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Incidence Rates of Gallstones and Kidney Stones Following Bariatric Surgery Compared to Dietary Management in Obese Individuals

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Abstract

Background: Rapid weight loss after bariatric surgery is known to increase the risk of cholelithiasis. This retrospective study aimed to compare the incidence rates of gallstone and kidney stone diseases in obese patients who underwent bariatric surgery *vs.* those who followed a diet plan.

Methods: The retrospective study included 100 obese patients aged 18 years or older with a Body Mass Index (BMI) of 35 or higher, 50 of whom underwent bariatric surgery and 50 followed a diet plan. Demographic and clinical data were collected and statistically evaluated.

Results: Women, particularly housewives, were found to undergo bariatric surgery more frequently than men ($p<0.05$). The incidence rate of new cases of gallstone disease after bariatric surgery (24%) was significantly higher than in those who followed a diet plan (4%) [($p=0.008$, OR(95%):7.58(1.59-35.95)]. The incidence rate of kidney stone disease was higher among patients who underwent surgery (20%) compared to those who followed a diet plan (6%), but the difference was not statistically significant ($p=0.07$). Additionally, a significant positive correlation was found between the incidence of gallstone disease and bariatric surgery, age, and BMI ($p<0.05$). Bariatric surgery was also significantly associated with a higher risk of developing kidney stones ($p<0.05$). No significant difference in the history and recurrence rates of gallstone and kidney stone diseases was found between the two groups ($p>0.05$).

Conclusion: Bariatric surgery may lead to a noticeable increase in the risk of developing gallstones and/or kidney stones in obese patients, particularly in older patients with a higher BMI.

Keywords: Aged, Bariatric surgery, Body Mas Index, Diet, Women, Gallstones, Incidence, Obesity, Weight loss

Introduction

Obesity, defined as a Body Mass Index (BMI) of 30 or higher, is a growing global health issue linked to numerous diseases, including hypertension, type 2 diabetes, cardiovascular conditions, gallstones, and certain cancers (1,2). It imposes substantial costs on individuals and healthcare systems through medical treatments and associated mortality. Despite significant investments in dietary and therapeutic interventions, obesity rates continue to rise, exacerbating related health complications such as gallstones (3,4).

One of the ways in which obesity increases the risk of gallstones is by raising the amount of cholesterol in the bile. When someone is overweight or obese, there is an imbalance between cholesterol, lecithin, and bile acids in the gallbladder. This disruption can impair gallbladder drainage, leading to the accumulation of cholesterol-rich bile and ultimately, the formation of gallstones (5).

While the surgical procedures are effective in achieving substantial weight loss and improving obesity-related comorbidities, they also come with certain risks, notably an increased likelihood of developing kidney stone diseases. Recent studies reveal a significant increase in the incidence of kidney stones among patients following bariatric surgery. For example, a 2023 study found that the risk of developing kidney stones nearly doubles within six months after surgery, underscoring the importance of careful monitoring and dietary management in this group (6). Additionally, another recent study reported that within the bariatric surgery population, patients with specific urinary abnormalities post-bariatric surgery, such as hyperoxaluria, elevated natriuresis (>97.75 *mmol*/24 *hr*), and reduced citrate levels (<288 *mg*/24 hr) are at higher risk for renal lithiasis. These factors collectively contribute to an increased predisposition to calcium oxalate kidney stones in certain individuals after surgery (7).

Gallstone disease affects people worldwide, with incidence rates ranging from 6 to 20%. Various factors contribute to the development of gallstones, including gender, age, BMI, metabolic syndrome, insulin resistance, non-alcoholic fatty liver, and type 2 diabetes mellitus. It's essential to be aware of these risk factors and take steps to maintain a healthy weight to reduce the risk of developing gallstones and other health problems associated with obesity (8,9). Currently, the first-line treatments for managing overweight, metabolic syndrome, and insulin resistance-all of which are obesity-related complications and significant risk factors for gallstones-involve diets, physical activity, lifestyle modification, and traditional medicine (10,11). However, in recent years, bariatric surgery has also become a popular method for treating obesity, particularly morbid obesity (12).

Unfortunately, rapid weight loss following bariatric surgery can result in cholelithiasis, which may occur due to damaged hepatic branches of the vagus nerve during surgery or disrupted nutrient passage through the gastro-duodenal tract. Gastric bypass, the most common type of weight-loss surgery, is known to increase the risk of cholelithiasis by altering enterohepatic circulation (13,14).

