entire distribution of BMI. The strongest associations of risk were observed for BMI in early adulthood⁽¹⁴⁾.

Associations between weight change and breast cancer risk in 61 335 postmenopausal women in the Women's Health Initiative Observational Study was evaluated. During a mean follow-up of 11.4 years with 3 061 incident breast cancers, postmenopausal women who lost weight had lower breast cancer risk than those with stable weight⁽¹⁵⁾.

A systematic review and meta-analysis of prospective studies searched in MEDLINE and EMBASE databases through January 2018 that reported the association between red meat and processed meat consumption with incident breast cancer identified 13 cohort, 3 nested case-control and two clinical trial studies. Comparing the highest to the lowest category, red meat (unprocessed) consumption was associated with a 6% higher breast cancer risk (pooled RR, 1.06; 95% confidence intervals (95%CI): 0.99–1.14; I² = 56.3%), and processed meat consumption was associated with a 9% higher breast cancer risk (pooled RR, 1.09; 95%CI, 1.03–1.16; I² = 44.4%)⁽¹⁶⁾.

Among postmenopausal women with a BRCA1 mutation, hormonal therapy use was not associated with increased risk of breast cancer; indeed, in this population, it was associated with a decreased risk⁽¹⁷⁾.

In a study assessed whole-exome sequencing results from 11 416 patients with breast cancer, ovarian cancer, or both and 3 988 controls, an increased risk of breast cancer was associated with PALB2, ATM, CHEK2, and MSH6 genes, whereas MSH6, RAD51C, TP53, and ATM genes were associated with an increased risk of ovarian cancer. In addition to confirming several well-known breast or ovarian cancer gene associations, this study identified MSH6 and ATM as possible moderate-risk breast and ovarian cancer predisposition genes, respectively⁽¹⁸⁾.

BIARIATRIC SURGERY AND ENDOMETRIAL CANCER

Bariatric surgery has been associated with reduced risk of overall cancer (hazard ratio = 0.71; 95% CI 0.59–0.85; *p* < 0.001). About half of the observed cancers were female-specific, and the incidence of these were lower in the surgery



group compared with the control group (hazard ratio = 0.68; 95% CI 0.52–0.88; $p = 0.004$). The surgical treatment benefit with respect to female-specific cancer was significantly associated with baseline serum insulin (interaction p value = 0.022), with greater relative treatment benefit in patients with medium or high insulin levels. Separate analyses of different types of female-specific cancers showed that bariatric surgery was associated with reduced risk of endometrial cancer (hazard ratio = 0.56; 95% CI 0.35–0.89; $p = 0.014$)⁽¹⁹⁾.

OVARIAN CANCER

One cohort study analyzed NSAID use and ovarian cancer diagnosis data from 2 prospective cohorts, 93 664 women in the Nurses' Health Study (NHS), who were followed up from 1980 to 2014, and 111 834 in the Nurses' Health Study II (NHSII), who were followed up from 1989 to 2015. Among the 205 498 women in both cohorts, there were 1 054 cases of incident epithelial ovarian cancer. Significant associations between aspirin and ovarian cancer risk were not observed when current versus nonuse of any aspirin was evaluated regardless of dose. However, when low-dose (≤ 100 -mg) and standard-dose (325-mg) aspirin were evaluated separately, an inverse association for low-dose aspirin (HR, 0.77), but no association for standard-dose aspirin (HR, 1.17; 95% CI, 0.92–1.49) was observed. Current use of nonaspirin NSAIDs was positively associated with risk of ovarian cancer compared with nonuse (HR, 1.19), and significant positive trends for duration of use ($P = .02$ for trend) and cumulative average tablets per week ($P = .03$ for trend) were observed. There were no clear associations for the use of acetaminophen⁽²⁰⁾.

All Danish women aged 15–49 years during 1995–2014 were categorised in one study as never users (no record of being dispensed hormonal contraception), current or recent users (≤ 1 year after stopping use), or former users (> 1 year after stopping use) of different hormonal contraceptives. Use of contemporary combined hormonal contraceptives was associated with a reduction in ovarian cancer risk in women of reproductive age—an effect related to duration of use, which diminished after stopping use. No protective effect from progestogen-only products was suggested⁽²¹⁾.

