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ORIGINAL ARTICLE

Increased incidence of cholecystectomy related to gallbladder disease in France: Analysis of 807,307 cholecystectomy procedures over a period of seven years



F. Bray^a, T. Balcaen^b, E. Baro^c, A. Gandon^d,
G. Ficheur^b, E. Chazard^{b,*}

^a Univ. Lille, CERIM EA2694, 59000 Lille, France

^b Univ. Lille, CHU Lille, CERIM EA2694, Department of Public Health, 59000 Lille, France

^c CHU Lille, Department of Public Health, 59000 Lille, France

^d CHU Lille, Department of Digestive Surgery, 59000 Lille, France

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KEYWORDS

Cholecystectomy;
Laparoscopic
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Open
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Nationwide database;
Epidemiology

Summary

Purpose: Gallstones are one of the most common abdominal reasons for admission to hospital. The aim of this study was to analyze trends and outcomes in patients undergoing cholecystectomy with gallbladder related disease in France from 2008 to 2014.

Patients and Methods: We carried out a population-based, retrospective cohort study using data extracted from the French nationwide hospital discharge database (PMSI). We included all patients having a cholecystectomy related to gallbladder disease from January 2008 to December 2014. Patients' demographics, primary diagnosis, procedure type, length of stay (LOS), admission in an intensive care unit, discharge disposition, complications, and in-hospital mortality were analyzed.

Results: Overall, 807,307 cholecystectomies were performed in France over the study period, with an increase in the national incidence rate from 167.5 (95%CI [166.5; 168.5]) to 182.6 (95%CI [181.6; 183.6]) per 100,000 inhabitants. Females accounted for 66.5% of procedures ($P < 0.001$). The mean age was lower for females than for males: 52.1 versus 60.2 ($P < 0.001$). The ratio of laparoscopic cholecystectomy significantly increased from 90% in 2008 to 94% in 2014 ($P < 0.001$). Average inpatient LOS decreased significantly from 6.5 days in 2008 to 4.7 days in 2014 ($P < 0.001$). Most common complication type was intra-abdominal (23.1%) for laparoscopic procedure (95%CI [22.7; 23.5]), and in-hospital mortality significantly decreased over time from 0.45% in 2008 to 0.38% in 2014 ($P < 0.005$).

Conclusion: Our results showed that the national incidence rate of cholecystectomy related to gallbladder disease increased from 2008 to 2014.

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* Corresponding author.

E-mail address: emmanuel.chazard@univ-lille.fr (E. Chazard).

Introduction

Gallstones are one of the most common abdominal reason for admission to hospital in developed countries, and account for a large part of healthcare expenditure [1]. The prevalence of gallstones increases with age in both sexes. In France, because of an increase in life expectancy and the maturation of the “baby boom” generation, the proportion of the population aged of 65 years old or more is expected to rise from 21% in 2005 to 31% in 2035 [2]. This will probably result in an increased number of patients presenting for treatment of gallstone-related disease.

In France, cholecystectomy is recommended for acute cholecystitis, for symptomatic cholelithiasis, polyp larger than 10 mm, and porcelain gallbladder. Many studies suggest that cholecystectomy should be performed immediately after the diagnosis of acute cholecystitis is established, before the inflammation becomes more intense, which increases the technical difficulty of surgery [3–5]. Other studies confirmed that early preference, taking into account medical and socio-economic aspects [6,7].

Few studies have reported the incidence of cholecystectomy in the general population. The incidence found in the literature ranges from 91 per 100,000 inhabitants in Taiwan to 116 per 100,000 in Sweden [8,9]. In France, no data about incidence of cholecystectomy has been available since 1973 [10].

Administrative databases are frequently used for observational studies in populations. Due to the compulsory health insurance system, these dates comprehend an exhaustive description of all surgical procedures that are performed, in profit or non-profit hospitals. One previous study described the epidemiology of cholecystectomy in France using an administrative database, but this study was based on local data, limiting the ability to generalize the results [11].

The aim of this study is to use a nationwide hospital discharge database to analyze trends and outcomes in patients undergoing cholecystectomy with gallbladder or gallstones related disease in France from 2008 to 2014.

