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ORIGINAL ARTICLE

Diarrhea after laparoscopic cholecystectomy: Associated factors and predictors

Tuan-Pin Yueh [a,b,c], Fong-Ying Chen [b], Tsyr-En Lin [c,d], Mao-Te Chuang [a,*]

[a] *Surgical Department, Saint Martin de Porres Hospital, Chiayi, Taiwan*
[b] *Department of Nursing, College of Medicine & Nursing, Hung Kuang University, Taichung, Taiwan*
[c] *Nursing Department, Saint Martin de Porres Hospital, Chiayi, Taiwan*
[d] *Department of Nursing, Chang Gung University of Science and Technology, Chiayi Campus, Chiayi, Taiwan*

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KEYWORDS
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Summary *Background:* Diarrhea is part of the postlaparoscopic cholecystectomy syndrome, but is not well defined. Published reports have ignored possible associated factors such as the preoperative excretion pattern, gastrointestinal disorders, personality disorders, the effect of drugs, unsanitary food, and high-fat diets.
Purpose: The aim of this study was to define the associated factors and predictors of postlaparoscopic cholecystectomy diarrhea (PLCD) at different time intervals after the operation and to identify the possible associated factors and predictors of PLCD. We also aimed to determine the effectiveness of a low-fat diet in these patients and to educate the patients about their diet after the operation.
Methods: Data were obtained from clinical records and preoperative interviews with patients, who were also interviewed or contacted by telephone 1 week after the operation, and then surveyed by telephone 3 months later using standardized questionnaires. A total of 125 consecutive patients who were adequately informed and who had assented to accepting a prescription of a low-fat diet after undergoing laparoscopic cholecystectomy participated in this prospective study.
Results: Thirty-eight patients (25.2%) had diarrhea 1 week after laparoscopic cholecystectomy and seven patients (5.7%) had diarrhea 3 months after laparoscopic cholecystectomy. The important predictors of PLCD at 1 week were a low-fat diet ($B = -0.177$, $p = 0.000$) and a high score on a preoperative diarrhea scale ($B = 0.311$, $p = 0.031$). There was no predictor for PLCD 3 months after laparoscopic cholecystectomy.

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

* Corresponding author. Surgical Department, Saint Martin de Porres Hospital, Number 565, Section 2, Daya Road, Chiayi, Taiwan.
E-mail address: chuang.maote@msa.hinet.net (M.-T. Chuang).

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Conclusion: We advise patients who have undergone laparoscopic cholecystectomy to follow a low-fat diet for at least 1 week to reduce the possibility of diarrhea, especially when they are ≤45 years of age, of male sex, and had a high preoperative tendency for diarrhea.

1. Introduction

Laparoscopic cholecystectomy is the gold standard treatment for symptomatic gallstones. In previously reported follow-up studies, postcholecystectomy symptoms were present in 12—47% of patients.[1,2] Between 25% and 43% of postcholecystectomy patients presented with pain and nonpain symptoms, respectively. Except for diarrhea, all the nonpain symptoms were significantly reduced postoperatively ($p < 0.05$).[3] Diarrhea is a symptom of various diseases[4,5] and is characterized by an increase in bowel movements and an increased liquidity of stools. The prevalence of diarrhea, one of the postcholecystectomy syndromes, has been reported as being between 0.9% and 35.6%.[6]

