## 2018.3 第3期

## 臺大醫院「減重暨代謝手術中心」電子報

## Center for Obesity, Life Style and Metabolic Surgery Newsletter

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美編製作:李佩容

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2018年3月7日-曾屏輝 醫師 Clinical implication and pathophysiology of metabolic factors in digestive disorders

## 減重暨代謝手術中心演講公告

# Exercise for obesity or overweight



主講者: 簡盟月物理治療師

臺灣大學物理治療學系專任副教授

臺大醫院復健科兼任物理治療師

時間: 107年5月2日(三) 10: 20-11: 20

地點: 慶學院202壽堂

減重暨代謝手術中心 敬邀

# 2018年1月10日演講照片台大醫學院202講堂



# 主講者:李佩玲醫師

台大醫院 睡眠中心 主任 台大醫院 減重暨代謝手術中心 副執行長 台大醫院 內科部 主治醫師



## 演講大鋼

睡眠一般分為淺睡期及深睡期。淺睡期包括了快速動眼期或作夢期;深睡期包括了非快速動眼期或非作夢期。整個夜晚的睡眠都由這兩種形式交替出現,整晚差不多有四到五個循環。快速動眼睡眠和腦力恢復有關,而非快速動眼睡眠則和體力恢復有關,所以一個晚上必須有這兩種形式睡眠,缺一不可。

睡眠呼吸中止是指睡覺中會反覆發生停止呼吸,並且造成缺氧與睡眠中斷的狀態,其中八成的患者是屬於「阻塞型」,是睡眠呼吸中止最常見的型態,源自上呼吸道於睡眠時發生塌陷,氣流阻滯而造成呼吸中斷,患病率為男性4.1%,女性2.1%。

肥胖是阻塞性睡眠呼吸中止症最重要的危險因子。肥胖造成的脂肪組織容易堆積於上呼吸道,一方面壓迫上呼吸道管徑,另一方面上呼吸道軟組織變得比較鬆軟,容易塌陷;此外,肥胖也會鈍化上呼吸道神經與肌肉的代償反應,使得在發生呼吸中止時,擴張上呼吸道的肌肉群無法有效地作用,延長呼吸中止的時間,造成缺氧情況更為嚴重。再者,因為肥胖的關係,胸壁軟組織增加,使得肺部擴張受限,因牽引作用的影響,連帶造成上呼吸道也容易塌陷。

睡眠呼吸中止的症狀以習慣性打鼾最為常見,其他症狀包含: 高血壓、白天過度嗜睡、夜尿等。若沒接受治療,容易引發心血 管疾病、代謝性疾病、神經等系統造成很大的潛在傷害。

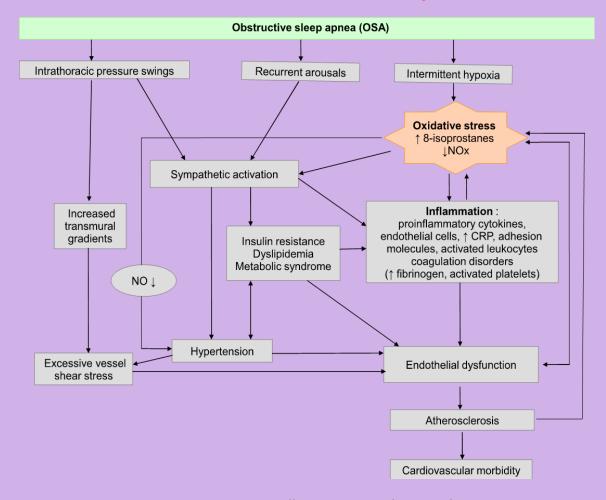
臨床上用來篩檢是否罹患睡眠呼吸中止的高危險群可使用問卷評估、身體檢查、睡眠檢查,調查相關的危險因子與臨床症狀後,做危險性的估計。常用的問卷有睡眠日誌、嗜睡量表、匹茲堡量表、STOP-Bang問卷,以及柏林問卷。睡眠檢查有整夜睡眠多項生理檢查(PSG)、陽壓呼吸器調整(CPAP titration)、日間多次入睡檢查(MSLT)、經皮二氧化碳(PtcCO2)、二十四小時血氧記錄,以及二十四小時腕動計(Actigraph)。

目前,標準診斷睡眠呼吸中止需要接受整夜睡眠多項生理檢查。嚴重度依呼吸中止或減弱指數(AHI,指睡眠中每小時呼吸發生中止或減弱的次數)而定,小於5次為正常、5-15次為輕度、15-30次為中度、大於30次為重度。

治療的方式有連續陽壓呼吸輔助器,是中度到重度和輕度到中度但有症狀的阻塞性睡眠呼吸中止的治療方法,一天約使用5.5-6小時才有效果;若有心血管疾病的患者則無效。另一種治療方式為口內矯正器,是藉由不同形式的矯正器將下顎舌頭及軟顎向前拉,打開呼吸道,以擴大呼吸道來減少呼吸阻塞。另外減重也可以降低睡眠呼吸中止的次數。不是所有人皆適合使用CPAP,有些需藉外科手術治療。懸壅顎咽整形術,移除喉部在睡眠時阻塞氣道的多餘組織。其他手術方法包括下顎骨前置術及上下顎骨前置術。

睡眠呼吸中止是種異質複雜的疾病,可能導致慢性間歇性缺氧和睡眠破碎,AHI是睡眠呼吸中止嚴重程度的替代指標,與疾病嚴重程度無關,治療上很重要,根據症狀、病人特異性去作單獨調整。

#### **Mechanism of OSA Consequence**



Jullian-Desayes I Sleep Medicine Reviews 2014

#### STOP-Bang 問卷

#### 以下問題回答為「是」或「否」:

第1題:打鼾:是否您打鼾很大聲(比說話還大聲,或者大聲到關著房門

都聽得見)?

第2題:疲倦:白天時,是否您時常感到疲倦或者容易打瞌睡?

第3題:觀察:有任何人曾觀察到您睡眠中會呼吸暫停嗎?

第4題:血壓:您是否有高血壓,或者正在服用高血壓藥物控制血壓?

第5題:身體質量指數BMI:BMI大於35kg/m<sup>2</sup>?

第6題:年齡:年紀大於50歲? 第7題:頸圍:頸圍大於40公分?

