



Cholecystectomy and ERCP in pregnancy: a nationwide register-based study

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Objective: The objective was to examine the outcomes of cholecystectomy and endoscopic retrograde cholangiopancreatography (ERCP) during pregnancy and compare these outcomes with those in nonpregnant women of fertile age.

Summary background data: Although both laparoscopic cholecystectomy and ERCP are considered safe and feasible in pregnant patients, there is still concern and uncertainty regarding gallstone intervention during pregnancy. This study aimed to investigate outcomes in pregnant patients compared to outcomes in nonpregnant patients.

Methods: Data on all female patients aged 18–45 years were retrieved from the Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography. The patients were divided into groups according to intervention: cholecystectomy, ERCP, or a combination thereof. Differences between pregnant and nonpregnant patients were analyzed.

Results: A total of 21 328 patients were included, with 291 cholecystectomy and 63 ERCP procedures performed in pregnant patients. At the 30-day follow-up, more complications after cholecystectomy were registered for pregnant patients. However, pregnancy was not a significant risk factor for adverse events when adjusting for previous complicated gallstone disease, intraoperative complications, emergency surgery, and common bile duct stones. There were no differences in outcomes when comparing cholecystectomy among the different trimesters. ERCP had no significant effect on outcomes at the 30-day follow-up.

Conclusion: Cholecystectomy, ERCP, and combinations thereof are safe during pregnancy.

Keywords: cholecystectomy, cholecystitis, cholelithiasis, ERCP, gallstones, pancreatitis, pregnancy

Introduction

Gallstones have a prevalence of 5.9–21.9% in the general population in Europe. Symptomatic gallstone disease, ranging from pain to complications such as cholecystitis, pancreatitis, cholangitis, and jaundice, affects ~20% of patients with gallstones, making it one of the most common reasons for admission to the hospital and for surgical intervention worldwide^[1–3]. The incidence of gallstones and symptomatic and/or complicated gallstone disease is affected by specific risk factors, including pregnancy; due to hormonal and physiological changes that affect bile composition and gallbladder emptying, the risk of

HIGHLIGHTS

- Managing gallstone disease during pregnancy is challenging.
- Cholecystectomy, ERCP, and combinations thereof are safe during pregnancy.

forming gallstones is increased. The formation of new sludge or stones during pregnancy is found on ultrasound examination in 10.9–31% and 2–6.3% of cases, respectively^[4–6]. The increased risk of developing gallstones in pregnancy and the high prevalence in the general population makes cholecystectomy the second most common reason for nonobstetric surgery in pregnancy, occurring in 1–8 per 10 000 pregnancies^[7,8]. Although considered safe and feasible and recommended in guidelines, there is still some controversy regarding the management of gallstone disease during pregnancy, including the timing of surgery^[3,9–11].

Another somewhat less studied intervention is ERCP, commonly used in addition to cholecystectomy or as a single treatment when there are gallstones or gallstone-related complications involving the bile ducts. Recent research has suggested that ERCP is safe during pregnancy, provided that the endoscopist is experienced and that measures are taken to minimize radiation exposure to the fetus^[12–15]. There are no current guidelines on the optimal strategy for ERCP during pregnancy; it may be performed as a single procedure or as an adjunct to cholecystectomy preoperatively, intraoperatively, or postoperatively.

An increasing number of pregnant patients with risk factors for gallstones and complications such as obesity, diabetes, and rapid weight loss after bariatric surgery suggests that this patient group

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will grow. There is also an increasing tendency toward the operative management of gallstone disease^[16–18].

The aim of this study was to describe current therapeutic practices for pregnant patients undergoing gallstone intervention in a national cohort and to evaluate outcomes in relation to a nonpregnant control group.

Materials and methods

The Swedish Registry of Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks) was created in 2005 to ensure the quality of care regarding biliary procedures nationwide. It comprises a comprehensive database of pre-operative, intraoperative, and postoperative parameters entered online by the surgeon or endoscopist and outcome parameters at the 30-day follow-up entered by a local coordinator at each participating hospital. The register is continuously validated and has demonstrated high completeness and correctness of data^[19]. Consent from the patients is required for participation, and there is a possibility for patients to withdraw all personal data from the register at any time. Annually, over 13 000 cholecystectomy and 9000 ERCP procedures are registered, giving a 90% national coverage rate^[20,21].

