Longitudinal study of gall stone prevalence at necropsy

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Abstract

A prospective study of the prevalence of gall stone disease at necropsy in a stable population has been undertaken over a 10 year period up to June 1988. In women, the prevalence of gall stone disease remained static but in men aged 50–59 years it rose from 7% (n=148) in the first three years to 18% (n=138) in the last three years (p<0·01) and in men aged 60–69 it rose from 12% (n=370) to 20% (n=366, p<0·01). In the latter age group the female: male ratio fell from 2:1 to 0.8:1. The proportion of deaths from coronary heart disease in men fell slightly in those over 70 during the study period. There was a fall in deaths from coronary heart disease in all age groups in women. Men with gall stones were less likely to have had a cholecystectomy than women, and overall 88% of gall stones remained in situ. In a parallel clinical study, the number of cholecystectomies carried out in the same district fell by 18% over the 10 years without any apparent change in the provision of resources. Cholecystectomy remained almost three times more frequent in women. National data indicate that there have been major changes in the average diet before and during the period of study in favour of reducing coronary heart disease. There has been no change in mortality from coronary heart disease in young men but if the observed increase in the prevalence of gall stones in men and the decrease in deaths from coronary heart disease in women are real phenomena, it seems likely that they are diet related.

In 1978, a prospective necropsy and clinical study of gall stone disease was undertaken to look for evidence of change in the prevalence, operation rates, and morbidity of gall stone disease over a period of time in a single health district. The preliminary findings were published after the first two years[1] but a further evaluation of the necropsy data has been undertaken after 10 years of the study. An increase in the prevalence of gall stones in men, which was not found in women, was an unexpected finding but two recent studies have reported an unusually high proportion of gall stones in older men.[2 3]

There are many necropsy studies of gall stone prevalence[4] but few have recorded a female to male ratio of much less than the expected 2:1,[5–8] and two of these were oriental studies in which subjects had a high proportion of pigment stones. There have been several studies of the prevalence of gall stones over time,[9–13] all of which showed an increase, although the Danish studies have shown a subsequent fall since the 1960s.[12 13] Bateson and Bouchier[14] did not find any evidence

of a real increase in Dundee from the turn of the century to 1973 but there was an increase from 1974–83,[15] and Brett and Barker, in an extensive review of the published reports,[4] found that the mean prevalence of gall stones in European countries rose from 10·5% before 1940 to 18·5% afterwards. These studies were not age adjusted, however, and Balzer et al[16] found that the prevalence of gall stones in Essen apparently increased from 8·2% to 15% in men and from 26% to 36% in women between 1940 and 1975 which was solely due to the increased age of the necropsy population. We have looked for factors that may account for the observed increase in the prevalence of gall stones in men over the past 10 years. There has been longstanding controversy over a possible relation between coronary heart disease and gall stones,[17 18] and it has recently been suggested that there may be a negative correlation.[19] This question was therefore addressed in both men and women. Only a small proportion of the UK population with gall stones undergo cholecystectomy[1] and the operation rate was examined over the same period in both the necropsy series and in the population served by the hospitals in the same health district.

Subjects and methods

A 10 year prospective necropsy study of the biliary tract was carried out between July 1978 and June 1988. All necropsy subjects aged 20 or over and resident in the South East Kent Health District were examined for the presence of gall stones or a cholecystectomy (gall stone disease). If a cholecystectomy had been carried out the presence of gall stones was assumed. (Of 300 consecutive cholecystectomies in 1980–5 carried out in the major hospital of the district, all were for stones).[20] The necropsy gall stone disease rates for each year were computed separately for men and women. Each rate was obtained by dividing the number of necropsy subjects with gall stone disease by the total number of necropsy subjects.

The necropsy rate for men and women resident in the district was taken as the number of necropsies in a given year divided by the number of issued death certificates. The numbers of certified deaths used in these computations were for people aged 15 and over but since there were only 20 deaths per year in people aged 15 to 19 this slight mismatch is of little consequence. The cholecystectomy rate at necropsy was taken as the number of necropsy subjects who had had a cholecystectomy divided by the number of necropsy subjects with gall stone disease.

