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Tubal Ectopic Pregnancy

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Approximately one in 100 pregnancies is ectopic, with the conceptus usually implanting in the fallopian tube. Some tubal ectopic pregnancies resolve spontaneously, but others continue to grow and lead to rupture of the tube.

- The risk of ectopic pregnancy is higher in women with damage to the fallopian tubes because of pelvic infections, pelvic surgery, or previous ectopic pregnancy, and in smokers.

- Intrauterine devices (IUDs) do not increase the absolute risk of ectopic pregnancy, but pregnancy that does occur with use of an IUD is more likely to be ectopic than intrauterine.

Primary treatment success and reduced risk of future pregnancy (intrauterine and/or ectopic) are prioritized outcomes for women with ectopic pregnancy who do not desire future fertility. However, treatment success and repeat intrauterine pregnancy are the prioritized outcomes for women with ectopic pregnancy who do desire future fertility. Given these individualized outcome preferences, even though data from randomized controlled trials are absent, the most effective treatment for ectopic pregnancy in women not desiring future fertility is salpingectomy.

Salpingotomy, salpingectomy, and methotrexate show similar rates of primary treatment success in women with ectopic pregnancy who desire future pregnancy; however, there is uncertainty over which treatment option is superior given the individualized outcome preference for this group of women and the absence of data from randomized controlled trials.

Salpingotomy by laparoscopy may lead to fewer complications and shorter recovery times compared with laparotomy, but

may also be less likely to remove all of the trophoblast.

Single- or multiple-dose methotrexate seems as likely as salpingotomy to eliminate trophoblast material and leave a patent fallopian tube in women with noninvasively diagnosed small ectopic pregnancies with no tubal rupture or bleeding, no sign of fetal cardiac activity, and low beta subunit of human chorionic gonadotropin (β -hCG) levels.

- About 15% to 40% of ectopic pregnancies may be suitable for such nonsurgical management.

- Adding mifepristone to systemic methotrexate seems unlikely to increase treatment success compared with methotrexate alone, other than in women with higher progesterone levels.

- Expectant management of unruptured ectopic pregnancies may lead to similar subsequent intrauterine pregnancy rates compared with surgery, but few studies have been done.

A single prophylactic dose of methotrexate after salpingotomy is more effective at reducing persistent trophoblast compared with salpingotomy alone.

Definition

Ectopic pregnancy is defined as a conceptus implanting outside the uterine endometrium. The most common implantation site is within the fallopian tube (95.5%), followed by ovarian (3.2%) and abdominal (1.3%) sites. The sites of tubal implantation in descending order of frequency are ampulla (73.3%), isthmus (12.5%), fimbrial (11.6%), and interstitial (2.6%). In this systematic review, we consider hemodynamically stable women with an unruptured tubal ectopic pregnancy, diagnosed by noninvasive or invasive techniques.

Incidence and Prevalence

About 10,000 ectopic pregnancies are diagnosed annually in the United Kingdom. The incidence of ectopic pregnancy in the United Kingdom is 11.1 per 1,000 pregnancies. Differing rates are reported in other countries such as Norway (14.9 per 1,000), Australia (16.2 per 1,000), and the United States (6.4 per 1,000). Since 1994, the overall rates of ectopic pregnancy and resulting mortality (0.35 per 1,000 ectopic pregnancies from 2003 to 2005) have been stable in the United Kingdom. Until recently, most epidemiologic studies failed to distinguish between ectopic pregnancies occurring in women who did not use contraception (reproductive failure) and in women who used contraception (contraceptive failure). A French population study undertaken from 1992 to 2002 found that, over the duration of the study, the rate of reproductive-failure ectopic pregnancies increased by 17%, whereas the rate of contraceptive-failure ectopic pregnancies decreased by 29%. Increasing rates of chlamydia infection, smoking, and assisted reproductive technology use may have contributed to the disproportionate increase in reproductive-failure ectopic pregnancies. Widespread use of dedicated early pregnancy assessment units and noninvasive diagnostic algorithms are likely to have contributed to increasing rates of ectopic pregnancy diagnosis.

