

審査の結果の要旨

氏名 杉田（柳澤）綾子

I examined the incidence of interventions, such as laser photocoagulation(LPC), vitrectomy(VR), and lower-limb amputations(LLA), for diabetic complications. And I elucidated the patient attributes related to the incidence of each intervention, and illustrated the temporal changes of cumulative incidence of each intervention whether the incidences of interventions for complications had decreased in recent years as clinical care and treatment environments had improved based on real-world claims data from Japan.

This retrospective longitudinal study used a 9-year claims database obtained from JMDC Inc. Patients aged 20–74 years old taking antidiabetic medications were included. They were divided into two groups: patients with newly initiated antidiabetic medication (Group 1, n = 42,788) and patients with continuing antidiabetic medication (Group 2, n = 85,337). The incidence rate for each intervention and patient attributes related to the incidence of each intervention were analyzed.

The results obtained from the analysis are shown below.

1. Group 1 consisting of 42,788 patients, among whom approximately 70% were men and 7% had received insulin and/or GLP-1 analogue since the initial prescription. Group 2 consisting of 85,337 patients; the proportion of gender were about the same as that in Group 1, though the proportion of users of insulin and/or GLP-1 analogue were over 15%. In Group 1, the incidence rate (IR) of first LPC, VR, and LLA were 7.12 (95% CI: 6.61–7.67), 2.57 (2.26–2.91), and 0.24 (0.16–0.36) per 1000 person-years, respectively. In the intervention for ocular complications, the IR of women tended to be higher than that of men and the incidence rate of all interventions of insulin and/or GLP-1analogue user were higher than for the users of oral antidiabetic agents. Furthermore, the IR of all the interventions was higher for the dependents than the insured individuals.

In Group 2, the IR of the first LPC, VR, and LLA were 9.14 (8.73–9.56), 3.34 (3.10–3.60), and 0.33 (0.26–0.42) per 1000 person-years, respectively. In the intervention for ocular complications, the IR of women tended to be higher than that of men. The IR of those with an older age, Type 1 diabetes, insulin and/or GLP-1 analogue users and high CCI score tended to be high in all interventions. In addition, similar to the result in Group 1, the IR for all the interventions was higher for the dependents than for the insured individuals.

2. In Group 1, older age was associated with an increased hazard ratio of the interventions for

retinopathy after adjustment by Cox's regression hazard models. The users of insulin and/or GLP-1 analogue were associated with increased risk of all the interventions. Gender differences of hazard ratio were found in LPC and LLA. In addition, the hazard ratios of dependents tended to be higher than that of insured individuals in all the interventions.

In Group 2, a similar trend was observed. Being older was mostly associated with an increased hazard ratio of interventions. The hazard ratio of insulin and/or GLP-1 analogue users tended to be high for all the interventions. The hazard ratios of dependents were also larger than that of insured individuals for all of the interventions. Higher CCI scores tended to be associated with larger hazard ratios in all the interventions.

3. I show the comparison of the cumulative incidence for each intervention between Period 1 (April 2009–March 2014) and Period 2 (April 2013–March 2018) in Group 1 and Group 2. This was calculated using Kaplan–Meier method. In Group 1, the incidence of LPC and VR for Period 1 and Period 2 did not differ over time ( $p = 0.90$ ,  $p = 0.83$ , respectively), the incidence of LLA was approximately halved ( $p = 0.01$ ). In Group 2, the incidence of all the interventions for Period 1 and Period 2 did not differ over time.

Based on the real-world claims data, I showed that the IR of LPC, VR, and LLA for patients with newly initiated antidiabetic medications were 7.12, 2.57, and 0.24 per 1000 person-years, respectively. Those for patients with continuing antidiabetic medication were about 1.3 times higher than the above group. Insulin and/or GLP-1 analogue users were associated with a higher IR for these interventions. The hazard ratio of all the interventions tended to be higher for dependents than for the insured person himself or herself in both groups. While there was a limited change in the cumulative IR of the intervention for retinopathy, the incidence of LLA declined by half.

The results of present study that investigated the IR of each intervention for severe diabetic retinopathy and diabetic serious lower-limb complications using large-scale real-world claims data are important and useful information for clinicians when considering the timing of referrals to ophthalmologists, dermatologists, and orthopedists in a clinical situation.

よって本論文は博士（医学）の学位請求論文として合格と認められる。