All female patients aged 18–45 years registered between 1 January 2009 and 12 March 2016, were identified in GallRiks, and relevant variables for these patients were extracted from the database and analyzed. BMI was not analyzed due to a large amount of missing data. The parameter ‘pregnant (yes/no)’ was used to identify patients who were pregnant during their procedure. The exclusion criteria were missing data for the pregnancy parameter, incorrectly coded entries, primary sclerosing cholangitis, suspected or confirmed malignancy and procedures performed as part of another surgery, such as liver resection or liver transplantation.

The patients were divided into groups based on procedure (cholecystectomy, cholecystectomy combined with ERCP and ERCP only) and pregnancy status.

A comparison of all cholecystectomies was made between pregnant and nonpregnant patients. The pregnant patients subjected to cholecystectomy were further divided and compared based on the trimester of pregnancy at the time of surgery.

All ERCP procedures performed during pregnancy were compared to all ERCP procedures performed in nonpregnant patients, including multiple ERCP procedures in the same patients, ERCP procedures performed in combination with cholecystectomy, and ERCP as the only procedure.

The ERCP procedures in the combination group were further divided into preoperative ERCP, intraoperative ERCP, and postoperative ERCP. To add complexity to this group, some patients underwent more than one ERCP procedure, and some patients were pregnant at the time of cholecystectomy but not pregnant at the time of ERCP, or vice versa. Therefore, all patients in the combination group who were pregnant during their cholecystectomy were compared to nonpregnant patients regarding outcomes after cholecystectomy.

The pregnant and nonpregnant patients who underwent only ERCP were also analyzed separately.

Comparisons were made between the different groups regarding baseline parameters (age, indication for surgery (emergency/planned surgery), intraoperative parameters (operation time, antibiotic

prophylaxis, antithrombotic prophylaxis, type of surgery, inpatient surgery, intraoperative cholangiography and results thereof and intraoperative complications) and postoperative parameters from the 30-day follow-up [length of stay (LOS), any postoperative complication and specific postoperative complications].

ASA classifications above 1 were grouped into a compound variable, ASA classification greater than 1. Previous episodes of cholecystectomy and pancreatitis were also grouped into one variable, previous complicated gallstone disease, for the multiple logistic regression analysis.

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, and the Strengthening the Reporting of cohort, cross-sectional, and case-control studies in Surgery (STROCCS) guidelines (Supplemental Digital Content 1, <http://links.lww.com/JS9/B171>), utilizing the respective checklists^[22,23].

Statistics

Data are presented as numbers (*n*) and percentages (%) or the median and interquartile range when applicable. Statistical analysis of differences between groups was made using the χ^2 test for categorical values and the Mann–Whitney *U* test for continuous variables. All tests were two-sided, and a *P* value <0.05 was considered significant.

Multiple logistic regression was used to adjust for confounders and examine whether pregnancy was a risk factor for complications at the 30-day follow-up. Kruskal–Wallis one-way analysis of variance was used for comparisons among trimesters. Stata MP statistical package version 17.0, 2021 (StataCorp LP, College Station) was used for all calculations.

Results

The database search yielded a total of 22 435 female patients aged 18–45. After exclusion and categorization, 21 328 patients were included and divided into different intervention groups (Fig. 1).

Cholecystectomy

Cholecystectomy was performed in 20 885 patients, 291 of whom were pregnant at the time of surgery (Fig. 1). Analysis of baseline data showed that pregnant patients were younger, ASA class greater than 1 was more common among pregnant patients, and most cholecystectomies in pregnant patients were performed as emergency surgeries. The indications for surgery also differed; more patients in the pregnant group had cholecystitis, pancreatitis, or jaundice. There were also more pregnant patients with a previous episode of pancreatitis. Antibiotic and antithrombotic prophylaxis were both more common in pregnant patients (Table 1).

A laparoscopic technique was used in the majority of patients in both groups, although less in pregnant patients than in nonpregnant patients. The conversion rates from laparoscopic to open surgery were similar (Table 2). Reasons for conversion in the pregnant group were severe cholecystitis in one case, common bile duct (CBD) stones necessitating open choledochotomy in one case, and bleeding in one case.

