Inflammation, Adipocyte Disfunction, and suboptimal outcome:

The Role of Neutrophile-Lymphocyte Ratio (NLR)

in Patients Undergoing Laparoscopic Sleeve gastrectomy

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CONFLICT OF INTEREST DISCLOSURE

I have

no potential conflict of interest

to report

Introduction- Prediction of Suboptimal weight loss

- 20-35% patients get suboptimal response to bariatric surgery

- To identify predictors of suboptimal response and implementing subsequent supportive therapy
  - Preoperatively factors predict 1 year, even further long duration
    - High food variability, mixed with too much factors
    - Cannot apply to “Adjust” patients’ loosing weight journey

Introduction- Prediction of Suboptimal weight loss

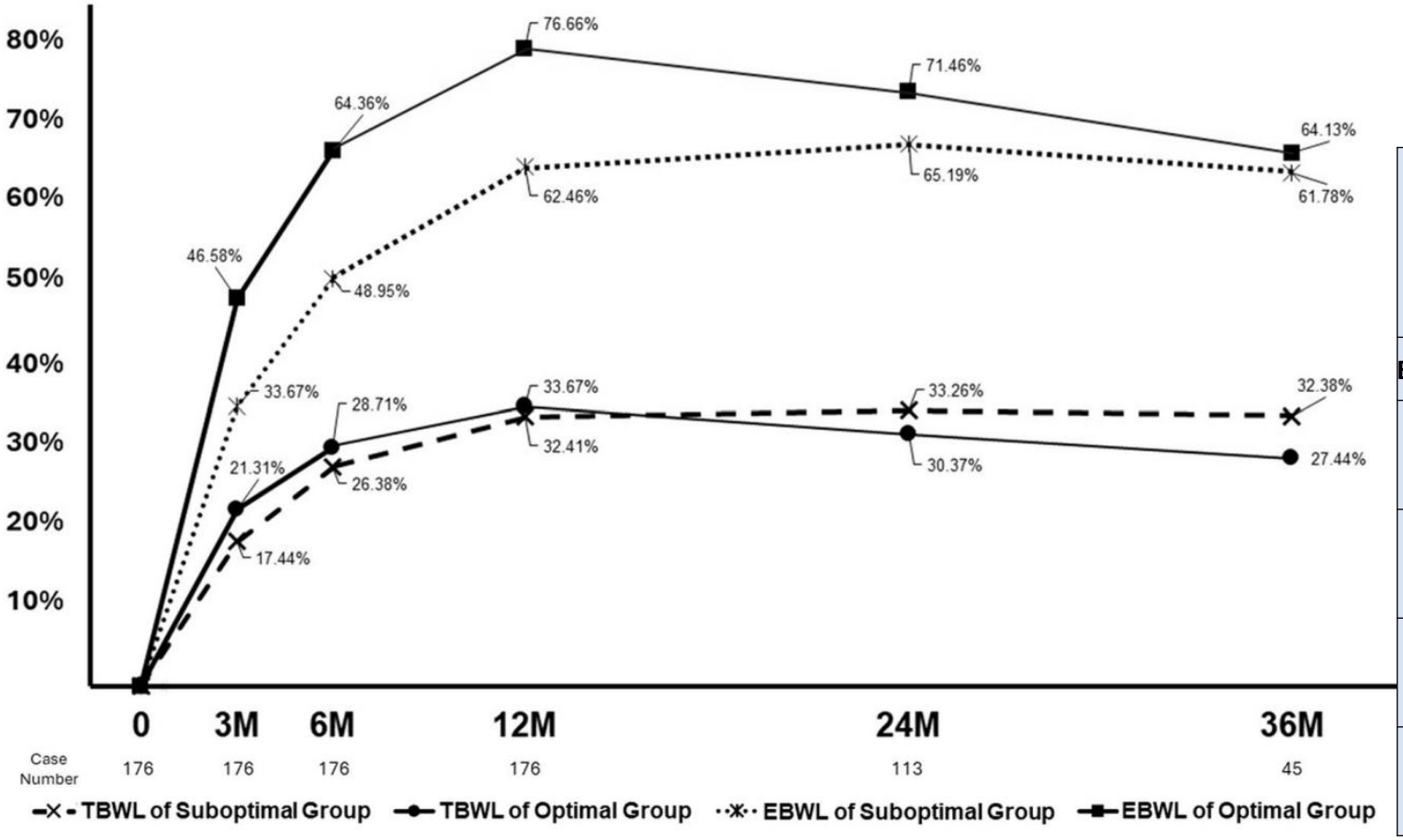
- Retrospectively analysis : **EBWL < 37.7% at POM 3** predicted suboptimal response in POM 6 (EBWL<50%)

