### Computed Tomographic Analysis of Gallbladder Stones: Correlation with Chemical Composition and In Vitro Shock-wave Lithotripsy

Myung Hwan Kim, M.D., Sung Koo Lee, M.D. and Young II Min, M.D.

Department of Internal Medicine, Asan Medical Center, Seoul, Korea

Kyung Sik Cho, M.D. and Yong Ho Auh, M.D.

Department of Radiology

Sung Gyu Lee, M.D.

Department of General Surgery

The recent advent of nonsurgical treatment for gallstones reguires accurate in vivo analysis of their chemical composition in order to select the best candidates. As a preliminary work, we undertook an in vitro CT examination of 53 surgically removed gallstones and compared their CT patterns with their chemical composition. Those results were correlated with in vitro lithotripsy of the gallstones. The CT appearances were classified as follows: laminated (43%), dense (32%), rimmed (11%), isodense (8%) and faint (6%).

The dense pattern contained a high calcium content. As the CT density increased, the calcium content increased, but the cholesterol content decreased proportionally. The number of shock waves needed to break down a gallstone less than 2 mm in size increased with stone volume and the cholesterol content increased but did not have any correlation with the calcium content level.

As a result we found the CT examination to be a very sensitive method in detecting small amounts of calcium content in gallstones and the CT pattern and density of the gallstones were well correlated with their chemical composition, therefore in vivo CT examinations for ESWL candidats are desirable.

Key Words: ESWL, Gallstone, CT

### INTRODUCTION

Recent advances in gallstone therapy, such as chemical dissolution, oral bile acid therapy, and extracorporeal shock-wave lithotripsy (ESWL), have generated interest in the ability of imaging

methods to determine the chemical composition of gallstones and potentially to predict the efficacy of these nonsurgical gallstone therapies<sup>1)</sup>.

The most important factor determining the result of this nonsurgical therapy is to find cholesterol stones consisting of the least amount of calcium. So we classified the calcification patterns and measured the Hounsefied units (HU) of gallstones by computed tomography (CT) and investigated the relationship between the CT finding and chemical composition. Also, we studied the factors of gallstones affecting response to ESWL.

Address correspondence to: Myung Hwan Kim, M.D., Department of Internal Medicine, Asan Medical Center, Kang-Dong P.O. Box 145, Seoul 134-600 (Fax: 484-2472) Tel: 02-480-3029

### **METHODS**

In anticipation of the role of CT in selecting patients for nonsurgical gallstone therapy such as ESWL, this study was undertaken to (a) determine the CT patterns of gallstone appearances, (b) correlate these patterns with their chemical composition, and (c) find the contributing factors to the number of shocks required to attain the endpoint (fragment stone size  $\leq 2 \text{ mm}$ ).

1) Gallbladder stones were surgically removed from 53 patients and maintained in normal saline.

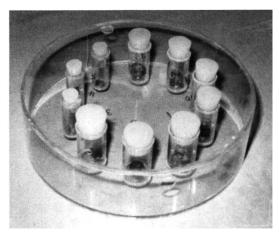


Fig. 1. Phantom for CT analysis.

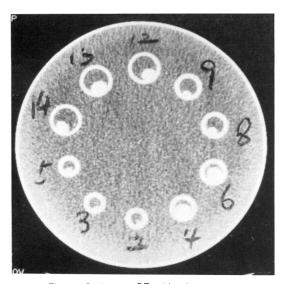


Fig. 2. Gallstone CT with phantom.

- 2) The color, diameter and volume of each stone were recorded, and the volume of each was measured by the water immersion method.
- 3) CT examinations (GE 9800 Quick) of gallstones were performed in custom-made plexiglass-and-water body phantom by 5 mm collimations (Fig. 1, 2).
- 4) CT attenuation values (Hounsefield units, HU) were obtained from the highest and lowest density area of a stone. The attenuation value of each stone was recorded as an average density of the above values.
- 5) Shock-wave lithotripsy (MPL 9000, Dornier) was performed with a saline-filled condom and the number of shocks required to attain the endpoint (fragment size  $\leq 2$  mm) was recorded (Fig. 3).
- 6) The chemical composition of the stones was measured by infrared spectroscopy.

### **RESULTS**

Five CT patterns could be indentified and categorized as dense (n=17), faint (n=3), rimmed (n=6), laminated (n=23) and isodense (n=4)



Fig. 3. Shock-wave lithotripsy with phantom.

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(Table 1). The dense pattern showed a homogenous increase in CT attenuation value. The laminated pattern showed alternating regions of higher and lower densities. The rimmed pattern showed a peripheral rim of higher attenuation value surrounding a homogenous, lower-density center. An isodense pattern was categorized when

a stone couldn't be seen within the saline-filled chamber. A faint pattern showed a slightly lower density than a dense pattern(Fig 4).

