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## **Population-based cohort study of outcomes following cholecystectomy for benign gallbladder diseases**

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**Background:** The aim was to describe the management of benign gallbladder disease and identify characteristics associated with all-cause 30-day readmissions and complications in a prospective population-based cohort

**Methods:** Data were collected on consecutive patients undergoing cholecystectomy in acute UK and Irish hospitals between 1 March and 1 May 2014. Potential explanatory variables influencing all cause 30-day readmissions and complications were analysed by means of

multilevel, multivariable logistic regression modelling using a two-level hierarchical structure with patients (level 1) nested within hospitals (level 2).

**Results:** Data were collected on 8909 patients undergoing cholecystectomy from 167 hospitals. Some 1451 cholecystectomies (16.3 per cent) were performed as an emergency, 4165 (46.8 per cent) as elective operations, and 3293 patients (37.0 per cent) had at least one previous emergency admission, but were operated on a delayed basis. The readmission and complication rates at 30 days were 7.1 per cent (633 of 8909) and 10.8 per cent (962 of 8909) respectively. Both readmissions and complications were independently associated with increasing ASA fitness grade, duration of surgery, and increasing numbers of emergency admissions with gallbladder disease before cholecystectomy. No identifiable hospital characteristics were linked to readmissions and complications.

**Conclusion:** Readmissions and complications following cholecystectomy are common and associated with patient and disease characteristics.

## **+A: Introduction**

Benign gallbladder disease is a major global health burden<sup>1</sup>. It is estimated that for every 100 000 of the world's population, 115 patients undergo cholecystectomy every year. In England alone, approximately 70 000 cholecystectomies are performed annually<sup>2</sup>. Among those fit for surgery, patients follow one of three pathways from presentation to definitive treatment linked to emergency admissions with gallbladder disease: emergency cholecystectomy during an emergency admission; elective cholecystectomy with no previous emergency admission; or delayed cholecystectomy following one or more previous emergency admissions with gallbladder pathology.

Variations in outcomes exist following these different patient pathways. When performed with no previous emergency admission, either as an index emergency or elective operation, cholecystectomy is associated with fewer gallbladder-specific complications, a shorter total length of hospital stay and similar operative complications compared with those among patients who have had one or more emergency admissions<sup>3-5</sup>. Many of these studies were conducted in specialized centres by enthusiasts. In contrast, population-level data from Hospital Episodes Statistics (HES)<sup>2</sup> and a retrospective study from Scotland<sup>6</sup> both suggested that emergency cholecystectomy may be associated with poorer surgical outcomes. The reasons for these differences are unclear, but may be due to patient, disease, surgical and hospital variables not fully realized in administrative data sets.

Patient outcomes are used to measure quality of healthcare, such as readmission, complication, reoperation and mortality rates<sup>6-13</sup>. The mortality rate is low following cholecystectomy, and therefore a poor measure of quality in this cohort<sup>14</sup>. In contrast, reducing hospital readmissions and complications after surgery can lower hospital costs and improve patient satisfaction<sup>15-17</sup>. The causes of readmission and complications after cholecystectomy have been poorly studied in large prospective series, but may vary according to patient pathways<sup>11</sup>.

Over the past 8 years, trainee-led networks in the UK have adopted a collaborative approach to deliver prospective population-level data collection, and measure patient, disease, surgical and hospital variables with short-term endpoints such as readmissions and complications<sup>18</sup>. Using these networks, a prospective, population-based cohort study was conducted to describe management of patients with benign gallbladder disease<sup>19</sup>, and identify patient, disease, surgical and hospital-related characteristics that might be associated with all-cause 30-day readmission and complications.

## **+A: Methods**

The study was carried out as described previously<sup>19</sup>. The study protocol did not require research registration as anonymized, observational data were collected. This was confirmed by the online National Research Ethics Service decision tool (<http://www.hra-decisiontools.org.uk/research/>), and further supported by written confirmation and advice from the Research and Development Director at University Hospitals Birmingham NHS Foundation Trust, UK. The study was registered as a clinical audit or service evaluation at each participating hospital under the supervision of a named senior investigator (consultant surgeon).

## **+B: Inclusion and exclusion criteria**

All patients undergoing cholecystectomy for benign gallbladder diseases in acute UK and Irish hospitals participating in this study between 1 March and 1 May 2014 were included. Patients were grouped according to the timing of cholecystectomy: emergency cholecystectomy, defined as cholecystectomy during an emergency admission; delayed cholecystectomy, defined as a scheduled cholecystectomy following an emergency admission with gallbladder disease in the preceding 12 months; or elective cholecystectomy, defined as a planned elective admission for cholecystectomy following referral by a family doctor and addition to the routine surgical waiting list from an outpatient department visit. Open, laparoscopic and laparoscopic procedures converted to open surgery were included. Cholecystectomies for a known gallbladder cancer or as a part of another surgical procedure. (such as pancreaticoduodenectomy) were excluded.

