

# Abstracts of the Alumni Association Memorial Lectures of the 76th Annual Meeting of the Medical Association of Nippon Medical School

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## Abstracts of the Alumni Association Medical Research Fund Prize Memorial Lecture (I)

### Gender-related Differences in Circulating Levels of Adipocytokine associated with Postoperative Complication following Major Surgery

Takeshi Matsutani<sup>1,2</sup>, Akihisa Matsuda<sup>1,2</sup>, Koji Sasajima<sup>1,2</sup> and Takashi Tajiri<sup>1</sup>

<sup>1</sup>Surgery for Organ Function and Biological Regulation, Graduate School of Medicine, Nippon Medical School

<sup>2</sup>Department of Surgery, Nippon Medical School Tama Nagayama Hospital

#### Introduction

Outcomes after hemorrhage and sepsis are affected by gender difference, as female animals tolerate trauma-hemorrhage and subsequent sepsis better than do male animals. Because immune dysfunction is a key factor in these processes, female animals show an enhanced immune response after trauma-hemorrhage, whereas male animals show a decreased immune response<sup>1</sup>. Few clinical studies have focused on the effect of gender difference on perioperative immune status after major abdominal surgery. The reported experimental and preliminary clinical data suggest that women have immunological advantages over men during the perioperative period<sup>2</sup>.

In recent years adipose tissue has received increased attention. The primary function of adipose tissue has traditionally been considered to be energy storage, but adipose tissue is now considered to be an endocrine/immune organ secreting a variety of biologically active molecules, conceptualized as adipokines<sup>3</sup>. Adiponectin, expressed specifically in adipose tissue, is an anti-inflammatory cytokine that antagonizes the effects of the proinflammatory cytokines. Leptin, the product of the *ob* gene, is also an adipocytokine secreted by adipose tissue. However, the mechanism of gender-related alterations in the innate function of adipose tissue after major surgery is still unknown.

The aim of this study was to investigate the effect of gender differences in innate inflammatory responses and the function of adipose tissue in patients undergoing major surgery.

#### Patients and Methods

The subjects were 19 patients (15 men and 4 women), who underwent subtotal esophagectomy through right

Table 1 Background of the patients

	Male (n=15)	Female (n=4)	
Age (yo)	64 ± 2	64 ± 7	N.S.
Operative time (minutes)	454 ± 31	393 ± 40	N.S.
Intraoperative blood loss (mL)	835 ± 118	602 ± 142	N.S.
Postoperative complications	Pneumonia; n=6 Wound infection; n=2	None	

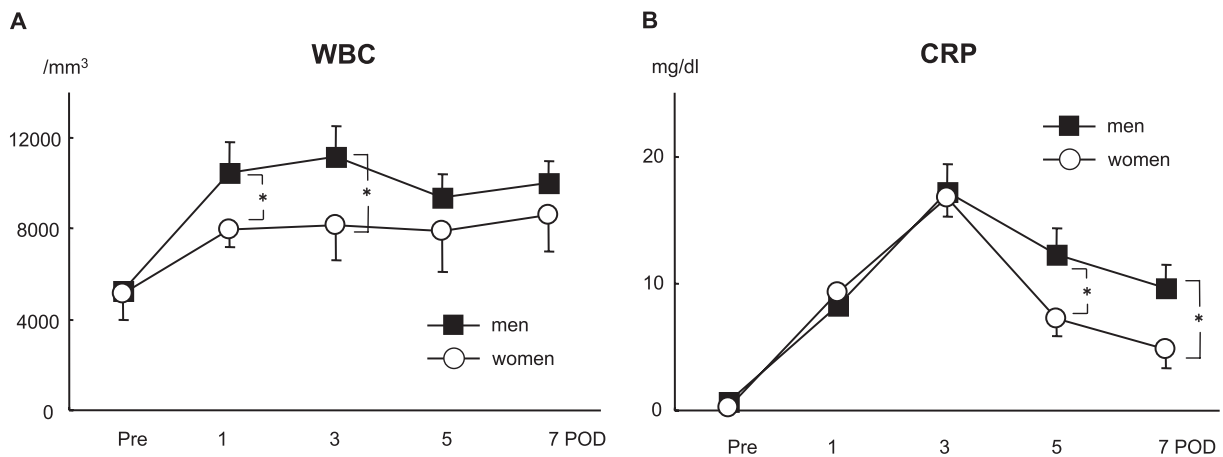


Fig. 1 Changes after surgery in WBC counts (A) and serum CRP levels (B) in men (closed squares) and women (open circles). The data are expressed as mean ± SE.