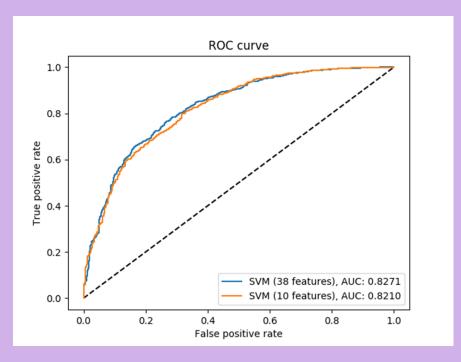
第8題:性別:男性。

#### 計分標準:

如果「三題以上」回答為「是」者,為阻塞性睡眠呼吸中止的危險群。

Anesthesiology 2008; 108:812-821

#### Prediction of OSA (AHI≥10) :38-Feats vs 10-Feats



Model	AUC	ACC	TPR	TNR	PPV	LR+	LR-
38-Feat	0.827	0.780	0.835	0.649	0.850	2.379	0.254
10-Feat	0.821	0.774	0.844	0.609	0.835	2.159	0.256

## Phenotyping with Multiple Trait: Sleep Disturbance, Sleepiness, Co-morbidities

822 moderate-to-severe OSA (AHI≥15/hr) clustered with Latent class analysis (LCA)

TABLE 1	Demographic and	clinical	characteristics (	of the	total	cohort	and by clu	sters

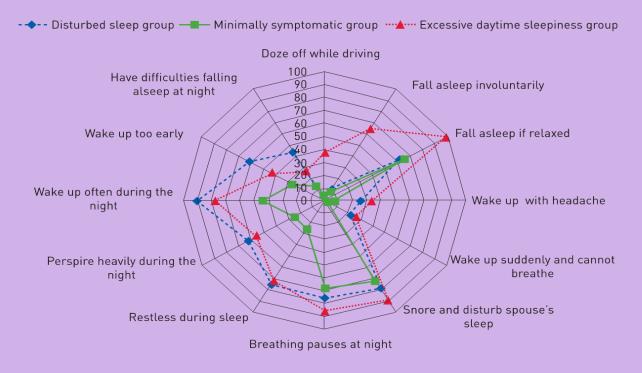
	Total cohort	Cluster 1	Cluster 2	Cluster 3	p-value
Subjects n	822	269	203	350	
% of total	100	32.7	24.7	42.6	
Males n (%)	666 (81.0)	211 (78.4)	170 (83.7)	285 (81.4)	0.336
Age years	$54.5 \pm 10.6$	$54.1 \pm 11.0$	$56.6 \pm 10.3$	$53.6 \pm 10.3$	0.005
BMI kg·m <sup>-2</sup>	33.5 ± 5.7	33.3 + 5.6	33.0 ± 5.6	34.0 + 5.8	0.130
AHI events·hour-1	$44.9 \pm 20.7$	43.8 ± 20.4	43.1 + 18.9	46.7 + 21.7	0.181
ODI events·hour <sup>-1</sup>	$35.5 \pm 20.2$	$34.0 \pm 18.4$	33.5 ± 18.9	37.8 ± 21.9	0.117
Minimum oxygen saturation %	76.2±8.0	$76.5 \pm 7.8$	$76.7 \pm 7.7$	$75.7 \pm 8.4$	0.385
SF-12 physical component score	40.3 ± 10.9	39.7 ± 10.5	45.4 ± 9.9	$37.7 \pm 10.7$	< 0.001
SF-12 mental component score	48.3 <u>+</u> 10.9	46.9 ± 11.2	52.9 <u>+</u> 9.6	46.6 ± 10.7	< 0.001

Cluster 1 Disturbed sleep group

Cluster 2 Minimally symptomatic group

Cluster 3 Excessive daytime sleepiness group

#### **Conditional Probability of 12 Symptoms within Cluster**



## Phenotyping with Multiple Trait: Symptoms, Co-morbidities, and Anthropometrics

 18,263 moderate-to-severe OSA (AHI≥15/hr) clustered with multiple correspondence analysis (MCA)

Table 1. Patients characteristics of the entire cohort and by clusters: Anthropometric and demographic characteristics.

	All clusters N = 18,263	Cluster 1 N = 1,823	Cluster 2 N = 4,200	Cluster 3 N = 3,363	Cluster 4 N = 2,715	Cluster 5 N = 3,511	Cluster 6 N = 2,642
Age (years)	59 [50; 67]	48 [41;55]	63 [56;71]	66 [60;74]	49 [40;57]	56 [48;63]	60 [54;66]
Gender (male)	13,465 (73.8)	1,427 (78.3)	3,138 (74.7)	2,349 (69.8)	2,209 (81.4)	2,432 (69.3)	1,910 (72.3)
BMI (kg/m²)	31 [27;36]	29 [26;35]	31 [27;35]	33 [29;38]	28 [25;33]	31 [27;36]	33 [29;37]
Waist circumference (cm)	109 [100;120]	104 [96;116]	108 [100;119]	115 [106;124]	100 [92;111]	108 [99;118]	113 [104;122]
Sedentary	3071 (16.8)	233 (12.8)	272 (6.5)	1021 (30.4)	90 (3.3)	538 (15.3)	917 (34.7)
Current smoker	2838 (15.5)	562 (30.8)	357 (8.5)	207 (6.2)	721 (26.5)	632 (18)	360 (13.6)
Former smoker	5366 (29.4)	338 (18.5)	1156 (27.5)	1570 (46.7)	324 (11.9)	912 (26)	1068 (40.4)
Systolic Blood pressure (mmHg)	130 [125;140]	130 [120;140]	130 [130;140]	140 [130;147]	130 [120;140]	130 [124;140]	140 [130;150]
Diastolic Blood pressure (mmHg)	80 [70;86]	80 [70;86]	80 [70;84]	80 [70;85]	80 [70;80]	80 [70;88]	80 [70;90]

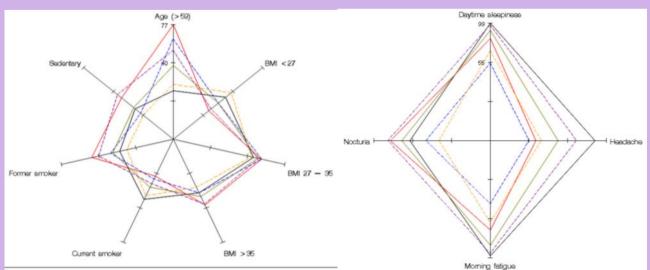
Table 2. Patients characteristics of the entire cohort and by clusters: Co-morbidities. Values in Numbers (%).