On the other hand, studies reveal that lifestyle and dietary modifications after surgery are crucial in reducing kidney stone incidence. Key strategies include maintaining adequate fluid intake, optimizing dietary composition to boost citrate levels and reduce oxalate intake, and emphasizing a diet rich in fruits and vegetables. These adjustments aim to decrease the supersaturation of stone-forming substances in urine, significantly lowering the risk of stone formation (15,16).

This study aims to investigate the incidence of gallstone and kidney stone diseases in obese patients who underwent bariatric surgery compared to those who followed a diet plan.

Materials and Methods

Study design and population

The data for this retrospective cohort study was obtained from obese patients who underwent bariatric surgery or followed a diet plan at a hospital in Ahvaz, Iran between 2017 and 2019. The study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences with Ethical Code: IR.AJUMS.REC.1399.713.

In this study, 100 obese patients aged 18-62 years (mean age of 35.41±10.94) were enrolled and divided into two groups based on treatment approach:1) bariatric surgery (n=50), and 2) diet therapy (n=50).

Demographic and clinical data were collected for each patient, including sex, age, BMI, history of gallstone and/or kidney stone diseases, new recurrence of gallstones or kidney stones, as well as lipid or kidney-related laboratory profiles. These data were then evaluated and compared between the two treatment groups.

Patients included in the analysis were aged 18 years or older, had a BMI greater than or equal to 35, and underwent bariatric surgery and/or followed a diet plan. Patients with underlying diseases or those taking medications known to cause kidney stones and/or gallstones, regardless of their obesity status, were excluded from the study. A nutritionist designed the diet based on dietary guidelines (17,18).

Assessments

Diagnosis of gallstone disease in a clinical setting depends on a combination of symptoms, physical examination, laboratory findings, and ultrasonography. Patients had been diagnosed with biliary colic, a repeated Right Upper Quadrant (RUQ) or epigastric pain, generally brought on by fatty meals. The pain spills over to the right shoulder or back and generally lasts 30 *min* to hours. Nausea and vomiting can also take place. If complications occur, *e.g.*, cholecystitis or choledocholithiasis, then fever and jaundice may be present. On inspection, a positive Murphy's sign, pain and interrupted inspiration on palpation of the RUQ, is a significant sign. RUQ tenderness and fever also indicate inflammation or infection. Laboratory investigations are normal in uncomplicated cases, but in cholecystitis it can demonstrate increased white blood cell counts, and in bile duct obstruction or liver involvement, increased bilirubin, alkaline phosphatase, and liver enzymes (ALT/AST). Ultrasound can detect gallstones, biliary sludge, gallbladder wall thickening, pericholecystic fluid, and a sonographic Murphy's sign, all of which are suggestive of gallstones or their complications (19).

Diagnostic criteria of kidney stones included a mixture of symptoms, physical examination, laboratory investigations, and imaging. Most patients had sudden onset of intense pain in the flank that radiated to the lower abdomen or renal colic and were usually accompanied by hematuria, nausea, vomiting, urgency, or pain with urination. Restlessness and agitation were also common. In physical examination, flank or costovertebral angle tenderness were evident. Urinalysis also detected hematuria in most cases and or crystals of calcium oxalate or uric acid. White blood cells, nitrites, or bacteria in cases with infection can be revealed. Elevated creatinine with obstruction, disturbances of electrolyte like hypercalcemia or hyperuricemia, and markers of inflammation such as WBC or CRP in cases of infection were evident. Moreover, ultrasonography is key to making the diagnosis definite. The gold standard is non-contrast abdominal and pelvic CT and can identify nearly all types of stones (20). Gallstones and kidney stones had been confirmed in our patients using an ultrasound scan.

Furthermore, the results of their lipid profile blood test measures were evaluated, which included total cholesterol, High-Density Lipoprotein (HDL), and Low-Density Lipoprotein (LDL). Based on the patients' medical records, the diet plan had been implemented and monitored over a period of 5 to 23 months, with the duration varying between patients. Based on the specific needs and underlying conditions of each patient, nutritionist recommended a combined diet plan involving the Mediterranean diet, high-protein, plant-based diet, and low-carb (keto) diets to promote long-term weight maintenance and overall health benefits, ensuring a balanced, sustainable, and personalized dietary strategy.

