

## ORIGINAL RESEARCH

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# Changes in mesenteric fat thickness and its clinical impact in bariatric surgery

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## Summary

Obesity, especially central obesity is associated with increased risk of metabolic syndrome, non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus. The study aimed to investigate the associations of the changes of abdominal fat thicknesses with changes of anthropometric indexes and improvements of metabolic phenotypes in patients with obesity and T2DM before and after bariatric surgery. Between April 2016 and January 2017, 34 adult patients with concurrent obesity and T2DM scheduled for different bariatric surgeries were prospectively evaluated by ultrasound before and 1-year after bariatric surgery to determine abdominal fat thicknesses (mesenteric fat, preperitoneal fat and subcutaneous fat) and NAFLD. At 1 year, of the 25 patients that finished the study, significant decrease in mesenteric-fat-thickness was associated with significant reduction of obesity, that is, BMI (−24%,  $p < .001$ ), remission of metabolic syndrome (32%,  $p = .008$ ), NAFLD (60%,  $p < .001$ ) and T2DM (44%,  $p < .001$ ). Lower baseline mesenteric fat thickness was associated with remission of metabolic syndrome. Lower baseline mesenteric-fat-thickness may have the potential to predict metabolic syndrome remission after bariatric surgery.

## KEYWORDS

bariatric surgery, diabetes, mesenteric fat thickness, metabolic syndrome, obesity, ultrasound

## What is already known about this subject?

- Obesity is associated with increased risk of metabolic syndrome, NAFLD and T2DM.
- Bariatric surgery is a known last resort treatment of obesity and its comorbidities.
- Visceral adipose tissue is more metabolically active than subcutaneous and retroperitoneal adipose tissues.

## What this study adds?

- Lower baseline mesenteric fat thickness gives higher benefit from bariatric surgery.
- Reduction of mesenteric fat gives greater weight loss and metabolic benefits.
- Mesenteric fat is highly sensitive to the effects of bariatric surgery than anthropometric indexes, preperitoneal fat and subcutaneous fat.

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## 1 | INTRODUCTION

Obesity, especially central obesity is associated with increased risk of metabolic syndrome (MetS), non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM),<sup>1</sup> with the probability and severity of these metabolic comorbidities increasing greatly with the increase in obesity. Obesity and its comorbidities are treatable, and common among them is the presence of dysfunctional,<sup>2</sup> inflamed<sup>3</sup> and increased visceral adipose tissue (VAT).<sup>4</sup> Interventions aimed at reducing adipose tissue mass or body weight have shown efficacy in the improvement of obesity, remission of T2DM, NAFLD and MetS. In particular, bariatric surgery has been shown to remarkably reduce body weight and massively improve metabolic profiles.<sup>5</sup>

Increased VAT even among the lean population has been shown to be sensitive and specific in predicting obesity related complications.<sup>6</sup> Mesenteric fat, as a specific VAT depot has been shown to be more metabolically active than subcutaneous and retroperitoneal adipose tissues.<sup>7</sup> In fact, Yang et al.<sup>8</sup> showed that mesenteric fat plays a crucial role in insulin resistance of T2DM and MetS. Further, our previous studies have shown that mesenteric fat has a high correlation with MetS and NAFLD.<sup>9,10</sup>

To our knowledge, there are no previous studies which investigated the changes of mesenteric fat in bariatric surgery. However, in the past 2 years, there has been five studies on mesenteric fat.<sup>11–15</sup> Thus, the aim of this study was to investigate the associations of the changes of abdominal fat thicknesses with changes of anthropometric indexes and improvements of metabolic phenotypes in patients with co-existing obesity and T2DM.

## 2 | MATERIALS AND METHODS

### 2.1 | Study participants

This study was a secondary study to Cheung et al.<sup>16–18</sup> study reported previously with a focus on diet, hedonic hunger, glycaemic control, metabolic control in participants with T2DM with and without obesity who were subjected to telephone lifestyle reinforcement and bariatric surgery interventions. In contrast, in this current study, ultrasound assessment of abdominal fat thicknesses was analysed in subjects who were only subjected to bariatric surgery intervention in the primary study. The study was approved by the Research Ethics Committee (CREC reference number 2016.240) and registered at [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT02938026, 19 October 2016). Written informed consents were obtained from all the participants. The study protocol complied with the Declaration of Helsinki and the Good Clinical Practice Guidelines of the International Conference on Harmonization (ICH-GCP) Standards. Thus, between April 2016 and January 2017, 34 adult Chinese participants with concurrent obesity and T2DM who underwent bariatric surgery were recruited consecutively to participate into this 1-year study after fulfilling the

selection criteria. Final analysis at 1 year involved 25 participants after nine withdrew from the study (Figure 1).

### 2.2 | Inclusion and exclusion criteria

The study included participants with age 18–65 years, obesity ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ), documented diagnosis of T2DM (as defined by World Health Organization) for  $\geq 6$  months, and of Chinese ethnicity. Exclusion criteria included: presence of type 1 diabetes mellitus, pregnancy, breastfeeding, medical conditions known to affect habitual dietary intakes, alcohol consumption limit of 30 g/d and 20 g/d for men and women respectively, malignancy diagnosed within 3 years, and previous bariatric surgery.

### 2.3 | Clinical assessment

The participants received their anthropometric measurements and biochemical evaluations on the pre-operation admission day (baseline) and at one-year follow-up. The participant's past medical history, drug

