Association between intrauterine device use and endometrial, cervical, and ovarian cancer: an expert review

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The intrauterine device is one of the most effective forms of contraception. Use of the intrauterine device has increased in the United States over the last 2 decades. Two formulations are commercially available in the United States: the levonorgestrel-releasing intrauterine device and the copper intrauterine device. The levonorgestrel intrauterine device releases progestin, causing endometrial suppression and cervical mucus thickening, whereas the primary mechanism of action of the copper intrauterine device is to create a local inflammatory response to prevent fertilization. Whereas the protective effects of combined hormonal contraception against ovarian and endometrial cancer, and of tubal sterilization against ovarian cancer are generally accepted, less is known about the effects of modern intrauterine devices on the development of gynecologic malignancies. The best evidence for a protective effect of intrauterine device use against cancer incidence pertains to levonorgestrel intrauterine devices and endometrial cancer, although studies suggest that both copper intrauterine devices and levonorgestrel intrauterine devices reduce endometrial cancer risk. This is supported by the proposed dual mechanisms of action including both endometrial suppression and a local inflammatory response. Studies on the relationship between intrauterine device use and ovarian cancer risk show conflicting results, although most data suggest reduced risk of ovarian cancer in intrauterine device users. The proposed biological mechanisms of ovarian cancer reduction (foreign-body inflammatory response, increased pH, anti-estrogenic effect, ovulation suppression) vary by type of intrauterine device. Whereas it has been well established that use of copper intrauterine devices confers a lower risk of cervical intraepithelial neoplasms, the effect of levonorgestrel intrauterine device use on cervical cancer remains unclear. Older studies have linked its use to a higher incidence of cervical dysplasia, but more recent literature has found a decrease in cervical cancer with intrauterine device use. Various mechanisms of protection are postulated, including device-related inflammatory response in the endocervical canal and prostaglandin-mediated immunosurveillance. Overall, the available evidence suggests that both levonorgestrel intrauterine devices and copper intrauterine devices reduce gynecologic cancer risk. Whereas there is support for the reduction of endometrial cancer risk with hormonal and copper intrauterine device use, and reduction of cervical cancer risk with copper intrauterine device use, evidence in support of risk reduction with levonorgestrel intrauterine device use for cervical and ovarian cancers is less consistent.

Key words: cervical cancer, endometrial cancer, gynecologic cancer, intrauterine device, ovarian cancer

Introduction

The intrauterine device (IUD) was first commercially available in the United States in 1964, and today is one of the most effective methods of contraception. Recent estimates show that approximately 4.4 million US women are currently using an IUD, representing a 2.5-fold increase from 2007 to 2017.[1–4] The rising popularity of the IUD is due in part to its superior effectiveness, high satisfaction, reversibility, and ease of use.[5] Whereas early iterations of the IUD included only inert materials such as plastic, modern devices available in the United States use either copper (Cu-IUD) or levonorgestrel (LNG-IUD, a type of hormone-releasing IUD) for enhanced contraceptive efficacy. In the United States, 1 copper-containing IUD (TCu380A IUD) and 4 levonorgestrel-releasing IUDs (including 52 mg, 19.5 mg, and 13.5 mg of levonorgestrel) are available for use. In addition to providing highly effective contraception, IUDs offer other noncontraceptive benefits, including avoidance of estrogen, and in the case of the LNG-IUD, treatment of heavy menstrual bleeding.[6–9]

Whereas the protective effects of combined hormonal contraception against endometrial and ovarian cancer, and of tubal sterilization against ovarian cancer are generally well accepted, less is known about the effects of modern IUDs on the development of gynecologic malignancies.[10,11] This article summarizes the current literature and provides a review of what is known about the use of IUDs and the development of endometrial, ovarian, and cervical cancers. We also review proposed mechanisms for the effect of IUD use on gynecologic cancer prevention.