To be able to calculate age-sex specific rates for gall stone disease and coronary heart disease at necropsy, both men and women were grouped

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by age decade – for example 50–9, 60–9 years etc). To investigate trends over time, rolling averages were used by plotting the age-sex specific rate for years one to three, followed by the rates for years two to four and so on.

The presence of death from coronary heart disease and the mean body mass index (BMI) as a measure of obesity were computed for men and women during the years 1978–81 and 1985–88 in order to investigate a possible correlation with trends seen in the gall stone disease rates over time (BMI=weight in kg/height in m²).[21] The height of subjects was measured with standard mortuary calipers. Death from coronary heart disease was recorded only where the pathologist considered this the principal cause. The annual number of cholecystectomies carried out in the two NHS hospitals and the one private hospital in the district was obtained from the operating theatre records.

Results

From July 1978 to June 1988, 8628 necropsies were carried out in the South East Kent District Health Authority. According to the Office of Population Censuses and Surveys (OPCS) Monitor PP1 89/1, the population for the district rose in 1988 by only 5% above the 1981 census figure of 256 200. For those aged 20 years and above there were 8563 necropsies. The prevalence of gall stone disease at necropsy in men aged 20 years and above rose from 15% (July 1978 to June 1981) to 21% (July 85 to June 88) but has remained stable for women (27% to 26%).

From 1978 to 1988 there was little change in the number of certified deaths. In the first three years (1978–81) there were 5035 deaths in men and 5018 in women. For the last three years (1985–8) there were 4907 deaths in men and 5395 in women, representing a 3% decrease and a 7% increase respectively. The proportion of those certified dead who were submitted to necropsy rose for both sexes: in men it increased from 26% to 32% (1978–81 to 1985–8) and in women from 18% to 23%. The mean age at necropsy rose during the study period from about 73 to 76 years in women and from 67 to 69 years in men. This

increase was entirely due to the number of subjects over 70 years rising by 40% for men and 44% for women (Tables I and II).

The necropsy gall stone prevalence rate increased quite considerably in men, particularly in those aged between 50 and 69 years (Figure A). The rate for females remained more or less stable (Figure B). From the first three years to the last three years, the prevalence in men aged 50–59 years increased from 7% to 18% ($0.001 < p < 0.01$, χ^2 test), from 12% to 20% ($0.001 < p < 0.01$) in men aged 60–69 years, and from 21% to 25% ($0.05 < p < 0.10$) in men aged 70–89 years. For women the corresponding changes in prevalence were from 28% to 24% in those aged 50–59 years ($p > 0.5$), from 20% to 16% in those aged 60–69 years ($0.4 < p < 0.5$), and from 29% to 28% ($p > 0.5$) in those aged 70–89 years. By 1988, prevalence rates in men were similar to those in women, so that the female to male ratio of gall stone disease for those aged 60–69 years fell from 2:1 to 0.8:1.

Mean BMI values for men and women (by age groups) in the first and last three years are shown in Tables I and II. The mean BMI values increased by about half a unit in both sexes and in most age groups between the beginning and the end of the study but in women aged 50–59 years the BMI increased by two units. In the first three years of the study men with and without gall stones had a similar BMI but during the last three years those with gall stones were slightly heavier. The women with gall stones were much heavier except for those aged 50–59 years in the last three years of the study, in whom there was little difference.

The numbers of male necropsy subjects who died from coronary heart disease are shown in Table I. Deaths from coronary heart disease increased by 6% for men aged 50–59 years between the first and the last three years of the study but decreased by up to 8% in older age groups. The reduction in deaths from coronary heart disease in women was more striking (Table II). This was greatest in the age group 50–59 years (14%), where there were small numbers, and in the group aged 80–89 years (12%) in which there was a large increase in the number of necropsies. The prevalence of gall stones in men who died of coronary heart disease was much the same as in those who died of other causes, although this rose from 7% to 18% in both groups for those aged 50–59 over the 10 year period. In women aged 50–59 years the prevalence of gall stones was twice as high in those who died from an illness other than coronary heart disease but the numbers were small and the trend was not apparent in the other age groups.