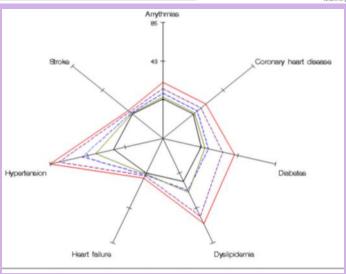
	All clusters N = 18,263	Cluster 1 N = 1,823	Cluster 2 N = 4,200	Cluster 3 N = 3,363	Cluster 4 N = 2,715	Cluster 5 N = 3,511	Cluster 6 N = 2,642
Cardiovascular and metabolic co-morbidities							
Coronary heart disease	1402 (7.7)	19 (1)	295 (7)	642 (19.1)	17 (0.6)	101 (2.9)	328 (12.4)
Arrhythmias	1562 (8.6)	28 (1.5)	343 (8.2)	689 (20.5)	22 (0.8)	139 (4)	341 (12.9)
Stroke	594 (3.3)	13 (0.7)	141 (3.4)	244 (7.3)	10 (0.4)	63 (1.8)	124 (4.7)
Heart failure	538 (2.9)	11 (0.6)	116 (2.8)	250 (7.4)	10 (0.4)	54 (1.5)	99 (3.7)
Hypertension	8462 (46.4)	254 (13.9)	2050 (48.8)	2857 (84.9)	115 (4.2)	1203 (34.3)	1988 (75.1)
Diabetes	2683 (14.7)	44 (2.4)	408 (9.7)	1306 (38.8)	7 (0.3)	221 (6.3)	697 (26.4)
Dyslipidemia	5552 (30.4)	195 (10.7)	922 (22)	2090 (62.1)	104 (3.8)	834 (23.8)	1407 (53.3)
Other co-morbidities							
Respiratory co-morbidities *	1171 (6.4)	56 (3.1)	229 (5.5)	388 (11.5)	56 (2.1)	178 (5.1)	264 (10)
Depression	2573 (14.1)	229 (12.6)	325 (7.7)	604 (18)	142 (5.2)	578 (16.5)	698 (26.4)

#### Table 3. Patients characteristics of the entire cohort and by clusters: Sleep characteristics. OSAS symptoms and functional scales.

	All cluster N = 18,263	Cluster 1 N = 1,823	Cluster 2 N = 4,200	Cluster 3 N = 3,363	Cluster 4 N = 2,715	Cluster 5 N = 3,511	Cluster 6 N = 2,642
Sleep characteristics	11 - 10,200	11 - 1,020	11 - 1,200	., - 0,000	.,	11 – 0,011	11 – 2,0 12
Self-reported sleep duration (hours)	7 [6; 8]	7 [6;8]	7.5 [6.5;8]	7.5 [6;8]	7 [6;8]	7 [6;8]	7 [6;8]
Short sleeper (<6h)	1465 (8)	168 (13.2)	206 (11)	284 (12.1)	175 (11.8)	342 (13.6)	290 (14.1)
Intermediate sleeper (6h-9h)	8558 (46.9)	970 (76.1)	1429 (76.3)	1662 (71.1)	1190 (80.5)	1860 (73.8)	1447 (70.4)
Very long sleeper (>9h)	1516 (8.3)	136 (10.7)	239 (12.8)	393 (16.8)	113 (7.6)	317 (12.6)	318 (15.5)
AHI (/h)	35 [26; 51]	31.6 [22;47]	34 [26;47.4]	40 [30;55]	31 [22;42]	34 [25;50]	39 [29;58]
ODI (/h)	27 [16; 45]	23 [13;40.9]	26 [15.9;41]	33 [21;50]	21 [11.8;35]	25 [14.2;42]	31 [18;51]
Time spent with nocturnal SaO2 below 90% (%)	34 [9; 104]	20 [5;72]	32 [9;91]	59 [18;148]	15 [4;50]	29 [8;89]	49 [15;130]
OSAS symptoms							
Snoring	16955 (92.4)	1818 (99.7)	3314 (78.8)	3226 (95.9)	2484 (91.5)	3434 (97.8)	2614 (98.8)
Self-declared daytime sleepiness	14451 (79.2)	1812 (99.4)	2261 (53.8)	2755 (81.9)	1856 (68.3)	3197 (91.1)	2577 (97.4)
Morning fatigue	12740 (69.8)	1770 (97.1)	1618 (38.5)	2293 (68.2)	1612 (59.4)	2975 (84.7)	2480 (93.7)
Nocturia	10647 (58.3)	1060 (58.1)	1670 (39.7)	2695 (80.1)	672 (24.7)	2361 (67.2)	2194 (82.9)
Headaches	6578 (36)	1567 (86)	446 (10.6)	632 (18.8)	667 (24.6)	1544 (44)	1726 (65.2)
Near miss accident	1389 (7.6)	348 (19.1)	77 (1.8)	133 (4)	158 (5.8)	305 (8.7)	368 (13.9)
Functional scales							
Pichot Scale	13 [6; 20]	16 [9;22]	7.5 [3;14]	12 [6;19]	10 [4;17]	14 [8;20]	16 [10;22]
Depression scale	3 [1; 7]	4 [1;7]	2 [0;5]	3 [1;7]	2 [0;5]	4 [1;7]	5 [2;8]
Epworth scale	10 [6; 14]	12 [8;15]	8 [5;12]	9 [6;13]	10 [6;14]	11 [7;14]	11 [7;14]

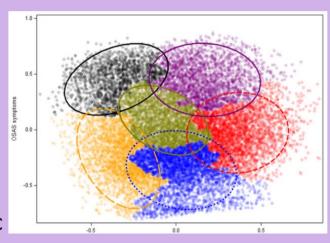
## Conditional Probability of Age, Risk Factors, Symptoms, Comorbidities





#### Cluster

- 1: Young symptomatic
- 2: Old obese
- 3: Multi-disease old obese
- 4: Young snorers
- 5: Drowsy obese
- 6: Multi-disease obese symptomatic



