Is out-of-hours cholecystectomy for acute cholecystitis associated with complications?

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Background: Existing data on the safety of out-of-hours cholecystectomy are conflicting. The aim of this study was to investigate whether out-of-hours cholecystectomy for acute cholecystitis is associated with a higher risk for complications compared with surgery during office hours.

Methods: This was a population-based cohort study. The Swedish Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography Register (GallRiks) was used to investigate the association between out-of-hours cholecystectomy for acute cholecystitis and complications developing within 30 days. Data from patients who underwent cholecystectomy between 2006 and 2017 were collected. Out-of-hours surgery was defined as surgery commencing between 19.00 and 07.00 hours on weekdays, or any time at weekends (Friday 19.00 hours to Monday 07.00 hours). Multivariable logistic regression analysis was used to assess the risk of complications, with time of procedure as independent variable. The proportion of open procedures and proportion of procedures exceeding 120 min were also analysed. Adjustments were made for sex, age, ASA grade, time between admission and surgery, and hospital-specific features.

Results: Of 11 153 procedures included, complications occurred within 30 days in 1573 patients (14.1 per cent). The adjusted odds ratio (OR) for complications for out-of-hours versus office-hours surgery was 1.12 (95 per cent c.i. 0.99 to 1.28). The adjusted OR for procedures completed as open surgery was 1.39 (1.25 to 1.54), and that for operating time exceeding 120 min was 0.63 (0.58 to 0.69).

Conclusion: Out-of-hours complications may relate to patient factors and the higher proportion of open procedures.

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Introduction

Laparoscopic cholecystectomy is one of the most common acute abdominal surgical procedures. The timing of surgery for acute cholecystitis has long been the subject of debate. It is recommended that surgery is performed soon after admission. In the newly updated Tokyo Guidelines (TG18), early laparoscopic cholecystectomy for acute cholecystitis is recommended regardless of the grade of severity, and a delayed procedure should be chosen only for selected high-risk patients. Although early cholecystectomy is widely recognized as the preferred approach, in clinical practice there is often delay owing to prioritization of more urgent procedures. Large studies have shown that the risk of complications, conversion to open surgery and prolonged operating time increases with each day that acute cholecystectomy is delayed. To improve the timeliness of care, acute-care surgery models have been developed, and undertaking laparoscopic cholecystectomy 24 h per day, 7 days a week has been discussed. In a systematic review from 2014, Nagaraja and colleagues reported shorter hospital stay, as well as a lower complication rate after acute cholecystectomy, when an acute-care surgery model was followed. Studies more specifically focused on out-of-hours surgery have shown...
no difference in duration of hospital stay or increased complication rate\textsuperscript{12,14}.

The impact of out-of-hours surgery for acute cholecystitis on outcome is not clear. The aim of this study was to investigate the association between out-of-hours cholecystectomy for acute cholecystitis and any complication developing within 30 days. The hypothesis was that out-of-hours surgery would be associated with a higher risk of complications. The proportion of procedures completed as open surgery was also investigated, as was the risk of a long procedure, defined as operating time exceeding 2 h.

**Methods**

This was a population-based cohort study based on data from the Swedish National Register for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (ERCP) (GallRiks). The Swedish National Board of Health and Welfare, Swedish Surgical Association and Swedish Society of Laparoscopic Surgery founded the register in 2005. It covers more than 90 per cent of all gallstone surgery and ERCP procedures performed in Sweden. Approximately 20 000 procedures (12 000 cholecystectomies and 8000 ERCP procedures) are registered annually. Data regarding indication for surgery, surgical technique, duration of operation, outcome and patient satisfaction are recorded\textsuperscript{16}. The Ethical Review Board at Karolinska Institutet (Stockholm, Sweden) approved the study (2018/506-31/2).

**Inclusion and exclusion criteria**

All patients registered in GallRiks as undergoing non-elective cholecystectomy for acute cholecystitis between 2006 and 2017 were included. The register has two options for reporting operating time: as duration of the procedure in minutes, or actual time of day for start and finish of surgery. Only procedures for which time of day was registered were included; procedures where duration only was recorded were excluded. Only centres reporting time of day for more than 1 per cent of procedures were included to avoid bias.

**Description of cohort**

Data from the register were collected retrospectively. Demographic and clinical data were recorded, including age, sex, ASA physical status grade, BMI, interval between admission and surgery, duration of operation, duration of hospital stay, any complication developing within 30 days (such as bile leak, common bile duct injury, surgical-site infection, abscess, thrombosis, pneumonia and bleeding) and death.

**Exposure**

Procedures performed out of hours were those that began between 19.00 and 07.00 hours on weekdays, or at any time during the weekend (from Friday 19.00 hours until Monday 07.00 hours).