The types of bariatric surgeries performed in this study population were sleeve gastrectomy and or gastric bypass (Roux-en-Y Gastric Bypass).

Sample size calculation

Based on the incidence rate of Gallstones in Shubayr *et al*'s study (61.4%) (21), with a margin of error (d) of 0.1, α=0.05, and Z $\alpha/2$=1.96 for 95% for desired confidence level, the minimum sample size was calculated to be at least 91 patients using the formula: $N= Z_{\alpha/2}{}^2 p (1-p)/d2$.

Statistical analysis

In this study, normally distributed continuous variables were presented as mean±SD, while categorical variables as number (percentage). The quantitative variables were compared between two groups using an independent samples t-test. Fisher's exact test was used to evaluate the qualitative variables. Both univariable and multivariable logistic regression analysis were conducted to precisely detect the association of bariatric surgery with related risk factors. The significance level was set at $p<0.05$. All statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY, USA).

Results

Demographics and medical history

Demographics and medical history were analyzed and are presented in table 1. A significant correlation was found between treatment approach and gender, age, marital status, occupation, and BMI ($p<0.05$). The majority of women elected to undergo bariatric surgery (70%), while the majority of men chose diet therapy (56%) as their treatment approach. The mean age of patients who underwent bariatric surgery (41.92±8.32 years) was significantly higher than that of patients who received diet therapy (28.9±9.27, p=0.0001). A total of 34 and 66% of patients were respectively single and married; most unmarried patients received diet therapy while the majority of married patients preferred bariatric surgery (Table 1). Of those who underwent bariatric surgery, the majority were housewives (48%), but of those who received diet therapy, the majority were government employees (50%). There was no significant difference between the two groups regarding underlying disease (renal diseases) and history of gallstone and/or kidney stone diseases ($p>0.05$).

Paired t-tests within each group showed a significant decrease in weight post-treatment compared to pre-treatment (p=0.0001) with no significant difference between the two groups ($p>0.05$). However, the mean difference in BMI pre- and post-treatment was significantly higher in the bariatric surgery group compared to the diet therapy group (p=0.006). Nonetheless, there was no significant difference in Total Weight Loss (TWL%) and/or Excess Weight Loss (EWL%) between the two groups of patients ($p>0.05$) (Table 1).

%TWL=[(initial weight-current weight)/initial weight] ×100

%EWL=[(initial weight-current weight)/initial weight -ideal weight]×100

Moreover, there was no significant difference in recurrence rates of gallstone and kidney stone diseases between the patients who underwent bariatric surgery and those who followed a diet plan ($p>0.05$). However, the incidence rate of gallstone disease was significantly higher in patients who underwent surgery (24%) compared to those on a diet plan (4%), with an odds ratio of 7.58 (95% CI:1.59-35.95, p=0.008). The incidence rate of kidney stone disease was also higher in the surgery group (20%) compared to the diet group (6%), but this difference was not statistically significant (p=0.07).

The duration of the diet therapy ranged from 5 to 23 days, with a mean of 12.54±4.04 days. On average, 3.02±0.71 years had passed since the diet therapy, while 3.98±0.65 years had passed since the bariatric surgery. The mean time interval between the surgery and new occurrence of gallstone disease ranged from less than half a year to 3 years, with a mean of 1.05±1.02 years. This was not significantly different from the mean-time interval in patients who followed a diet plan (0.57±0.53 years, >1 year to 1 year, p=0.25). Similarly, there was no significant difference in the meantime interval between treatment and new occurrence of kidney stone disease between the two groups (1.30±1.2 years *vs*. 0.57±0.53 years, p=0.14) (Table 1).

Table 1. Comparison of demographic and clinical features between the two groups of obese patients who underwent bariatric surgery and or followed a diet plan

Variables	Obese patients underwent bariatric surgery (n=50)	Obese patients treated with diet plan (n=50)	p-value[1]
	Frequency (%) and/or mean (SD)		
Gender			
Male	15(30%)	28(56%)	0.01* OR (95%):2.97 (1.30-6.76)
Female	35(70%)	22(44%)	

Contd. table 1.