The mean ages for each age group changed very little in either sex. In the first three years and in the last three years the mean age for men in the 50–59 years group was 56. For men and women in the 60–69 years group the mean age was 65 years in both time periods. The proportion of subjects with gall stone disease who had had a cholecystectomy at necropsy rose more steeply for men (from 5% to 11%) than for women (14% to 16%) over the study. The increase in cholecystectomy rates in men, however, did not account for the overall increase in gall stone disease in

TABLE I *Prevalence of gall stones by decade compared with coronary heart disease (CHD) and body mass index (BMI) over a 10 year period in men (first and last three years)*

	Age (yrs)			
	50–59 No (%)	60–69 No (%)	70–79 No (%)	80–89 No (%)
July 1978–June 1981				
Gall stones	10 (6·8)	43 (11·6)	82 (18·9)	52 (25·0)
No gall stones	138	327	353	156
CHD	91 (61·5)	206 (55·7)	238 (54·7)	102 (49·0)
Gall stones+CHD	6 (6·6)	19 (9·2)	44 (18·5)	28 (27·5)
Gall stones/no CHD	4 (7·0)	24 (14·6)	38 (19·3)	24 (22·6)
Mean BMI:				
Gall stones	24·3	24·3	24·7	22·7
No gall stones	25·0	24·6	22·9	22·0
All subjects	25·0	24·6	23·2	22·2
July 1985–June 1988				
Gall stones	25 (18·1)	72 (19·7)	133 (22·7)	90 (29·0)
No gall stones	113	294	454	220
CHD	93 (67·4)	201 (54·9)	278 (47·4)	141 (45·5)
Gall stones+CHD	17 (18·3)	43 (21·4)	46 (16·6)	37 (26·2)
Gall stones/no CHD	8 (17·6)	29 (17·6)	88 (28·5)	53 (31·4)
Mean BMI:				
Gallstones	26·5	25·0	24·2	23·1
No gall stones	25·5	24·5	23·5	22·4
All subjects	25·7	24·6	23·7	22·6

men aged 50–59 years in whom in the last three years only one of the 25 subjects with gall stones had had an operation.

The number of cholecystectomy operations carried out in the three hospitals in the district over the same period as the necropsy study fell slightly in both sexes from 68 per 100 000 population per annum in 1978–81 to 56 per 100 000 per annum in 1985–8 (17·6%). The mean age of patients having a cholecystectomy rose from 51·3 to 52·8 years in women and from 58·1 to 59·4 in men.

Overall, of 1880 necropsy subjects with gall stone disease, 88% remained unoperated at the time of death.

TABLE II *Prevalence of gall stones by decade compared with coronary heart disease (CHD) and body mass index (BMI) over a 10 year period in women (first and last three years)*