## **+B: Outcome measures**

Planned analyses comprised a description of current management of benign gallbladder disease with readmission and complication rates. Variations in 30-day complication and readmission rates were studied as well as predictive factors for these events. A list of recorded complications with their definitions is available in *Table S1* (supporting information).

#### **+B: Data quality**

To standardize data quality, a quality assurance programme was developed<sup>19</sup>. This included a detailed study protocol, pilot phase, and a requirement for a minimum of 95 per cent data completeness at submission. Case ascertainment, including readmission to a different hospital from where cholecystectomy was performed, and data accuracy, were validated by independent investigators at selected hospitals, who checked data from 10 per cent of patients against original medical records. These independent investigators were not involved in the original data collection.

#### **+B: Explanatory variables**

Patient, disease and hospital characteristics were considered as potential explanatory variables influencing the performance of emergency cholecystectomy. A full list including definitions has been published previously<sup>19</sup>. Briefly, patient characteristics included: age, sex, ASA fitness grade (I, normal healthy patient; II, mild systemic disease; III, severe systemic disease; IV, severe systemic disease that is a constant threat to life; V, moribund patient who is not expected to survive without the operation) and BMI (less than 17.9 kg/m<sup>2</sup>, underweight; 18.0–24.9 kg/m<sup>2</sup>, normal; 25.0–29.9 kg/m<sup>2</sup>, overweight; 30.0–34.9 kg/m<sup>2</sup>, moderate obesity; 35.0 kg/m<sup>2</sup> and above, severe or very severe obesity). The following disease characteristics were considered: indication (biliary colic, cholecystitis, pancreatitis, common bile duct (CBD) stones), ultrasound findings (gallbladder wall thickness, dilated

CBD), findings from other radiological investigations (CT, magnetic retrograde cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP)) and total number of emergency admissions with biliary symptoms in the 12 months before cholecystectomy.

Surgical characteristics included degree of difficulty according to the Nassar score<sup>20</sup> and surgical approach (laparoscopic, open or laparoscopic converted to open surgery). Hospital characteristics, including type (university or not), specialist hepatobiliary centre and acute hospital status, were recorded along with the number of consultants within the reporting hospital performing cholecystectomy, hospital country, number of beds within the reporting hospital (less than 100, 101–500, 501–1000, more than 1000) and presence of an on-site ERCP service. The hospital's policy regarding the ease of performing intraoperative cholangiography and use of dedicated emergency gallbladder operating lists were considered. The consultant's presence, specialty and grade were also recorded at the time of cholecystectomy.

#### **+B: Statistical analysis**

Results are reported in accordance with the STROBE statement for observational studies<sup>21</sup>. Crude rates of emergency cholecystectomy at each hospital were calculated for all patients. Descriptive statistics were obtained for all variables. Median values with interquartile range (i.q.r.) are reported. The  $\chi^2$  test or Fisher's exact test, as appropriate, was used to identify differences between categorical variables.

To investigate the relationship between 30-day readmission and complication rates and the variables studied, data were analysed using multilevel, multivariable logistic regression modelling. Both 30-day readmission and complication rates were recorded as binary outcome measures, requiring a logistic analytical approach. These data comprise a

two-level hierarchical structure, with patients at level 1, nested within hospitals at level 2. Multilevel (hierarchical) modelling was selected owing to the structure of the data. Patient outcomes are not independent of each other as patients are clustered within hospitals. This clustering introduces multilevel dependency or correlation among patient observations that can have implications for model parameter estimates. Because of this dependency among observations, multilevel modelling has advantages over other approaches, such as logistic regression analysis, which assume that observations are independent.

Before model building, variables were investigated for potential confounding relationships using correlation and scatter plots. As the variables included in this study could be viewed as being on a causal path potentially linking each variable to the outcome, they were assessed during model building and none were excluded. Variable collinearity was also tested using variance inflation factor scores.

Variables were included in the models if they were found to be significant at the 5 per cent level. The forward and back Collett method<sup>22</sup> was used to select variables for inclusion.

To investigate between-hospital variation, the random intercept model was extended to a random coefficient model, including each variable in turn, allowing the factor to vary across hospitals. Results are expressed as adjusted odds ratios (ORs) with 95 per cent confidence intervals (c.i.).

