Sphincter of Oddi dysfunction: Psychosocial distress correlates with manometric dyskinesia but not stenosis

Ethelle Bennett, Peter Evans, John Dowsett, John Kellow

AIM: To compare postcholecystectomy patients with Sphincter of Oddi (SO) dyskinesia and those with normal SO motility to determine the psychosocial distress, gender and objective clinical correlates of dyskinesia, and contrast these findings with comparisons between SO stenosis and normal SO motility.

METHODS: Within a cohort of seventy-two consecutive postcholecystectomy patients with suspected SO dysfunction, manometric assessment identified subgroups with SO dyskinesia (n = 33), SO stenosis (n = 18) and normal SO motility (n = 21). Each patient was categorized in terms of Milwaukee Type, sociodemographic status and the severity of stress-coping experiences.

RESULTS: Logistic regression revealed that in combination certain psychological, sociodemographic and clinical variables significantly differentiated SO dyskinesia, but not SO stenosis, from normal SO function. Levels of psychosocial stress and of coping with this stress (i.e. anger suppressed more frequently and the use of significantly more psychological coping strategies) were highest among patients with SO dyskinesia, especially women. Higher levels of neuroticism (the tendency to stress-proneness) further increased the likelihood of SO dyskinesia.

CONCLUSION: A motility disturbance related to psychosocial distress may help to explain the finding of SO dyskinesia in some postcholecystectomy patients.

INTRODUCTION

Sphincter of Oddi (SO) dysfunction (SOD), characterized by recurring episodes of severe biliary-like abdominal pain following cholecystectomy, is one of a number of functional disorders of the biliary tract [1]. However, based on SO manometry, which is the “gold standard” for the diagnosis of SOD, the condition is a heterogeneous one, currently considered within the context of the functional disorders, but known to include both stenotic and non-stenotic (functional) groups. Thus, SO dyskinesia can be differentiated from SO stenosis, a structural defect of the sphincter orifice.

Unlike other functional gastrointestinal disorders (FGIDs) [2], the psychosocial and gender concomitants of SOD have received little attention. In particular, psychosocial issues specifically relating to SO dyskinesia have not been addressed. Although two previous studies have implicated psychosocial factors in the genesis of symptoms in SOD, patients were not differentiated manometrically [3,4]. A more recent study found that health-related quality of life is impaired, and abuse histories are common, in SOD patients, but again patients were not differentiated manometrically [5].

Given the strength of the relations between psychosocial disturbance and alterations in gastrointestinal transit, motor activity and sensitivity previously documented...
in irritable bowel syndrome (IBS), our central hypothesis was that a similar association may exist with respect to SO dyskinesia. While the term stress or chronic stress can be viewed as a generic or umbrella term to include all features of a social stressor situation including psychophysiological effects, we have applied the term psychosocial distress to represent a person’s experience of and transactions with a stressor situation including on-going attempts to gain or regain emotional and psychological equilibrium/control.

The aims of the present study, therefore, were to determine, among subgroups of postcholecystectomy patients exhibiting SO dyskinesia, SO stenosis (± dyskinesia) or normal SO motor activity: (1) whether levels of psychosocial distress are higher in patients with manometrically proven SO dyskinesia than in those with normal SO motor activity, and (2) whether higher levels of psychosocial distress are specific to SO dyskinesia (that is, relative to patients with SO stenosis), and (3) whether the presence of objective clinical criteria, according to the Milwaukee classification, influences these associations. We chose specific psychological assessments of emotional state, personality and coping behaviour based on previously documented associations in other FGIDs. Thus, during an individual’s exposure to high levels of threat, powerful emotions such as fear, anger, anxiety and frustration are aroused and coping strategies, strongly influenced by personality and past experiences, are employed in an attempt to reduce the impact of both the emotions and the situation. A high level on any cluster of these psychological dimensions suggests high levels of psychosocial distress.

