


# Is Opioid Addiction a Sufficient Predicting Factor for Common Bile Duct Dilatation? A Sonographic Study

Journal of Diagnostic Medical Sonography  
26(3) 137–142  
© The Author(s) 2010  
Reprints and permission: <http://www.sagepub.com/journalsPermissions.nav>  
DOI: 10.1177/8756479310366470  
<http://jdm.sagepub.com>  


Ahmad Rezaee, MD<sup>1</sup>, Behzad Narouie, MD<sup>2</sup>,  
Mohammad Ghasemi-Rad<sup>3</sup>, Emad Nosair, MD<sup>4</sup>,  
Farshid Mohebi, MD<sup>1</sup>, and Sharareh Sanei Sistani, MD<sup>1</sup>

## Abstract

In the absence of hepatobiliary symptoms, opioid consumption has been shown to cause dilatation of the common bile duct (CBD). The main objective of this study was to measure with sonography CBD diameters in opioid addicts as compared with nonaddicts. The research was done on 208 individuals; 104 were opioid addicts using various routes of administration (inhalation, oral, or intravenous), and 104 had no history of addiction (control group). All patients underwent abdominopelvic sonography, and the internal diameters of the proximal part of the CBD were recorded. The average CBD diameter in the control group was  $4.13 \pm 1.14$  mm, which significantly increased to  $8.16 \pm 2.54$  mm in the case group. A significant increase in the average diameter of CBD in the case group with the oral route was  $10.7 \pm 2.26$  mm, compared with  $7.5 \pm 1.64$  mm and  $7.6 \pm 3.05$  mm, respectively, for those using inhalation and intravenous routes. The diameter of CBD was age dependent. The dilatation of the CBD detected by sonography occurring in opioid addicts in all age groups was attributed principally to the effect of opioids. Oral administration of opioid caused the highest dilatation effect on CBD.

## Keywords

common bile duct, sonography opioid addicts

Since the late 1980s, sonography has become a major diagnostic modality in suspected biliary diseases as it is inexpensive, available, and noninvasive.<sup>1</sup> Transabdominal sonography accurately identifies dilatation of the common bile duct (CBD) with a sensitivity of 96% and a specificity of 95%, but it is less accurate (sensitivity 55%–77%, specificity 98%) in detecting CBD stones.<sup>2,3</sup> The etiology of CBD dilatation also might be observed by sonography in conditions of obstruction such as CBD stones, tumors of the pancreatic head or tumors of Vater's ampula, masses, and enlarged hilar lymph nodes of the liver. However, when the etiology of the obstruction is not evident, more investigations are required to discover the cause of CBD dilatation.

In the absence of an obvious cause for mechanical obstruction for dilated CBD by sonography, predicting factors have been found to explain the dilated CBD. Among these factors are age, body mass index (BMI), portal vein diameter, and opioid addiction.<sup>4</sup> It is important clinically to consider these predicting factors to save the time and

expense of further assessment by invasive methods to discover the etiology of CBD dilatation.

The number of opioid addicts of newer opioids, such as heroin—the most widely abused semisynthetic form—is on the increase orally, intravenously, or by inhalation.<sup>5</sup>

Contraction of biliary smooth muscle is known to be one of the important effects of opioids. The sphincter of Oddi (SOD) may contract, resulting in reflux of biliary and pancreatic secretions and elevated plasma amylase and

<sup>1</sup>Zahedan University of Medical Sciences, Zahedan, Iran

<sup>2</sup>Ali-ebne-Abitaleb Hospital, Zahedan University of Medical Sciences, Iran

<sup>3</sup>Urmia University of Medical Sciences, Urmia, Iran

<sup>4</sup>University of Sharjah, Sharjah, United Arab Emirates

## Corresponding Author:

Behzad Narouie, MD, Ali-ebne-Abitaleb Hospital, Zahedan University, no 300, 1st ally, Jonobi St, Farhangian, Zahedan, Iran 571676311