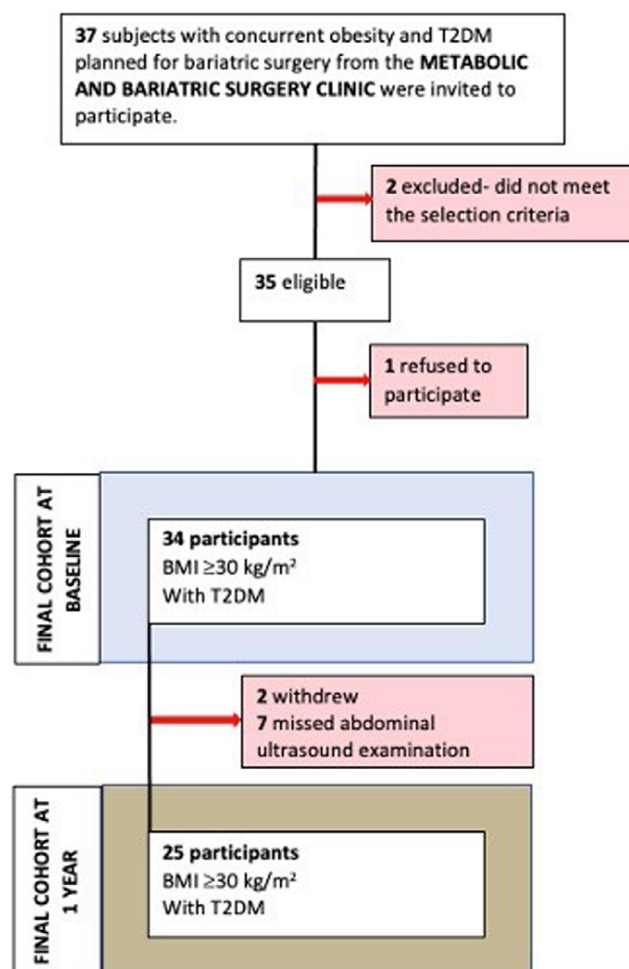


FIGURE 1 Flow chart for study participants.

history/current use of medications, smoking history and alcohol consumption were recorded at baseline.

### 2.3.1 | Clinical and anthropometric measurements

Anthropometric measurements including body weight, body height, body mass index (BMI), waist and hip circumferences, diastolic and systolic blood pressures were recorded. Blood tests including liver enzymes, glucose and lipids were conducted after 8 h of fasting. The harmonised criteria<sup>19</sup> was used to define metabolic syndrome, that is, the presence of at least any three of five of the following: (1) central obesity (waist circumference  $\geq 90$  cm in Asian men and  $\geq 80$  cm in Asian women); (2) triglycerides  $\geq 1.7$  mmol/L; (3) reduced high-density lipoprotein-cholesterol ( $<1.0$  mmol/L in men and  $<1.3$  mmol/L in women); (4) blood pressure  $\geq 130/85$  mmHg and (5) fasting plasma glucose  $\geq 5.6$  mmol/L, or receiving treatment for any of the above metabolic abnormalities.

### 2.3.2 | Remission of clinical conditions—Definitions

- *Metabolic syndrome* remission was defined as the presence of 2 or less, of the 5 MetS diagnostic components.
- *T2DM remission* was defined according to the Association of British Clinical Diabetologists (ABCD) and the Primary Care Diabetes Society (PCDS),<sup>20</sup> that is: (1) the absence of any medications for T2DM for at least 6 months (2) weight loss (3) glycated haemoglobin (HbA1c)  $< 6.5\%$  or fasting plasma glucose level  $< 7.0$  mmol/L.
- *Remission of dyslipidaemia* was defined as triglycerides  $< 1.7$  mmol/L; increased high-density lipoprotein-cholesterol ( $> 1.0$  mmol/L in men and  $> 1.3$  mmol/L in women) and not receiving any lipid treatment.
- *Remission of hypertension* was defined as blood pressure  $< 130/85$  mmHg and not receiving antihypertensive drugs.

## 2.4 | Ultrasound imaging

All 25 participants had ultrasound examinations of the abdomen performed a day before surgery (baseline), and at 1 year after surgery. The abdominal ultrasound was performed to diagnose NAFLD, measure the subcutaneous, preperitoneal and mesenteric fat thicknesses. A single sonographer blind to clinical data conducted the examinations using the ultrasound machines (Philips iU22 Eindhoven, The Netherlands, and Siemens Acuson S3000, CA USA).

## 2.5 | Measurements of abdominal fat thickness

The scanning protocol and measurements of the abdominal fat thickness used in the study were as described by Liu et al.<sup>21</sup> Briefly, mesenteric leaves were seen around the paraumbilical region, which

appeared as tubular structures separated by thin linear hyperechoic peritoneal layers. The preperitoneal and subcutaneous fat thicknesses were also measured in the midline between the xiphoid process and the umbilicus in longitudinal and transverse sections respectively. The measurements of three thickest mesenteric leaves, preperitoneal and subcutaneous fat layers were made, and the mean value was taken for analysis. The inter-operator and intra-operator intraclass correlation coefficients of mesenteric, preperitoneal and subcutaneous fat thickness were reported by the same group in previous study, which ranged from 0.89 to 0.99.<sup>21</sup>

## 2.6 | Diagnosis of NAFLD

The determination of NAFLD and its severity were according to the criteria set by Scatarige et al.<sup>22</sup> These included: reduced ultrasound penetration of deep liver, poor visualisation of portal veins, diaphragm and increase of hepatic echogenicity. NAFLD remission was defined as the absence of all NAFLD diagnostic and grading criteria as described by Scatarige et al.<sup>22</sup> that is, reduced ultrasound penetration of deep liver, poor visualisation of portal veins, diaphragm and increase of hepatic echogenicity.

## 2.7 | Bariatric surgery

Three experienced bariatric surgeons performed five different bariatric surgery methods: Laparoscopic sleeve gastrectomy ( $n = 18$ ), Roux-en-Y gastric bypass ( $n = 10$ ), single loop duodenojejunal bypass with sleeve gastrectomy ( $n = 4$ ), laparoscopic mini gastric bypass ( $n = 1$ ) and laparoscopic greater curvature plication ( $n = 1$ ) in accordance with the departmental standard protocols. Given that the primary aim of Cheung et al. study<sup>16</sup> was comparing the effects of usual care, telephone lifestyle reinforcement programme and bariatric surgery on dietary characteristics, hedonic hunger and metabolic control, bariatric surgery methods were grouped as one (not as individual methods) and their effect were assessed as such.

## 2.8 | Statistical analysis

All continuous variables were expressed as mean  $\pm$  SD, unless stated otherwise and in this case, median was used. Categorical variables were expressed as number (percentage). Comparisons between two groups were analysed using Mann–Whitney and Fischer's exact tests accordingly. Wilcoxon and McNemar's tests were used to compare matched data accordingly. Correlations between variables were analysed with Pearson's correlation coefficient. Subjects with missing data at follow up were excluded in the final analysis. Multiple linear regression analysis with multiple comparisons was used to predict causation among variables. All tests were two sided and  $p$ -values  $< .05$  were considered

statistically significant. Statistical analyses were performed with software (SPSS, version 25.0; IBM, Chicago, IL).

