英文題目: Nonalcoholic Fatty Liver Disease and Diabetes Mellitus Overlapping Gene Signature in Morbidly Obese Patients Undergoing Bariatric Surgery- preliminary report

中文題目:非酒精性脂肪肝和糖尿病在接受減重手術病態性肥胖病人之共同基因印記-初步報告

作 者:高偉育¹⁻⁵,王偉⁶,林源峰³,蘇建維^{4,5},張君照^{1,2},陳志榮⁷

服務單位:¹台北醫學大學附設醫院內科部胃腸科;²台北醫學大學醫學院醫學 系;³台北醫學大學臨床醫學研究所;⁴台北榮民總醫院內科部胃腸科;⁵陽明大學 醫學院醫學系;⁶台北醫學大學附設醫院外科部一般外科;⁷台北醫學大學附設醫 院病理部

Background: Bariatric surgery is emerging as a valuable treatment option for morbidly obese patients with type 2 diabetes mellitus (DM). The prevalence rate of nonalcoholic fatty liver disease (NAFLD) has been reported up to 74% to 90% of morbidly obese patients. NAFLD is a complex disease with interaction of genetic and environmental factors. This study is aimed to identify NAFLD and DM overlapping gene signature in morbidly obese patients underwent bariatric surgery.

Methods: The Gene Expression Omnibus (GEO) is a database repository of sequenceand array-based data. We used the keywords "bariatric surgery", "diabetes", "nonalcoholic fatty liver disease" to search the GEO repository for materials for our study. We downloaded a series matrix file in which the data were normalized with *GeneSpring*. We selected differentially expressed genes (DEGs) between the NAFLD and no NAFLD groups, the DM and no DM groups which exhibited a 1.5-fold change (FC >1.5-fold) and a p value of <0.05.

Results: There were 14, 194, 7 results for "bariatric surgery", "diabetes", "nonalcoholic fatty liver disease" in the GEO database, respectively. The GSE58979 dataset contained 16 group I (<5% steatosis), 13 group II (NAFLD, 30-50% steatosis), 14 group III (NASH) and 10 group IV (NASH + fibrosis F2-F3). The GSE15653 dataset contained 5 lean control subjects undergoing elective cholecystectomy and 13 obese subjects (9 with type 2 DM) undergoing gastric bypass surgery. DEGs between the NAFLD and no NAFLD groups, the DM and no DM groups were 343 and 679 genes, respectively. NAFLD and DM overlapping gene signature revealed ACTA2, ANXA1, CCL8, IL1B, INSIG1, MT1M, RCAN1, TNFAIP6.

Conclusions: Further clinical cohort studies are warranted to investigate the predicted biomarkers and pathways using online databases in morbidly obese patients undergoing bariatric surgery. It may help clinical physicians for the identification of patients most likely to benefit from bariatric surgery.

Keywords: Nonalcoholic fatty liver disease; Diabetes mellitus; Bariatric surgery; Gene signature

Table 1. NAFLD and DM overlapping 8-gene signature expression

Gene	NAFLD	DM
ACTA2	-0.64359	0.628312
ANXA1	0.814897	0.957755
CCL8	1.230522	0.646791
IL1B	0.79868	-0.74024
INSIG1	0.694476	0.716084
MT1M	0.975163	0.711199
RCAN1	0.806639	-1.03352
TNFAIP6	0.907797	0.835478

Figure 1. NAFLD and DM overlapping gene signature expression pattern

