Effects of low-fat food on gallbladder contraction and ultrasound image quality

Abstract

Objective: To examine the impact of consuming a navel orange, a low-fat food, on gallbladder contraction and ultrasound image quality.

Materials and Methods: 66 healthy Chinese participants underwent ultrasonographic evaluation of gallbladder volume (GBV) and anterior wall thickness (AWT) after fasting for at least six hours and again 120 minutes after consuming a navel orange. An experienced sonographer rated the quality of the gallbladder images on a five-point Likert scale.

Results: There was no significant change in GBV (14.15 cm^3 preprandial vs. 14.00 cm^3 preprandial, $p=0.073$), AWT (0.154 cm vs. 0.157 cm, $p=0.101$), or image quality (both rated 5, $p=1.000$) after orange intake. GBV correlated with body mass index ($p<0.05$). Among various age groups, no significant differences in all measured parameters in both preprandial and postprandial states were observed (All, $p>0.05$).

Conclusion: Navel oranges may be an alternative to fasting for gallbladder ultrasound preparation without affecting image quality.

Key words: Gallbladder volume and anterior wall thickness; ultrasound; low fat food; image quality; fasting.

Introduction

Food and gallbladder contraction are closely related. Fatty and protein-rich foods stimulate cholecystokinin (CCK) release, promoting gallbladder contraction to empty bile into the duodenum for lipid digestion.[1] Therefore, in theory, low-fat foods induce unremarkable gallbladder contraction. However, existing research, often focused on subjects with obesity, suggests that low-fat diets result in weaker gallbladder contraction, a finding not necessarily applicable to individuals without obesity, who contribute to a greater population size.[2,3] Moreover, studies in healthy subjects present conflicting results, with some indicating that a low-fat diet encourages gallbladder contraction, while others report the opposite.[4,5] This discrepancy underscores the need to explore the effects of low-fat diets on gallbladder contraction in a broader, healthy population.

Ultrasonography is a widely available and safe imaging modality that has been effectively used in clinical and research settings.[6] Fasting for at least six hours prior to the clinical ultrasound examination is a common preparation to ensure gallbladder distension and visualization.[7] A properly distended gallbladder prevents physiologic wall thickening, which can be caused by fat-rich food intake and regarded as an imaging characteristic of certain gallbladder diseases such as inflammatory and neoplastic pathologies.[8] Postprandial gallbladder wall thickening should therefore be avoided to ensure accurate diagnosis of hepatobiliary conditions in a gallbladder ultrasound examination. Nonetheless, fasting beforehand can cause hypoglycaemia, particularly in patients with diabetes mellitus,[9] potentially causing severe neurological outcomes such as seizures and brain damage if left untreated.[10]

Thus, it is important to identify low-fat foods that patients, especially those with diabetes mellitus, can consume before an ultrasound examination. These foods should maintain the quality of the ultrasound image by ensuring the gallbladder remains properly distended without pseudo wall thickening. To date, limited research has explored this, with only one study showing that low-fat foods do not significantly affect ultrasound image quality,[11] highlighting the gap in research on low fat food's impact on gallbladder ultrasound imaging. However, the low-fat foods adopted in that study had a high glycaemic index, which is not suitable for patients with diabetes mellitus. Therefore, this study was designed to investigate whether consuming a navel orange (which has a low glycaemic index) as a low-fat food before an ultrasound examination can affect gallbladder contraction and image quality. This research could enhance patient comfort, compliance and align with personalised medicine principles, particularly benefiting patients with diabetes mellitus by potentially eliminating the need for fasting during patient preparation.

Materials and Methods

Study Participants

This cross-sectional prospective study was performed between January and February 2024. All procedures were performed in compliance with relevant laws and institutional guidelines and have been approved by the Institutional Review Board (HSEARS no. 20231214005). 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.

The study included healthy male and female Chinese participants between the ages of 18-65 years, and body mass index (BMI) of 18.5-24.9 kg/m^2. The BMI interpretation for Asian populations was used with BMI of 18.5-23.0 kg/m^2 and 23.0-24.9 kg/m^2 indicating normal weight and overweight participants, respectively.[12] Exclusion criteria were pregnancy, current use of medication that interfere with gastrointestinal physiology (e.g., nonsteroidal anti-inflammatory drugs like Ibuprofen, some antibiotics like amoxicillin, etc.), presence of clinically relevant diseases especially diabetes mellitus, cholelithiasis, other biliary diseases, and any previous biliary surgery.

