

Impact of Ursodeoxycholic Acid on Gall Stone Formation Post Bariatric Surgery

Afra Amin, Yasir Arafat, Mohammed Alkhatat, Mohammad Eledreesi, Sultan Alotaibi, Omniyyah Bakheet

Taif Aramid Forces Hospital, Taif, Saudi Arabia

Email: ph.afraa.91@hotmail.com

How to cite this paper: Amin, A., Arafat, Y., Alkhatat, M., Eledreesi, M., Alotaibi, S. and Bakheet, O. (2023) Impact of Ursodeoxycholic Acid on Gall Stone Formation Post Bariatric Surgery. *Surgical Science*, 14, 240-251.

<https://doi.org/10.4236/ss.2023.143028>

Received: February 16, 2023

Accepted: March 28, 2023

Published: March 31, 2023

Copyright © 2023 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Introduction: Bariatric surgery is identified as highly effective therapy for obesity and help to loss weight that is become important public health priority because it increases the risk of condition including diabetes, cardiovascular disease, and several types of cancer whether by accomplishing mini-gastric bypass, Gastric bypass (Roux-en-Y) and sleeve gastrectomy [1] rapid weight loss increased incidence risk of gall stone formation [2]. Ursodeoxycholic acid is a bile acid which affect a reduction in cholesterol in biliary fluid primary by dispersing the cholesterol and forming a liquid-crystal phase [2], it's can play a significant role in preventing of gall stone formation. **Objective:** Study potential effect of Ursodeoxycholic acid (UDCA) on gall stone formation after bariatric surgery. **Methods:** This study Cross-sectional Trials, review of all patient underwent bariatric surgery November 2021-Jun 2022, Taif Military Hospital in the department of surgery, the sample of study will be around 143 participants or more, data collection all patient underwent bariatric surgery. **Results:** A Total of 160 patients underwent bariatric surgery in Taif Armed Forces Hospitals from 2015 to 2021. Of these, 53 were male (33.1%) and 107 were female (66.9%). only 33 patients (20.6%) received Ursodeoxycholic acid, and 127 patients (79.4%) weren't proscribed for them. However, 40 patients (25%) develop gall stone and underwent cholecystectomy, three of them were on Ursodeoxycholic acid (9%) and 37 patients weren't on Ursodeoxycholic acid (29%). which shows that Ursodeoxycholic acid remarkable reduce the risk of gall stone formation post weight reduction surgery. **Conclusion:** In conclusion, bariatric procedures come with the risk of leading to the formation of gallstones. This is especially in the stage when a patient experiences rapid loss of weight. This is why a preventive measure is necessary and UDCA have been considered for this purpose. This study has shown that patients who use UDCA are less bound to have gallstone formations.

Keywords

Ursodeoxycholic Acid, Gallstone, Bariatric Surgery

1. Introduction

Patients of Bariatric Surgery face problems related to gallstone after the Bariatric Surgery which can be effectively mitigated by using Ursodeoxycholic acid (UCDA) to dissolve the gall stone without operation. In that case, the present discussion has prophesied to conduct research upon the application of UDCA and its impact upon the dissolving of the gallstone with fewer side effects. This study has proposed an appropriate background has been evaluated in this study which encompasses the statistical rate of this application. On the other hand, a description of the research rationale, objectives and others had been proposed in this study.

1.1. Background

Bariatric surgery is identified as highly effective therapy for obesity and help to loss wight that is become important public health priority because it increases the risk of condition including diabetes, cardiovascular disease, and several types of cancer whether by accomplish mini-gastric bypass, Gastric bypass (Roux-en-Y) and sleeve gastrectomy (Sylke Haal *et al.*, 2020) [1]. Rapid weight loss increased incidence risk of gall stone formation (Francisco Heine Ferreira Machado *et al.*, 2019) [2].

Ursodeoxycholic acid is a bile acid which affects a reduction in cholesterol in biliary fluid primary by dispersing the cholesterol and forming a liquid-crystal phase (Francisco Heine Ferreira Machado *et al.*, 2019) [2], it can play a significant role in preventing of gall stone formation.