Etiology and Risk Factors

The etiology of ectopic pregnancy is unclear. Ectopic pregnancies arising from reproductive failure should be considered as separate entities from those arising from contraceptive failure, with differing etiologies, risk factors, and reproductive outcomes. The main risk factors for reproductive-failure ectopic pregnancies are previous ectopic pregnancy, previous pelvic inflammatory disease, previous pelvic and tubal surgery, infertility, smoking, and use of assisted conception. The main risk factor for contraceptive-failure ectopic pregnancy is IUD failure. IUDs do not increase the absolute risk of ectopic pregnancy, but a pregnancy occurring with an IUD is more likely to be ectopic than intrauterine. Other risk factors for ectopic pregnancy include prior spontaneous miscarriage, endometriosis,

uterotubal anomalies, and prior in utero exposure to diethylstilbestrol. However, less than one-half of diagnosed ectopic pregnancies are associated with risk factors.

Prognosis

As the pregnancy advances, tubal ectopic pregnancies may either diminish in size and spontaneously resolve, or increase in size and eventually lead to tubal rupture, with consequent maternal morbidity and mortality. There are no reliable clinical, sonographic, or biological markers (e.g., serum β -hCG, serum progesterone) that can predict rupture of tubal ectopic pregnancy. Maternal mortality following ectopic pregnancy is an uncommon short-term outcome in resource-rich countries. The 2003 to 2005 U.K. Confidential Enquiry into Maternal Deaths cited ectopic pregnancy as a cause of 10 maternal deaths (0.47 per 100,000 pregnancies). Short-term maternal morbidity relates to pain, transfusion requirement, and operative complications. Primary treatment success and long-term fertility outcomes depend on the clinical characteristics of the ectopic pregnancy (e.g., whether the ectopic pregnancy occurred in a woman using contraception, with tubal rupture, or with contralateral tubal disease) and the type of surgical or

Clinical Questions

What treatments improve outcomes in women with unruptured tubal ectopic pregnancy?

Beneficial	Salpingectomy (more effective than salpingotomy and methotrexate in women not desiring future fertility; unknown if superior to salpingotomy or methotrexate in women desiring future fertility)
Likely to be beneficial	Methotrexate (single- or multiple-dose systemic; in women desiring future fertility; however, unknown if superior to salpingectomy) Methotrexate (systemic prophylactic) following salpingotomy Salpingotomy* (in women desiring future fertility; however, unknown if superior to salpingectomy or methotrexate)
Unknown effectiveness	Expectant management of unruptured ectopic pregnancies
Unlikely to be beneficial	Methotrexate plus mifepristone (systemic combination no better than systemic methotrexate alone)

*—Categorization based on consensus.

medical treatment chosen. A 10-year follow-up of ectopic pregnancies showed that the rate of repeat ectopic pregnancy was much higher in women with an IUD in place at the time of the index ectopic pregnancy, compared with women whose ectopic pregnancies were not associated with IUD use. By contrast, the rate of intrauterine pregnancy was 1.7 times higher (fecundity rate ratio, 1.7; 95% confidence interval [CI], 1.3 to 2.3) in women who had an IUD in place at the time of the index ectopic pregnancy compared with women whose index ectopic pregnancy was not associated with IUD use. Short- and long-term consequences on health-related quality of life and psychological issues (e.g., bereavement) are also important, but are rarely quantified.

A pregnancy of unknown location is the absence of pregnancy localization (either intrauterine or extrauterine) by transvaginal ultrasonography when serum β -hCG levels are below the discriminatory zone (1,000 to 1,500 IU per L [1,000 to 1,500 mIU per mL]). One observational study of pregnancies of unknown location has shown that 55% spontaneously resolve, 34% are subsequently diagnosed as viable, and 11% are subsequently diagnosed as ectopic pregnancies.

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