### 3 | RESULTS

#### 3.1 | Study participants—Baseline analysis

The 25 participants who completed the study (as nine subjects that withdrew from the study were excluded) had: 56% men, mean age  $43 \pm 10$  years and BMI  $37 \pm 5$  kg/m<sup>2</sup>. Table 1 summarises the details.

#### 3.2 | Anthropometric outcomes

At 1 year after surgery, participants showed a mean percentage total body weight loss of  $-24 \pm 6\%$ ,  $p < .001$  (women:  $-25 \pm 8\%$ ,  $p = .005$

and men:  $-23 \pm 6\%$ ,  $p = .001$ ). All anthropometric indexes had significant reduction after surgery ( $p < .001$ ; Table 2).

#### 3.3 | Abdominal fat thickness outcomes

At 1 year after surgery, there was significant percentage decrease in subcutaneous fat thickness (SFT) ( $-7 \pm 30\%$ ,  $p = .032$ ), preperitoneal fat thickness (PFT) ( $-25 \pm 17\%$ ,  $p < .001$ ) and mesenteric fat thickness (MFT) ( $-46 \pm 14\%$ ,  $p < .001$ ). Among the three abdominal fat layers, the MFT had the highest percentage loss (Table 2).

#### 3.4 | Associations of changes in abdominal fat thickness and anthropometric indexes

The percentage change in SFT correlated with the percentage change in both body weight ( $r = 0.448$ ,  $p = .018$ ) and BMI ( $r = 0.449$ ,  $p = .018$ ).

Variables	All (n = 25)	Women (n = 11)	Men (n = 14)	p-Value <sup>a</sup>
Age (years)	$43 \pm 10$	$43 \pm 9$	$44 \pm 11$	.681
Body weight (kg)	$104 \pm 19$	$91 \pm 15$	$114 \pm 17$	<b>.002</b>
Body mass index (kg/m <sup>2</sup> )	$36 \pm 5$	$35 \pm 6$	$38 \pm 4$	.071
Waist circumference (cm)	$118 \pm 12$	$113 \pm 13$	$122 \pm 9$	<b>.049</b>
Waist to hip ratio	$1.01 \pm 0.1$	$0.97 \pm 0.1$	$1.04 \pm 0.1$	<b>.012</b>
Subcutaneous fat thickness (cm)	$3.23 \pm 1.34$	$3.86 \pm 1.34$	$3.02 \pm 1.26$	.171
Preperitoneal fat thickness (cm)	$1.74 \pm 0.45$	$1.81 \pm 0.56$	$1.60 \pm 0.35$	.273
Mesenteric fat thickness (cm)	$1.21 \pm 0.24$	$1.20 \pm 0.19$	$1.23 \pm 0.28$	.870
Fasting plasma glucose (mmol/L)	$8.40 \pm 3$	$7.71 \pm 3$	$8.94 \pm 3$	.273
HbA1c (%)	$7.86 \pm 1.6$	$7.18 \pm 1.2$	$8.39 \pm 1.6$	.084
Antidiabetic drug use, n (%)	25 (100)	11 (100)	14 (100)	1.000 <sup>b</sup>
Diastolic blood pressure (mmHg)	$82 \pm 9$	$80 \pm 8$	$83 \pm 10$	.179
Systolic blood pressure (mmHg)	$134 \pm 15$	$127 \pm 11$	$139 \pm 16$	.079
Mean arterial pressure (mmHg)	$98 \pm 10$	$94 \pm 6$	$102 \pm 12$	.154
Antihypertensive drug use, n (%)	20 (80)	9 (82)	11 (79)	1.000 <sup>b</sup>
Total cholesterol (mmol/L)	$4.12 \pm 0.7$	$4.22 \pm 0.8$	$4.04 \pm 0.7$	.681
HDL-cholesterol (mmol/L)	$1.15 \pm 0.3$	$1.16 \pm 0.4$	$1.15 \pm 0.25$	.934
LDL-cholesterol (mmol/L)	$2.21 \pm 0.7$	$2.28 \pm 0.8$	$2.15 \pm 0.6$	.762
Triglycerides (mmol/L)	$1.81 \pm 1.03$	$2.00 \pm 1.4$	$1.66 \pm 0.5$	.913
Lipid lowering drug use, n (%)	18 (72)	8 (73)	10 (71)	1.000 <sup>b</sup>
ALP (IU/L)	$67 \pm 21$	$65 \pm 17$	$68 \pm 24$	.956
ALT (IU/L)	$57 \pm 43$	$44 \pm 28$	$66 \pm 51$	.163
Metabolic syndrome, n (%)	25 (100)	11 (100)	14 (100)	1.000 <sup>b</sup>
Diabetes, n (%)	25 (100)	11 (100)	14 (100)	1.000 <sup>b</sup>
Hypertension, n (%)	22 (88)	9 (82)	13 (93)	.565 <sup>b</sup>
Dyslipidaemia, n (%)	25 (100)	11 (100)	14 (100)	1.000 <sup>b</sup>
NAFLD, n (%)	25 (100)	11 (100)	14 (100)	1.000 <sup>b</sup>

Note: Bold indicates significant value ( $p < .05$ ).

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; HbA1c, glycated haemoglobin; HDL, high density lipoproteins; LDL, low density lipoproteins; NAFLD, non-alcoholic fatty liver disease.

<sup>a</sup>Mann-Whitney U test.

<sup>b</sup>Fischer's exact test.

**TABLE 1** Baseline anthropometric indexes, abdominal fat thickness, clinical and metabolic parameters of participants.

**TABLE 2** Anthropometric indexes, abdominal fat thickness, clinical and metabolic parameters of subjects at baseline and 1 year after surgery in all participants.

