

## Correspondence



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### Conflict of Interest

No potential conflict of interest relevant to this  
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# Protective and therapeutic effects of metformin on gynecologic cancers

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To the editor:

Currently, in the aspect of drug repositioning, metformin which is the first line drug of choice for type 2 diabetes mellitus (T2DM) has been considered as a kind of therapeutic drug for gynecologic cancers based on its antitumor effects [1]. The main antitumor action of metformin occurs through activation of adenosine monophosphate activated protein kinase, which inhibits the phosphatidylinositol 3-kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) pathway stimulating cellular proliferation and activates p53. Additionally, it has been reported that metformin down-regulates cyclin D1 expression and telomerase activity.

So far, clinical studies have reported that metformin reduces cancer risk and improves survival rates in diabetic women having uterine endometrial and ovarian cancers only [2,3]. Clinical result on uterine cervical cancer has been limited. By the way, in the volume 27 May of this journal, a retrospective clinical study regarding the impact of T2DM on early stage cervical cancer patients who underwent surgery was published and this article pointed out that metformin did not affect the prognosis [4]. In association with the effect of metformin on cervical cancer, more recently, another retrospective cohort study analyzing 181 women with diabetes and cervical cancer gave us the result that cumulative dose of metformin was recognized as an independent factor decreasing the risk of cancer-specific mortality. In this study, researchers also found that metformin decreased the risk of cervical cancer in a dose-dependent fashion [5]. There were some differences in research purposes and materials between the two studies. The former mainly aimed to evaluate the impact of T2DM on cervical cancer and analyzed early stage patients treated by surgery only, while the latter studied the impact of metformin use on mortality after cervical cancer in older women with diabetes.

Drug repositioning is very meaningful in cancer therapy considering time and expenditure for new drug discovery and clinical trials of it. While T2DM is common in old women and has been acknowledged as a risk factor for cervical cancer as well as other gynecologic cancers, the effect of metformin has been analyzed based on only diabetic women with gynecologic cancer. Conclusively, researchers should consider prospective clinical trial evaluating the impact of metformin on gynecologic cancer patients without diabetes for its therapeutic use.

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