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Methods

Data sources

A comprehensive literature search for eligible studies was conducted using

Medline through Ovid in March of 2022. Three separate searches were conducted to investigate the association of IUD use with endometrial, cervical, and ovarian cancer. Using the Medline database, the MeSH (Medical Subject Headings) terms "exp intrauterine devices" AND "endometrial neoplasms" were used, as well as "Intrauterine device*," "iud*," "endometrial cancer*," and "exp ovarian neoplasms" to broaden the search to include all alternative search words. A similar search was conducted on Medline to study cervical and ovarian cancer risk using the same MeSH terms: "exp intrauterine devices," "Intrauterine device*," and "iud" AND "uterine cervical neoplasms" or "ovarian neoplasms." Again, alternative MeSH terms were included in the search to account for variability. Studies were limited to the English language.

Study selection criteria

For the purposes of this review, case reports were excluded. To focus on contemporary IUDs, all studies published from 1993 onward in which both never-users and ever-users of IUDs were evaluated for the incidence of gynecologic cancers were included.

Endometrial cancer

Epidemiology and evidence

Endometrial cancer (EC) is the most common gynecologic malignancy in the United States, with an estimated 66,570 new cases and 12,940 deaths in 2021.[12,13] The endometrioid type is the most common histologic variant of EC, and endometrial intraepithelial neoplasia (EIN) is a precursor to endometrioid adenocarcinoma.[7] It is well known that unopposed estrogen is a key risk factor for the development of EIN and subsequently EC.[14,15] Once diagnosed, oral progestins and LNG-IUDs are acceptable nonsurgical treatment options for EIN and EC.[7,16]

Because of their location within the uterine body, IUDs may offer prevention against EC via a local inflammatory-like reaction and/or endometrial suppression.[17,18] Although a number of case−control and cohort studies have shown a decreased risk of EC following the use of an IUD, most are retrospective in design and/or rely exclusively on epidemiologic data.[17,19−25] Most recently, a 2018 population-based prospective study from Norway found that those exposed to an LNG-IUD were nearly 80% less likely to develop EC when compared with those unexposed (relative risk [RR], 0.22; 95% confidence interval [CI], 0.13−0.40).[26] An earlier study by Soini et al,[27] which looked at women using an LNG-IUD specifically for heavy menstrual bleeding, found a dose response in risk reduction of 50% and 75% based on historic use of either 1 or 2 LNG-IUDs, respectively (RR, 0.50; 95% CI, 0.35−0.70; and RR, 0.25; 95% CI, 0.05−0.73). These findings are further supported by a 2015 pooled analysis of 18 observational studies included in the Epidemiology of Endometrial Cancer Consortium. This analysis reviewed 18 retrospective studies from 1980 to 2009 with 8801 EC cases and 15,357 controls. Detailed data on IUD type, quantitative duration of use, and ages of initiation and discontinuation were available. The analysis found a more modest decrease in odds of EC (odds ratio [OR], 0.81; 95% CI, 0.71−0.91) with IUD use; however, many of the included studies were older, reflecting the use of either inert plastic IUDs or early formulations of the Cu-IUD.[18] Despite this difference in type of IUD exposure, Felix et al[18] also found that longer duration of IUD use (≥10 years) compared with never-use was more protective against EC (OR, 0.61; 95% CI, 0.52−0.71). It is important to note that although most of these studies do not provide the dosage of hormone within the IUD, the 52-mg LNG-IUD is shown to decrease risk and also treat EC.[7]

Proposed mechanism

EC is thought to mostly evolve from precursor lesions (endometrial hyperplasia) related to unopposed estrogen exposure.[28] EC and endometrial hyperplasia share the same risk factors (unopposed estrogen therapy, obesity, diabetes mellitus, nulliparity, early menarche, and late menopause), all related to excess estrogen relative to progesterone.[15] Normally, estrogen's proliferative effects on the endometrium are balanced by endogenous progesterone-induced differentiation.[29] In the absence of sufficient progesterone, estrogen-induced oncogenesis takes place via unregulated gene transcription.[28]