Bariatric Surgery is a weight-loss operation that encompasses the procedure of gastric bypass, sleeve gastrectomy and others (Magouliotis *et al.*, 2017) [3]. Stated that fast burn of the carollers by emphasising the metabolism procedure which causes gall stone. In order to mitigate this health issue, doctors use Ursodeoxycholic Acid to reduce the potential of both symptomatic and asymptomatic gallstones. The procedure of the rapid weight loss process is mainly conducted with the help of abdominal ultrasound. Most of the patients are being screened for up to 12 months. A recent trend in health orientation and prevalence of weight loss among individuals in Australia and the UK must be communicated here.

Intervention strategies for weight management possess underlying threats for individuals where RCTs are carried out that also agree to this fact such as reduction of weight using bariatric surgeries to have a direct impact on the development of gall stones. As per the survey, 35% - 38% of the patients who underwent bariatric surgery faced problems related to the gallstone (Della Penna *et al.*, 2019) [4]. In that case, doctors use 900 mg of Ursodeoxycholic Acid daily for 6 months

to reduce the threat of GS. As per the view of (Haal *et al.*, 2021) [5], UDCA dissolved the gall stones by solubilising cholesterol in bile. As per the study of Cholecystectomy, weight loss based on very low-calorie dieting causes gall stones which can be effectively mitigated by the use of 900 mg of Ursodeoxycholic Acid daily for 6 months (Thomas CC Boerlage *et al.*, 2017) [6].

On a similar note, inhibition of the VDLC or very-low-calorie dieting causes the increasing cholesterol within the body. Based on that, previous research for anticipating gallstone issues has found that Ursodeoxycholic Acid possesses the prospective potential for managing gallstone issues (Figure 1). The study of (Della Penna *et al.*, 2019) [4]. Outlined that, almost 50% of patients benefited from the UDCA treatment in terms of dissolving the gallstones without operation. As per the views of (Elgohary, El Azawy & Omar., 2021) [7]. laparoscopic cholecystectomy cannot be expanded as an impact of using UDCA which does not encompass any painful process. Along with this, the patients also get relief from abdominal pain after the obesity treatment. It tries to improve the effectiveness of Cholecystectomy. The doctors provide UDCA to the patients after 3 days of the operation which started to dissolve the cholesterol effectively.