MATERIALS AND METHODS

Patients
The study population comprised seventy-two consecutive postcholecystectomy patients with biliary-like pain consistent with SOD [64 women, mean age 45 (SD ± 12) years], referred to the Gastrointestinal Investigation Unit for SO manometry. The presence of recurrent biliary-like pain fulfilling the criteria for SOD was confirmed from responses on the Bowel Disease Questionnaire (BDQ) and defined according to the Rome criteria, namely - episodes of pain in the right upper quadrant or epigastrium, rated by the patients as severe or very severe, steady and lasting from 30 min to 6 h. In all patients, organic disease had been excluded on the basis of normal physical examination, negative screening blood tests, negative gastroduodenoscopy and upper abdominal ultrasound or computed tomography scan, and the absence of calculi and strictures as demonstrated by endoscopic retrograde cholangiopancreatography (ERCP). Approval for the procedures was given by the Medical Research Ethics Committee of the Royal North Shore Hospital, and all subjects gave written informed consent.

Clinical assessment
SO Milwaukee Type was determined according to Hogan et al., with patients sub-grouped into patients with objective clinical criteria (Types I & II), including abnormalities of the biliary tree at cholangiography or abnormalities in hepatic biochemistry associated with episodes of pain, and patients without objective criteria (Type III) but with recurrent episodes of biliary-like pain. Thus, biliary-type I patients exhibited elevated liver biochemistries documented on two or more occasions, delayed contrast drainage, and a dilated common bile duct with a corrected diameter equal to or greater than 12 mm at ERCP; biliary-type II patients exhibited only one or two of the above criteria; while biliary-type III patients exhibited none of the above criteria.

SO manometry
Manometry of the SO was performed in standard fashion according to the technique of Toouli et al., using an Olympus JFIT10 duodenoscope and a triple-lumen catheter with inner lumen diameters each of 0.5 mm, an outer diameter of 1.7 mm and side holes radially oriented 2 mm apart (Wilson-Cook Medical, Winston-Salem, NC, USA). SO manometric tracings were analyzed by two experienced observers, blinded to the results of the symptom questionnaire. The following parameters were determined: basal sphincter pressure, peak sphincter pressure, and phasic wave contractile frequency and propagation. Abnormalities of these parameters were defined as values outside normal ranges established previously using an identical recording technique: basal pressure < 40 mmHg, contractile frequency < 8/min, and proportion of retrograde contractions < 50%. Complete inhibition of phasic contractions following cholecystokinin (CCK) was considered a normal CCK response. Failure of such a response, including a “paradoxical response” of the sphincter to CCK (i.e. increase in either the basal pressure and/or phasic contractions), was considered an abnormal response. SO manometric recordings were classified as either: (1) sphincter dyskinesia, defined as an abnormally high basal pressure resolving after CCK, or an abnormally high phasic contractile frequency, and/or an elevated proportion of retrograde contractions, and/or an abnormal response to CCK in the absence of sphincter stenosis or (2) sphincter stenosis, defined as an abnormally high basal pressure persisting after CCK irrespective of the presence of some features of dyskinesia or (3) normal sphincter motor function. The presence of SO stenosis had hierarchical importance over any other feature of dyskinesia in stratifying patients.

Psychosocial assessments
Psychometric measures assessed sociodemographic and psychological factors. The following data were collected prior to the SO manometry.

Sociodemographic data: Sex, age, marital status, highest education level, current employment status (i.e. whether working full-time, part-time or unemployed) and highest occupation level of self and father.

Emotional distress/mood state: Depression - in particular the affective component of a depressed mood state - was assessed using The Centre of Epidemiological Studies...
Depression Scale\textsuperscript{(19)} and state anxiety using the Spielberger State and Trait Anxiety Inventory (STAI)\textsuperscript{(20)}. Responses on these scales reflect complementary dimensions of psychosocial distress arising from stressful life situations.

**Personality traits:** Trait anxiety (the tendency to anxious states) was also assessed from responses on the STAI\textsuperscript{(20)}, and neuroticism (high scores reflect a tendency to stress-proneness and to excessive worry) and extraversion (orientation to things external or internal) were assessed using the Eysenck Personality Inventory\textsuperscript{(21)}.

**Coping style:** The Defense Style Questionnaire (DSQ 40) measured the tendency to use emotion-focused coping defenses or strategies to reduce emotional distress classified as mature (e.g. using humor, suppression, anticipation, sublimation), immature (e.g. using denial, acting out, being passive aggressive) and/or neurotic (e.g. using pretense (pseudo-altruism), idealization, undoing, reaction formation)\textsuperscript{(22)}. Normative and reliability data from patient and non-patient groups show these factors to have the internal consistency and the temporal stability of a trait measure - the mature dimension proving to be the primary discriminating factor\textsuperscript{(23)}.