The participants had their anthropometric measurements (weight, height) taken and underwent gallbladder ultrasound scanning. Pregnancy status and any use of medication were self-reported. BMI was computed using the standard formula: weight (kg)/height^2 (m^2). If the participant met all the set selection criteria, they were then recruited in the study.

The study participants were clustered into groups with respect to sex and age. Age was clustered according to Geifman and Rubin[13] as follows: young adults (19-24 years), adults (25-44 years), middle aged (45-64 years), and aged (65-79 years). Considering that there was only 1 subject of 65 years old in this study, the range for the middle-aged group was extended from age 64 to age 65.

Low fat food administration

A navel orange containing 0.21g of fat per serving[14] and weighing between 145g and 150g was used as a “low fat food”[15] in all the participants. A navel orange was chosen because it has a low glycaemic index, low fat content, and high fibre content. It is also nutrient-dense, affordable, widely available, and therefore suitable for people with diabetes. Prior to consumption, the navel orange was peeled and sliced then given to each participant. Participants were instructed to finish it within 10 minutes and then wait for 120 minutes before their second gallbladder ultrasound examination. During the waiting time, they were not allowed to consume any food or drink except water. Figure 1 illustrates the subject flow chart on the day of examination.

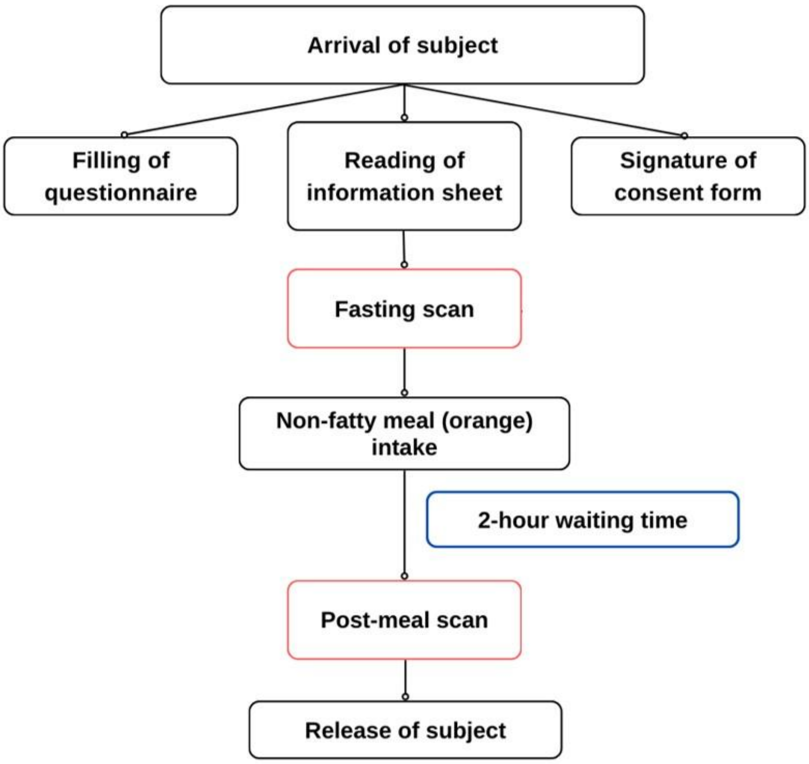

Figure 1. Illustrates the flow chart of subjects on the scanning day.

Ultrasound protocol

The gallbladder was evaluated by real-time ultrasound examination in the Ultrasound Laboratory of the institute with a Samsung RS80A ultrasound machine (Samsung Medison Co., Ltd., Seoul, Republic of Korea), equipped with a 1-7 MHz curvi-linear array transducer. Participants were instructed to fast for at least six hours prior to ultrasound examination, with their fasting state confirmed by self-declaration. To reduce inter-scanner variability, all scans were performed by a single operator. This decision was made after confirming the reliability of the measurements taken by this operator and an experienced sonographer with over 15 years of experience in abdominal ultrasound scanning. Two sets of measurements were performed; at fasting state (after six hours) and 120 minutes after consuming a navel orange to determine postprandial gallbladder volume and anterior wall thickness.