thoracotomy with 3-field lymph node dissection for squamous cell carcinoma of the esophagus. All of the women were postmenopausal. None of the patients had received any medication with known effects on the immune system during the 4 weeks before the operation. All patients requiring surgical intervention received standard surgical care and postoperative treatment in the intensive care unit. This study was approved by the Ethics Committee of Nippon Medical School, and informed consent for this study was obtained from all patients before surgery.

The number of the white blood cells (WBCs) and serum levels of C-reactive protein (CRP) were measured before the operation and on postoperative days (PODs) 1, 3, 5, and 7. Preoperative plasma levels of adiponectin and leptin were assayed with a commercially available enzyme-linked immunosorbant assay kit (Quantikine; R&D Systems Inc., Minneapolis, MN, USA) according to the manufacturer's instructions.

Data are presented as the mean ± SE (standard error). A P value < 0.05 was considered to indicate significance for all statistical analyses.

### Results and Discussion

The background factors for the 19 patients with esophageal carcinoma are listed in **Table 1**. There were no significant differences in terms of age, duration of surgery, or intraoperative blood loss between male and female patients. However, postoperative complications were observed in 8 men (53%) and in 0 women. The women had a significantly lower morbidity rate due to postoperative complication than did the men. These findings suggest that male patients might develop postoperative immune suppression after esophagectomy, whereas female patients have an immunological advantage during the early postoperative period.

The number of WBCs in men was slightly lower than that in women, with significant differences in WBC counts on POD 1 ( $p < 0.05$ ) and on POD 3 ( $p < 0.05$ ; **Fig. 1A**). Serum levels of CRP in both groups gradually

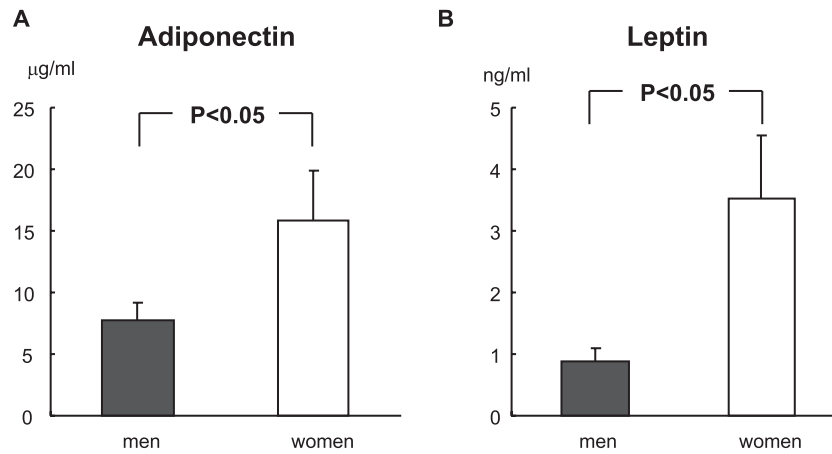


Fig. 2 Preoperative plasma adiponectin (A) and leptin levels (B) in men and women. The data are expressed as mean  $\pm$  SE.

increased after surgery and peaked on POD 3 (**Fig. 1B**). Serum levels of CRP levels in both men and women were significantly higher after surgery than before surgery. In men these inflammatory responses on POD 5 and 7 were significantly higher than those in women. **Fig. 2A** shows that preoperative adiponectin levels were 52% lower in men than in women. Furthermore, preoperative leptin levels in men were lower than those in women (**Fig. 2B**). In the present study, we have demonstrated that preoperative levels of adiponectin and leptin were lower in male patients than in female patients with esophageal cancer and have clearly shown lower inflammatory responses in women after surgery. We have previously reported that the preoperative adiponectin level is an independent risk factor for postoperative infection following gastrointestinal surgery<sup>3</sup>. The immunological advantages may improve the short- and long-term results of abdominal surgery.

Although we do not know the hormonal status, differences in immune response were clearly evident between men and women. Because variations in circulating levels of sex hormones might not explain all observations, our study confirmed a gender difference in postoperative complications after esophagectomy, with a benefit in women.

## References

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