氏 授与した学位 専攻分野の名称 学位授与番号 学位授与の日付 学位授与の要件	YANG TITI(楊 媞媞)   博 士   医 学   博 甲第 7210 号   2025年3月25日   医歯薬学総合研究科 病態制和学専攻   (学位規則第4条第1項該当)
学位論文題目	Vascular dysfunction in women with recurrent pregnancy loss: Possible association with antiphospholipid antibodies (不育症の女性における血管機能障害:抗リン脂質抗体との関連の可能性)
論文審查委員	教授 大塚文男 教授 大内淑代 准教授 江口 潤

## 学位論文内容の要旨

Antiphospholipid antibodies (aPL) are a key factor in recurrent pregnancy loss (RPL) and cardiovascular disease. This retrospective study assessed vascular function in 569 women with RPL and 55 healthy controls by blood tests for antiphospholipid antibodies and accelerated cardiography (APG). According to the results, women with RPL had significantly lower vascular elasticity, as evidenced by a lower pulse wave difference index (DPI:  $115.6 \pm 4.1$ ), compared with controls ( $117.0 \pm 2.3$ ). Among women with RPL, those with at least one aPL antibody had a lower DPI compared with those without any antibody. Notably, those with anti- $\beta_2$  glycoprotein I ( $a\beta_2$ GP I) IgG positivity had significantly lower DPI and higher remained blood volume (RBV), indicating impaired vascular function. Regression analysis showed that ab<sub>2</sub>GP I IgG and body mass index (BMI) were negatively correlated with DPI. These findings suggest that subclinical vascular dysfunction is present in women with RPL during their reproductive years, potentially linked to the presence of a62GP I IgG.In addition, we suggest that this noninvasive APG measurement opens the possibility of future vascular testing in women with RPL, helping to predict cardiovascular risk in women with RPL and encouraging improvements in their lifestyles to reduce vascular dysfunction. Further research will elucidate the mechanisms of RPL, its association with vascular dysfunction, and effective treatments.

## 論文審査結果の要旨

Antiphospholipid antibodies (aPL) are a key factor in recurrent pregnancy loss (RPL) and cardiovascular disease. The present study is a retrospective study that assessed vascular function in 569 women with RPL and 55 healthy controls by blood tests for antiphospholipid antibodies and accelerated cardiography (APG). According to the results, women with RPL had significantly lower vascular elasticity, as evidenced by a lower pulse wave difference index (DPI:  $115.6 \pm 4.1$ ), compared with controls ( $117.0 \pm 2.3$ ). Among women with RPL, those with at least one aPL antibody had a lower DPI compared with those without any antibody. Notably, those with anti-B<sub>2</sub> glycoprotein I (aB<sub>2</sub>GP I) IgG positivity had significantly lower DPI and higher remained blood volume (RBV), indicating impaired vascular function. Regression analysis showed that  $a\beta_2$ GP I IgG and body mass index (BMI) were negatively correlated with DPI. These findings suggest that subclinical vascular dysfunction is present in women with RPL during their reproductive years, potentially linked to the presence of  $a\beta_2 GP I IgG$ . It was also suggested that this noninvasive APG measurement opens the possibility of future vascular testing in women with RPL, helping to predict cardiovascular risk in women with RPL and encouraging improvements in their lifestyles to reduce vascular dysfunction.

This research has provided important knowledge on RPL and attained to the valuable achievement. Therefore, this student is eligible for the Ph.D. degree.