GRADES OF GALLBLADDER DISEASES USING THE GALLBLADDER CONTRACTION INDEX: A PILOT STUDY

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Summary: The aim of this study was to develop a pilot model for the assessment of the severity of gallbladder diseases based on gallbladder contraction index, clinical and sonographic appearances of the gallbladder. The gallbladder contraction index (GBCI) was obtained as the average of the first ten and the first 20minutes contraction indices. A range of 5% to 77% previously obtained in normal subjects was adopted in this study. Gallbladder contraction index in combination with other variables: sonographic appearances and clinical presentations were used for the grading of gallbladder diseases in the present study. This pilot model may have a good diagnostic performance but a clinical prospective evaluation is needed to confirm its actual value.

Key Words*: Milk ultrasonography, gallbladder contraction index, gallbladder disease.*

Introduction

Milk Ultrasonography (MU) is a cholecystodynamic study whereby gallbladder emptying or refilling is assessed by ingestion of milk. Some of the peptides (hormones) for example, cholecystokinin, gastrin, neurotesin, somatostatin, vasoactive intestinal polypeptide, substance P, bombesin, and the endomorphins, have been demonstrated to occur in the brain (Long *et al,* 1984). CCK is present in both the brain and gut and is therefore a neuropeptide, possibly with a neurotransmitter role, as well as a hormone. In the gut the highest tissue concentrations are in the upper small intestine but it can be detected in the ileum. CCK is present in both the mucosa and the muscle of the intestine. In the mucosa it is present in the endocrine cell (Long, *et al,* 1984).

Motility disorders occur when a physiological pattern of motility is disrupted, or absent or replaced by an aberrant pattern (Wingate, 1984). Hence, the mathematical analysis of minute- by- minute ultrasonography measurements of gallbladder volume variations yields both physiological and pathological insight (Pallota, 2003) Clinicians have in their diagnostic armamentarium a wide range of techniques for the preoperative evaluation of gallbladder, such as physical examination, biochemical examination, gray and colour Doppler ultrasonography, axial computed tomography, scintigraphy and magnetic resonance imaging. Several studies have used ultrasonography to evaluate gallbladder contraction index, GBCI (Ugwu, *et al*, 2007,Ugwu[a];2006, Pons *et al,* 2003, Siegel *et al,*2000, Cay *et al,* 2006, Acalovschi *et al,* 2004, Guliter, *et al,* 2003), but none has come up with a grading pattern for gallbladder diseases. Meanwhile no model for grading has been proposed to assist in the determination of the severity of gallbladder disease, prognosis and treatment algorithm.

In the present study, we aimed to develop a model to be used in the grading of gallbladder diseases.

Materials and Methods

This was a prospective study. Fifty normal, apparently healthy adult Nigerians, with no history of hepatobiliary disease or any other disease known to affect gallbladder motility were studied (Ugwu[b]; 2006). The GBCI ranged from 5% to 77% in normal subjects (Ugwu[b]; 2006). Hence a benchmark of 5% was used for the formulative design.

Five subjects with history of gallbladder diseases were assessed in this pilot study. Approval for the study was given by Jeomedic ultrasound center Research Board, Abakaliki,

Ebonyi State, according to the Helsinki Declaration (1996). Informed consent was obtained from each subject. Subjects were advised to report to the department in the morning having fasted overnight and without breaking fast. Three serial ultrasound scans were carried out on each subject as follows:

(a)   Before drinking a tin of full cream milk (165mls). Trade name-

        Three crowns   (Frieshland Foods, WAMCO, Lagos, Nigeria)

(b)   10 minutes postprandial;

(c)   20minutes postprandial.

These procedures were used to assess the variations of gallbladder prolate ellipsoid volume with bile emptying (contraction). Ultrasound studies were performed using sono line SL-1 (siemens medical systems, U.S.A Inc, Ultrasound group Issaquah (WA) with a sector transducer of 3.5 MH_Z frequency. The skin of the right upper quadrant was covered with ultrasound gel and the probe applied to it. After visualization of the maximal gallbladder longitudinal outline, the length and maximal anteroposterior diameter (height) were measured on arrested respiration either in supine or oblique position (fig 1). Thereafter, the probe was turned through 90^0 (fig 2) to obtain the maximal coronal diameter (width). The electronic calipers cross one another at 90^0 to make 3-othorgonal plane measurements. The 3 measurements were repeated 10 minutes and 20 minutes postprandial. Gallbladder volume was obtained using the volume calculation for the prolate ellipsoid (length x width x height x 0.523) (Ho, *et al,* 1998). Gallbladder contraction index (GBCI) is the percentage decrement of postprandial size (volume) from the initial size (Ho *et al,* 1998). The 10th minute GBCI and the 20th minute GBCI were computed for each subject and the average of two used as the actual (GBCI.)

Cholecystodynamic Analysis

Descriptive Statistical technique was used. The gallbladder contraction indices were expressed as percentages and graded as shown in the table 2.
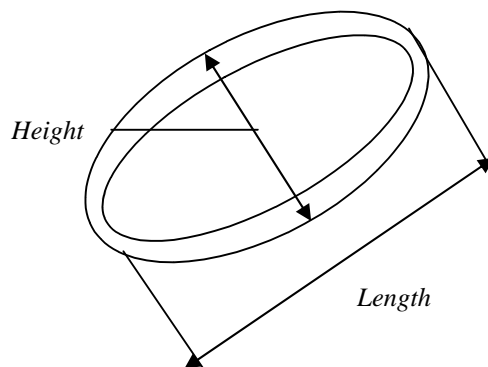

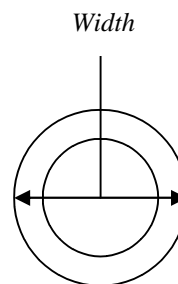*Fig 1 A line drawing showing a longitudinal section of the gallbladder.*

Fig 2: A line drawing showing a transverse section of the gallbladder.