Inpatient surgery was more common in the pregnant group. Fewer intraoperative cholangiography examinations were performed in the pregnant group, and CBD stones were more common. There were significant differences in the intraoperative

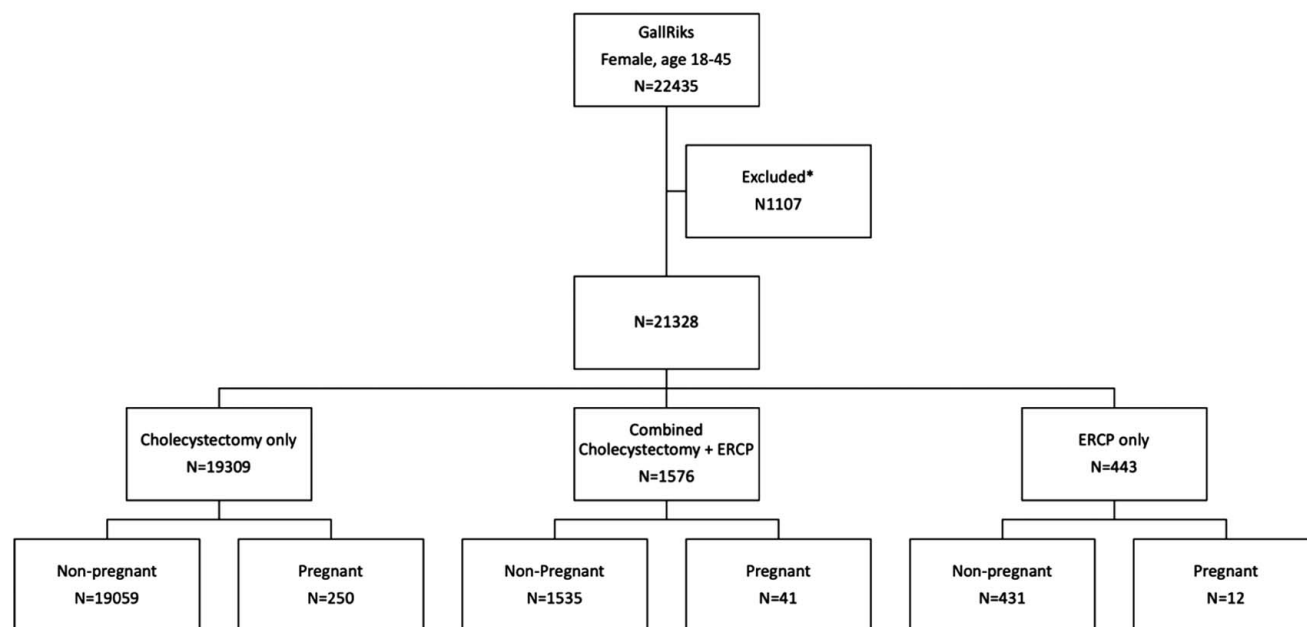


Figure 1. Flowchart. Flowchart of patients after exclusion and division into different groups. *Exclusion due to duplicate or faulty entries, malignancy or primary sclerosing cholangitis.

management of CBD stones detected on cholangiography (Table 2). There were few intraoperative complications in both groups, including bleeding, bile duct injury, and bowel perforation, with no significant differences. Only one intraoperative complication was registered for a pregnant patient, a bleeding requiring conversion to open surgery. The patient was discharged 4 days later without any further complications.

The LOS was longer in the pregnant group, and when considering all complications, there were more postoperative complications at the 30-day follow-up in the pregnant group. However, the only significant difference in specific complications was in the prevalence of bile leakage. The most common specific complication in both groups was postoperative infection requiring antibiotic treatment (Table 2).

The ‘other complication’ parameter in the 30-day follow-up of pregnant patients contained text answers including nausea, pain, urinary tract infection, urinary retention, pneumonia, diarrhea, and elevated liver enzymes. One of the complications mentioned was a miscarriage that occurred in week 13 of the pregnancy. The patient had undergone laparoscopic cholecystectomy in week 12, with cholecystitis as an indication. No intraoperative or other postoperative complications were registered for this patient.

There were a few cases of re-exploration registered at the 30-day follow-up, with no significant differences between pregnant and nonpregnant patients. All three pregnant patients who underwent re-exploration underwent exploratory laparoscopy in the immediate postoperative period due to pain. Re-exploration yielded no findings in any of these patients; however, one was subsequently diagnosed with pancreatitis and one with pneumonia.

