Incidence and risk factors for development of cholelithiasis after bariatric surgeries in Egypt: a prospective cohort study

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Background
Although bariatric surgeries have proved their safety and effectiveness, they have many adverse effects and complications such as increasing the risk of cholelithiasis. Previous reports measured the incidence of cholelithiasis after bariatric surgeries, but further studies are needed.
The present study was designed for identifying the rate of occurrence of cholelithiasis after performance of bariatric surgeries in morbidly obese patients and exploring risk factors for postsurgical occurrence of cholelithiasis.
Patients and methods
We included 160 patients who underwent bariatric surgeries and followed them from the first day of surgery to at least 1 year. Ultrasound results of patients were collected.
We assessed the primary outcome of our study, which was detection of the incidence of occurrence of de novo cholelithiasis in the first year following the bariatric surgeries. We also assessed the secondary outcome of our study, which was determining preoperative risk factors for development of cholelithiasis.
Results
Of the included 160 patients, 13.75% (n=22) developed postoperative cholelithiasis.
The majority (90%) of the patients were asymptomatic.
Incidence of cholelithiasis was higher in patients who underwent laparoscopic sleeve gastrectomy more that patients who underwent single anastomosis sleeve ileal or laparoscopic mini-gastric bypass (P=0.049).
We found significant associations between cholelithiasis occurrence and patients age (P=0.0.037), smoking, duration of follow-up, percent decrease in weight at 6 and 12 months ($P<0.001$), diabetes (P=0.011), hypertension (P=0.039), dyslipidemia (P=0.027), obstructive sleep apnea (P=0.034), preoperative weight (P=0.023), and type of performed surgery (P=0.012).
Conclusions
The incidence of cholelithiasis after preforming bariatric surgery was higher in laparoscopic sleeve gastrectomy more than other procedures, older age of the patients, and high BMI of more than 40 kg/m^2.

Keywords:
bariatric surgery, cholelithiasis, risk factors

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Introduction

Obesity is now considered one of the most prevalent global health problems, and its incidence is markedly increased, reaching ~35–40% in men and women [1]. The association between obesity and many diseases and many complications highlighting the need for effective solutions for the management of obesity. The recent resolution of morbid obesity in person who failed in diet and physical activity trials was bariatric surgery [2]. Bariatric surgeries have many types, such as Roux-en-Y gastric bypass, single anastomosis ileal bypass, laparoscopic mini-gastric bypass, and laparoscopic sleeve gastrectomy (LSG). Among these surgical procedures, LSG was the commonest performed surgical subtype [3]. Although bariatric surgeries have proved their safety and effectiveness, they have many adverse effects and complications, such as increasing the risk of cholelithiasis. The incidence globally varied from 2 to 50% [4,5], but in some localities locally, the incidence rate is 2.3–3.5% [6]. Previous reports showed that patients who underwent LSG were less liable to have cholelithiasis as complication [7]. Moreover, after bariatric surgery, rapid weight loss was found to be strongly correlated with development of cholelithiasis [6]. Aldriweesh

et al. [8], measured the incidence of cholelithiasis after bariatric surgeries. However, further studies are needed.

The aim of our present study was to evaluate the incidence and risk factors for development of cholelithiasis in different techniques of bariatric surgery.

Patients and methods

Study design

The current prospective cohort study was done in General Surgery Hospitals, Faculty of Medicine, Zagazig University, in the period from March 2015 to May 2019. The study was approved by the local ethical committee of Faculty of Medicine, Zagazig University. We designed the study for identifying the rate of occurrence of cholelithiasis after performance of bariatric surgery in morbidly obese patients and exploring the risk factors for postoperative occurrence of cholelithiasis.

We included all patients who underwent bariatric surgeries [LSG, single anastomosis sleeve ileal (SASI) bypass, and laparoscopic mini-gastric bypass] after acquiring written confirmed consents from all patients, and the inclusion criteria of our study were patients aged from 18 to 60 years with morbid obesity who were admitted to undergo any subtype of bariatric surgeries.

The exclusion criteria were presence of preoperative cholelithiasis, gall bladder polyp as detected by abdominal ultrasound, past history of performing cholecystectomy, past history of performing previous bariatric surgeries, and any patient with missed follow-up data.

