

## GALLBLADDER DISEASE AND THE HEART

P. M. BROOKS, M.R.A.C.P.\*

*National Heart Foundation, Hobart*

AND

ROBERT CUTFORTH, M.D., F.R.C.P., M.R.A.C.P.†

*Royal Hobart Hospital*

*Med. J. Aust.*, 1973, 1: 340-342.

Fifty patients subjected to operation for gallbladder disease undertook cardiac stress tests before and two months after surgery. Fourteen showed evidence of preexisting coronary heart disease and this was unaltered by operation. Squeezing the gallbladder during surgery provoked arrhythmias in six out of 10 patients with coronary heart disease and in two out of 14 of those without demonstrable heart disease. Removal of a diseased gallbladder may decrease the arrhythmia potential, particularly in patients with associated coronary heart disease, but does not alter the angina threshold.

THE effect of chronic inflammatory gallbladder disease upon the heart has been argued for many years. Single cases and small series have been reported in which angina-like pain or cardiac arrhythmias have been relieved by cholecystectomy (Straus and Hamburger, 1924; Fitzhugh

\* Research Assistant.

† Cardiologist.

Address for reprints: Dr R. Cutforth, Cardiac Investigation Centre, 37 Argyle Street, Hobart, Tas. 7000.

and Wolferth, 1935; Wakefield, 1947). Much experimental work has been done in man and animals, in which various manipulations of the gallbladder and associated viscera have caused changes in the electrocardiogram (Ravdin *et alii*, 1942; Scherf and Schott, 1953; Mendelsohn and Monheit, 1956; De Masi and Akdamar, 1969). Cardiac pain is not always easily distinguished from that arising in the gallbladder or other viscera and confusion can exist not only in the clinical interpretation but also in the interpretation of special investigations and therapeutic trials used to "confirm" the cause of the pain. When morphine is given for pain of biliary origin, transaminase levels may rise, although the heart may be normal. The pain of biliary colic can be relieved by glyceryl trinitrate, as can angina (Goodman and Gilman, 1965). Freidman (1968) concluded that several factors have to be appreciated before one can be certain of a causative association between one disease and another. In the Framingham survey no firm conclusions could be drawn about the relationship of gallbladder disease to coronary artery disease despite the fact that 5,200 adults were followed up for 10 years.

This study reports the effect of cholecystectomy on the cardio-vascular system in a number of patients suffering from gallbladder disease.

**MATERIAL AND METHODS**

Fifty patients aged between 16 and 77 years were studied, before and after cholecystectomy. The initial testing consisted of a careful history, a physical examination, ECG, chest X-ray examination, barium swallow test to exclude the possibility of hiatus hernia, haemoglobin estimation, white cell count, ESR, and one or more cardio-vascular stress tests. Stress testing was by supine bicycle exercise with or without atrial pacing as previously described (Brooks and Cutforth, 1971). Bicycle exercise was started at 50 watts and the work load was increased by 25 watts every 2 minutes until pain or ECG changes occurred (positive result) or until a heart rate of 90% of the maximum predicted for age was reached (negative result). Inability to reach the maximum heart rate in the absence of pain or ECG changes was graded as equivocal (Ellestad *et alii*, 1969). Approximately 2 months after operation, clinical examination, electrocardiography and a further stress test were carried out.

In addition, at operation in 24 patients the exposed gallbladder was subjected to pressure by squeezing after ligation of the cystic duct. An ECG was taken before induction of anaesthesia, during the whole period of pressure application and continuously for the next 2 minutes. Anaesthesia was induced with thiopentone sodium and maintained with a nitrous oxide/oxygen mixture and muscle relaxants. A standard premedication of pethidine, 100 mg, and promethazine, 50 mg, was given intramuscularly 1 hour before surgery.

**RESULTS**

Twenty-nine patients (58%) had normal preoperative and postoperative stress test results and had no evidence of coronary heart disease. Two out of 14 (14%) of this normal group developed nodal bradycardia during manipulation of the gallbladder.