Diarrhea in many postcholecystectomy patients is multifactorial in origin.[7] Evidence about the important factors in postcholecystectomy diarrhea have so far been controversial. Postcholecystectomy diarrhea may be associated with the malabsorption of bile acid.[8—10] However, shortening of the gut transit time by accelerating passage through the colon may lead to postcholecystectomy diarrhea.[11] Postcholecystectomy diarrhea may also be due to increased amounts of bile acid presented to the large bowel.[12] Published reports of the prevalence of postcholecystectomy diarrhea have so far originated from uncontrolled or retrospective data and ignore preoperative diarrhea, the effects of drugs, possible changes in diet, and functional bowel syndromes.[13] For example, when high-fat diets were assessed, 20% of patients had postcholecystectomy diarrhea, which showed that cholecystectomy may decrease tolerance towards fatty foods.[14] Approximately 5—25% of patients receiving antibiotics may have antibiotic-associated diarrhea.[15] Diarrhea may also be related to bacterial overgrowth in the small intestine.[16] Diarrhea may be associated with ulcerative colitis,[17,18] Crohn's disease,[19,20] diverticular disease,[21,22] and an imbalance in intestinal fluid secretion.[23] Bacteria enteropathogens cause approximately 80% of travelers' diarrhea.[24] Irritable bowel syndrome may induce diarrhea,[25,26] while the presence of mood and anxiety disorders are related to irritable bowel syndrome.[27] Consequently, we suspected that postlaparoscopic cholecystectomy diarrhea (PLCD) may coexist with multiple factors; previous reports were rarely directed specifically and prospectively towards the associated factors and predictors of PLCD. We therefore designed this study to include the preoperative excretion pattern, gastrointestinal problems, personality disorders, effects of drugs, unsanitary food, and high-fat diets in order to understand the real associated factors and predictors of PLCD.

2. Methods

This prospective longitudinal study project was approved by the Research Ethics Committee (serial number 10B-011) at Saint Martin De Porres Hospital. We studied 125 patients diagnosed with gallstones and admitted to the surgical department of a regional teaching hospital in south Taiwan for laparoscopic cholecystectomy from September 2010 to August 2011. The exclusion criteria were known dumping syndrome, ulcerative colitis, stool incontinence, and treatment with antibiotics for more than 2 weeks before the operation. The procedure was clearly explained to the patients and informed consent was obtained in a preoperative interview. All the patients were educated to follow a low-fat diet for 3 months after the operation, and then they completed the questionnaires, including a basic properties questionnaire and all the standardized questionnaires. We interviewed or surveyed the patients by telephone 1 week after the operation and again 3 months later to complete the standardized questionnaires. Two patients were excluded due to their rejection of follow up.

In the prestudy phase, we consulted the Eating Behavior Questionnaire in Kristal et al[28] to complete low-fat diet assessment scales including avoidance, exclusion, modification, and replacement of fat as seasoning (15 items, total 75, ≥60 indicates a significant tendency towards a low-fat diet). We also referred to the Five-Factor Model of Personality in McCrae and Costa[29] to complete negative personality assessment scales, involving neuroticism and conscientiousness (19 items, total 95, ≥76 indicates a significant negative personality tendency). According to the definition of diarrhea as three or more bowel movements of liquid stools a day,[4,5] we developed diarrhea assessment scales (2 items, total 10, ≥8 indicates diarrhea). In addition, in terms of the studies about gastrointestinal disease causing diarrhea,[16—24] we completed assessment scales for gastrointestinal problems (6 items, total 6, ≥1 indicating gastrointestinal problems). Based on prescribed drugs which may induce diarrhea, such as drugs for hypertension, infection, gout, peptic ulcers, diabetes mellitus, insomnia, laxatives, and antibiotics,[15,30—33] we completed drug-induced diarrhea scales (9 items, total 45, ≥17 indicates a drug problem). Referring to the ingestion of food contaminated with bacteria, especially *E. coli*, as the major cause of diarrhea in patients,[24] we developed assessment scales for unsanitary food (4 items, total 20, ≥5 indicates a tendency towards unsanitary food).

Designed by a modified five-level Likert item (never = 1, seldom = 2, occasionally = 3, frequently = 4, always = 5), all the questionnaires were revised by five specialists, including a gastroenterologist, a general

Table 1 *t* test to check associated factors between patients with and without diarrhea.