We collected and reviewed all patients who met the inclusion criteria of the study.

We followed patients from the first day of surgery to at least 1 year postoperatively.

Demographic data of patients such as age, sex, socioeconomic standard, smoking status height, weight, BMI, total weight loss percentage, and presence of comorbid conditions were collected.

We reviewed patients' laboratory results such as total bilirubin, high-density lipoprotein, low-density lipoprotein, and triglycerides.

We collected all ultrasound results of the patients.

We assessed the primary outcome of our study, which was detection of the incidence of occurrence of de novo cholelithiasis in the first year following the bariatric surgeries. We also assessed the secondary outcome of our study, which was determining the preoperative risk factors for development of cholelithiasis.

We followed our patients by serial laboratory tests and abdominal ultrasound every 6 months or if the patient developed manifestations suggestive of gallstone disease.

Statistical analysis

We analyzed the data using SAS v. 9.4 (SAS Institute Inc., Cary, North Carolina, USA). We analyzed descriptive variables as percentages and frequencies for the categorical variables, but we analyzed the numerical variables as mean and SD.

We compared risk factors between patients who developed gallstones and those who did not develop them using independent t test for continuous variables and χ^2 test for categorical variables. We used analysis of variance for comparing between total weight loss percentage and EBMIL% between patients who developed gallstones and those who did not develop them during the follow-up time. We considered a P value of less than 0.05 as significant.

Results

We included 160 patients who underwent bariatric surgeries. Patients included 108 (67.5%) females and 52 (32.5%) males, with a mean age of 32.73±9.28 years, and the median follow-up duration of most patients was 20 months (range, 10–36 months).

The performed surgical procedures were LSG in 96 (60%) patients, SASI in 42 (26.25%) patients, and laparoscopic mini-gastric bypass in 22 (13.75%) patients.

Of the included 160 patients, 13.75% (n=22) developed postoperative cholelithiasis.

The majority, ~20 (90%) patients, were asymptomatic during follow-up.

Of the patients who were symptomatic in the form of upper abdominal pain and dyspepsia, one (5%) patient underwent cholecystectomy, and one (5%) patient of the patients who presented with manifestation of calcular obstructive jaundice, which were abdominal pain, mild elevation of bilirubin, and GGT was

managed by supportive medical treatment by ursodeoxycholic acid, antispasmodic, analgesics, and antibiotic and then cholecystectomy later on after improvement of symptoms.

The incidence of cholelithiasis was higher in patients who underwent LSG more than the patients who underwent SASI or laparoscopic mini-gastric bypass (P=0.049); this is owing to the higher number of patients who underwent LSG.

No statistically significant differences were found between patients who underwent different bariatric surgical procedures and patients' age or sex, smoking, presence of diabetes, hypertension, dyslipidemia, or presence of obstructive sleep apnea (Table 1).

There is a statistically nonsignificant difference between type of surgery and either duration of follow-up, percent of weight loss at 6 or 12 months, preoperative body weight, or preoperative or postoperative BMI.

There is a statistically significant difference between type of surgery and postoperative body weight (P=0.034). On LSG comparison, the difference is significant between mini-gastric bypass and LSG groups. Within each type of surgery, there is a significant decrease in body weight and BMI postoperatively (Table 2 and Figs 1–5).

We found significant associations between cholelithiasis occurrence and patients' age (P=0.0.037), smoking, duration of follow-up, percent decrease in weight at 6 and 12 months (P<0.001), diabetes (P=0.011), hypertension (P=0.039), dyslipidemia (P=0.027), obstructive sleep apnea (P=0.034), preoperative weight (P=0.023), and type of performed surgery (P=0.012). We found no significant association between cholelithiasis and either preoperative BMI or sex (Table 3).

