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J Gynecol Oncol Vol. 26, No. 3:240-241
http://dx.doi.org/10.3802/jgo.2015.26.3.240
pISSN 2005-0380 · eISSN 2005-0399

Journal of Gynecologic Oncology
jgo

Impact of statins on risk and survival of ovarian cancer

To the editor: While statins have been clearly shown to decrease mortality and morbidity in cardiovascular diseases, the role of statins as an anti-cancer agent is less well defined. Predicted through new guidelines published by American College of Cardiology, it is said that around 30% of Americans in the age group 40 to 75 will be using statins even if they do not have cardiovascular disease [1]. Recently, statin's beneficial effect on cancer survival has also been highlighted in many studies. A Danish study [2] reported that people who have used statins have 20% lower chance of cancer deaths compared with those who have not used statins. Similarly studies have also shown that statins lower the incidence of common cancers such as breast, prostate and colorectal. This anticancer activity of statins is due to inhibition of isoprenoid biosynthesis which is essential for cancer growth and metastasis [3,4].

Ovarian cancer has the worst prognosis among gynecological cancers. It has been estimated that ovarian cancer causes approximately 15,000 deaths in USA annually [5]. Therefore, identification of protective factors and possible agents associated with increased survival can have great implications. Statin's role in ovarian cancer has been controversial with varying opinions. In order to collect all the evidence, we conducted a literature search utilizing Medline (PubMed and Ovid) and Cochrane Library to identify studies related to statins effect on incidence and survival in ovarian cancer. Eight relevant citations were found and are summarized in **Table 1**. Only three studies [6-8] were found which reported the effect of statin therapy on ovarian cancer survival while the others [9-13] only reported risk of ovarian cancer.

Habis et al. [6] reported a decrease in hazards of disease-specific death (adjusted hazard ratio, 0.23; p=0.04) among statin users in non-serous papillary epithelial ovarian cancer. Similarly Elmore et al. [7] showed significantly longer survival in statin users (62 months) compared with non-users (46 months, p=0.04). Out of the six studies [8-13] reporting risk of ovarian cancer, only one found a significant reduction in ovarian cancer incidence with statin usage. Baandrup et al. [9] documented a decrease risk only with respect to mucinous ovarian cancer enforcing the need for further subgroup analysis.

When findings of five studies [8,10-13] were pooled in a

Table 1. Summary of the evidence regarding impact of statin therapy on risk and survival of ovarian cancer

Study	Type of study	Size of population	Primary outcome variable	Conclusion
Habis et al. (2014) [6]	Retrospective cohort	442	Progression-free survival and disease-specific survival	Improved survival among statin users was not seen except in non-serous papillary epithelial ovarian cancer
Elmore et al. (2008) [7]	Retrospective cohort	126	Progression-free survival and overall survival	Improved survival was seen in statin users
Lavie et al. (2013) [8]	Case control study	Cases, 12; matched controls, 126	Risk of ovarian cancer and survival	Decreased risk along with improved survival was reported
Baandrup et al. (2015) [9]	Case control study	Cases, 4,103; matched controls, 58,706	Risk of epithelial ovarian cancer	Decreased risk seen in mucinous ovarian cancer. No association with epithelial subtype
Yu et al. (2009) [10]	Retrospective cohort	73,336	Risk of ovarian cancer	Non-significant decrease in ovarian cancer risk was found
Kaye et al. (2004) [11]	Case control study	Cases, 91; controls, 7,393	Risk of ovarian cancer	Statins have no substantial effect on ovarian cancer risk
Friedman et al. (2008) [12]	Retrospective cohort	361,859	Risk of ovarian cancer	No association was found
Clearfield et al. (2001) [13]	Randomized controlled trial	997	Risk of ovarian cancer	No difference in frequency of cancer between statin users/non-users was reported

meta-analysis conducted by Liu et al. [14], a significant 21% risk reduction was seen (relative risk [RR], 0.79; 95% confidence interval [CI], 0.64 to 0.98). The RR reduction was found to be 52% when long term statin usage was considered (RR, 0.48; 95% CI, 0.28 to 0.80). In conclusion, we suggest that statins impact on ovarian cancer warrants further investigation with larger randomized controlled trials as observational studies are subject to bias and may lead to false slight benefits. Effect of statins with respect to different histological subtypes also need to be further studied.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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http://dx.doi.org/10.3802/jgo.2015.26.3.240