Pregnancy as a risk factor for any complication at the 30-day follow-up was significant in the univariable analysis. However, when adjusting for previous complicated bile stone disease, intraoperative complications, emergency surgery and CBD stones on cholangiography, the risk was not significantly elevated in the pregnant group (Table 3).

Table 1
Comparison of preoperative parameters of all cholecystectomies in nonpregnant and pregnant patients.

Parameter	N	Nonpregnant (n= 20 594)	Pregnant (n= 291)	Differences between groups (P)
Preoperative data				
Age, years	20 885	34 (28–40)	29 (25–34)	< 0.001
ASA > 1	20 885	6015 (29)	111 (38)	0.001
Previous complicated gallstone disease				
Cholecystitis	20 885	1089 (5)	11 (4)	0.253
Pancreatitis	20 885	848 (4)	22 (8)	0.004
Emergency surgery	20 885	5764 (28)	198 (68)	< 0.001
Indication				
Cholecystitis	20 885	2240 (11)	61 (21)	< 0.001
Pancreatitis	20 885	620 (3)	31 (11)	< 0.001
Jaundice	20 885	1347 (7)	35 (12)	< 0.001
Biliary colic	20 664	14 797 (73)	157 (55)	< 0.001

Values in parenthesis are percentages except when median (interquartile range).
ASA, American Society of Anesthesiologists.

Cholecystectomy during different trimesters of pregnancy

Most patients underwent surgery in the second trimester ($n=159$), followed by the first trimester ($n=114$), and the third trimester ($n=18$). Comparison of the three trimesters showed differences in age but not in the indication for surgery or frequency of emergency surgery (Supplementary Table 1, Supplemental Digital Content 2, <http://links.lww.com/JS9/B172>). There were significant differences in the frequency of antithrombotic prophylaxis, LOS, and proportion of

Table 2**Comparison of outcome of all cholecystectomies in nonpregnant and pregnant patients.**

Parameter	N	Nonpregnant (n = 20 594)	Pregnant (n = 291)	Differences between groups (P)
Perioperative data				
Operating time, minutes	20 810	84 (61–112)	84 (60–113)	0.700
Inpatient surgery	20 885	13 538 (66)	271 (93)	< 0.001
Laparoscopic surgery	20 802	19 488 (95)	245 (85)	< 0.001
Intraoperative cholangiography	20 797	18 390 (90)	185 (64)	< 0.001
Antithrombotic prophylaxis	20 806	5932 (29)	119 (41)	< 0.001
Antibiotics, prophylaxis or therapy	20 807	4158 (20)	81 (28)	0.001
Conversion to open surgery	20 802	459 (2)	3 (1)	0.238
CBD found on cholangiography	20 797	2066 (10)	49 (17)	< 0.001
Intraoperative management of CBD stones				
No specific intraoperative management	2114	265 (13)	3 (6)	< 0.001
Preparing for postoperative ERCP	2114	317 (15)	7 (14)	
Intraoperative ERCP	2114	725 (35)	25 (51)	
Flushed or manipulated to duodenum	2114	270 (13)	5 (10)	
Transcystic stone extraction	2114	322 (16)	5 (10)	
Laparoscopic choledochotomy	2114	47 (2)	0 (0)	
Open choledochotomy	2114	119 (6)	4 (8)	
Perioperative complications				
Any Complication	20 796	258 (1)	1 (0.3)	0.276
Bleeding	20 885	64 (0.3)	1 (0.3)	0.599
Postoperative data				
LOS, days	19 997	1 (0–1)	1 (1–2)	< 0.001
Complications at 30-day follow-up				
Any Complication	19 931	1191 (6)	25 (9)	0.035
SSI, antibiotics	19 929	589 (3)	9 (3)	0.781
Bleeding	19 930	114 (0.6)	0 (0)	0.206
Bile leak	19 930	181 (1)	6 (2)	0.030
Reoperation	19 929	190 (1)	3 (1)	0.825
Other	19 930	637 (3)	15 (5)	0.039
ERCP				
ERCP or ERCPs performed	20 885	1576 (8)	41 (14)	< 0.001

Values in parenthesis are percentages except when median (interquartile range).