## Phenotyping with Complex Trait: Sleep Disturbance, Sleepiness, Co-morbidities PAP Adherence

**Table 1:** Demographic and clinical characteristics of the ISAC symptom clusters

	Baseline Characteristics								
Variable	Overall	Disturbed Sleep	Minimally Symptomatic	Sleepy	p*				
N (%)	706 (100)	229 (32.4)	170 (24.1)	307 (43.5)	4				
Male, %	80.6%	77.7%	84.1%	80.8%	0.278				
Age, years	54.7 ± 10.3	54.4 ± 10.8	56.8 ± 10.0	53.8 ± 10.0	0.008				
BMI, kg/m <sup>2</sup>	33.6 ± 5.7	33.7 ± 5.6	$33.0 \pm 5.4$	34.0 ± 5.9	0.194				
AHI, events/hour	45.9 ± 19.9	44.8 ± 18.8	43.6 ± 18.0	47.9 ± 21.5	0.135				
ODI, events/hour	36.3 ± 19.8	34.4 ± 17.4	34.5 ± 18.6	38.7 ± 21.9	0.132				
SaO <sub>2</sub> Nadir	76.1 ± 8.1	76.4 ± 7.9	76.5 ± 7.6	75.5 ± 8.5	0.447				
% Time SaO <sub>2</sub> <90	14.1 ± 18.2	13.3 ± 18.7	12.4 ± 16.2	15.7 ± 18.8	0.166				
SF-12 Physical <sup>†</sup>	40.1 ± 11.0	39.7 ± 10.7	45.2 ± 10.0	37.6 ± 10.7	<0.0001				
SF-12 Mental <sup>†</sup>	48.3 ± 10.7	47.2 ± 11.1	52.7 ± 9.8	46.8 ± 10.2	<0.0001				

Table 3: Comparisons of PAP adherence and usage among symptom clusters

		Sympton	n Clusters	
Variable	Disturbed Sleep	Minimally Symptomatic	Sleepy	р
N (%)	229 (32.4)	170 (24.1)	307 (43.5)	-
Any PAP Usage, n (%)	140 (61.1)	102 (60.0)	215 (70.0)	0.034 <sup>†</sup>
PAP Usage Group, n (%)				0.085
Full User	112 (48.9)	84 (49.1)	165 (53.8)	
Partial User	28 (12.2)	18 (10.6)	50 (16.3)	
Non-user	89 (38.9)	68 (40.0)	92 (30.0)	
Hours PAP Usage <sup>‡</sup>				
Mean ± SD	6.5 ± 2.3	6.2 ± 1.7	6.4 ± 1.9	0.596
Median (Range)	6.9 (0.1, 10.4)	6.5 (0.3, 9.7)	6.9 (0.6, 10.4)	0.160
Nights PAP Used <sup>‡</sup>				
Mean ± SD	24.2 ± 6.6	23.8 ± 6.2	24.5 ± 5.9	0.720
Median (Range)	28 (1, 28)	26 (1, 28)	27 (2, 28)	0.183

