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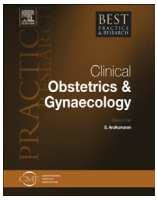

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Epidemiology of epithelial ovarian cancer

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Globally, ovarian cancer is the seventh most common cancer in women and the eighth most common cause of cancer death, with five-year survival rates below 45%. Although age-standardised rates are stable or falling in most high-income countries, they are rising in many low and middle income countries. Furthermore, with increasing life-expectancy, the number of cases diagnosed each year is increasing. To control ovarian cancer we need to understand the causes. This will allow better prediction of those at greatest risk for whom screening might be appropriate, while identification of potentially modifable causes provides an opportunity for intervention to reduce rates. In this paper we will summarise the current state of knowledge regarding the known and possible causes of epithelial ovarian cancer and discuss some of the main theories of ovarian carcinogenesis. We will also briefly review the relationship between lifestyle and survival after a diagnosis of ovarian cancer.

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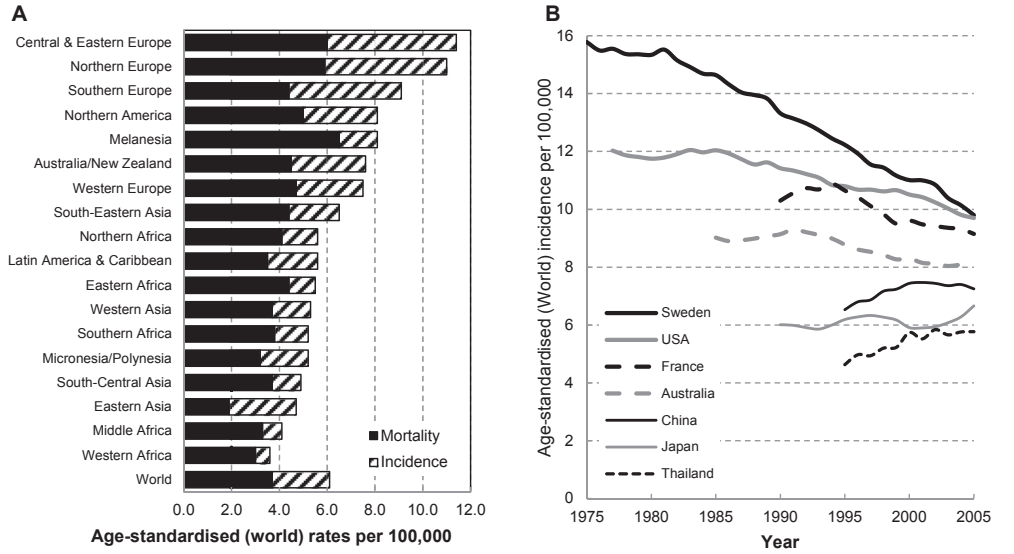

Figure 1. (A) Ovarian cancer incidence and mortality rates in 2012, age-standardised to the world population, by geographic region (Drawn from [1]), (B) Ovarian cancer incidence rates, age-standardised to the world population, in selected countries over time (Drawn from [2]).

Introduction

Globally, 240,000 women are diagnosed with ovarian cancer every year and, with five-year survival below 45%, it is responsible for 150,00 deaths making it the 7th most common cancer and 8th most common cause of cancer death among women [1]. Figure 1A shows that age-standardised incidence rates are highest in northern and central/eastern Europe, intermediate in north America, Australia and western Europe and lowest in Asia and Africa. Rates have been decreasing in most high incidence countries but increasing in many low incidence countries (Figure 1B) thus the differences today are less marked than 30 years ago [2]. Rates also vary by ethnicity within countries such that in the United States, rates in non-Hispanic white women are approximately 30% higher than African-American and Asian women and 12% higher than Hispanic women [3].

Ovarian cancer is rare in women under 40 years of age and most cancers in this age group are germ cell tumours. Above age 40, more than 90% are epithelial tumours and the risk increases with age, peaking in the late 70s. Despite being classified as ovarian, a high proportion of high-grade serous cancers are now thought to originate from the fallopian tube. In the following discussion the term 'ovarian cancer' refers to epithelial cancers that arise in the ovary or fallopian tube as well as the histologically similar primary peritoneal cancers.

Risk factors

It is well established that women with a family history of ovarian cancer are themselves at higher risk of the disease. The risk for women with one affected first-degree relative is about three times that for women with no affected relatives [4], and even higher for those whose relative was diagnosed below the age of 50 [5]. A high proportion of hereditary cancers are due to mutations in the BRCA genes, however BRCA mutations are also common among women with ovarian cancer who do not have a family history of either breast or ovarian cancer [6]. BRCA1 mutation carriers have an estimated 40–50% risk of developing ovarian cancer by age 70, compared to 10–20% for BRCA2 [7]. Most cancers associated with BRCA mutations are high-grade serous tumors. Lynch syndrome or hereditary non-polyposis colon cancer (HNPCC) caused by mutations in genes involved in DNA mismatch repair also increases risk of ovarian cancer, particularly non-serous cancer [8]. Mutations in other genes including

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