論文審査の要旨及び担当者 (甲)乙 第 報告番号 号 氏 名 VU CHI HOANG VIET 男 論文審查担当者 眼科学 坪 田 主 杳 内科学 原 耳鼻咽喉科学 小 中 仁 11 郁 内科学 竹 内 勤 学力確認担当者: 審査委員長:中原 仁 試問日:平成31年 1月16日 (論文審査の要旨) 論文題名: Influence of Meibomian Gland Dysfunction and Friction-Related Disease on the Severity of Dry Eye (ドライアイの重症度におけるマイボーム腺機能不全と摩擦関連疾患の影響) Dry eye disease (DED) is a multifactorial disease of the tears and ocular surface that is the result of compromises in the quality or quantity, or both, of the tears and ocular surface. It is not uncommon to encounter more than 1 risk factor in a patient with DED, therefore it is necessary to determine the contribution of each risk factor to DED as a whole. Given this approach, in this study, the author evaluated the influence of meibomian gland dysfunction (MGD), a common cause of DED, separately and in the influence of meibonian gland dysfunction (MGD), a common cause of DED, separately and in combination with friction related diseases (FRD), a new term proposed to include a set diseases arising from frictional force between the eyelid and the ocular surface, on DED and dry eye subgroups. The Japanese dry eye diagnostic criteria was adopted in this research. The question of what about other criteria using internationally and how difference they are compared with the Japanese criteria were asked. The response was: several diagnostic criteria were used in Europe and America. Different tests and different cut-off value were utilized, for example TBUT was less than 10s instead of less than 5s in the Japanese criteria. In this study, the Dry Eye Related Quality of Life Score (DEQS) was used to evaluate the subjective symptoms but the score of DEQS was not provided in the paper. In response to the question of the relationship between the DEQS score and MGD and FRD, unpublished data were shown. There was no significant association between the DEQS score and MGD/FRD. 86% of the patients in this study were female so what was the cause of the sex difference in DED. The answer was: it is widely accepted that DED occurs more frequently in women than in men. Several hypothesis were proposed to explain this observation and one of them was the interpretation of the results, could the conclusion of FRD is the cause of DED be made. The answer was it is difficult to conclude if the association between FRD and DED is because of a causal effect. In response to the difficult to conclude if the association between FRD and DED is because of a causal effect. In response to the question of how the results could be applied to dry eye treatment, the following answer was made. The results of this study suggested a broader approach in management of DED. It is necessary to take into account other DED-related conditions such as MGD and FRD in order to treat DED in a more comprehensive way. Furthermore, the results emphasized the important role of an unstable tear film in the mechanism of DED. It is in accordance with new definition and diagnostic criteria developed by the Asian Dry Eye Societies. This new definition led to development of a new strategy called "tear film oriented therapy". In this study, good correlation was shown between MGD, FRD and the severity of DED, however it was difficult to conclude if the association was because of a causal effect or not. Since it is a cross-sectional study, difficult to conclude if the association was because of a causal effect or not. Since it is a cross-sectional study, causal inference could not be made. Furthermore, in this study the patients were not follow-up therefore it was impossible to provide longitudinal data. Suggestion regarding conducting a cohort study was made. Regarding the question about why the diagnostic criteria of MGD were based on a Yes-No criteria rather than a spectrum scale and how the results would be affected if a spectrum scale was used. The answer was: MGD was detected via the presence of clinical signs such as altered meibomian gland secretion and changes in eyelid morphology. At first, to diagnose MGD, MGD score was graded and MGD probable group was made to include patients who had MG abnormalities but did not meet the diagnostic criteria of definite MGD. Ocular surface findings were compared between no-MGD, probable MGD and definite MGD groups. No significant difference was found between no-MGD and probable MGD group (data not shown in the paper). In addition, the diagnostic criteria using in this study was derived from the Japanese diagnostic criteria for MGD which was widely recognized. MGD which was widely recognized. In this study, 9 participants were excluded because of disqualification. Question about what were the detailed reasons of disqualification in these cases was asked. Answer: the investigators at the study sites were in charge of deciding those who were ineligible for the study based on the exclusion criteria. It is difficult to provide the detailed answer to this question. Regarding the question about by using the Japanese Dry eye diagnostic criteria in this study, there would be a possibility that patients with no symptoms be recruited. The answer was: indeed such cases could have been included; however in fact all patients in this study had subjective symptoms. Regarding the question of should hypersecretion of the meibomian glands should be considered as a disease because it is commonly believed that the more meibum is secreted the more benefit

considered as a disease because it is commonly believed that the more meibum is secreted the more benefit the ocular surface will have. The answer was: in MGD, not only the quality but also the quantity of meibum is changed. These abnormalities can lead to abnormalities of the tear film resulting in evaporative dry eye. Based on this answer, suggestion about dividing these 2 conditions when evaluating the influence on DED was proposed. The question of what was the clinically relevant suggestion of this study was asked. The answer was: this study suggested that a more comprehensive way should be made when approaching DED. DED related conditions such as MGD and FRD should be taken into account and be treated probably. From this response, suggestion about future research regarding the effect of FRD treatment on the severity of DED was proposed.