Because of their growth-inhibitory effects on the endometrium, progestogens are an ideal endometrial tumor suppressor through activation of progesterone receptors that induce differentiation and cell cycle arrest. Progesterone receptor signaling has also been shown to reduce inflammation and counter invasion associated with metastatic disease.[30] In addition, progestogens acts as inhibitors of the estrogen receptor, which blocks endometrial cell mitosis and promotes apoptosis leading to the production of secretory endometrium.[31] Promotion of secretory endometrium leads to decidual loss, allowing for shedding of endometrial lining with subsequent removal of premalignant and hyperplastic endometrial cells.

The LNG-IUD delivers progestin directly to the endometrium, counteracting the stimulatory effect of estrogen through stromal decidualization and down-regulation of proliferative signaling pathways. This results in low endometrial cellular proliferation leading to glandular atrophy.[6] The LNG-IUD has been shown to inhibit the proliferation-stimulating action of insulin-like growth factor-1 by stromal insulin growth factor-binding proteins, which may be a molecular mechanism causing endometrial epithelial atrophy.[29]

Compared with oral therapy, the LNG-IUD releases a continuous supply of local levonorgestrel to the endometrium, avoiding peaks/troughs of oral administration, eliminating compliance problems, and limiting contraindications and adverse effects (eg, vaginal bleeding, nausea, weight gain) because the systemic concentrations of levonorgestrel are much lower than with oral therapy.[32] Early studies showed that with the use of the LNG-IUD compared with oral progestin therapy, the concentration of levonorgestrel in the endometrium was higher. In a study that looked at

endometrial tissue samples with LNG-IUD use and those with oral therapy, the total levonorgestrel in the endometrium reached up to 660 ng vs 2.3 ng for the oral therapy.[33]

The Cu-IUD has been associated with reductions in both endometrial mitotic activity and estrogen receptor concentrations, which inhibits endometrial growth, offering protection against EC.[6] Both Cu-IUDs and hormonal IUDs cause chronic uterine inflammation, which reduces endometrial hyperplasia.[34]

Given these effects, studies have shown that those exposed to the LNG-IUD have a reduced risk of EC.[26,27] A summary of the evidence is provided in Table 1.

Cervical cancer

Epidemiology and evidence

Cervical cancer is the third most common gynecologic cancer in the United States, with approximately 14,000 new cases each year.[35] In resource-rich nations, cervical cancer is both less common and deadly than uterine and ovarian cancer, in large part because of screening and vaccination efforts.[36] Persistent infection with high-risk human papillomavirus (HPV) is a known risk factor for the development of cervical cancer and cervical intraepithelial neoplasia, although other factors are involved in cervical carcinogenesis.[37] Identified cofactors for cervical cancer include tobacco smoking, multiparity, and infection with other sexually transmitted diseases.[38] The results of studies evaluating the association of IUDs with cervical cancer have been inconsistent because of failure to control for important confounding variables (eg, sexual history) (Table 2).[37,43]

Although older studies have shown an association between IUD use and the incidence of cervical dysplasia, 2 large meta-analyses found a statistically significant decrease in cervical cancer with IUD use.[39,40,44,45] A large prospective cohort study (EPIC Cohort) provided evidence that IUD use conferred a reduced risk of cervical cancer.[37] Skorstengaard et al[41] found that women with normal cytology at time of IUD insertion had a 37% to 42% lower risk of severe precancerous cervical lesions at follow-up. In addition, it was found in 2 studies that Cu-IUD users had lower risk of high-grade cervical lesions than hormonal IUD users (RR, 0.38; 95% CI, 0.16−0.78).[41,42] In women with low-grade lesions, there was a decreased progression to higher-grade lesions with the use of LNG-IUD compared with Cu-IUD or oral contraceptive use.[41] When compared with noncontraceptive users, Loopik et al[46] found that both oral contraceptive and IUD users had an increased risk of developing cervical intraepithelial neoplasia grade ≥3, and the risk was highest for oral contraceptive users. Notably, this study did not account for sexual activity, an important confounding variable, which limits the validity of Loopik's findings.