Age(18-62 year):35.41±10.94	41.92±8.32	28.9±9.27	0.0001*
Marital status			
Single	7(14%)	27(54%)	0.0001*
Married	43(86%)	23(46%)	OR (95%):7.21 (2.72-19)
Educational status			
Under diploma	5(10%)	3(6%)	
Diploma	23(46%)	28(56%)	0.54
Well-educated	22(44%)	19(38%)	
Job			
Housewife	24(48%)	10(20%)	
Self-employment	19(38%)	2(4%)	
Governmental position	7(14%)	25(50%)	0.0001*
Student	0	12(24%)	
Jobless	0	1(2%)	
Underlying disease	10(20%)	9(18%)	0.99
History of gallstone disease	7(14%)	5(10%)	0.76
History of kidney stones	3(6%)	4(8%)	0.99
Weight before treatment	118.88±20.04	114.70±18.88	0.28
Weight after treatment	87.16±17.34	86.18±16.81	
p-value (paired t test)	0.0001	0.0001	0.77
Difference of mean weight	-(31.72±10.44)	-(28.52±5.79)	0.06
Total Weight Loss (TWL%)	45.56±21.35	39.81±17.90	0.15
Excess Weight Loss (EWL%)	56.86±16.84	61.59±18.58	0.18
BMI before treatment	42.64±5.14	39.08±5.80	0.002*
BMI after treatment	31.25±4.94	29.31±5.07	0.05
p-value[2] (paired t test)	0.0001	0.0001	
Difference of mean BMI	-(11.38±3.45)	-(9.77±2.15)	0.006*
Recurrence of gallstone disease	6(12%)	5(10%)	0.99
Recurrence of kidney stone disease	3(6%)	4(8%)	0.21
Incidence or new occurrence of gallstone disease after treatment	12(24%)	2(4%)	0.008* OR (95%):7.58 (1.59-35.95)
Incidence or new occurrence of kidney stone disease after treatment	10(20%)	3(6%)	0.07

p-value[1]: intergroup comparison of variables via independent t-test and or χ^2 test.

p-value[2]: intragroup comparison of variables via a paired t-test.

*p-value < 0.05 is significant.

BMI: Body Mass Index.

The results of bivariate analysis showed no significant association between gender and history of gallstone disease (p=0.22), kidney stone history (p=1), recurrence of gallstone disease(p=0.1), recurrence of kidney stone disease (p=1), incidence or new occurrence of gallstone disease after treatment (p=0.57), incidence of kidney stone disease after treatment (p=0.55), lipid profile status before or after treatment (p>0.05), and kidney function before treatment (p=0.57). However, the mean age of patients who experienced the first occurrence of gallstone disease (43.36±8.16 years) was significantly higher than those without such an illness experience (34±11 years, p=0.003). There was no significant difference in mean age between patients with other clinical conditions mentioned above and those without these conditions (p>0.05).

Lipid profile status and kidney function

There was no significant difference in the effect

Table 2. Comparison of lipid profile status between and kidney function between two groups of obese patients underwent bariatric surgery and/or diet plan

Variables	Obese patients underwent bariatric surgery (n=50)	Obese patients underwent diet plan (n=50)	p-value
Lipid profile status before treatment			
Normal	35(70%)	37(74%)	0.82
Abnormal	15(30%)	13(26%)	
Lipid profile status after treatment			
Normal	48(96%)	47(94%)	0.99
Abnormal	2(4%)	3(6%)	
Kidney function before treatment			
Normal	48(96%)	49(98%)	0.99
Abnormal	2(4%)	2(1%)	
Kidney function after treatment			
Normal	50(100%)	50(100%)	/
Abnormal	0	0	

*p-value <0.05 is significant.

Table 3. Unadjusted and adjusted odds ratios and 95% CIs for new occurrence of gallstone disease in obese patients based on logistic regression

	Unadjusted or (95% CI)	p-value	Adjusted or (95% CI)	p-value
Bariatric surgery	7.58(1.60_35.93)	0.01*	3.78(0.68-20.76)	0.12
Gender	1.39(0.45_4.30)	0.57	/	/
Age	1.09(1.02_1.15)	0.006*	1.05(0.97-1.12)	0.18
BMI	1.12(1.01_1.23)	0.02*	1.07(0.96-1.20)	0.19
Underlying disease	0.291(0.036_2.371)	0.25	/	/
Marital status	3.556(0.748_16.912)	0.11	/	/

*p-value <0.05 is significant.