	PLCD 1 week							PLCD 3 months						
	Diarrhea (n = 38)			Nondiarrhea (n = 85)			*t* test	Diarrhea (n = 9)			Nondiarrhea (n = 114)			*t* test
	Mean ± SD	Max.	Min.	Mean ± SD	Max.	Min.		Mean ± SD	Max.	Min.	Mean ± SD	Max.	Min.	
BMI	25.76 ± 5.23	44.6	17.8	25.79 ± 4.92	41.0	15.2	−0.31	24.73 ± 5.19	32.9	19.2	25.86 ± 5.00	44.6	15.2	−0.65
LFD	50.47 ± 13.62	75	19	66.74 ± 5.55	75	40	−7.10***	39.89 ± 8.74	56	29	49.42 ± 12.10	71	19	−2.31*
NP	58.63 ± 11.77	89	42	57.20 ± 7.31	86	43	0.69	61.33 ± 16.24	89	44	57.35 ± 8.11	87	42	0.73
PRLCD	3.82 ± 2.85	10	2	2.82 ± 1.70	10	2	2.00*	3.78 ± 3.07	10	2	3.08 ± 2.08	10	2	0.94
DID	16.71 ± 4.27	29	13	17.22 ± 4.70	31	11	−5.75	11.56 ± 3.97	21	9	12.57 ± 4.21	25	9	−0.70
UF	4.05 ± 0.32	6	4	4.02 ± 0.22	6	4	0.59	4.00 ± 0.00	4	4	4.13 ± 0.52	7	4	−0.75

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.
BMI = body mass index (kg/m^2); DID = drug-induced diarrhea; LFD = low-fat diet; Max. = maximum value; Min. = minimum value; NP = negative personality; PLCD = postlaparoscopic cholecystectomy diarrhea; PRLCD = prelaparoscopic cholecystectomy diarrhea; UF = unsanitary food.

surgeon, a nutritional specialist, and two senior nurses to complete the development and validation of the assessment scales. The content validity indexes of all the questionnaires ranged from 0.84 to 0.96. Among the dimensions used were the following: clarity of wording, appropriateness of the item for the target population, and relevance of the item to the underlying construct. The scale of all the items was as follows: very unsuitable =1, not suitable = 2, average = 3, suitable = 4, quite suitable = 5. For each item, the item content validity index was computed as a rating for the raters multiplied by the number of raters, divided by five multiplied by the number of specialists ($5 \times 5 = 25$). For example, an item rated as 4 by four raters and 5 by one rater would have a content validity index of 0.84 [$(4 \times 4) + (1 \times 5) \div 25 = 0.84$)] which was considered an acceptable value.

In addition to the 125 patients in the formal study, 25 patients diagnosed with gallstones and receiving laparoscopic cholecystectomy were used to test the questionnaires. Five patients were used to test the validity and to modify the questionnaires until the questions could be clearly answered; another 20 patients were used to test the questionnaires and for rechecking 2 weeks later to test the reliability (test-retest method). This showed a high correlation with $r > 0.7$. We used the Cronbach α to test the internal consistency of the prodromal and formal studies. The results were acceptable, with α between 0.76 and 0.89. Before the study, the sample size was estimated using the *a priori* sample size calculator for multiple regression. The minimum required sample size was 97 ($\alpha = 0.05$, number of predictors = 6, anticipated effect size = 0.15, desired statistical power level = 0.8). Statistical analysis was conducted using SPSS Statistical Analysis System software version 15.0 (SPSS, Chicago, IL, USA), including the two-sample *t* test, correlation, and binary logistic regression.

3. Results

Table 1 presents the results of applying the *t* test to check the differences in variables between the diarrhea and nondiarrhea groups. In the nondiarrhea group, the patients who followed a low-fat diet were superior to those in the diarrhea group 1 week postlaparoscopic cholecystectomy (PLC) ($p < 0.001$) and 3 months PLC ($p < 0.05$). In the group with diarrhea, there were more patients with a high preoperative tendency towards diarrhea than there were in the nondiarrhea group 1 week PLC ($p < 0.05$).

When applying the *t* test to check the low-fat diet variable, we found that more female patients followed a low-fat diet than male patients 1 week PLC ($p < 0.001$) and that more patients >45 years old followed a low-fat diet than patients ≤45 years both 1 week PLC ($p < 0.001$) and 3 months PLC ($p < 0.001$). We also found that more male patients had diarrhea than female patients 1 week PLC ($p < 0.001$) and that more patients aged ≤45 years had diarrhea than patients >45 years 1 week PLC ($p < 0.05$).