### **Changes in Symptoms within and between Cluster**

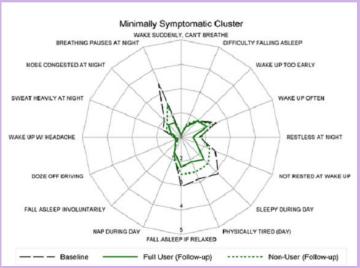
			Estimate (95% CI)®		Overall	Pairw	ise Differences Estimates**	
	Symptom Measures	Disturbed Sleep (DS)	Minimally Symptomatic (MS)	Sleepy (S)	p <sup>®</sup>	DS vs. MS	DS vs. S	MS vs. S
	Epworth Sleepiness Scale	-2.06 (-2.64, -1.48) <sup>§</sup>	-1.33 (-2.00, -0.66) <sup>§</sup>	-5.31 (-5.81, -4.81) <sup>§</sup>	<0.0001	-0.19 (-0.42, 0.04)	0.84 (0.65, 1.04)	1.03 (0.82, 1.25) <sup>¶</sup>
•	I feel sleepy during the day	-0.94 (-1.13, -0.75) <sup>§</sup>	-0.68 (-0.91, -0.46) <sup>§</sup>	-1.41 (-1.57, -1.24) <sup>§</sup>	<0.0001	-0.22 (-0.47, 0.03)	0.40 (0.18, 0.62) <sup>¶</sup>	0.62 (0.38, 0.86) <sup>¶</sup>
Fatigue	I fall asleep involuntarily during the day	-0.04 (-0.21, 0.13)	-0.04 (-0.24, 0.16)	-1.31 (-1.45, -1.16) <sup>§</sup>	<0.0001	0.00 (-0.24, 0.25)	1.18 (0.97, 1.39) <sup>¶</sup>	1.18 (0.94, 1.41) <sup>¶</sup>
ø	I fall asleep if I relax (TV)	-0.56 (-0.73, -0.39) <sup>§</sup>	-0.58 (-0.78, -0.39) <sup>§</sup>	-1.21 (-1.36, -1.07) <sup>§</sup>	<0.0001	0.02 (-0.19, 0.23)	0.53 (0.35, 0.71) <sup>1</sup>	0.51 (0.31, 0.70) <sup>¶</sup>
ess	I take a nap during the day	-0.48 (-0.65, -0.30) <sup>§</sup>	-0.01 (-0.22, 0.19)	-0.58 (-0.73, -0.43) <sup>§</sup>	<0.0001	-0.36 (-0.56, -0.15) <sup>¶</sup>	0.08 (-0.10, 0.26)	0.44 (0.24, 0.63) <sup>¶</sup>
Sleepir	I doze off at the steering wheel when driving	-0.11 (-0.23, 0.02)	-0.09 (-0.24, 0.05)	-0.82 (-0.92, -0.71) <sup>§</sup>	<0.0001	-0.02 (-0.26, 0.23)	0.92 (0.71, 1.13) <sup>¶</sup>	0.94 (0.71, 1.17) <sup>¶</sup>
•	I feel physically tired during the day	-1.07 (-1.25, -0.88) <sup>§</sup>	-0.53 (-0.74, -0.32) <sup>§</sup>	-1.54 (-1.70, -1.39) <sup>§</sup>	<0.0001	-0.48 (-0.73, -0.23) <sup>¶</sup>	0.43 (0.21, 0.64) <sup>¶</sup>	0.91 (0.67, 1.15) <sup>¶</sup>
ted	I have difficulties falling asleep at night	-0.28 (-0.44, -0.13) <sup>5</sup>	-0.03 (-0.21, 0.15)	-0.01 (-0.14, 0.13)	0.021	C/3	O3	C3
ia-Related	## € ☐ ☐ ☐ ## ## ## ## ## ## ## ## ## ## ##	-0.54 (-0.73, -0.35) <sup>§</sup>	0.09 (-0.13, 0.31)	-0.04 (-0.2, 0.13)	<0.0001	-0.46 (-0.68, -0.25) <sup>¶</sup>	-0.37 (-0.55, -0.19) <sup>¶</sup>	0.09 (-0.11, 0.29)
Ē	I wake up often during the night	-0.90 (-1.1, -0.69) <sup>9</sup>	-0.26 (-0.50, -0.03)	-0.92 (-1.1, -0.74) <sup>9</sup>	<0.0001	-0.46 (-0.68, -0.23) <sup>11</sup>	0.02 (-0.18, 0.21)	0.47 (0.26, 0.69)
nso		-1.25 (-1.46, -1.05) <sup>§</sup>	-0.13 (-0.37, 0.11)	-1.10 (-1.27, -0.92) <sup>§</sup>	<0.0001	-0.81 (-1.04, -0.59) <sup>¶</sup>	-0.11 (-0.31, 0.08)	0.70 (0.49, 0.91) <sup>1</sup>
_	I feel rested when I wake up	1.27 (1.07, 1.47) <sup>§</sup>	0.52 (0.29, 0.74)	1.69 (1.52, 1.86) <sup>§</sup>	<0.0001	0.60 (0.36, 0.83) <sup>¶</sup>	-0.34 (-0.54, -0.13) <sup>¶</sup>	-0.93 (-1.16, -0.71) <sup>1</sup>
	I wake up suddenly and feel as if	-0.51 (-0.65, -0.37) <sup>§</sup>	-0.04 (-0.20, 0.12)	-0.53 (-0.65, -0.41) <sup>§</sup>	<0.0001	-0.55 (-0.80, -0.30) <sup>¶</sup>	0.03 (-0.19, 0.25)	0.58 (0.35, 0.82) <sup>¶</sup>
Apneic	I have been told that I stop breathing at night	-1.29 (-1.55, -1.04) <sup>§</sup>	-1.32 (-1.62, -1.03) <sup>5</sup>	-1.77 (-1.99, -1.55) <sup>§</sup>	0.009	0.02 (-0.25, 0.29)	0.32 (0.09, 0.56) <sup>¶</sup>	0.30 (0.05, 0.56)
Ap	Any loud snoring	0.02 (0.01, 0.07)	0.06 (0.02, 0.17)	N/A	N/A	0.35 (0.11, 1.09)	N/A	N/A
	I snore loudly and it disturbs my  •□□●Ⅲ●•●Ⅲ□	0.10 (0.05, 0.19)	0.14 (0.07, 0.28)§	0.02 (0.01, 0.05) <sup>§</sup>	<0.0001	0.70 (0.30, 1.66)	5.01 (2.11, 11.9) <sup>¶</sup>	7.14 (2.86, 17.8) <sup>¶</sup>
	My nose is congested at night	-0.28 (-0.48, -0.08) <sup>5</sup>	-0.25 (-0.48, -0.02)	-0.54 (-0.71, -0.37) <sup>§</sup>	0.065	O3	C/3	C)3
	I wake up with a headache	-0.30 (-0.42, -0.17) <sup>5</sup>	-0.08 (-0.23, 0.07)	-0.50 (-0.61, -0.39) <sup>§</sup>	<0.0001	-0.23 (-0.44, -0.03)	0.21 (0.04, 0.39)	0.44 (0.25, 0.64) <sup>¶</sup>
Other	I perspire heavily during the night	-0.90 (-1.08, -0.72) <sup>§</sup>	-0.26 (-0.47, -0.05)	-0.65 (-0.81, -0.5) <sup>§</sup>	<0.0001	-0.49 (-0.70, -0.28) <sup>¶</sup>	-0.19 (-0.37, -0.01)	0.30 (0.10, 0.50)
Ŭ	Presence of RLS	0.43 (0.26, 0.72) <sup>9</sup>	0.57 (0.25, 1.26)	0.33 (0.21, 0.52) <sup>9</sup>	0.445	OB	OB	CB
	1.1 11 1.1 1.1 11 11							

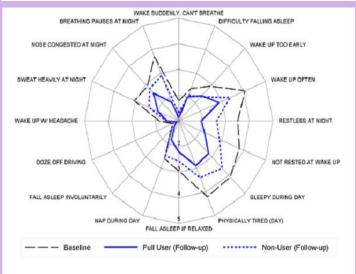
### Changes in Co-morbidities, BMI, BP, and QoL Among Clusters

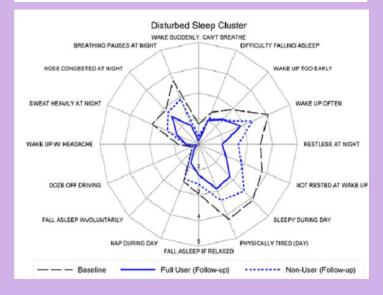
Table 5: Adjusted models for changes in comorbidities, BMI, blood pressure and quality of life within and between symptom clusters