BMI: Body Mass Index.

of treatment between patients who underwent bariatric surgery and those who followed a diet plan. Specifically, 30% of bariatric surgery patients and 26% of diet plan patients had abnormal lipid profile status, but most returned to normal after treatment. Similarly, only 4 cases had abnormal kidney function before treatment, but their renal function improved after treatment with no significant difference between the two groups (p>0.05). (Table 2).

Associations of bariatric surgery with incidence of gallstone disease

Based on the results of the unadjusted logistic regression analysis, there was a significant positive correlation between the new occurrence of gallstone disease and bariatric surgery, age, and BMI (p<0.05). However, after conducting an adjusted logistic regression analysis taking into account the impact of age and BMI as independent variables included in the model, the effect of bariatric surgery on the increased risk of gallstones formation was found to be nonsignificant (Adjusted OR (95% CI): 3.78 (0.68_20.76), p=0.12) (Table 3).

Table 4. Unadjusted odds ratios and 95% cls for new occurrence of kidney stone disease in obese patients based on logistic regression

	Unadjusted or (95% CI)	p-value
Bariatric surgery	3.9(1-15.22)	0.04*
Gender	1.65(0.51-5.33)	0.4
Age	1(0.95-1.05)	0.9
BMI	1.05(0.95-1.16)	0.33
Underlying disease	0.319(0.039-2.621)	0.28
Marital status	1.184(0.337-4.167)	0.79

*p-value <0.05 is significant.

BMI: Body Mass Index.

Association of bariatric surgery with incidence of kidney stone disease

According to unadjusted logistic regression analysis, there appears to be a significant positive correlation between bariatric surgery and the incidence of kidney stone disease [OR (95% CI): 3.9(1_15.22), p=0.04]. It is important to note that there was no significant association between the new occurrence of kidney stone disease and gender, age, BMI, underlying disease, and marital status ($p<0.05$) (Table 4).

Discussion

This study found that bariatric surgery increases significantly the risk of developing both gallstones and kidney stones compared with diet therapy. Specifically, gallstones developed within about three years or less of surgery, and kidney stones developed in 0.5 to three years after surgery. Additionally, older age and higher BMI were identified as the primary risk factors for both diseases, while gender and weight loss from diet had not significant correlations. These findings are consistent with previous reports of a high incidence of gallstone formation following bariatric surgery-induced rapid weight loss in up to one-third of patients (22,23).

Numerous studies have indicated that bariatric surgery, older age, and high BMI are risk factors for developing gallstones (24-26). Additionally, some studies have suggested that rapid weight loss caused by surgery or very low-calorie diets may also increase the risk of cholelithiasis (27). However, present study did not find a significant association between gallstone formation and either gender or diet-induced weight loss. Instead, we found that bariatric surgery, older age, and high BMI are the primary risk factors for developing gallstones.

The baseline differences in gender, age, and BMI between the bariatric surgery and diet therapy groups could introduce confounding bias, as these factors may independently influence the occurrence of gallstones and kidney stones. For instance, the higher proportion of females, older age, and higher BMI in the surgery group could skew the results, making it difficult to determine whether the differences in disease occurrence are due to the treatment or these confounding variables. To address this, statistical adjustments such as multivariable analysis have been used to control for these differences and isolate the effect of the treatment on stone formation.

In this study, nutritionists chose short-term diet therapy (<23 months) for a considerable percent of patients due to various reasons based on each patient's condition, including the need for rapid improvement in health markers, such as blood sugar, cholesterol, and blood pressure, particularly for those with severe obesity or obesity-related diseases. Short-term diets can provide quick, motivating results and may be used to break unhealthy eating patterns or prepare for medical procedures like surgery. However, these diets carry risks, such as nutritional deficiencies and rebound weight gain if not followed by long-term lifestyle changes. In many cases, short-term diets are used to jumpstart weight loss, which is then followed by a more sustainable, long-term eating plan to maintain results and promote overall health (28). Nonetheless, the best approach, whether a combined strategy or long-term diet therapy-should be tailored to the patient's specific needs, health goals, preferences, and lifestyle.