**Emotional suppression/expression:** The Courtauld Emotional Control Scale\textsuperscript{(24)} assessed the tendency to suppress unwanted emotions such as anger and anxiety and the Anger Expression Scale\textsuperscript{(25)} assessed the tendency to hold in anger (anger-in) to express anger (anger-out) and to control and/or resist becoming angry (anger-control). Anger-in and anger-out are empirically independent, factorially orthogonal dimensions\textsuperscript{(26)}. Differences in the physiological effects of suppression vs expression of powerful emotions on autonomic, neuroendocrine and digestive functioning underlie the inclusion of these scales.

**Locus of control of behavior:** This scale\textsuperscript{(27)} assessed the extent to which a person believes that personal efforts more than external factors can achieve a positive outcome.

Each of the above measures has established reliability and validity and relevance with respect to the investigation of the hypothesized links between psychosocial distress and the development of SO dyskinesia.

**Statistical analysis**

Univariate and multivariate analyses were performed to compare the SO dyskinesia subgroup, and for comparison purposes the SO stenosis subgroup, with the normal SO motility subgroup, on a range of clinical, sociodemographic and psychological factors\textsuperscript{(28)}. The relation of individual continuous variables such as age, sociodemographic and psychosocial factors was assessed by logistic regression, while \( \chi^2 \) analyses were performed to determine any sex or clinical differences with respect to SO subgroups. Using a Stepwise regression - a model-building procedure by which sample data (not the investigator) determines order of entry into the model - an optimal subset of clinical, sociodemographic and psychological factors that had independent, statistically significant effects in relation to SO subgroups was then identified.

### RESULTS

SO manometry revealed evidence of SO dyskinesia (with no stenosis) (\( n = 33 \)), SO stenosis (\( n = 18 \), some with concurrent SO dyskinesia features (\( n = 8 \)), or normal SO motility (i.e. no SO dyskinesia or SO stenosis (\( n = 21 \)). The three groups did not differ with respect to age, gender, or any of the independent clinical variables (Table 1), sociodemographic or psychological variables assessed.

When logistic regression was used to determine the effect of combinations of independent variables in relation to manometric outcome, however, a particular subset of clinical demographic and psychological variables significantly differentiated SO dyskinesia from normal SO motility (Table 2). In this model, variables positively associated with SO dyskinesia were being female, and the psychological variables of frequently suppressing anger, frequently using stress coping strategies, and neuroticism (the propensity to an overly anxious response to stressors). The negative association with abnormal motility (or positive association with normal motility) was related to the sociodemographic background, namely a lower occupational status of the patient’s father. The variables of anxiety and depression were not associated with SO dyskinesia, nor were there positive associations with objective clinical criteria.

In contrast, duplicate analyses revealed no significant differences between patients with SO stenosis and those with normal SO motor activity, on psychosocial distress and gender and also on objective clinical criteria (data

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**Table 1** Clinical features of the post-cholecystectomy patient subgroups of SO dyskinesia, SO stenosis with or without dyskinesia and normal SO motility (mean ± SD) (%)

| Type       | SO dyskinesia (\( n = 33 \)) | SO stenosis (\( n = 18 \)) | Normal SO motility (\( n = 21 \)) |
|------------|-------------------------------|-------------------------------|-----------------------------------|
| Age (yr)   | 45 ± 10                       | 44 ± 13                       | 48 ± 16                           |
| Gender: % female | 91                             | 89                            | 86                               |
| SOD        |                               |                               |                                  |
| Type I     | 2 (6)                         | 2 (11)                        | 0 (0)                            |
| Type II    | 19 (58)                       | 12 (67)                       | 14 (67)                          |
| Type III   | 12 (36)                       | 4 (22)                        | 7 (33)                           |

*\( P > 0.05 \) for all comparisons. SO: Sphincter of Oddi; SOD: SO dysfunction.*

