










# Evaluation of morphometry in extrahepatic bile ducts in preoperative and postoperative periods in diabetic and non-diabetic patients with cholelithiasis

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## Abstract

**Aim:** The aim of this study was to find out and to compare the effect of cholecystectomy performed due to gallstone on the extrahepatic bile ducts morphometry in diabetic and non-diabetic patients.

**Material and Methods:** Three groups consisting of a total of 120 individuals. Diabetic patients with cholelithiasis (DC group) consisted of 40 person, non-diabetic patients with cholelithiasis (N-DC group) consisted of 40 person and healthy group (H group) consisted of 40 person. Laparoscopic cholecystectomy was performed on individuals with cholelithiasis.

DHC (ductus hepaticus communis) diameter was measured below hepatic canal bifurcation from mucosa to mucosa by ultrasonography. The measurements were conducted in preoperative period and in the third and sixth postoperative months.

**Results:** There were no significant differences between DC and N-DC groups in terms of DHC diameters in preoperative period and postoperative third and sixth months. In both DC and N-DC groups, DHC diameters in postoperative third and sixth months were found to show a small but statistically significant increase.

**Conclusion:** This study showed a small but statistically significant dilatation in DHC following cholecystectomy. In addition, no statistically significant difference was found between DC and N-DC groups in terms of post- cholecystectomy DHC dilatation.

**Keywords:** Diabetes mellitus; ductus hepaticus communis; extrahepatic bile ducts; gallstone; morphometry; surgery

## INTRODUCTION

The person who found that gallstones (cholelithiasis) can cause a disease was the great anatomist and physician Vesalius. Cholelithiasis is considered to be the most prevalent and most costly gastrointestinal system disease. The rate of cholelithiasis is between 10 and 15% in the Western world among adults (1, 2).

Cholelithiasis is more frequent in women when compared with men and its prevalence in women is about 2-3 times higher than men (3). An increase has been found in the incidence of cholelithiasis recently. Decrease in physical activity and changes in life style increase the risk of developing cholelithiasis. There are two types of gallstones as cholesterol and pigment stones and 70% of gallstones are cholesterol stones, while 30% are pigment stones (4). 40-60% of patients with cholelithiasis are

reported to live symptom-free. These days, laparoscopic cholecystectomy is recommended as standard cholecystectomy method (5).

Diabetes mellitus is an endocrine and metabolism disease in which carbohydrate, fat and protein metabolism break down due to absence or insufficient functioning of the insulin hormone (6). In the advanced periods of diabetes, there is an increase in the risk of complications specific for this disease such as neuropathy, retinopathy, renal failure and atherosclerosis. Diabetes mellitus causes pathological changes in biochemical, morphological and functional characteristics of tissue and organs (6, 7).

It has been reported that ultrasonography is the primary imaging tool with a high specificity and sensitivity to assess the gallstones and the enlargement in intrahepatic and extrahepatic bile ducts (8). As a non-

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invasive imaging method that does not use radiation, ultrasonography can be used fast, repeatedly, with low cost and safety (9). The significance of ultrasonographic assessment of bile ducts in pre-operative period to prevent the possible complications during cholecystectomy is being emphasized (10). It has been claimed that the measurement of choledochus diameter in post-operative period can be useful for distinguishing patients with permanently enlarged canals from patients who have newly enlarged canals (11). A short time after it has begun to be used, ultrasonography has been accepted as the most sensitive measurement method of ductus hepaticus communis (DHC) and choledochus canal diameter. In a great number of retrospective studies, it has been stated that although there is not an obvious increase in DHC diameter in most of the patients after cholecystectomy, they have been found to have a tendency for a small amount of DHC dilatation (12, 13, 14).

The purpose of this study is to find out how cholecystectomy performed for cholelithiasis influences the extrahepatic bile ducts morphometry of diabetic patients with cholelithiasis (DC) and non-diabetic patients with cholelithiasis (N-DC)