The strongest evidence on the matter comes from Castellsagué et al,[39] who reported the results of a large epidemiologic study of over 20,000 women from the International Agency for Research on Cancer and Institut Catala d'Oncologia to evaluate the effect of IUD use on the risk of

TABLE 1
Studies evaluating intrauterine devices and endometrial cancer

Author, y	Type of study	Type of IUD included	OR/RR	95% CI
1. Castellsagué et al,[17] 1993	Case−control study	Unknown	0.51	0.33−0.79
2. Felix et al,[18] 2015	Pooled analysis	Inert, Cu-IUD, progesterone-releasing, combination	0.81	0.74−0.90
3. Parazzini et al,[19] 1994	Case−control study	Not obtained	0.40	0.10−1.00
4. Rosenblatt and Thomas,[20] 1996	Case−control study	Stainless steel, inert, or unknown	0.74	0.4−1.33
5. Hill et al,[21] 1997	Case−control study	Lippes loop, Dalkon Shield, safety coil, Cu-IUD, Majzlin spring, unknown	0.61	0.41−0.89
6. Sturgeon et al,[22] 1997	Case−control study	Cu-IUD, inert, unknown	0.56	0.30−1.00
7. Benshushan et al,[23] 2002	Case−control study	Unknown	0.37	0.19−0.95
8. Tao et al,[24] 2006	Case−control study	Unknown	0.53	0.43−0.65
9. Wernli et al,[25] 2006	Cohort study (prospective)	Unknown	0.56[a]	0.35−0.88
10. Soini et al,[27] 2014	Observational study	LNG-IUD	0.59[b]	0.45−0.76
11. Beining et al,[34] 2008	Meta-analysis	Unknown	0.54	0.47−0.62
12. Jareid et al,[26] 2018	Cohort study (prospective)	LNG-IUD	0.22	0.13−0.40

1. OR of EC and ever-use of IUD. 2. Pooled OR of EC and ever-use of IUD. 3. RR of EC and ever-use of IUD. 4. OR of EC and ever-use of IUD. 5. OR of EC and ever-use of IUD. 6. RR of EC and ever-use of IUD. 7. OR of EC and ever-use of IUD. 8. OR of EC and ever-use of IUD. 9. Hazard ratio showing decreased risk of EC and ever-use of IUD. 10. Incidence ratio of EC and use of LNG-IUD. 11. Pooled OR of EC and ever-use of IUD. 12. RR of EC and ever-use of LNG-IUD.

CI, confidence interval; *Cu-IUD*, copper intrauterine device; *EC*, endometrial cancer; *IUD*, intrauterine device; *LNG-IUD*, levonorgestrel-releasing intrauterine device; *OR*, odds ratio; *RR*, relative risk.

[a] Hazard ratio; [b] Incidence ratio.

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TABLE 2
Studies evaluating intrauterine devices and cervical cancer or precancer

Author, y	Type of study	Type of IUD included	OR/RR	95% CI
1. Castellsagué et al,[39] 2011	Meta-analysis	Unknown	0.55	0.42–0.70
2. Cortessis et al,[40] 2017	Meta-analysis, systematic review	Unknown	0.64	0.53–0.77
3. Skorstengaard et al,[41] 2021	Cohort study (retrospective)	Cu-IUD LNG-IUD	0.58 0.63	0.52–0.65 0.57–0.69
4. Spotnitz et al,[42] 2020	Cohort study (retrospective)	Cu-IUD LNG-IUD	0.38	0.16–0.78

1. OR of cervical cancer with ever-use of an IUD. 2. OR of cervical cancer with ever-use of an IUD. 3. aRR of cervical intraepithelial neoplasia grade ≥3 given for Cu-IUD compared with OCP and aRR given for LNG-IUD compared with OCP. 4. RR of cervical cancers for Cu-IUD use compared with LNG-IUD use.

aRR, absolute risk reduction; *CI*, confidence interval; *Cu-IUD*, copper intrauterine device; *IUD*, intrauterine device; *LNG-IUD*, levonorgestrel-releasing intrauterine device; *OCP*, oral contraception pill; *OR*, odds ratio; *RR*, relative risk.

