ORIGINAL SCIENTIFIC REPORT

The Impact of Depression in Patients Undergoing Emergency Abdominal Surgery: An Exploratory Study

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Accepted: 9 November 2022 / Published online: 19 November 2022
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Abstract

Background Depression is associated with poorer outcomes in many disease states. However, its significance in abdominal surgery is unknown. This study investigated rates of depression in emergency abdominal surgery patients and its effects on outcomes.

Methods A retrospective cohort study was conducted across two UK sites and included all adult patients undergoing emergency abdominal surgery. Primary outcome was the complication rate in depressed patients, including the incidence of post-operative delirium. Secondary outcomes included mortality, time to oral intake and analgesia.

Results Two hundred and ten patients were identified. The commonest indication for surgery was appendicitis (53.3%) followed by small bowel obstruction (9.5%). There was a 17% (n = 36) incidence of depression amongst patients, most of whom (n = 26, 72.2%) were taking antidepressants. Depression was associated with male sex (M:F 27:9 \( p = 0.003 \)), higher median BMI (28 vs. 25 \( p = 0.013 \)) and previous surgery (47.2% vs. 28.7% \( p = 0.032 \)). Despite a higher incidence of post-operative delirium, increased time to oral analgesia and greater 30-day readmission rates in the depression cohort, multivariate analyses showed depression was not a significant independent predictor of these (OR 2.181, 95%CI 0.310–15.344; \( p = 0.433 \), OR 0.07, 95%CI 0.499–1.408; \( p = 0.348 \) and OR 1.367, 95%CI 0.102–18.34, respectively). Complication and mortality rates between depressed and non-depressed individuals were similar.

Conclusion Significant numbers of patients undergoing emergency abdominal surgery have depression, but this did not adversely affect post-operative outcomes. The study included relatively small numbers of participants undergoing procedures with straightforward recovery. Larger population studies are therefore required and should focus on investigating the association between major emergency surgeries with post-operative delirium and uncontrolled pain.

Introduction

The negative impact of depression on post-operative morbidity has been documented in the previous literature. Persistent activation of the hypothalamic–pituitary–adrenal axis in chronic depression impairs key immune modulators such as tumour necrosis factor alpha, conferring a higher risk of post-operative infection [1]. Similarly, principle neurophysiological disturbances in delirium relate to immune dysregulation and abnormal stress responses [2]. Compromised circadian rhythm is acutely perpetuated and
exacerbated by physiological stress including surgery [2]. It is therefore not surprising that research has shown greater vulnerability to post-operative delirium in patients with depression compared to those with normal baseline cognition. In spite of this, the impact of depression in patients undergoing emergency abdominal surgery is unknown.

Emergency abdominal surgery is performed in over 50,000 patients a year in the UK [3]. It is an important public health arena in which there are constant efforts to improve outcomes, a prime example being the National Emergency Laparotomy (NELA) audit [4]. NELA is a nationally commissioned audit designed to improve the results of emergency laparotomy through the provision of comparative data from all providers of emergency laparotomy in the UK. The previous literature has highlighted an association between depression and an increased risk of post-operative mortality in coronary artery bypass surgery [5]. Furthermore, in 2012, a study found that the rate of cardiac events in the post-operative period, including arrhythmias and heart failure, was significantly raised in patients with chronic depression [6]. Forty-five per cent of individuals with depression were re-hospitalised with recurrent angina; almost threefold the number reported in those without. Research has also identified a twofold increase in post-operative delirium in depressed patients undergoing spinal surgery [7]. Post-operative delirium itself is associated with inferior surgical outcomes and higher mortality rates [8]. Despite evidence that depression may play a detrimental role in surgical outcomes, data relating to its impact in general and abdominal surgery remain limited.

We hypothesised that depression places patients undergoing emergency abdominal surgery at higher risk of worse post-operative outcomes compared to non-depressed counterparts. The aim of this study was therefore to identify the incidence of clinical depression and investigate the impact of the diagnosis on outcomes after emergency abdominal surgery.

## Materials and methods

The study complied with the Declaration of Helsinki and was approved by the local Audit Committee.

### Study design and setting

A retrospective cohort study was conducted of all consecutive patients undergoing emergency surgery from March to June of 2021. This was undertaken at two district general hospitals in the UK.