TABLE 1  
Positive Bicycle Exercise Test Results<sup>1</sup>

Case Number	Age (Years)	Duration of Test (Minutes)		End Point Heart Rate	
		Pre-operative	Post-operative	Pre-operative	Post-operative
1	44	8	9	130	125
2	77	6	5	115	120
3	64	7	6	150	135
4	69	6	6	140	150
5	70	3	4	130	140
6	64	4	4	150	145
7	76	4	5	115	140
8	60	6	6	131	140
9	54	4	5	105	120
10	54	8	7	130	125
11	64	4	5	115	120
12	66	8	6	142	125
13	47	6	6	150	135
14	54	6	5	131	131
15	57	4	8	130	155
16	64	4	7	136	142
17	51	8	6	150	135
18	64	6	6	140	150

<sup>1</sup> Cases 15 to 18: the preoperative test result was considered equivocal because of failure of patient to achieve adequate heart rate; Cases 19 to 50 inclusive had negative test results.

Fourteen patients (28%) had a history of coronary artery disease and had positive stress test results before and after operation. All these patients were over 40 years of age (range 44 to 77 years). It was concluded that removal

of the gallbladder had had no detectable effect on the cardio-vascular system in these patients. However, the 14 patients who had chest pain before operation, noticed a decrease in frequency of their pain after operation, but in the absence of changes in the stress test results, the significance of these subjective feelings is dubious. Six out of 10 (60%) of this abnormal group developed some form of arrhythmia on gallbladder manipulation, 3 developing ventricular extrasystoles, 2, nodal rhythm, and 1, atrial extrasystoles. All arrhythmias were eliminated by atropine therapy and did not recur on remanipulation of the gallbladder (Tables 1 and 2).

Four patients (Cases 15 to 18) who failed to reach an adequate heart rate on bicycle exercise before operation and whose stress test results were therefore classed as equivocal, had positive test results postoperatively. Two (Cases 15 and 16) gave positive results because of a more vigorous performance on the bicycle, and 2 were found to give positive results at the preoperative level of exertion.

TABLE 2  
Results of Preoperative and Postoperative Stress Tests and of Gallbladder Manipulation during Surgery

Number of Patients (Total 50)	Preoperative Stress Test Results		Postoperative Stress Test Results		Gall-Bladder Manipulated during Surgery	Arrhythmias
	Negative	Positive	Negative	Positive		
29	29	—	29	—	14	2
14	—	14	—	14	10	6
4	—	Equivocal	—	4	—	—
3	3	—	3	—	—	—
Isolated T-wave changes						

**T-Wave Changes**

One patient, a 19-year-old girl (Case 19) with striking tenderness in the gallbladder region, had negative T waves in Leads II, III, VF, V4 to V6 in the resting ECG before operation. Her exercise test produced no change and the result was classed as normal. At operation she was found to have a normal gallbladder which was not removed. Two months later her resting ECG had returned to normal and the result of her stress test was again negative. No firm diagnosis was reached.

T-wave inversion was seen in 2 other patients with negative stress test results. In one, the T-wave changes reverted to normal after operation, while in the other T-wave inversion in AVL changed to T-wave inversion in Lead III. Direct hiatus hernia was detected in 4 patients. Traction was applied to the cardia of the stomach of these patients during operation without producing any change in ECG results.

**DISCUSSION**

No patient with a positive exercise test result before surgery showed any significant objective improvement in the cardio-vascular system after cholecystectomy.

Of those with proven coronary heart disease who were monitored during surgery, 6 out of 10 developed arrhythmias during gallbladder manipulation, compared with 2 out of 14 of those with negative stress test results. All arrhythmias were eliminated by atropine and were probably caused by reflexes acting through the vagus. Cullen and Reese (1952) using a potassium-24 clearance technique in dogs showed that distension of the common

bile duct reduced myocardial blood flow. This effect was abolished by section of the vagi. If a similar reflex exists in man it would provide an adequate explanation for our findings.