Table 1 Comparison between the studied groups regarding baseline characteristics

Parameters	Total (N=160) [n (%)]	Type of surgery [n (%)]			P
		LSG (N=96)	SASI (N=42)	Min-gastric bypass (N=22)	
Sex					
Female	108 (67.5)	66 (68.8)	28 (66.7)	14 (63.6)	0.891
Male	52 (32.5)	30 (31.2)	14 (33.3)	8 (36.4)	
Age (year)					
Mean±SD	32.73±9.28	32.13±9.73	32.43±9.68	35.91±5.37	0.221
Smoking (yes)	22 (13.8)	16 (16.7)	2 (4.8)	4 (18.2)	0.165
Diabetes (yes)	33 (16.4)	22 (22.9)	6 (14.3)	5 (11.7)	0.497
Dyslipidemia (yes)	40 (25)	25 (26)	7 (16.7)	8 (36.4)	0.209
Hypertension (yes)	32 (20)	24 (25)	4 (9.5)	4 (18.2)	0.096
Obstructive sleep apnea	43 (26.9)	23 (24.0)	16 (38.1)	4 (18.2)	0.149
Cholelithiasis	22 (13.8)	10 (10.4)	8 (19.0)	4 (18.2)	0.049

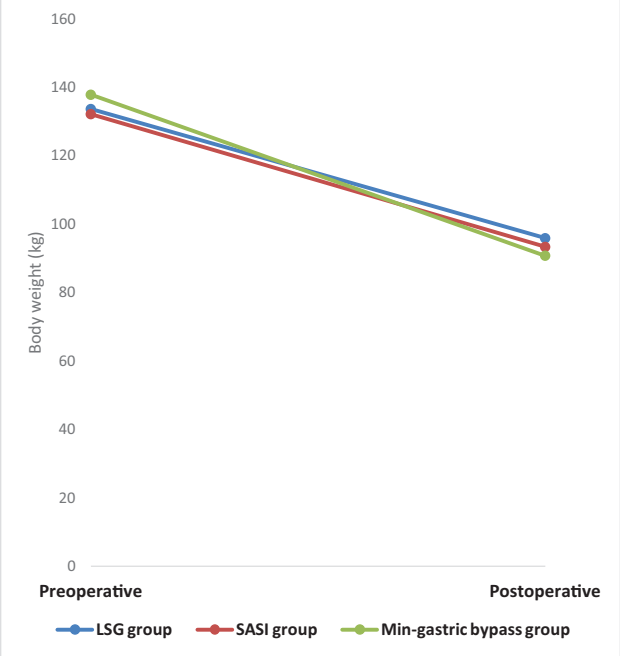
LSG, laparoscopic sleeve gastrectomy; SASI, single anastomosis sleeve ileal.

Table 2 Comparison between the studied groups regarding outcome parameters

Parameters	Type of surgery (mean±SD)			P
	LSG (N=96)	SASI (N=42)	Min-gastric bypass (N=22)	
Weight preoperatively	133.59±11.6	132.1±11.99	137.77±6.35	0.153
Weight postoperatively:	95.63±8.62	93.29±8.51	90.73±7.36	0.034*
LSD	P_1=0.136	P_2=0.251	P_3=0.015*	
P_4	<0.001**	<0.001**	<0.001**	
Pre–BMI	48.13±4.99	49.71±5.38	47.64±4.48	0.166
BMI (kg/m^2)	29.46±7.84	31.4±6.36	30.36±7.87	0.93
P_4	<0.001**	<0.001**	<0.001**	
% of weight loss at 6 months	25.5±3.13	24.88±3.01	26.2±2.53	0.431
% of weight loss at 12 months	33.05±3.53	33.0±3.73	32.43±2.97	0.108
Duration of follow-up [n (%)]				
<1 year	40 (41.7)	27 (64.3)	13 (59.1)	0.125
1–2 years	48 (50)	13 (31)	7 (31.8)	
>2 years	8 (8.3)	2 (4.8)	2 (9.1)	

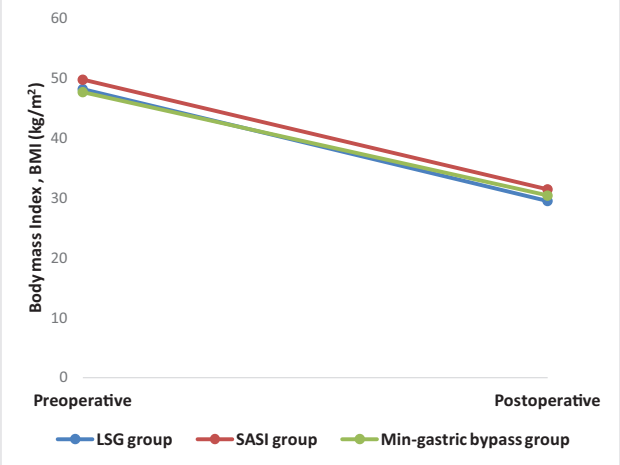
LSG, laparoscopic sleeve gastrectomy; SASI, single anastomosis sleeve ileal. *P value less than 0.05 is statistically significant. P1 the difference between LSG and SASI groups.