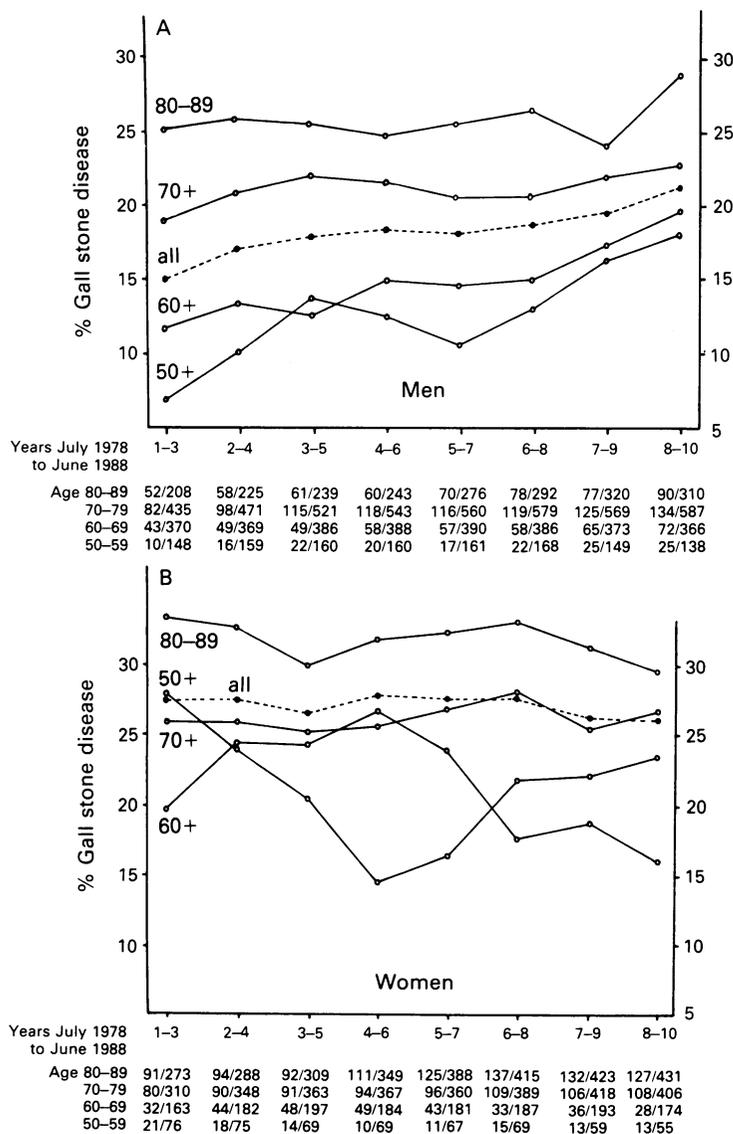|	Age (yrs)			
	50–59 No (%)	60–69 No (%)	70–79 No (%)	80–89 No (%)
July 1978–June 1981				
Gall stones	21 (27·6)	32 (19·6)	80 (25·8)	91 (33·3)
No gall stones	55	131	230	182
CHD	33 (43·4)	79 (48·5)	152 (49·0)	140 (51·3)
Gall stones+CHD	6 (18·2)	15 (19·0)	33 (21·7)	47 (33·6)
Gall stones/no CHD	15 (34·9)	17 (20·2)	47 (29·8)	44 (33·1)
Mean BMI:				
Gall stones	25·0	25·2	25·0	23·9
No gall stones	23·6	24·0	23·1	21·6
All subjects	24·0	24·2	23·6	22·4
July 1985–June 1988				
Gall stones	13 (23·6)	28 (16·1)	108 (26·6)	127 (29·5)
No gall stones	42	146	298	304
CHD	16 (29·1)	76 (43·7)	176 (43·4)	169 (39·2)
Gall stones+CHD	2 (12·5)	13 (17·1)	50 (28·4)	43 (25·4)
Gall stones/no CHD	11 (28·2)	15 (15·3)	58 (25·2)	84 (32·1)
Mean BMI:				
Gallstones	26·0	27·2	25·1	23·9
No gall stones	26·2	24·1	23·9	22·4
All subjects	26·1	24·6	24·2	22·8

Discussion

The rise in the prevalence of gall stone disease in men and the fall in the number of deaths from coronary heart disease in women may be real phenomena but both observations are unexpected and it is possible that they may be chance findings.

It has been suggested that the variations that have been observed between regions[19] may be based on too few data,[15] since prevalence rates for gall stone disease in Leeds between 1910 and 1926[22] are very similar to those in Dundee between 1974 and 1983.[15] This does not, however, necessarily mean that any fluctuations in the prevalence of gall stone disease over time or place or between sexes are of no significance or that examination of these trends will fail to give any clue to cause.

Most studies show that the prevalence of gall stones rises with age and the difference between the sexes remains roughly parallel.[1 9 10 19] In the Pima Indians, however, the prevalence of gall stones in men rises towards that of women by the age of 60 years[23] and similar observations have been made by Crump[5] and Horn[24] in other populations. Other studies show a weaker trend with loss of the sex difference only in the very elderly.[15] In Fredericksberg, the female:male ratio between 1925 and 1955 fell from 3·3 to 1·6[11] but has subsequently fluctuated between 1·7 and 1·3 up to 1985.[12] In this study the prevalence in all male age groups over 50 rose towards the female prevalence over a 10 year period.

We found no evidence of an inverse relation between gall stone disease and coronary heart disease except in so far as the former rose in men and the latter fell in women. United Kingdom statistics[25] show a slight fall in coronary heart disease in men from 1978–87 but the reduction in deaths from coronary heart disease in men in the present study is small and is virtually confined to those over 70 years. The fall in the number of deaths from coronary heart disease in women is unexpected in relation to national statistics and it is possible that a bias occurred in the latter part of the study because an increased necropsy rate in subjects over 70.