CBD, common bile duct stone; ERCP, endoscopic retrograde cholangiopancreatography; LOS, length of stay; SSI, surgical site infection.

laparoscopic surgeries, with a significantly lower proportion of patients in trimester 3 undergoing laparoscopic surgery (Supplementary Table 2, Supplemental Digital Content 3, <http://links.lww.com/JS9/B173>). More CBD stones were found on cholangiography in the third trimester. Only one intraoperative complication was recorded, that is, bleeding requiring conversion in a patient in the second trimester complication was recorded, a bleeding requiring, as previously described. No differences among trimesters were observed in postoperative complications at the 30-day follow-up (Supplementary Table 2, Supplemental Digital Content 3, <http://links.lww.com/JS9/B173>).

ERCP

A total of 2665 ERCP procedures were identified in GallRiks. Of these, 63 ERCP procedures were performed during pregnancy in 55 patients; among them, eight underwent two ERCP procedures. The most common type of ERCP was intraoperative ERCP in the pregnant group and only ERCP in the nonpregnant group (Supplementary Table 3, Supplemental Digital Content 4, <http://links.lww.com/JS9/B174>).

The median week of pregnancy at the time of the procedure was 17 (9–20). Patients who underwent ERCP during pregnancy were younger, and the indication was more often acute, but there was no

Table 3**Univariable and multivariable analysis of risk factors for any postoperative complication at 30-day follow-up.**

	N	Unadjusted			Adjusted		
		OR	95% CI	P	AOR	95% CI	P
Pregnancy	20 885	1.56	1.03–2.36	0.037	1.23	0.81–1.88	0.335
Previous complicated gallstone disease ^a	20 885	1.32	1.09–1.59	0.003	1.39	1.15–1.67	0.001
Intraoperative complication	20 794	4.04	2.95–5.54	< 0.001	3.99	2.89–5.50	< 0.001
Emergency surgery	20 885	1.94	1.72–2.18	< 0.001	1.63	1.43–1.84	< 0.001
CBD stones on cholangiography	20 797	2.90	2.52–3.35	< 0.001	2.45	2.11–2.85	< 0.001

^aCombined variable of complicated bile stone disease preoperative: previous cholecystitis and previous pancreatitis.

CBD, common bile duct stone.

Table 4
Comparison of Outcome of all ERCPs performed in pregnant versus nonpregnant patients.

	Total number (<i>N</i>)	Nonpregnant <i>N</i> = 2602	Pregnant <i>N</i> = 63	Differences between groups (<i>P</i>)
Perioperative data				
ERCP time (minutes)	2642	25 (17–37)	20 (15–33)	0.062
Inpatient procedure	2665	2174 (84)	57 (91)	0.168
Sphincterotomy	2651	2302 (89)	56 (89)	1.000
Intraoperative complications				
Any complication	2651	54 (2)	1 (2)	1.000
Postoperative complication at 30-days follow-up				
Any complication	2494	472 (19)	13 (22)	0.623
Pancreatitis	2494	195 (8%)	0 (0%)	0.013
LOS	2362	1 (1–2)	1 (1–2)	0.673

Values in parenthesis are percentages except when median (interquartile range).
ERCP, endoscopic retrograde cholangiopancreatography; LOS, length of stay.

difference in ASA class greater than 1, inpatient status, or LOS (Supplementary Table 3, Supplemental Digital Content 4, <http://links.lww.com/JS9/B174>). Intraoperative complications were uncommon (Table 4). The single complication in the pregnant group was bile leakage observed as contrast agent leakage during the procedure. No additional ERCP procedures or other procedures were registered for this patient. There was also no significant difference in any complication at the 30-day follow-up, but when comparing specific complications at the 30-day follow-up, ERCP procedures during pregnancy were associated with more cases of bile leakage and fewer cases of post-ERCP pancreatitis. For patients who underwent both ERCP and cholecystectomy during the same admission, no difference was found in 30-day complications between cholecystectomy and ERCP. All cases of bile leakage originated from the cystic duct and were thus probably complications of cholecystectomy. No cases of postoperative pancreatitis were registered for pregnant patients (Table 4).