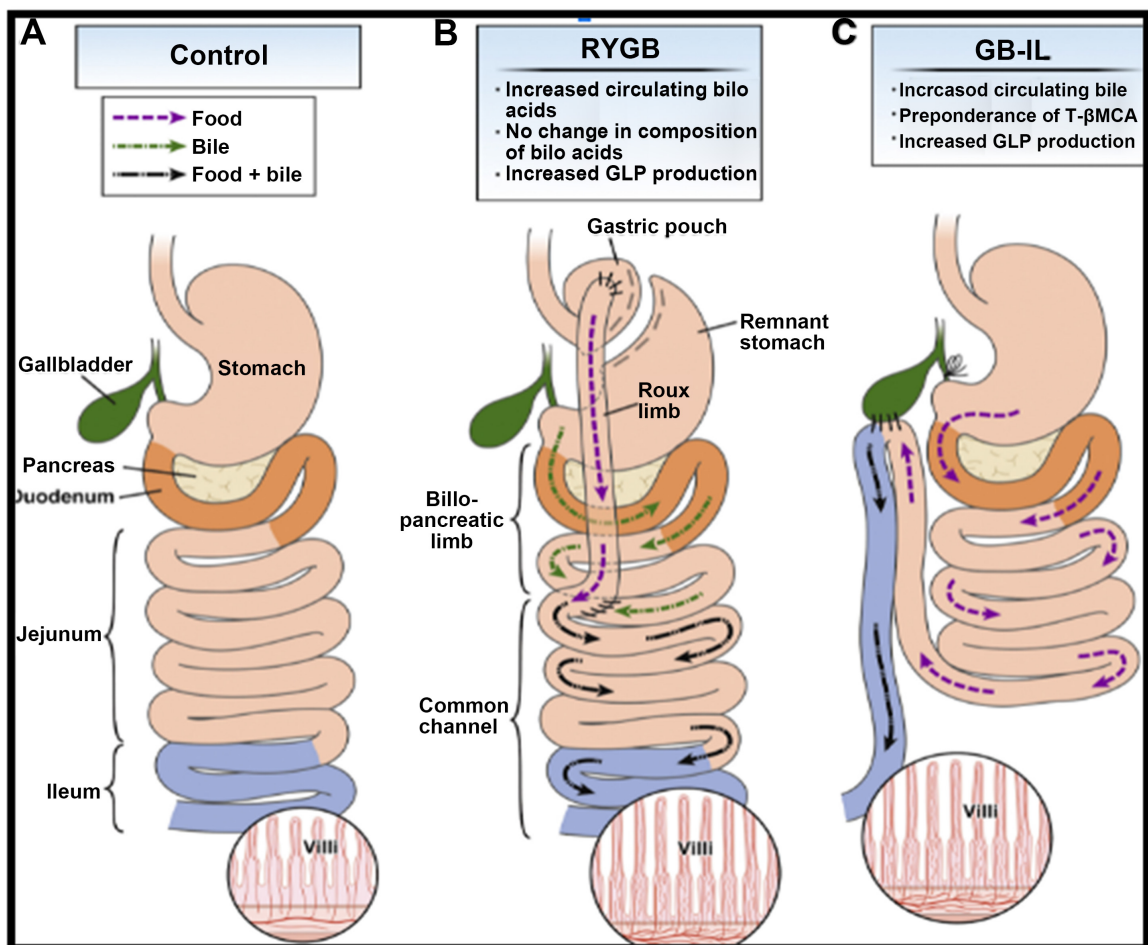


Figure 1. Importance of Ursodeoxycholic Acid to mitigate the potential of gall stone after Bariatric Surgery (source: Elgohary, El Azawy & Omar, 2021) [7].

On the other hand, improvement within the logistic regression has shown that application of the UDCA is also able to detect the asymptomatic gall-stone appropriately which improved the baseline, $p = 0.046$ (Elgohary, El Azawy & Omar, 2021) [7]. In addition, application of UDCA before sleeve gastrectomy surgery patients benefited from the low risk of symptomatic gall store with abdominal pain. Apart from this, the application of the UDCA protected the injured cholangiocytes from the toxic materials of the surgery. In this next step, the composition of UDCA stimulated the impaired biliary secretion which mitigates the mechanism of the gall stone (Coupaye *et al.*, 2017) [8]. Stated that detoxification of hydrophobic bile acids has also been simulated as an impact of applying the UDCA. At the last step, this composition inhibits the apoptosis of hepatocytes which dissolves the gall stone.

1.2. Rationale

Obesity is one of the most significant problems in this present era which affected the mental and physical health of a human being in his present era rapid trend of weight loss influenced by social media. In order to mitigate this problem, the community started to have clinical Bariatric Surgery to lose their weight fast by increasing the metabolism. However, preventive measures are required for these issues and carious medical research has been carried out for identifying prospective methods of intervention of gallstone issues for such patients. More to the context, most of the patients are affected due to the gall stone as the after-effect of this surgery. In that case, those patients also have to undergo gall stone surgery which creates the abdominal problem of the patients. As per the opinion of (Boerlage *et al.*, 2017) [9]. Doctors implement UDCA to mitigate the problem of gall stone after weight-loss surgery. It has been evidence that the application of the UDCA dissolved the bad cholesterol in bile. As an impact, it reduces the chances of gall stone operation after Bariatric Surgery. More to the context, the application of the UDCA is going to be used in the dissolution therapy in future to mitigate the potential of surgery.

2. Methods

Approval:

Ethical approval will be obtained from Al Hada Armed Forces Hospital, research center, Kingdom of Saudi Arabia, before the commencement of the study.

Ethical approval:

Human ethics clearance certificate for postgraduate dissertation study from institutional research review board, ibn Sina National Collage for Medical studies, Title of the protocol “Impact of Uresodeoxycholic acid on gall stone formation post bariatric surgery” protocol identification: 022CPP-PG-16122021.

Study design:

This study cross sectional Control Trials, review of all patients underwent bariatric surgery from 2015 till 2021, will be conducted at Taif Military Hospital in

the department of surgery.

Sample size:

The minimum sample size according to Alpha 5%, Beta 20% and Df: 5, therefore, the sample of study will be around 143 participants or more.

