RESEARCH ARTICLE

Recreational Physical Activity and Risk of Ovarian Cancer: a Meta-analysis

Li-Min Zhou

Abstract

Our aim was to access the association between recreational physical activity (RPA) and risk of ovarian cancer (OC). The studies were retrieved from the PubMed and Embase databases up to February 20th, 2014. Risk ratios (OR) and 95% confidence intervals (CI) were used to estimate effect sizes. Random-effects or fixed-effects models were used to pool the data. The trim and fill method was applied for sensitivity analysis. Begg’s rank correlation test and Egger’s regression asymmetry test were employed to assess the publication bias. A total of 6 studies (435398 participants including 2983 OC patients) were included in this meta-analysis. The overall estimate indicated that there was weakly inverse association between RPA and OC risk (RR=0.90, 95% CI: 0.72-1.12, p=0.335). Meanwhile, for prospective cohort studies, a result consistent with the overall estimate was obtained (RR=1.12, 95% CI: 0.88-1.42, p=0.356). However, for case control studies, the pooled estimate of RR was 0.76 (95% CI: 0.64-0.90, p=0.002), indicating a clear significant association between RPA and OC risk. In addition, the sensitivity analysis indicated a significant link between RPA and risk of OC after removing Lahmann’s study (RR=0.80, 95% CI: 0.68-0.93, p=0.004). No significant publication bias was found (Begg’s test: p=1.00; Egger’s test: p=0.817). In conclusion, our meta-analysis indicated a weakly inverse relationship between RPA and the occurrence of OC.

Keywords: Recreational physical activity - ovarian cancer - meta-analysis

Asian Pac J Cancer Prev, 15 (13), 5161-5166

Introduction

Ovarian cancer (OC) is the leading cause of death from gynecological malignancy among women (Society, 2005; Lin et al., 2013). Epithelial OC is the most common histologic type of OC, constituting more than 90% of all cases of ovarian cancer (Kim et al., 2012). It was reported that epithelial OC and related cancers lead to 15,000 deaths in the US annually, representing the fifth leading cause of death from cancer among women (Siegel et al., 2011). In China, the burden of ovary cancer will continue to be relative stable due to the aging population (Wang, 2014). Although the molecular etiology about OC was continuously investigated (Samuels et al., 2011; Munksgaard et al., 2012), the overall survival rate of OC was still not improved in the last 20 to 30 years (Vaughan et al., 2011). In Robert’s study, the poor prognosis of OC was usually attributed to advanced stage at diagnosis and inadequate chemotherapy (Burger et al., 2011), but it was difficult to solve these technical problems. Therefore, the prevention of OC seems to be particularly important.

Physical activity (PA) has been proved to have protective effect against cancers of the colon and breast and possibly of the endometrium and prostate as well (Thune, 2000; Vainio et al., 2002). However, it remains unclear whether PA is associated with the reduction of OC risk. Although a number of studies have examined the relationship between PA and OC, the results of them were inconsistent (Tavani et al., 2001; Zhang et al., 2003; Anderson et al., 2004; Hannan et al., 2004). Tavani et al. (2001) and Hannan et al. (2004) reported that there was no significant association between PA and OC (Tavani et al., 2001; Hannan et al., 2004), while significant association between PA and OC was found by Zhang et al. (2003) and Anderson et al. (2004). This may be attribute to the different definitions of PA, different parameters of PA (type, frequency, duration, intensity), and different methods of measurement.

In this study, we included studies that the intensity of PA was estimated by a specific metabolic equivalent (MET) value. The MET values were abstracted from the Compendium of Physical Activities and defined as the ratio of work metabolic rate to a standard resting metabolic rate (1.0 (4.184 kJ)·kg⁻¹·h⁻¹) (Ainsworth et al., 2000). Then the association between recreational PA (RPA) and the risk of OC was explored by this meta-analysis.

Materials and Methods

Search strategy

We performed the pre-established search strategies and retrieved literatures in a systematic way from the...
In the present meta-analysis, we aimed to evaluate the potential association between physical activity and ovarian cancer risk. The PubMed and Embase library were searched for relevant articles. Inclusion and exclusion criteria were established to select studies for the meta-analysis. After screening, six studies were included, and the quality of these studies was assessed. The statistical analysis was performed using Stata11.0 software, and the effect size was calculated. A total of 438 potentially relevant studies were selected, and the quality of the included studies was assessed. The overall effect size was calculated, and the heterogeneity was evaluated.