All two-way interactions were assessed and no significant interactions were identified in the final models. Model testing was performed using likelihood ratio tests, Wald tests, and residual and deviance plots. Owing to the binary nature of the outcome data, the multilevel logistic regression model deviates from the normal assumptions that underlie regression models and as such these were not tested for. However, testing for the assumption of



independent co-variance structure between random effects was not possible as no explanatory variables were included at level 2.

Missing data accounted for 0.8 per cent of the data set. Models were fitted with missed data and therefore all available data were included.

All statistical analyses were performed using Stata® version 12 (StataCorp, College Station, Texas, USA). The multilevel, multivariable logistic regression modelling was carried out in MLwiN version 2.14 (<http://www.cmm.bristol.ac.uk/MLwiN>).

#### +A: **Results**

Data were collected on 8909 patients undergoing cholecystectomy from 167 hospitals. Case ascertainment and accuracy of collected data was above 95.3 and 99.2 per cent respectively, compared with information from 10 per cent of patients checked independently against the original medical records.

The median age of the cohort was 51 (38–64) years. The numbers of patients undergoing emergency, delayed and elective cholecystectomy were 1451 (16.3 per cent), 3293 (37.0 per cent) and 4165 (46.8 per cent) respectively. A total of 3713 patients (41.7 per cent) had at least one emergency admission with acute gallbladder disease before cholecystectomy. Elective cholecystectomy was mainly undertaken for biliary colic, in younger women with a low ASA fitness grade, who did not require additional radiological tests or interventions (such as MRCP or ERCP) compared with patients who had delayed and emergency cholecystectomy (*Table 1*). Patients with biliary colic underwent elective surgery (73.3 per cent) more frequently, whereas cholecystitis and pancreatitis were more frequently treated by delayed cholecystectomy (53.0 and 64.0 per cent respectively). Elective cholecystectomy was more likely to be completed laparoscopically, was less difficult as

assessed by the operating surgeon, and with fewer intraoperative complications (bile contamination, stones spilled, bleeding, bowel and significant biliary injury), compared with delayed and emergency cholecystectomy (*Table 2*). The difference in incidence of bile duct injury, however, did not reach statistical significance. The median duration of an elective procedure was 60 (45–79) min compared with 65 (50–90) and 80 (60–110) min for delayed and emergency cholecystectomy respectively.

#### **+B: Outcomes at 30 days**

Readmission and complication rates at 30 days were 7.1 per cent (633 of 8909) and 10.8 per cent (962 of 8909) respectively (*Table 3*). The rates of readmission, overall complications and individual complications at 30 days were higher in the delayed and emergency groups than in the elective group. Both readmission and complication rates differed according to the number of surgical admissions (*Fig. 1*). Readmission rates among patients with no, one or at least two surgical admissions before cholecystectomy were 6.1, 7.2 and 12.9 per cent respectively; corresponding complication rates were 8.9, 11.8 and 19.1 per cent.

Reoperations were more frequent following delayed cholecystectomy, although this difference was not statistically significant. The 30-day mortality rate was higher when cholecystectomy was performed as an emergency or delayed operation, but again this difference was not statistically significant.

#### *+C: Thirty-day readmission rate*

The null random intercept model containing no exploratory variables was used to test variation across the 167 hospitals, and demonstrated a statistically significant between-hospital variance (likelihood ratio statistic 11.57,  $P = 0.003$ ). Estimates of the hospital effects obtained from the null model showed the hospital effects in rank order together with 95 per cent confidence intervals (*Fig. 2*). Only two of 167 hospitals (1.2 per cent) had 30-day

readmission rates higher than the rest. When the model was extended to include explanatory variables, duration of surgery and greater number of surgical admissions before the index surgery were associated with a higher risk of readmission, whereas there was no difference in readmissions between emergency and delayed operation (*Table 4*). Elective cholecystectomy, younger patients and ASA score I–II were associated with a lower risk of readmission. The variables included in this multilevel model accounted for 97 per cent of the detected variation. BMI, indication for cholecystectomy and hospital-related variables were not independently associated with readmission.

#### *+C: Thirty-day complication rate*

The null random intercept model demonstrated significant between-hospital variance (likelihood ratio statistic 74.80,  $P = 0.003$ ). Eleven hospitals (6.6 per cent) had a significantly different 30-day complication rate from the others (*Fig. 3*). When the model was extended to include explanatory variables, age, ASA grade, surgical admission type, number of admissions and duration of surgery were again associated with complications (*Table 5*). In addition, having an open or a laparoscopic procedure converted to open surgery and a greater degree of operative difficulty were associated with a higher risk of complications. These variables accounted for 93 per cent of the detected variation. Other patient categories, disease and hospital factors were not independently associated with the outcomes measured.