HORMONAL CONTRACEPTION AND DIAGNOSIS OF LEUKEMIA IN THEIR CHILDREN

In a nationwide cohort of 1 185 157 liveborn children between 1996 and 2014 listed in the Danish Medical Birth Registry, 606 children were diagnosed with leukaemia (465 with lymphoid leu-

kaemia and 141 with non-lymphoid leukaemia) in the Danish Cancer Registry. Children born to women with recent use of any type of hormonal contraception were at higher risk for any leukaemia than children of women who never used contraception (HR 1.46, 95% CI 1.09–1.96; $p = 0.011$); and for exposure during pregnancy the risk was 1.78 (0.95–3.31; $p = 0.070$). No association was found between timing of use and risk for lymphoid leukaemia. The findings suggest the maternal hormonal use affects non-lymphoid leukaemia development in children⁽²²⁾.

VULVAR AND VAGINAL CANCER

During approximately 4 years of follow-up in 8,798 females, 40 vulvar LSILs and 46 vulvar HSILs were diagnosed in 68 females, and 118 vaginal LSILs and 33 vaginal HSILs were diagnosed in 107 females. Females developing vulvar (41.2%) or vaginal (49.5%) lesions also had cervical lesions, whereas 6.5% of females with cervical lesions had vaginal or vulvar lesions. At least 1 of the 14 HPV genotypes was detected in females with vulvar LSIL (72.5%), vulvar HSIL (91.3%), vaginal LSIL (61.9%), and vaginal HSIL (72.7%). Considering only HPV-positive lesions, the nine most common genotypes causing cervical cancer and anogenital warts (6, 11, 16, 18, 31, 33, 45, 52, and 58) were found in 89.4% of vulvar LSILs, 100% of vulvar HSILs, 56.0% of vaginal LSILs, and 78.3% of vaginal HSILs. In conclusion, most vulvar and vaginal lesions were attributable to at least 1 of the 14 HPV genotypes analyzed. Effective immunization programs could potentially prevent substantial numbers of HPV-related vulvar and vaginal LSILs and HSILs⁽²³⁾.

OVERWEIGHT-ASSOCIATED CANCER

In 2014, approximately 631 000 persons in the United States received a diagnosis of a cancer associated with overweight and obesity, representing 40% of all cancers diagnosed. Overweight- and obesity-related cancer incidence rates were higher among older persons (ages ≥ 50 years) than younger persons; higher among females than males; and higher among non-Hispanic black and non-Hispanic white adults compared with other groups. Incidence rates for overweight- and obesity-related cancers during 2005–2014 varied by age, cancer site, and state. Excluding colorectal cancer, incidence rates increased significantly among persons aged 20–74 years; decreased among those aged ≥ 75 years⁽²⁴⁾.

PROSTATE CANCER

In a case-control study that included 3 030 patients with pancreatic cancer and 123 136 ref-



erence controls, 6 genes were independently associated with pancreatic cancer, with odds ratios between 2.58 and 12.33 after correction for multiple comparisons. In aggregate, these genes were observed in 5.5% of patients with pancreatic cancer⁽²⁵⁾.

Accumulating evidence suggest that *Propionibacterium acnes* may play a role in prostate carcinogenesis. A large cohort of young men born in Sweden between 1952 and 1956, who underwent mandatory assessment for military conscription around the age of 18 (n = 243,187) were identified. The cohort was followed through linkages to the Swedish Cancer Register to identify the occurrence of prostate cancer until December 31, 2009. A total of 1 633 men were diagnosed with prostate cancer during a median follow-up of 36.7 years. A diagnosis of acne was associated with a statistically significant increased risk for prostate cancer (adjusted HR: 1.43 95% CI: 1.06–1.92), particularly for advanced stage disease (HR: 2.37 95% CI 1.19–4.73). A diagnosis of acne classified as severe conferred a sixfold increased risk of prostate cancer (HR: 5.70 95% CI 1.42–22.85). Data from this large prospective population-based cohort add new evidence supporting a role of *P. acnes* infection in prostate cancer⁽²⁶⁾.

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