Email: [medman11@hotmail.com](mailto:medman11@hotmail.com)

lipase levels.<sup>6</sup> Chronic spasm of SOD in opioid addicts may cause biliary stasis and dilatation of CBD. Opioid addicts with no biliary symptoms have been shown to have dilated CBD.<sup>7-10</sup>

However, the previous studies are deficient in using an adequate number of samples of opioid addicts and in considering the effect of age and mode of opioid administration on the CBD diameter. So, the main objective of this work was to study the effect of chronic opioid abuse on the diameter of CBD in opioid addicts as compared with nonaddicts in different age groups using transabdominal sonography.

## Materials and Methods

### Patients

In this prospective cross-sectional study, 208 participants >20 years old participated; 104 had a history of opioid addiction (case group; 93 men [89.4%] and 11 women [10.6%]), and another 104 were without a history of opioid abuse (control group; 86 men [82.7%] and 18 women [17.3%]). All participants were matched regarding sex and age, and they underwent abdominopelvic sonographic examination. They were classified into different age groups of 20 to 29, 30 to 39, 40 to 49, 50 to 59, and  $\geq 60$  years old. The study was approved by a research committee, and an informed written consent was taken from all patients.

The study selected the participants from those admitted to the general hospital between January 2008 and February 2009 who were complaining of symptoms other than hepatobiliary ones. The data obtained from sonography, along with the age of the individuals and the routes of opioid administration among opioid addicts (oral, intravenous, or by inhalation), were recorded in questionnaires and tables. Opioid addiction was determined by the patient's report and also from those accompanying the patient as relatives or close friends. Patients have been ensured that the data will remain confidential and that their names have been omitted from the form. The study included those who have used only one route for opioid consumption.

### Exclusion Criteria

This study excluded patients younger than 20 years old and those with opioid addiction for less than 1 year. Because of the cultural issues of the area, we did not rely on the patient's answer about the duration of addiction, but we did choose a minimum of a 1-year addiction for patients to be involved in this study. All those with multiple routes of opioid consumption were excluded from the study. Those with a history or symptoms of hepatitis, cirrhosis, biliary stones, purulent cholangitis, acute or chronic cholecystitis, inflammatory bowel disease, or biliary, hepatic, or pancreatic tumors were excluded from sampling.

Also, those who underwent surgical procedures such as cholecystectomy or sphincterotomy were not included in this study. Moreover, those who, upon abdominal sonography, were found to have signs of hepatomegaly or diseases in the liver, biliary passages, gallbladder, and pancreas were ruled out of the current study. All other comorbidities were also excluded.

### Scanning Technique

The ultrasonography machine used was a LOGIQ 7 (GE Healthcare, Piscataway, New Jersey) with a 3.5-MHz multifrequency convex probe. Transabdominal sonography was conducted on individuals in a fasting state, in a supine position, and in the parasagittal plane. To avoid interobserver variability, sonography was made and interpreted by a single radiologist.

Based on previous studies<sup>4,11</sup> that recorded a strong correlation for CBD diameter in proximal and distal parts, the measurements of the CBD diameter in this study were calculated in the proximal part close to the genu of the CBD (Figures 1-3)<sup>12,13</sup> and parallel to the portal vein. Measurement was made from inner-to-inner walls of the ducts by using electronic calipers and during maximal inspiration.

In the current study, the diameter of a CBD in an adult between 4 and <6 mm was considered normal, between 6 and 7 mm was considered equivocal, and >7 mm was considered dilated.<sup>1,14,15</sup>

### Statistical Analysis

We used SPSS 15 (SPSS, Inc, an IBM Company, Chicago, Illinois) for analyzing the data. The comparison of averages was done using one-way analysis of variance (ANOVA; Tukey HSD). A *P* value <.05 was considered significant for each of the mentioned tests.

