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## 肉类摄入与卵巢癌发病及预后关系的研究进展

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• 综述 •

# 肉类摄入与卵巢癌发病及预后关系的研究进展

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**Abstract:** The incidence of ovarian cancer ranks third in gynecological malignant tumors and the mortality rate ranks first. The research on its pathogenic factors and prognosis has attracted more and more scholars' attention. As a daily food, various carcinogens produced during the preservation process of meat may lead to ovarian cancer and poor prognosis. Numerous epidemiological studies have explored the relationship between meat intake and risk as well as prognosis of ovarian cancer. This paper reviews aforementioned topic.

**Key words:** Ovarian cancer; Meat; Incidence; Prognosis

**摘要:** 卵巢癌发病率居妇科恶性肿瘤第三位, 死亡率居首位, 对其发病因素和预后情况的研究受到越来越多学者关注。肉类作为日常食物, 在保藏加工过程中产生的各类致癌物都可能导致卵巢癌变及预后不良。国内外已有多项流行病学研究探讨了肉类摄入与卵巢癌发病及预后的关系, 本文就上述两种关系进行综述。

**关键词:** 卵巢癌; 肉类; 发病; 预后

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## 0 引言

卵巢癌(ovarian cancer, OC)是常见的妇科恶性肿瘤之一, 2018年全球预计有29.5万人被确诊为OC, 约有18.5万人死于该病<sup>[1]</sup>。我国OC年龄标准化发病率为5.37/10万, 年龄标准化死亡率为2.22/10万<sup>[2]</sup>, 但由于我国人口基数较大, OC发病形势仍不容乐观。OC早期缺乏特异性临床症状, 多数患者在Ⅲ期(51%)或Ⅳ期(29%)被诊断出来, 五年生存率分别为42%和26%<sup>[3]</sup>。

遗传<sup>[4]</sup>、人体测量因素<sup>[5]</sup>、激素和生殖因素<sup>[6]</sup>被证实与OC的发病风险相关。膳食和特定的营养成分在OC发展中的作用尚不清楚, 现有流行病学证据在建立相关性方面也不一致<sup>[7]</sup>。肉类食物含有高生物价值的蛋白质和重要的微量元素, 如B族维生素, 铁(游离铁和血红素铁)和锌<sup>[8]</sup>, 因此明确肉类摄入与OC关系的研究进展, 对其一级预防和改善预后具有重要意义。

## 1 肉类摄入在卵巢癌发病过程中的作用

### 1.1 脂肪、血红素铁

肉类脂肪含量为10%~30%, 主要成分是甘油三酯和各种类型脂肪酸, 同时还含有少量卵磷脂、胆固醇、游离脂肪酸等。膳食脂肪主要通过激素相关机制影响OC的发生, 研究表明高膳食脂肪摄入可能使卵巢上皮细胞暴露于高水平的内源雌激素, 进而通过细胞损伤和增殖诱导卵巢癌变<sup>[9]</sup>。

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有研究显示，膳食脂肪包括饱和脂肪和反式脂肪的摄入可能会增加OC的发病风险<sup>[10]</sup>。

肉类食物尤其是红肉中含有大量容易被人体吸收的血红素铁，这可能是导致红肉相比于白肉与癌症更具有关联性的生物学机制之一。血红素铁被证明可促进内源性N-亚硝基化合物（N-nitroso compounds, NOCs）的产生，以及介导人体和啮齿动物消化道中脂质氧化产物的形成，从而引起黏膜细胞增殖以发挥其致癌作用<sup>[11]</sup>。

### 1.2 烹调加工产生的致癌物

肉类在保藏、烹调、加工过程中会产生一系列的致癌物，其中许多已被证实可诱发多种动物肿瘤<sup>[12-13]</sup>。肉类蛋白质烹调过程中由于燃烧不完全可产生杂环胺（heterocyclic amine, HCAs），其污染水平主要由肉的种类、烹饪方式、烹调温度决定。HCAs需要经过代谢活化才具有致癌性，机体的解毒能力与代谢活化的相对强度是决定其致癌性的重要因素之一。HCAs可诱导细胞色素P450酶系（cytochromeP450, CYP450），促进自身的代谢活化，但这种诱导作用有明显的种属、器官、性别差异<sup>[14]</sup>。肉类在保藏过程中还可能会产生另外一类致癌物——NOCs。迄今为止尚未发现一种动物对NOCs的致癌作用有抵抗力，不仅如此，多种给药途径都能引起试验动物肿瘤的发生，反复多