Thirty-one patients (25.2%) had diarrhea at 1 week PLC and seven (5.7%) had diarrhea at 3 months PLC. Six patients (4.9%) had significant negative personality traits. Ninety-one patients (73.9%) followed a low-fat diet at 1 week PLC

and 34 patients (27.4%) followed a low-fat diet at 3 months PLC. Sixty-three patients (51.2%) had drug-induced diarrhea at 1 week PLC and 26 patients had drug-induced diarrhea (22.1%) at 3 months PLC. Two patients (1.6%) consumed unsanitary food at 1 week PLC and seven patients (5.7%) consumed unsanitary food at 3 months PLC.

The associated factors analysis showed that a low-fat diet, high preoperative tendency for diarrhea, male sex, and age $\leq$45 years had significant correlations with diarrhea at 1 week PLC (Table 2) and following a low-fat diet and age $\leq$45 years had significant correlations with diarrhea at 3 months PLC (Table 3). Patients who did not follow a low-fat diet experienced more diarrhea at both 1 week PLC ($r = -0.651$, $p < 0.001$) and at 3 months PLC ($r = -0.206$, $p < 0.05$). Age $\leq$45 years ($r = 0.211$, $p < 0.05$), male sex ($r = 0.271$, $p < 0.01$), and high preoperative tendency for diarrhea ($r = 0.213$, $p < 0.05$) had significant positive correlations with diarrhea at 1 week PLC, but only age $\leq$45 years ($r = 0.187$, $p < 0.05$) had significant positive correlations with diarrhea at 3 months PLC. This suggests that a low-fat diet can decrease the tendency for diarrhea PLC.

To check the predictors for diarrhea PLC, we performed binary logistic regression (Table 4). The important predictors of diarrhea at 1 week PLC ($R^2 = 0.593$) were a low-fat diet ($B = -0.177$, $p < 0.001$) and a high preoperative tendency towards diarrhea ($B = 0.311$, $p < 0.05$), whereas there was no predictor for diarrhea at 3 months PLC.

4. Discussion

Fisher et al[6] reported that 17% of patients had troublesome diarrhea PLC. PLCD was independently associated with younger age, especially age <50 years, and postoperative food intolerance. A coexistence of age <50 years with a high body mass index and male sex was predictive of PLCD.[6] According to the definition of diarrhea as three or more bowel movements of liquid stools daily without precipitating factors,[4,5] our study showed diarrhea in 25.2% and 5.7% of patients at 1 week and at 3 months PLC, respectively. Male sex and age $\leq$45 years in patients 1 week PLC and age $\leq$45 years in patients 3 months PLC predict a tendency towards diarrhea if the patients do not follow a low-fat diet. A low-fat diet and high preoperative tendency towards diarrhea were the predictors at 1 week PLC.

Comparing the results of Fisher et al[6] with our study, age <50 years and male sex were associated with PLCD in both studies, whereas body mass index was not unanimously associated with PLCD. We suggest further study to check whether body mass index is associated with PLCD.

Lublin et al[3] noted preoperative diarrhea and postoperative diarrhea in 19% and 21% of their patients, respectively. Pain and nonpain symptoms were presented postoperatively in 25% and 45% of patients, respectively. The most common nonpain symptom PLC was indigestion (45%), fatty food intolerance (41%), heartburn (38%), and nausea (35%). All symptoms were reduced except diarrhea.[3] Laparoscopic cholecystectomy may decrease the tolerance towards fatty foods and result in diarrhea.[14] In our study, a low-fat diet has significant negative correlations with PLCD at both 1 week and 3 months PLC. The important predictor of PLCD at 1 week PLC was a low-fat diet.

In the study of Hearing et al,[13] most patients with postoperative diarrhea already had diarrhea before the operation.[13] Our study matches the result that a high preoperative tendency for diarrhea was a predictor of diarrhea 1 week after the operation and has significant positive correlations with this factor.