#### **+A: Discussion**

This study evaluated the current management and outcomes of cholecystectomy for benign gallbladder disease in the UK and Ireland. Readmissions and complications were common and varied across the 167 hospitals studied. An emergency or delayed operation and greater numbers of surgical admissions before the index surgery were associated with a higher risk of readmission and complications. Intraoperative features, such as difficulty, duration and

operative method, were also associated with poorer outcomes across hospitals. Importantly, the hospital characteristics analysed did not influence these associations.

Readmission and complication rates at 30 days were similar to those reported previously. Other studies<sup>2,6,12,23–26</sup> have described patient and hospital factors, both independently and in combination, linked to complications and readmissions. Factors associated with readmission or complication in the present study were analysed by means of hierarchical modelling. The advantage of this type of analysis was that it allowed the effects of patient variables on certain outcomes to be considered independently of hospital variables that may also influence outcomes<sup>27</sup>. Age, ASA grade, duration of surgery, operative approach and degree of operative difficulty were all associated with worse outcomes, as demonstrated previously<sup>25,28</sup>.

Increasing numbers of emergency admissions before cholecystectomy were independently associated with both readmission and complication rates here. This supports a pathway in which definitive cholecystectomy should be performed during the first admission. Emergency cholecystectomy was mainly carried out in younger patients and those presenting with cholecystitis, whereas older patients and those requiring further investigations tended to be discharged and brought back for a delayed cholecystectomy.

Delayed cholecystectomy can result in emergency readmissions and poorer outcomes<sup>29–33</sup>. Logistical barriers to emergency cholecystectomy, such as lack of prompt access to specialist investigations and emergency theatre availability, appear to explain differences in service provision. Hospital policy and surgeon or patient preference may contribute to delaying cholecystectomy. Increasing the numbers of emergency cholecystectomies by addressing modifiable barriers, such as reducing the number of surgical

admissions with gallbladder pathology before cholecystectomy, would improve outcomes. This is generalizable to healthcare providers outside the UK and Ireland.

In contrast to previous studies, there was no statistical difference in readmissions and complications when emergency and delayed cholecystectomies were compared, suggesting that the delayed cohort was not homogeneous. Definitions of emergency and delayed cholecystectomy varied in previous studies. Some considered emergency or early cholecystectomy to comprise operations performed within 48–72 h of symptom onset<sup>5</sup>. A population-based study<sup>4</sup> of 14 200 patients in Canada showed that patients experienced fewer complications when cholecystectomy was performed within 7 days of hospital admission. A study<sup>3</sup> in Switzerland demonstrated that a 6-day delay in performing emergency cholecystectomy was associated with a higher conversion rate (12 per cent at day 0 *versus* 18 per cent at day 6), more complications (5.7 *versus* 13 per cent respectively) and the reoperation rate almost double in the delayed compared with the emergency group (0.8 *versus* 0.5 per cent).

There are limitations to the present study. The data represent a 2-month snapshot of practice and this may account for unexpected observations, such as the inverse association between age and risk of readmission. However, short intensive data collection allowed surgical teams to contribute meaningful numbers of patients with high levels of accuracy and without additional resources. The number of patients who did not undergo cholecystectomy is unknown. It seems intuitive that those with less co-morbidity are more likely to be offered cholecystectomy. The overall models accounted for nearly 90 per cent of the variations in outcomes seen across the hospitals studied, suggesting the presence of other factors not characterized in this study. Despite these limitations, the accuracy of the data set was validated independently and it contained variables not typically collected in similar studies.

Sweden<sup>34</sup>, Denmark<sup>35</sup> and Switzerland<sup>25</sup> use prospective registries of cholecystectomy for continual quality improvement. Although this is costly and time-consuming, the results of this prospective population-based cohort study demonstrate that cholecystectomy following multiple surgical admissions is linked to 30-day complications and readmissions. Measuring numbers of surgical admissions before cholecystectomy provides a simple quality improvement metric. There needs to be a focus on offering emergency rather than delayed cholecystectomy for patients presenting with acute benign gallbladder disease.

