

171 Risk Indicators of Delayed Gastric Emptying in 296 Patients with Functional Dyspepsia

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Some pts with functional dyspepsia (FD) present with delayed gastric emptying (GE). The association between this digestive motor abnormality and dyspeptic symptoms has never been investigated in a large FD population. We prospectively evaluated clinical features, dyspeptic symptoms and GE of solids in 296 strictly selected FD pts (118 M, 178 F; 39 ± 12 yrs; 62 ± 12 kg; m ± SD). Epigastric pain or burning, postprandial fullness (PF), nausea and vomiting were each graded 0 to 3 according to their intensity. Including criteria were total score ≥3 with at least one symptom ≥2, in the absence of organic, systemic, metabolic diseases. GE of a mixed meal (638 kcal) was measured scintigraphically (99mTc-chicken liver) and expressed as GE rates (k; %emptied/min). Results were compared to those of 50 healthy controls (HC; 30 M, 20 F; 35 ± 12 yrs; 67 ± 11 kg). The two groups were not matched for sex (P < 0.05), age (P < 0.05) and body weight (BW) (P < 0.01). GE was delayed in FD (k = 0.47 ± 0.20) vs HC (k = 0.67 ± 0.18; F = 36.70; P < 0.001; ANOVA standardized for sex, age and BW). Relevant PF (≥2) was more frequent in pts with delayed GE compared to pts without delayed GE (92.1% vs 80.2%; P < 0.01). No difference was detected in the frequency of pain (44.7% vs 54.9%), nausea (31.2% vs 28.6%) and vomiting (13.2% vs 10.4%). Logistic regression analysis showed that the presence of relevant PF and changes in BW were independently associated with delayed GE. Odd ratios (OR) and 95% confidence intervals (95%-CI) are reported in the table:

	OR	(95%-CI)	P value
PF (≥2)	2.449	(1.11–5.39)	0.019
BW (kg)	0.965	(0.94–0.99)	0.001

Conclusions: FD pts present delayed GE compared to HC, irrespectively of sex, age and BW. The presence of relevant PF and low BW are independent risk indicators of delayed GE in FD pts.

172 Gallbladder Stones (GBS) Do Not Recur True to Type After Medical Dissolution Therapy

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Primary gallbladder stones (GBS) may be: (i) solitary or multiple, and (ii) radio- and CT-lucent (and therefore cholesterol-rich) or radio-opaque and calcium-containing. Medical treatments which dissolve or remove the stones but leave the GB behind suffer the disadvantage of GBS recurrence (10–15% p.a. to plateau at approx 50% by 5 yr). Little is known about the composition of recurrent stones and whether they recur "true-to-type". **Methods:** Therefore, in 20 patients with recurrent stones detected 5–74 mo (mean 26 ± SEM 4 mo) after being rendered stone-free with oral bile acids (OBA, n = 5), lithotripsy (ESWL) + adjuvant OBA (n = 6), MTBE (n = 3), or percutaneous cholecystolithotomy (PCCL, n = 6), we compared pre-treatment and post-recurrence GBS number, maximum gallstone CT attenuation scores (CT scores < 100 Hounsfield Units (HU) predict cholesterol-rich, potentially dissolvable, stones), and, in 13, the dissolvability of the recurrent radio- and CT-lucent stones with OBA (n = 11) or ESWL + OBA (n = 2). **Results:** Stone number Before treatment, 4 patients had solitary and 16 had multiple stones, but on recurrence, the GBS were not true-to-type in 8 of the 20. Thus, 4 patients who initially had solitary GBS, developed multiple recurrent stones, while 4 of the 16 who originally had had multiple GBS, developed solitary recurrent stones. **Stone lucency/attenuation** As a result of selection, before dissolution treatment (OBA, ESWL+OBA or MTBE) the primary stones were all radiolucent with maximum CT scores < 100 (mean 41, range 10–74) HU. After recurrence, the mean GBS attenuation score increased to 55 HU (NS), being unchanged in 6, decreased in 3 and increased in 5 – two of whom developed calcium-containing stones (HU scores of 118 and 176). The discrepancy between primary and recurrent stone attenuation was even more marked in those treated by PCCL, all of whom initially had radio-opaque stones with a median CT score of 351 (range 100–969) HU. On recurrence, only one had calcified stones (HU 140) while the remaining 5 had CT-lucent stones (25–98 HU, p < 0.01). **Dissolvability** Of the 13 patients whose recurrent radio- and CT-lucent stones were treated with OBA (n = 11) ± ESWL (n = 2), all showed evidence of GBS dissolution (complete in 8 and partial in 5 after 2 to 15 mo OBA) – suggesting that the recurrent stones were, indeed, cholesterol-rich. **Summary:** In 13 of 20 patients (65%) the number or composition of recurrent GBS differed from that of the original stones. Thus, GBS do not recur true-to-type. However, irrespective of original GBS composition, recurrent stones are usually radio- and CT-lucent, and therefore cholesterol-rich and potentially dissolvable with medical therapy.