Another study[11] found that cholecystectomy shortens the gut transit time by accelerating passage through the colon and that these sequelae develop early and persist for at least 4 years after cholecystectomy. The post-cholecystectomy diarrhea syndrome probably represents a magnification of these colonic sequelae. From our result, the preoperative diarrhea scale is positively related to diarrhea at 1 week postoperation and could be a predictor of this, although there is no significant correlation with diarrhea at 3 months postoperation. We think there must be some adaptive mechanisms after cholecystectomy. The PLCD will continue to decrease with time after the operation.

Our study shows that patients who did not follow a low-fat diet tended to have significantly more likelihood of diarrhea at 1 week PLC and at 3 months PLC. Moreover, a low-fat diet is a predictor of PLCD at 1 week PLC, but not at 3 months PLC. All our patients were instructed to maintain

Table 2 Associated factors analysis for postlaparoscopic cholecystectomy diarrhea 1 week after the operation ($n = 123$).

	PLCD	Male sex	≤45 y	>45 y	BMI	LFD	NP	PRLCD	DID	UF
PLCD	1									
Male sex	0.271**	1								
≤45 y	0.211*	0.090	1							
>45 y	−0.100	−0.130	0.518***	1						
BMI	−0.003	−0.169	−0.073*	0.110	1					
LFD	0.651***	−0.298**	−0.264**	0.110	0.051	1				
NP	0.075	0.001	0.064	0.024	−0.134	0.045	1			
PRLCD	0.213*	−0.024	0.013	0.037	0.033	0.105	0.361***	1		
DID	−0.052	−0.078	−0.442***	0.278**	0.049	0.090	0.086	0.052	1	
UF	0.053	−0.101	0.175	−0.91	0.259**	0.092	0.063	−0.068	−0.0581	1

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.
BMI = body mass index (kg/m^2); DID = drug-induced diarrhea; LFD = low-fat diet; NP = negative personality; PLCD = postlaparoscopic cholecystectomy diarrhea; PRLCD = prelaparoscopic cholecystectomy diarrhea; UF = unsanitary food.

Table 3 Associated factors analysis for postlaparoscopic cholecystectomy diarrhea 3 months after the operation ($n = 123$).

	PLCD	Male sex	≤45 y	>45 y	BMI	LFD	NP	PRLCD	DID	UF
PLCD	1									
Male sex	0.036	1								
≤45 y	0.187 *	0.090	1							
>45 y	−0.132	−0.130	0.518***	1						
BMI	−0.059	−0.169	−0.073	0.110	1					
LFD	−0.206*	−0.177	−0.247**	0.122	0.080	1				
NP	0.117	0.123	0.064	−0.024	−0.134	0.085	1			
PRLCD	0.085	−0.024	−0.013	0.037	0.033	0.149	0.361***	1		
DID	−0.063	−0.070	−0.443***	0.288**	0.041	0.080	0.006	0.016	1	
UF	−0.068	0.009	0.093	−0.103	−0.107	0.055	0.268***	0.083	−0.052	1

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.
BMI = body mass index (kg/m^2); DID = drug-induced diarrhea; LFD = low-fat diet; NP = negative personality; PLCD = postlaparoscopic cholecystectomy diarrhea; PRLCD = prelaparoscopic cholecystectomy diarrhea; UF = unsanitary food.

a low-fat diet, but male patients and those aged ≤45 years tended to have low compliance. In the multivariate analysis, only a low-fat diet and preoperative diarrhea remained significant predictors. The effect of sex and age was confounded by the low compliance of the corresponding group. Male sex and age were not direct predictors of PLCD because the effect was cancelled out during multivariate analysis, high compliance with a low-fat diet was very important. Surgeons and nurses could use our data to counsel patients regarding postoperation expectations and advise them (especially male patients ≤45 years of age with a high preoperative tendency towards diarrhea) to follow a low-fat diet for at least 1 week to reduce the possibility of diarrhea.

