Lithotripsy and Related Techniques for Gallstone Treatment

Adapted from the Proceedings of The Third International Symposium on Biliary Lithotripsy, Munich, Germany, September 13–15, 1990.

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Mosby Year Book

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A Year Book Medical Publishers imprint of Mosby–Year Book, Inc.

Mosby–Year Book, Inc.
11830 Westline Industrial Drive
St. Louis, MO 63146

1 2 3 4 5 6 7 8 9 0 CLMV 95 94 93 92 91

Library of Congress Cataloging-in-Publication Data

Lithotripsy and related techniques for gallstone treatment /
[edited by] Gustav Paumgartner, H. Joachim Burhenne.
p. cm.
Includes bibliographical references and index.
ISBN 0-8151-6624-9
1. Gallstones—Treatment. 2. Ultrasonic lithotripsy.
I. Paumgartner, G. (Gustav) II. Sauerbruch, Tilman
III. Sackmann, Michael
IV. Burhenne, H. Joachim (Hans Joachim),
1925- .
[DNLM: 1. Cholelithiasis—therapy.
2. Lithotripsy—methods. WI
755 L776]
RD547.L57 1991– 91-22617
617.5'56—dc20 CIP
DNLM/DLC
for Library of Congress

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Cholesterol Nucleation Time: A Potentially Valuable Parameter for Prediction of Gallstone Recurrence After Successful Dissolution Therapy

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Previous studies suggest that at least 30% to 50% of patients with complete gallstone dissolution by oral bile acid therapy will develop recurrent stones over a 3- to 5-year period when bile acid treatment is withdrawn.[5, 6] Villanova et al.[9] have demonstrated that patients who had multiple gallstones seem to be at greater risk of recurrence after successful stone dissolution than those who originally had solitary stones.

Abnormally rapid nucleation of cholesterol from supersaturated gallbladder bile is of key importance in primary gallstone formation and might therefore be a major determinant of gallstone recurrence.[3, 6, 7]

It seemed possible that different cholesterol nucleation times or nucleation-promoting activity in the gallbladder bile of patients with multiple stones as compared with those with solitary stones might be responsible for the different rates of stone recurrence.

This is supported by earlier observations of Gollish et al.,[1] who reported a shortened nucleation time in all patients with multiple gallbladder stones while half of their patients with solitary stones (four of eight patients) needed more than 4 days to develop cholesterol crystals. More recently, van Erpecum et al.[8] also found rapid nucleation in bile from patients with multiple gallstones but normal nucleation in most gallbladder bile from patients with a single stone.

Groen et al.[2] have isolated, by concanavalin A–sepharose chromatography of gallbladder bile, a glucose/mannose-containing, 130 kilodalton (kD) glycoprotein with strong cholesterol nucleation-promoting activity in model bile. The activity was found in the majority of gallbladder bile investigated, and high nucleation-promoting activity titers were observed in bile from patients with multiple cholesterol stones. The activity titer in bile was not correlated to the total protein content, cholesterol saturation index, and total lipid concentration. The data of Groen et al.[2] are of particular interest and the relationship between the 130 kD glycoprotein and the pathogenesis of multiple cholesterol gallstones seems to be evident.

We have recently compared cholesterol nucleation times in the gallbladder bile of 59 patients with solitary and 42 patients with multiple gallstones.[4] A clear separation was observed between two groups, one with pigment and mixed and the other with cholesterol stones (Fig 41–1). The results of the median cholesterol nucleation time in the gallbladder bile of these patients are illustrated (Fig 41–1). Long nucleation times exceeding 21 days were usually observed in bile from patients with pigment or

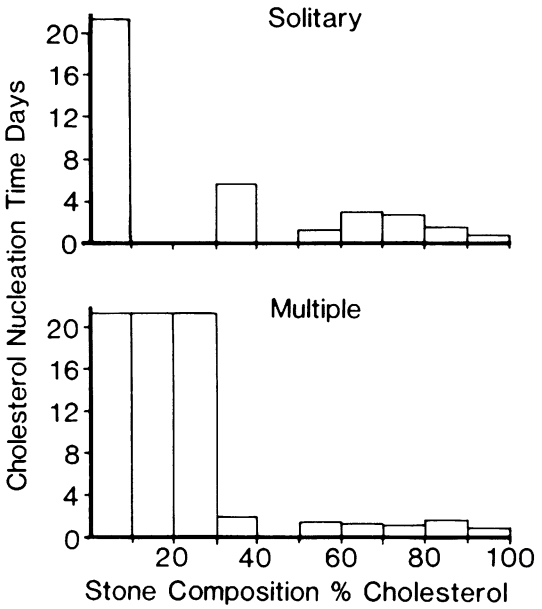

Fig 41–1.
Median cholesterol nucleation time in the gallbladder bile from 59 patients with solitary and 42 patients with multiple stones.

mixed stones, while abnormal nucleation was seen mostly in the bile of patients with cholesterol stones. However, nucleation times were significantly longer in bile from solitary than in bile from multiple cholesterol stone carriers. Only 1 of 32 patients with multiple stones as compared with 10 of 54 patients with a single stone had a normal nucleation time (>4 days). Furthermore, over a wide range of cutoff levels for cholesterol nucleation times the percentage of patients with abnormal nucleation in their gallbladder bile was consistently higher in patients with multiple than in patients with solitary stones. At a cutoff level of 4 days abnormal nucleation in gallbladder bile occurred in 80% of patients with solitary and in about 95% of patients with multiple stones. This is far above the known rate of stone recurrence in those patients. However, highly abnormal nucleation below 1 day was observed in 40% of patients with solitary and 55% of patients with multiple cholesterol stones. These rates are comparable to the percentage of long-term stone recurrence in those patients.[9]

Rapid nucleation of cholesterol in gallbladder bile may predispose to gallstone recurrence in patients with cholesterol gallstones. The value of cholesterol nucleation times in the prediction of gallstone recurrence could be proved by follow-up of patients with successful stone dissolution in whom sampling of gallbladder bile prior to therapy has been possible.

Acknowledgment

We thank Benedikta Zündt for her excellent technical assistance and her help in preparation of the manuscript.

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