次接触或一次大剂量给药都能诱发肿瘤，且均有剂量—效应关系。动物试验方面，NOCs的致癌作用证据充分，大量人群流行病学研究也显示人类某些癌症可能与NOCs有关<sup>[14]</sup>。但是关于HCAs和NOCs在OC发生发展过程中所起到的病因学作用尚不清楚。

## 2 文献质量评价

纽卡斯尔—渥太华质量评估量表（NOS）用于评估原始研究包括队列研究（表1）和病例对照研究（表2）的质量，分数越高表示原始研究质量越好。

## 3 肉类摄入与卵巢癌发病的关系

本综述归纳了肉类摄入与OC发病关系的7项队列研究<sup>[15-21]</sup>和11项病例对照研究<sup>[22-32]</sup>（表3），发表时间均在2000年之后，研究地区涉及北美洲（美国、加拿大、墨西哥）、欧洲（意大利、荷兰、瑞典）、亚洲（中国、日本）以及大洋洲（澳大利亚）。7项队列研究尽管在研究地区、队列规模、人群饮食习惯、调整的混杂因素上各不相同，但所得出的结论一致——即肉类摄入与OC发病之间不存在关联。与队列研究相比，另外11项病例对照研究则观察到了较多有统计学意义的结果。例如，最近在中国<sup>[31]</sup>和意大利<sup>[32]</sup>进行的研究显示过多

表1 纳入综述的队列研究的方法学质量\*

Table1 Methodological quality of cohort studies included in the review\*

References	Representativeness of Exposed cohort	Selection of unexposed cohort	Ascertainment of exposure	Outcomes of interest does not appear at start of study	Control for important factor or additional factor <sup>†</sup>	Assessment of outcome	Follow-up long enough for outcomes to occur <sup>‡</sup>	Adequacy of follow-up of cohort <sup>§</sup>	Using Energy-adjusted model
Bertone, <i>et al</i> <sup>[15]</sup> , 2002, USA	☆	☆	☆	☆	☆	☆	☆	☆	☆
Larsson, <i>et al</i> <sup>[16]</sup> , 2005, Sweden	☆	☆	☆	☆	☆☆	☆	☆	☆	-
Kiani, <i>et al</i> <sup>[17]</sup> , 2006, USA	☆	☆	☆	☆	☆	☆	☆	☆	☆
Sakauchi, <i>et al</i> <sup>[18]</sup> , 2007, Japan	☆	☆	☆	☆	☆	☆	☆	☆	-
Schulz, <i>et al</i> <sup>[19]</sup> , 2007, Europe	☆	☆	☆	☆	☆☆	☆	-	☆	-
Cross, <i>et al</i> <sup>[20]</sup> , 2007, USA	☆	☆	☆	☆	☆☆	☆	-	☆	☆
Gilsing, <i>et al</i> <sup>[21]</sup> , 2011, Netherlands	☆	☆	☆	☆	☆☆	☆	☆	☆	☆

Notes: \*: a study could be awarded a maximum of one star for each item except for the item Control for important factor or additional factor. The definition/explanation of each column of the Newcastle-Ottawa Scale is available from [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp); ☆: the cohort study meets this methodological description; -: the cohort study does not meet the methodological description; †: a maximum of two stars could be awarded for this item. Studies that controlled for total energy intake receive one star, whereas studies that controlled for other important confounders such as parity, oral contraceptive use receive an additional star; ‡: a cohort study with a follow-up time >10 years is assigned one star; §: a cohort study with a follow-up rate >75% is assigned one star