### Population

All adults who underwent emergency abdominal surgery over the study time frame were eligible for inclusion. This included appendicectomy, which although has a typically short and uneventful recovery, the study was designed to investigate all aspects of the emergency surgical take with the aim of enabling the results of this study to translate into everyday practice. Appendicectomy is the commonest abdominal emergency operation, and we wished to identify whether depression would impact outcomes even in such mostly uncomplicated surgeries.

Patients under 16 years of age, admissions who did not proceed to surgery and all elective cases were excluded.

### Definition and outcomes

Depression was defined as a formal diagnosis of clinical depression on admission registered in the medical notes. Duration and severity of depression were not recorded.

The primary outcome was the complication rate in depressed patients, including the incidence of post-operative delirium. Secondary outcomes included mortality, length of stay and time to oral intake and time to oral analgesia.

### Data collection

Data collected included demographics, diagnosis of depression and use of antidepressant medication, past medical history, American Society of Anaesthesiology (ASA) score, body mass index (BMI), smoking and history of COVID-19 infection. Operative details included diagnosis, indication for surgery, operation type, need for re-operation and blood loss. This was categorised into four categories, namely < 100 millilitres (mls), 101-500mls, 501-999mls and > 1000mls. Post-operative data comprised of intensive care (ITU) admission, time to oral intake, mobilisation, flatus and length of stay.

Complications were stratified according to Clavien–Dindo grades [9], including the incidence of post-operative delirium. This was defined as an acute disturbance in attention and awareness with additional change in baseline cognition [10]. Its presence was diagnosed using the Delirium Rating Scale and based on documentation by the independent treating doctors in the medical notes [11]. Readmission within 30 days of discharge was noted. The use of patient-controlled analgesia was more common in the depressed cohort, and were used for a longer period before transition to oral analgesia alone.

Peri-operative mortality was defined as either in-hospital mortality or death within 30 days of surgery in case of earlier discharge.
Statistical analysis

Normal quantile plots were used to test for normality. Nonparametric data are expressed as median with interquartile range (IQR) and categorical data as absolute number and percentage. Continuous data were analysed using Mann–Whitney U. Fisher’s exact test or Chi-square test was used to compare categorical data.

Binary logistic regression was used to identify independent factors predictive of delirium and readmission rates, whilst a multiple linear regression model was used to identify time to oral analgesia. The models contained both categorical and continuous predictor variables, and these were added in a stepwise regression analysis. Significance levels were set at $p < 0.05$ to enter and $p > 0.1$ for removal. Variables included, depending on the model, were the following: sex, age, BMI, smoker status, history of COVID infection, depression, use of antidepressants, presence of co-morbidities, ASA, previous surgery, operative approach, ITU admission, time to oral intake, flatus or mobilisation, LOS and complications. A two-tailed $p$ value of less than 0.05 was considered to be significant. All data analyses were performed using SPSS version 27 (SPSS Inc., Chicago IL).

Results

Study demographics and incidence of depression

Two hundred and ten patients were included over the study timeframe. The overall median age was 42 years with an equal sex distribution (Table 1). A quarter of the study population were smokers, but generally independent with an overall performance status of 0. Five per cent ($n = 11$) had a history of proven COVID-19 infection. Half had at least one co-morbidity.

Thirty-six patients (17%) had a diagnosis of depression. These individuals were more often male with a significantly higher BMI and more likely to have had previous surgery (Table 1). Amongst those with depression, most ($n = 26$, 72.2%) were on antidepressant medication on admission. In all but two cases (7.6%), patients were treated with a single agent. The majority ($n = 21$, 80%) of these were selective serotonin reuptake inhibitors (SSRIs), typically sertraline or citalopram. The remainder were prescribed a mixture of atypical, tetracyclic or tricyclic antidepressants.

Indications for surgery

Acute appendicitis accounted for over half the cases in the study population (Table 2). Thereafter, small bowel obstruction was the most frequent diagnosis, followed by biliary disease (Table 2). Sixty per cent ($n = 12$) of patients presenting with small bowel obstruction had adhesions as a result of previous surgery, the rest being equally due to hernias ($n = 3$) or primary disease, i.e. Crohn’ (5) or malignancy (2).