**Table 2** Clinical, psychosocial and demographic variables which significantly differentiated between SO dyskinesia and normal SO motility in postcholecystectomy patients: logistic regression model of best fit

| Effect size and significance | B     | SE    | \( P \)-value |
|------------------------------|-------|-------|---------------|
| Female sex                   | 5.023 | 1.981 | 0.01          |
| Frequent suppression of anger | 2.399 | 1.239 | 0.05          |
| Frequent use of mature coping strategies | 0.232 | 0.085 | 0.006         |
| Frequent use of immature coping strategies | 0.03  | 0.057 | 0.026         |
| Infrequent use of neurotic coping strategies | 0.004  | 0.266 | 0.091        |
| Higher occupational status of father | 1.475 | 0.588 | 0.01        |
| Neuroticism (stress-proneness) | 4.901 | 4.901 | 0.02        |

*\( ^{3} \)See text for further details; Model variance explained = 36.3%; B: Regression coefficient.*
DISCUSSION

The novel finding in this study was the identification of a cluster of psychosocial and gender factors which together differentiate postcholecystectomy patients with manometric SO dyskinesia - but not those with SO stenosis - from those with normal SO motor activity. In comparison with the normal motor activity group, patients with SO dyskinesia, especially women, used significantly more stress-management strategies that were problem-focused (i.e. they suppressed anger more frequently) and emotion-focused (i.e. they frequently used mature and immature but not neurotic coping strategies), findings which implicitly represent on-going attempts to reduce psychosocial stress. While the prominence of the emotion anger (but not depression or anxiety) in the stress-copying profile reveals the potent nature of the psychosocial distress, for each individual the effectiveness of the particular range of coping strategies used to reduce emotional distress (and the associated physiological responses) is unclear. Thus, although patients with SO dyskinesia displayed a preference for strategies such as anticipation, humor, suppression, and sublimation (especially adaptive in the short term), other less effective (immature) strategies such as passive aggression and denial were also employed from time to time. Neurotic coping was rare in this group.

Our other major finding was that the biopsychosocial model of SO dyskinesia described above was, in essence, independent of objective clinical non-manometric criteria. This was despite the fact that the distribution of our patients with manometric evidence of SOD according to the Milwaukee classification was generally in keeping with that of other published reports: half of our patients with Type I exhibited stenosis, 61% of Type II exhibited sphincter dyskinesia, and 75% of Type III exhibited sphincter dyskinesia. The fact that our patients with Type III SOD exhibited a higher overall proportion of manometric dysfunction than published reports may reflect the fact that we employed CCK provocation, which is not now routinely undertaken in Units performing SO manometry. Moreover, our use of CCK considerably strengthens the distinction between SO hypertension due to sphincter hypertonicity and that due to a true fixed stenosis.

The significant association between psychosocial distress and sphincter dyskinesia is a new finding with respect to the sphincter of Oddi. It is, however, conceptually consistent with reports of similar links between stress and alterations in gut motility and sensation in patients with FGID categorized as IBS[8,9] and with the severity[10,11] and the extent (number of regions) of gut stasis[12], especially gastric stasis, in mixed gender groups. Similar relations have been reported with respect to functional gut symptomatology. For example, higher levels of distress, assessed as outlined above, and also an objective measure of life stress, namely chronic stressor threat, are associated with a larger number of FGID syndromes[13], with the overall intensity of FGID symptoms, and with the direction and extent of change in symptom intensity over time[7]. Also for patients with FGID, anger provoked in real life situations is the emotion which most strongly contributes to the net severity and extent of symptoms[14] and sensorimotor dysfunction[15,16], while anger provoked in the laboratory inhibits antral motor activity in patients with these disorders in contrast to its enhancing effects on antral motor activity in healthy control subjects[17,18]. Consistent with all of these findings, the psychosocial distress model which described postcholecystectomy patients with SO dyskinesia in this study also included anger and female gender; these findings suggest both the potency of the stressful input on the one hand, and perhaps the more subtle and discriminating influence of sex hormones in SO motility on the other.