Material and methods

Data Source

We carried out a population-based, retrospective cohort study using data extracted from the French national hospital discharge database (PMSI). The PMSI is based on standardized discharge reports from all patients admitted to acute care profit or non-profit hospitals in France. Each discharge report describes the patient’s background and procedures. Diagnoses are encoded using the International Classification of Diseases, 10th revision (ICD-10) either as primary or associated diagnosis, and therapeutic or diagnostic procedures are recorded according to the French terminology of medical procedures (CCAM). Discharge reports are compulsory and are the basis of hospitals funding. The data provided were anonymized. The PMSI data include a unique and constant patient identifier, which enables to link the different stays of the same patient, even when the same patient is admitted in different hospitals. Incidence rates were calculated using population data provided by the French National

Institute for Statistics and Economic Studies. Approval from the French data protection agency (CNIL) was obtained to conduct the present study.

Study population

All hospital discharge records in France from January 1, 2008 to December 31, 2014 were considered. As cholecystectomies can frequently be performed during other digestive surgical procedures, the principal diagnosis had to be considered. Thus, all the patients having a cholecystectomy procedure code (Table 1) and a principal diagnosis of gallbladder or gallstone related disease (Table 2) were included. In order to compute the number of inpatients stays in relation with gallstones, a second extraction was performed based on diagnoses, using all kinds of gallstones.

Patients outcomes

For each patient, the following information was analyzed: age, sex, hospitalization date, primary diagnosis (i.e. reason for admission), type of cholecystectomy (laparoscopic versus open cholecystectomy), source of admission, length of stay (LOS, defined as the number of days), stays in an intensive care unit (ICU), discharge disposition, complications, and in-hospital mortality. Outcomes were secondarily identified by ICD-10 codes and categorized as intra-abdominal, hemorrhage, infection, renal, cardiac, transfusions, pulmonary, or anesthesia complications (Table 3). For each patient, a unique constant identifier was available.

Patient analysis

For each patient, the healthcare pathway was described. The first stay with cholecystectomy was tagged as the index stay, and all further stays (even in different hospitals) were considered to search for complications. Only readmissions within a delay of 30 days after the surgery were considered, as usually done by other authors. Then we analyzed the reason for admission of all these stays, to define potential complications.

Statistical analyses

Descriptive statistics were calculated for the variables of interest. Percentages were reported to describe categorical variables, means and standard deviations (SD) were reported to describe the distribution of the symmetrically distributed continuous variables, and medians and quartiles were reported for continuous variables with skewed distributions. Ninety-five percent confidence intervals (95%CI) of means were calculated using the central limit theorem. Ninety-five percent confidence intervals of categorical variables were calculated using the binomial distribution. Independence between categorical variables was tested using Chi² or exact Fisher test, and independence between categorical and quantitative variables were tested using Student’s *t*-test or analysis of variance (Anova). All tests were 2-sided, with $P < 0.05$ considered statistically significant. All analyses were performed using R software version 3.3.1 and R Studio version 0.99.903.

Table 1 Inclusion criteria: surgical procedures of cholecystectomy.

CCAM Code	Wording
HMFA001	Cholecystectomy with choledochojejunostomy by laparotomy
HMFA002	Cholecystectomy with choledochogastrostomy or choledochoduodenostomy, laparotomy
HMFA003	Laparoscopic cholecystectomy with removal of bile duct stone by choledochotomy, laparotomy
HMFA004	Cholecystectomy with transcystic removal of common bile duct stone, laparotomy
HMFA005	Laparoscopic cholecystectomy, with choledochojejunostomy by laparotomy
HMFA006	Laparoscopic cholecystectomy with choledochoduodenostomy by laparotomy
HMFA007	Cholecystectomy, laparotomy
HMFA008	Cholecystectomy with removal of bile duct stone by choledochotomy, laparotomy
HMFC001	Cholecystectomy with transcystic removal of common bile duct stone, by laparoscopy
HMFC002	Cholecystectomy with removal of bile duct stone by choledochotomy, by laparoscopy
HMFC003	Cholecystectomy with choledochogastrostomy or choledochoduodenostomy, by laparoscopy
HMFC004	Cholecystectomy, Laparoscopic
HMFC005	Cholecystectomy with choledochojejunostomy by laparoscopy

Table 2 Inclusion criteria: principal diagnoses of gallstones or gallbladder disease.