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acquiring HPV infection and progression to cervical cancer. After adjusting for covariates (ie, age, education, marital status, number of cytologic screenings, number of sexual partners, parity, condom use), there remained a strong inverse association between IUD use and cervical cancer risk (OR, 0.55; 95% CI, 0.42–0.70; $P<.0001$), squamous cell carcinoma (OR, 0.56; 95% CI, 0.43–0.72; $P<.0001$), and adenocarcinoma and adenosquamous carcinoma (OR, 0.46; 95% CI, 0.22–0.97; $P=.035$).[6,39] Results also showed that the risk of cervical cancer was reduced by half after the first year of IUD use when compared with those who had never used an IUD.[39]

Proposed mechanism

There are a number of possible mechanisms to explain the potential protective effect of IUD use against development of cervical cancer. One possibility is a device-related inflammatory response in the endocervical canal.[39] The insertion and removal of IUDs can also cause a protective effect through the elimination of cervical intraepithelial neoplasia.[39] Much like with EC, it has become widely accepted that the Cu-IUD creates a sterile and inflammatory reaction on cervical mucus. The chronic inflammatory response in the endometrium, endocervical canal, and cervix may change the course of HPV infection, a known underlying risk factor for the development of cervical intraepithelial neoplasia and cervical cancer.[39] Copper also has antitumor effects by inhibiting cell growth and protecting against carcinogenesis through increasing prostaglandin levels in the uterine and tubal fluids causing chronic inflammation.[47]

The effect of LNG-IUDs on local immunity and its impact on carcinogenesis is more complex. Although LNG-IUDs decrease prostaglandin levels, which may suppress local immunity, they may have a protective effect by increasing the number of Langerhans cells (LC), which are important for immunosurveillance of the squamous epithelium.[48,49] It has been shown that progesterone increases the amount of LCs in the vaginal epithelium.[48,50] However, no studies have investigated the effect of hormonal contraceptives on the ability of LCs to bind and clear virions.[50] Conversely, one study suggests that differences in immunomodulation between Cu-IUDs and hormonal IUDs may cause LNG-IUD users to clear HPV infections at a slower rate and be more susceptible to infection than Cu-IUD users because of the effects of these IUDs on innate antiviral factors.[50] One study investigated the role of hormonal contraceptives in susceptibility to viral infections and found that users of LNG-IUDs had decreased expression of human beta-defensins and secretory leukocyte protease inhibitors, both important for antiviral activity.[50] Others propose that the insertion or removal of an IUD causes local inflammation with increased neutrophils and macrophages (similar to the effects occurring in punch biopsies during colposcopy), and elimination of precancerous cells.[39]

Ovarian cancer

Epidemiology and evidence

Ovarian cancer is the deadliest of all gynecologic cancers, and each year accounts for >22,000 deaths worldwide.[51] Symptoms are typically vague and nonspecific, and there is currently no accurate screening test. Because of this, up to 75% of women with ovarian cancer present at a late stage, and experience recurrence following treatment, with 5-year survival of <50%.[51,52] Because of the late detection, poor prognosis, and lack of screening for cervical cancer, risk-reduction strategies are of primary importance to reduce the incidence of this deadly disease.