表2 纳入综述的病例对照研究的方法学质量\*

Table2 Methodological quality of case-control studies included in the review\*

References	Adequate definition of cases	Representativeness of cases	Selection of control subjects	Definition of control subjects	Control for important factor or additional factor†	Exposure assessment	Same method of ascertainment for all subjects	Non-response rate‡	Using Energy-adjusted model
Tavani, <i>et al</i> <sup>[22]</sup> , 2000, Italy	☆	☆	☆	☆	-	-	☆	☆	-
Bosetti, <i>et al</i> <sup>[23]</sup> , 2001, Italy	☆	☆	☆	☆	☆☆	☆	☆	☆	-
Mccann, <i>et al</i> <sup>[24]</sup> , 2001, USA	☆	☆	☆	☆	☆	☆	☆	☆	-
Salazar-Martinez, <i>et al</i> <sup>[25]</sup> , 2002, Mexico	☆	☆	-	☆	☆☆	☆	☆	☆	☆
Zhang M, <i>et al</i> <sup>[26]</sup> , 2002, China	☆	☆	-	☆	☆☆	☆	☆	-	-
McCann, <i>et al</i> <sup>[27]</sup> , 2003, USA	☆	☆	☆	☆	☆☆	☆	☆	☆	-
Pan, <i>et al</i> <sup>[28]</sup> , 2004, Canada	☆	☆	☆	☆	☆☆	☆	☆	-	☆
Hu, <i>et al</i> <sup>[29]</sup> , 2008, Canada	☆	☆	☆	☆	☆	☆	☆	-	☆
Kolahdooz, <i>et al</i> <sup>[30]</sup> , 2010, Australia	☆	☆	☆	☆	☆☆	☆	☆	☆	-
Lee, <i>et al</i> <sup>[31]</sup> , 2013, China	☆	☆	☆	☆	☆☆	☆	☆	☆	-
Rosato, <i>et al</i> <sup>[32]</sup> , 2018, Italy	☆	☆	☆	☆	☆☆	☆	☆	☆	-

Notes: \*: a study could be awarded a maximum of one star for each item except for the item Control for important factor or additional factor. The definition/explanation of each column of the Newcastle-Ottawa Scale is available from [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp); ☆: the case-control study meets this methodological description; -: the case-control study does not meet the methodological description; †: a maximum of two stars could be awarded for this item. Studies that controlled for total energy intake receive one star, whereas studies that controlled for other important confounders such as parity, oral contraceptive use receive an additional star; ‡: one star is assigned if there is no significant difference in the response rate between control subjects and cases by using the chi-square test ( $P>0.05$ )

摄入加工肉制品是OC发病的危险因素，并与之前研究<sup>[30]</sup>相呼应。红肉摄入在早期两项研究<sup>[22-23]</sup>中得到正相关的结果，而后一些研究<sup>[27-30]</sup>均未发现二者之间的关联。McCann等<sup>[27]</sup>研究显示摄入家禽肉可降低OC的发病风险，而其他研究<sup>[23,26,28-30]</sup>未得出二者之间的关联。有两项研究<sup>[23,30]</sup>显示鱼肉摄入可能会降低OC的发病率，其他相关研究<sup>[26,28-29]</sup>均未发现二者之间的关联。

#### 4 肉类摄入与卵巢癌预后的关系

与发病相比，肉类摄入与OC预后关系的流行病学研究较少，目前共有4项研究<sup>[33-36]</sup>（表4）。Nagle等<sup>[33]</sup>研究纳入了1990—1993年间确诊的609例OC患者，随访截止时394例OC患者死亡，结果显示红肉和白肉摄入与OC预后之间不存在关联。Dolovec等<sup>[34]</sup>的研究选取1994—1998年间确诊的341例OC患者并进行随访，随访截止时176例OC患者死亡，结果显示一些肉类食物摄入水平高的OC患者存在更高的死亡风险，趋势性检验 $P<0.01$ 。对

肉类进行亚组分析发现红肉和腌制肉摄入是OC预后的危险因素，而白肉和鱼肉摄入与OC预后之间不存在关联。Thomson等<sup>[35]</sup>研究为探索健康饮食指数（healthy eating index, HEI）与OC预后之间的关系，纳入了1993—1998年间确诊的636例OC患者，随访截止时354例OC患者死亡，结果显示更高质量的饮食模式与OC诊断后全因死亡率降低相关，但没有具体的HEI成分评分项目与死亡率降低存在统计学上的关联。最近一项关于诊断前饮食与OC预后关系的研究<sup>[36]</sup>发现鱼肉摄入是OC预后的保护因素，而其他肉类（红肉、家禽肉、加工肉）摄入与OC预后不存在关联。