There was no significant correlation between negative personality traits and PLCD at 1 week and at 3 months after the operation. Our study only looked at the personality scale before the operation because personality does not change over time. The patient with diarrhea with negative personality traits had overadjustment to the environment and affective vulnerability.[34] Personality traits and emotional state may affect the physiology of the gut,[35] and may play a role in how symptoms are interpreted and experienced, which can affect treatment.[36,37] The frequency of diarrhea in the patient with negative personality traits of conscientiousness and neuroticism was improved by focus management plans and increased by distress.[38] The patients with negative personality traits may suffer from disease-associated anxiety and be misunderstood by colleagues or friends, which could induce them to be overreactive, with affective neuroticism and vulnerability, and this could lead to an increased tendency towards diarrhea. After the operation, the disease-associated anxiety should be relieved and they should receive more psychological support from friends and families. The tendency towards diarrhea improved and this could explain why there was no significant correlation between negative personality and PLCD scales 1 week and 3 months PLC in our study. However, disease-associated anxiety and postoperative diarrhea are far beyond the scope of this work and further work is suggested.

Table 4 Binary logistic regression analysis for postlaparoscopic cholecystectomy diarrhea ($n = 123$).

Variable	PLCD at 1 week *B*	PLCD at 3 months *B*
Sex	0.756	−0.233
≤45 y	−0.177	0.789
>45 y	−0.485	−0.846
BMI	−0.005	−0.028
LFD	−0.177***	−0.078
NP	0.018	0.041
PRLCD	0.311*	0.115
DID	0.019	0.049
UF	1.638	−9.271
Constant	0.915	35.307
R^2	0.593	0.230

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.
BMI = body mass index (kg/m^2); DID = drug-induced diarrhea; LFD = low-fat diet; NP = negative personality; PLCD = postlaparoscopic cholecystectomy diarrhea; PRLCD = prelaparoscopic cholecystectomy diarrhea; UF = unsanitary food.

Literature reviews have reported that diarrhea may be caused by gastrointestinal problems.[39–41] However, none of our 123 consecutive patients had gastrointestinal problems, so this factor was not discussed further. Many studies have shown that diarrhea may be induced by drugs, such as those used to treat hypertension, infection, gout, peptic ulcers, diabetes mellitus, insomnia, or laxatives and antibiotics.[15,30,31] More than 700 types of drugs have been shown to be involved in causing diarrhea, and drug-induced diarrhea is mentioned in about 7% of all adverse drug effects.[32,33] In our study, there was no significance between drug-induced diarrhea and PLCD at 1 week and 3 months PLC.

Dupont[24] reported the ingestion of food contaminated with bacteria, especially *E. coli*, as a major cause of diarrhea. In our study, the scales for unsanitary food 1 week PLC and PLCD at 1 week, and unsanitary food 3 months PLC and PLCD at 3 months were all unrelated. We think patients will pay more attention to their diet PLC, especially if they have been educated in how to eat after the operation. The possibility of eating contaminated food is decreased, leading to a reduced tendency towards diarrhea.

According to Martin et al,[42] 136 adults who followed a low-fat diet had a preference for low-protein foods rather

than high-protein or carbohydrate foods and significantly larger increases in cravings for low-fat foods. Compared with women, men had larger decreases in appetite ratings. The prescription of diets that promoted the restriction of certain types of foods lead to reduced preferences and cravings for the foods that were targeted for restriction. In our study, we interviewed patients preoperatively and postoperatively and educated them to follow a low-fat diet. This education program will gradually change their eating habits and lead to a tendency towards no diarrhea because of the avoidance of high-fat and unsanitary foods after the operation.

5. Conclusion

PLCD continues to decrease as time passes. Male patients $\leq$45 years at 1 week PLC and patients $\leq$45 years at 3 months PLC have a tendency for diarrhea as they do not tend to follow a low-fat diet. Patients with a high tendency for preoperative diarrhea also have a tendency for diarrhea at 1 week PLC. Patients not following a low-fat diet at 1 week PLC and at 3 months PLC also a have tendency for diarrhea. The important predictors of PLCD 1 week after the operation are a low-fat diet and preoperative diarrhea tendency. There is no predictor for PLCD 3 months after the operation. We advise patients who have undergone laparoscopic cholecystectomy to follow a low-fat diet for at least 1 week to reduce the possibility of diarrhea, especially when they are of male sex and $\leq$45 years of age and have a high tendency towards preoperative diarrhea. The relation between disease-associated anxiety and postoperative diarrhea needs to be studied further.

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