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**Supporting information**

Additional supporting information may be found in the online version of this article:

**Appendix S1** Definitions of complications (Word document)

**Typesetter: please refer to marked-up figures**

**Fig. 1** Thirty-day **a** readmission rate and **b** complication rate according to number of emergency admissions before cholecystectomy

**Fig. 2** Plot examining hospital effects (residuals) and corresponding 95 per cent confidence intervals for 30-day readmissions

**Fig. 3** Plot examining hospital effects (residuals) and corresponding 95 per cent confidence intervals for 30-day complications

**Table 1** Patient and disease characteristics, and radiological investigations according to performance of emergency, delayed or elective cholecystectomy

|                                     | All patients<br>( <i>n</i> = 8909) | Emergency<br>cholecystectomy<br>( <i>n</i> = 1451) | Delayed<br>cholecystectomy<br>( <i>n</i> = 3293) | Elective<br>cholecystectomy<br>( <i>n</i> = 4165) | <i>P</i> * |
|-------------------------------------|------------------------------------|--|--|---|------------|
| Age (years)                         |                                    |  |  |   | < 0.001    |
| < 40                                | 2534 (28.4)                        | 441 (30.4)   | 859 (26.1)                                       | 1234 (29.6)                                       |            |
| 40–60                               | 3531 (39.6)                        | 510 (35.1)   | 1161 (35.3)                                      | 1860 (44.7)                                       |            |
| 61–80                               | 2602 (29.2)                        | 435 (30.0)   | 1108 (33.6)                                      | 1059 (25.4)                                       |            |
| > 80                                | 242 (2.7)                          | 65 (4.5)   | 165 (5.0)  | 12 (0.3)  |            |
| Sex                                 |                                    |  |  |   | < 0.001    |
| F                                   | 6565 (73.7)                        | 1000 (68.9)  | 2189 (66.5)                                      | 3,376 (81.1)                                      |            |
| M                                   | 2344 (26.3)                        | 451 (31.1)   | 1104 (33.5)                                      | 789 (18.9)  |            |
| BMI (kg/m <sup>2</sup> )            |                                    |  |  |   | 0.033      |
| < 17.9                              | 41 (0.5)                           | 6 (0.4)  | 17 (0.5)   | 18 (0.5)  |            |
| 18.0–24.9                           | 1749 (20.6)                        | 262 (19.4)   | 667 (21.1)                                       | 820 (20.5)  |            |
| 25.0–29.9                           | 3101 (35.7)                        | 494 (36.6)   | 1108 (35.1)                                      | 1429 (35.8)                                       |            |
| 30.0–34.9                           | 2078 (24.4)                        | 337 (25.0)   | 805 (25.5)                                       | 936 (23.4)  |            |
| ≥ 35.0                              | 1600 (18.8)                        | 250 (18.5)   | 560 (17.7)                                       | 790 (19.8)  |            |
| Unknown                             | 410                                | 102  | 136  | 172   |            |
| ASA fitness grade                   |                                    |  |  |   | < 0.001    |
| I–II                                | 7897 (89.4)                        | 1220 (85.0)  | 2873 (87.9)                                      | 3804 (92.1)                                       |            |
| ≥ III                               | 937 (10.6)                         | 216 (15.0)   | 396 (12.1)                                       | 325 (7.9)   |            |
| Unknown                             | 75                                 | 15   | 24   | 36  |            |
| Indication                          |                                    |  |  |   | < 0.001    |
| Colic                               | 4683 (52.6)                        | 295 (20.3)   | 955 (29.0)                                       | 3433 (82.5)                                       |            |
| Cholecystitis                       | 2581 (29.0)                        | 795 (54.8)   | 1369 (41.6)                                      | 417 (10.0)  |            |
| Pancreatitis                        | 851 (9.6)                          | 268 (18.5)   | 545 (16.6)                                       | 38 (0.9)  |            |
| CBD stone                           | 589 (6.6)                          | 83 (5.7)   | 386 (11.7)                                       | 120 (2.9)   |            |
| Polyp                               | 135 (1.5)                          | 2 (0.1)  | 16 (0.5)   | 117 (2.8)   |            |
| Dyskinesia                          | 31 (0.3)                           | 1 (0.1)  | 9 (0.3)  | 21 (0.5)  |            |
| Acalculous                          | 28 (0.3)                           | 6 (0.4)  | 11 (0.3)   | 11 (0.3)  |            |
| Other                               | 2 (0.0)                            | 0 (0)  | 0 (0)  | 2 (0.0)   |            |
| Missing                             | 9                                  | 1  | 2  | 6   |            |
| No. of admissions<br>before surgery |                                    |  |  |   | < 0.001    |
| 0                                   | 5196 (58.3)                        | 913 (62.9)   | 118 (3.6)  | 4165 (100.0)                                      |            |
| 1                                   | 2859 (32.1)                        | 361 (24.9)   | 2498 (75.9)                                      | 0 (0.0)   |            |
| 2                                   | 623 (7.0)                          | 121 (8.3)  | 502 (15.2)                                       | 0 (0.0)   |            |
| ≥ 3                                 | 231 (2.6)                          | 56 (3.9)   | 175 (5.3)  | 0 (0.0)   |            |
| Ultrasonography<br>performed        | 8539 (96.0)*                       |  |  |   |            |
| Ultrasound findings                 |                                    |  |  |   |            |
| Thick-walled                        | 2855 (32.8)†                       | 729 (51.9)   | 1412 (43.6)                                      | 714 (17.6)  | < 0.001    |
| CBD dilated                         | 1398 (16.0)‡                       | 289 (20.6)   | 793 (24.5)                                       | 316 (7.8)   | < 0.001    |
| CT performed                        | 1307 (14.8)§                       | 290 (20.1)   | 680 (20.8)                                       | 337 (8.2)   | < 0.001    |
| MRCP performed                      | 2301 (26.1)¶                       | 417 (28.9)   | 1319 (40.2)                                      | 565 (13.8)  | < 0.001    |