#### 5 讨论

本文所纳入的队列研究均未发现肉类摄入（红肉、白肉、加工肉）与OC发病存在关联，病例对照研究方面仅中国一项研究<sup>[26]</sup>显示新鲜肉类摄入是OC发病的危险因素，红肉在两项意大利研究<sup>[22-23]</sup>中被发现可能会诱发摄食者罹患OC，另外



表3 已经发表的肉类摄入与卵巢癌发病关系的研究信息

Table3 Published information on relationship between meat consumption and incidence of ovarian cancer

References	Study design	N	Control size/ Cohort size	Measure of exposure and range of exposure	Effect estimates OR(95%CI)	Covariates
Tavani, <i>et al</i> <sup>[22]</sup> , 2000, Italy	Case-control study	971	4770	Red meat (servings/week) >6 vs. ≤3	1.30(1.10-1.60)	Age, gender, education level, age of interview, smoking, alcohol, fruits, vegetables and fat intake
Bosetti, <i>et al</i> <sup>[23]</sup> , 2001, Italy	Case-control study	1031	2411	Red meat (servings/week) >5.4 vs. <2.2 Fish (servings/week) >2.9 vs. <0.9 Poultry (servings/week) >3.4 vs. <0.9 Processed meat (servings/week) >29 vs.<19	1.53(1.13-2.05) 0.51(0.38-0.70) 0.83(0.57-1.21) 1.21(0.98-1.49)	Age, research center, education level, age of interview, fertility, oral contraceptives, energy intake
Mccann, <i>et al</i> <sup>[24]</sup> , 2001, USA	Case-control study	496	1425	Meat (servings/month) >25 vs. ≤9	1.17(0.80-1.71)	Age, education, region of residence, regularity of menstruation, family history of ovarian cancer, parity, age at menarche, oral contraceptive use, and remaining food groups
Salazar-Martinez, <i>et al</i> <sup>[25]</sup> , 2002, Mexico	Case-control study	84	629	Meat T3 vs. T1	1.35(0.58-3.14)	Age, total energy intake, number of live births, recent changes in weight, physical activity and diabetes
Zhang M, <i>et al</i> <sup>[26]</sup> , 2002, China	Case-control study	254	652	Fresh meat(kg/year) ≥22.75 vs. ≤7.45 Poultry(kg/year) ≥7.50 vs. ≤1.50 Fish(kg/year) ≥22.55 vs. ≤3.90	1.98(1.00-3.80) 0.77(0.40-1.40) 1.45(0.80-2.80)	Age at interview, education, living area, BMI, smoking, alcohol drinking, tea drinking, family income, marital and menopause status, parity, tubal ligation, oral contraceptive use, physical activity, family history of ovarian cancer, total energy intake, and all the variables listed above except subgroups of vegetables
Bertone, <i>et al</i> <sup>[15]</sup> , 2002, USA	Cohort study	301	80258	Main dish of beef, pork,lamb: ≥2-4 times/week vs. 1-3times/month Mixed dish of beef, pork, lamb: ≥2-4 times/week vs. <1 time/month Hamburger: ≥1 time/week vs. <1 time/month Chicken with skin: ≥1time/week vs. <1 time/month Chicken without skin: ≥1 time/week vs. <1 time/month	1.30(0.93-1.82) 0.87(0.58-1.31) 0.86(0.63-1.17) 0.98(0.73-1.32) 0.82(0.62-1.07)	Age, parity, age at menarche, menopause status/postmenopausal hormone use, tubal ligation, smoking status