Isolated T-wave changes can be seen in such a wide variety of cardiac and non-cardiac abnormalities that it is unwise to assign a specific cause to those seen in these cases. It is possible that they represent vector changes due to alteration in heart position caused by shift in the diaphragm or mediastinum.

#### CONCLUSIONS

These results failed to demonstrate any real association between gallbladder disease and coronary artery disease. The arrhythmias detected during gallbladder manipulation were vagally mediated and occurred more frequently in the presence of clinically documented coronary heart disease. Removal of a diseased gallbladder may decrease the arrhythmia potential in patients with coronary heart disease but in this series did not alter the threshold of angina.

#### ACKNOWLEDGEMENT

This work was supported by Research Grant-in-Aid, No. G. 697, National Heart Foundation of Australia.

#### REFERENCES

- BROOKS, P. M., and CUTFORTH, R. (1971), The value of the atrial pacing test, *Med. J. Aust.*, 1: 470.
- CULLEN, M. L., and REESE, H. L. (1952), Myocardial circulatory changes measured by clearance of Na<sup>24</sup>—effect of common duct distension on myocardial circulation, *J. appl. Physiol.*, 5: 281.
- DE MASI, C. J., and AKDAMAR, K. (1969), Electrocardiography during upper gastrointestinal endoscopy. *Gastroint. Endosc.*, 16: 33.
- ELLESTAD, M. H., ALLEN, W., WAN, M. C. K., and KEMP, C. L. (1969), Maximal treadmill stress testing for cardiovascular evaluation, *Circulation*, 39: 517.
- FITZHUGH, T. jr., and WOLFERTH, C. C. (1935), Cardiac improvement following gallbladder surgery—electrocardiographic evidence in cases with associated myocardial disease, *Ann. Surg.*, 101: 478.
- FREIDMAN, G. (1968), The relationship between coronary heart disease and gallbladder disease, *Ann. intern. Med.*, 68: 222.
- FREIDMAN, G., KANNEL, W. B., and DAWBER, T. R. (1966), The epidemiology of gallbladder disease: observations in the Framingham study, *J. Chron. Dis.*, 19: 273.
- GOODMAN, L. S., and GILMAN, A. (1965), *The Pharmacological Basis of Therapeutics*, 3rd Edition, MacMillan, London.
- HAMPTON, A. G., BECKWITH, J. R., and WOOD, E. J. (1959), The relationship between heart disease and gallbladder disease, *Ann. intern. Med.* 50: 1135.
- KAUFMAN, J., and LUBERA, R. (1967), Preoperative use of atropine and electrocardiographic changes, *J. Amer. med. Ass.*, 200: 197.
- KIESSLING, C. E., SCHAAF, R. S., and LYLE, A. M. (1964), A study of T wave changes in the electrocardiograms of normal individuals, *Amer. J. Cardiol.*, 13: 598.
- MENDELSON, D. jr., and MONHEIT, R. (1956), Electrocardiographic and blood pressure changes during and after biliary tract surgery, *New Engl. J. Med.*, 254: 307.
- PATERSON, H. A. (1954), The association of gall stones and heart disease, *Ann. Surg.*, 139: 683.
- RAVDIN, I. S., ROYSTER, H. P., and SANDERS, G. B. (1942), Reflexes originating in the common duct giving rise to pain simulating angina pectoris, *Ann. Surg.*, 115: 1055.
- SCHERF, D., and SCHOTT, A. (1953), Extrasystoles and allied arrhythmias, Heinemann, London.
- STRAUS, D. C., and HAMBURGER, W. W. (1924), The significance of cardiac irregularities in reference to the operability of cases of cholelithiasis, cholecystitis and duodenal ulcer, *J. Amer. med. Ass.*, 82: 706.
- WAKEFIELD, H. (1947), The association of gallbladder disease with heart disease, clinical and experimental observations, *Med. Clin. N. Amer.*, 161.