Results

Table 1. Model Development

STAGES	GBCI	CLINICAL EVIDENCE	SONOGRAPHY EVIDENCE
1	<5%	+	+
2A	<5%	-	+
2B	<5%	+	-
2C	>5%	+	+
3A	>5%	-	+
3B	>5%	+	-
3C	<5%	-	-

GBCI=Gallbladder Contraction Index
(+) = Presence of Clinical / Sonographic Evidence
(-) = Absence of Clinical / Sonographic Evidence

Table 2 shows gallbladder contraction indices in some patients with positive histories of gallbladder diseases
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Table 2: Gallbladder contraction indices in patients with positive history of gallbladder diseases

S/N	Sex	Clinical History	GBCI (%)	Grade/Remark
1	M	Hepatomegaly, mild ascites, Lymphadenopathy, cholecystitis (4mm wall thickness) cholelithiasis (9. 6mm cholelith), gall bladder attack.	-2	Grade 1
2	M	Acalculous cholecystitis. six months post medication. Normal wall thickness. No gall bladder attack.	36.31	Improvement To Normality.
3	M	Cholelithiasis. six months post medication, reduced gall bladder attack, No cholelith seen.	48.45	Grade 3. Recorded Improvement.
4	F	Chronic cholecystitis (7.4mm wall thickness), cholelithiasis (multiple calculi averaging 7.4mm), six weeks post partum, gall bladder attack.	-75.32	Grade 1
5	M	2.2mm asymptomatic solitary cholelith. No gall attack incidental finding during an untargeted abdominal sonography. Normal wall thickness.	12.25	Grade 3

Model Development

GBCI is used in this model as a cholecystodynamic variable. Other variables are clinical evidence and sonographic signature of gallbladder diseases (e.g. wall thickening and intracavitary masses)

In this model, grade 1 is the most severe and grade 3 is the least severe.

Grade 1:
GBCI < 5% + clinical evidence of gallbladder disease + sonography evidence of gallbladder disease.

Grade 2:
GBCI < 5% + sonographic evidence of gallbladder disease + no clinical evidence of gallbladder disease.
Or
GBCI < 5% + Clinical evidence of gallbladder disease + No sonographic evidence of gallbladder disease.
Or
GBCI > 5% + clinical evidence of gallbladder disease + sonographic evidence of gallbladder disease.

Grade 3:
GBCI > 5% + sonographic evidence of gallbladder disease + no clinical evidence of gallbladder disease.
Or
GBCI > 5% + clinical evidence of gallbladder disease + No sonographic evidence of gallbladder disease.
OR
GBCI < 5% + no sonographic evidence of gallbladder disease + no clinical evidence of gallbladder disease.

Discussion

At present, there has not been any model based on contractility used for assessing very severe (Grade 1), moderately severe (Grade 2) and mild (Grade 3) gallbladder diseases even though several dynamic studies (Ugwu[b],*et al,* 2007, Pons, *et al,* 2003, Siegel *et al,* 2000,Cay *et al,* 2006, Acalovschi *et al,* 2004, Guliter *et al,* 2003) have been carried out on the gallbladder. This present study is the first.

However, it should be taken into account that the definition of parameters used might be interpreted in different ways by independent investigators when applying models. That makes it essential to use reproducible and clearly defined parameters, as recently suggested (Zimmerrman *et al,* 2000), which is especially true for categorical variables. We tried to use a clear definition for the main variable, which is the GBCI. The mathematical formula used for GBCI was

$$\frac{(V1-V2) \times 100}{V1 \quad 1}$$

where V1 is the Initial Gallbladder Volume
V2 is the Postprandial Gallbladder Volume

This model is a mathematical formula, and clinicians may be reluctant to use it. Actually, it is simple to use. Only a computer or even simply a hand calculator is needed. Once all the parameters to be used in the model are obtained in the evaluation of a given gallbladder in fasting and postprandial phases, their values (measurements) are applied to the model's mathematical formula, and result will allow the estimation of the severity of the disease. A possible limitation of this proposed model is the use of two-dimensional ultrasound to determine gallbladder volume and contraction index, which has been shown to have significant problem when compared with gold standard (dynamic scintigraphy). Further studies in this field apart from being carried out on a larger samples of both normal subjects and patients with gallbladder diseases to give high power (enough sample size) would need to be compared with crossover studies using gold standards. In this case, the gold standards would be dynamic cholescintigraphy (DCS) and possibly surgical pathology. The use of dynamic ultrasonography (DUS) may have contributed to the wide variability in the percentages (Ugwu[b], 2006) used to identify normal gallbladder function (5%-77%) in this paper. This could obviously be due to the use of ellipsoid formula in volume determination for various gallbladder shapes and contours.

Finally, we propose this model for predicting gallbladder disease severity and affirm that the prospective evaluation of this model in large series of subjects in different racial and socio-cultural background would further determine its actual value.

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