

可能藉由影響脂肪細胞的脂解功能而降低減重手術效果  
Elevated Neutrophil-Lymphocyte Ratio may decrease weight loss effect after Laparoscopic Sleeve Gastrectomy by impairing Lipolysis function of Adipocyte.

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Introduction

Low-grade subclinical inflammation plays an important role in the development of obesity. The neutrophil-lymphocyte ratio (NLR) is a well-known indicator of subclinical inflammation. We previously demonstrated that preoperative NLR shows the potential to be used as a prognostic biomarker for predicting successful weight loss at POM3 after LSG. Preoperative NLR < 2.36 did predict successful weight loss (EBWL>37.7%) at POM3 (AUC = 0.635, p=0.032).

The adipocyte function did associate with body weight loss after bariatric surgery. However, There are seldom research discussing the association between adipocyte function, inflammation, and weight loss effect after bariatric surgery.

Our study has two aims: 1: To identify whether NLR<2.36 is a significant predictive factor for adequate weight loss, which was defined as POM\_EBWL>37.7% in morbid obese patients who underwent LSG, by multivariate analysis. 2: To explore the difference of adipocyte function between patients with NLR<2.36 and NLR ≥ 2.36.

Method

Prove the predict efficiency of NLR

Retrospectively, we included patients who had undergone LSG at our institution between January 2019 and April 2021. (Table 1) An excessive body weight loss (EBWL) of >37.7% at 3 months postoperatively (POM3) was defined as a successful operation. We do multivariate analyzed the correlation between NLR and postoperative weight change after LSG.

Total		N=100	
Age (yrs)	Mean (SD)	39.16	(11.23)
Sex (M/F)	(M/F)	44/56	
Basic clinical characteristics.			
Weight (Kilograms)	Mean (SD)	117.33	(24.10)
Body mass index (BMI)	Median (IQR)	40.13	(7.87)
Follow up interval(months)	Mean (SD)	20.83	(8.04)
Hypertension	n (%)	63	(63%)
Diabetes Mellitus	n (%)	43	(43%)
Dyslipidemia	n (%)	36	(36%)

Abbreviation: IQR: interquartile range, SD: standard deviation

Table 1. Demographic data of included patients for NLR analysis

Adipocyte function evaluation

We collected the omental visceral (omVAT) and subcutaneous adipose tissue (SAT) from 8 patients who undergone LSG. The adipocyte function was evaluated by following method:

1. Adipocyte Isolation

Visceral adipose tissue was rinsed twice with Phosphate buffered saline (PBS) to remove residual blood. Mince the tissue into about 1mm size with scissors and thumb forceps, then transfer to a 50 mL centrifuge tube, added collagenase I(1.5mg/mL) with gently shaking, digest the adipose tissue at 37°C for 30 minutes in a water bath. Shake centrifuge tube every 10 minutes to allow the enzyme to fully digest the tissue. Cells were then filtered through a polypropylene filter (100 μM mesh) and centrifuge (500 x g, 1 minute) to collect the floating adipocytes.

2. Western blot:

Protein extraction of adipocytes used cell lysis buffer (RIPA). Appropriate amount of protein mixed with loading dye, heated in a dry bath at 95°C for 5 minutes to denature the protein, and then Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDA-PAGE) was performed, and transferred onto Polyvinylidene Fluoride (PVDF) membrane. Membrane was blocked with 5% skimmed milk and incubated with primary antibodies, then subsequently incubated with HRP-conjugated secondary antibodies for 1 hour at room temperature. Bands were visualized through the ECL using Bio-RadChemiDoc XRS+ system.

Result

Variables	Standard Error(SE)	t-statistic	p value
Age	0.005036	-5.0260	0.60110
Pre-operative BMI > 50	0.165900	-1.5910	0.11740
Pre-operative Neutrophil-Lymphocyte ratio (NLR) <2.36	0.097130	2.3860	0.0205 *
Pre-operative Body weight	0.002334	-0.3504	0.0009 *
Pre-operative HOMA-IR	0.014790	01.9000	0.06270
Pre-operative HbA1c level	0.036800	-1.2930	0.20150
Pre-operative Hypertension	0.122900	01.3430	0.18490
Pre-operative Diabetes mellitus	0.099090	00.4650	0.64390
Pre-operative Dyslipidemia	0.110900	-2.9930	0.0041 *

Abbreviation: BMI: Body mass index, \*P < .05

Table 2. Multivariate regression of predicting EBWL > 37.7% in the POM3

Result 1: NLR<2.36 did predict better weight loss at POM3

A total of 100 patients were included (Table 1). Compared with the success group (POM3 EBWL > 37.7%), the failure group exhibited a significantly higher initial bodyweight, body mass index, incidence of dyslipidemia, and NLR. In the multivariate analysis, preoperative NLR < 2.36 exhibited a positive effect for predicting successful weight loss in patients. However, higher preoperative body weight (P = .0009) and preoperative dyslipidemia (P = .0045) demonstrated a negative effect in achieving EBWL > 37.7% at POM3. (Table 2)