McCann, <i>et al</i> <sup>[27]</sup> , 2003,USA	Case-control study	124	696	Red meat (g/month) <2224 vs. <766 Poultry (g/month) >1189 vs. <369	1.22(0.61-2.44) 0.45(0.22-0.92)	Age, education, total months menstruating, difficulty becoming pregnant, oral contraceptive use (ever/never), menopausal status and total energy
Pan, <i>et al</i> <sup>[28]</sup> , 2004, Canada	Case-control study	422	2135	All meat product Q4 vs. Q1 Fresh red meat Q4 vs. Q1 Chicken Q4 vs. Q1 Fish Q4 vs. Q1 Processed meat Q4 vs. Q1	0.91(0.67-1.24) 0.78(0.57-1.06) 0.99(0.71-1.37) 1.16(0.85-1.59) 0.98(0.72-1.33)	10-year age group, province of residence, education, alcohol consumption, cigarette pack-years, BMI, total caloric intake, recreational physical activity, number of live births, menstruation years, and menopause status
Larsson, <i>et al</i> <sup>[16]</sup> , 2005, Sweden	Cohort study	288	66651	Red meat (servings/week) ≥4 vs. <2 Fish (servings/week) ≥4 vs. <1	1.00(0.70-1.46) 1.00(0.72-1.41)	Age, BMI, educational level, parity, use of oral contraceptives and postmenopausal hormones, total energy intake, and quartiles of consumption of fruits, vegetables, and dairy products
Kiani, <i>et al</i> <sup>[17]</sup> , 2006, USA	Cohort study	71	13281	Total meat index(servings/week) ≥1 vs. 0 Beef index(servings/week) ≥1 vs. 0 Fish(servings/week) ≥1 vs. 0 Poultry(servings/week) ≥1 vs. 0	1.69(0.88-3.24) 1.09(0.50-2.38) 1.39(0.73-2.62) 1.23(0.66-2.32)	Age, parity and BMI
Sakauchi, <i>et al</i> <sup>[18]</sup> , 2007, Japan	Cohort study	77	63541	Pork≥3-4 times/week vs.≤1-2 times/month Beef≥1-2 times/week vs. Seldom Chicken≥3-4 times/week vs. ≤1-2 times/month Fish almost every day vs. ≤1-2times/month Dried or salted fish: ≥3-4times/week vs. ≤1-2times/month	1.59(0.62-4.08) 1.24(0.50-3.05) 1.13(0.40-3.17) 1.33(0.59-2.98) 2.80(1.14-6.89)	Age, menopausal status, number of pregnancies, history of sex hormone use, BMI, physical activity, and education
Schulz, <i>et al</i> <sup>[19]</sup> , 2007, Europe	Cohort study	581	325731	Meat(g/week) ≥109 vs. <64 Red meat(g/week) ≥55 vs. <25 Fish(g/week) ≥44 vs. <17 Poultry(g/week) ≥23 vs. <8 Processed meat(g/week) ≥42 vs. <17	0.78(0.52-1.17) 1.04(0.70-1.56) 0.90(0.56-1.43) 1.05(0.75-1.47) 1.25(0.81-1.92)	BMI, parity, menopausal status, ever use of oral contraceptives, total energy intake, education, smoking, and hormone replacement therapy use at baseline, unilateral ovariectomy