## Results

The mean age was  $39.5 \pm 12.67$  years in the case group and  $38.8 \pm 13.33$  years in the control group. The average diameter of the CBD increased with age in the control group:  $3.5 \pm 0.7$  mm in the 20- to 29-year-old group and  $6.02 \pm 1.1$  mm in the  $\geq 60$ -year-old group, which is still <7 mm, the commonly accepted upper range of normal. The average diameter of the CBD was compared with different age groups using the one-way ANOVA test, and a significant difference was found between the average diameters of the CBD of the various age groups ( $F = 11.3$ ,  $P = .001$ ; Table 1).

The average diameter of the CBD increased with age in the case group:  $6.8 \pm 1.9$  mm in the 20- to 29-year-old group and  $11.3 \pm 2.3$  mm in the  $\geq 60$ -year-old group. The average diameter of the CBD was compared with the different age groups using the one-way ANOVA test, and a



**Figure 1.** Common bile duct sonography of a patient with an intravenous opioid addiction.



**Figure 2.** Common bile duct sonography of a patient with an oral opioid addiction.



**Figure 3.** Common bile duct sonography of a patient with an inhalational opioid addiction.

**Table 1.** Relation of Average CBD Diameter and Age in the Control Group

Age Group, y	Number of Cases	Common Bile Duct Diameter, mm, Mean ± SD (Range)
20–29	35	3.5 ± 0.7 (2.0–5.2)
30–39	26	4.04 ± 0.9 (2.9–6.8)
40–49	23	4.2 ± 0.8 (2.5–5.6)
50–59	12	4.6 ± 1.5 (3.0–7.6)
60	8	6.02 ± 1.1 (4.3–7.6)
Mean 38.8 ± 13.33		4.13 ± 1.14 (2.0–7.6)

$F = 11.3, P = .001.$

**Table 2.** Relation of Average CBD Diameter and Age in the Case Group

Age Group, y	Number of Cases	Common Bile Duct Diameter, mm, Mean ± SD (Range)
20–29	31	6.8 ± 1.9 (3.6–11.3)
30–39	27	7.6 ± 2.2 (4.0–12.3)
40–49	27	8.7 ± 2.6 (4.8–15.1)
50–59	12	9.7 ± 1.6 (7.0–12.3)
60	7	11.3 ± 2.3 (7.8–14.8)
Mean 39.5 ± 12.67		8.16 ± 2.54 (3.6–14.8)

$F = 8.74, P = .001.$

**Table 3.** Percentage of Individuals and Their CBD Diameters in the Case

Groups (n)	Common Bile Duct Diameter		
	Normal (<6 mm)	Equivocal (6–7 mm)	Dilated (>7 mm)
Control (104)	n (%)	n (%)	n (%)
	97 (93.3)	4 (3.8)	3 (2.9)
Case (104)	n (%)	n (%)	n (%)
	24 (23.1)	13 (12.5)	67 (64.4)

significant difference was found between the average diameters of the CBD of the various age groups ( $F = 8.74, P = .001$ ; Table 2).

The average diameter of CBD in the opioid addicts (case group) was  $8.16 \pm 2.54$  mm, which is significantly higher than that of the non-opioid addicts (control group), which was  $4.13 \pm 1.14$  mm. The average diameter of CBD in every age category in the case group was significantly higher than that in the corresponding age category of the control group.

The percentage of those having dilated CBD (>7 mm) in the case group was 64.4%, and this was significantly higher ( $P < .001$ ) than the percentage of those having dilated CBD in the control group (2.9%) in all age categories (Table 3).