Inclusion criteria:

Data collection all patients underwent bariatric surgery.

Exclusion Criteria:

Exclusion patient who underwent cholecystomy before bariatric surgery, patient who already diagnosed with gall stone before bariatric surgery.

Tools for data collection: data collection sheet.

Outcome measurement: Gall stone formation—rapid weight reduction.

Statistical analysis:

- software proposed to be used: SPSS V.25 software statistical subroutines;
- Statistical subroutines(tests): Chi-Square test;
- level of significance less than 0.05.

3. Results

A Total of 160 patients underwent bariatric surgery in Taif Armed Forces Hospitals from 2015 to 2021. Of these, 53 were male (33.1%) and 107 were female (66.9%). The mean age was 34 years. Type of operation shown that laparoscopic sleeve gastrectomy done for 150 patients (93.8%), laparoscopic mini-gastric bypass done for 9 patients (5.6%) and laparoscopic roux en y gastric bypass done for single patient (0.6%). of these only 33 patients (20.6%) received Ursodeoxycholic acid, and 127 patients (79.4%) wasn't proscribed for them. Compliance of patients to duration of usage shown that 27 patients used for 5 - 6 months (81.8%), 4 patients more than 6 months (12.12%) and two patients less than 5 months (6.06%).

With the same pattern for the other variables, among the comorbidities, there was a higher prevalence of diabetes mellitus (10%), HTN was (6.2%), dyslipidemia (6.8%), psychiatric disorder (7.5%) and thyroid disorder (5.6%) on the other hand, asthma, gastritis, contraceptive show (3.1%) and prostate disorder (1.8%) no other factor was associated with the formation of gallstones other than UDCA use (**Table 1** & **Table 2**).

However, 40 patients (25%) develop gall stone and underwent cholecystectomy, three of them were on Ursodeoxycholic acid (9%) and 37 patients wasn't on Ursodeoxycholic acid (29%). which shown that Ursodeoxycholic acid remarkable reduce the risk of gall stone formation post wight reduction surgery (**Table 3**).

4. Discussion

It has been shown through research that up to 30% of patients develop gallstones following bariatric surgery (Abouzeid & Shoka, 2018) [10]. The period when weight loss accelerates is when the gallstone occurrence becomes most common.

Table 1. Characteristic of patients.

Characteristic	Variation	No. of patient (Percentage)
Age	0 - 19	12 (7.5%)
	20 - 29	97 (60.6%)
	40 - 59	51 (31.9%)
Gender	Male	53 (33.1%)
	Female	107 (66.9%)
Types of surgery	laparoscopic sleeve gastrectomy	150 (93%)
	laparoscopic mini-gastric bypass	9 (5.6%)
	laparoscopic roux en y gastric bypass	1 (0.6%)
Comorbidities	Hypertension	6.2%
	Diabetes mellitus	10%
	Dyslipidemia	6.8%
	Asthma	3.1%
	Gastritis	3.1%
	Thyroid's disorder	5.6%
	Contraceptive	3.1%
	Prostate disorder	1.8%
	Psychiatric disorder	7.5%
	Non	61.25%
Duration of usage of UDCA	1 - 2 Month	2 (1.3%)
	3 - 4 Month	3 (1.9%)
	5 - 6 Month	24 (15%)
	7 - 8 Month	1 (0.6%)
	More than 8 Month	3 (1.9%)
	Non	127 (79.4%)
US Finding postoperative	Yes	67 (41.9%)
	No	93 (58.1%)
Use of UDCA	Yes	33 (20.6%)
	No	127 (79.4%)
Develop of gall stone post bariatric surgery	Yes	43 (26.9%)
	No	117 (73.1%)

Table 2. Outcome: proportion of patients who use UDCA and who not use and develop of gall stone post bariatric surgery.

		Develop of gall stone		Total
		Yes	No	
Use of UDCA	Yes	4	29	33
	No	88	39	127

Table 3. Number of patients who underwent cholecystectomy post bariatric surgery.