Results

The procedures and outcomes of literature search were clearly shown in Figure 1. The meta-analysis included 6 studies, and the quality assessment of included studies was shown in Table 2. All the selected studies were high quality. The characteristics and information of the included studies are shown in Table 1. The 6 included articles were 3 prospective cohort studies (Bertone et al., 2001; Patel et al., 2006; Lahmann et al., 2009; Rossing et al., 2010) and 3 case control studies (Bertone et al., 2002; Pagan et al., 2005; Patel et al., 2006; Lahmann et al., 2009; Rossing et al., 2010). Four researches were conducted in American (Bertone et al., 2001; 2002; Patrick et al., 2005; Patel et al., 2006; Rossing et al., 2010). The other two studies were conducted in European (Lahmann et al., 2009) and Canada (Pagan et al., 2005), respectively. A total of 435398 participants including 2983 OC patients were included in this meta-analysis (Bertone et al., 2001; Bertone et al., 2002; Pan et al., 2005; Patel et al., 2006; Lahmann et al., 2009; Rossing et al., 2010).
Table 1. Characteristics of 6 Included Studies on Recreational Physical Activity and the Ovarian Cancer

<table>
<thead>
<tr>
<th>Study reference</th>
<th>Location</th>
<th>Period</th>
<th>Age (year)</th>
<th>Length of follow-up</th>
<th>Cases/Cohort</th>
<th>Type of measurement</th>
<th>Exposure range</th>
<th>Adjusted RRs (95% CI)</th>
<th>Adjustment for covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lahmann 2009</td>
<td>Europe</td>
<td>51.5</td>
<td>9.3</td>
<td>731/234740</td>
<td>questionnaire</td>
<td>baseline MET-hours/wk</td>
<td>&lt;12</td>
<td>1.15 (0.94,1.41)</td>
<td>Education, BMI, parity, age at menarche, menopausal status, unilateral oophorectomy, use of oral contraceptives, type of physical activity</td>
</tr>
<tr>
<td>Patel 2006</td>
<td>USA, 1992-2001</td>
<td>50-74</td>
<td>9</td>
<td>314/59695</td>
<td>questionnaire</td>
<td>baseline MET-hours/wk</td>
<td>&gt;24</td>
<td>1.05 (0.85,1.31)</td>
<td>Age, race, BMI, family history of breast or ovarian cancer, use of oral contraceptives, type of physical activity</td>
</tr>
<tr>
<td>Bertone 2001</td>
<td>USA, 1980-1996</td>
<td>30-55</td>
<td>16</td>
<td>377/92825</td>
<td>questionnaire</td>
<td>Cumulative average (1980-1996), MET-hr/wk</td>
<td>&lt;0</td>
<td>0.87 (0.58,1.30)</td>
<td>Age, parity, age at menarche, oral contraceptive use and duration, menopausal status/postmenopausal hormone use, tubal ligations, smoking status</td>
</tr>
</tbody>
</table>

Table 2. Methodological Quality of Cohort Studies Included in the Meta-analysis

<table>
<thead>
<tr>
<th>First author</th>
<th>Representativeness of the exposed cohort</th>
<th>Selection of the unexposed cohort</th>
<th>Ascertainment of exposure</th>
<th>Outcome of interest not present at start of study</th>
<th>Control for important factor or additional factor</th>
<th>Outcome assessment</th>
<th>Follow-up long enough for outcomes to occur</th>
<th>Adequacy of follow-up of cohorts</th>
<th>Total quality scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bertone</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>☆</td>
<td>8</td>
</tr>
<tr>
<td>Lahmann</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>☆</td>
<td>7</td>
</tr>
<tr>
<td>Patel</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>---</td>
<td>☆</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 2. Methodological Quality of Cohort Studies Included in the Meta-analysis

<table>
<thead>
<tr>
<th>First author</th>
<th>Case definition adequate</th>
<th>Representativeness of the cases</th>
<th>Selection of Controls</th>
<th>Same method of ascertainment for cases and controls</th>
<th>Control for important factor or additional factor</th>
<th>Definition of Controls</th>
<th>Ascertainment of exposure</th>
<th>Non-Response rate</th>
<th>Total quality scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossing</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>---</td>
<td>☆</td>
<td>7</td>
</tr>
<tr>
<td>Pan</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>---</td>
<td>☆</td>
<td>7</td>
</tr>
<tr>
<td>Bertone</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>☆</td>
<td>---</td>
<td>---</td>
<td>☆</td>
<td>7</td>
</tr>
</tbody>
</table>

*One star represents one score: 1 A study could be awarded a maximum of one star for each item except for the item Control for important factor or additional factor; 2 A maximum of 2 stars could be awarded for this item.
Limin Zhou

Meta-analysis

The summary of the meta-analysis for the association between RA and risk of OC was shown in Figure 2. The heterogeneity test showed that there was significant heterogeneity among studies (I^2=56.6%, p=0.042), so random effects model was applied to calculate the effect sizes. The overall estimate of RR was 0.90 (95%CI: 0.72-1.12, p=0.335), which indicated that high level RPA would decrease the risk of OC compared with the low level RPA, but the result was not significant. According to the study type, the subgroup analysis was performed (Figure 3). For case control studies, the pooled estimate (RR=0.76, 95%CI: 0.64-0.90, p=0.002) indicated that the high level RPA significantly decreased the risk of OC compared with the low level RPA. For prospective cohort studies, the pooled estimate of RR was 1.12 (95% CI: 0.88-1.42, p=0.356), which showed a consistent result with the summary meta-analysis.