		Estimate (95% CI) <sup>©</sup>		Overall	Pairw	Pairwise Differences Estimates**		
Measure	Disturbed Sleep (DS)	Minimally Symptomatic (MS)	Sleepy (S)	p <sup>®</sup>	DS vs. MS	DS vs. S	MS vs. S	
Hypertension	0.67 (0.32, 1.41)	2.25 (0.93, 5.40)	0.97 (0.52, 1.82)	0.116	C/3	OS	O3	
Cardiovascular Disease	0.65 (0.18, 2.39)	5.40 (1.34, 21.8)	1.16 (0.37, 3.64)	0.083	C3	Œ	O3	
Obstructive Lung Disease	1.38 (0.58, 3.28)	1.12 (0.37, 3.41)	1.11 (0.52, 2.35)	0.925	C3	OS	O3	
Diabetes Mellitus	2.07 (0.51, 8.40)	4.15 (0.69, 25.1)	N/A	N/A	0.50 (0.05, 4.66)	N/A	N/A	
Body Mass Index	0.66 (0.37, 0.96) <sup>§</sup>	0.66 (0.32, 1.01) <sup>§</sup>	0.35 (0.09, 0.60) <sup>§</sup>	0.188	C/3	OS	O3	
Diastolic Blood Pressure	-0.11 (-1.37, 1.16)	-2.58 (-4.06, -1.10) <sup>§</sup>	-2.81 (-3.9, -1.71) <sup>§</sup>	0.004	0.26 (0.06, 0.46)	0.28 (0.11, 0.46) <sup>¶</sup>	0.02 (-0.17, 0.22)	
Systolic Blood Pressure	2.01 (0.20, 3.81)	-0.41 (-2.53, 1.70)	1.31 (-0.25, 2.88)	0.223	C3	O	O3	
SF-12 Physical Component	0.96 (-0.27, 2.20)	1.23 (-0.21, 2.67)	4.82 (3.77, 5.88) <sup>§</sup>	<0.0001	-0.03 (-0.22, 0.16)	-0.38 (-0.55, -0.22) <sup>¶</sup>	-0.36 (-0.53, -0.18) <sup>¶</sup>	
SF-12 Mental Component	3.26 (1.77, 4.75) <sup>§</sup>	0.61 (-1.12, 2.35)	2.80 (1.53, 4.07) <sup>§</sup>	0.057	C3	OB	O3	

### **Symptom Profile at Baseline and PAP**







Baseline ----Adherent ——
Non-adherent

#### 李佩玲醫師和曾屏輝醫師一起研究發表的論文

RESEARCH ARTICLE

A Higher Proportion of Metabolic Syndrome in Chinese Subjects with Sleep-Disordered Breathing: A Case-Control Study Based on Electrocardiogram-Derived Sleep Analysis

Ping-Huei Tseng<sup>1</sup>, Pei-Lin Lee<sup>1,2</sup>, Wei-Chung Hsu<sup>1,2,3</sup>, Yan Ma<sup>4</sup>, Yi-Chia Lee<sup>1</sup>, Han-Mo Chiu<sup>1</sup>, Yi-Lwun Ho<sup>1</sup>, Ming-Fong Chen<sup>1</sup>, Ming-Shiang Wu<sup>1\*</sup>, Chung-Kang Peng<sup>4</sup>

Table 3. Logistic regression analysis for sleep-disordered breathing based on metabolic parameters.

		Univariate analyses	,	Multivariate analyses			
Variables	Crude OR	95% CI	P-value*	Adjusted OR	95% CI	<i>P</i> -value*	
BMI	1.27	1.10-1.46	.001				
Waist circumference	1.10	1.04–1.16	< .001	1.10	1.04–1.16	.001	
Systolic blood pressure	1.03	1.00-1.05	.03				
Fasting blood glucose	1.03	1.01-1.05	.01				

Table 4. Comparison of metabolic syndrome and its various components between subjects with sleep-disordered breathing and the control group.

Metabolic syndrome component	SDB (n = 40)	Control (n = 80)	OR (CI)	<i>P</i> -value*
Waist circumference (central obesity)	29 (72.5)	34 (42.5)	3.6 (1.6-8.1)	.002
High blood pressure	19 (47.5)	29 (36.3)	0.6 (0.7–3.4)	.23
Low HDL	14 (35.0)	21 (26.3)	1.5 (0.7–3.4)	.32
Hyperglycemia	18 (45.0)	21 (26.3)	2.3 (1.0-5.1)	.04
Hypertriglyceridemia	17 (42.5)	29 (36.3)	1.3 (0.6–2.8)	.50
Number of MS components	2.4 ± 1.6	1.7 ± 1.4		.01
Metabolic syndrome	18 (45.0)	18 (22.5)	2.8 (1.2-6.3)	.01

Tseng PH PLoS ONE 2016

# 2018年3月7日演講照片台大醫學院202講堂



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## 演講大鋼

多年來在健檢中心和腸胃科門診發現,做大腸鏡時常看到息肉,那麼多健康的人來做也是有息肉,然而做超音波時也發現,脂肪肝的比例很高,讓我相當驚訝,所以,每次做完超音波時都會跟病人衛教飲食運動體重要多注意,後來發現很多銀行的員工來做健檢,體型不胖但都有脂肪肝合併脂肪胰。

代謝方面,診斷最確定的就是「糖尿病」,過去腸胃方面的研究,糖尿病和胃食道逆流、消化性潰瘍、胃輕癱(gastroparesis)、胃排空延遲等有關。然而肥胖和胃食道逆流也有相關。這些代謝性疾病跟腸胃會有什麼相關性,理論上和癌症有關之外,對糖尿病的人會不會影響藥物的吸收,血糖的控制,甚至吃不下影響營養方面問題,這個部分值得我們深入進一步的研究。

當胃排空的時間延遲時,將發生「胃輕癱(gastroparesis)」。正常蠕動情況下,神經信號會告訴胃部肌肉收縮的時間,這些肌肉將食物從胃移動到十二指腸,胃輕癱時,神經或肌肉被損壞,導致腸蠕動減慢或完全停止,因此,食物無法從胃裡正常移出。嚴重的症狀,如噁心、嘔吐、吃飯時很快感到飽足感、腹脹。為確認問題,需進行的檢查包括胃排空掃描、上胃腸道攝影、核磁共振。患病率為糖尿病患者的5-12%,此問題經常被忽視。

胃食道逆流是台灣正在出現的一個新問題,在健檢的內視鏡中發現西元2003年到2006年有15.7%,西元2009年有29.2%。係指實門括約肌功能障礙,或腹內壓升高引起胃內酸性內容物逆流至食道所引起的結果。這些人常和三高、生活方式、飲食、肥胖、抽菸、喝酒、幽門螺旋桿菌有關。肥胖和胃食道逆流有很大的相關因素,其他因素有:裂孔疝氣、增加胃內壓力、胃容量受損、下食道括約肌功能障礙、荷爾蒙變化。臨床的患者常主訴「感覺喉嚨有液體出來」,嚴重者會影響睡眠。許多人因為症狀輕微,罹患胃食道逆流以為吃個電視廣告的胃藥就好了,導致食道長期被胃酸侵蝕,久了為了適應強酸的環境而產生變性,即所謂的

