論　文　内　容　要　旨

Influence of donor liver telomere and G-tail on clinical outcome after living donor liver transplantation

（ドナーテロメアやGテールの生体肝移植後の臨床所見に関する影響）

PLoS ONE 14(3): e0213462, 2019 in press.

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It has been reported that donor age affects patient outcomes after liver transplantation, and that telomere length is associated with age. However, to our knowledge, the impact of donor age and donor liver telomere length in liver transplantation has not been well investigated. This study aimed to clarify the influence of the length of telomere and G-tail from donor livers on the outcomes of living donors and recipients after living donor liver transplantation. The length of telomere and G-tail derived from blood samples and liver tissues of 55 living donors, measured using the hybridization protection assay. The length of telomeres from blood samples was inversely correlated with ages, whereas G-tail length from blood samples and telomere and G-tail lengths from liver tissues were not correlated with ages. Age, telomere, and G-tail length from blood did not affect postoperative liver failure and early liver regeneration of donors. On the other hand, the longer the liver telomere, the poorer the liver regeneration tended to be, especially with significant difference in donor who underwent right hemihepatectomy. We found that the survival rate of recipients who received liver graft with longer telomeres was inferior to that of those who received liver graft with shorter ones. An elderly donor, longer liver telomere, and higher Model for End-Stage Liver Disease score were identified as independent risk factors for recipient survival after transplantation. In conclusion, telomere shortening in healthy liver does not correlate with age, whereas longer liver telomeres negatively influence donor liver regeneration and recipient survival after living donor liver transplantation. These results can direct future studies and investigations on telomere shortening in the clinical and experimental transplant setting.

Liver transplantation (LT) is a standard treatment for end-stage liver disease and liver malignancies. In a globally aging society, a declining pool for living donor liver transplantation (LDLT) and cadaver LT has become a critical issue. The possibility and safety of donations from marginal donors should be considered, particularly those of elderly and obese donors. It remains controversial whether donor age impairs recipient outcomes after LDLT [1]. However, the impact of donor age on the outcome of both donors and recipients after LDLT has not been studied. For a long time, the liver was recognized as an organ that could regenerate; yet, the mechanism of liver regeneration is remains unclear. Eukaryotic organisms senesce as they get older, and organ function and regeneration ability decline. It has been reported that liver regeneration in elderly

people and rats after hepatectomy slows down [2]. The residual capacity of hepatic function is thought to be correlated with liver regeneration. However, only a few studies have focused on the effects of aging liver tissues on liver regeneration and postoperative outcomes. Thus, it is necessary to clarify the relationship between liver regeneration and age. Telomeres, double-stranded DNA containing repeat sequences of5'-TTAGGG-3'at the ends of chromosomes, appear to be deeply involved in tissue regeneration, lifespan, and cell division [3, 4]. It has been reported that telomere length decreases as the time of cell division increases [3, 4]. According to the general theory, telomere length is inversely correlated with age. In addition, it has been reported that the telomeric 3'-overhang (G-tail) length is associated with a risk of cardiovascular events [5, 6]. However, the significance of telomere/G-tail length in LT has not been well studied. We investigated the influence of telomere and G-tail length from donor blood and liver tissues on donor liver regeneration and recipient outcome after LDLT.