**Outcomes**

The primary outcome was any complication (yes/no) within 30 days. Types of complication are shown in Table S1 (supporting information). Secondary outcomes were proportion of procedures completed as open surgery, and proportion of procedures with operating time exceeding 120 min.
## Table 1 Demographic and clinical data according to timing of operation

| Outcome                          | Office hours (n = 6443) | Out of hours (n = 2710) | P‡  |
|----------------------------------|-------------------------|-------------------------|-----|
| **Complication**                 |                         |                         |     |
| No                               | 7294 (86-4)             | 2286 (84-4)             |     |
| Yes†                             | 1149 (13-6)             | 424 (15-6)              | 0-008|
| Surgical approach*              |                         |                         | <0-001|
| Laparoscopic                     | 6007 (71-3)             | 1678 (62-1)             |     |
| Laparoscopic, converted to open  | 1355 (16-1)             | 418 (15-5)              |     |
| Open                             | 1067 (12-7)             | 608 (22-5)              |     |
| **Duration of surgery (h)**     |                         |                         | <0-001|
| < 2                              | 3734 (44-2)             | 1616 (59-6)             |     |
| ≥ 2                              | 4709 (55-8)             | 1094 (40-4)             |     |
| **Potential confounders**        |                         |                         |     |
| Age (years)*                     |                         | <0-001                  |     |
| ≤ 50                             | 3099 (36-8)             | 901 (33-3)              |     |
| > 51, ≤ 75                       | 4368 (51-9)             | 1395 (51-6)             |     |
| > 75                             | 952 (11-3)              | 406 (15-0)              |     |
| Sex*                             |                         | 0-558                   |     |
| F                                | 4368 (51-8)             | 1375 (50-8)             |     |
| M                                | 4071 (48-2)             | 1333 (49-2)             |     |
| ASA fitness grade                |                         | <0-001                  |     |
| I                                | 3170 (37-5)             | 948 (35-0)              |     |
| II                               | 4142 (49-1)             | 1345 (49-6)             |     |
| III                              | 1077 (12-8)             | 375 (13-8)              |     |
| IV                               | 52 (0-6)                | 40 (1-5)                |     |
| V                                | 2 (0-0)                 | 2 (0-1)                 |     |
| Time since admission (days)*     |                         | <0-001                  |     |
| 0                                | 619 (7-7)               | 521 (19-4)              |     |
| 1                                | 3021 (37-6)             | 1142 (42-5)             |     |
| 2                                | 2308 (28-7)             | 616 (23-0)              |     |
| 3                                | 1066 (13-3)             | 224 (8-3)               |     |
| 4–7                              | 871 (10-8)              | 149 (5-6)               |     |
| ≥ 8                              | 152 (1-9)               | 32 (1-2)                |     |
| BMI (kg/m²)*                     |                         | 0-725                   |     |
| ≤ 25                             | 1372 (25-4)             | 381 (24-8)              |     |
| > 25, ≤ 30                       | 2246 (41-6)             | 665 (43-3)              |     |
| > 30, ≤ 35                       | 1190 (22-1)             | 331 (21-5)              |     |
| > 35                             | 587 (10-9)              | 160 (10-4)              |     |
| Proportion surgery out of hours (per centre) | <0-001                |                         |     |
| ≤ 0.1                            | 1187 (14-1)             | 71 (2-6)                |     |
| > 0.1, ≤ 0.2                     | 2622 (31-1)             | 459 (16-9)              |     |
| > 0.2, ≤ 0.3                     | 2206 (26-1)             | 760 (28-0)              |     |
| > 0.3, ≤ 0.4                     | 1518 (18-0)             | 750 (27-7)              |     |
| > 0.4                            | 910 (10-8)              | 670 (24-7)              |     |
| Proportion of procedures with the time of day registered (per centre) | <0-001                |                         |     |
| ≤ 0-1                            | 94 (1-1)                | 43 (1-6)                |     |
| > 0-1, ≤ 0-3                     | 726 (8-6)               | 215 (7-9)               |     |
| > 0-3, ≤ 0-5                     | 1997 (23-7)             | 692 (25-5)              |     |
| > 0-5, ≤ 0-7                     | 4007 (47-5)             | 1063 (39-2)             |     |
| > 0-7                            | 1619 (19-2)             | 697 (25-7)              |     |