Sci Rep 10, 12788 (2020).
Doi: 10.1038/s41598-020-69714-4

- The proportion of optimal response increase after dietary adjustment.
- Still 52% patients who did not achieve **EBWL of 37.7% at POM 3** have suboptimal response (EBWL ≥ 50%) by POM 6 even after dietary adjustments
  - **The preoperative predictor of POM 3**: Less bias : short period, less food variety

Obes Surg 2022;32(2):398–405.
Doi: 10.1007/s11695-021-05776-1

Introduction- POM3 did predict Mid-term (POY2) effect



- POM3_EBWL < 37.7% **significantly lower** EBWL at POM6, POM12, POM24

	EBWL_3M < 37.7%		EBWL_3M ≥ 37.7%		
EBWL Median(IQR)	N=45		N=131		P
EBWL_03M	33.67%	(5.07%)	46.58%	(13.05%)	<0.001*
EBWL_06M	48.95%	(7.63%)	64.36%	(15.60%)	<0.001*
EBWL_12M	62.46%	(11.31%)	76.66%	(21.49%)	<0.001*
EBWL_24M	65.19%	(19.55%)	71.46%	(14.44%)	0.007*

Obes Surg. 2024 Jul;34(7):2317-2328. doi: 10.1007/s11695-024-07315-0.

Introduction- POM3 did predict Mid-term (POY2) effect

Independent variable	Univariant analysis		Multivariant analysis		
	OR	*p*	Adjust OR	95% CI	*p*
Age	1.005	0.739			
Gender (Female)	[illegible]	0.073	[illegible]	[illegible]	0.011*
Preoperative BMI	[illegible]	[illegible]	[illegible]	[illegible]	<0.001*
Diabetes	0.733	0.371			
Hypertension	1.087	0.811			
Hyperlipidemia	**1.629**	**0.172**	2.391	(0.966–5.920)	0.060
TDQ	[illegible]	[illegible]			
CHQ	1.006	0.924			
HbA1C	[illegible]	[illegible]			
HOMA_IR	0.991	0.463			
TG	1.000	0.744			
HDL-C	1.020	0.211			
LDL-C	1.006	0.257			
NLR ≥ 2.36	**2.800**	**0.004**	**2.915**	**(1.257–6.760)**	**0.013***

Preoperative Risk factors:

Female , High Preoperative BMI

High NLR (NLR≥ 2.36)

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Aim of stdudy

Our study has aimed to explore the possible impact of preoperative Neutrophil-to-Lymphocyte Ratio (**NLR≥2.36**), which may indicated to chronic inflammation,

on **gut hormone, Microbiota and adipocyte function,**.

Method

- Proved by Eda Hospital IRB (EMRP58108N, EMRP22110N)
- Inclusion Criteria
  - Prospectively enrolled Adult patients (age≥18),
    BMI≥37 kg/m2 or a BMI≥32 kg/m2 with obesity-related comorbidities
  - **Primary LSG** April 2020/10 to 2023/11.
  - Preoperative analysis, Serum storage , Stool sample , and Adipocyte tissue collection

- **73 Included patients.**
  - 2 groups: Higher NLR (NLR≥ 2.36) and Lower group (NLR<2.36)
  - Propensity Score match by Age, BMI and Gender.
  - Finally 44 patients included for further analysis.