173 Does Biliary Pain Have a Muscular Origin?

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Aims: to determine if biliary pain is related to gallbladder (GB) contractility.

Methods: 23 patients admitted for elective cholecystectomy were asked to complete a pain questionnaire describing the last attack of biliary pain. The questionnaire included a visual linear analogue scale (VAS) (0–10) and the McGill word score (0–20) and pain rating index (0–78).

GB's were obtained at cholecystectomy. 6 strips were taken from the GB and mounted in organ baths containing Krebs solution at 37°C, pH 7.4, aerated with 95% O₂ and 5% CO₂ and connected to an isometric force displacement transducer. Cumulative concentrations of 0.01–500 nM CCK-8 were added to the organ baths. Results were expressed in grams of developed tension.

Results: VAS scores ranged from 3.6 to 10. The number of words chosen ranged from 3 to 17 and the pain rating index from 6 to 50. Maximal contractile response in-vitro ranged from 0.28 to 5.7 g of developed tension. Linear regression analysis showed a significant correlation between the number of words chosen and maximal contractile response (p = 0.0064) and also between pain rating index and maximal contractile response (p = 0.0025). There was no correlation between the linear analogue results and the in-vitro results.

Conclusion: The pain associated with biliary colic as analyzed with the McGill pain questionnaire correlates well with the maximal isometric response of the gallbladder in-vitro.

174 The Effect of Bile Lipid Concentration (BLC) and Biliary Deoxycholic Acid (DCA) on the Solubilization of Biliary Cholesterol (CH) in Vesicles

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Background: CH is solubilised in bile by phospholipids (PL) alone as vesicles, and by PL and bile acids (BA) as mixed micelles. CH microcrystals form from unstable vesicles with a high CH:PL molar ratio. These unstable vesicles, may arise due to increased BLC. An increase in the proportion of biliary DCA is associated with a rise in cholesterol saturation and rapid nucleation of cholesterol microcrystals—factors important in the pathogenesis of CH-rich gallbladder stones (GBS). However the effect of DCA on the distribution of CH between vesicles and micelles and on the vesicular CH:PL molar ratio (VCH:PL), is unknown. **Methods:** Therefore, in 43 GB bile samples from patients with and without GBS, we measured total biliary BA, PL and CH concentration, and derived BLC and CH saturation indices (CSIs). The vesicular and micellar fractions were separated by sucrose density gradient ultracentrifugation and the range of spontaneous variations in: (i) the % of total biliary CH in vesicles (VCH%), (ii) the VCH:PL, (iii) the vesicular concentration of CH [VCH] and (iv) the micellar concentration of CH [MCH] in mmol determined. Total biliary BA composition was measured by HPLC. Linear and multiple regression analyses were then performed to determine the influence of (i) BLC and (ii) DCA on the partitioning of CH between micelles and vesicles. **Results:** The ranges of spontaneous variations were as follows: CSI 0.90–1.90; BLC 73.9–279.8 mM; VCH% 26.1–89.2%; VCH:PL, 0.36–1.47; [VCH] 3.2–18.5 mM and [MCH] 2.0–14.9 mM, while the mean BA composition (% of total ± SEM) was: 40.3 ± 1.9% cholic acid, 37.3 ± 1.2% chenodeoxycholic acid and 21.2 ± 1.5% DCA with <2% of lithocholic and ursodeoxycholic acid. CSI correlated positively with the VCH% (r = 0.65; p < 0.001), the VCH:PL (r = 0.73; p < 0.001) and the [VCH] (r = 0.69; p < 0.001). There was no relationship between the BLC and the CSI, although as the BLC increased, the fraction of cholesterol in vesicles (% VCH) reduced (r = 0.53; p < 0.001) while the [VCH] increased (r = 0.42, p < 0.01). Since the CSI also correlated positively with % DCA (r = 0.54; p < 0.001), it was not surprising that the % DCA was linearly related to the VCH:PL (r = 0.53; p < 0.001) and [VCH] (r = 0.59; p < 0.001) but there was no significant relationship with the [MCH]. Multiple regression analysis confirmed that: (i) both the CSI (p < 0.001) and the BLC (p < 0.001) were independent determinants of [VCH] (r = 0.88) and similarly (ii) both the CSI (p < 0.002) and the % DCA (p < 0.05) also determined the [VCH] (r = 0.74) independently of each other. **Interpretation:** Relative increases in BLC and the % DCA (by virtue of its hydrophobicity) favour the partitioning of CH to vesicles, as opposed to micelles which, in turn, leads to a rise in the VCH:PL and an increase the propensity of vesicular CH to precipitate microcrystals – an early step in CH-GBS formation.