Variable	Baseline (n = 25)	1-year After surgery (n = 25)	% Change	p-Value
Body weight (kg)	104 ± 19	79 ± 18	−24 ± 6	<.001 <sup>a</sup>
Body mass index (kg/m <sup>2</sup> )	36 ± 5	28 ± 5	−24 ± 7	<.001 <sup>a</sup>
Waist circumference (cm)	118 ± 12	100 ± 13	−16 ± 5	<.001 <sup>a</sup>
Waist to hip ratio	1.01 ± 0.1	0.96 ± 0.1	−4 ± 5	<.001 <sup>a</sup>
Subcutaneous fat thickness (cm)	3.23 ± 1.34	2.94 ± 1.18	−7 ± 30	.032 <sup>a</sup>
Preperitoneal fat thickness (cm)	1.74 ± 0.5	1.28 ± 0.3	−25 ± 17	<.001 <sup>a</sup>
Mesenteric fat thickness (cm)	1.21 ± 0.2	0.65 ± 0.2	−46 ± 14	<.001 <sup>a</sup>
Fasting plasma glucose (mmol/L)	8.40 ± 3	5.26 ± 1	−32 ± 20	<.001 <sup>a</sup>
HbA1c (%)	7.86 ± 2	5.81 ± 0.5	−24 ± 14	<.001 <sup>a</sup>
Antidiabetic drug use, n (%)	25 (100)	11 (44)	−56	<.001 <sup>b</sup>
Diastolic blood pressure (mmHg)	82 ± 9	78 ± 12	−4 ± 15	.187 <sup>a</sup>
Systolic blood pressure (mmHg)	134 ± 15	127 ± 14	−5 ± 12	.049 <sup>a</sup>
Mean arterial pressure (mmHg)	98 ± 10	93 ± 11	−4 ± 13	.100 <sup>a</sup>
Antihypertensive drug use, n (%)	20 (80)	13 (52)	−28	.039 <sup>b</sup>
Total cholesterol (mmol/L)	4.12 ± 0.7	4.10 ± 0.8	−2 ± 25	.668 <sup>a</sup>
HDL-cholesterol (mmol/L)	1.15 ± 0.3	1.48 ± 0.4	31 ± 27	<.001 <sup>a</sup>
LDL-cholesterol (mmol/L)	2.21 ± 0.7	2.16 ± 0.7	−5 ± 47	.627 <sup>a</sup>
Triglycerides (mmol/L)	1.81 ± 1	1.01 ± 0.5	−39 ± 23	<.001 <sup>a</sup>
Lipid lowering drug use, n (%)	18 (72)	14 (56)	−16	.344 <sup>b</sup>
ALP (IU/L)	67 ± 21	73 ± 34	7 ± 22	.353 <sup>a</sup>
ALT (IU/L)	57 ± 43	31 ± 21	−21 ± 75	.003 <sup>a</sup>
Metabolic syndrome, n (%)	25 (100)	17 (68)	−32	.008 <sup>b</sup>
Diabetes (%)	25 (100)	14 (56)	−44	.001 <sup>b</sup>
Hypertension (%)	22 (88)	16 (64)	−24	.109 <sup>b</sup>
Dyslipidaemia (%)	25 (100)	17 (68)	−32	.016 <sup>b</sup>
NAFLD (%)	25 (100)	10 (40)	−60	<.001 <sup>b</sup>

Note: Bold indicates significant value ( $p < .05$ ).

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; eGFR-estimated glomerular filtration rate; HbA1c, glycated haemoglobin; HDL, high density lipoproteins; LDL, low density lipoproteins; NAFLD, non-alcoholic fatty liver disease.

<sup>a</sup>Wilcoxon's test used.

<sup>b</sup>McNemar's test used.

The percentage change in PFT correlated with the percentage change in waist to hip ratio ( $r = -0.455$ ,  $p = .033$ ), while the percentage change in MFT correlated with the percentage change in both body weight ( $r = 0.517$ ,  $p = .012$ ), and BMI ( $r = 0.517$ ,  $p = .012$ ).

### 3.5 | Blood biochemistry outcomes

Fasting plasma glucose ( $p < .001$ ), HbA1c ( $p < .001$ ), HDL-cholesterol ( $p < .004$ ) and Triglycerides ( $p < .001$ ) had significant percentage reduction at 1 year after surgery.

### 3.6 | Clinical characteristics

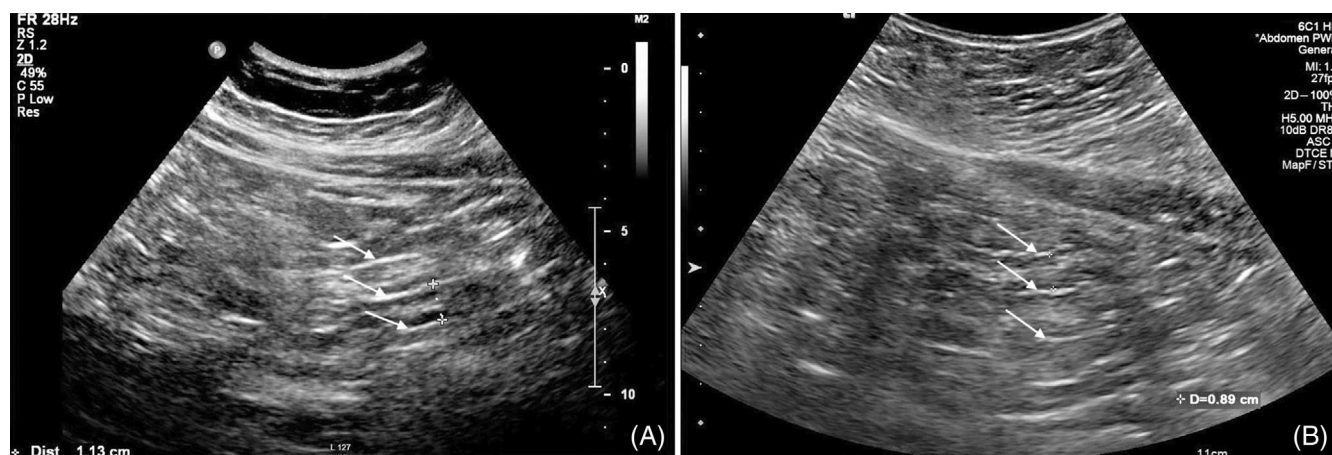
MetS remission was achieved in 8 (32%,  $p = .008$ ) out of 25 patients. T2DM remission was achieved in 11 (44%,  $p = .001$ )

out of 25 patients. Dyslipidaemia remission was achieved in 8 (32%,  $p = .016$ ) out of 25 patients. Hypertension was achieved in 6 (24%,  $p = .109$ ) out of 25 patients. Details are summarised in Table 2.