	Number of patients		Percentage	
On UDCA	3		9%	
Without UDCA	37		29%	
NON	120		75%	

	N	MINIMUM	MAXIMUM	MEAN	Std. Deviation
Use of UDCA	160	1.00	2.00	1.7938	0.40588
Develop of gall stone	160	1.00	2.00	1.7313	0.44470

Use of UDCA	PEARSON CORRELATION	1	-0.170-*
	SIG (2-tailed)		0.32
	N	160	
Develop gall stone post operation	PEARSON CORRELATION	-0.170-*	
	Sig (2-tailed)	0.32	
	N	160	

*Correlation is significant at the 0.05 level (2-tailed).

It has also been suggested by studies that when weight loss was above between 1.5 - 1.7 Kg/week, it increases the risk of occurrence of gallstones. The same is the case when weight loss translates to 24% of the weight a patient had before the surgery. While there has been some research conducted in this area, this study shows the reason why gallstone post-bariatric surgery remains inconclusive and largely contentious in the research circles.

The findings in this study show that even where UDCA was used, the risk of occurrence of gallstone still exists. This borders on the efficacy of the use of UDCA. However, the results point to fewer patients who used UDCA ending up in need of cholecystectomy. This is consistent with what other studies have done in examining the prophylactic effect that UDCA has when used after losing weight suddenly and in a rapid manner. Post-Post-Laparoscopic sleeve gastrectomy (LSG) studies, while few also suggest that UDCA posts good results in the prevention of occurrence of gallstone when patients are in the phase of rapid loss of weight.

Consistent with the findings of this study that UDCA are effective, (UY *et al.* 2008) [11] concluded that UDCA are recommendable and with satisfactory efficacy levels. For UY *et al.* the study was a meta-analysis comprising five RCTs and had 521 participating patients. An even larger meta-analysis comprising 1836 patients was conducted by (Stokes *et al.* 2014) [12]. Reported that of those who were under UDCA, only 5% forming gallstones. This is as compared to the 23% who were in the control group. For this study, the conclusion was that UDCA was effective and additionally that diet that had high-fat content was also a primary modality of prevention of gallstone when in the stage of sudden and

rapid loss of weight.

These results reflect the findings of this study that show of 33 patients, only 4 developed gallstones where UDCA was used. This is as compared to 88 developing gallstones out of 127 and only 39 not forming gallstones.

The results in this study also indicate the length of use as being a factor in efficacy and require a comparison of studies on the impact of dropout. Essentially, it appeared that longer use also impacted on the formation of gallstones. This is an indicator of the UDCA's prophylactic role as shown in the 12th month following LSG in a study by (Stocker, 2003) [13]. Stone formation could be high early in the period post-surgery. However, a decrease is then experienced as it could be related to the UDCA unleashing its efficacy along the path of continued use.

However, it is also important to consider the very factor of rapid weight loss. It correlates with the formations of gallstones both in UDCA and control groups (Magouliotis *et al.*, 2017) [14]. At a stage where weight loss is not as rapid, the formation of gallstones also tends to reduce. While the explanation for this is not articulately presented, some pathophysiological findings have hypothesized some explainers. For instance, some point to the hypomotility of the gallbladder while others establish associations with the level of acidity of the prostaglandins (Uy *et al.*, 2008) [11].

The current study did not delve into the question of the safety of UDCA. However, this was covered in a different study by (Welbourn & Pournaras, 2021) [14], where only two participants showed suffering side effects with adverse symptoms. These include body aches. Diarrhea and skin rash were also observed among other effects. With the effects getting adverse, discontinuation was recommended for the affected patients. However, this study helps solidify the case for this drug especially as it appertains to its safety. Essentially, side effects would only be suffered by a negligible no of patients.

The current study also does not capture dropout and provides an account for it. However, there are indications that the drug is not particularly liked by patients. This is because of its size that comes as a large capsule. This causes swallowing difficulties minding that the patients have been through procedures that have restrictive implications (Welbourn & Pournaras, 2021) [14].

Even as the findings point to positive outcomes, it is to be noted that gallstones are prevalent following bariatric surgery. However, a method that is universally agreed upon for prevention does not exist. Notwithstanding, evidence of the use of UDCA is documented in many studies. Besides, the studies also attest to the safety of the drug. However, its use is still not widespread owing to different problems. It is still not yet known how best to select high-risk patients that require UDCA to prevent gallstones.