175 The Effect of Octreotide (OT) on Meal-Stimulated Gallbladder (GB) Emptying in Control Subjects and Acromegalic Patients

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Background: Up to 60% of acromegalic patients treated with octreotide develop GB stones – in part because of impaired GB emptying – but there is controversy about the influence of acromegaly itself on GB motor function, and whether the OT-induced dysmotility affects fasting (FV) or residual (RV) GB volume, the extent of GB emptying (ejection fraction or EF, and the delta volume or DV – that is, FV minus RV) or the rate of GB emptying (RGE in ml/min). **Methods:** To study this, we used a randomised, double-blind, placebo (saline)-controlled, cross-over design to examine the effects of a single dose (50 µg) of OT given sub-cut 30 min before a fat-rich liquid meal ("Ensure"), on all 5 parameters of GB emptying, assessed by ultrasound, in 6 non-acromegalic control subjects and 8 stone-free non-OT treated acromegalic patients. **Results:** Before OT, the fasting GB vol in the acromegalic patients (49.8 ± SEM 7.1 ml) was more than 3 times that in controls (15.8 ± 1.9; $p < 0.005$), but in response to a meal, acromegalic GBs emptied faster (RGE 0.97 ± 0.19 vs 0.26 ± 0.04 ml/min; $p < 0.005$) and to a greater extent (DV 33.8 ± 5.5 vs 9.5 ± 1.2 ml; $p < 0.005$) than did those in the controls, and while the % GB emptying was also slightly greater (EF 74.3 ± 2.4 vs 66.3 ± 2.3%; $p < 0.03$), the RV in the acromegalics (10.9 ± 1.2 ml) was still more than twice that in the controls (5.0 ± 1.0 ml; $p < 0.02$). OT markedly inhibited meal-stimulated GB emptying in the acromegalics with significant reductions in the DV (to 10.7 ml; $p < 0.02$), EF (to 23.1%; $p < 0.002$) and the RGE (to 0.44 ml/min; $p < 0.02$) and a significant increase in the RV (to 38.8 ml; $p < 0.002$), but OT's effects were even more marked in the controls, where it completely abolished GB emptying. **Summary/conclusions:** These results confirm that acromegalic patients have cholecystomegaly (larger FVs than controls) and show that in response to a meal, their GBs expel a greater than normal volume of bile (DV and EF) more rapidly than normal (RGE) but despite this, are left with increased residual GB volumes. OT inhibits GB emptying more in controls than in acromegalic patients and since chronic OT treatment induces GBS, this suggests that the residual volume is more important than the speed of GB emptying, or the amount of bile expelled, in the pathogenesis of GBS.

176 Cholelithiasis in Diabetes Mellitus: Predisposing Factors

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The aim of our work was to study the factors concerning the increased prevalence of cholelithiasis (CL) (gallstones or previous cholecystectomy) in adult subjects with diabetes mellitus (DM).

Materials and methods: 2000 DM patients: 1227(61.35%) females and 773(38.65%) males consecutively hospitalised in our Department with an average age of 58.34 ± 11.43 years were prospectively investigated.

Results: Among the 2000 DM patients, insulin-dependent DM (IDDM) was present in 353(17.65%) subjects and 49 (13.86%) of them presented CL, whereas among the 1647 (82.35%) non-insulin-dependent DM (NIDDM) patients, 401 (24.35%) presented CL, the difference between the 2 CL prevalences being statistically significant ($p < 0.01$). Overall 450(22.5%) of the DM patients had CL (154 gallstones and 296 previous cholecystectomies). After adjustment for age, body mass index and sex, using multiple logistic regression, the overall prevalence of CL in our DM patients was 22.1%.

Further on we calculated OR = odds ratio (95% confidence interval) concerning the risk of appearance of CL for the following risk factors:

- DM: IDDM-OR = 0.50 (0.36 < OR < 0.70); NIDDM-OR = 2.00 (1.43 < OR < 2.79)
- Duration of DM: under 10 years-OR = 0.88 (0.70 < OR < 1.10) and over 10 years-OR = 1.14 (0.91 < OR < 1.43)
- Sex: females-OR = 3.05 (2.36 < OR < 3.95) and males-OR = 0.33 (0.25 < OR < 0.42)
- obesity-OR = 1.91 (1.48 < OR < 2.46)
- Hyperlipoproteinemia (HLP)-OR = 1.16 (0.85 < OR < 1.58)
- Age: under 50 years-OR = 0.61 (0.48 < OR < 0.78) and over 50 years-OR = 1.64 (1.20 < OR < 2.08)

Conclusions: In our study, the factors which seem to determine the increased prevalence of CL in DM, are: NIDDM, female sex, obesity, age over 50 years, HLP, duration of DM over 10 years.