There is only very limited data available relating to psychosocial associations with SOD. Psychological disturbance has been implicated in one study[19] in the recurrence of biliary-type pain in some patients following cholecystectomy. In comparison to healthy controls, psychological factors assessed indirectly in terms of the number of concurrent multisystem gastrointestinal and non-gastrointestinal symptoms, was higher in patients with a diagnosis of SOD. However, patients were not differentiated manometrically in this study. In another report, psychological disturbance (anxiety, somatization, depression and obsessive-compulsive behavior) was found to be higher in patients with SOD Type III[20] than in other types. Interestingly, our findings did not confirm significantly higher levels of anxiety and depression in patients evaluated according to their manometric findings and not their Milwaukee criteria alone. In a longitudinal study, Jorgensen et al[21] reported that psychological vulnerability (assessment prior to cholecystectomy in terms of the severity of multisystem somatic and neurotic symptoms) predicted failure to achieve a full recovery post-operatively, after controlling for age, sex, pre-operative pain characteristics, history of disease, type of surgery, histology and complications. The contribution of the present study is the notion that a stress-related sensorimotor dysfunction may help to explain the presence and the persistence of the syndrome for some patients with a diagnosis of SO dyskinesia, while high rates of recovery following endoscopic sphincterotomy in patients with manometric features of SO stenosis[22,23] suggest that fixed structural or anatomical defects may explain the syndrome in others. Indeed, an important feature of the stress-related sensorimotor dysfunction in this study is that it was determined in the absence of confounding influences arising from the presence of SO stenosis.

We are aware of the potential limitations of our
findings, especially the potential selection bias because patients with certain personality or mood-state characteristics may be more likely to seek medical attention than other patients, and also that recurrent pain may have influenced some of their responses to the various questionnaires. However, we sought to limit any such bias by also including patients with the same symptoms who had presented for medical care but were found to have sphincter stenosis. Moreover, as all patients reported intermittent episodes of pain as severe or very severe it was not feasible to relate the psychosocial measures to pain scores. Further studies will be required to confirm and extend these findings, as they are of potential clinical importance given that the psychological distress levels including clinical levels of anxiety and depression may be eminently treatable (e.g. with medication and/or psychotherapy). Although individual psychotherapies (e.g. biofeedback, cognitive-behavioral, psychodynamic, hypnotherapy), achieve reductions in emotional distress and symptom severity in patients with IBS, an integrated psychophysiological approach to the management of these disorders that is sensitive to the unique nature of each stressor situation would seem most likely to be helpful long term.

In summary, the close association found, for the first time, in this study between psychosocial distress and SO dyskinesia, but not between psychosocial distress and SO stenosis or normal SO motor activity, suggests that, for some patients with a diagnosis of SO dyskinesia, a stress-related motor dysfunction may help to explain the recurrence of their biliary-like symptoms following cholecystectomy. This is consistent with pathophysiological models of the FGIDs in general.

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COMMENTS

*Background*
Sphincter of Oddi (SO) dysfunction (SOD) is one of a number of functional disorders of the biliary tract. It is known to include both stenotic and nonstenotic (functional) groups. Thus, SO dyskinesia can be differentiated from SO stenosis, a structural defect of the sphincter orifice. Unlike other functional gastrointestinal disorders, the psychosocial and gender concomitants of SOD have received little attention. In particular, psychosocial issues specifically relating to SO dyskinesia have not been addressed.

*Research frontiers*
Because of the strong relationships between psychosocial disturbance and alterations in gastrointestinal transit, motor activity and sensitivity previously documented in irritable bowel syndrome, we hypothesized that a similar association may exist with respect to SO dyskinesia.

*Innovations and breakthroughs*
This is the first study to identify a cluster of psychosocial and gender factors which together differentiate postcholecystectomy patients with manometric SO dyskinesia - but not those with SO stenosis - from those with normal SO motor activity. The findings suggest that a stress-related motor dysfunction may help to explain the recurrence of biliary-like symptoms following cholecystectomy. This is consistent with pathophysiological models of the functional gastrointestinal disorders in general.

*Applications*
These findings are of potential clinical importance given that psychological distress levels including clinical levels of anxiety and depression may be eminently treatable (e.g. with medication and/or psychotherapy).

*Terminology*
Sphincter of Oddi dysfunction: a disorder characterized by recurring episodes of severe biliary-like abdominal pain following cholecystectomy. Sphincter dyskinesia: an abnormally high basal pressure resolving after cholecystokinin (CCK), or an abnormally high phasic sphincter contractile frequency, and/or an elevated proportion of retrograde contractions, and/or an abnormal response to CCK in the absence of sphincter stenosis. Sphincter stenosis: an abnormally high basal pressure persisting after CCK irrespective of the presence of some features of dyskinesia.

*Peer review*
It is a solid research, well-written paper with reasonable conclusion. Although there are limitations to the study, these are nicely outlined and discussed.
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