**Table 4.** Average Diameters of CBD in Different Routes of Administration Among Oral Addicts and Control Groups

Mode of Administration	Number of Opioid Addicts	Common Bile Duct Diameter, mm, Average $\pm$ SD (Range)
Oral	30	10.7 $\pm$ 2.26 (6.8–15.1)
Inhalation	69	7.05 $\pm$ 1.64 (3.6–11.6)
Intravenous	5	7.6 $\pm$ 3.05 (0.75–12.3)

The average diameter of the CBD among those with an oral route of opioid addiction was 10.7  $\pm$  2.26 mm, which is significantly higher than those with inhalation or intravenous routes, 7.05  $\pm$  1.64 mm and 7.6  $\pm$  3.05 mm, respectively (Table 4).

## Discussion

The present study shows that the average diameter of CBD in 104 nonaddict controls with an average age of 38.8  $\pm$  13.33 years was 4.13  $\pm$  1.14 mm. This result coincides with a normal diameter of the CBD in healthy individuals in different age groups listed in textbooks,<sup>14</sup> as well as with findings by Reinus et al.,<sup>1</sup> who suggested that the normal CBD diameter should be between 5 and 8 mm, and Bowie,<sup>15</sup> who considered 6 mm the upper limit of normal for the common bile duct as measured by sonography.

Correlation between CBD diameter in sonography and age has been specified in previous studies by Niederau et al.,<sup>11</sup> Rumack et al.,<sup>14</sup> Bowie,<sup>15</sup> Wu et al.,<sup>16</sup> and Kaim et al.,<sup>17</sup> who showed that the mean width of CBD in asymptomatic elderly (>75 years) was 6.5  $\pm$  2.5 mm and recommended the upper limit of 10 mm. However, in the study of Chuah et al.,<sup>8</sup> the average diameter of CBD in 7 healthy patients with an average age of 64.43  $\pm$  8.72 years was 8.3  $\pm$  5.95 mm. In contrast, Horrow et al.<sup>18</sup> did not find an association between age and CBD diameter in an asymptomatic population. Horrow et al. did not consider the respiratory phase for duct measurements, which was accounted for in our study; maximum ultrasonographic CBD diameter can increase in deep inspiration.<sup>19</sup>

Our results show a significant increase ( $F = 11.3$ ,  $P = .001$ ) in the average diameters of CBD with age in both the control and case groups. Regarding the asymptomatic control group, the average diameter was 3.5  $\pm$  0.7 mm in the 20- to 29-year-old group and 6.02  $\pm$  1.1 mm in the  $\geq$ 60-year-old group. This means that the average CBD diameter in all age groups did not exceed 7 mm, the commonly accepted conventional upper range of normal. However, only 2.9% of this group (104 individuals) had dilated CBD (>7 mm).

The effect of aging on CBD dilatation may be explained by fragmentation of the longitudinal smooth myocyte bands

and intervening connective tissues, as well as loss of the reticulo-elastic network of the duct wall by aging.<sup>17</sup>

Regarding the case group of opioid addicts, our results show that the average CBD diameter was 6.8  $\pm$  1.9 mm (equivocal to dilated) in the 20- to 29-year-old group and 11.3  $\pm$  2.3 mm (dilated) in the  $\geq$ 60-year-old group. This means that the upper limit of the normal diameter (7 mm) had been reached from the first age group onwards. Moreover, of the 104 opioid addicts, 64.4% had developed a dilated CBD (>7 mm).

The results of the present study show that opioid addiction in the case group caused a significant increase ( $P < .001$ ) in the average CBD diameter (8.16  $\pm$  2.54 mm) compared to the mean CBD diameter in the asymptomatic nonaddicts (4.13  $\pm$  1.14 mm).

Also, the average diameter of CBD in every age group within opioid addicts (case group) was significantly higher than that in the same age group of the nonaddicts (control group).

These results are in accordance with the results of Chuah et al.,<sup>8</sup> Katznuq,<sup>6</sup> Helm et al.,<sup>9</sup> and Joehl et al.<sup>10</sup> Thompson<sup>20</sup> mentioned that all narcotics increase the internal pressure of biliary ducts, but the biggest increase is with morphine.