Considering the relation between the CT pattern and the chemical composition of the gallstone, we observed the highest cholesterol content (104.  $8\pm69.5\,\text{mg}\%$ ) in the isodense stones and the

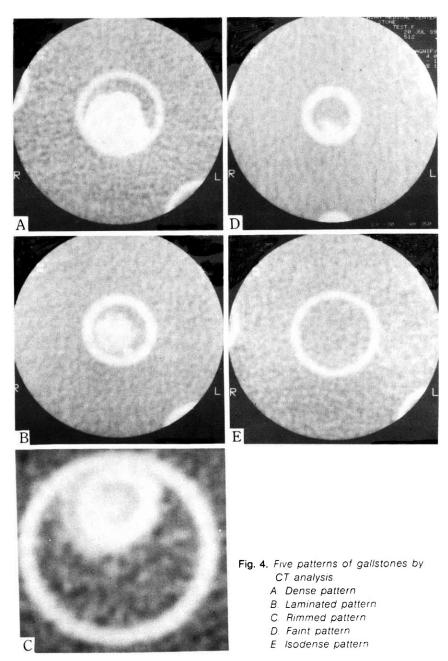


Table 1. Distribution of CT Patterns of Gallstones

Pattern	Total Stone Population (%)
Dense	17 ( 32)
Laminated	23 ( 43)
Rimmed	6 ( 11)
Isodense	4 (8)
Faint	3 ( 6)
Total	53 (100)

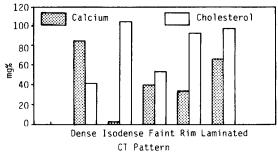


Fig. 5. Chemical Composition.

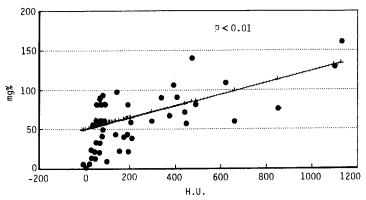


Fig. 6. H.U. vs calcium.

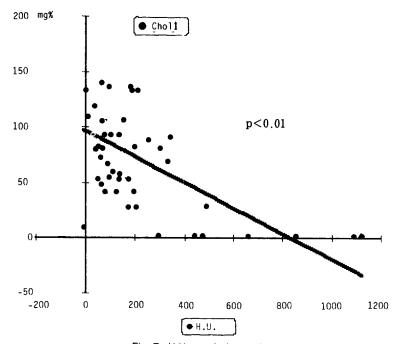


Fig. 7. H.U. vs cholesterol.

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lowest  $(3.3\pm2.3\,\text{mg\%})$  in the dense stones. In contrast, the highest calcium content  $(84.4\pm42.4\,\text{mg\%})$  was measured in the dense stones and the lowest  $(41.4\pm26.3\,\text{mg\%})$  in the isodense stones (Fig. 5).

Considering the relation between the Hounsefield units and the chemical composition of the gallstones, a negative correlation betweeen the attenuation values and cholesterol content and a positive correlation between the calcium content and attenuation values (Hounsefield unit) were observed (p < 0.01)(Fig. 6, 7).

Classifying the gallstones in 4 subgroups by

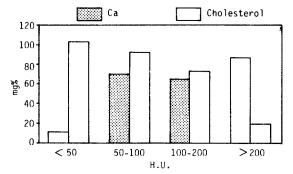


Fig. 8. H.U. vs chemical composition.

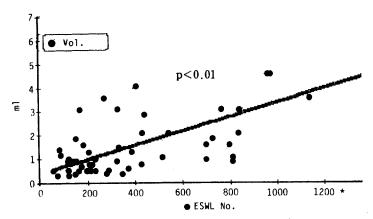


Fig. 9. Stone volume vs shock-wave number.

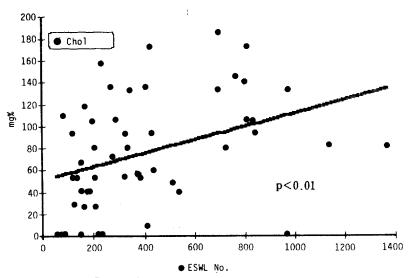


Fig. 10. Cholesterol vs shock-wave number.

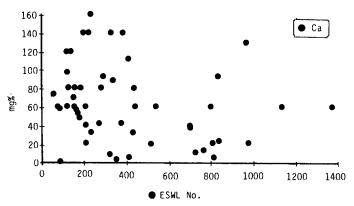


Fig. 11. Calcuim vs shock-wave number.

Hounsefield unit such as  $\leq$  50, 50-100, 100-200 and > 200, the stones with  $\leq$  50 Hounsefield unit showed the lowest calcium content (16.9 $\pm$ 14.3 mg%) and highest cholesterol content (163.3 $\pm$ 47 mg%)(Fig. 8).