「巴瑞特氏食道」Barrett's esophagus,它是食道腺癌的癌前病變。

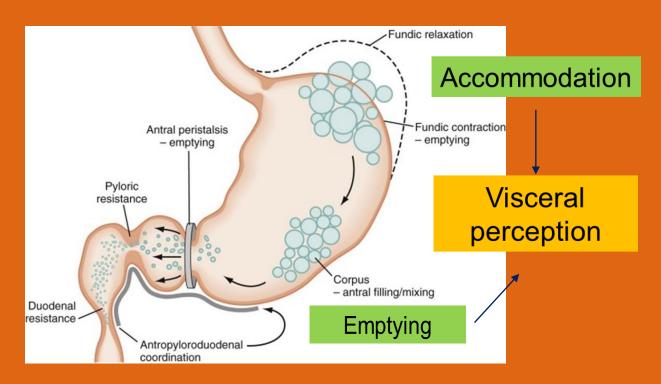
胃排空,指食物由胃排入十二指腸的過程,不同食物的排空 速度是不相同,在台大醫院做是喝一包燕麥片來測半小時、一小 時、兩小時、三小時。許多疾病能引起胃排空減慢,如胃潰瘍、 糖尿病引起的胃輕癱等。

食道壓力檢查,從鼻子放一條0.4公分的管子,管子上有刻度可以測壓力,主要用來評估食道的蠕動功能和下食道括約肌的壓力。藉由食道壓力檢查,可以明確看到裂孔疝氣,食道的收縮功能。

目前正進行的是和解剖所謝教授合作在胃腸道運動障礙和症 狀的感覺神經,不但看糖尿病,還有楊博仁醫師的病態性肥胖的 患者,術前術後做食道壓力檢查,當然,更早之前是建立動物研 究。

腸胃道和代謝方面相關,其實,兩者中間的關係相當複雜, 我們常用臨床來驗證。

## Gastric motility/physiology



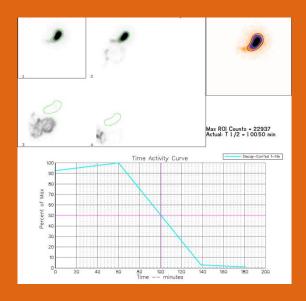
Koch KL. Physiological basis of electrogastrography

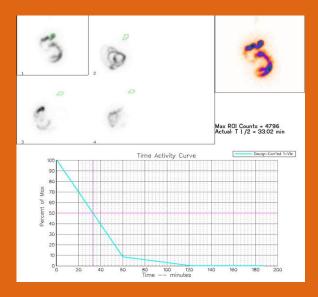
## 台大醫院核子醫學部 semi-solid (oatmeal) GET

檢查項目 報告時間 2017/07/30 Gastric emptying time - Semisolid 報告內容 NUCLEAR MEDICINE STUDY: Gastric emptying time study RADIOPHARMACEUTICAL: 1.0 mCi Tc-99m DTPA (diethylenetriamine pentaacetic acid) in oatmeal (1 pack with 200 mL water) per Os within 20 minutes. SCANNING PROTOCOL: 30 sec/frame for 60min , then static images at 2nd, and 3rd hrs (from LAO 30 degree for 30sec). CLINICAL HISTORY: Suspect familial amyloid polyneuropathy, for GI evaluation. In supine position, the gastric emptying time study showed: \* During the first 60 minutes, the estimated time of half emptying (T1/2) of stomach is 550.79 minutes (normal 52.9 ± 34.4 minutes). \* During the overall 180 minutes, the time of half emptying (T1/2) of stomach is 399.82 minutes. (normal 51.8  $\pm$  13.8 minutes). \* During the first 60 minutes, the estimated time of half emptying (T1/2) of gastric fornix is 70.10 minutes. \* The 1st-hour transit is 10%. \* The percentage of tracer remained in the stomach after - 30th minutes residual is 94%. (normal 63.6 ± 14.3%) 1st-hour residual is 90%. ((normal  $41.5 \pm 14.0\%$ )) 2nd-hour residual is 69%. (normal 9.3  $\pm$  7.8%) 3rd-hour residual is 63%. (normal 2.0  $\pm$  2.4%) Reference values from healthy volunteers were listed below (Tseng PH et al. J Gastroenterol Hepatol 2014): \* The upper (95th percentile) and lower (5th percentile) limits were: - 0.5h gastric retention values: 88% and 35% - 1 hr gastric retention values: 65% and 16% - 2 hr gastric retention values: 28% and 1% - 3 hr gastric retention values: 8% and 0%. Impression GET after 30th minutes residual: 94%, 1 hour residual: 90%, 2 hour residual: 69%, 3 hour residual: 63%. Severely prolonged gastric emptying time was 鄭媚方 PACS影像 開魰PACS影像 開啟PACS影像(Mobile) 顯示修改記錄 🗌 報告醫師

### Morbid obesity and gastric emptying

33 male, BMI: 54.6, DM





T1/2: 100.5 min T1/2: 33.0 min

#### 曾屏輝醫師和楊偉勛教授一起研究發表的論文

OPEN & ACCESS Freely available online



## Association of Esophageal Inflammation, Obesity and Gastroesophageal Reflux Disease: From FDG PET/CT Perspective

Yen-Wen Wu<sup>1,2,3,4,9</sup>, Ping-Huei Tseng<sup>1,5,9</sup>, Yi-Chia Lee<sup>1,7</sup>, Shan-Ying Wang<sup>3</sup>, Han-Mo Chiu<sup>1</sup>, Chia-Hung Tu<sup>1</sup>, Hsiu-Po Wang<sup>1</sup>, Jaw-Town Lin<sup>8,9</sup>, Ming-Shiang Wu<sup>1</sup>, Wei-Shiung Yang<sup>1,5,6</sup>\*

- Esophageal inflammation demonstrated by FDG PET/CT correlates with endoscopic findings and symptomatology of GERD.
- Obesity markers, both visceral and general, are independent determinants of esophageal inflammation.

