Body measures in relation to gastro-oesophageal reflux

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Association between overweight and gastro-oesophageal reflux disease (GORD) has become established in large-scale analytical epidemiological research. There is a dose-dependent association between increasing body mass index and GORD

An association between overweight and gastro-oesophageal reflux disease (GORD) has long been suspected and observed in case series. Recently, this association has become established in large-scale analytical epidemiological research.^{1,2} In a recent meta-analysis based on the available literature, it was concluded that there is a dose-dependent association between increasing body mass index (BMI) and GORD, usually assessed as typical reflux symptoms—that is, heartburn or regurgitation.³ The precise strength of this association is difficult to assess, but it seems that persons with a BMI >30 kg/m² are at an about twofold increased risk of GORD than persons of normal weight. Interestingly, it seems that any increase in BMI, even within the range of what is considered normal BMI, is associated with a gradually increased risk of reflux symptoms.² A similar finding has been observed with regard to the relation between increased BMI and adenocarcinoma of the oesophagus,⁴ a cancer closely linked with GORD.⁵

In the present issue of *Gut*, Corley *et al*⁶ (see page 756) present a large cohort study that not only evaluates BMI in relation to GORD, but also evaluates the role of objectively measured abdominal diameter, with and without adjustment for BMI. Moreover, the study addresses the possible ethnic differences with regard to body composition and GORD. Intriguingly, the association between high BMI and symptoms of GORD was particularly strong among whites than among blacks and Asians. Moreover, after adjustment for BMI, the abdominal diameter correlated with symptoms of GORD in whites only, whereas no such correlation was identified in blacks or Asians. This is a new and possibly valid finding, but it needs to be confirmed by future studies before it can be considered true. Some potential methodological sources of error in the study might contribute to explain the findings. As pointed out by

the authors, a particular problem might have been the differential misclassification of the outcome (GORD) between ethnic groups, which could distort effects of the true relation between measures of body composition with regard to reflux. Moreover, the cross-sectional design makes it impossible to reliably assess the timing of the relation between the exposure (body measures) and the outcome (GORD) under study. Yet, the reported prevalence of GORD seems to vary greatly in different geographical areas and between ethnic groups according to the available literature, and the results of the current study further indicate the possibility of ethnic biological differences in the development of GORD.

If a true ethnic difference in the aetiology of GORD is confirmed by future research, it might open a discussion of the occurrence of GORD-related diseases, including oesophageal adenocarcinoma.⁵ Adenocarcinoma of the oesophagus is considerably more common in whites than in other ethnic groups.^{7,8} Thus, ethnic differences in the development of GORD might explain or at least contribute to the ethnic differences in the incidence of oesophageal adenocarcinoma. In this context, it should be stressed that the strong link between GORD and oesophageal adenocarcinoma should encourage further research that focuses on the aetiology of GORD. Such research might be the key to understanding the aetiology of oesophageal adenocarcinoma, a highly lethal cancer with a rapidly increasing incidence in Western populations, particularly among white males.^{7,8}

The current study by Corley *et al*⁶ also suggests a lack of difference between sexes with regard to the relation between increased BMI and GORD. This result is in contrast with some population-based studies, where a substantially stronger association between BMI and reflux was found among females than males.^{1,9} Some data indicate that exposure to

oestrogen might have a role in promoting reflux among women.^{1,9} It has also been hypothesised that oestrogen might relax the lower oesophageal sphincter and thereby facilitate reflux.¹⁰ As data are conflicting, there is a continued need to assess the possibility of sex differences in the occurrence of GORD in future studies.

In the current issue of *Gut*, El-Serag *et al*¹¹ (see page 749) present an interesting study that evaluates the role of body measures in relation to GORD. They objectively measured various anthropometric variables, including waist circumference, in relation to objectively measured 24 h pH measurements of oesophageal acid exposure. The cross-sectional design and the risk of selection bias should not materially hamper this study, as reverse causality and selection due to obesity is unlikely. The study provides objective data regarding both the exposure (body measures) and the outcome (GORD). Moreover, the study includes waist and hip circumference, which has rarely been evaluated. Much of the previous research has been based on self-reported weight and height, and subjective symptoms of GORD. The current study by El-Serag *et al*¹¹ provides further evidence for an association between obesity and GORD, as the acid exposure was higher in obese persons, a finding in line with the previous literature. An interesting finding was that the obesity effect on oesophageal acid exposure was attenuated by adjustment for waist circumference, indicating that the association between obesity and GORD might be mediated by waist circumference. This information gives some clues to the biological mechanism of the association between BMI and GORD.