Values in parentheses are percentages. *Variable has missing values; percentages are based on available numbers †Of which 63 were bile duct injuries: 48 (0-6 per cent) in office hours, 15 (0-6 per cent) out of hours. χ² test.
Table 2 Univariable and multivariable logistic regression analyses for association between timing of operation and complications

| Time of day                  | No. of patients | Complications (%) | Univariable analysis | Multivariable analysis\(^1\) |
|------------------------------|-----------------|-------------------|----------------------|-----------------------------|
|                              |                 |                   | Odds ratio           | P                           |
|                              |                 |                   |                      |                             |
| Office hours                 | 8443            | 13.6              | 1.00 (reference)     | 1.00 (reference)            |
| Out of hours                 | 2710            | 15.6              | 1.18 (1.04, 1.33)    | 0.008                       |
| Age (years)\(^*\)           |                 |                   |                      |                             |
| ≤ 50                         | 4000            | 10.3              | 1.00 (reference)     | 1.00 (reference)            |
| > 50, ≤ 75                   | 5763            | 14.5              | 1.47 (1.29, 1.66)    | < 0.001                    |
| > 75                         | 1358            | 23.9              | 2.72 (2.32, 2.30)    | < 0.001                    |
| Sex\(^*\)                   |                 |                   |                      |                             |
| F                            | 5743            | 12.8              | 1.00 (reference)     | 1.00 (reference)            |
| M                            | 5404            | 15.5              | 1.25 (1.13, 1.40)    | < 0.001                    |
| ASA grade                    |                 |                   |                      |                             |
| I–II                         | 9605            | 12.7              | 1.00 (reference)     | 1.00 (reference)            |
| III–V                        | 1548            | 22.7              | 2.02 (1.77, 2.31)    | < 0.001                    |
| Time since admission (days)\(^*\) |     |                   |                      |                             |
| 0                            | 1140            | 16.4              | 1.29 (1.08, 1.55)    | 0.005                       |
| 1                            | 4163            | 13.2              | 1.00 (reference)     | 1.00 (reference)            |
| 2                            | 2924            | 13.3              | 1.01 (0.88, 1.16)    | 0.920                       |
| 3                            | 1290            | 14.0              | 1.07 (0.90, 1.29)    | 0.437                       |
| 4–7                          | 1020            | 15.5              | 1.21 (1.00, 1.46)    | 0.055                       |
| ≥ 8                          | 184             | 23.9              | 2.07 (1.46, 2.94)    | < 0.001                    |
| Proportion of surgery out of hours (per centre) |  |                   |                      |                             |
| ≤ 0.1                        | 1258            | 10.5              | 1.00 (reference)     | 1.00 (reference)            |
| > 0.1, ≤ 0.2                 | 3081            | 14.9              | 1.49 (1.21, 1.83)    | < 0.001                    |
| > 0.2, ≤ 0.3                 | 2966            | 13.6              | 1.35 (1.09, 1.66)    | 0.005                       |
| > 0.3, ≤ 0.4                 | 2268            | 16.0              | 1.63 (1.31, 2.01)    | < 0.001                    |
| > 0.4                        | 1580            | 13.7              | 1.35 (1.07, 1.70)    | 0.011                      |
| Proportion of procedures with time of day registered (per centre) |  |                   |                      |                             |
| ≤ 0.1                        | 137             | 8.0               | 1.00 (reference)     | 1.00 (reference)            |
| > 0.1, ≤ 0.3                 | 941             | 14.9              | 2.00 (1.05, 3.80)    | 0.034                       |
| > 0.3, ≤ 0.5                 | 2689            | 13.9              | 1.85 (0.99, 3.46)    | 0.054                       |
| > 0.5, ≤ 0.7                 | 5070            | 13.3              | 1.75 (0.94, 3.26)    | 0.078                       |
| > 0.7                        | 2316            | 16.2              | 2.22 (1.19, 4.15)    | 0.013                       |

Values in parentheses are 95 per cent confidence intervals. \(^*\)Variable has missing values. \(^1\)Multivariable analysis based on 10690 valid procedures (463 missing).

Statistical analysis

Out-of-hours surgery was compared with office-hours surgery for acute cholecystitis using univariable and multivariable logistic regression analyses. The following possible confounders were considered: sex, age (sorted on an ordinal scale), BMI (ordinal scale) and ASA grade (dichotomized into I–II and III–V). Adjustment was also made for interval between admission and surgery (ordinal scale), hospital-specific factors such as the extent to which the hospital recorded time of day for the procedure (indexed as proportion of procedures with a time of day registered), and proportion of procedures performed out of hours at each hospital. Odds ratios (ORs) are reported with 95 per cent confidence intervals; a two-tailed test with \(P<0.050\) was considered significant. In the logistic regression analyses, calculations were performed with complete data only (missing data excluded).
Table 3 Univariable and multivariable logistic regression analyses for association between time of operation and open surgery