Result 1: No Differences Between Preoperative Gut hormone

Total Include: 44 patients

Similar Demographic data Between High NLR (NLR≥ 2.36) Group and Lower Group

Except high-selective CRP

	NLR ≥ 2.36		NLR < 2.36		
	N= 20		N= 24		p
Age, median (IQR) y	37.84	(13.95)	33.98	(19.29)	0.944
Gender					
Female	10	50.00%	17	70.83%	0.218
Male	10	50.00%	7	29.17%	
BMI median (IQR)	41.37	(8.08)	40.34	(7.68)	0.370
WC median (IQR) cm	120	(32.0)	116.35	(18.2)	0.081
HC median (IQR) cm	124.75	(16.4)	124	(19.7)	0.577
Comorbidity:					
DM	10	50.00%	8	33.33%	0.359
HTN	20	100.00%	20	83.33%	0.114
Hyperlipidemia	11	55.00%	17	70.83%	0.352
Laboratory data median (IQR)					
HbA1C %	6.25	(1.3)	5.21	(4.49)	0.242
HOMA-IR	5.98	(7.75)	5.45	(3.55)	0.248
C-peptide ng/mL	4.44	(2.37)	4.29	(1.26)	0.981
TCH mg/dL	179	(41.5)	192.5	(50.5)	0.588
TG mg/dL	152.5	(91)	150.5	(103.3)	0.850
HDL-C mg/dL	44.0	(12.8)	46.0	(14.5)	0.364
LDL-C mg/dL	121.0	(40.3)	112.5	(59.0)	0.841
hsCRP mg/L	8.94	(14.71)	3.67	(5.19)	**0.030#**

Result 1: No Differences Between Preoperative Gut hormone

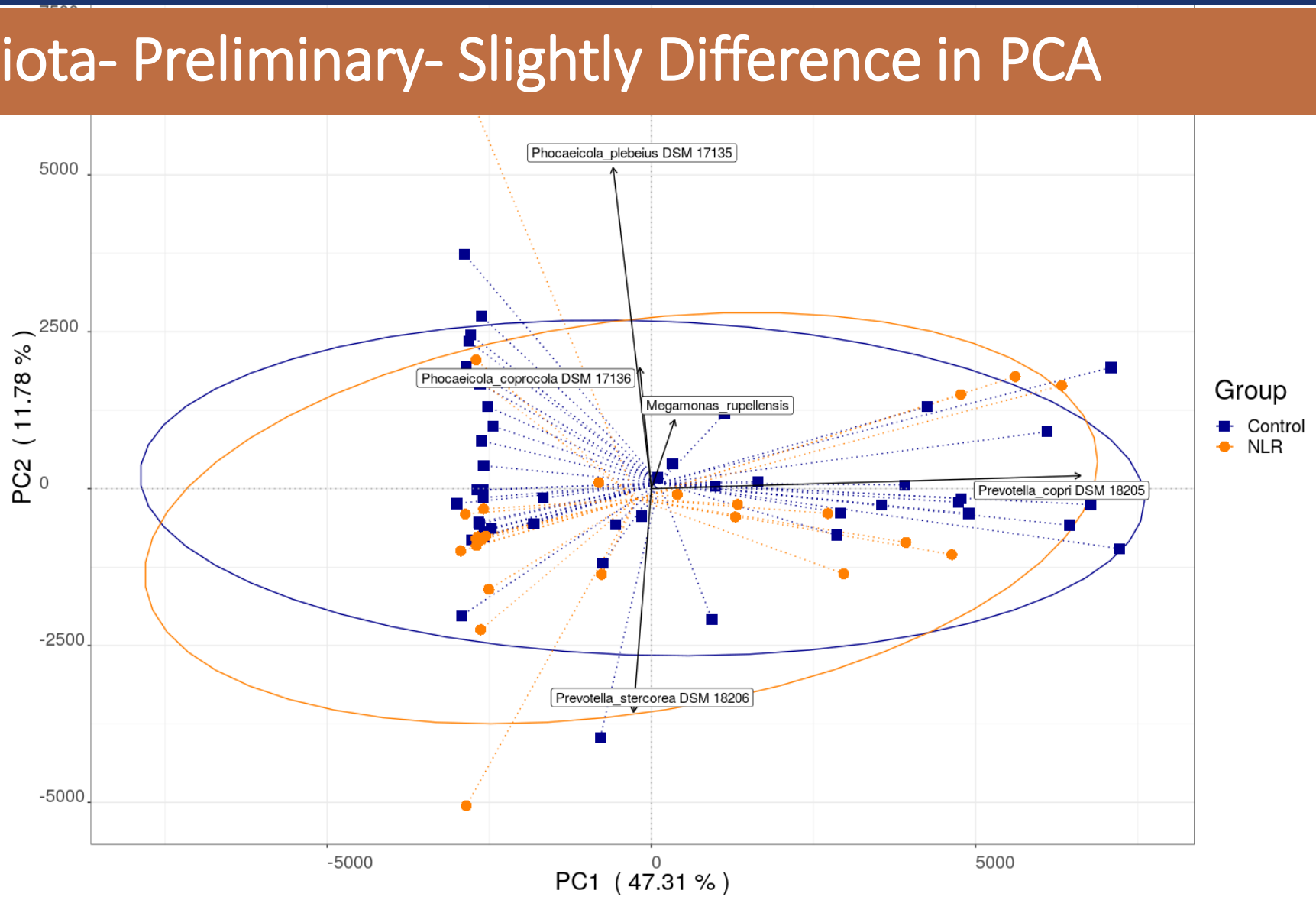
	NLR ≥ 2.36	NLR < 2.36	p
GIP Successful Detect	N= 20	N= 24	
GIP Median (IQR)	12.11 (13.29)	7.61 (11.18)	0.220
GLP-1 Successful Detect	n= 20	n= 24	
GLP-1 Median (IQR)	128.11 (94.32)	126.41 (110.16)	0.480
Ghrelin Successful Detect	n= 19	n= 24	
Ghrelin Median (IQR)	154.30 (956.30)	184.77 (2227.7)	0.392
Leptin Successful Detect	n= 3	n= 7	
Leptin Median (IQR)	44.00 (NA)	90.65 (224.80)	0.517