Sensitivity analyses and publication bias

In the sensitivity analysis, it demonstrated that the pooled RR was 0.80 (95% CI: 0.68-0.93, p=0.004) after removing the Lahmann’s study (Lahmann et al., 2009), while after removing the others articles, the results were all consistent with the initial statistical analysis.

For all studies, no evidence of publication bias was observed in this meta-analysis (Begg’s test: p=1.00; Egger’s test: p=0.817).

Discussion

OC is the leading cause of death from gynecological malignancy. PA may have potentially prevented effect on the occurrence of OC. In this study, we evaluated the association between RPA and risk of OC. The results demonstrated that there was weakly inverse association between RPA and risk of OC. However, for the case control studies, the outcome showed a significant association between RPA and risk of OC. In addition, the sensitivity analysis also indicated the significant association between RPA and risk of OC after removing Lahmann’s study (Lahmann et al., 2009).

Several plausible biologic mechanisms have been proposed for the protective effect of PA on OC. Hormonal factors have been reported to be associated with OC risk in the general population (Salehi et al., 2008; Antoniou et al., 2009). Exposures to endogenous hormones such as estrogens, androgens, and gonadotropins have been proved increase ovarian epithelial cell proliferation, whereas exposure to progesterone could decrease stimulation of ovarian epithelial cells (Cramer et al., 1983; Risch, 1998; Rimann et al., 2004). PA was associated with decreased levels of circulating estrogen and progesterone in premenopausal women and serum estradiol, estrogens and androgens in postmenopausal women (Kramer et al., 1996; Westerlind, 2003). It was reported that PA could decrease postmenopausal estrogen levels directly or indirectly through reducing peripheral fat stores, which was the major source of postmenopausal estrogen production (Cauley et al., 1989; Friedenreich, 2001). In addition, PA may decrease OC risk through a reduction in chronic inflammation (Campbell et al., 2007) which has been proved to play a role in OC (Ness et al., 1999). Moreover, PA may also influence OC risk through a reduction in obesity, especially central obesity, which has been shown to increase OC risk (Pan et al., 2004). In summary, the association of PA and the reduction of OC risk might relate to the mechanisms such as alterations in the levels of endogenous sex hormones, reduction of chronic inflammation and even the weight loss. Further studies were required to investigate these speculations.

Many previous studies have confirmed the role of PA on the prevention of cancer (Kruk et al., 2006; Kruk, 2007; Wu et al., 2009). Even dance has been considered a therapy for cancer prevention (Aktas et al., 2005). People with cancer have a lower quality of life; PA is related to better quality of life of cancer survivors (Lee et al., 2013). Although weakly inverse relationship between RPA and the occurrence of OC was found in this study, PA may be play roles in the development of OC and improving the
quality of life of OC patients.

The consistent result has also been proved by a recent mate-analysis published in 2007. There were some differences between our study and that one. Firstly, this study updated the included study and two articles (Lahmann et al., 2009; Rossing et al., 2010) published after 2007 were included. The second one was that the cases in our study were patents with OC while in that study were patients with the most common OC, epithelial OC (Zhao et al., 2013). Furthermore, the intensity of RPA was estimated by MET value in the included studies of this meta-analysis. Thus, the influence of different evaluation criteria of RPA intensity on the results was avoided in this study. However, the evaluation criteria of RPA intensity were different in the included studies of that meta-analysis.

There were some advantages of this meta-analysis. The first one was that the included studies were all high quality studies. Second, the estimates were adjusted with covariates such as age, education, smoking status and body mass index, which could decrease the recall and selection bias. Besides, Begg’s and Egger’s tests proved no significant publication bias among the included studies. However, some limitations of this study should be mentioned. First of all, only 6 studies were included in this study. More studies were needed to be done to verify the results of this meta-analysis. Secondly, the included studies were all observational studies. Though we adjusted the studies with covariates such as age, education and smoking, the association between the RPA and the risk of OC would be affected by other unknown confounders. Of the third, the RPA levels were divided based on the self-administered questionnaire, so it might have a certain bias due to no accurate measurement and time standards. The fourth one was that the included studies were all carried out in European and American area. So it is necessary to develop investigations of Asian, African and Latino in order to assess the applicability of our results. Furthermore, the significant heterogeneity was found among the studies. Further studies were needed to explore the source of heterogeneity.

In conclusion, our meta-analysis indicated a weakly inverse relationship between RPA and the occurrence of OC.

References


DOI:http://dx.doi.org/10.7314/APJCP.2014.15.13.5161

Effect of Recreational Physical Activity on Ovarian Cancer Development