Intra-operative outcomes

Patients with or without depression were broadly well matched with regard to operative outcomes (Table 3). Average time to surgery was one day, with a similar distribution of open and laparoscopic surgery. Blood loss was no different. Pre-operative ITU admission was significantly higher amongst depressed patients, and these individuals were also more likely to be admitted to ITU post-operatively, albeit this did not meet statistical significance.

Post-operative outcomes

The use of patient-controlled analgesia was more common in the depressed cohort, and were used for a longer period before transition to oral analgesia alone (Table 4). Regression analysis revealed four independent predictors of time to oral analgesia alone, namely ITU stay (Odds Ratio 0.255, 95% Confidence Intervals 0.428–2.774; $p < 0.001$), time to flatus (OR 0.206, 95%CI 0.049–0.416; $p=0.014$), time to oral intake (OR 0.323, 95%CI 0.017–0.416; $p=0.001$) and LOS (OR 0.303, 95%CI 0.059–0.171; $p < 0.001$). Depression, conversely, was not an independent predictor (OR 0.07, 95%CI 0.001–0.1; $p = 0.348$). Nagelkerke $R^2$ 0.749).

Depressed patients also had greater readmissions rates, although logistic regression revealed this was not a predictive factor (OR 1.367, 95%CI 0.310–15.344; $p = 0.433$). In our model (Nagelkerke $R^2$ 0.386), only BMI (OR 1.095, 95%CI 1.022–1.193 $p = 0.046$) and age (OR 0.09, 95%CI 0.966–0.925 $p = 0.034$) were found to be significant variables.
Whilst non-significant, there was a trend towards longer length of stay and time to mobilisation in the depression group. A quarter of depressed patients suffered a complication, compared to 17% of non-depressed patients ($p = 0.344$). There were no Clavien–Dindo grade 4 complications, but four patients died, with an equal incidence between the two groups.

Subgroup analysis (not shown) demonstrated no differences between medicated and non-medicated depressed individuals in all study outcomes.

**Discussion**

A correlation between depression and poor outcomes in elective surgery has been documented in the previous literature [12–15]. This is the first study to investigate this relationship in patients undergoing emergency abdominal surgery.

We found depression was common, but did not significantly adversely affect post-operative outcomes. The incidence of depression in our cohort was 17%, slightly lower than the nationally reported figure of 21%, but similar to other reported studies in surgery [16]. The likelihood of accurately diagnosing depression in an acute setting is much lower than in outpatient practice [17]. This has been heightened by the extraordinary impact of the COVID-19 crisis on hospital services, where access to direct psychiatric assessment is limited and staff shortage across surgical specialties is at its highest. Due to its potential impact on post-operative recovery, there is an argument to be made for efficacious hospital-based liaison psychiatry programmes, aimed at improving the diagnosis and management of depression in surgical patients.

We identified a significant increase in post-operative delirium in the depressed cohort undergoing emergency abdominal surgery. This link is not limited to emergency abdominal surgery and has been extensively documented in other elective surgical patients. Elsamadicy et al. [7] identified a twofold higher rate of post-operative delirium in depressed patients undergoing elective spine surgery, and Falk et al. found a strong association between pre-operative depression and post-operative delirium in cardiac surgery [18]. It has been suggested that depression and