Despite the positive metabolic outcomes associated with bariatric surgery (29), research suggests that individuals who undergo obesity surgeries may be at an increased risk of developing kidney stones (30,31). This increased risk can be attributed to changes in urine composition after surgery, such as low levels of urine volume or citrate and high levels of urine oxalate, which result in elevated levels of urine Calcium oxalate Supersaturation (CaOx SS) and subsequent kidney stone formation (32). Postoperative acute weight loss can lead to increased mobilization and secretion of cholesterol into bile, producing bile supersaturation and reduced gallbladder motility, both pivotal in gallstone development (33). Regarding kidney stones, bariatric surgery, particularly malabsorptive forms like Roux-en-Y gastric bypass (RYGB), also leads to fat malabsorption. This increases the concentration of free fatty acids in the intestine, which bind calcium and reduce its availability to pair with oxalate to form insoluble complexes. Consequently, freer oxalate is absorbed by the colon, leading to hyperoxaluria, a strong risk factor for calcium oxalate stone disease. Furthermore, such patients often have low urinary citrate and low urine output, which are other risk factors (34). Recognition of these pathophysiologic mechanisms underscores the necessity for long-term dietary management and metabolic follow-up following surgery.

The present study found that kidney stones appeared within a range of 0.5 to three years after surgery, which is consistent with previous reports (34,35). Furthermore, findings of the present study indicated that the risk of kidney stone formation was significantly higher in obese patients who underwent bariatric surgery compared to those who received diet therapy. However, neither gender nor age were considered as associated risk factors for kidney stone formation in this patient population. Present findings are in contrast to a recent study by Prochaska *et al* (36), which found that gender can play a significant role in urine composition and kidney stone risk after surgery. Specifically, their results suggested that women may be at a higher risk due to higher levels of urine calcium oxalate supersaturation and lower urine volume compared to men (37).

As for preventative measures, dietary models high in fiber, monounsaturated fats (such as olive oil and fish), vegetable protein, fruit, and vitamin C supplementation have been shown to be effective in reducing the risk of developing gallstones and kidney stones (37). A diet rich in fruits and vegetables can also help decrease urine citrate levels while increasing urine volume, thereby decreasing the risk of stone formation (36,37). Adequate fluid intake is also associated with a decreased risk of stone formation through its effect on urine volume (37). This study provides important insights into the risks associated with obesity treatments, specifically the increased risk of kidney stone formation after bariatric surgery. It is crucial for healthcare providers and patients to be aware of these potential risks when considering treatment options for obesity.

In addition to dietary changes and fluid intake, there are other preventative measures that can be taken to reduce the risk of kidney stone formation, such as regular physical activity (38) and reducing sodium intake (39). Patients who have undergone bariatric surgery should also receive ongoing monitoring and counseling from their healthcare provider to ensure proper care and management.

Strengths and limitations of the study

This study offers valuable insights into the relationship between obesity treatments and post-surgical complications. However, it also holds several limitations. Firstly, the retrospective nature of the study relies on incomplete medical records, and the failure to accurately record urine analysis results limits the ability to assess urine composition, which is crucial for understanding stone formation. Additionally, the retrospective design carries inherent biases (*e.g.*, selection bias, recall bias) that could impact the validity of the results. Moreover, baseline differences in gender, age, and BMI between the two treatment groups introduce confounding bias, which may affect the interpretation of the results. Additionally, only general lipid profile and kidney function data were available, while detailed urine composition tests were missing. The presence of wide 95% confidence intervals in some analyses suggests that the results may be less precise, affecting their reliability. This article gives a good comparison but does not discuss novel treatments to prevent gallstones or kidney stones after bariatric surgery.

Conclusion

Bariatric surgery leads to greater BMI reduction than diet plans, but increases the risk of gallstones and kidney stones, particularly in older and high-BMI patients. While bariatric surgery remains an effective option for managing obesity, more research is needed to assess its risks and benefits. Lifestyle changes, such as diet and exercise, should be considered as alternatives or complements to surgery. Moreover, healthcare providers must balance risks and benefits based on patient characteristics.

Ethical approval

The local institutional ethics committee of study center oversaw the proceedings and documentation; The study followed the principles outlined in the updated 2018 Declaration of Helsinki and its later amendments, and approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences with Ethical Code:IR.AJUMS.REC.1399.713.

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Conflict of Interest

There was no conflict of interest in this manuscript.

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