|                |             |           |            |           |         |
|----------------|-------------|-----------|------------|-----------|---------|
| ERCP performed | 960 (10.9)# | 139 (9.6) | 670 (20.5) | 151 (3.7) | < 0.001 |
|----------------|-------------|-----------|------------|-----------|---------|

Values in parentheses are percentages. CBD common bile duct; MRCP magnetic retrograde cholangiopancreatography; ERCP endoscopic retrograde cholangiopancreatography. Data missing for \*12, †219, ‡212, §101, ¶93 and #105 patients. \*\* $\chi^2$  test or Fisher's exact test, as appropriate.

**Table 2** Surgical and hospital-related factors in 8909 cholecystectomies according to performance of emergency, delayed or elective cholecystectomy

|                            | All patients<br>(n = 8909) | Emergency<br>cholecystectomy<br>(n = 1451) | Delayed<br>cholecystectomy<br>(n = 3293) | Elective<br>cholecystectomy<br>(n = 4165) | P‡      |
|----------------------------|----------------------------|--|--|---|---------|
| Grade of operating surgeon |                            |  |  |   |         |
| Junior trainee             | 403 (4.5)                  | 91 (6.3)                                   | 114 (3.5)                                | 198 (4.8)                                 | < 0.001 |
| Senior trainee             | 1488<br>(16.7)             | 278 (19.2)                                 | 503 (15.3)                               | 707 (17.0)                                | < 0.001 |
| Consultant                 | 7007<br>(78.7)             | 1080 (74.5)                                | 2675 (81.3)                              | 3252 (78.2)                               | < 0.001 |
| Missing                    | 11                         | 2  | 1  | 8   |         |
| Consultant present         | 7755<br>(89.5)*            | 1178 (85.9)                                | 2940 (90.9)                              | 3637 (89.6)                               | < 0.001 |
| Consultant specialty       |                            |  |  |   | < 0.001 |
| Oesophagogastric           | 3416<br>(38.5)             | 560 (38.8)                                 | 1220 (37.1)                              | 1636 (39.5)                               |         |
| HPB                        | 1918<br>(21.6)             | 314 (21.8)                                 | 634 (19.3)                               | 970 (23.4)                                |         |
| Colorectal                 | 1958<br>(22.1)             | 352 (24.4)                                 | 831 (25.3)                               | 775 (18.7)                                |         |
| Breast                     | 348 (3.9)                  | 42 (2.9)                                   | 137 (4.1)                                | 169 (4.1)                                 |         |
| Vascular                   | 373 (4.2)                  | 57 (3.9)                                   | 141 (4.3)                                | 175 (4.2)                                 |         |
| Other                      | 863 (9.7)                  | 117 (8.1)                                  | 327 (9.9)                                | 419 (10.1)                                |         |
| Missing                    | 33                         | 9  | 3  | 21  |         |
| Operative method           |                            |  |  |   | < 0.001 |
| Laparoscopic               | 8523<br>(95.7)             | 1343 (92.6)                                | 3105 (94.3)                              | 4075 (97.8)                               |         |
| Converted                  | 297 (3.3)                  | 77 (5.3)                                   | 152 (4.6)                                | 68 (1.6)                                  |         |
| Open                       | 89 (1.0)                   | 31 (2.1)                                   | 36 (1.1)                                 | 22 (0.5)                                  |         |
| Hospital type              |                            |  |  |   | < 0.001 |
| Non-university             | 4843<br>(54.4)             | 687 (47.3)                                 | 1915 (58.2)                              | 2241 (53.8)                               |         |
| University                 | 4066<br>(45.6)             | 764 (52.7)                                 | 1378 (41.8)                              | 1924 (46.2)                               |         |
| Tertiary HPB centre        |                            |  |  |   | < 0.001 |
| No                         | 6602<br>(74.1)             | 941 (64.9)                                 | 2588 (78.6)                              | 3073 (73.8)                               |         |
| Yes                        | 2307<br>(25.9)             | 510 (35.1)                                 | 705 (21.4)                               | 1092 (26.2)                               |         |
| Acute hospital             |                            |  |  |   | < 0.001 |
| No                         | 561 (6.3)                  | 13 (0.9)                                   | 222 (6.7)                                | 326 (7.8)                                 |         |
| Yes                        | 8348<br>(93.7)             | 1438 (99.1)                                | 3071 (93.3)                              | 3839 (92.2)                               |         |
| Day case                   |                            |  |  |   | < 0.001 |
| No                         | 1297<br>(97.1)             | 1297 (97.1)                                | 958 (29.2)                               | 822 (19.8)                                |         |