Studies examining the relationship between ovarian cancer risk and IUD use have shown conflicting results, although the trend is toward a reduced risk of ovarian cancer in IUD users (Table 3).[10,11,26,53-55] Reports by Ness et al[10,53] demonstrated reduced risk of ovarian cancer in IUD users (OR, 0.80; 95% CI, 0.6–1.0; and OR, 0.75; 95% CI, 0.59–0.95, respectively). A large Norwegian study that included >100,000 women found a strongly reduced risk of ovarian cancer with LNG-IUD exposure (RR, 0.53; 95% CI, 0.32–0.88).[26] Similarly, a study by Soini et al[49] found that LNG-IUD users had decreased risk for invasive ovarian cancer via standardized

TABLE 3
Studies evaluating intrauterine devices and ovarian cancer

Author, y	Type of study	Type of IUD included	OR/RR	95% CI
1. Ness et al,[10] 2011	Case–control study (retrospective)	Unknown	0.75	0.59–0.95
2. Wheeler et al,[11] 2019	Meta-analysis, systematic review	Unknown	0.68	0.62–0.75
3. Jareid et al,[26] 2018	Cohort study (prospective)	LNG-IUD	0.53	0.32–0.88
4. Ness et al,[53] 2001	Case–control study (retrospective)	Unknown	0.80	0.60–1.00
5. Soini et al,[49] 2016	Cohort study (prospective)	LNG-IUD	0.59 (invasive OC)[a] 0.76 (borderline OC)[a] 0.49 (mucinous OC)[a] 0.55 (endometrioid OC)[a] 0.75 (serous OC)[a]	0.47–0.73 0.57–0.99 0.24–0.87 0.28–0.98 0.55–0.99
6. Balayla et al,[54] 2021	Meta-analysis, systematic review		0.67[b] 0.58[c]	0.60–0.74 0.47–0.71
7. Huang et al,[55] 2015	Cohort study (prospective)	Unknown	0.86 (ever-user of IUD)[d] 0.62 (long-term IUD use)[d]	0.60–1.24 0.40–0.97
8. Tworoger et al,[56] 2007	Cohort study (prospective)	Unknown	1.76	1.08–2.85
9. D'Alessandro et al,[57] 2022	Meta-analysis, systematic review	LNG-IUD	0.66	0.41–1.08
10. Yang et al,[58] 2021	Case–control study	Cu-IUD, Lippes, Dalkon Shield, safety coil, inert, progesterone-releasing	0.96	0.81–1.14
11. Chesang et al,[59] 2021	Case–control study (retrospective)	Unknown	1.25	0.81–1.93

1. OR of OC with ever-use of an IUD. 2. OR of OC with ever-use of an IUD. 3. OR of OC with ever-use of an LNG-IUD. 4. OR of OC with ever-use of an IUD. 5. Incidence ratios showing decreased risk OC with use of LNG-IUD. 6. ORs showing reduction of OC with using any type of IUD[b] and LNG-IUD.[c] 7. Hazard ratios showing reduction in OC in both ever-users of IUDs and with long-term IUD use >20 years. 8. RR of OC with ever-use of an IUD. 9. OR of OC with ever-use of LNG-IUD. 10. OR of epithelial OC and ever-use of an IUD. 11. OR of OC and ever-use of an IUD.

CI, confidence interval; *Cu-IUD*, copper intrauterine device; *IUD*, intrauterine device; *LNG-IUD*, levonorgestrel-releasing intrauterine device; *OC*, ovarian cancer; *OR*, odds ratio; *RR*, relative risk.

[a] Incidence ratio; [b] OR showing reduction of ovarian cancer with using any type of IUD; [c] OR showing reduction of ovarian cancer with using LNG-IUD; [d] Hazard ratio.