Figure 1



Multiple line graph showing body weight among the studied groups preoperatively and postoperatively.

Figure 2



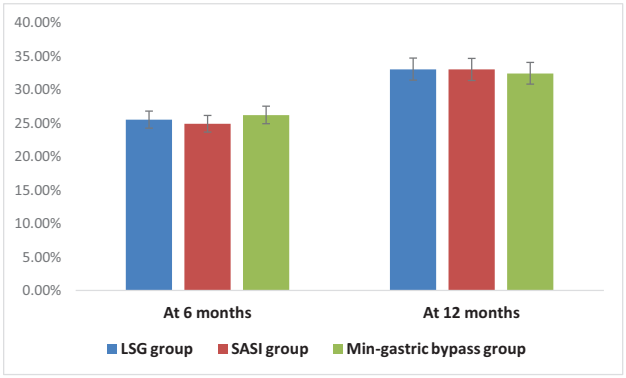
Multiple line graph showing BMI among the studied groups preoperatively and postoperatively.

Percent of weight loss at 6 months significantly increased the risk of cholelithiasis by 56.667, whereas percent of weight loss at 12 months more than 30% nonsignificantly protected against that risk ($P<0.001$) (Table 4).

Discussion

In the current study, we found that the incidence of cholelithiasis after preforming bariatric surgery was ~13.75%, and the incidence was higher in LSG

Figure 3



Multiple bar chart showing percent change in body weight at 6 and 12 months among the studied groups.

more than other procedures, which is similar to the results of Aldriweesh *et al.* [8]; although former studies reported rates of ~50%, many studies showed that the incidence rates were 2.3 and 3.5% [6,9].

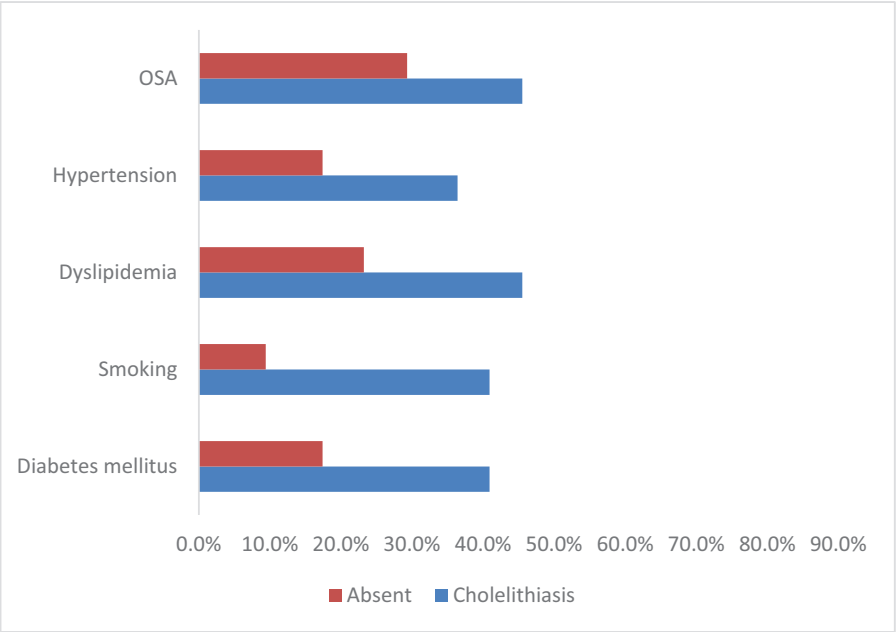
We found that sex has no role in cholelithiasis development. Similarly, many studies showed that sex has not been associated with development of cholelithiasis after performing bariatric surgeries [6,8,10], whereas previous studies reported sex as a risk factor for development of cholelithiasis [5,11,12].