| Time of day                        | No. of patients | Open surgery (%) | Univariable analysis | Multivariable analysis† |
|-----------------------------------|-----------------|------------------|----------------------|-------------------------|
|                                   |                 |                  | Odds ratio           |                        |
|                                   |                 |                  | P                    |                        |
|                                   |                 |                  |                      |                        |
| Office hours                      | 8429            | 28.7             | 1.00 (reference)     | 1.00 (reference)        |
| Out of hours                      | 2704            | 37.9             | 1.52 (1.39, 1.66)    | < 0.001                 |
| Age (years)*                      |                 |                  |                      |                        |
| ≤ 50                              | 3998            | 17.8             | 1.00 (reference)     | 1.00 (reference)        |
| > 50, ≤ 75                        | 5751            | 34.7             | 2.46 (2.23, 2.71)    | < 0.001                 |
| > 75                              | 1352            | 54.5             | 5.55 (4.85, 6.35)    | < 0.001                 |
| Sex*                             |                 |                  |                      |                        |
| F                                 | 5735            | 27.2             | 1.00 (reference)     | 1.00 (reference)        |
| M                                 | 5392            | 35.0             | 1.44 (1.33, 1.56)    | < 0.001                 |
| ASA grade                         |                 |                  |                      |                        |
| I–II                              | 9598            | 28.1             | 1.00 (reference)     | 1.00 (reference)        |
| III–V                             | 1535            | 48.9             | 2.44 (2.19, 2.73)    | < 0.001                 |
| Time since admission (days)*      |                 |                  |                      |                        |
| 0                                 | 1136            | 31.3             | 1.02 (0.89, 1.18)    | 0.783                   |
| 1                                 | 4159            | 30.8             | 1.00 (reference)     | 1.00 (reference)        |
| 2                                 | 2919            | 30.1             | 0.96 (0.87, 1.07)    | 0.502                   |
| 3                                 | 1288            | 31.1             | 1.02 (0.89, 1.16)    | 0.834                   |
| 4–7                               | 1017            | 36.0             | 1.26 (1.09, 1.46)    | 0.002                   |
| ≥ 8                               | 183             | 40.4             | 1.52 (1.13, 2.06)    | 0.006                   |
| Proportion of surgery out of hours (per centre) |                 |                  |                      |                        |
| ≤ 0.1                             | 1253            | 35.4             | 1.00 (reference)     | 1.00 (reference)        |
| > 0.1, ≤ 0.2                      | 3075            | 22.9             | 0.54 (0.47, 0.63)    | < 0.001                 |
| > 0.2, ≤ 0.3                      | 2963            | 30.7             | 0.81 (0.71, 0.93)    | < 0.001                 |
| > 0.3, ≤ 0.4                      | 2266            | 26.8             | 0.67 (0.58, 0.78)    | < 0.001                 |
| > 0.4                             | 1576            | 49.7             | 1.81 (1.55, 2.11)    | < 0.001                 |
| Proportion of procedures with time of day registered (per centre) |                 |                  |                      |                        |
| ≤ 0.1                             | 137             | 12.4             | 1.00 (reference)     | 1.00 (reference)        |
| > 0.1, ≤ 0.3                      | 940             | 33.9             | 3.63 (2.14, 6.13)    | < 0.001                 |
| > 0.3, ≤ 0.5                      | 2682            | 36.4             | 4.03 (2.41, 6.74)    | < 0.001                 |
| > 0.5, ≤ 0.7                      | 5062            | 25.8             | 2.45 (1.47, 4.10)    | < 0.001                 |
| > 0.7                             | 2312            | 35.9             | 3.96 (2.37, 6.63)    | < 0.001                 |

Values in parentheses are 95 per cent confidence intervals. *Variable has missing values. †Multivariable analysis based on 10671 valid procedures (482 missing).

Classification tree analysis was used to identify exposure variables associated with complications, and to identify groups of patients with different risks of complications. The χ² automatic interaction detection algorithm was used to construct the tree. Analysis began with all data in one group. Every possible split for each variable was considered, in order to find the split that led to the strongest association with the outcome (any complication). The resulting groups were split until any one of the following stop criteria was reached: tree depth limited to three levels; no group from parent nodes with fewer than 100 patients was formed; and no split with a Bonferroni adjustment less than 0.05 was executed. Missing data were included in the tree analysis, as specified in the relevant figure.