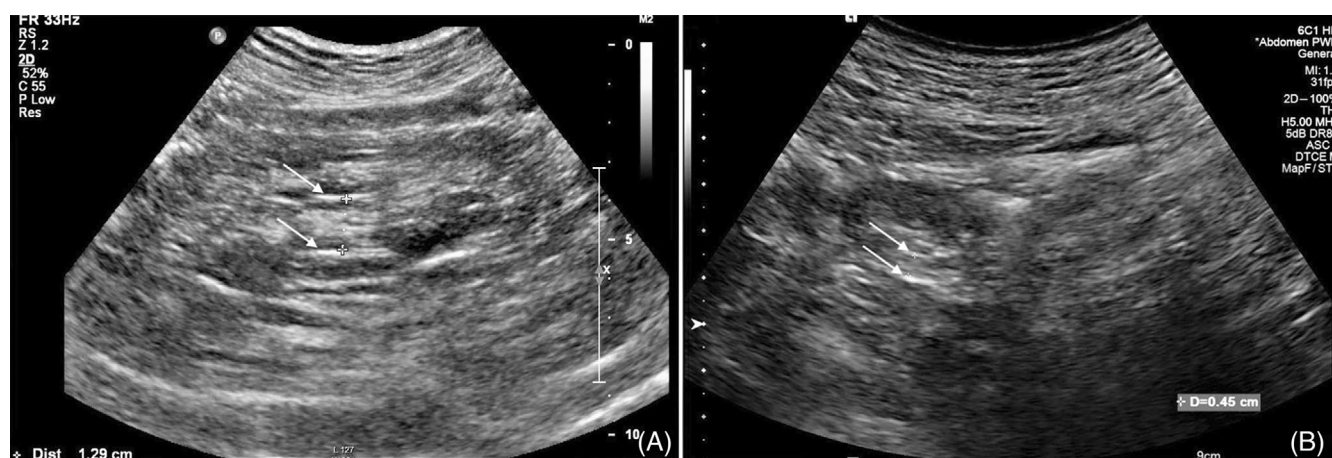
In both the groups of persistent and remission of MetS, MFT had the highest percentage decrease when compared to other abdominal fat thicknesses and anthropometric indexes ( $p < .001$ ). The MFT had a trend of higher percentage decrease in patients with remission of MetS than in those with persistent MetS (Figures 2 and 3), though not statistically significant (−51% vs. −43%,  $p = .124$ ; Table 3).

The baseline MFT in patients with remission of MetS was lower than those with persistent MetS with marginal statistical significance (1.03 cm vs. 1.23 cm,  $p = .055$ ). The baseline measurements of other abdominal fat thickness and anthropometric indexes did not have significant difference between groups ( $p > .05$ ).





**FIGURE 2** (A) is the mesenteric fat thickness (1.13 cm) before surgery and (B) is mesenteric fat thickness at 1 year after surgery (0.89 cm). Percentage reduction of mesenteric fat thickness of  $-21\%$  was achieved in this patient who did not have remission of metabolic syndrome at 1 year after surgery. Measurements made between two peritoneal surfaces (white arrows) as illustrated by the distance between callipers.



**FIGURE 3** (A) is mesenteric fat thickness (1.29 cm) before surgery and (B) is mesenteric fat thickness at 1 year after surgery (0.45 cm). Percentage reduction of mesenteric fat thickness of  $-65\%$  was achieved in this patient who had remission of Metabolic syndrome at 1 year after surgery. Measurements made between two peritoneal surfaces (white arrows) as illustrated by the distance between callipers.

In both groups of persistent and remission of T2DM, no significant difference between the baseline abdominal fat thicknesses and anthropometric indexes (all  $p > .05$ ) were found (Table 4).

### 3.7 | NAFLD remission

NAFLD remission was achieved in 15 (60%,  $p < .001$ ) out of 25 patients (Table 2). In participants who had remission of NAFLD, the baseline data showed significantly lower PFT ( $1.53 \pm 0.4$  cm vs.  $1.99 \pm 0.4$ ,  $p = .012$ ) than in those who did not (Table 5). However, at 1 year after surgery the percentage reduction in MFT in those with remission of fatty liver was significantly higher than it was with PFT ( $-51\%$  vs.  $-24\%$ ,  $p = .001$ ).

In all the measured abdominal fat layers and anthropometric indexes regardless of whether the participants had persistent or

remission of the metabolic conditions, the MFT consistently showed the highest percentage loss ( $p < .001$ ), while the largest percentage loss was observed in patients who had remission of MetS and NAFLD (Tables 3 and 5, respectively).

### 3.8 | Remission rates

To confirm the outcomes above, an analysis of those in remission of MetS, T2DM and NAFLD was conducted. The baseline median values of the whole cohort in each of the three fat depots, BMI and WC were used to determine the remission rates of each metabolic condition between those below and above the respective median values. It was shown generally that the remission rates of MetS, T2DM and NAFLD were higher in those whose baseline values were below the baseline median values. However, the remission rates were not

**TABLE 3** Showing anthropometric indexes, abdominal fat compartments and their changes in those who remained with and those who lost metabolic syndrome diagnosis at 1 year after surgery.

Variables	Remained with metabolic syndrome (n = 17)				Lost metabolic syndrome (n = 8)				<i>p</i> -Value <sup>b,2</sup>	<i>p</i> -Value <sup>b,3</sup>
	Baseline	1 year after surgery	% Change	<i>p</i> -Value <sup>a,1</sup>	Baseline	1 year after surgery	% Change	<i>p</i> -Value <sup>a,1</sup>		
BW (kg)	104 ± 21	79 ± 19	−24 ± 6	<b>&lt;.001</b>	104 ± 15	79 ± 17	−25 ± 8	<b>.005</b>	.816	.954
BMI (kg/m <sup>2</sup> )	37 ± 6	29 ± 6	−24 ± 6	<b>&lt;.001</b>	36 ± 3	27 ± 4	−25 ± 8	<b>.005</b>	.771	.854
WC (cm)	120 ± 12	102 ± 14	−15 ± 6	<b>&lt;.001</b>	115 ± 11	95 ± 12	−17 ± 4	<b>.005</b>	.382	.256
WHR	1.01 ± 0.1	0.97 ± 0.04	−3.86 ± 5	<b>.006</b>	0.99 ± 0.1	0.93 ± 0.1	−5.61 ± 5	<b>.028</b>	.522	.954
SFT (cm)	3.67 ± 1.3	3.23 ± 1.2	−9 ± 22	.088	2.78 ± 1	2.30 ± 1	−0.6 ± 48	.249	.081	.841
PFT (cm)	1.74 ± 0.5	1.34 ± 0.3	−25 ± 17	<b>.001</b>	1.60 ± 0.4	1.15 ± 0.3	−30 ± 16	<b>.028</b>	.466	.916
MFT (cm)	1.23 ± 0.2	0.71 ± 0.2	−43 ± 15	<b>&lt;.001</b>	1.03 ± 0.2	0.53 ± 0.2	−51 ± 14	<b>.028</b>	.055	.124