## MATERIALS AND METHODS

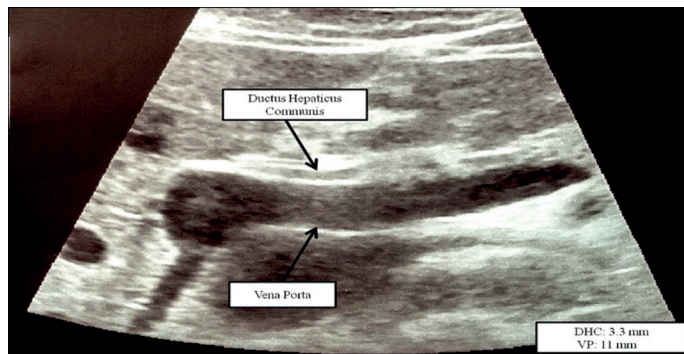
Our prospectively designed study was started after ethical board approval was taken. Besides, informed consent was obtained from the participants in the study. One hundred and twenty individuals consisting of 3 groups were assessed. The first group was formed with 20 male – 20 female diabetic individuals with cholelithiasis (DC), the second group was formed with 20 male – 20 female non-diabetic individuals with cholelithiasis (N-DC) and the third group was formed with 20 male – 20 female healthy individuals (H). Individuals who did not have an existing liver and pancreas disease and history, those who had not received any bile duct surgery or intervention previously and those who did not have gallstones in bile ducts were included in groups with cholelithiasis (DC and N-DC).

The individuals in the healthy group were chosen from individuals who had not undergone liver, gallbladder and bile duct and pancreas diseases and who had not undergone abdominal surgery before.

Laparoscopic cholecystectomy was performed on the individuals with cholelithiasis by different surgeons. All ultrasonographic examinations were performed by a single radiologist who participated in the study, with the same ultrasound device.

The morphometry of the extrahepatic biliary tracts of the individuals in DC and N-DC groups were examined three times: in the preoperative period, in the postoperative third and sixth months with ultrasonography, while the morphometry of the extrahepatic biliary tracts of the individuals in the healthy group was examined once.

Morphometrically, DHC diameter of the individuals in DC and N-DC group and H group was measured from mucosa to mucosa below the DHC bifurcation (Figure 1). All the measurements were performed while the patient was holding breath in deep inspiration for the measurements not to be influenced. Toshiba Aplio 500 ultrasonography device was used in the measurements.



**Figure 1.** DHC diameter measurement with ultrasonography

Biostatistical Analysis: Kolmogorov Smirnov test was used to analyze normality distribution of the data and the data were not found to be normally distributed. Mann Whitney U test was used to analyze whether there were statistical differences between individuals with cholelithiasis (DC and N-DC) and individuals in H group in terms of age, weight, height and Body Mass Index (BMI) values. Kruskal Wallis H Test was conducted to analyze whether there were statistical differences between age, weight, height and BMI values of all groups. Spearman's rho correlation was conducted on all groups to analyze the correlation between preoperative DHC and age, weight, height and BMI. Kruskal Wallis Test was conducted to compare the DHC diameter values of DC, N-DC and H groups in preoperative period. Mann Whitney U test was conducted to compare the pre-operative and postoperative third month and postoperative third month and postoperative sixth month DHC diameter values of DC and N-DC groups. Mann Whitney U test was conducted to compare the preoperative and postoperative (third and sixth month) DHC diameter values of DC and N-DC groups.

Median, minimum (min) and maximum (max) values were given to the data that were not normally distributed.  $p < 0.05$  values were considered as statistically significant. IBM SPSS Statistics 22.0 for Windows program was used for statistical analyses.

## RESULTS

The age range of the individuals who participated in the study was 17 to 85 years. Median age of all the individuals was found as 47.5 years. Ages of the individuals with cholelithiasis were higher when compared with the H group and statistically significant difference was found between the groups in terms of age ( $p < 0.05$ ), while no statistically significant difference was found in terms of weight, height and BMI (Table 1).

**Table 1. Age, weight, height and BMI median (min-max) values of individuals with cholelithiasis and healthy individuals**

|                                 | Age (year) | Weight (kg)   | Height (cm)   | BMI               |
|---------------------------------|------------|---------------|---------------|-------------------|
| Individuals with cholelithiasis | 52 (18-85) | 77.5 (55-115) | 166 (150-185) | 27.4 (20.2-44.9)  |
| Healthy individuals             | 39 (17-79) | 72.5 (49-105) | 170 (150-187) | 25.75 (17.7-41.6) |
| p value                         | <0.001     | 0.497         | 0.102         | 0.132             |

(BMI: Body Mass Index)

Kruskal Wallis H Test was conducted on the data to find out whether there were differences between age, weight, height, and BMI values of the groups. As a result of the analysis, statistically significant difference was found between groups in terms of age, weight, and BMI values ( $p < 0.05$ ), (Table 2).

The correlation between preoperative DHC diameters and age, weight, height and BMI was analyzed in all groups. DHC diameters were found to have a positive weak correlation with age in all groups (Table 3).

When preoperative DHC diameters of the three groups (DC, N-DC, H) were compared, no statistically significant difference was found ( $p > 0.05$ ), (Table 4).