To study the association between time of day and the outcomes any complication and procedure completed as open surgery, these outcomes were also modelled in separate logistic regression analyses, adjusted for sex, age and ASA grade (the variables most strongly associated
### Table 4: Univariable and multivariable logistic regression analyses for association between time of operation and duration of operation exceeding 2 h

| Time of day                  | No. of patients | Duration of surgery > 2 h (%) | Univariable analysis | Multivariable analysis† |
|------------------------------|-----------------|-------------------------------|----------------------|-------------------------|
|                              |                 |                               | Odds ratio | P       | Odds ratio | P       |
| Office hours                 | 8443            | 55.8                          | 1.00 (reference)     | < 0.001                | 1.00 (reference)     | < 0.001 |
| Out of hours                 | 2710            | 40.4                          | 0.82 (0.69, 0.96)    | < 0.001                | 0.92 (0.76, 1.11)    | < 0.001 |
| Age (years)*                 |                 |                               |                      |                        |                      |
| ≤ 50                         | 4000            | 51.0                          | 1.00 (reference)     | 1.00 (reference)       | 1.00 (reference)     | 1.00 (reference) |
| > 50, ≤ 75                   | 5763            | 53.3                          | 1.10 (1.01, 1.19)    | 0.023                  | 1.08 (1.00, 1.18)    | 0.065   |
| > 75                         | 1358            | 49.6                          | 0.95 (0.84, 1.07)    | 0.384                  | 0.96 (0.84, 1.10)    | 0.531   |
| Sex*                         |                 |                               |                      |                        |                      |
| F                            | 5743            | 51.0                          | 1.00 (reference)     | 1.00 (reference)       | 1.00 (reference)     | 1.00 (reference) |
| M                            | 5404            | 53.1                          | 1.09 (1.01, 1.17)    | 0.025                  | 1.08 (1.00, 1.17)    | 0.054   |
| ASA grade                    |                 |                               |                      |                        |                      |
| I–II                         | 9605            | 51.7                          | 1.00 (reference)     | 1.00 (reference)       | 1.00 (reference)     | 1.00 (reference) |
| III–V                        | 1548            | 54.1                          | 1.10 (0.99, 1.23)    | 0.084                  | 1.12 (0.99, 1.26)    | 0.063   |
| Time since admission (days)* |                 |                               |                      |                        |                      |
| 0                            | 1140            | 39.8                          | 0.71 (0.63, 0.82)    | < 0.001                | 0.81 (0.70, 0.92)    | 0.002   |
| 1                            | 4183            | 48.1                          | 1.00 (reference)     | 1.00 (reference)       | 1.00 (reference)     | 1.00 (reference) |
| 2                            | 2924            | 55.5                          | 1.36 (1.20, 1.54)    | < 0.001                | 1.26 (1.15, 1.39)    | < 0.001 |
| 3                            | 1290            | 58.4                          | 1.55 (1.34, 1.78)    | < 0.001                | 1.51 (1.30, 1.75)    | < 0.001 |
| 4–7                          | 1020            | 60.9                          | 1.68 (1.46, 1.93)    | < 0.001                | 1.48 (1.29, 1.71)    | < 0.001 |
| ≥ 8                          | 184             | 52.2                          | 1.18 (0.88, 1.58)    | 0.281                  | 1.05 (0.78, 1.42)    | 0.739   |
| Proportion of surgery out of |                 |                               |                      |                        |                      |
| hours (per centre)           |                 |                               |                      |                        |                      |
| ≤ 0.1                        | 1258            | 60.8                          | 1.00 (reference)     | 1.00 (reference)       | 1.00 (reference)     | 1.00 (reference) |
| > 0.1, ≤ 0.2                 | 3081            | 58.2                          | 0.90 (0.79, 1.03)    | 0.112                  | 0.78 (0.67, 0.91)    | 0.001   |
| > 0.2, ≤ 0.3                 | 2966            | 50.9                          | 0.67 (0.59, 0.77)    | < 0.001                | 0.65 (0.56, 0.75)    | < 0.001 |
| > 0.3, ≤ 0.4                 | 2268            | 46.7                          | 0.56 (0.49, 0.65)    | < 0.001                | 0.64 (0.55, 0.75)    | < 0.001 |
| > 0.4                        | 1580            | 42.2                          | 0.48 (0.41, 0.56)    | < 0.001                | 0.57 (0.48, 0.67)    | < 0.001 |
| Proportion of procedures with |                 |                               |                      |                        |                      |
| time of day registered (per   |                 |                               |                      |                        |                      |
| centre)                      |                 |                               |                      |                        |                      |
| ≤ 0.1                        | 137             | 57.7                          | 1.00 (reference)     | 1.00 (reference)       | 1.00 (reference)     | 1.00 (reference) |
| > 0.1, ≤ 0.3                 | 941             | 42.8                          | 0.55 (0.38, 0.79)    | 0.001                  | 0.47 (0.32, 0.69)    | < 0.001 |
| > 0.3, ≤ 0.5                 | 2689            | 51.7                          | 0.78 (0.55, 1.11)    | 0.171                  | 0.70 (0.48, 1.00)    | 0.051   |
| > 0.5, ≤ 0.7                 | 5070            | 55.5                          | 0.91 (0.66, 1.29)    | 0.069                  | 0.78 (0.54, 1.11)    | 0.167   |
| > 0.7                        | 2316            | 48.4                          | 0.69 (0.49, 0.97)    | 0.035                  | 0.68 (0.48, 0.99)    | 0.042   |

Values in parentheses are 95 per cent confidence intervals. *Variable has missing values. †Multivariable analysis based on 10 690 valid procedures (463 missing).