ERCP as the only procedure was performed during pregnancy in 12 patients. Two of these patients underwent two ERCP procedures during pregnancy. In nonpregnant patients, ERCP as the only procedure was performed in 609 patients; among them, 127 underwent one to six additional ERCP procedures. A comparison of the index ERCP was performed between pregnant and nonpregnant patients. The pregnant patients were younger, and their procedure times were shorter. The median pregnancy week at which ERCP procedures were performed was week 14 (9–21). No significant differences were seen in indications or complications. The single pregnant patient in this group who had a postoperative complication at the 30-day follow-up had bile obstruction due to remaining CBD stones, requiring another ERCP procedure during pregnancy.

Cholecystectomy and ERCP in Pregnancy

Among the patients who were pregnant during cholecystectomy, 41 (14%) underwent one or more ERCP procedures compared to 1576 (8%) of the nonpregnant patients ($P < 0.001$). The most common combination for patients treated with one ERCP procedure was intraoperative ERCP for pregnant patients and preoperative ERCP for nonpregnant patients. For patients treated with two or more ERCP procedures, the most common combination was intraoperative ERCP and postoperative ERCP in both groups. None of the pregnant patients underwent more than two ERCP procedures (Fig. 2).

Since pregnancy is a dynamic condition, some patients were pregnant at the time of surgery but not pregnant at the following postoperative ERCP ($n = 3$). There were also cases where patients were not pregnant during preoperative ERCP but were later pregnant during cholecystectomy ($n = 3$).

Pregnant patients subjected to combination treatment were younger, and among these patients, surgery was more often performed as an emergency procedure, and pancreatitis was more common as a specific primary indication (Table 5). The only difference in outcome parameters was the frequency of inpatient procedures ($n = 1268$ (83%) vs. 41 (100%), $P = 0.003$).

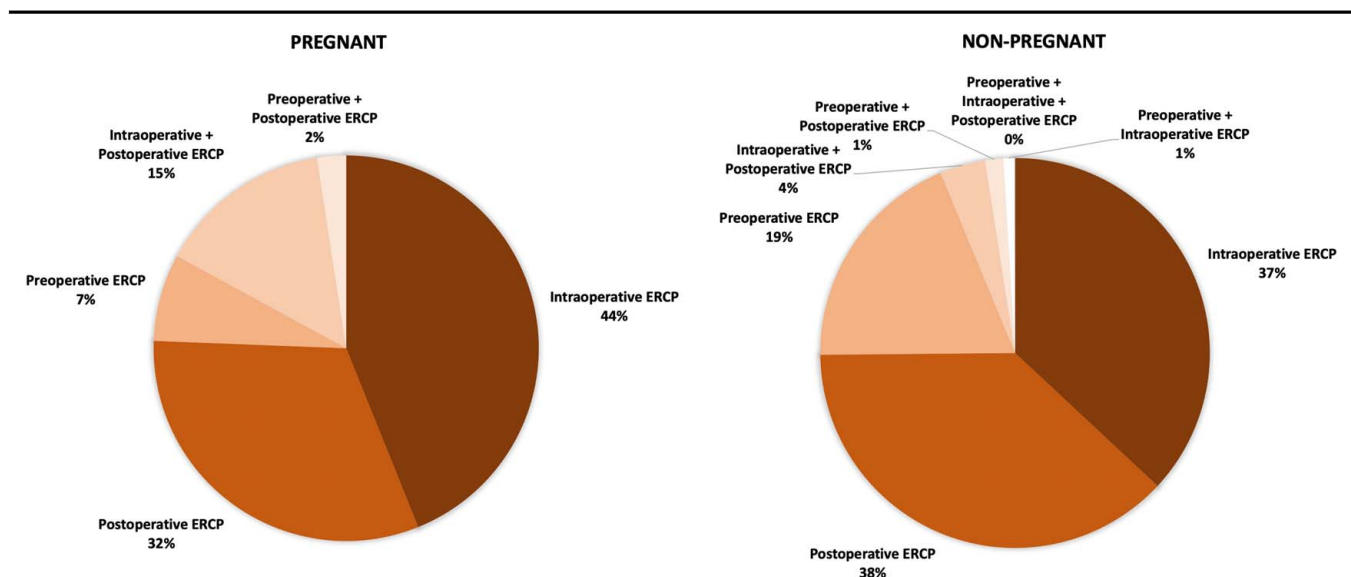


Figure 2. Type of ERCP. Frequency of type of ERCP or ERCP combination for patients who were or were not pregnant during cholecystectomy.