Each participant was instructed to lie on their back with their hands positioned under their head to widen the spaces between the ribs. The gallbladder was examined using a subcostal approach in supine or right anterior oblique positions with the portal vein in view as a main landmark. The largest gallbladder length and height, as well as the anterior wall thickness, were measured and recorded in the longitudinal view. The largest gallbladder width was measured from the widest diameters in the transverse view. Three measurements of length and remaining each parameter (i.e. width, height and anterior wall thickness) at the fundus and body were made, and the mean values were used for analysis as shown in Figure 2. The wall thickness (cm) was measured at the anterior wall of the gallbladder because it has a better intrinsic contrast than measuring on the posterior wall. All measurements were obtained from inner wall to inner wall. The volume of the gallbladder was then calculated using the ellipsoid formula:[16] $L \times W \times H \times \frac{\pi}{6}$, where L, W, and H is the gallbladder length (cm), width (cm), and height (cm), respectively.

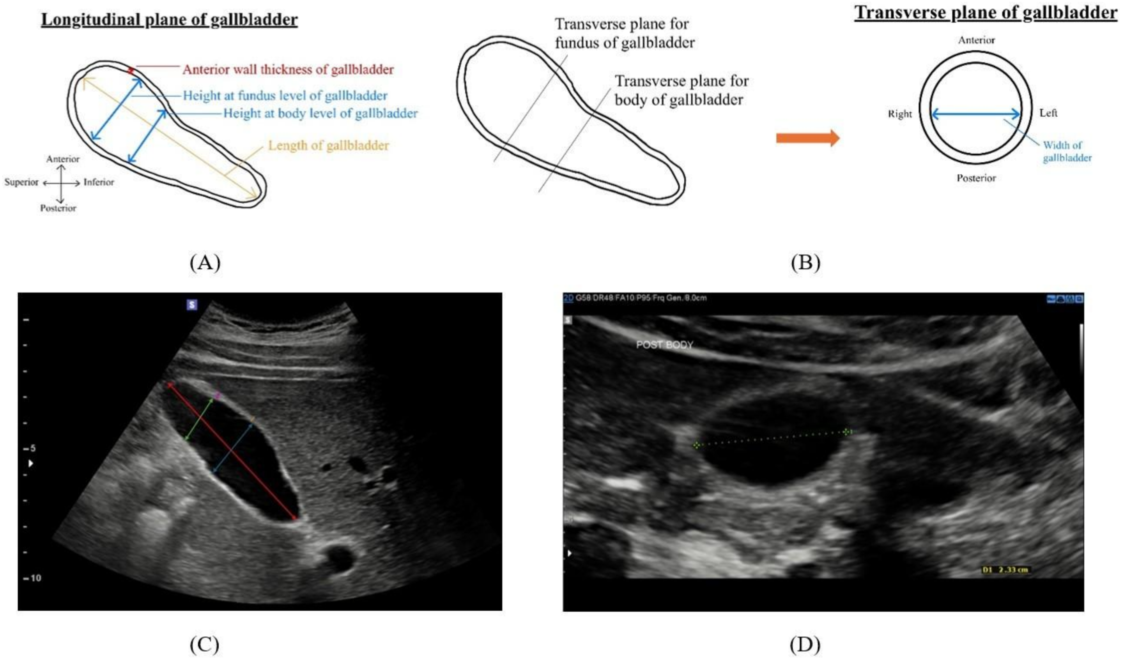

Figure 2. Illustrates the technique used to measure the dimensions of the gallbladder. Image (A) provides a schematic longitudinal view detailing the measurements of length, height, and anterior wall thickness, while image (C) displays the actual ultrasound image corresponding to these measurements. Image (B) shows a schematic longitudinal view indicating the points at which the gallbladder's width was measured in the transverse plane, and image (D) presents the actual transverse ultrasound image from which the width was measured.