续表3 Table3 continued

References	Study design	Cases	Control size/ Cohort size	Measure of exposure and range of exposure	Effect estimates OR(95%CI)	Covariates
Cross, <i>et al</i> <sup>[20]</sup> , 2007, USA	Cohort study	149	199312	Red meat(g/1000kcal) 62.7 vs. 9.8 Processed meat(g/1000kcal) 22.6 vs. 1.6	1.19(0.89-1.59) 1.23(0.92-1.63)	Age, education, marital status, family history of cancer, race, BMI, smoking, frequency of vigorous physical activity, total energy intake, alcohol intake, and fruit and vegetable consumption
Hu, <i>et al</i> <sup>[29]</sup> , 2008, Canada	Case-control study	442	5039	Total meat Q4 vs. Q1 Red meat Q4 vs. Q1 Fresh fish T3 vs. T1 Smoked fish T3 vs. T1 Poultry T3 vs. T1 Processed meat Q4 vs. Q1	1.10(0.80-1.50) 1.00(0.70-1.50) 1.40(0.90-2.20) 1.30(0.70-2.60) 0.80(0.40-1.50) 1.10(0.70-1.60)	10-yr age group, province, education, BMI, alcohol use, pack-year smoking, total of vegetable and fruit intake, and total energy intake, number of live birth and years of menstruation
Kolahdooz, <i>et al</i> <sup>[30]</sup> , 2010, Australia	Case-control study	793	2984	Total meat (servings/week) ≥12 vs. <6 Red meat (servings/week) ≥7 vs. <3 Total fish (servings/week) ≥4 vs. <1 Fatty fish (servings/week) ≥6 vs. <1 Nonfatty fish (servings/week) ≥4 vs. <1 Poultry (servings/week) ≥3 vs. <1 Processed meat (servings/week) ≥4 vs. <1	1.06(0.87-1.30) 1.07(0.80-1.42) 0.76(0.62-0.94) 0.79(0.65-0.98) 0.86(0.70-1.05) 0.83(0.67-1.03) 1.18(1.15-1.21)	Age, age-squared, oral contraceptive use, level of education, parity, energy intake
Gilting, <i>et al</i> <sup>[21]</sup> , 2011, Netherlands	Cohort study	340	62573	Total fresh meat (g/week) 145.8 vs. 45.2 Fresh red meat (g/week) 129.6 vs. 36.2 Fish (g/week) 28.2 vs. 0 Processed meat (g/week) 25.6 vs. 0 Beef (g/week) 50.4 vs. 2.2 Pork (g/week) 71.2 vs. 3.5	0.97(0.63-1.47) 0.93(0.61-1.42) 1.01(0.71-1.43) 0.83(0.59-1.20) 1.15(0.81-1.64) 1.08(0.75-1.59)	Age, total energy intake, parity, use of oral contraceptives
Lee, <i>et al</i> <sup>[31]</sup> , 2013, China	Case-control study	500	500	Preserved meat (g/d) >9 vs. ≤9	1.52(1.16-1.99)	Age, BMI, physical activity, total energy intake, parity, oral contraceptive use, menopausal status, marital status, education level, smoking status, alcohol drinking, family history of ovarian or breast cancer
Rosato, <i>et al</i> <sup>[32]</sup> , 2018, Italy	Case-control study	2002	5478	Processed meat (g/d) ≥20 vs. <10	1.49(1.30-1.71)	age, study centre, year of interview, education, tobacco smoking, alcohol drinking, body mass index, age at menarche, parity, oral contraceptives, hormone replacement therapy, status menopausal and age at menopause, family history of ovarian cancer, vegetables consumption, fruit consumption, and total energy intake

Note: BMI: body mass index

表4 已经发表的肉类摄入与OC预后关系的研究信息

Table4 Published information on relationship between meat intake and prognosis of ovarian cancer

References	Country	Average follow-up time/year	Deaths (n)	Total (n)	Dietary variable	Hazard ratio (95%CI)	Adjusted confounding factors
Nagle, <i>et al</i> <sup>[33]</sup> , 2003	Australia	7.3	394	609	Red meat(serves/d): >0.86 vs. <0.4 White meat (serves/d): >0.54 vs. <0.3	0.76(0.58-1.00) 0.78(0.60-1.01)	FIGO stage, age at diagnosis, grade, total energy intake, BMI
Doloeck, <i>et al</i> <sup>[34]</sup> , 2010	USA	Not mentioned	176	341	Meat (servings/week): 11.4 vs. 2 Red meat (servings/week): 5 vs. 0.2 White meats and fish (servings/week): 5 vs. 0.5 Cured/processed meats (servings/week): 5.7 vs. 0.4	2.28(1.34-3.89) 2.82(1.42-5.59) 0.97(0.58-1.63) 1.91(1.07-3.42)	Age at diagnosis, race, stage, grade, residual lesions, smoking status, BMI, oral contraceptive use, parity, and total energy intake
Thomson, <i>et al</i> <sup>[35]</sup> , 2014	USA	Not mentioned	354	636	HEI score(meat and beans): 10 points vs. <7.5 points	0.83(0.59-1.17)	Age at diagnosis, stage, race, diabetes, physical activity, total energy, waist circumference, family history of ovarian cancer
Playdon, <i>et al</i> <sup>[36]</sup> , 2017	Australia	Not mentioned	547	811	Total meat(servings/d): ≥2 vs. <1 Red meat(servings/week): ≥6 vs. <2 Total fish(servings/week): ≥3 vs. <1 Oily fish(servings/week): ≥2 vs. None Poultry(servings/week): ≥2 vs. <1 Processed meat (servings/week): ≥2 vs. <1	0.98(0.71-1.35) 1.21(0.89-1.64) 0.74(0.57-0.95) 0.80(0.58-1.11) 0.98(0.80-1.20) 1.08(0.86-1.35)	Age at diagnosis, International Federation of Gynaecology and Obstetrics (FIGO) stage, amount of residual disease, grade, tumour subtype, smoking status, BMI, physical activity index, marital status, and daily caloric intake