Note: *p*-Value<sup>1</sup> for the parameter change before and after surgery. *p*-Value<sup>2</sup> for the difference in the baseline parameters between the groups of 'remained with metabolic syndrome' and 'lost metabolic syndrome'. *p*-Value<sup>3</sup> for the difference in the percentage change of the parameters between the groups of 'remained with metabolic syndrome' and 'lost metabolic syndrome'. Bold indicates significant value (*p* < .05).

Abbreviations: BMI, body mass index; BW, body weight; MFT, mesenteric fat thickness; PFT, preperitoneal fat thickness; SFT, subcutaneous fat thickness; WC, waist circumference; WHR, waist hip ratio.

<sup>a</sup>Wilcoxon's test used.

<sup>b</sup>Mann-Whitney *U* test.

**TABLE 4** Showing anthropometric indexes, abdominal fat compartments and their changes in those who remained with and those who lost T2DM diagnosis at 1 year after surgery.

Variables	Remained with T2DM (n = 14)				Lost T2DM (n = 11)				<i>p</i> -Value <sup>b,2</sup>	<i>p</i> -Value <sup>b,3</sup>
	Baseline	1 year after surgery	% Change	<i>p</i> -Value <sup>a,1</sup>	Baseline	1 year after surgery	% Change	<i>p</i> -Value <sup>a,1</sup>		
BW (kg)	108 ± 20	82 ± 18	−25 ± 6	<b>&lt;.001</b>	98 ± 18	75 ± 18	−24 ± 7	<b>.001</b>	.834	.662
BMI (kg/m <sup>2</sup> )	38 ± 5	29 ± 5	−25 ± 7	<b>&lt;.001</b>	35 ± 5	27 ± 5	−24 ± 7	<b>.001</b>	.801	.708
WC (cm)	119 ± 13	100 ± 16	−16 ± 6	<b>&lt;.001</b>	117 ± 11	97 ± 10	−15 ± 4	<b>.001</b>	.906	.525
WHR	1.00 ± 0.1	0.95 ± 0.1	−4 ± 5	<b>.011</b>	1.01 ± 0.1	0.97 ± 0.1	−6 ± 4	<b>.013</b>	.956	.622
SFT (cm)	3.36 ± 1.6	3.05 ± 1.4	−0.3 ± 32	.170	3.43 ± 1.0	2.83 ± 0.9	−14 ± 26	.110	.229	.325
PFT (cm)	1.69 ± 0.5	1.35 ± 0.4	−21 ± 17	<b>.005</b>	1.69 ± 0.5	1.19 ± 0.2	−30 ± 16	<b>.005</b>	.948	.187
MFT (cm)	1.16 ± 0.2	0.65 ± 0.2	−46 ± 12	<b>.002</b>	1.18 ± 0.3	0.66 ± 0.3	−45 ± 18	<b>.003</b>	.720	.902

Note: *p*-Value<sup>1</sup> for the parameter change before and after surgery. *p*-Value<sup>2</sup> for the difference in the baseline parameters between the groups of 'remained with T2DM' and 'lost T2DM'. *p*-Value<sup>3</sup> for the difference in the percentage change of the parameters between the groups of 'remained with T2DM' and 'lost T2DM'. Bold indicates significant value (*p* < .05).

Abbreviations: BW, body weight; BMI, body mass index; MFT, mesenteric fat thickness; PFT, preperitoneal fat thickness; SFT, subcutaneous fat thickness; WC, waist circumference; WHR, waist hip ratio.

<sup>a</sup>Wilcoxon's test used.

<sup>b</sup>Mann-Whitney *U* test.

significantly different between those below and above the reference values (all, *p* > .05). Details are shown in Table 6.

### 3.9 | Relationship between anthropometric/abdominal fat parameters with metabolic syndrome

A multiple linear regression analysis showed that among the measured baseline parameters (BMI, WC, PFT, SFT), baseline MFT (*p* = .079, though borderline significant) seemed to have a stronger relationship with MetS remission at 1 year after surgery. It was further shown that

baseline BMI (*p* = .037) had a stronger relationship with T2DM remission, while PFT had a stronger relationship with NAFLD remission (*p* = .032) at 1 year after surgery (Table 7).

## 4 | DISCUSSION

This was the first study to assess the relationship of mesenteric fat change in patients with obesity who underwent bariatric surgery. Ultrasound could be used to longitudinally assess different abdominal fat depots in patients with obesity, particularly the mesenteric fat, a

**TABLE 5** Showing anthropometric indexes, abdominal fat compartments and their changes in those who remained with and those who lost fatty liver disease diagnosis at 1 year after surgery.

Variables	Remained with fatty liver disease (n = 10)				Lost fatty liver disease (n = 15)					
	Baseline	1 year after surgery	% Change	p-value <sup>a,1</sup>	Baseline	1 year after surgery	% Change	p-Value <sup>a,1</sup>	p-Value <sup>b,2</sup>	p-Value <sup>b,3</sup>
BW (kg)	110 ± 21	88 ± 19	−20.0 ± 6	<b>.008</b>	100 ± 18	74 ± 16	−27 ± 6	<b>&lt;.001</b>	.213	<b>.011</b>
BMI (kg/m <sup>2</sup> )	38 ± 7	31 ± 6	−20 ± 7	<b>.008</b>	36 ± 4	27 ± 4	−27 ± 6	<b>.001</b>	.610	<b>.013</b>
WC (cm)	123 ± 13	108 ± 15	−12 ± 5	<b>.008</b>	116 ± 10	95 ± 10	−18.0 ± 4	<b>&lt;.001</b>	.213	<b>.006</b>
WHR	1.03 ± 0.1	0.99 ± 0.02	−3.7 ± 6	.086	0.99 ± 0.1	0.94 ± 0.1	−4.5 ± 4	<b>.002</b>	.095	.910
SFT (cm)	3.85 ± 1.6	3.53 ± 1.6	−7 ± 23	.263	3.13 ± 1.1	2.63 ± 0.8	−7 ± 33	.078	.336	.846
PFT (cm)	1.99 ± 0.4	1.45 ± 0.3	−25 ± 21	<b>.017</b>	1.53 ± 0.4	1.18 ± 0.3	−24.4 ± 15	<b>.001</b>	<b>.012</b>	.946
MFT (cm)	1.16 ± 0.4	0.80 ± 0.3	−35.2 ± 13	<b>.012</b>	1.17 ± 0.2	0.57 ± 0.2	−51.3 ± 12	<b>.001</b>	.887	<b>.012</b>