|                                   |             |             |             |             |         |
|-----------------------------------|-------------|-------------|-------------|-------------|---------|
| Yes                               | 39 (2.9)    | 39 (2.9)    | 2324 (70.8) | 3337 (80.2) |         |
| Missing                           | 132         | 115         | 11          | 6           |         |
| Emergency cholecystectomy list    |             |             |             |             | < 0.001 |
| No                                | 6036 (67.8) | 993 (68.4)  | 2225 (67.6) | 2818 (67.7) |         |
| <i>Ad hoc</i>                     | 984 (11.0)  | 152 (10.5)  | 403 (12.2)  | 429 (10.3)  |         |
| Once per week                     | 646 (7.3)   | 162 (11.2)  | 212 (6.4)   | 272 (6.5)   |         |
| More than once per week           | 788 (8.8)   | 138 (9.5)   | 292 (8.9)   | 358 (8.6)   |         |
| Elective surgery only at hospital | 455 (5.1)   | 6 (0.4)     | 161 (4.9)   | 288 (6.9)   |         |
| Nassar operative difficulty score |             |             |             |             | < 0.001 |
| 1                                 | 3554 (40.2) | 360 (25.1)  | 1146 (35.1) | 2048 (49.5) |         |
| 2                                 | 2644 (29.9) | 374 (26.1)  | 942 (28.9)  | 1328 (32.1) |         |
| 3                                 | 1814 (20.5) | 423 (29.5)  | 775 (23.8)  | 616 (14.9)  |         |
| 4                                 | 821 (9.3)   | 278 (19.4)  | 397 (12.2)  | 146 (3.5)   |         |
| Missing                           | 76          | 16          | 33          | 27          |         |
| IOC                               |             |             |             |             | < 0.001 |
| Not performed                     | 7770 (87.9) | 1121 (78.0) | 2869 (87.6) | 3780 (91.6) |         |
| Planned                           | 965 (10.9)  | 295 (20.5)  | 354 (10.8)  | 316 (7.7)   |         |
| Unplanned                         | 105 (1.2)   | 22 (1.5)    | 54 (1.6)    | 29 (0.7)    |         |
| Missing                           | 69          | 13          | 16          | 40          |         |
| CBD exploration                   | 282†        | 99 (6.9)    | 113 (3.4)   | 70 (1.7)    | < 0.001 |

Values in parentheses are percentages. HPB hepatobiliary; IOC, intraoperative

cholangiography; CBD, common bile duct. Data missing for \*244 and †75 patients. ‡ $\chi^2$  test.

**Table 3** Thirty-day readmission and complications according to performance of emergency delayed or elective cholecystectomy.

|                              | Emergency cholecystectomy<br>( <i>n</i> = 1451) | Delayed cholecystectomy<br>( <i>n</i> = 3293) | Elective cholecystectomy<br>( <i>n</i> = 4165) | <i>P</i> ‡ |
|------------------------------|---|---|--|------------|
| Readmissions                 | 138 (9.5)                                       | 270 (8.2)                                     | 225 (5.4)                                      | < 0.001    |
| All complications            | 223 (15.4)                                      | 420 (12.8)                                    | 319 (7.7)                                      | < 0.001    |
| Intraoperative complications |   |   |  |            |
| Stones spilt                 | 222 (15.3)                                      | 400 (12.1)                                    | 224 (5.4)                                      | < 0.001    |
| Bleeding                     | 195 (13.4)                                      | 302 (9.2)                                     | 257 (6.2)                                      | < 0.001    |
| Bowel injury                 | 8 (0.6)   | 22 (0.7)                                      | 19 (0.5)                                       | 0.479      |
| CBD injury                   | 5 (0.3)   | 12 (0.4)                                      | 7 (0.2)  | 0.232      |
| Postoperative complications  |   |   |  |            |
| Collections                  | 44 (3.0)  | 88 (2.7)                                      | 57 (1.4)                                       | < 0.001    |
| Surgical-site infection      | 38 (2.6)  | 78 (2.4)                                      | 76 (1.8)                                       | 0.114      |
| Pancreatitis                 | 13 (0.9)  | 19 (0.6)                                      | 4 (0.1)  | < 0.001    |
| CBD stone                    | 30 (2.1)  | 28 (0.9)                                      | 25 (0.6)                                       | < 0.001    |
| Bile leak                    | 32 (2.2)  | 52 (1.6)                                      | 37 (0.9)                                       | < 0.001    |
| Respiratory                  | 29 (2.0)  | 69 (2.1)                                      | 29 (0.7)                                       | < 0.001    |
| Reimaging                    | 172 (11.8)                                      | 300 (9.1)                                     | 206 (4.9)                                      | < 0.001    |
| Radiological drain           | 16 (1.1)  | 37 (1.1)                                      | 16 (0.4)                                       | < 0.001    |
| Relaparoscopy or laparotomy  | 7 (0.5)   | 27 (0.8)                                      | 27 (0.6)                                       | 0.399      |
| 30-day mortality             | 3 (0.2)   | 6 (0.2)                                       | 2 (0.05)                                       | 0.160      |