Food purchasing for home consumption from 1961 onwards[25] does show a steady decline in the amounts of butter, milk, cream, eggs, red meat, sugar, and white bread. The mean of the indices for these items consumed per person per week, where 1980=100, fell from 129 in 1976 to 65 in 1987. There was a corresponding increase in the purchase of brown bread, non-fresh fruit and vegetables, poultry, and other fats from a mean of 77 in 1976 to 131 in 1987. The total fat content of the average British diet has fallen since 1971,

A

Years July 1978 to June 1988	1–3	2–4	3–5	4–6	5–7	6–8	7–9	8–10
Age 80–89	52/208	58/225	61/239	60/243	70/276	78/292	77/320	90/310
70–79	82/435	98/471	115/521	118/543	116/560	119/579	125/569	134/587
60–69	43/370	49/369	49/386	58/388	57/390	58/386	65/373	72/366
50–59	10/148	16/159	22/160	20/160	17/161	22/168	25/149	25/138

B

Years July 1978 to June 1988	1–3	2–4	3–5	4–6	5–7	6–8	7–9	8–10
Age 80–89	91/273	94/288	92/309	111/349	125/388	137/415	132/423	127/431
70–79	80/310	90/348	91/363	94/367	96/360	109/389	106/418	108/406
60–69	32/163	44/182	48/197	49/184	43/181	33/187	36/193	28/174
50–59	21/76	18/75	14/69	10/69	11/67	15/69	13/59	13/55

Prevalence of gall stone disease at necropsy in men (A) and women (B) between 1978 and 1988

with a major reduction in the use of saturated fat and a slight increase in polyunsaturates. There have therefore been major changes in the national diet both preceding and during the period of study but these may not accurately reflect changes in the diets of men and women in this district, and it is possible that dietry risk for gall stones and coronary heart disease may start at a young age and have a different effect in the two sexes. The static prevalence of gall stone disease in women in the present study may be explained by a saturation effect, in that women with a predisposition to gall stone disease have already reached a plateau prevalence but the male prevalence is unsaturated and continues to rise.

The evidence from studies into the role of diet in gall stone disease using control groups, matched pairs,[26-28] or intervention therapy[29 30] is often contradictory and has mostly been in women. The role of refined carbohydrates and fibre depleted diets in the pathogenesis of gall stones has been supported by Heaton[31] but although there is some evidence that refined sugar may be pathogenic for gall stones,[26] at least in men under 50,[27] the case for dietary fibre is less secure. If the rise in gall stone disease is real, the dietary evidence would run counter to both theories since the consumption of sugar has almost halved over the period of the study and the purchase of fibre rich food has almost doubled.[25] Obese people synthesise excess cholesterol and have supersaturated bile[32] but although most studies have shown a clear correlation between obesity (BMI) and gall stone disease in women,[33 34] this is not the case in men.[27 33 35] In this study there did seem to be an association between gall stone disease and BMI in men in the last three years but this trend is stronger in women. Slimming treatment may be a risk factor for gall stone disease[33] but there was a slight increase in the BMI in both sexes over the period of the study.

The necropsy cholecystectomy rate for gall stone disease was 11·6%, which is close to that found in the nine British towns in 1977-8 (11·4%)[19] so the vast majority of patients with gall stones do not undergo operation in this country and there is a low gall stone related death rate.[1] The clinical cholecystectomy rate in this district fell for both sexes during the study, although there was no evident change in the provision of surgical resources. It has long been known that cholecystectomy rates per head of population may vary as much as fivefold between countries[36 37] and have little relation to the prevalence of gall stones.[15 38] Cholecystectomy rates in Canada[39] rose to a peak in 1972-3. In Quebec province this was over 450 operations per 100 000 population per annum, twice the rate of Newfoundland province, which in turn was twice the rate expected in the UK.[1 36] Cholecystectomy rates also rose to a peak in Scotland in 1976, with 120 operations per 100 000 in those health boards with the most surgeons – twice the rate in those with the least surgical resources.[40]

As well as the modest fall in cholecystectomy rates noted in the present study, rates have fallen substantially in Canada[39] and Sweden,[41] and to a lesser extent in Scotland.[42] In Saudi Arabia, however, there has been an enormous increase.[43]

Operation rates vary for economic and many other reasons[44] but it is possible that the present fall seen in most centres is due to a realisation that the symptomatic outcome of cholecystectomy is sometimes disappointing.[20]

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