Image grading

On completion of each ultrasound examination, the ultrasound image of the gallbladder in the longitudinal view was frozen, captured, and converted as JPEG files for easy review. The quality of the image from preprandial and postprandial ultrasound examinations of each participant was evaluated by a Sonographer with over 25 years of experience in performing abdominal ultrasound examinations. The Sonographer was blinded to the nature of the images (fasting or postprandial) and participants' identity. The image quality was rated based on gallbladder visualization using a five-point Likert scale (1 - very poor visualization of gallbladder; 2 - poor visualization of gallbladder; 3 - average visualization of gallbladder; 4 - good visualization of gallbladder, 5 - very good visualization of gallbladder).

Statistical analysis

To ensure the reliability of the study results, Power analysis was conducted with the G* Power software (version 3.1.9.7). Initially, the Cohen's d using the magnitude of the difference between the gallbladder volumes during preprandial and postprandial states was determined. This calculation resulted in an effect size of 0.5. A two-tailed analysis was then performed with this effect size, setting the significance level (alpha) at 0.05 and using a sample size of 66 participants. The analysis revealed a high statistical power (1- β err prob) of 0.97, indicating a very low likelihood of a Type II error. Statistical power analyses were also conducted separately for subgroups based on sex and age. The results showed a high statistical power of 0.92 for the sex-based sub-analysis and 0.80 for the age-based analysis. This indicates that the study's findings are not only statistically significant but also practically meaningful.

All continuous variables were expressed as median (minimum to maximum) unless stated otherwise. The Shapiro-Wilk test was used to determine data distribution pattern. Comparisons between two groups were performed by the Mann-Whitney U test. For comparisons among three groups, the Kruskal-Wallis test was performed and for those that reached significance level, a post hoc analysis was performed. To compare pre- and postprandial differences, the Wilcoxon signed-rank test was used.

The intra-rater and inter-rater reliability tests were conducted to ensure the consistency of the measurements using Intra-class Correlation Coefficient (ICC). ICC values below 0.5, 0.5-0.75, 0.75- 0.90 and >0.90, indicate poor, moderate, good, and excellent reliability, respectively.[17] This analysis was based on a mean-rating (k=3), absolute agreement, and 2-way mixed-effects model for intra-rater reliability and a 2-way random model for inter-rater reliability. These reliability tests were conducted on the first 10 participants before proceeding to the remaining participants. For the image quality score, all the preprandial and postprandial longitudinal images were used to determine the reproducibility of the scores. These images were scored twice to determine the reproducibility of the image quality scores.

Partial correlations test and multiple linear regression analysis while controlling for age and sex were used to assess the associations between body mass index, gallbladder volume and anterior wall thickness. All tests were two sided and p-values <0.05 were considered statistically significant. Statistical analyses were performed with the SPSS software (version 28.0; IBM, Chicago, IL).

Results

Participants characteristics

66 healthy individuals (33 men and 33 women; median age, 28 (20-65 years); median BMI, 21.25 (18.51-24.90kg/m^2) participated in this study. Males were significantly older, with a median age of 35 (21-61 years), compared to the females, who had a median age of 26 (20-65years), p=0.024. However, there was no significant difference in BMI between sexes. The median BMI for males was 21.70 (18.50-24.90kg/m^2), while for females it was 20.30 (18.50-24.90kg/m^2), p=0.715.

Reliability test

The inter-rater reliability for gallbladder volume and anterior wall thickness measurements were excellent (ICC=0.982, 95% CI 0.931-0.995) and (ICC=0.972, 95% CI 0.196-0.948), respectively. The intra-rater reliability was excellent for both gallbladder volume (ICC=0.995, 95% CI 0.980-0.999), and gallbladder anterior wall thickness measurements (ICC=0.967, 95% CI 0.809-0.992). The intra-rater reliability of ultrasound image quality grading was excellent (ICC=1.000).

Whole study cohort outcomes

There was no significant difference between preprandial and postprandial gallbladder volume (14.15cm^3 vs. 14.00cm^3, p=0.073). Similarly, there was no significant difference between preprandial and postprandial gallbladder anterior wall thickness (0.154cm vs. 0.157cm, p 0.101). Notably, all wall thickness measurements were below 0.3cm. There was no significant difference in image quality score between the preprandial and postprandial images (5 vs 5, p=1.000).