| Study Demographics | All n = 210 | Diagnosis of depression n = 36 | No diagnosis of depression n = 174 | p value |
|--------------------|-------------|-------------------------------|---------------------------------|---------|
| Age, years         | 42 (30–61)  | 44.5 (31.7–55)                | 40 (30–62.2)                    | 0.751   |
| Sex, M:F           | 110:111     | 27:9                          | 82:92                           | **0.003** |
| BMI                | 25.6 (22–44.5) | 28 (25–33)                  | 25 (23–28.1)                    | **0.013** |
| Smoker, n (%)      | 54 (25.7)   | 9 (25)                        | 45 (25.9)                       | 0.999   |
| Performance status | 0 (0–0)     | 0 (0–1)                       | 0 (0–0)                         | 0.057   |
| ASA                | 2 (1–2)     | 2 (2–2)                       | 2 (1–2)                         | 0.151   |
| History of COVID, n (%) | 11 (5) | 2 (5.5)                     | 9 (5.1)                         | 0.919   |
| Co-morbidity, n (%) | 103 (49)  | 20 (55.6)                    | 83 (47.7)                       | 0.465   |
| 1 only             | 46 (21.9)   | 8 (22.2)                      | 38 (21.8)                       | 0.999   |
| ≥ 2                | 57 (27.1)   | 12 (33.3)                     | 45 (25.9)                       | 0.411   |
| Cardiac            | 36 (17.1)   | 4 (11.1)                      | 32 (18.4)                       | 0.343   |
| Respiratory        | 27 (12.9)   | 8 (22.2)                      | 19 (10.9)                       | 0.054   |
| Malignancy         | 22 (10.5)   | 4 (11.1)                      | 18 (10.3)                       | 0.999   |
| Endocrine/diabetes | 23 (10.9)  | 2 (5.6)                       | 21 (12.1)                       | 0.318   |
| Renal              | 4 (1.9)     | 2 (5.6)                       | 2 (1.1)                         | 0.318   |
| Rheumatic/MS       | 10 (4.8)    | 4 (11.1)                      | 6 (3.4)                         | 0.071   |
| Haematological     | 7 (3.3)     | 1 (2.8)                       | 6 (3.4)                         | 0.999   |
| Gastrointestinal   | 30 (14.3)   | 7 (19.4)                      | 23 (13.2)                       | 0.308   |
| Infectious disease | 2 (0.95)    | 1 (2.8)                       | 1 (0.6)                         | 0.314   |
| Previous surgery, n (%) | 77 (36.6) | 17 (47.2)                  | 50 (28.7)                       | **0.032** |

Data expressed as median (interquartile range) unless otherwise stated. Comparisons are between the patients with and without depression. MS = Musculoskeletal
delirium have similar pathophysiological pathways. Whilst rates of delirium were higher in depressed patients undergoing emergency abdominal surgery, our analysis revealed depression was not an independent predictor of this. However, it is worth noting that the 95% confidence intervals were large, potentially indicating the study was underpowered. O’Sullivan et al. discussed the intricate overlap in principle neurophysiological disturbances seen in both delirium and depression. Vulnerability to delirium was demonstrated in patients with compromised circadian regulation, seen in acute physiological stress but also in patients with depressive illness [19]. Given that existing research has consistently established poor surgical outcomes and higher mortality rates in patients with post-operative delirium, it is important to continue to explore and understand this potential association.

We observed an association with prolonged use of intravenous analgesia pumps in the depressed cohort. This finding confirmed the results of previous studies that have shown pre-operative depression negatively influences post-operative pain [20].

Moreover, evidence suggests greater intensity of post-operative pain may increase the risk of post-operative delirium [21]. Indeed in a trial of 60 men, Duggleby and Lander found that pain and not analgesic intake predicted mental status decline after surgery [22].

Despite mounting evidence that depression plays a critical role in every aspect of post-operative recovery, it is scarcely considered during pre-operative patient assessment. The ASA grading system is the primary method used to classify patient risk with regard to intra- and post-operative complications, yet psychiatric diagnoses are yet to be formally factored into this classification system [23]. Similarly, they are neither included in the p-possum score [24]. More research in the field is required to both recognise and indeed optimise the management of such disorders to improve the overall assessment and care of patients.

The majority of the depressed patients were receiving some form of pharmaceutical antidepressant therapy, although the study failed to note a difference in outcomes between medicated and non-medicated individuals. This alludes to a need to re-evaluate current therapeutic practices in light of the increasing incidence of depression amongst the general population, not least in light of COVID-19’s unprecedented negative influence on the psychological well-being of the general population. Depression rates have doubled over the past year and are predicted to continue to rise [25]. It is therefore more pertinent than ever that surgeons identify and effectively address the presence of depressive illness. In terms of identification, this not only includes confirming known cases but also identifying undiagnosed cases through proactive history taking; the Patient Health Questionnaire-Two and Patient Health Questionnaire-Nine could serve as useful templates for questioning [26]. Research is still required to show which post-operative interventions would be most beneficial to these identified with depression, and a multimodal approach will likely be required involving psychiatry, pharmacology, physiotherapy and pain team services.