Moreover, we showed that age was found to be a risk factor for development of cholelithiasis after performing bariatric surgeries, and we observed that older age of the patients has been associated with higher risks of developing cholelithiasis, which is similar to results of Aldriweesh *et al.* [8] and Alimogullari and Bulus [13], but studies about correlation with age were few.

A previously found risk factor for development of cholelithiasis after performing bariatric surgeries is higher BMI, which primarily has a vital role in the pathophysiology of development of cholelithiasis.

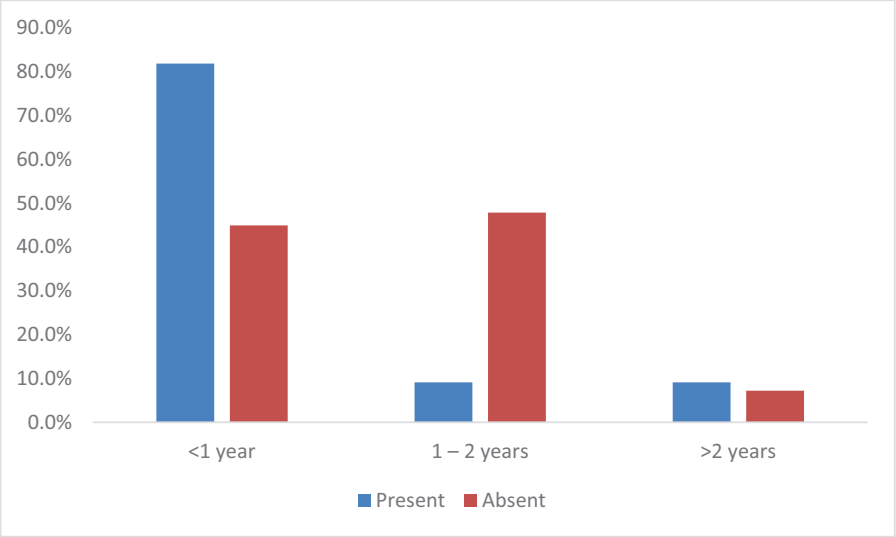
We found that high BMI of more than 40 kg/m^2 was associated with postoperative development of cholelithiasis, which was similar to results of Grover and Kothari [10], which might be attributed to that elevation of BMI is associated with higher cholesterol levels in those patients, which leads to cholelithiasis [14]. Aldriweesh *et al.* [8] have not found any associations between BMI and development of cholelithiasis, but they have not explained their findings.

Figure 4



Multiple bar chart showing relation between special habits, comorbidities, and occurrence of cholelithiasis.

Figure 5



Multiple bar chart showing relation between duration of follow-up and occurrence of cholelithiasis.

The rate of occurrence of cholelithiasis was compared with the type of performed bariatric surgery according to complexity of the performed procedure and whether the procedure is malabsorptive or restrictive.

We found a higher incidence of cholelithiasis in LSG than other bariatric procedures, which was similar to Aldriweesh *et al.* [8]; this might be owing to interfering with bile signaling, movement, and saturation [13].

Sneineh *et al.* [15] found a general cholelithiasis rate of 6.2% after bariatric surgery and found that the incidence after Roux-en-Y gastric bypass was ~14.5%, which was higher than that occurred in other performed procedures such as LSG, mini-gastric bypass, or laparoscopic gastric band (4.4, 7.5, and 4.1%, respectively).

Yardimci *et al.* [16] found that the risks of cholelithiasis development after LSG is near to the healthy population.