In terms of the association between variables, it was shown that both preprandial and postprandial gallbladder volumes correlated with BMI (r=0.368, p=0.003 and r=0.462, p<0.001, respectively) after controlling for sex and age. However, this association was not observed between the anterior wall thickness and both in preprandial and postprandial gallbladder volumes (r=0.087, p=0.492 and r=0.063, p=0.619, respectively) after controlling for sex and age. In fact, these outcomes were reflected in the multiple linear regression analysis that showed that BMI (R2=0.142, p=0.004) and (R2=0.264, p<0.001) was the only independent predictor of preprandial and postprandial gallbladder volumes, respectively, after controlling for age and sex. However, this relationship was not observed between the anterior wall thickness and both preprandial and postprandial gallbladder volumes (R2=0.083, p=0.424 and R2=0.080, p=0.388, respectively).

Sub-analysis between sex

There were significant differences between males and females in preprandial (p=0.004) and postprandial (p=0.001) gallbladder volumes. However, there were no significant differences between sexes in preprandial (p=0.166) and postprandial (p=0.264) gallbladder anterior wall thickness. Similarly, both preprandial and postprandial image quality scores were not significantly different between sexes (Both, p=0.722). In terms of the percentage difference between sexes, there was no significant differences in the percentage changes in the gallbladder volume (males; -4.39% vs. females; -0.97%, p= 0.937) and in anterior wall thickness [males; 0.00% vs. females; 0.00%, p= 0.697). Details are shown in Table 1.

Sub analysis among age groups

The study cohort was further clustered into age groups [young adult = 29, adult = 10, middle age = 27]. There were no significant differences among the 3 age groups in preprandial (p=0.886) and postprandial (p=0.507) gallbladder volume, preprandial (p=0.390) and postprandial (p=0.740) anterior wall thickness and preprandial (p=0.785) and postprandial (p=0.752) in image quality scores. In terms of BMI among age groups, a significant difference was only between the young adult and the adults (20.30 vs. 22.10kg/m^2, p=0.029). Details are summarized in Table 2.

Table 1 shows the gallbladder volume, anterior wall thickness and image quality score of the participants.

Variable	Category [all subjects (n=66), males (n=33), females (n=33)]	Measurements			P-value‡	P-value*	P-value§
		Pre-prandial	Postprandial	Percentage change (%)			
Gall bladder volume (cm^3)	All subjects	14.15 (5.16-29.37)	14.00 (5.78-29.19)	-4.02 (-38.74-65.35)	0.073	-	-
	Males	16.43 (5.16-29.37)	15.62 (5.78-29.19)	-4.39 (-38.74-65.35)	0.081	0.004	0.001
	Females	13.50 (6.95-19.32)	12.10 (6.74-17.97)	-0.97 (-38.34-48.04)	0.480		
Gall bladder anterior wall thickness (mm)	All subjects	0.154 (0.12-0.21)	0.157 (0.12-0.21)	0.00 (-14.00-18.99)	0.101	-	-
	Males	0.157 (0.12-0.21)	0.160 (0.12-0.21)	0.00 (-7.87-10.84)	0.166	0.166	0.264
	Females	0.150 (0.13-0.20)	0.153 (0.13-0.19)	1.00 (-14.00-18.99)	0.355		
Image quality score	All subjects	5 (4-5)	5 (4-5)	0 (-20-25)	1.000	-	-
	Males	5 (4-5)	5 (4-5)	0 (-20-25)	1.000	0.722	0.722
	Females	5 (4-5)	5 (4-5)	0 (0)	1.000		

Data presented as median (range), ‡= Wilcoxon test between pre and post prandial measurements *= Mann-Whitney test for pre-prandial measurements between males and females, §= Mann-Whitney test for post-prandial measurements between males and females.

Table 2. shows the gall bladder volume, anterior wall thickness and image quality with respect to clustered age groups.