### Table 2 Diagnoses in the Study Population

| Diagnoses                  | Overall $n = 210$ | Diagnosis of depression $n = 36$ | No diagnosis of depression $n = 174$ |
|----------------------------|-------------------|---------------------------------|-------------------------------------|
| Colitis-related complication | 8 (3.8)           | 2 (5.6)                         | 6 (3.4)                            |
| Small bowel obstruction    | 20 (9.5)          | 4 (11.1)                        | 16 (9.2)                           |
| Appendicitis               | 112 (53.3)        | 14 (38.9)                       | 98 (56.3)                          |
| Biliary colic              | 4 (1.9)           | 2 (5.6)                         | 2 (1.1)                            |
| Acute cholecystitis        | 12 (5.7)          | 4 (11.1)                        | 8 (4.6)                            |
| Gallstone pancreatitis     | 6 (2.9)           | 1 (2.8)                         | 5 (2.9)                            |
| Colorectal cancer          | 10 (4.8)          | 0 (0.0)                         | 10 (5.7)                           |
| Diverticular disease       | 12 (5.7)          | 3 (8.3)                         | 9 (5.2)                            |
| Intra-abdominal hernia     | 4 (1.9)           | 0 (0.0)                         | 4 (2.3)                            |
| Iatrogenic                 | 4 (1.9)           | 1 (2.8)                         | 3 (1.7)                            |
| Upper gastrointestinal perforation | 10 (4.8) | 1 (2.8)                         | 9 (5.2)                            |
| Stoma-related complication | 3 (1.4)           | 1 (2.8)                         | 2 (1.1)                            |
| Intussusception            | 1 (0.5)           | 1 (2.8)                         | 0 (0.0)                            |
| Small bowel cancer         | 2 (1.0)           | 0 (0.0)                         | 2 (1.1)                            |
| Miscellaneous              | 2 (1.0)           | 2 (5.6)                         | 0 (0.0)                            |

All data expressed as absolute number (percentage)
Nevertheless, it is also worth noting that a third of patients diagnosed with depression who did not take medication before surgery had similar complications to patients with no depression. This is not only reassuring to surgeons but also to patients, who may be concerned that if an individual stops taking oral antidepressants before major surgery they may relapse. Evidence based on this study indicate this is not the case.

There were limitations to this study. Appendicitis was the most common indication for theatre in our cohort. With a relatively short and uncomplicated post-operative recovery, this may have skewed the effects of depressive illness. Complications are more likely to be seen after major operations, when comprising of a prolonged and difficult post-operative period. Although dual-centred, the study was relatively small, and given the wide confidence intervals, it may well have been underpowered. In turn, this may have undermined the effect of depression on outcomes in emergency abdominal surgery. Both these limitations suggest that future studies would benefit from investigating patients from a less heterogeneous population, undergoing more complicated surgery such as laparotomy. Because this was an exploratory study, however, a power calculation was not undertaken, but now having identified the incidence of depression in this cohort, such work can be appropriately powered to reach greater statistical accuracy and avoid any potential for a type II error in particular. The study observed patients during the COVID pandemic lockdown. This deterred individuals from presenting to hospital and resulted in a shift towards medical management of surgical diseases where possible. In addition to this, the lack of access to mental health services and face-to-face GP appointments has resulted in under-reporting and therefore underdiagnosis of depression. These factors