In postoperative third month measurements, DHC diameter values of 63 patients were found to be higher when compared with the preoperative values, while the remaining 17 patients were found to have equal preoperative values. In postoperative sixth month measurements, DHC diameter values of 73 patients were found to be higher when compared with the preoperative values, while the remaining 7 patients were found to have equal preoperative values. Besides, postoperative sixth month DHC diameter values were found to be higher than postoperative third month measurements. In DC and N-DC groups, statistical analysis showed significant difference between preoperative and postoperative third month and postoperative third month and postoperative sixth month DHC diameters ( $p < 0.05$ ), (Table 5).

**Table 2. Age, weight, height and BMI median (min-max) values of DC, N-DC and H groups**

| Groups  | Gender | Age (year)   | Weight (kg)   | Height (cm)     | BMI                |
|---------|--------|--------------|---------------|-----------------|--------------------|
| DC      | Male   | 58 (30-82)   | 85.5 (72-100) | 173.5 (160-182) | 28.85 (25.2-32.87) |
|         | Female | 52.5 (30-80) | 83 (53-115)   | 160 (150-173)   | 32.2 (20.2-44.9)   |
| N-DC    | Male   | 49.5 (18-85) | 72.5 (60-85)  | 170 (160-185)   | 25 (20.4-29)       |
|         | Female | 46.5 (25-79) | 65 (55-85)    | 162.5 (150-172) | 24.3 (20.9-30.4)   |
| H       | Male   | 39 (18-79)   | 72.5 (55-105) | 175 (160-187)   | 24.25 (17.9-34.2)  |
|         | Female | 41 (17-57)   | 72.5 (49-100) | 162 (150-173)   | 27.4 (17.7-41.6)   |
| p value |        | <0.001       | <0.001        | 0.257           | <0.001             |

(BMI: Body Mass Index, DC: Diabetic patients with cholelithiasis, N-DC: Non-diabetic patients with cholelithiasis, H: Healthy group)

**Table 3. Analysis results of the correlation between preoperative DHC diameters and age, weight, height and BMI in all groups**

| Groups | Parameter    | Spearman's rho correlation | Age    | Weight | Height | BMI    |
|--------|--------------|----------------------------|--------|--------|--------|--------|
| DC     | DHC diameter | r                          | 0.361  | -0.131 | -0.033 | -0.097 |
|        |              | p                          | 0.022  | 0.420  | 0.841  | 0.550  |
| N-DC   | DHC diameter | r                          | 0.589  | 0.013  | -0.242 | 0.163  |
|        |              | p                          | <0.001 | 0.938  | 0.138  | 0.320  |
| H      | DHC diameter | r                          | 0.403  | 0.138  | -0.005 | 0.153  |
|        |              | p                          | 0.010  | 0.395  | 0.977  | 0.347  |

(DHC: Ductus Hepaticus Communis, BMI: Body Mass Index, DC: Diabetic patients with cholelithiasis, N-DC: Non-diabetic patients with cholelithiasis, H: Healthy group)

**Table 4. Median (min-max) values of preoperative DHC diameters of DC, N-DC and H groups**

| Groups  | Gender | Preoperative DHC diameter (mm) |
|---------|--------|--------------------------------|
| DC      | Male   | 3 (1.6-4.1)                    |
|         | Female | 3 (1.8-5)                      |
| N-DC    | Male   | 2.8 (1.5-4.5)                  |
|         | Female | 2.95 (1.6-4.4)                 |
| H       | Male   | 2.9 (1.4-5.5)                  |
|         | Female | 2.35 (1.5-4.5)                 |
| p value |        | 0.799                          |

(DHC: Ductus Hepaticus Communis, DC: Diabetic patients with cholelithiasis, N-DC: Non-diabetic patients with cholelithiasis, H: Healthy group)

**Table 5. Preoperative and postoperative 3rd month and postoperative 3rd month and postoperative 6th month DHC diameters comparison of DC and N-DC groups (p values)**

| Groups | Preoperative / postoperative 3rd month | Postoperative 3rd month / postoperative 6th month |
|--------|--|---|
| DC     | <0.001                                 | <0.001  |
| N-DC   | <0.001                                 | <0.001  |

(DHC: Ductus Hepaticus Communis, DC: Diabetic patients with cholelithiasis, N-DC: Non-diabetic patients with cholelithiasis)

We compared DC and N-DC groups to see the effects of diabetes mellitus on preoperative and postoperative bile duct morphometry. No statistically significant difference was found between DC and N-DC groups in terms of preoperative, postoperative third month and postoperative sixth month DHC diameters ( $p>0.05$ ), (Table 6).