A continuous time model for weekday data was used to visualize the distribution of risk for the outcomes, studied over the course of the day, with restricted cubic splines for the variables time of day and age. The model discontinuity at midnight was ignored for simplicity.

Statistical analyses were done using SPSS® version 25 (IBM, Armonk, New York, USA) and R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

### Results

Of 135 054 patients recorded in GallRiks between 2006 and 2017, 11 153 were included in the analyses (Fig. 1). Demographic and clinical data for groups of patients who
had surgery within office hours or out of hours are shown in Table 1.

A complication within 30 days was registered for 1573 of 11153 patients (14.1 per cent). The proportion of complications in the out-of-hours group was higher than that in the office-hours group (15.6 versus 13.6 per cent; crude OR 1.18), but this difference disappeared when adjustments were made (adjusted OR 1.12, 95 per cent c.i. 0.99 to 1.28) (Table 2). The proportion of open procedures was higher in the out-of-hours group (37.9 versus 28.7 per cent; adjusted OR 1.39, 1.25 to 1.54) (Table 3), whereas operating time exceeding 120 min was less common when surgery was performed out of hours (40.4 versus 55.8 per cent; adjusted OR 0.63, 0.58 to 0.69) (Table 4).

The tree analysis showed that age was the variable most strongly associated with complications, and the risk increased with age (Fig. 2). Patients aged below 50 years had a 10.3 per cent risk of developing a complication, whereas the risk was 23.9 per cent among those older than 75 years. At the next level, ASA grade was the variable with the strongest association; the risk of complication within each age and ASA category is shown in Fig. 2. Patients aged less than 50 years with ASA grade I–II had the lowest risk of complication (10.0 per cent), whereas patients over 75 years old with ASA grade III–V had the highest risk (27.4 per cent). Sex, BMI and proportion of surgery performed out of hours (at each centre) were also associated with risk of complication. Out-of-hours surgery was not associated with complications at any level.

A continuous time model was used to visualize the variation in outcome depending on when surgery began during the 24 h of the weekday (Fig. 3). There was a shift in risk of complication from around 10–11 per cent during the day, to 15 per cent in the early out-of-hours period. This observation is subject to large error owing to the small number of procedures commencing after 20.00 hours and associated complications. The proportion of open procedures increased as the day progressed, from around 25 per cent at 10.00 hours to 30 per cent at 15.00 hours, and rising to approximately 40 per cent by midnight.

The surgical approach changed over the study interval. Open cholecystectomy was common in the early part, with 431 of 925 procedures (46.6 per cent) completed by an open technique in 2009. In 2017, however, only 263 of 1622 cholecystectomies (16.2 per cent) were completed using an open approach.
Discussion

In this large population-based cohort study, the risk of complications was higher among patients who underwent acute cholecystectomy out of hours than in those operated during office hours. However, after adjusting for possible confounders related to the patient and hospital, the difference in risk between groups no longer persisted. The tree analysis showed that age and ASA were the factors most strongly associated with complications, and the highest risk of complications was seen among the oldest patients with an ASA grade of III–V. Sex, BMI and hospital-specific features all seemed to be more highly associated with outcome than time of day when surgery commenced. There was a significantly higher risk of open surgery in the out-of-hours group (OR 1.39), together with a lower risk of prolonged surgery (over 2 h) in the same group (OR 0.63).

The continuous time model showed that the cut-off point for out-of-hours surgery (weekday operations starting between 19.00 and 07.00 hours) was reasonably matched with the change in complication risk, but differences in outcome regarding open surgery were not as clearly associated with the normal on-call shifts in Sweden.

The results of this analysis are in line with those of other studies, but the present cohort was much larger. Conversion to open surgery is often necessary owing to complicated surgical conditions, and is still advocated as a back-up strategy for acute cholecystitis. Known preoperative risk factors for conversion, apart from acute cholecystitis, include male sex, age over 60 years, gallbladder wall thickness greater than 4–5 mm, and a contracted gallbladder. In the present cohort, the proportion of procedures that were converted from laparoscopic to open surgery, or began as open surgery, was high (31.0 per cent), which is probably related to the study interval, which spanned the years 2006–2017. Until the mid-1990s, open cholecystectomy was the standard procedure for acute cholecystitis, and cholecystitis was considered a relative contraindication to a laparoscopic procedure. This situation changed at the end of the 1990s, after a number of studies showed that acute laparoscopic surgery was equally safe. The present study suggests an overall change in surgical practice occurred over the study period. Until 2009, approximately half of procedures were completed by an open approach, whereas in the later years the vast majority (over 80 per cent) were completed laparoscopically. However, the role of open surgery, even as a back-up procedure, is possibly changing, as it is not necessarily considered an easier way out for surgeons today, who are more or less exclusively trained in the laparoscopic technique.