The study conducted by Bachar et al.<sup>21</sup> revealed an age-dependent increase in the diameter of the extrahepatic bile duct with a gradual dilatation of a rate of 0.04 mm/y. He also suggested that the upper normal limit of the duct in elderly persons be set at 8.5 mm.

The present results show that the effect of aging on the diameter of CBD in both control and opioid addict groups is likely due to the assumption that the duration of opioid addiction increases when the patients get older. It has been evidenced that CBD dilatation correlates with the years of opioid addiction.<sup>6</sup> Unfortunately, because of cultural difficulties we faced in collecting accurate information from the addicts or from their families about the duration of addiction, we found it unreliable to include the effect of duration of opioid addiction on CBD diameter in this study and only included those with a minimum 1 year of addiction.

CBD dilatation in opioid addicts is probably due to the spastic effect of morphine on SOD<sup>9</sup> or to the contraction of the biliary smooth muscle produced by opioids,<sup>10</sup> resulting in a chronic increase in CBD internal pressure and therefore its dilatation.<sup>22</sup>

It must be mentioned that no age group in the controls showed dilatation of the CBD (>7 mm), but this limit had been reached in all age groups of the opioid abusers. This means that in opioid addicts without evidence of hepatobiliary disease, dilatation of the CBD by sonography may not be needed for further investigations, irrespective of the age of the addict.

Our results show that chronic opioid administration via the oral route caused the higher significant effect ( $P < .05$ ) on increasing the diameter of CBD ( $10.7 \pm 2.26$  mm) than either the intravenous route ( $7.05 \pm 1.64$  mm) or by inhalation ( $7.6 \pm 3.05$  mm). However, no previous literature described the relation between the opioid-induced CBD dilatation and the route of opioid administration.

The greater effect of chronic oral morphine intake on CBD dilatation is perhaps due to either easier accessibility of the oral route than inhalation or intravenous administration or the higher plasma concentration of the drug or the duration of opioid addiction. The bioavailability of opioids and their metabolites, morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G), depends on the route of their administration. Following chronic oral morphine, the blood levels of M6G markedly exceed those of morphine itself, giving its greater potency and high concentrations. Also, oral morphine seems to have a longer duration of action than intravenous or inhaled morphine.<sup>23</sup> In a previous study by Hoskin et al.,<sup>24</sup> the mean ratio of the area under the concentration-time effect curve for M6G/morphine in plasma after oral and buccal morphine was 11:1 compared with 2:1 after intravenous morphine.

In conclusion, the diameter of CBD is age dependent. The dilatation of the CBD detected by sonography occurring in opioid addicts in all age groups was attributed principally to the effect of the opioid and not likely to the effect of age. Oral administration of opioids caused the highest dilatation effect on CBD compared with the inhalation or intravenous routes.

### Acknowledgments

We acknowledge the Clinical Research Development Center of Ali-ebne-Abitaleb hospital Zahedan, Iran, for its help in preparing this manuscript.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the authorship and/or publication of this article.

### Funding

The author(s) received no financial support for the research and/or authorship of this article.