**Table 6. Median (min-max) values of preoperative, postoperative 3rd month and postoperative 6th month DHC diameters of DC and N-DC groups**

| Groups  | DHC diameter (mm) |                         |                         |
|---------|-------------------|-------------------------|-------------------------|
|         | Preoperative      | Postoperative 3rd month | Postoperative 6th month |
| DC      | 3 (1.6-5)         | 3.3 (1.6-5.6)           | 3.6 (1.7-5.6)           |
| N-DC    | 2.95 (1.5-4.5)    | 3.25 (1.5-4.6)          | 3.35 (1.5-4.9)          |
| p value | 0.686             | 0.654                   | 0.679                   |

(DHC: Ductus Hepaticus Communis, DC: Diabetic patients with cholelithiasis, N-DC: Non-diabetic patients with cholelithiasis)

## DISCUSSION

Gallstones (cholelithiasis) are considered as a global health problem in the world. Approximately 30,000,000 people have gallstones in the USA and 750,000 cholecystectomy are performed each year (15).

Gallstone prevalence increases with age (16). In our study, the ages of individuals with cholelithiasis were found to be significantly higher when compared with healthy individuals.

Gallstones are reported to be seen more frequently in obese women (17). According to the results of our study, although individuals with cholelithiasis were found to have higher weight and BMI values, no statistically significant difference was found between individuals with cholelithiasis and healthy individuals in terms of weight and BMI.

It has been reported in literature that individuals with cholelithiasis and diabetes have higher BMI values than the control group. Obesity, high BMI and diabetes mellitus are risk factors for gallstone formation (18, 19). Our results showed that ages, weights and BMI values of individuals in DC group were significantly higher than those of N-DC and H group.

A great number of studies have been conducted assessing the correlation between characteristic features such as age, weight, height and BMI and extrahepatic bile ducts. In Kaude's study, while choledochus diameter was 2.8 mm in individuals 20 years old and younger, it was 4.1 mm in individuals 71 years old and older (20). Admassie et al. found positive correlation between choledochus canal diameter and weight, but no correlation was found with height (21). Reinus et al. did not find such a correlation between choledochus diameter and weight (22). According to the correlation analysis results we conducted, a positive weak correlation was found between DHC diameter and age in three groups (DC, N-DC and H); while no significant correlation was found between DHC diameter and weight, height and BMI. In addition, when pre-operative DHC diameters of DC, N-DC and H groups were compared, no statistically significant difference was found.

The theory of compensatory dilatation development after cholecystectomy was put forward by Oddi for the first time. Since then, it has been the subject of long and important discussions in radiographic, sonographic and surgical literature and it has been concluded that there is a need for more advanced research (14, 23). More recent studies with long term follow up have reported minimal increase in bile duct diameters after cholecystectomy (24). In a study researching the changes in bile duct after laparoscopic cholecystectomy, bile duct diameter was measured right below DHC bifurcation, at the intersection level of hepatic artery and at the level of pancreas head. Bile duct average diameters measured 24 hours after surgery and postoperative day 7 were not found to be statistically significantly different when compared with preoperative measurements. Three months after cholecystectomy, the

bile duct was found to be significantly wider at each of the three points ( $p < 0.05$ ). Six months after cholecystectomy, bile duct was found to be wider at proximal and distal part when compared with preoperative measurements. In this study, mild but statistically significant dilatation tendency was found in bile duct after cholecystectomy (11). In our study, statistically significant increase was found in postoperative third month and postoperative sixth month DHC diameter of both DC and N-DC groups, although the increase was small.

Biliary dyskinesia due to diabetic autonomous neuropathy was found to increase gallbladder size in diabetic patients (25). In literature review, no study was found about the effects of diabetes on extrahepatic bile duct morphometry. In order to show the effects of diabetes mellitus on preoperative and postoperative extrahepatic bile duct morphometry, we compared preoperative, postoperative third month and postoperative sixth month DHC diameters and found no statistically significant difference between preoperative, postoperative third month and postoperative sixth month DHC diameters of DC and N-DC groups.

Cholecystectomy was found to cause a small but statistically significant increase in postoperative DHC diameter values of both DC and N-DC group in our study. No statistically significant difference was found between the preoperative and postoperative DHC diameters of DC and N-DC groups. Based on this result, it was concluded that diabetes mellitus did not influence bile ducts morphometry in preoperative and postoperative period. We believe that our study will shed a light on distinguishing between physiological and pathological dilatation that can develop in postoperative period in extrahepatic bile ducts and also help in terms of preventing misdiagnosis and mistreatment that may develop in post-operative period.