Essentially, use cannot be random without mapping out who needs it and who does not (Abouzeid & Shoka, 2018) [10]. There are also the risks of the side effects that are known to lead to distortion of trust between the patient and the doctor.

Essentially, this study showed how UCDA could be shown to be preventive of gallstones. However, the study has not delved into the mode of work of the UCDA for it to result in a preventive effect. There is also the fact that gallstones are related to rapid weight loss following a bariatric procedure. However, studies are yet to establish the association between the rapid loss of weight and the conventional factors such as age, gender, and physiological condition of patients (Li *et al.*, 2009) [15].

This could be because such factors could not be experimented on as they are not modifiable. There is also a degree of contradictory outcomes from the studies on various elements of UDCA usage. This all points to a developing body of knowledge with respect to this area. These are considerable areas of interest for future research to help answer some lingering questions.

While the scope of the study and its findings focus on use of UDCA, some studies have established a connection between the timing and the bariatric surgery. There are certain measures that if undertaken before the surgery could help mediate the risk of gallstone. In one such study by (Lim *et al.* 2010) [16], the case of a patient who needed bariatric and gallbladder removal was considered. In the study, it was found that the removal of the gallbladder first before undertaking the weight loss procedure helped to control the risk of developing post-bariatric complications. The importance of this study is that it shifts the focus more on prevention by getting UDCA out of the equation. With some reservations still hanging over UDCA, it is important to consider alternatives some of which such as study propounds (Moon *et al.* 2014) [17]. This particular study examined over 79,000 patients some who underwent cholecystectomy and another set of over 36,000 who underwent Roux-en-Y bypass. While a bulk of the patients were undergoing one of the procedures, 2650 were scheduled for both. It was found that of those who first had Roux-en-Y bypass stood 35 percent more chance of developing complications in comparison with those who first had cholecystectomy. To have both operations simultaneously led to the doubling of the risk of complications.

In establishing the use of UDCA, the same study found that gallstones are not supposed to have surgical redress. Surgical treatment had proven to only lead to aggravation when in fact, some patients would be healthy and untroubled even when they have gallstones. Dietary interventions after bariatric surgeries have been explained to be associated with egg-size reduction of the stomach (Dhabuwala *et al.*, 2000) [18]. It has also been linked to the reordering of the intestines that induces bypass of food on parts of it. Gallstone surgical intervention may therefore only go to further interfere with the gut system thereby broadening risks. This notwithstanding, studies have shown that patients have to discuss with their doctors about the need for operations, have extensive understanding of their gallstone and post-surgical state and the order of procedures in order to minimize risks and complications.

Concerns over UDCA use is that some studies on certain post-bariatric surgeries reported inefficacy. This means that its efficacy does not apply to all post-

bariatric surgery gallstone problems. Evidence for use of UDCA is authoritative but this does not mean it is conclusive. This is the reason why all options have to be considered especially the dietary intervention based on the knowledge that 80% of gallstones develop from cholesterol (Sreenarasimhaiah, 2004) [19]. This pre-suggests the kind of foods that should be avoided in creating concerted interventions that supplement the use of UDCA.

5. Conclusions

In conclusion, bariatric procedures come with the risk of leading to the formation of gallstones. This is especially in the stage when a patient experiences rapid loss of weight. This is why a preventive measure is necessary and UDCA have been considered for this purpose. This study has shown that patients who use UDCA are less bound to have gallstone formations. Essentially, this relates to when its prophylactic use. From the findings of the study as well as discussions along with previous studies, the length of use is a key factor as well. Use for over six weeks is associated with higher preventive power. However, sensitivities regarding the use of this drug revolve around its safety. However, the study has demonstrated in comparison with other studies, which UDCA are safe and that few people are bound to manifest adverse side effects.

It is important to note that the use of the drug remains quite limited. This is accredited to the varied research studies and findings of the use, factors around the patients, and questions regarding efficacy and risks. It is imperative that future studies focus on how to establish the risks of patients to gallstones in order to profile those who need the drug and those who do not. This is because there are some who would not develop gallstones even without using UDCA. Ascertaining those who are at risk and having a more targeted approach will add to credibility of findings that vouch for their use. This however points to the developing nature of this research area. Emergent studies are also taking varying perspectives that need to harmonize in order to build a consolidated knowledge around post-bariatric procedures. The sparseness of knowledge and its fragmented nature could be contributing to the speculation and continued uncertainty on interventions for post-bariatric surgery. However, it is reasonable that surgical interventions be avoided as most of the studies have found and this affirms the use of UDCA in the meantime.