Variables	**Category** [young adult (n=29), adult (n=10), middle aged (n= 27)]	**Pre-prandial**	**Postprandial**	**Percentage change (%)**	**P-value[¥]**	**P-value[*]**	**P-value[§]**
Body mass index (kg/m^2)	Young adult	20.30 (18.50-24.80)	20.30 (18.50-24.80)	-	-	0.011[p]	-
	Adult	22.10 (19.50-24.90)	22.10 (19.50-24.90)	-	-		
	Middle aged	21.90 (18.60-24.90)	21.90 (18.60-24.90)	-	-		
Gall bladder volume (cm^3)	Young adult	13.85 (6.02-26.30)	12.96 (5.78-23.75)	-5.67 (-38.74-48.04)	0.082	0.886	0.507
	Adult	14.60 (7.32-29.37)	16.21 (8.12-26.28)	0.33 (-29.34-26.34)	0.646		
	Middle aged	14.16 (5.16-26.86)	14.01 (6.21-29.19)	-0.97 (-31.89-65.35)	0.486		
Gall bladder anterior wall thickness (mm)	Young adult	0.153 (0.12-0.20)	0.156 (0.12-0.19)	1.09 (-14.00-18.99)	0.076	0.390	0.740
	Adult	0.158 (0.13-0.19)	0.158 (0.13-0.20)	0.00 (-3.54-3.95)	0.564		
	Middle aged	0.155 (0.12-0.21)	0.158 (0.12-0.21)	0.00 (-5.45-3.70)	0.739		
Image quality score	Young adult	5 (4-5)	5 (4-5)	0 (-20-0)	0.317	0.785	0.752
	Adult	5 (4-5)	5 (4-5)	0 (0-25)	0.317		
	Middle aged	5 (4-5)	5 (4-5)	0 (-20-25)	1.000		

Data presented as median (range), ¥= Wilcoxon test between pre and post prandial measurements *= Kruskal-Wallis test for pre-prandial measurements among age groups, p denotes that post-Hoc analysis was performed, §= Kruskal-Wallis test for postprandial measurements among age groups.

Discussion

This study evaluated the effects of a low-fat food (navel orange) on gallbladder contractility vis-à-vis gallbladder volume, anterior wall thickness and image quality as determined by ultrasonography. The results showed that there was no significant difference before and after orange intake in all sonographic measurements and image quality score. Also, in terms of different age groups and between sexes, there was no statistically significant difference in all sonographic measurements and image quality scores before and after a navel orange intake, except for gallbladder volumes between sexes in both preprandial and postprandial states.

The lack of significant change in gallbladder volume in the postprandial state in this study is in concordance with previous similar studies.[5,18] However, a magnetic resonance imaging study noted a significant decrease in gallbladder volume 65 minutes after consuming low-fat food, contrasting the results of this study. This discrepancy could be due to the different fat composition, observation time points (65 vs. 120 minutes) or imaging technique used. Moreover, this current study further showed that there was no significant difference in the gallbladder volume and image quality among various age groups like the findings in a previous study.[19] Furthermore, a regression analysis revealed that age and sex did not independently predict gallbladder volume at both preprandial and postprandial states, meaning they did not significantly influence gallbladder contractility. Instead, BMI was a significant predictor in both preprandial and postprandial states. This result agrees with the findings of Wedmann et al.[20] Gallbladder volume is typically measured to evaluate gallbladder contraction.[21] Therefore, these outcomes may suggest that the effect of orange intake on gallbladder contraction may not be significantly influenced by age or sex. However, these outcomes could be attributed to lower levels of cholecystokinin (CCK) release by foods low in fat, as CCK is a key hormone that stimulates gallbladder contraction,[22] offering a possible explanation for the above observations.

Contrastingly, despite a non-significant change in gallbladder volume between the preprandial and postprandial states in the whole cohort and in both sexes, there was a significant difference in the gallbladder volume between them in both states, with males having a significantly larger gallbladder volume than females. This outcome agrees with a previous study.[21] The probable explanation for this outcome could be that men typically have larger internal organs than women, and gallbladder volume tends to be proportional to body size.[23,24] Although not significant, the BMI for males in this study was slightly higher than that for females, and a study has shown that higher BMI correlates with higher gallbladder volume.[25] Besides, hormonal factors have also been linked to changes in the gallbladder volume.[22]

Oestrogen, for example, is known to influence gallbladder motility by reducing gallbladder contractions, leading to a more concentrated bile and consequently a smaller gallbladder volume in females.[26,27] Based on these considerations and the fact that the percentage changes in the gall bladder volumes and anterior wall thicknesses between sexes were not significantly different between them, it is postulated that the consistently smaller gallbladder volume observed in females, both before and after eating, may be attributed to these factors rather than gallbladder dysfunctionality (biliary dyskinesia) or pathology in the females.