Prolonged operating time has previously been shown to be associated with a higher complication rate, which is in line with the present results.

These findings support early cholecystectomy in the treatment of acute cholecystitis. No evidence was forthcoming that time of day of operation affects the risk of complications after surgery for acute cholecystitis. The proportion of open operations was significantly higher in the out-of-hours group, which in turn probably affected morbidity. However, even if there is no contraindication...
to out-of-hours surgery, there might be other reasons for delaying the procedure until office hours. As this is a large population-based cohort study based on data from a national register with high coverage\textsuperscript{16}, the results probably apply to the Swedish population in general.

There are limitations to this study, including the risk of selection bias. Of more than 26,000 patients who underwent surgery for acute cholecystitis, 11,153 were included in the analyses. The main reason for missing data was lack of registration of time of day of the procedure. To reduce study bias, adjustments were made for factors that may have influenced the way in which time of surgery was reported. An index for each centre included was calculated, based on how frequently the time of procedure was reported. Also taken into consideration was the extent to which the reporting centre performed cholecystectomy

| Table 5 Univariable and multivariable logistic regression analyses, including BMI for association between time of operation and complications |
|---------------------------------------------------------------|
| Time of day                                                                             | No. of patients | Complications (%) | Univariable analysis | Multivariable analysis |
|                                                                                         |                |                  | Odds ratio | P       | Odds ratio | P       |
| Office hours                                                                             | 8443           | 13-6             | 1.00 (reference) | 1.00 (reference) |
| Out of hours                                                                             | 2710           | 15-6             | 1.18 (1.04, 1.33) | 0.008 | 1.08 (0.91, 1.28) | 0.406 |
| Age (years)\textsuperscript{a}                                                             |                |                  |            |        |            |        |
| ≤ 50                                                                                     | 4000           | 10-3             | 1.00 (reference) | 1.00 (reference) |
| > 50, ≤ 75                                                                                 | 5783           | 14-5             | 1.47 (1.29, 1.66) | < 0.001 | 1.50 (1.27, 1.78) | < 0.001 |
| > 75                                                                                     | 1358           | 23-9             | 2.72 (2.32, 3.20) | < 0.001 | 2.80 (2.21, 3.55) | < 0.001 |
| Sex\textsuperscript{a}                                                                      |                |                  |            |        |            |        |
| F                                                                                       | 5743           | 12-8             | 1.00 (reference) | 1.00 (reference) |
| M                                                                                       | 5404           | 15-5             | 1.25 (1.13-1.40) | < 0.001 | 1.33 (1.15-1.54) | < 0.001 |
| ASA grade                                                                               |                |                  |            |        |            |        |
| I–II                                                                                    | 9605           | 12-7             | 1.00 (reference) | 1.00 (reference) |
| III–V                                                                                   | 1548           | 22-7             | 2.02 (1.77-2.31) | < 0.001 | 2.33 (1.10-1.60) | 0.004 |
| Time since admission (days)\textsuperscript{a}                                             |                |                  |            |        |            |        |
| 0                                                                                       | 1140           | 16-4             | 1.29 (1.08-1.55) | 0.005 | 1.19 (0.92-1.53) | 0.180 |
| 1                                                                                       | 4163           | 13-2             | 1.00 (reference) | 1.00 (reference) |
| 2                                                                                       | 2924           | 13-3             | 1.01 (0.88-1.16) | 0.920 | 1.02 (0.85-1.22) | 0.844 |
| 3                                                                                       | 1290           | 14-0             | 1.07 (0.90-1.29) | 0.437 | 1.01 (0.80-1.28) | 0.924 |
| 4–7                                                                                     | 1020           | 15-5             | 1.21 (1.00-1.46) | 0.055 | 1.21 (0.94-1.54) | 0.137 |
| ≥ 8                                                                                     | 184            | 23-9             | 2.07 (1.46-2.94) | < 0.001 | 2.07 (1.33-3.21) | 0.001 |
| BMI (kg/m\textsuperscript{2})\textsuperscript{a}                                           |                |                  |            |        |            |        |
| ≤ 25                                                                                    | 1753           | 13-6             | 1.00 (reference) | 1.00 (reference) |
| > 25, ≤ 30                                                                               | 2911           | 14-9             | 0.97 (0.76-1.25) | 0.818 | 1.17 (0.98-1.40) | 0.080 |
| > 30, ≤ 35                                                                               | 1521           | 13-6             | 1.08 (0.86-1.37) | 0.497 | 1.01 (0.81-1.25) | 0.936 |
| ≥ 35                                                                                     | 747            | 16-0             | 0.85 (0.65-1.10) | 0.203 | 1.27 (0.97-1.66) | 0.081 |
| Proportion surgery out of hours (per centre)                                             |                |                  |            |        |            |        |
| ≤ 0.1                                                                                   | 1258           | 10-5             | 1.00 (reference) | 1.00 (reference) |
| > 0.1, ≤ 0.2                                                                             | 3081           | 14-9             | 1.49 (1.21-1.83) | < 0.001 | 2.07 (1.56-2.75) | < 0.001 |
| > 0.2, ≤ 0.3                                                                             | 2966           | 13-6             | 1.35 (1.09-1.66) | 0.005 | 1.61 (1.20-2.16) | 0.002 |
| > 0.3, ≤ 0.4                                                                             | 2268           | 16-0             | 1.63 (1.31-2.01) | < 0.001 | 1.45 (1.08-1.95) | 0.015 |
| > 0.4                                                                                   | 1580           | 13-7             | 1.35 (1.07-1.70) | 0.011 | 1.30 (0.93-1.83) | 0.124 |
| Proportion of procedures with time of day registered (per centre)                        |                |                  |            |        |            |        |
| ≤ 0.1                                                                                   | 137            | 8-0              | 1.00 (reference) | 1.00 (reference) |
| > 0.1, ≤ 0.3                                                                             | 941            | 14-9             | 2.00 (1.05-3.80) | 0.034 | 3.28 (1.45-7.41) | 0.004 |
| > 0.3, ≤ 0.5                                                                             | 2689           | 13-9             | 1.85 (0.99-3.46) | 0.054 | 2.35 (1.07-5.17) | 0.034 |
| > 0.5, ≤ 0.7                                                                             | 5070           | 13-3             | 1.75 (0.94-3.26) | 0.078 | 1.94 (0.89-4.24) | 0.097 |
| > 0.7                                                                                   | 2316           | 16-2             | 2.22 (1.19-4.15) | 0.013 | 2.57 (1.17-5.69) | 0.019 |