PLoS One. 2014 Mar 18;9(3):e92001

## Associations of Circulating Gut Hormone and Adipocytokine Levels with the Spectrum of Gastroesophageal Reflux Disease

Ping-Huei Tseng  $^{1,2},$  Wei-Shiung Yang  $^{1,2,3},$  Jyh-Ming Liou  $^1,$  Yi-Chia Lee  $^1,$  Hsiu-Po Wang  $^1,$  Jaw-Town Lin  $^{1,4,5},$  Ming-Shiang Wu  $^1*$ 

	GERD (n = 104)	Control (n = 50)	P*
Age, yr	45.6 ± 12.8	44.4 ± 12.9	0.584
Male gender, n (%)	31 (29.8%)	25 (50.0%)	0.02*
BMI, kg/m <sup>2</sup>	22.4 ± 3.0	22.8 ± 2.6	0.397
Abdominal girth, cm	79.9 ± 9.9	83.7 ± 11.4	0.093
Hip girth, cm	94.7 ± 7.1	97.7 ± 10.3	0.096
H. pylori infection, n (%)	28 (26.9%)	0	
Fasting blood glucose, mg/dL	84.9 ± 11.9	89.2 ± 19.2	0.145
Triglycerides, mg/dL	106.9 ± 58.9	119.6 ± 62.1	0.132
Total cholesterol, mg/dL	205.5 ± 43.8	216.9 ± 43.3	0.223
Peptide hormones			
Ghrelin, pg/mL	162.4 (82.0–240.4)	160.5 (81.8–258.9)	0.647
PYY, pg/ml	80.1 (49.8–108.3)	99.4 (65.8-131.9)	0.057
Adiponectin, μg/mL	9.0 (6.8–11.1)	7.7 (6.3–9.5)	0.087
Leptin, ng/mL	8.4 (5.1–12.8)	7.7 (4.4–13.3)	0.427

Patients with Barrett's esophagus appeared to have lower adiponectin levels and lower ghrelin levels than those without BE

#### 曾屏輝醫師和楊偉勛教授一起研究發表的論文

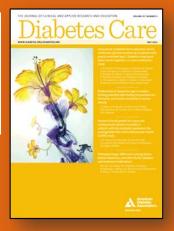
Epidemiology/Health Services Research

ORIGINAL ARTICLE

## Association of Diabetes and HbA<sub>1c</sub> Levels With Gastrointestinal Manifestations

PING-HUEI TSENG, MD<sup>1,2</sup> YI-CHIA LEE, MD, PHD<sup>1,3</sup> HAN-MO CHIU, MD, PHD<sup>1</sup> CHIEN-CHUAN CHEN, MD<sup>1</sup> WEI-CHIH LIAO, MD, MSC<sup>1</sup>
CHIA-HUNG TU, MD, MSC<sup>1,3</sup>
WEI-SHIUNG YANG, MD, PHD<sup>1,2,4</sup>
MING-SHIANG WU, MD, PHD<sup>1</sup>

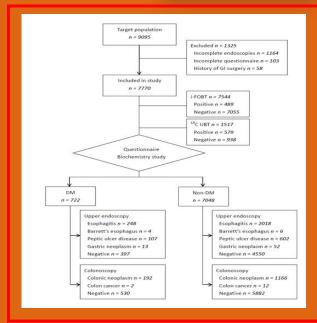




**OBJECTIVE** To determine the prevalence of gastrointestinal (GI) manifestations associated with diabetes mellitus (DM) in a Taiwanese population undergoing bidirectional endoscopies.

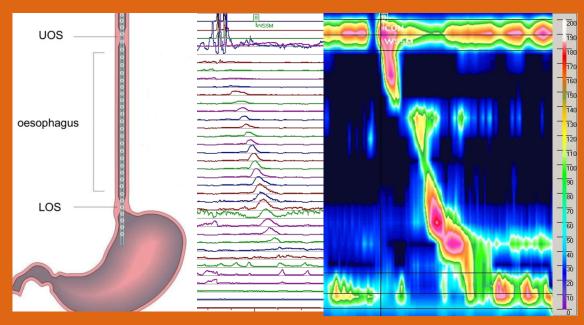
RESEARCH DESIGN AND METHODS Subjects voluntarily undergoing upper endoscopy/colonoscopy as part of a medical examination at the National Taiwan University Hospital were recruited during 2009. Diagnosis of DM included past history of DM, fasting plasma glucose ≥126 mg/dL, or glycated hemoglobin (HbA(1c)) ≥6.5%. Comparisons were made between diabetic and nondiabetic subjects, subjects with lower and higher HbA(1c) levels, and diabetic subjects with and without complications, respectively, for their GI symptoms, noninvasive GI testing results, and endoscopic findings. RESULTS Among 7,770 study subjects, 722 (9.3%) were diagnosed with DM. The overall prevalence of GI symptoms was lower in DM subjects (30.3 vs. 35.4%, P = 0.006). In contrast, the prevalence of erosive esophagitis (34.3 vs. 28.6%, P = 0.002), Barrett's esophagus (0.6 vs. 0.1%, P = 0.001), peptic ulcer disease (14.8 vs. 8.5%, P < 0.001), gastric neoplasms (1.8 vs. 0.7%, P = 0.003), and colonic neoplasms (26.6 vs. 16.5%, P < 0.001) was higher in diabetic subjects. Diagnostic accuracy of immunochemical fecal occult blood test for colonic neoplasms was significantly decreased in DM (70.7 vs. 81.7%, P < 0.001). Higher HbA(1c) levels were associated with a decrease of GI symptoms and an increase of endoscopic abnormalities. Diabetic subjects with complications had a higher prevalence of colonic neoplasms (39.2 vs. 24.5%, P = 0.002) than those without

CONCLUSIONS DM and higher levels of HbA(1c) were associated with lower prevalence of GI symptoms but higher prevalence of endoscopic abnormalities



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### High resolution manometry (HRM)



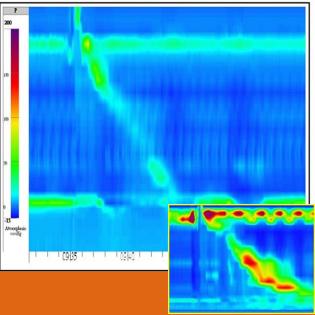
More channels: 4~8 -> 22~36

Replace pressure levels by colors(esophageal pressure topography, EPT)

### Morbid obesity and esophagus

44 male, BMI: 39.7





Hiatal hernia Reflux esophagitis, LA Gr.A 100% failed contractions (DCI<100) !! **Absent contractility**