*Conflict of interest: The authors declare that they have no competing interest.*

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*Ethical approval: This study was carried out following approval by the Research and Ethics Committee of Malatya Inonu University, Malatya, Turkey*

## REFERENCES

- Portincasa P, Ciaula AD, Bonfrate L, et al. Therapy of gallstone disease: What it was, what it is, what it will be. *World J Gastrointest Pharmacol Ther* 2012;3:7-20.
- Stinton LM, Myers RP, Shaffer EA. Epidemiology of gallstones. *Gastroenterol Clin N Am* 2010;39:157-69.
- Aerts R, Penninckx F. The burden of gallstone disease in Europe. *Aliment Pharmacol Ther* 2003;18:49-53.
- Chowdhury AH, Lobo DN. Gallstones. *Surgery (Oxford)* 2011;29:610-7.
- Akat AZ, Doğanay M, Koloğlu M, et al. Evaluation of 1000 laparoscopic cholecystectomies performed in one institution. *T Klin J Med Sci* 2002;22:133-41.
- Memisogullari R, Taysi S, Bakan E, et al. Antioxidant status and lipid peroxidation in type II diabetes mellitus. *Cell Biochem Funct* 2003;21:291-6.
- Memişoğulları R, Bakan E. Levels of ceruloplasmin, transferrin, and lipid peroxidation in the serum of patients with Type 2 diabetes mellitus. *J Diabetes Complications* 2004;18:193-7.
- Hanbidge AE, Buckler PM, O'Malley ME, et al. From the RSNA refresher courses: imaging evaluation for acute pain in the right upper quadrant. *Radiographics* 2004;24:1117-35.
- Berk RN, Cooperberg PL, Gold RP, et al. Radiography of the bile ducts: a symposium on the use of new modalities for diagnosis and treatment. *Radiology* 1982;145:1-9.
- Targarona EM, Bendahan GE. Management of common bile duct stones: controversies and future perspectives. *HPB(Oxford)* 2004;6:140-3.
- Valkovic P, Miletic D, Zelic M, et al. Dynamic changes in the common bile duct after laparoscopic cholecystectomy: a prospective longitudinal sonographic study. *Ultraschall Med* 2011;32:479-84.
- Bruneton JN, Roux P, Fenart D, et al. Ultrasound evaluation of common bile duct size in normal adult patients and following cholecystectomy. A report of 750 cases. *Eur J Radiol* 1981;1:171-2.
- Hunt DR, Scott AJ. Changes in bile duct diameter after cholecystectomy: a 5-year prospective study. *Gastroenterology* 1989;97:1485-8.
- Parulekar SG. Ultrasound evaluation of common bile duct size. *Radiology* 1979;133:703-7.
- Nakeeb A, Comuzzie AG, Martin L, et al. Gallstones: genetics versus environment. *Ann Surg* 2002;235:842-9.
- Arik MK, Türk N, Süner A. The incidence of metabolic syndrome in patients with operation for gallbladder. *Medeniyet Med J* 2010;25:158-63.
- Williams K, Tchernof A, Hunt KJ, et al. Diabetes, abdominal adiposity, and atherogenic dyslipoproteinemia in women compared With men. *Diabetes* 2008;57:3289-96.
- Liu CM, Hsu CT, Li CY, et al. A population-based cohort study of symptomatic gallstone disease in diabetic patients. *World J Gastroenterol* 2012;18:1652-9.
- Saxena R, Sharma S, Dubey DC. Gallbladder disorder in type 2 diabetes mellitus cases. *J Hum Ecol* 2005;18:169-71.
- Kaude JV. The width of the common bile duct in relation to age and stone disease. An ultrasonographic study. *Eur J Radiol* 1983;3:115-7.
- Admassie D. Ultrasound assessment of common bile duct diameter in Tikur Anbessa Hospital, Addis Ababa, Ethiopia. *Ethiop Med J* 2008;46:391-5.
- Reinus WR, Shady K, Lind M, et al. Ultrasound evaluation of the common duct in symptomatic and asymptomatic patients. *Am J Gastroenterol* 1992;87:489-92.
- Edmunds R, Katz S, Garciano V, et al. The common duct after cholecystectomy. Interval report. *Arch Surg* 1971;103:79-81.
- Horror MM. Ultrasound of the extrahepatic bile duct: issues of size. *Ultrasound Q* 2010;26:67-74.
- Gitelson S, Oppenheim D, Schwartz A. Size of the gallbladder in patients with diabetes mellitus. *Diabetes* 1969; 8:493-8.