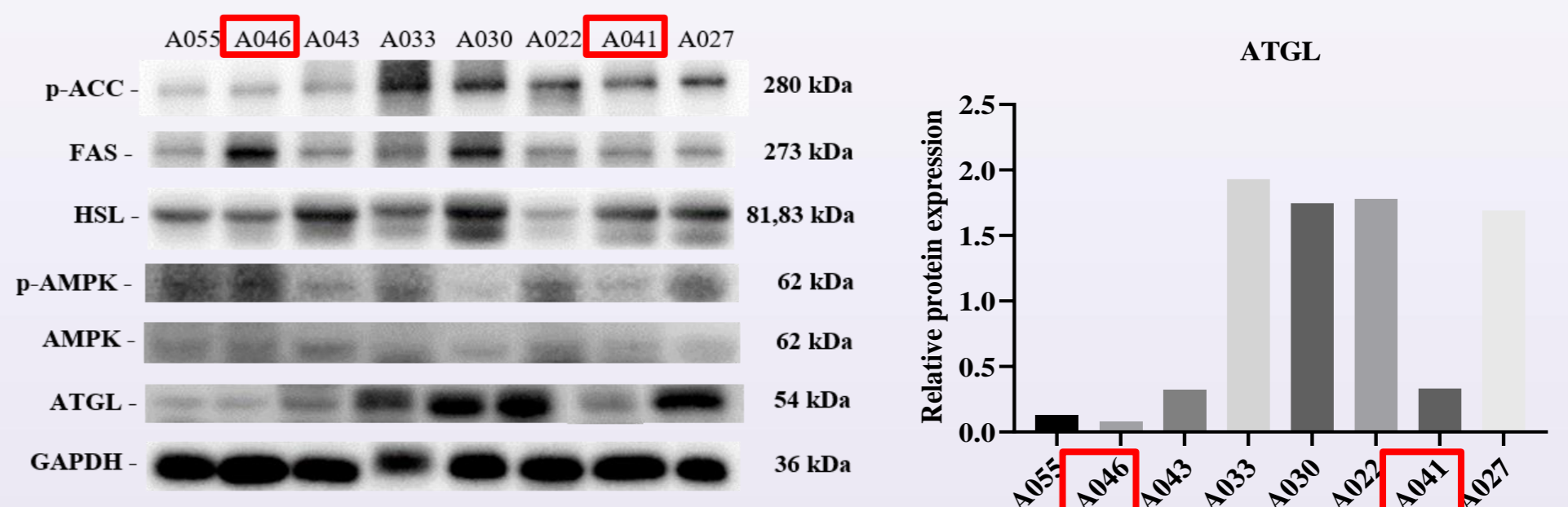
Result 2: NLR ≥ 2.36 deteriorate the lipolysis function of Adipocyte

A total of 8 patients' (mean age 35.6 years, mean BMI 46.3) omental fat and subcutaneous fat were collected for analysis. 2 of them had high NLR (NLR ≥ 2.36) and 6 of them had lower NLR. It had trend to elder age and higher initial BMI in higher NLR group without significant difference (Table 3)

		NLR ≥ 2.36 N = 2	NLR < 2.36 N = 6	p value
Pre-operative parameters				
Age (Year)	Mean(SD)	40.32(18.86)	34.06(13.10)	0.609
Body mass index(BMI)	Mean(SD)	57.38(9.97)	42.59(8.68)	0.088
Gender (Female)	N(%)	1(50%)	6(100%)	0.250
Hypertension(%)	n (%)	2(100%)	4(66.66%)	1.000
Diabetes Mellitus(%)	n (%)	0(0%)	1(16.67%)	1.000
Dyslipidemia(%)	n (%)	1(50%)	3(50%)	1.000

Table 3. Demographic data of included patients based on preoperative NLR

In adipocyte function, there is no obviously difference between low NLR (NLR<2.36) and High NLR (NLR ≥ 2.36) in lipogenic and lipolysis function of SAT. As omVAT, we identify no differences in lipogenic function. However, adipose triglyceride lipase (ATGL) in omVAT, as a key enzyme of lipolysis, is significantly lower in high NLR group (p=0.025) (Table 4).



omVAT	NLR ≥ 2.36 (Marked) Mean ± SD	NLR < 2.36 Mean ± SD	P-value
FAS	0.29 ± 0.11	0.33 ± 0.12	0.700
p-ACC	0.84 ± 0.49	1.38 ± 0.61	0.304
HSL	1.04 ± 0.23	1.73 ± 0.56	0.153
p-AMPK /AMPK	2.92 ± 2.36	1.73 ± 1.73	0.462
ATGL	0.21 ± 0.18	1.27 ± 0.81	0.025

Table 4. the difference of Lipolysis function between different NLR group

Conclusion

Preoperative NLR < 2.36 exhibited a positive effect in predicting successful EBWL at POM3. High NLR may deteriorate the lipolysis function and lead poorer weight loss effect after LSG. Further study should be done to confirm the association between poor weight loss, inflammation, and adipocyte dysfunction.