Conflicts of Interest

The authors declare no conflicts of interest regarding publication of this paper.

References

- [1] Haal, S., Guman, M.S.S., de Brauw, L.M., van Veen, R.N., Schouten, R., Paul, F., Gerdes, V.E.A., Dijkgraaf, M.G.W. and Voermans, R.P. (2020) Ursodeoxycholic Acid for the Prevention of Symptomatic Gallstone Disease after Bariatric Surgery: Study Protocol for a Randomized Controlled Trial (UPGRADE Trial). *Trials*, **21**, Article No. 676. <https://doi.org/10.1186/s13063-020-04605-7>

- [2] Machado, F.H.F., de Castro Filho, H.F., de Albuquerque Lima Babadopulos, R.F., Rocha, H.A.L., de Carvalho Rocha, J.L. and de Moraes Filho, M.O. (2019) Ursodeoxycholic Acid in the Prevention of Gallstones in Patients Subjected to Roux-en-Y Gastric Bypass. *Acta Cirúrgica Brasileira*, **34**, e20190010000009. <https://doi.org/10.1590/s0102-865020190010000009>
- [3] Magouliotis, D.E., Tasiopoulou, V.S., Svokos, A.A., Svokos, K.A., Chatedaki, C., Sioka, E. and Zacharoulis, D. (2017) Ursodeoxycholic Acid in the Prevention of Gallstone Formation after Bariatric Surgery: An Updated Systematic Review and Meta-Analysis. *Obesity Surgery*, **27**, 3021-3030. <https://doi.org/10.1007/s11695-017-2924-y>
- [4] Penna, D.A., Lange, J., Hilbert, J., Archid, R., Königsrainer, A. and Quante, M. (2019) Ursodeoxycholic Acid for 6 Months after Bariatric Surgery Is Impacting Gallstone Associated Morbidity in Patients with Preoperative Asymptomatic Gallstones. *Obesity Surgery*, **29**, 1216-1221. <https://doi.org/10.1007/s11695-018-03651-0>
- [5] Haal, S., Guman, M.S., Boerlage, T.C., Acherman, Y.I., de Brauw, L.M., Bruin, S. and Voermans, R.P. (2021) Ursodeoxycholic Acid for the Prevention of Symptomatic Gallstone Disease after Bariatric Surgery (UPGRADE): A Multicentre, Double-Blind, Randomised, Placebo-Controlled Superiority Trial. *The Lancet Gastroenterology & Hepatology*, **6**, 993-1001. [https://doi.org/10.1016/S2468-1253\(21\)00301-0](https://doi.org/10.1016/S2468-1253(21)00301-0)
- [6] Boerlage, T.C.C., Haal, S., de Brauw, L.M., Acherman, Y.I.Z., Bruin, S., van de Laar, A.W.J.M., Moes, D.E., van Wagenveld, B.A., de Vries, C.E.E., van Veen, R., Schouten, R., Dijkgraaf, M.G., Fockens, P., Gerdes, V.E.A. and Voermans, R.P. (2017) Ursodeoxycholic Acid for the Prevention of Symptomatic Gallstone Disease after Bariatric Surgery: Statistical Analysis Plan for a Randomised Controlled Trial (UPGRADE Trial). *BMC Gastroenterology*, **17**, Article No. 164. <https://doi.org/10.1186/s12876-017-0674-x>
- [7] Elgohary, H., Azawy, E.M. and Omar, W. (2021) The Incidence of Gallstones after Bariatric Surgery and Its Association with Weight Loss. *International Journal of Surgery Open*, **33**, e100340. <https://doi.org/10.1016/j.ijso.2021.100340>
- [8] Coupaye, M., Calabrese, D., Sami, O., Msika, S. and Ledoux, S. (2017) Evaluation of Incidence of Cholelithiasis after Bariatric Surgery in Subjects Treated or Not Treated with Ursodeoxycholic Acid. *Surgery for Obesity and Related Diseases*, **13**, 681-685. <https://doi.org/10.1016/j.soard.2016.11.022>
- [9] Boerlage, T.C., Haal, S., de Brauw, L.M., Acherman, Y.I., Bruin, S., van de L.A.W. and Voermans, R.P. (2017) Ursodeoxycholic Acid for the Prevention of Symptomatic Gallstone Disease after Bariatric Surgery: Study Protocol for a Randomized Controlled Trial (UPGRADE Trial). *BMC Gastroenterology*, **17**, Article No. 164. <https://doi.org/10.1186/s12876-017-0674-x>
- [10] Abouzeid, T.A. and Shoka, A.A. (2018) Should We Prescribe Ursodeoxycholic Acid after Laparoscopic Sleeve Gastrectomy? A Two-Center Prospective Randomized Controlled Trial. *The Egyptian Journal of Surgery*, **37**, 349-354. https://doi.org/10.4103/ejs.ejs_29_18
- [11] Uy, M.C., Talingdan-Te, M.C., Espinosa, W.Z., Daez, M., Lourdes, O. and Ong, J.P. (2008) Ursodeoxycholic Acid in the Prevention of Gallstone Formation after Bariatric Surgery: A Meta-Analysis. *Obesity Surgery*, **18**, 1532-1538. <https://doi.org/10.1007/s11695-008-9587-7>
- [12] Stokes, C.S., Gluud, L.L., Casper, M. and Lammert, F. (2014) Ursodeoxycholic Acid and Diets Higher in Fat Prevent Gallbladder Stones during Weight Loss: A Meta-Analysis of Randomized Controlled Trials. *Clinical Gastroenterology and Hepatology*, **12**, 1090-1100. <https://doi.org/10.1016/j.cgh.2013.11.031>

