Labels in figure: seed, sprout, peritoneal recurrence, - obesity, - cytology(+), - pT3, stealth metastasis, distant recurrence, lymph node recurrence

News Release

Title
Detailed Analysis of the Effect of Obesity on Ovarian Cancer Recurrence from Stealth Tumor Cells Residing in the Abdominal Cavity: Peritoneal-specific recurrence-free survival and overall survival are predominantly shorter in the high BMI group

Key Points
　・Although basic research has shown that adipose tissue supports the progression of ovarian cancer, some clinical studies have shown limited effect of obesity on the prognosis of ovarian cancer, and experts have been divided in their opinions about the effect of obesity on the prognosis of ovarian cancer.

　・By focusing on cases in which complete surgical resection was achieved after intraperitoneal dissemination had occurred, the research group analyzed in detail the effect of obesity on recurrence from stealth ovarian cancer cells latent in the abdominal cavity.

　・The research group found that peritoneum-specific recurrence-free survival and overall survival were significantly shorter in the high BMI group.

Summary

A research group consisting of Graduate Student Shohei Iyoshi, Assistant Professor Masato Yoshihara, Professor Hiroaki Kajiyama (Department of Obstetrics and Gynecology), Assistant Professor Ryo Emoto, and Professor Shigeyuki Matsui (Department of Biostatistics) from the Graduate School of Medicine, Nagoya University (Dean: Professor Hiroshi Kimura) reported that obesity is an independent prognostic factor in intraperitoneal recurrence after initial surgery for ovarian cancer (OvCa), using a large patient cohort and statistical modeling.

OvCa is one of the deadliest cancers in the field of gynecologic oncology and shows a characteristic mode of progression, called direct dissemination, via accumulating ascites. It is also known that OvCa cells are selectively metastasizing into the intraperitoneal adipose tissues, such as the omentum and mesentery, and that adipocytes provide energy to the proliferating cancer cells, thereby supporting their growth. However, clinical studies analyzing the relationship between obesity and OvCa progression have often reported results showing that obesity has no effect on prognosis, and experts have been divided in their opinions.

Using a large data set of approximately 5,000 patients with malignant ovarian tumors collected over a 35-year period in the Tokai region (Tokai Ovarian Tumor Study Group), the research group analyzed in detail the effect of obesity on the intraperitoneal recurrence in patients who once had intraperitoneal dissemination and whose tumors had been removed at the initial surgery completely. The results showed that the time to intraperitoneal recurrence was significantly shorter in the group with higher BMI at diagnosis. In addition to being a factor for identifying high-risk groups for early recurrence in postoperative follow-up, these results suggest that targeting adipose tissue may be a new therapeutic target for refractory OvCa.

Research Background

OvCa possess one of the poorest prognoses in the field of gynecological oncology. Because of the lack of subjective symptoms and the lack of established screening methods, it is often detected in an advanced stage, with multiple micro-metastases called peritoneal dissemination, in which cancer cells metastasize directly into peritoneal cavity through accumulating ascites. In such cases, OvCa cells are known to show a high selectivity for adipocyte-rich tissues such as the omentum and mesentery. Basic studies have shown that adipocytes support the proliferation of OvCa cells in peritoneal dissemination sites by providing energy to cancer cells as fatty acids and by forming a cancer microenvironment that is preferable to cancer cells. On the other hand, some clinical studies using actual patient data have reported that obesity does not affect prognosis, and experts have been divided in their opinions. Recently, it has also been reported that the impact of obesity on OvCa prognosis varies depending on the advanced stage of ovarian cancer, and thus, more detailed analysis has been demanded.

Research Results

The study used data from a total of approximately 5,000 patients with malignant ovarian tumors collected over a 35-year period in the Tokai Ovarian Tumor Study Group. Patients with stage IIB and IIIC epithelial OvCa who had achieved complete resection of the visible lesion at initial surgery (R0) were included. 280 patients who satisfied study criteria were included in the study and classified into high BMI group (BMI ≥ 25, n = 37), normal BMI group (18.5 ≤ BMI < 25, n = 201), and low BMI group (BMI ≤ 18.5, n = 42) based on their BMI at diagnosis. In addition to overall survival and progression-free survival, peritoneum-specific recurrence-free survival was evaluated. Thus, the research group investigated the effect of obesity on peritoneal recurrence from latent OvCa cells.

The results showed that both peritoneum-specific recurrence-free survival and overall survival were significantly shorter in the high BMI group than in the normal BMI group (p = 0.028 and 0.018, HR = 1.87 and 1.95, respectively). On the other hand, there were no significant differences in peritoneum-specific recurrence-after survival or peritoneum-specific recurrence-free interval among the various BMI groups. Multivariate analysis identified obesity as an independent prognostic factor in addition to pT3 staging and positive ascites cytology. In addition, no significant difference in the distribution of recurrence sites between these two groups was detected. These results suggest that in OvCa recurrence from stealth cancer cells, adipose tissue plays pro-tumoral roles and supports their growth.

Research Summary and Future Perspective

These results suggest that obesity in OvCa patients can be a predictor of recurrence in OvCa cases in which complete resection has been achieved, and that targeting adipose tissue may be a new therapeutic strategy for refractory OvCa.

Publication

Japanese ver.
https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Obe_220720.pdf