Result 2: Microbiota- Preliminary- Slightly Difference in PCA

Principal Component Analysis

Slightly difference

Need further evaluation



Result 3: Adipocyte function

- Randomly select 10 patients to do adipose tissue analysis.
  - Omental visceral (omVAT) and subcutaneous adipose tissue (SAT)
  - Adipocyte function were detected by immunohistochemistry and western blot.
  - Bands were visualized using Bio-RadChemiDoc XRS+ system.

Successful Adipocyte western blot : 8 patients

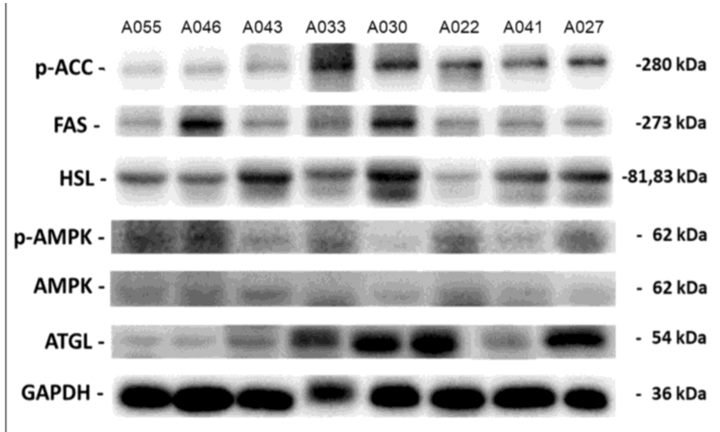
	N= 8	
Age, median (IQR) y	30.52	(27.56)
Gender		
Female	7	87.50%
Male	1	12.50%
BMI median (IQR)	45.45	(15.62)
WC median (IQR) cm	117.5	(30.6)
HC median (IQR) cm	133	(36.1)
Comorbidity:		
DM	1	12.50%
HTN	6	75.00%
Hyperlipidemia	4	50.00%
Laboratory data median (IQR)		
HbA1C %	5.75	(0.5)
HOMA-IR	4.11	(5.12)
C-peptide ng/mL	3.69	(2.08)
TCH mg/dL	187.5	(59)
TG mg/dL	154	(228)
HDL-C mg/dL	42.5	(28)
LDL-C mg/dL	102	(45)
hsCRP mg/L	3.71	(8.23)