Table 3 Operative Outcomes According to a Diagnosis of Depression or Not

| Diagnosis of depression (n = 36) | No diagnosis of depression (n = 174) | p value |
|----------------------------------|-------------------------------------|---------|
| **Time to surgery, days, median (IQR)** | | |
| 1 (0–2) | 1 (0–2) | 0.632 |
| **Operation** | | |
| Laparoscopic | 25 (69.4) | 133 (76.4) | 0.669 |
| Open | 11 (30.6) | 38 (21.8) | 0.282 |
| Converted to open | 0 (0.0) | 3 (1.7) | 0.999 |
| **Operation** | | |
| Lap/open adhesiolysis | 5 (13.9) | 9 (5.2) | 0.072 |
| Subtotal colectomy | 2 (5.6) | 3 (1.7) | 0.204 |
| Diagnostic laparoscopy only | 2 (5.6) | 1 (0.6) | 0.078 |
| Hernia repair (abdominal) | 0 (0.0) | 4 (2.3) | 0.999 |
| Hartmanns | 2 (5.6) | 9 (5.2) | 0.999 |
| Left hemicolecotmy | 0 (0.0) | 1 (0.6) | 0.900 |
| Right hemicolecotmy | 1 (2.8) | 7 (4.0) | 0.999 |
| Lap/open appendicectomy | 13 (36.1) | 97 (55.7) | 0.043 |
| Lap cholecystectomy | 6 (16.7) | 15 (8.6) | 0.216 |
| Perforated duodenal ulcer repair | 1 (2.8) | 7 (4.0) | 0.999 |
| Defunctioning colostomy | 0 (0.0) | 4 (2.3) | 0.999 |
| Small bowel resection | 0 (0.0) | 8 (4.6) | 0.356 |
| Loop ileostomy formation | 0 (0.0) | 1 (0.6) | 0.900 |
| Other | 4 (11.1) | 8 (4.6) | 0.129 |
| **Blood Loss, millimetres** | | |
| < 100 | 27 (75) | 147 (84.5) | 0.222 |
| 101–500 | 9 (25) | 23 (13.2) | 0.079 |
| 501–1000 | 0 (0.0) | 0 (0.0) | n/a |
| Intra-operative complication | 4 (11.1) | 8 (4.6) | 0.129 |
| Pre-operative ITU admission | 2 (5.6) | 0 (0.0) | 0.029 |
| Post-operative ITU admission | 9 (25) | 26 (14.9) | 0.146 |

Data expressed as absolute number (percentage) unless otherwise stated. Lap = laparoscopic, ITU = intensive care unit
could have most likely confounded some of the results of the study. Finally, as a retrospective analysis, this study was potentially susceptible to recall bias and inaccurate documentation.

### Conclusion

Our data demonstrated a significant number of patients undergoing emergency abdominal surgery have depression. This led to a trend of higher rate of post-operative delirium and longer time to oral analgesia use alone, although these do not meet statistical significance in our study.

More research is required to verify the effect of depression in emergency surgery, with an emphasis on larger trials of patients undergoing major surgery.

### Declarations

**Conflict of interest** The authors did not receive support from any organisation for the submitted work and have no relevant financial or non-financial interests to disclose or conflicts of interest.

**Ethical approval** The study complied with the Declaration of Helsinki and was approved by the local audit committee.

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Table 4  Post-Operative Outcomes

|                          | Diagnosis of depression n = 36 | No diagnosis of depression n = 174 | p value |
|--------------------------|--------------------------------|-----------------------------------|---------|
| Time to oral intake, days| 1 (0–3)                        | 1 (0–1)                           | 0.147   |
| Time to mobilisation, days| 2 (1–5)                        | 1 (0–1)                           | 0.174   |
| Time to flatus, days     | 1 (0–3)                        | 1 (0–2)                           | 0.292   |
| Time to oral analgesia, days| 1 (0–5)                     | 0 (0–1)                           | 0.017   |
| Length of stay, days     | 4 (2–13)                       | 3 (2–9)                           | 0.297   |
| Post-operative delirium, n (%) | 4 (11)                      | 3 (1.7)                           | 0.017   |
| Complication n (%)       | 9 (25)                         | 30 (17)                           | 0.344   |
| Clavien–Dindo, n (%)     | 3 (8)                          | 8 (4.6)                           | 0.404   |
| I                        | 4 (11)                         | 18 (10.3)                         | 0.773   |
| II                       | 1 (2.7)                        | 1 (0.6)                           | 0.310   |
| IIIa                     | 1 (2.7)                        | 3 (1.7)                           | 0.529   |
| IIIb                     | 0 (0.0)                        | 0 (0.0)                           | n/a     |
| IVa                      | 0 (0.0)                        | 0 (0.0)                           | n/a     |
| IVb                      |                                 |                                   |         |
| Mortality, n (%)         | 1 (2.7)                        | 3 (1.7)                           | 0.529   |
| Readmission, n (%)       | 4 (11)                         | 10 (5.7)                          | < 0.0001|

Data expressed as median (interquartile range) unless otherwise stated
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