### References

1. Reinus WR, Shady K, Lind M, Scott R: Ultrasound evaluation of the common duct in symptomatic and asymptomatic patients. *Am J Gastroenterol* 1992;87:489–492.
2. Stott MA, Farrands PA, Guyer PB, Dewbury KC, Brown- ing JJ, Sutton R: Ultrasound of the common bile duct in patients undergoing cholecystectomy. *J Clin Ultrasound* 1991;19:73–76.
3. Yarmenitis SD: Ultrasound of the gallbladder and the biliary tree. *Eur Radiol* 2002;12:270–282.
4. Adibi A, Givechian B: Diameter of common bile duct: what are the predicting factors? *J Res Med Sci* 2007;12:121–124.
5. Albertson TE, Offerman S, Kenyon NJ: How recreational drugs affect asthma, in Gershwin ME, Albertson TE (eds): *Current Clinical Practice: Bronchial Asthma: A Guide for Practical Understanding and Treatment*. 5th ed. Totowa, NJ, Humana, 2006, pp 327–340.
6. Katzung BG: *Basic & Clinical Pharmacology*. 10th ed. New York, McGraw-Hill, 2007.
7. Farahmand H, PourGholami M, Sheikh Fathollah M: Chronic extrahepatic bile duct dilatation: sonographic screening in the patients with opioid addiction. *Korean J Radiol* 2007;8:212–215.
8. Chuah SY, Leong CK, Pang CW: Dilated common bile duct in opioid addicts with and without biliary symptoms: implication for research in AIDS cholangiopathy. *Singapore Med J* 2003;44:261–267.
9. Helm JF, Venu RP, Geenen JE, et al: Effects of morphine on the human sphincter of Oddi. *Gut* 1988;29:1402–1407.
10. Joehl RJ, Koch KL, Nahrwold DL: Opioid drugs cause bile duct obstruction during hepatobiliary scans. *Am J Surg* 1984;147:134–138.
11. Niederau C, Müller J, Sonnenberg A, et al: Extrahepatic bile ducts in healthy subjects, in patients with cholelithiasis, and in postcholecystectomy patients: a prospective ultrasonic study. *J Clin Ultrasound* 1983;11:23–27.
12. Sutton D. *Textbook of Radiology and Imaging: Abdominal and Gastrointestinal Tract*. 7th ed., vol. 1. London, Churchill Livingstone, 2003.
13. McGahan JP, Goldberg BB: *Diagnostic Ultrasound*. 2nd ed. New York, Informa Healthcare, 2008.
14. Rumack CM, Wilson SR, Charboneau JW: *Diagnostic Ultrasound*. 2nd ed. St. Louis, MO, Mosby, 1988.
15. Bowie JD: What is the upper limit of normal for the common bile duct on ultrasound: how much do you want it to be? *Am J Gastroenterol* 2000;95:897–900.
16. Wu CC, Ho YH, Chen CY: Effect of aging on common bile duct diameter: a real-time ultrasonographic study. *J Clin Ultrasound* 1984;12:473–478.
17. Kaim A, Steinke K, Frank M, et al: Diameter of the common bile duct in the elderly patient: measurement by ultrasound. *Eur Radiol* 1998;8:1413–1415.
18. Horrow MM, Horrow JC, Niakosari A, Kirby CL, Rosenberg HK: Is age associated with size of adult extrahepatic bile duct? Sonographic study. *Radiology* 2001;221:411–414.
19. Wachsberg RH: Respiratory variation of extrahepatic bile duct diameter during ultrasonography. *J Ultrasound Med* 1994;13:617–621.
20. Thompson DR: Narcotic analgesic effects on the sphincter of Oddi: a review of the data and therapeutic implications

- in treating pancreatitis. *Am J Gastroenterol* 2001;96:1266–1272.
21. Bachar GN, Cohen M, Belenky A, Atar E, Gideon S: Effect of aging on the adult extrahepatic bile duct: a sonographic study. *J Ultrasound Med* 2003;22:879–882.
  22. Wu SD, Zhang ZH, Jin JZ, et al: Effects of narcotic analgesic drugs on human Oddi's sphincter motility. *World J Gastroenterol* 2004;10:2901–2904.
  23. Gutstein HB, Akil H: Opioid analgesics, in Brunton LL, Lazo JS, Parker KL (eds): *Goodman & Gilman's the Pharmacological Basis of Therapeutics*. 11th ed. New York, McGraw-Hill, 2006.
  24. Hoskin PJ, Hanks GW, Aherne GW, Chapman D, Littleton P, Filshie J: The bioavailability and pharmacokinetics of morphine after intravenous, oral and buccal administration in healthy volunteers. *Br J Clin Pharmacol* 1989;27:499–505.