Result 3: High NLR deteriorated OmVAT ATGL Function

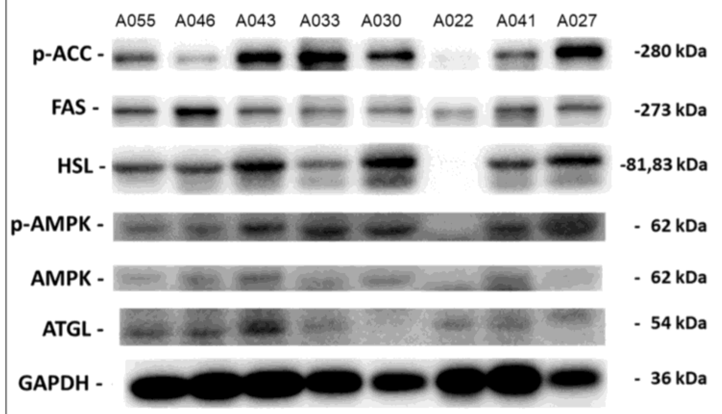
SAT	NLR ≥ 2.36 Mean ± SD	NLR < 2.36 Mean ± SD	*p*-value
FAS	0.59 ± 0.03	0.60 ± 0.33	0.968
p-ACC	[illegible]	[illegible]	0.378
HSL	1.16 ± 0.40	2.17 ± 1.41	0.203
p-AMPK/AMPK	[illegible]	[illegible] 0.69	0.150
ATGL	0.03 ± 0.02	0.09 ± 0.09	0.421

High NLR (NLR≥ 2.36)
deteriorated
Omental fat (OmVAT)
ATGL (Lypolysis) Function

omVAT	NLR ≥ 2.36 Mean ± SD	NLR < 2.36 Mean ± SD	*p*-value
FAS	0.29 ± 0.11	0.33 ± 0.12	0.700
p-ACC	[illegible]	[illegible]	[illegible]
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***



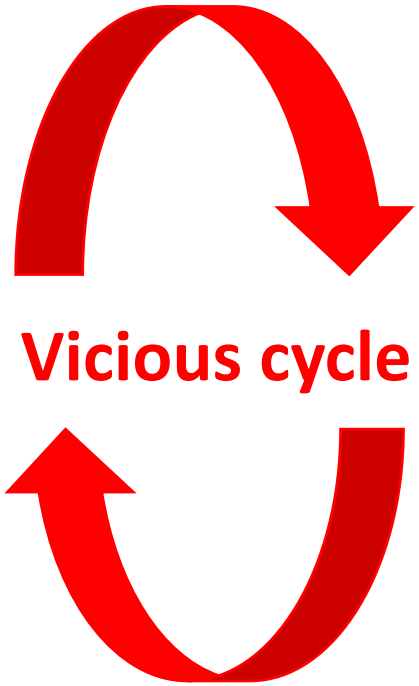
Omental Visceral fat (omVAT)



Subcutaneous fat (SAT)

Discussion

- Chronic inflammation in adipose tissue can disrupt adipocyte function.
  - impaired secretion of adipokines , increased fibrosis
  - **abnormal lipid storage and adipogenesis**



- **Expand Adipocyte** May further trigger Chronic inflammation
  - Nutrient overload ➔ adipose tissue hyperplasia, hypertrophy, or dysfunction
  - Increase chronic inflammation via adipocyte death, hypoxia, and mechanical stress,

Discussion

- Our study indicates that an elevated Neutrophil-to-Lymphocyte Ratio (NLR) predicts worse weight loss outcomes, linking higher NLR with reduced lipolysis.
  - suggests that prolonged obesity and chronic inflammation could impair lipolytic function, potentially undermining the effectiveness of bariatric surgery.

- GLP-1 was also reported to reduce lipogenic effect, increase lipolysis and reduce adiposity in human adipocytes.
  - ➔ effective adjuvant therapy after BS in this situation.

- Further study is necessary to validate the result and clarify the interaction

Conclusion

High Neutrophil-to-Lymphocyte Ratio (NLR ≥ 2.36), leads poorer effect

1. May **impair** adipocyte functionality, lower adipose triglyceride lipase (**ATGL**) in omental visceral adipose tissue (**omVAT**).
   ➔ Potential to diminish the effectiveness of LSG

2. No significant overall differences in gut hormone levels
3. Preliminary ,Difference in Microbiota

➔ necessity for more in-depth research to clarify the interaction

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