在中国<sup>[31]</sup>、意大利<sup>[32]</sup>和澳大利亚<sup>[30]</sup>开展的三项研究均发现加工肉可能是OC发病的危险因素，在美国<sup>[27]</sup>、意大利<sup>[23]</sup>和澳大利亚<sup>[30]</sup>开展的三项研究发现白肉的摄入可能是OC发病的保护因素，其中一项研究<sup>[30]</sup>发现多脂鱼的摄入可降低OC的发病风险，而当暴露因素变为非多脂鱼摄入时，二者之间的相关性消失，此结果提示鱼肉中含有的 $\omega$ -3多不饱和脂肪酸可能是其降低OC发病风险的活性物质。

经济合作与发展组织最新发布的全球肉类摄入水平数据显示，2017年澳大利亚人均肉类消费量为90.3千克居首位，美国以人均肉类消费量90.1千克次之，而亚洲国家如中国和日本的人均肉类消费量相对较低，仅为49.8千克和39.7千克，且欧美国家以家禽肉为主要肉类摄入，而亚洲国家则以猪肉为主要的肉类摄入（<https://doi.org/10.1787/fa290fd0-en>）。对本综述纳入研究按照不同地区分析可以发现，肉类摄入充足的欧美国家较其他国家地区可以观察到更多有统计学意义的结果。亚洲国家在加工肉摄入的效应上较其他肉类相对显著，可能与该地区人群习惯通过腌制、发酵、烟熏等加工工艺处理肉类以增强风味和储藏性有关，与此同时在加工过程中使用的防腐剂（亚硝酸盐和硝酸盐等）以及加工处理方式（烘烤和熏烤等）都会使得肉制品中致癌物含量大大增加。日本的一项队列研究<sup>[18]</sup>通过半定量的食物频率问卷调查发现，摄入咸鱼每周超过3~4次的人群与几乎不摄入该类食物的人群相比OC死亡风险显著增加（ $HR=2.80$ ,  $95\%CI: 1.14-6.89$ ）。另一项在我国开展的病例对照研究<sup>[31]</sup>发现南方妇女加工肉类的摄入与OC发病风险呈正相关，其中在当地很受欢迎的咸肉、咸鱼和腊肉都分别观察到了与卵巢癌发病之间显著的正相关。

开展预后方面流行病学研究地区较少，目前仅涉及美国和澳大利亚，有两项研究<sup>[33,36]</sup>发现肉类摄入（红肉和鱼肉）是OC预后的保护因素，Dolovec等的研究<sup>[34]</sup>却显示肉类摄入（除白肉以外的肉类）会增加OC死亡风险，但该研究局限之处在于缺乏OC患者在生存期间临床治疗和生活方式方面的信息，而这类混杂因素可能会导致观察到生存结果而非诊断前肉类摄入的效应，影响结果的真实性。最近的一项澳大利亚研究<sup>[36]</sup>显示鱼肉摄入可能是OC预后的保护因素，而其他类型的肉类包括多脂鱼均未发现与OC预后相关，且与之前研究结果存在明显差异，这提示需要更多学者重视OC预后方面的研究，以获得更多充分的证据。

综上所述，肉类摄入是OC发病的危险因素尚无确凿证据，但加工肉类在病因学机制及流行病学研究方面都有证据支持其致癌作用。目前预后方面开展的流行病学研究难以得出二者之间的真实关联结果，仍需要开展更多地区研究以增强结论的真实性。

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