Table 5
Comparison of preoperative parameters in cases of cholecystectomies in combination with ERCP between nonpregnant and pregnant patients.

Parameter	N	Nonpregnant N=1535	Pregnant N=41	Difference between groups (P)
Preoperative data				
Age	1576	34 (27–39)	29 (25–35)	0.002
ASA > 1	1576	402 (26)	15 (37)	0.136
Previous complicated gallstone disease				
Cholecystitis	1576	102 (7)	1 (2)	0.282
Pancreatitis	1576	124 (8)	4 (10)	0.698
Emergency surgery	1576	842 (56)	32 (78)	0.003
Indication				
Cholecystitis	1576	254 (16)	7 (17)	0.929
Pancreatitis	1576	95 (6)	9 (22)	< 0.001
Jaundice	1576	451 (29)	15 (37)	0.318
Biliary colic	1567	655 (42)	17 (41)	0.852

Values in parenthesis are percentages except when median (interquartile range).
 ASA, American Society of Anesthesiologists.

Discussion

Cholecystectomy, ERCP, and combinations thereof were found to be as safe for pregnant as for nonpregnant women in this national cohort regarding intraoperative and postoperative complications at the 30-day follow-up. Although there were some differences in indications and patient characteristics, pregnancy does not seem to be a risk factor for adverse events. No differences in outcomes were found between surgery in the first, second or third trimester.

The different indications and higher number of cases of complicated gallstone disease in the pregnant population might indicate a higher threshold for cholecystectomy in this group. In the pregnant group, there was a higher frequency of antibiotic and antithrombotic prophylaxis, open surgery was more common, more procedures were performed as inpatient procedures, and the LOS was longer. One explanation for these findings is that they may indicate a more careful approach in these patients. Additionally, fewer intraoperative cholangiography examinations were performed in pregnant patients. Intraoperative cholangiography is otherwise routinely performed in all cholecystectomies in Sweden^[24].

Overall, there were few intraoperative complications for cholecystectomy and/or ERCP in any of the groups. Although more complications were seen for cholecystectomy in the pregnant group at the 30-day follow-up, most of these complications were of a less consequential type. There is reason to believe that the follow-up of pregnant patients is more rigorous, which perhaps explains some of the complications identified at the 30-day follow-up.

Multiple studies have previously confirmed the safety and feasibility of cholecystectomy during pregnancy, mainly focusing on surgical outcome parameters^[11,25–28]. A large study by Rios-Diaz *et al.* of pregnant women with cholecystitis found, contrary to guidelines, that most patients were managed nonoperatively, with increased readmission and twice the risk for maternal-fetal complications. In this study, no subgrouping of patients according to trimester was performed. There is a current controversy regarding the timing of surgery. A study by Fong *et al.* examined

outcomes when surgery was performed in the third trimester compared to three months postpartum and found that pregnant patients had longer in-hospital stays, a higher frequency of open surgery, more readmissions, and less favorable composite maternal outcomes, including preterm delivery. The conclusion was to delay cholecystectomy if possible^[29]. Another study by Hong *et al.*^[10] confirmed a longer LOS and greater incidence of preterm delivery if surgery was performed in the third trimester, but there were no differences in composite outcome variables compared to cholecystectomy in the first or second trimester. Our study confirms the favorable outcome of surgery regardless of trimester but lacks data regarding maternal-fetal outcome parameters. Most patients underwent cholecystectomy in the second trimester, in accordance with previous studies^[30].

ERCP during pregnancy is less studied than cholecystectomy, but the literature suggests that it is safe, provided that it is performed by high-volume practitioners to minimize the procedure and radiation time and maximize the success rate. It is also recommended that other measures be taken to protect the fetus from radiation and to avoid unnecessary procedures by performing rigorous preoperative examinations^[12,15,31]. Our data mainly confirm the safety of ERCP during pregnancy concerning procedural outcomes. A discrepancy from previous reports in the literature was that there were no cases of post-ERCP pancreatitis in the pregnant group. This contradicts a previous study by Tang *et al.*^[32] that found a higher incidence of post-ERCP pancreatitis in the pregnant group. The higher frequency of intraoperative ERCP, usually performed with the rendezvous technique, in the pregnant group might explain this difference^[33]. The shorter procedure time among the pregnant patients subjected to ERCP in our study might be attributed to greater endoscopist experience.