In the study by El-Serag *et al*, however, no differences were found between sexes or ethnic groups with regard to body measures and acid exposure of the oesophagus. Thus, this study does not provide much support for the ethnic differences found in the article by Corley *et al*.⁶

Intensified epidemiological research of the risk factors for GORD, such as those exemplified by the studies of Corley *et al*⁶ and El-Serag *et al*¹¹ should be encouraged. The physiology of GORD has been extensively studied and the physiological mechanisms have been well defined, but the actual underlying factors that actually cause GORD deserve much more attention. It is surprising that the available literature in this field is so sparse. Therefore, more detailed studies on various possible risk factors for GORD are warranted. As GORD is usually a chronic or recurrent disease, the available epidemiological research has suffered

from the problems of cross-sectional design. A further development of the aetiological research of GORD would therefore be to assess incident cases of GORD. Such research would supply us with a reliable estimation of the incidence of GORD and also increase the validity of the aetiological research of GORD.

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Sphincter of Oddi dysfunction

Prospective comparison of secretin-stimulated MRCP with manometry in the diagnosis of sphincter of Oddi dysfunction types II and III

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Is the role of secretin in causing a choleresis clinically significant enough to be a “stress test” for biliary SOD?

Every specialty in Medicine has its orphan diagnosis; in ophthalmology it's “dry eyes”, in gynaecology “dyspareunia”, in rheumatology “fibromyalgia” and the list goes on. In gastroenterology, the vast diagnostic and therapeutic wasteland is irritable bowel syndrome (IBS). However, deep within IBS (or more correctly, chronic functional abdominal pain syndrome) there is an almost impenetrable jungle, called sphincter of Oddi Dysfunction (SOD). It is not a place for the faint-hearted. SOD as a fashionable diagnosis first appeared on the radar screen in a 1989 *N Engl J Med* paper: a group of US investigators published their experience of endoscopic (biliary) sphincterotomy (EBS) in patients with postcholecystectomy pain.¹ The authors divided SOD into three categories depending on the presence or absence of transiently abnormal liver serologies and/or common bile duct (CBD) dilatation. “Typical” biliary-type pain was needed to make the SOD diagnosis. Type I patients had “typical” biliary pain, transient serum transaminase elevations to at least 1.5 times the

upper limit of normal with normalisation between attacks on ≥ 2 occasions, and a CBD ≥ 12 mm in diameter. Type II patients had pain and enzyme elevations or a dilated CBD, but not both. Type III patients had a pain syndrome alone. (The original classification included delayed drainage of contrast from the bile duct after ERCP as an addition criterion. Most investigators have dropped this from the classification, as it has been shown to be unreliable). The so-called Milwaukee Classification of SOD has survived unchanged for 17 years, despite growing evidence that it is flawed and in need of revision.² This is not intended as a criticism of the original investigators, who tried their best to make sense of a difficult pain syndrome in a demanding group of patients. Under the recently promulgated Rome III Criteria,³ SOD is now part of a biliary dyskinesia syndrome that includes gallbladder dysmotility in those who have not had that organ surgically removed. Most ERCP endoscopists who see cases of postcholecystectomy pain feel that type I SOD should be dropped from the classification. It is not a

motility disturbance but a mechanical (papillary) stenosis of the biliary outlet. It is effectively treated by EBS, with $>95\%$ long-term “cure” rates.⁴ Indeed, this outcome is so predictable that we do not bother to perform sphincter of Oddi manometry (SOM) in the patients: the result is the same regardless of the sphincter pressure measured. SOM is a technically demanding technique used to measure biliary and pancreatic sphincter pressures. Typically, SOM is limited to large referral centres, which can justify the investment in expensive equipment to help evaluate patients with postcholecystectomy pain syndromes and idiopathic pancreatitis.⁵ On the heels of biliary SOD came an inevitable attempt to similarly classify pancreatic sphincter dysfunction.⁶ A useful discussion of pancreatic SOD is beyond the scope of this commentary, but it will suffice to say that it is imperfect and even more confusing to many of us than biliary SOD! Unfortunately, SOM has developed a bad reputation for causing post-ERCP pancreatitis, especially in patients with type III SOD.⁷ As Freeman *et al*⁸ have pointed out however, the act of performing pressure measurement is not the problem, the risk comes from instrumenting a normal or hypersensitive duodenal papilla and perfusing a catheter within the confines of a small-calibre (ie, normal) pancreatic duct. Efforts have been made to reduce this risk using catheters with simultaneous aspiration during perfusion, with reported benefit in the hands of enthusiasts.⁹ Post-ERCP pancreatitis (PEP) rates of 15–20% after SOM are not uncommon,¹⁰ although routine stenting of the pancreatic duct after manometry (with or without sphincterotomy) is probably lowering these numbers.

The term “Holy Grail” is much abused these days, but if you define it as a much-desired object or goal that transforms