Note: p-Value<sup>1</sup> for the parameter change before and after surgery. p-Value<sup>2</sup> for the difference in the baseline parameters between the groups of 'remained with NAFLD' and 'lost NAFLD'. p-Value<sup>3</sup> for the difference in the percentage change of the parameters between the groups of 'remained with NAFLD' and 'lost NAFLD'. Bold indicates significant value ( $p < .05$ ).

Abbreviations: BW, body weight; BMI, body mass index; MFT, mesenteric fat thickness; PFT, preperitoneal fat thickness; SFT, subcutaneous fat thickness; WC, waist circumference; WHR, waist hip ratio.

<sup>a</sup>Wilcoxon's test used.

<sup>b</sup>Mann-Whitney U test.

depot of VAT, after weight loss intervention. In relation to other imaging methods such as computed tomography (CT) and Magnetic Resonance Imaging (MRI) which can assess visceral fat, ultrasound has the advantage of being generally affordable, readily available and radiation free. In addition, previous studies<sup>23–28</sup> have shown that ultrasound assessment of mesenteric fat change may be more specific to the visceral fat reduction compared to CT and MRI which usually include extraperitoneal fat in the visceral fat assessment.

In this study, it was shown that bariatric surgery was not only efficacious in significantly reducing different abdominal fat thicknesses and anthropometric indexes but also resulted in remission of 60%, 32% and 44% of NAFLD, MetS and T2DM, respectively. This was in concordance with earlier studies.<sup>29,30</sup>

Although no significant differences were observed, when comparing those with persistent and remission of MetS, MFT tended to have a higher percentage decrease when compared to PFT/SFT and all anthropometric indexes. This may indicate that mesenteric fat could be more sensitive to the effect of bariatric surgery than other measures of obesity. The underlying mechanism for this outcome is not clear. However, given that the mesenteric fat depot has the most visceral fat quantity, highly metabolically active, highly vascularised, rich in blood supply, highly innervated and has a larger difference in gene expression than other abdominal fat depots like the omentum, preperitoneal fat and subcutaneous fat,<sup>8,23,31,32</sup> it can be postulated that its response to the effects of bariatric surgery is stronger than other fat depots, driven by an instant need for energy in view of acute negative energy balance. This in turn results in early restoration of efficient energy metabolism, manifested as improvement of metabolic aberrations. Thus, mesenteric fat has the highest percentage loss than the other measures of obesity. Indeed, the above postulation is further supported by the findings of Andrew et al.<sup>32</sup> in a baboon study where they performed mesenteric visceral lipectomy using liquefaction

technology. The results showed reversal of insulin resistance and significant weight loss in contrast to subcutaneous fat liposuction<sup>33</sup> and omentectomy<sup>34</sup> where the metabolic outcomes were inconsistent. Suggesting that among the various fat depots, reduction of mesenteric fat depot appears to give greater weight loss and metabolic benefits.

We also found lower baseline MFT in patients with remission of MetS after surgery. This outcome was further consolidated in the regression analysis which showed that baseline MFT tended to have a stronger relationship with MetS remission. Also, there was higher remission of MetS in subjects whose baseline MFT was below the median value than in those above the median. These outcomes are in line with an earlier study by Weiss et al.<sup>35</sup> in which the lower baseline visceral fat (VAT) area as shown by CT was associated with the remission of MetS after bariatric surgery. These results suggest that lower baseline MFT might predict remission of MetS. In other words, the patients with lower baseline MFT may benefit more from bariatric surgery. This outcome could be partly explained by the established fact that free fatty acid release increases with an increase in VAT mass.<sup>36</sup> The free fatty acids induce insulin resistance and inflammation in the major insulin target tissues like the skeletal muscle, liver and endothelial cells, hence, they play a critical role in the development of insulin resistance and metabolic syndrome.<sup>37</sup> It could then be postulated that metabolic aberrations experienced in higher VAT mass are greater than in lower VAT mass, thus, subjects with lower baseline MFT tend to have a higher remission of MetS after surgery because their metabolic condition may not be as worse as those with higher baseline MFT.

In those with persistent or remission of T2DM, there were no significant differences in both the baseline and percentage decrease in abdominal fat layers and anthropometric indexes. However, the subcutaneous fat thickness (and preperitoneal fat thickness) tended to



**TABLE 6** Showing the remission rates between those below and above baseline median values of the whole cohort in each measured parameter of participants in remission of metabolic syndrome, T2DM and NAFLD.

Metabolic Syndrome (n = 8)															
MFT			PFT			SFT			BMI			WC			
	Remission rate, n (%)	Baseline median value (cm)	p-Value	Remission rate, n (%)	Baseline median value (cm)	p-Value	Remission rate, n (%)	Baseline median value (cm)	p-Value	Remission rate, n (%)	Baseline median value (kg/m <sup>2</sup> )	p-Value	Remission rate, n (%)	Baseline median value (cm)	p-Value
Below median value	5 (38.5)	1.21	.673	6 (40)	1.74	.402	5 (38.5)	3.23	.673	6 (37.5)	35.84	.202	5 (38.5)	117.5	.673
Above median value	3 (25)			2 (20)			3 (25)			2 (22.2)			3 (22.2)		
T2DM (n = 11)															
Below median value	7 (53.8)	1.21	.428	6 (40)	1.74	.697	5 (38.5)	3.23	.695	9 (56.3)	35.84	.428	8 (61.5)	117.5	.111
Above median value	4 (33.3)			2 (20)			6 (50)			2 (22.2)			3 (25)		
NAFLD (n = 16)															
Below median value	9 (69.2)	1.21	.688	12 (80)	1.74	.053	9 (69.2)	3.23	.688	11 (68.8)	35.84	.226	10 (76.9)	117.5	.226
Above median value	7 (58.3)			4 (40)			7 (58.3)			5 (55.6)			6 (50)		

Note: Mann-Whitney U test. P-value for the difference between remission rates in those below and above median values for each measured parameter. Bold indicates significant value ( $p < .05$ ).