-
- [13] Stocker, D.J. (2003) Management of the Bariatric Surgery Patient. *Endocrinology and Metabolism Clinics*, **32**, 437-457. [https://doi.org/10.1016/S0889-8529\(03\)00002-1](https://doi.org/10.1016/S0889-8529(03)00002-1)
- [14] Welbourn, R. and Pournaras, D.J. (2021) Bariatric Surgery, and Prophylaxis against Symptomatic Gallstone Disease. *The Lancet, Gastroenterology & Hepatology*, **6**, 972-973. [https://doi.org/10.1016/S2468-1253\(21\)00383-6](https://doi.org/10.1016/S2468-1253(21)00383-6)
- [15] Li, V.K.M., Pulido, N., Fajnwaks, P., Szomstein, S. and Rosenthal, R. (2009) Predictors of Gallstone Formation after Bariatric Surgery: A Multivariate Analysis of Risk Factors Comparing Gastric Bypass, Gastric Banding, and Sleeve Gastrectomy. *Surgical Endoscopy*, **23**, 1640-1644. <https://doi.org/10.1007/s00464-008-0204-6>
- [16] Lim, L.R.B., Blackburn, G.L. and Jones, D.B. (2010) Benchmarking Best Practices in Weight Loss Surgery. *Current Problems in Surgery*, **47**, 79-104. <https://doi.org/10.1067/j.cpsurg.2009.11.003>
- [17] Moon, R.C., Teixeira, A.F., DuCoin, C., Varnadore, S. and Jawad, M.A. (2014) Comparison of Cholecystectomy Cases after Roux-en-Y Gastric Bypass, Sleeve Gastrectomy, and Gastric Banding. *Surgery for Obesity and Related Diseases*, **10**, 64-68. <https://doi.org/10.1016/j.soard.2013.04.019>
- [18] Dhabuwala, A., Cannan, R.J. and Stubbs, R.S. (2000) Improvement in Co-Morbidities Following Weight Loss from Gastric Bypass Surgery. *Obesity Surgery*, **10**, 428-435. <https://doi.org/10.1381/096089200321594291>
- [19] Sreenarasimhaiah, J. (2004) Prevention, or Surgical Treatment of Gallstones in Patients Undergoing Gastric Bypass Surgery for Obesity. *Current Treatment Options in Gastroenterology*, **7**, 99-104. <https://doi.org/10.1007/s11938-004-0030-4>