Values in parentheses are 95 per cent confidence intervals. *Variable has missing values. †Multivariable analysis based on 6615 valid procedures (4538 missing).
of hours, calculated as a proportion. These variables were adjusted for in the analyses.

Previous studies have shown that the risk of complications increases with each day after admission. Therefore, admission to surgery (with the exception of same-day surgery). To overcome the problem of complications owing to delay in surgery, adjustment was made for time since admission.

BMI should have been included as a confounder in the logistic regression analysis, but because many BMI data were missing from the database, regression analyses were undertaken without this variable. However, a regression model analysis for complications was performed with BMI included, which showed similar results regarding the outcome (Table 5). A BMI of 40 kg/m² or more is by definition classified as ASA grade III, so obesity was adjusted for indirectly in the analyses. The impact of BMI alone is also illustrated in the tree analysis; it showed an association with risk of complications, but only for a selected group of patients (aged 50–75 years, with ASA grade III–V).

The decision to undertake cholecystectomy out of hours may have been influenced by other factors, in particular the severity of cholecystitis and the general condition of the patient, which were not registered in GallRiks. The register does not include data on severity of disease, so this was not adjusted for. There may have been patients with perforated cholecystitis or septicaemia who underwent surgery out of hours, in order to avoid rapid deterioration. This could explain the relatively large proportion of procedures being completed by an open approach out of hours, and thus may have confounded the outcome. The proficiency of the surgeon was not taken into account in these analyses, as this information is not recorded in the register. This limitation cannot easily be accounted for with the available data. The higher proportion of open procedures, together with shorter operating times out of hours, may reflect that more senior surgeons performed the procedures. These surgeons may have been trained in open acute cholecystectomy before the introduction of laparoscopic surgery.

By dividing continuous variables into categories, there was a risk of residual confounding. Furthermore, one cannot exclude a difference in risk of complications for procedures undertaken out of hours versus during office hours that was not detectable in this material.

Despite these limitations, in the present study, out-of-hours surgery was not associated with a higher risk of complications. The higher proportion of open surgery out of hours must not be overlooked in terms of morbidity, and the overall benefit of daytime surgery should be considered.

Disclosure

The authors declare no conflict of interest.

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**Supporting information**

Additional supporting information can be found online in the Supporting Information section at the end of the article.