理委員会の審査を受け、指針に従い臨床情報は匿名化し個人情報に十分配慮した。
個人遺伝子情報に関する保護と管理は、「ヒトゲノム・遺伝子解析研究に関する倫理指針」に基づいて行うものとした。試料・データはすべて連結可能匿名化とし、個人識別に関するデータは個人識別情報管理分担者が管理した。データは研究室に設置した専用コンピューターにて一括管理し、データアクセスは研究従事者がパスワードを用いて行った。また、各症例の遺伝子発現情報の管理、情報解析も専用コンピューターに一括して保存し、部外者のアクセスを禁じた。

C．研究結果

1. 初回観察時の平均HbA_{1c}、BMI、HOMA-IRは7.5%、29kg/m^2、3.9であった。
2. 2型糖尿病、高血圧、脂質異常症、メタボリックシンドロームの罹患率は各々76、35、64、38%であった。
3. 平均観察期間3.0±2.1年間で肝線維化は11人（28%、FL：NASH 10：1）が悪化、12人（31%、FL：NASH 3：9）が改善、16人（41%、FL：NASH 7：9)が不変であった。
4. 単変量解析では、線維化改善群で初回肝生検時のAST（P=0.04）およびHbA_{1c}低下量（⊿HbA_{1c}、P=0.01）が有意に高値を示した。
5. 一方、BMI やインスリン抵抗性マーカーであるHOMA-IR、QUICKI、筋インスリン抵抗性、肝インスリン抵抗性はいずれも線維化進展と相関しなかった。
6. 多変量解析（重回帰分析）により年齢、性、BMIで補正すると、⊿HbA_{1c}のみが肝線維化進展の予測因子であった（P=0.03)。
7. 各種治療法をCox比例ハザードモデルで解析したところ、インスリン治療が肝線維化を改善する独立した予知因子であった。

D．考察

血糖コントロールの改善は、BMI、インスリン抵抗性にも増して、日本人NAFLD患者の肝病理改善を予知する。分担研究者は以前に、2型糖尿患者の肝臓では、非糖尿病患者に比し、血管新生因子、線維化のマスター因子TGF-βファミリー、コラーゲン等の遺伝子発現が亢進することを観察しており、今回の知見を裏付けるものと考える。

E．結論

肥満といった既知のNASH危険因子だけでなく、厳格な血糖コントロールがNAFLDの肝線維化阻止のために重要である。また、超速効型インスリン各食前投与を主体としたインスリン治療が、NAFLDの病理を改善する可能性が示唆された。

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H. 知的財産権の出願・登録状況

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Ⅲ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

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