Abbreviations: BMI, body mass index; MFT, mesenteric fat thickness; NAFLD, non-alcoholic fatty liver disease; PFT, preperitoneal fat thickness; SFT, subcutaneous fat thickness; T2DM, type 2 diabetes mellitus; WC, waist circumference.

have a higher percentage decrease in patients with T2DM remission. Although our results were not statistically significant, Andersson et al.<sup>38</sup> showed that a significant reduction in subcutaneous fat cell volume or decrease in estimated subcutaneous adipose tissue area was strongly associated with improvement in insulin sensitivity. The probable explanation for this outcome in our study as opposed to Anderson et al. could be related to T2DM and lipid therapies our cohort was on, as these treatments are known to alter body adiposity.<sup>39</sup>

With regards to those who had persistent or remission of NAFLD, there was a significantly lower baseline preperitoneal fat in those with remission of NAFLD. This outcome was further consolidated in the regression analysis that showed that PFT had a stronger relationship with NAFLD remission. However, no significant difference in the baseline MFT was seen, yet there was a significant reduction in MFT (and preperitoneal fat but to a lesser degree) in those with remission of NAFLD after surgery. In agreement with our study, Kim et al.<sup>40</sup> showed no significant difference in the baseline VAT area between participants with remission or persistent NAFLD. They further showed that significant reduction in the VAT area (and subcutaneous adipose tissue area but to a lesser degree) was significantly associated with regression of NAFLD.<sup>40</sup> These results suggest that significant reduction especially in the MFT coupled with minimal reduction in the preperitoneal fat thickness post-surgery is vital in the remission of NAFLD. In fact, this current study showed that mesenteric fat had the largest percentage decrease among all obesity indexes and abdominal fat layers, which was also associated with improved metabolic profiles. Thus, the assessment of mesenteric fat as well as preperitoneal fat might have an added advantage over traditional anthropometric indexes in assessing obesity and its related comorbidities in patients.

Concerning the relationship between MFT and anthropometric indexes, the percentage change in MFT correlated with the percentage change in both body weight and BMI but not with waist circumference and waist to hip ratio. These outcomes were consistent with an earlier study that assessed this relationship using VAT area.<sup>35</sup> Thus, highlighting the importance of assessing the amount of mesenteric fat (VAT). Mesenteric fat deposition in individuals with obesity leads to hypertrophic adipocytes to release several specific proinflammatory cytokines.<sup>41</sup> These proinflammatory cytokines play a significant role in the pathogenesis of MetS, T2DM and NAFLD.<sup>41</sup> Moreover, it is a known fact that mesenteric fat is drained by the portal circulation, thus, the increased supply of free fatty acids following visceral lipolysis are deposited directly into the liver. Consequently, contributing to the pathogenesis of insulin resistance, dyslipidaemia, cardiometabolic disease (components of MetS) and NAFLD.<sup>42</sup>

This study was limited by a small sample size, which could explain in part, some of the marginal significant outcomes reported. As the primary study did not investigate the effects of each bariatric surgery but instead grouped all surgery types as one despite their variability in malabsorption ability, the effect of each bariatric surgery method on mesenteric fat, preperitoneal fat, subcutaneous fat, weight, waist circumference and remission of NAFLD/metabolic syndrome/T2DM could not be established. Thus, this is another limitation of this study. Finally,

**TABLE 7** Showing regression analysis of the measured parameters in predicting remission of metabolic syndrome, T2DM and NAFLD at 1 year after surgery.

Metabolic Syndrome remission				T2DM remission			NAFLD remission		
	Standardised coefficients beta	t	p-Value	Standardised coefficients beta	t	p-Value	Standardised coefficients beta	t	p-Value
(Constant)		−0.592	.561		0.371	.715		−1.540	.140
BMI	−.516	−1.233	.232	−.958	−2.245	<b>.037</b>	−.457	−1.163	.259
WC	.299	0.783	.443	.477	1.224	.236	.536	1.493	.152
PFT	.188	0.878	.391	.154	0.704	.490	.466	2.321	<b>.032</b>
SFT	.264	1.158	.261	.176	0.758	.458	.179	0.837	.413
MFT	.432	1.857	<b>.079</b>	.263	1.105	.283	−.085	−0.389	.702

Note: Bold indicates significant value ( $p < .05$ ).

Abbreviations: BMI, body mass index; MFT, mesenteric fat thickness; NAFLD, non-alcoholic fatty liver disease; PFT, preperitoneal fat thickness; SFT, subcutaneous fat thickness; T2DM, Type 2 diabetes mellitus; WC, waist circumference.

this was a single centre study with Chinese population, thus, caution must be taken in the generalisation of the results. Therefore, future studies to reproduce our findings are warranted with a larger sample size, multicentre and a homogeneous bariatric surgery procedure.

In conclusion, ultrasound can be used to longitudinally assess different abdominal fat depots of patients with obesity, particularly the mesenteric fat, a depot of VAT, after weight loss intervention. A significant decrease in MFT was associated with significant reduction of obesity, and with the remission of MetS and NAFLD. Lower baseline MFT may have the potential to predict MetS remission after bariatric surgery.

## AUTHOR CONTRIBUTIONS

Chileka Chiyanka, Kin Hung Liu, Winnie Chiu Wing Chu, Lorena Tsui Fun Cheung, Alice Pik Shan Kong, Simon Kin Hung Wong and Enders Kwok Wai Ng participated in study design. Kin Hung Liu and Lorena Tsui Fun Cheung collected data. Simon Kin Hung Wong and Enders Kwok Wai Ng performed bariatric surgeries. Chileka Chiyanka analysed the data and wrote the manuscript. Kin Hung Liu, Lorena Tsui Fun Cheung and Winnie Chiu Wing Chu reviewed and edited the manuscript. All authors revised the manuscript, approved the final manuscript as submitted and agreed to be accountable for all aspects of the work. Winnie Chiu Wing Chu is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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