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incidence ratio (SIR, 0.59; 95% CI, 0.47−0.73) and for borderline ovarian tumors (SIR, 0.76; 95% CI, 0.57−0.99). Two meta-analyses found that there was a 30% to 41% decrease in ovarian cancer risk with ever-use of any type of IUD.[11,54] A study from China found that longer duration of IUD use, >20 years, decreased the risk of development of ovarian cancer by 38%.[55]

In contrast, other studies have not found decreased ovarian cancer risk with IUD use. Tworoger et al[56] found an increased incidence of ovarian cancer in IUD users (RR, 1.76; 95% CI, 1.08−2.85); however, the IUDs used in this study were from the 1970s and 1980s, predating the contemporary Cu-IUDs and hormonal IUDs used today. A meta-analysis analyzing previous data showed a preventive role of LNG-IUD for ovarian cancer, but this was not statistically significant (OR, 0.66; 95% CI, 0.41−1.08).[57] Other case−control studies also found no association between ever-use of IUDs and ovarian cancer risk (combined RR, 0.94; 95% CI, 0.81−1.08) and (OR, 1.24; 95% CI, 0.81−1.93).[58,59]

Proposed mechanism

Whereas both the Cu-IUD and LNG-IUDs cause a localized foreign-body inflammatory response that activates local immune cells to target occult microscopic cancer cells, the proposed biological mechanisms of ovarian cancer reduction vary by type of IUD and are similar to the mechanisms observed in risk reduction of other gynecologic malignancies.[11] In addition to creating a local inflammatory response, Cu-IUDs increase the pH of the reproductive tract, which has been linked to prevention of carcinogenesis by altering the cervical microenvironment to decrease HPV infection in the development of cancer and cervical intraepithelial neoplasia.[11,60] Alternatively, LNG-IUDs thicken cervical mucus, suppress the endometrium, and exert an antiestrogenic effect on the reproductive tract that suppresses endometrial proliferation. Because LNG-IUDs reduce menstruation and often cause amenorrhea, in theory they may decrease retrograde menstruation and reduce the potential of carcinogenic cells entering the fallopian tubes and abdominal cavity.[27] The inhibition of estrogen is also believed to prevent ovarian cell division and contribute to reduction in carcinogenesis.[11] LNG-IUDs may also affect carcinogenesis within the ovaries through ovulation suppression via the hypothalamic−pituitary axis, although this effect is less common and likely inconsistent.[26,61]

The data remain limited on IUD characteristics and duration of use, both of which likely modify IUD effect on ovarian cancer. Two studies show varying lengths of duration of use that confer a decreased risk of ovarian cancer. One study showed a decreased risk with a shorter duration of ever-use of IUD of <4 years vs another showing that >20 years of IUD use is beneficial to decrease the risk of ovarian cancer.[10,55]

Summary

Most studies suggest that IUDs of all types (even with short-term use) potentially reduce gynecologic cancer risk. Evidence strongly supports reduction of EC risk with IUD use. Although less definitive, evidence also suggests reduction of risk with IUD use for both cervical and ovarian cancer. Thus, a potential noncontraceptive benefit of using IUDs as a contraceptive device is that IUD use may offer protection from gynecologic malignancies. However, it is evident that there are gaps in the literature, particularly with regard to high-quality data on modern IUD use and its effect on developing endometrial, cervical, and particularly ovarian cancers. Our current understanding about the association of IUD use with risk of gynecologic malignancies is limited by the current body of literature. Most studies used in this review were unable to detail the dosage of levonorgestrel, duration of IUD use, or exact type of IUD used. In addition, some of the studies pooled data from use of antiquated IUDs, which limits the ability to extrapolate the noncontraceptive clinical benefits of modern IUDs. However, it is impactful to observe an overall protective benefit because of decreased risk of gynecologic malignancies with ever-use of IUDs alone. It is increasingly important for clinicians to have detailed evidence in regard to the specifics of current IUDs to provide complete counseling. Additional epidemiologic studies should assess the association of IUD use with gynecologic malignancies while controlling for important confounding variables. Because of the increase in IUD use in the United States, it is important to continue to evaluate the impact of contemporary IUDs on gynecologic malignancies.[1] ■

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