This study showed that the thickness of the gallbladder anterior wall in the preprandial and postprandial states was less than 0.3cm, with no significant difference between the two states. Since a gallbladder wall thickness greater than 0.3 cm indicates impaired function,[28] these findings suggest that the participants in this study had normal gallbladder function, as all exhibited wall thicknesses within the normal range. Furthermore, changes in the wall thickness are typically seen as indicators of the degree of gallbladder contraction.[29] Therefore, these results indicate that consuming navel oranges may not significantly affect gallbladder contraction, as evidenced by the minimal non-significant change in wall thickness.

Given these findings, this study suggests having navel orange as an alternative to the fasting preparation before a clinical gallbladder ultrasound examination especially in the normal weight population. A minimum of 6-hour fasting beforehand is commonly required to ensure optimal image quality.[7] The main reason is to prevent gallbladder wall thickening in postprandial contracted gallbladder, which not only can hinder gallbladder visualization but can also lead to misdiagnosis, as it is regarded as an imaging feature of certain biliary diseases such as inflammatory and neoplastic pathologies.[8] Fasting preparation has a major drawback, which is fasting hypoglycaemia, especially in patients with diabetes mellitus on medication as it increases their risk of suffering.[9] Untreated hypoglycaemia can lead to life-threatening neurological consequences including seizures and brain damage.[10] Therefore, fasting preparation could be avoided especially for patients with diabetes mellitus. This study used a navel orange, with an average glycaemic index of 40,[30] making it suitable for both healthy people and patients with diabetes mellitus who are recommended to consume foods of low glycaemic index of 55 or less.[31] Moreover, since patients with diabetes mellitus have been shown to have diminished sensitivity of gallbladder smooth muscle to CCK and with fewer CCK receptors on gallbladder wall,[32] these results are likely to be applicable to this population.

Study Limitations

This study has several limitations. Firstly, the population studied was relatively homogenous, consisting only of healthy normal and overweight Chinese volunteers. A more diverse population including subjects with varying BMIs (lean and with obesity) with and without diabetes mellitus in different ethnicities would verify the clinical significance of a navel orange. Secondly, the image quality was only rated by one grader. This could possibly introduce a bias given that ultrasound is generally subjective in nature. However, the rater has over 25 years' experience in abdominal sonography, thus minimising this possible bias. Thirdly, the postprandial ultrasound was set at 120 minutes to assess gallbladder contraction. Given that the maximum gallbladder contraction among people can vary, the study outcomes may not be applicable at other time points, thus, it will be desirable in future studies to monitor the gallbladder across different time periods to completely capture the time course of gallbladder emptying. Fourthly, the study did not measure CCK levels to determine how it correlates with changes in the gallbladder volume and wall thickness as measured by ultrasound. Finally, the study only evaluated the gallbladder at both preprandial and postprandial states. It remains unknown how eating a navel orange might influence the amount of gas in the intestines, which is another reason why fasting is instituted before an abdominal ultrasound examination. Therefore, caution in the generalisation and interpretation of these results should be exercised.

Conclusion

This study showed that a navel orange has no significant effect on gallbladder contraction and gallbladder ultrasound image quality in normal weight participants. Eating a navel orange up to two hours before a gallbladder ultrasound could serve as an alternative to a full six-hour fast, as long as no other foods are consumed. This approach might be beneficial for patients with diabetes mellitus. Foods that share similar characteristics with navel oranges i.e. low glycaemic index, low fat content, high fibre content, high nutrient density, affordability, and wide availability could also potentially be used in the same way. However, caution is advised because these foods have not been specifically studied in this context. Future studies on the effect of a navel orange and any similar foods on gallbladder contractility, image quality and bowel gas involving a diverse population with varying BMIs with and without diabetes mellitus are therefore warranted.

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