The wide variety of different types of ERCP in conjunction with cholecystectomy suggests that knowledge was lacking during the studied time period of which approach is the best. The timing of ERCP is one aspect where local differences may necessitate different approaches. As our study suggests, intraoperative ERCP is the favored strategy in Sweden as well as in the authors' hospital. In a review by Ricci *et al.*^[34] of nonpregnant patients, intraoperative ERCP seemed to be the best alternative. Although not specified in this study, most intraoperative ERCP procedures in Sweden are performed as rendezvous procedures, as recommended by guidelines. The number of patients in this study is too small to draw reliable conclusions of which strategy is superior during pregnancy^[33,35]. The significantly higher number of pregnant patients undergoing ERCP in combination with cholecystectomy is probably indicative of a higher threshold for intervention in this patient group.

Regarding the treatment of CBD stones, novel techniques such as nonradiation ERCP, endoscopic ultrasound (EUS)-guided ERCP, and other strategies such as intraoperative stent placement, either laparoscopic or endoscopic, and subsequent postpartum stone removal are other techniques that need to be further evaluated^[31].

A higher ASA score among the pregnant patients does not necessarily mean that these patients had more comorbidities since in the ASA classification, a patient with a normal pregnancy is given a score of 2, even if otherwise healthy^[36]. There might also be a bias in the ASA classification that is dependent on the registering surgeon or endoscopist^[37].

The differences in age at the time of the procedure between pregnant and nonpregnant patients are probably caused by more cholecystectomy and ERCP procedures being performed with increasing age.

Although GallRiks is well established and validated, all register studies have limitations. In GallRiks, one of these is the definition and registration of 30-day follow-up parameters. This is performed by a local coordinator at each hospital, and interpretations can thus differ. There is also a risk of selection bias in the primary registration performed by the surgeon or endoscopist, where, as an example, adverse events might be omitted or downplayed. The 30-day limit of follow-up also means that complications occurring after this time period are not registered. For patients who underwent both cholecystectomy and ERCP during the same admission, there was no difference in the procedure that caused complications during the 30-day follow-up period, making the interpretation of this parameter somewhat difficult. Additionally, for certain parameters, such as BMI, there were many missing values, making these parameters difficult to interpret in a meaningful way. The different types of ERCP procedures have their own advantages and disadvantages, but when dividing them into subgroups, the numbers of cases in this study were too small to draw any reliable conclusions regarding different management strategies for CBD stones. GallRiks does not include any maternal-fetal parameters, so possible adverse events regarding birth or the subsequent child were not analyzed. The miscarriage registered as a complication at the 30-day follow-up was the only maternal-fetal adverse event registered. Although not specific to the register, adverse maternal-fetal events of this magnitude would probably be registered if they occurred within the 30-day follow-up period. Even considering these disadvantages, and since there are hardly any ethically acceptable means of studying this patient group in a randomized double-blind placebo-controlled study, the authors' opinion is that this study can contribute to the growing body of knowledge about managing gallstone disease in this particular patient group.

In conclusion, cholecystectomy and ERCP, either by themselves or in conjunction, seem to be a safe way to manage gallstones and their complications in pregnancy. The differences seen at the 30-day follow-up after cholecystectomy disappeared when adjusting for confounders, confirming that pregnancy is not a risk factor for complications at the 30-day follow-up.

Ethical approval

Ethical approval was obtained by the Regional Human Ethics Committee in Lund, Sweden on the (Dnr 2014/177).

Consent

Agree, the study has ethical committee approval, and in Sweden, all patients are asked if their data can be stored in quality registers. The consent forms are not available for researchers, but this structure regarding the national quality registers, as GallRiks in this study, is safe and robust for the patients.

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Author contribution

J.H.: conceptualization, investigation, data analysis, writing – original draft; J.N.: conceptualization, data analysis, supervision, writing – review and editing; B.A.: conceptualization, investigation, data analysis, supervision, writing – review and editing.

Conflicts of interest disclosure

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Provenance and peer review

It was not invited.

Data availability statement

Data underlying this study will be shared upon reasonable request to the corresponding author.

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