



Patients with functional constipation do not have increased prevalence of colorectal cancer precursors

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the preferred treatment goal or acknowledgement that liver transplantation is an expensive intervention if all it achieves is "controlled drinking patterns".

The principle of a structured management programme is the one that has not been comprehensively explored in the UK. There have been pockets of work such as the report of a pilot psychological intervention programme in Birmingham,⁵ but at the time of writing there are only three dedicated addiction specialists working in the seven transplant centres. These are likely to do little to deal with interunit inconsistencies in both candidate selection and support after transplant. At the same time, we could question whether we are putting unreasonable pressure on to donor recipients. If we are to share the sense of being custodian to the donor liver then, surely, we also have a responsibility to provide comprehensive and consistent support packages to the patients we select. This acknowledges a process of reciprocity, as after all, no unit would tolerate transplanting a patient and then asking them to leave the hospital and source appropriate immunosuppression.

We strongly agree with O'Grady's assertion that current transplant service provision is poor, but dealing with this could backfire. Equity of access and referral to transplant centres may well benefit from closer scrutiny, and it is likely that large pockets of referral come from district general hospitals where clinicians have close links with the transplant units. However, other units may have poor liaison and referral rates either due to clinical naivety or ethical judgements on suitability of referral for a patient with ALD. Either way, if we are already in an era of donor shortage to increase referral activity could open up the floodgates and potentially overwhelm current transplant assessment procedures.

Finally, we worry that O'Grady, by permissive acceptance that the general population drinks more than the Department of Health recommended guidelines on alcohol "because their peers do", may be undermining long-standing health promotion advice.⁶ We only have to look at the response of the general public to the 21 and 14 units/week becoming 3-4 and 2-3 units/day (they began quoting 28 and 21 units, respectively) to realise that clear unambiguous advice is the first starting point for alcohol education. After that, brief interventions for alcohol advice are proved to be effective for those with hazardous/harmful levels of consumption,^{7,8} and for those with an alcohol dependence then timely appropriate referral to specialist alcohol services are vital.

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Author's response

Webb and Shepherd's contribution to the debate on liver transplantation for alcohol-related liver disease is welcome, not least as it comes from an extremely important, but underdeveloped element of the multidisciplinary approach to the management of this issue. They point out that only three of the liver transplant programmes in the UK have dedicated addiction specialists. I believe this is unacceptable, as there is evidence that dealing with this would further improve the outcomes after liver transplantation for alcohol-related liver disease. I, therefore, endorse their comments on the fundamental importance of support structures after transplantation, although not necessarily at precisely the same pitch as the supply of immunosuppressive treatment.

Any assessment of a clinical service must include key data on outcomes, and in the context of liver transplantation, evaluation of patient and graft survival rates are inescapable. Disease recurrence affects these parameters, and it is appropriate to undertake comparisons between different aetiologies of liver disease indicating the need for transplantation. These analyses do not necessarily prove efficacy, but can establish lack of inferiority, and this is important information when evaluating disease recurrence and outcomes.

The term "apparently arbitrary tests" was used in the paragraph that tried to articulate some patient perspectives on the assessment process. The term was certainly not meant to be critical of the tools used by individual addiction specialists, but to reflect how a patient might view the lack of agreement in how they should be assessed and the absence of widely adopted, standardised, transparent and reproducible assessment protocols.

Webb and Shepherd are quite right to say "clear and unambiguous advice is the first starting point for alcohol education". The Department of Health recommendations are helpful for a significant section of the population. However, these recommendations are ignored by a sizable cohort, as in that mindset they lack tangible credibility. Furthermore, there is no strong evidence that these recommendations have been successful in reducing overall alcohol consumption. I argue for additional public health intervention for the population of alcohol consumers who reject the

council of perfection and this is best delivered before they establish a need for referral to either addiction or medical services. I view this as pragmatic engagement of the population at risk rather than permissive erosion of effective health promotion advice.