Table 3 Relation between incidence of cholelithiasis and the studied parameters

Parameters	Total (*N*=160) [*n* (%)]	Cholelithiasis [*n* (%)]		*P*
		Yes (*N*=22)	No (*N*=138)	
Age (mean±SD)	32.73±9.28	28.91±7.65	33.33±9.4	0.037*
Sex (female)	108 (67.5)	14 (63.6)	94 (68.1)	0.677
Smoking	22 (13.8)	9 (40.9)	13 (9.4)	<0.001**
Diabetes	33 (20.6)	9 (40.9)	24 (17.4)	0.011*
Dyslipidemia	42 (26.3)	10 (45.5)	32 (23.2)	0.027*
Hypertension	32 (20)	8 (36.4)	24 (17.4)	0.039*
Obstructive sleep apnea	43 (26.9)	10 (45.5)	33 (29.3)	0.034*
Duration of follow-up				
<1 year	80	18 (81.8)	62 (44.9)	
1–2 years	68	2 (9.1)	66 (47.8)	0.015*
>2 years	12	2 (9.1)	10 (7.2)	
Type of surgery				
LSG	96 (60)	10 (45.5)	86 (62.3)	
SASI	42 (26.3)	8 (36.4)	34 (24.6)	0.012
Mini-gastric bypass	22 (13.8)	4 (18.2)	18 (13.0)	
Baseline BMI	48.48±5.05	48.0±3.94	48.55±5.22	0.556
Preoperative weight (kg)	133.78±11.21	137.14±6.24	133.24±11.74	0.023*
% decrease in weight at 6 months>25%	32 (38.1)	20 (90.9)	12 (19.4)	<0.001*
% decrease in weight at 12 months>30%	114 (71.2)	22 (100)	92 (66.7)	0.001*

LSG, laparoscopic sleeve gastrectomy; SASI, single anastomosis sleeve ileal. **P* value less than 0.05 is statistically significant. **Highly significant.

Table 4 Multivariate analysis of predictors of cholelithiasis among the studied patients

	B	*P*	AOR	95% CI	
				Lower	Upper
% weight loss at 6 months (>25)	4.037	<0.001*	56.667	10.425	308.01
% weight loss at 12 months (<30)	–20.839	0.998	0	0.0	

AOR, adjusted odds ratio; CI, confidence interval. **P* value less than 0.05 is statistically significant.

We found an association between occurrence of cholelithiasis and presence of comorbid conditions in the patients, which is different from the results of previous studies that found no association between comorbid conditions and cholelithiasis [8,9,17]. Guzmán *et al.* [17] found that hypertension was a protective factor against occurrence of cholelithiasis. Owing to a lack of consensus regarding the association between occurrence of cholelithiasis and comorbid conditions, there was a gap in the medical knowledge in such a point.

We found an association between metabolic syndromes such as diabetes mellitus or hyperinsulinemia and occurrence of cholelithiasis, but hyperinsulinemia was shown to be a risk factor for development of cholelithiasis in some studies after bariatric surgery, similar to previous studies [12,18].

Rapid weight loss after bariatric surgery was defined as weight loss of more than 1.5 kg per week. We showed that 28.94% loss of weight was found to be associated with a higher risk for development of cholelithiasis during the first postoperative year, which is similar to the results of Alsaif *et al.* [6], Reshetnyak [19], and Lammert *et al.* [12]. Moreover, previous reports found that cholelithiasis is associated with 25–30% weight loss [20]. On the contrary, some reports found no association between degree of weight lost and occurrence of cholelithiasis [4,17]. Current management guidelines are preoperative radiological and laboratory tests for assessment of possible risks of cholelithiasis development, which if present will be better to make prophylaxis concomitant cholecystectomy [21]. However, there is still a lack of consensus regarding this topic.The mechanisms of postbariatric surgery occurrence of cholelithiasis are not clearly understood, but the following precaution may help in reducing their risks: (a) prophylaxis ursodeoxycholic acid might be used for about 6 months postoperatively to prevent cholelithiasis, but there is insufficient evidence for supporting its efficacy. (b) Avoidance of drugs that lead to biliary dysfunction such as gemfibrozil or octreotide preoperatively might help in prevention of cholelithiasis development [22]. (c) There is a need for a perioperative education

program for patients mainly done by a qualified dietitian to guide postoperative diet of the patient for reducing the risks of cholelithiasis and ensuring healthy diet. (d) Preoperative use of prophylactic cholagogue and choleretic agents might help in reducing the incidence of cholelithiasis [6,8,21].

Conclusion

In the current report, we explored and assessed the risks of cholelithiasis occurrence after bariatric surgeries, and we found that the incidence of cholelithiasis after performing bariatric surgery was ~13.75%, and the incidence was higher in LSG more than other procedures. Older age of the patients and high BMI of more than $40\,kg/m^2$ were associated with postoperative development of cholelithiasis. Sex was not related to occurrence of cholelithiasis.

We concluded that the incidence of cholelithiasis after bariatric surgery is relatively low. However, further future studies including larger samples size and longer duration of follow-up duration are needed for confirmation our findings.

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Conflicts of interest

There are no conflicts of interest.

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