177 Colonoscopic Screening in First-Degree Relatives of Patients with Colorectal Cancer (CCR): A Prospective, Multicentre, Case-Control Study

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First-degree relatives of patients with common CCR carry an increased risk of CCR. Feasibility and efficiency of colonoscopy in this group are however not well defined.

The 488 first-degree relatives (R), aged from 40 to 75 years, of 195 patients with common colorectal cancer examined in 16 french general hospitals were invited to a colonoscopic screening. Each examined relative was matched by center with two controls (C) for sex, age and symptoms. Logistic regression taking account of sex, age, center, and group (R or C) was used to determine the risk of colorectal tumor.

186 relatives (38% of total group), of mean age 54 years, were examined. Odds ratios (OR) for colorectal tumors observed in R vs C, adjusted for center, sex and age were as follows: adenomas OR = 1.5 (95% CI: 1.0–2.4); adenomas < 1 cm OR = 1.2 (95% CI: 0.7–1.9); adenomas > 1 cm OR = 2.5 (95% CI: 1.1–5.4); adenomas with villous structures OR = 2.8 (95% CI: 1.0–7.9); adenomas with moderate to severe dysplasia OR = 3.1 (95% CI: 0.9–10.1); carcinoma OR = 7.2 (95% CI: 1.4–37.8).

Sex and age were preeminent risk factors for adenomas in R and C, but R seemed to be more prone to high-risk adenomas (> 1 cm, villous structure, moderate to severe dysplasia) or cancer.

In conclusion, a history of CCR in a first-degree relative must be taken into account in CCR screening policy. Genetic predisposition to common CCR might concern adenomas growth.

178 Polypectomy of Adenomas in the Prevention of Clinical Colorectal Cancer. 10 Years Follow Up of a Prospective, Controlled Population Study in Telemark, Norway

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400 men and women aged 50–59 years (20 of each sex from each year of age) were drawn by randomization from the population registry of the municipalities of Porsgrunn and Skien in the county of Telemark, Norway, to be offered a screening examination of the rectum and sigmoid colon using a colonoscope. An equal control group was similarly drawn from the same registry. 324 individuals (81%) attended for the initial screening examination in 1983. A finding of polyps qualified for full colonoscopy.

In the screening phase of the study neoplasms were found in 57 individuals, including one case of Dukes' stage A carcinoma, two cases of intra-mucosal carcinoma and one individual with severe dysplasia in an adenoma. Controls were at no stage invited to have a screening examination.

After 10 years, information reported to the Norwegian Cancer Registry has revealed presence of no new carcinomas in 324 attending for screening, one case in 76 not attending and 5 cases in the control group of 400 individuals. All cases of new carcinomas were diagnosed due to symptoms and not in the course of screening. 3 of the 6 cancer patients have died from their cancer.

As far as we know, this is the first prospective, controlled study regarding the benefit of polypectomy in cancer prevention.

179 Diagnostic Value of Somatostatin Receptor Scintigraphy in Neuroendocrine Tumors

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Somatostatin receptor scintigraphy with 111 In-pentetreotide, (Octreoscan 111), is a technique recently proposed for demonstrating the presence of receptor positive neuroendocrine tumors and their metastases. We performed this technique in 20 patients: 12 males and 8 females, ranging in age from 21 to 68 years; all patients had biochemical and/or histological diagnosis of neuroendocrine tumor (16 gastrinomas, 1 pancreatic somatostatinoma with hepatic metastases, 1 carcinoid with hepatic metastases, 1 medullary carcinoma of thyroid, and 1 nonfunctioning pancreatic islet cell tumor with hepatic metastases). Nine of the 16 patients with gastrinoma had familial multiple endocrine neoplasia type 1 (MEN 1). One of these nine patients had a pancreatic gastrinoma with liver metastases and massive carcinoid proliferation of the gastric body. Each patient was studied at 4, 24 and 48 hours after injection of 180–220 MBq of Octreoscan 111 (Mallinckrodt Diagnostica, Petten Holland). Total body planar imaging was performed using a Philips gamma camera (Gammadiagnost TOMO) equipped with a medium energy parallel