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It has always been a controversial subject whether patients with functional constipation have a higher risk of developing colorectal cancer. Watanabe *et al*¹ showed an increase in relative risk (RR) 1.31 of colorectal cancer in those with constipation.¹ Roberts *et al*² showed an association with >twofold risk of colon cancer (OR 2.36) adjusted for age, race, sex and relevant confounders.² On the other hand, both studies by Dukas *et al*³ and Kune *et al*,⁴ after adjusting for age, sex and other risk factors showed no increase in risk.

Colorectal cancer develops through the adenoma-carcinoma sequence.⁵ Thus, we aimed to compare the prevalence of colorectal adenomas in patients with long-standing functional constipation to an age, sex and risk factors-matched control group in a prospective study. The result indirectly gives insight into the risk of development of colorectal cancer in patients with chronic constipation.

Patients with long-standing constipation, satisfying the Rome II criteria⁶ were recruited from the Constipation Clinic of Queen Mary's Hospital, Hong Kong. Exclusion criteria include constipation predominantly from irritable bowel syndrome, secondary causes for constipation, those who had a colonoscopy done in the past 10 years, or those under active medical care for gastrointestinal complaints. Healthy controls were recruited from the general population who had no symptoms of constipation and did not satisfy the Rome II criteria. In addition, they were matched for age, sex, smoking history, diabetes and family history of colorectal cancer, with those in the constipated group. Subjects aged ≥ 50 years in both groups were invited for assessment by colonoscopy. Colonoscopy was repeated the next day for those with poor bowel preparation. The withdrawal time of the colonoscopy procedure was >6 min to minimise the chance of lesions being missed.⁷ Incomplete examination was excluded for analysis. Advanced colonic lesion was defined as the presence of cancer, or adenomas with villous component, or with high dysplasia, or ≥ 1 cm. The calculated sample size was 200 people in each group, assuming the polyp prevalence in Hong Kong was 24%,⁸ with an OR of 2.36² for developing colorectal cancer or adenoma.

In all, 220 consecutive patients with constipation and 235 controls were invited for screening colonoscopy. The colonoscopy procedure failed in six patients due to presence of multiple sharp bends, whereas 20 controls

Table 1 Demographic data and prevalence of colonic lesions of the constipated and control groups

	Constipated group % (n = 214)	Control group % (n = 215)	p Value
Demographic data			
Age (years), mean (SD)	61 (9)	61 (8)	0.93
Sex (female)	73.8	75.8	0.64
History of smoking	4.7	6	0.53
Diabetes	5.6	8.4	0.26
Family history of colorectal cancer	6.1	5.6	0.83
Prevalence of colonic lesion			
Endoscopic polyp	18.7	20.5	0.64
Adenoma	12.1	13	0.79
Hyperplastic polyp	2.8	4.7	0.31
Advanced colonic lesions	3.7	4.7	0.64
Colorectal cancer	0.47	0	0.32

defaulted or refused the screening colonoscopy. Twelve patients and one control had unsatisfactory bowel preparation requiring colonoscopy to be repeated.

The demographic data in both groups were comparable as they were purposely matched (table 1). There was no difference in terms of endoscopic polyps, adenomas, hyperplastic polyp, advanced colonic lesion or colorectal cancer (table 1).

It has been a laymans' concept that constipated patients may have higher risk of developing colorectal cancer owing to the accumulation of "toxic substances". However, this has never been proved. The studies reporting a possible link between constipation and the development of colorectal cancer, however, were mostly questionnaire based results and were retrospective.^{1 2} Our study confirms the results of the prospective study by Dukas *et al.*³ Moreover, Nascimbeni *et al*⁹ have assessed the frequency of aberrant crypt

foci in patients with sigmoid colorectal cancer and those with diverticular disease, and found that mean aberrant crypt foci did not often vary according to constipation, laxative use or melanos coli in either group.

We have extrapolated our results and concluded that there is no increased risk in constipated patients of developing colorectal cancer, when compared with age, sex and other risk factors-matched controls in the general population. The results can be extrapolated because most colorectal cancer develops through the adenoma-carcinoma sequence.⁵

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