Values in parentheses are percentages. CBD, common bile duct. \* $\chi^2$  test.

**Table 4** Multilevel random intercept logistic regression analysis of association between patient and surgery characteristics with all-cause 30-day readmission following cholecystectomy

|                               | Odds ratio        | <i>P</i> |
|-------------------------------|-------------------|----------|
| Random intercept              | 0.07 (0.06, 0.09) | < 0.001  |
| Patient factors               |                   |          |
| Age (years)                   |                   |          |
| < 40                          | 1.00 (reference)  |          |
| 40–60                         | 0.78 (0.63, 0.95) | 0.014    |
| 61–80                         | 0.72 (0.58, 0.91) | 0.005    |
| > 80                          | 0.56 (0.33, 0.94) | 0.028    |
| ASA fitness grade             |                   |          |
| I–II                          | 1.00 (reference)  |          |
| II–IV                         | 1.47 (1.14, 1.90) | 0.003    |
| Surgical factors              |                   |          |
| Surgery admission type        |                   |          |
| Delayed                       | 1.00 (reference)  |          |
| Emergency                     | 0.91 (0.68, 1.21) | 0.519    |
| Elective                      | 0.48 (0.35, 0.66) | < 0.001  |
| No. of surgical admissions    |                   |          |
| 0                             | 1.00 (reference)  |          |
| 1                             | 1.50 (1.11, 2.03) | 0.009    |
| ≥ 2                           | 1.59 (1.18, 2.14) | 0.002    |
| Duration of surgery (per min) | 1.01 (1.00, 1.01) | 0.043    |

Values in parentheses are 95 per cent confidence intervals.



**Table 5** Multilevel random intercept logistic regression of the association between patient and surgery characteristics with all-cause 30-day complications following cholecystectomy

|  | Odds ratio        | <i>P</i> |
|--|-------------------|----------|
| Random intercept                                 | 0.06 (0.04, 0.07) | < 0.001  |
| Patient factors                                  |                   |          |
| Age (years)                                      |                   |          |
| < 40   | 1.00 (reference)  |          |
| 40–60  | 0.78 (0.65, 0.95) | 0.012    |
| 60–80  | 0.98 (0.80, 1.19) | 0.838    |
| > 80   | 1.52 (1.08, 2.16) | 0.018    |
| ASA fitness grade                                |                   |          |
| I–II   | 1.00 (reference)  |          |
| II–IV  | 1.44 (1.17, 1.78) | 0.001    |
| Surgical factors                                 |                   |          |
| Surgical admission type                          |                   |          |
| Delayed  | 1.00 (reference)  |          |
| Emergency  | 1.01 (0.80, 1.29) | 0.902    |
| Elective   | 0.61 (0.46, 0.81) | < 0.001  |
| No. of surgical admissions                       |                   |          |
| 0  | 1.00 (reference)  |          |
| 1  | 1.36 (1.05, 1.75) | 0.021    |
| ≥ 2  | 1.28 (0.99, 1.65) | 0.055    |
| Method of operation                              |                   |          |
| Laparoscopic                                     | 1.00 (reference)  |          |
| Open   | 1.77 (1.04, 3.01) | 0.034    |
| Laparoscopic converted to open                   | 2.59 (1.91, 3.52) | < 0.001  |
| Duration of surgery (per min)                    | 1.01 (1.01, 1.01) | 0.003    |
| Level of operation difficulty (per Nassar level) | 1.22 (1.12, 1.33) | < 0.001  |

Values in parentheses are 95 per cent confidence intervals.