A positive correlation between stone volume and the number of shocks required to attain the endpoint (fragment stone  $\leq 2$  mm) was observed (p<0.001, Fig. 9). The number of shockwaves needed to break down gallstones less than 2 mm in size increased as the cholesterol content increased but did not have any correlation with the calcium content level(Fig. 10, 11).

#### DISCUSSION

Gallstone lithotripsy and chemolysis represent dramatic departures from the traditional surgical treatment of cholelithiasis<sup>2)</sup>. Since the 1980's many reports show a tendency of a higher prevalence of cholesterol gallstones in Korea<sup>3)</sup>. So there is the future possibility that nonsurgical therapy of gallstones will be utilized more frequently in our country.

Extracorporeal shock wave lithotripsy (ESWL) usually requires adjuvant oral bile acid therapy to achieve complete dissolution of gallstones<sup>4)</sup>. Of course, adjuvant litholytic therapy is only of value in cholesterol stones<sup>5)</sup>. Normally these stones are radiolucent, but radiolucent gallstones frequently contain significant calcium deposits. Their detection is important in the evaluation of patients for medical gallstone dissolution therapy<sup>1,5)</sup>.

Plain X-ray of the abdomen and oral cholecystography are the diagnostic methods presently

used for distinguishing calcified from radiolucent stones<sup>6~8)</sup>. It has been shown that, in about 20% of the patients, the radiolucent stones contain significant amounts of calcium<sup>9)</sup>. This finding is probably responsible for many of the treatment failures. Hence more sensitive diagnostic aids are desirable for detecting calcium in radiolucent stones.

With the advent of chemical dissolution and lithotripsy for the treatment of gallstones, use of imaging techniques to determine the chemical composition of gallstones has become important. Although CT has been proposed as a means of selecting patients for these nonsurgical therapies, investigation into the significance of the CT appearances of gallstones has been limited. Our results suggest that the CT appearances and CT density (Hounsefield unit) relate closely to the concentration of cholesterol.

A study by Hickman et al.<sup>10)</sup> reveals that stones with a CT density of 50 HU or greater are not soluble in chenodeoxycholic acid, whereas 50% of those with a density of less than 50 HU show significant dissolution. Our data also showed that gallstones with a density of less than 50 HU had the highest cholesterol and lowest calcium content.

Although CT is less sensitive than abdominal sonography in detecting gallstones<sup>11)</sup>, our data show that five CT patterns can be indentified that have varied chemical compositions. Among the five patterns, gallstones with isodense patterns had the highest cholesterol and lowest calcium content. As above, the CT density and CT pattern may be of help in distinguishing between non-cholesterol and cholesterol stones. Only the latter

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are amenable to adjuvant litholytic therapy, which may be important for the complete disappearance of the fragments. Considering the cost of ESWL and following oral bile acid therapy, a computed tomographic scan would be a cost effective patient selection parameter if the stones do not float on oral cholecystography<sup>12)</sup>.

In summary, the CT appearances and density of gallstones will be a useful finding to predict the chemical composition and success of nonsurgical therapy for gallstones. Also, in vivo CT analysis of gallstones for selection of ESWL candidates is desirable, because ESWL is a very expensive treatment modality.

### CONCLUSION

The role of CT in predicting the chemical composition of gallstones and selecting patients for ESWL was investigated.

- 1) Five CT patterns could be identified and categorized as dense (n=17), faint (n=3), rimmed (n=6), laminated (n=23) and isodense (n=4).
- 2) The highest cholesterol content (104.8 $\pm$ 69.5 mg%) was encountered in isodense stones and the lowest (41.4 $\pm$ 26.6 mg%) in dense stones. The highest calcium content (84.4 $\pm$ 42.4 mg%) in dense stones. The hishest calcium content (84.4 $\pm$ 42.4 mg%) was encountered in dense stones and the lowest (3.3 $\pm$ 2.3 mg%) in isodense stones.
- 3) A negative correlation was noted between the attenuation values (Hounsefield units) and cholesterol content (p<0.001), and there was a positive correlation between the calcium content and attenuation values (p<0.01).
- 4) Stones with a density of less than 50 Hounsefield units showed the lowest calcium content ( $16.9\pm14.3\,\text{mg}\%$ ) and the highest cholesterol content ( $163.3\pm47\,\text{mg}\%$ ).
- 5) There was a positive correlation between stone volume and the number of shocks required to attain the endpoint (fragmented stone  $\leq 2$  mm) (p $\leq 0.001$ ).

In conclusion, the CT appearance and CT density of gallstones can predict their chemical compositions and outcome of nonsurgical gallstone therapy.

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