Principal diagnosis	ICD10 codes
Malignant tumor	C23, C24, C240, C241, C248, C249
Benign tumor	D135, K835
Cholelithiasis	K80, K802, K805, K808, K831, K820
Cholecystitis	K800, K801, K804, K81, K810, K811, K818, K819
Cholangitis	K803, K830, K8700
Other disease of the gallbladder	K82, K821, K822, K823, K824, K828, K829
Other disease of the biliary tract	K832, K833, K834, K838, K839, K87, K870, K8708, K871
Other acute pancreatitis	K85, K850, K852, K853, K858
Acute biliary pancreatitis	K851
Trauma	S361, S3610, S3611

Table 3 Cholecystectomy complications: primary, related or associated diagnoses.

Complications	ICD10 Codes
Cardiac	E86, I26, I269, I46, I460, I469, I80*, I978, I979, J81, R092, T800, T811
Intra-abdominal	K20, K210, K219, K29*, K30, K430-2, K436, K437, K439, K56, K560, K562-7, K591, K65*, K91*, N328, R10*, R11, S36*, S37*, T81, T812, T8130, T815, T818, Y61, Y610, Y611, Y618, Y619, Y620, Y652, Y83, Y834, Y836, Y838, Y839
Hemorrhagic	I772, K625, K661, K922, R58, S35*, T145, T810, T817, Y446, Y60*
Renal	N10, N170-2, N178, N179, N19, N328, N390, N99, N990, N991, N994, N998, N999, R33
Pulmonary	J690, J709, J80, J95, J95*, J960*, T175, Z991
Infectious	A41*, K750, T802, T813, T814, Y62, Y621, Y628, Y629
Anesthetic	T882-7, Y484, Y653
Anemic	D500, D62, Y650, Z513, T803-5

Results

Procedures

From 2008 to 2014, 807,307 cholecystectomies were performed in France. The national incidence rate increased from 167.5 [166.5; 168.5] to 182.6 [181.6; 183.6] per 100,000 inhabitants (Fig. 1). Over the study period, the average patient age was 55.3 [55.3; 55.4]. The mean age decreased slightly from 56 in 2008 to 55 in 2014 ($P < 0.001$). Regarding gender distribution, 536,782 (66.5%) were females and 270,525 (33.5%) were males ($P < 0.001$). The mean age was lower for females than for men: 52.1 versus 60.2 ($P < 0.001$).

Table 4 reports demographic characteristic and outcomes of patients undergoing cholecystectomy, Fig. 1 pictures

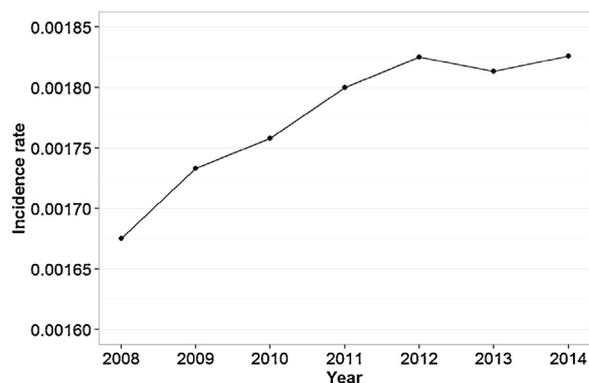


Figure 1. Trends in cholecystectomies performed in France from 2008 to 2014.

Table 4 Description of inpatient stays with cholecystectomy for gallstone or gallbladder diseases in France, 2008–2014.

	2008	2009	2010	2011	2012	2013	2014	P
Number of stays	107,152	111,450	113,602	116,882	119,077	118,899	120,245	
Incidence rate (per 100,000 inhabitants)	168	173	176	180	183	181	183	
Mean age (years)	56.0	55.6	55.6	55.2	55.1	55.0	55.0	***
Male (%)	32.9	33.1	33.6	33.5	33.6	33.9	33.9	***
Primary diagnosis (%)								***
Cholecystitis	71.4	72.4	73.0	73.2	73.6	73.4	74.0	
Cholelithiasis	23.7	22.6	22.2	22.0	21.8	22.0	21.3	
Cholangitis	1.47	1.50	1.48	1.42	1.40	1.27	1.31	
Acute biliary pancreatitis	1.16	1.25	1.29	1.33	1.26	1.30	1.38	
Other gallbladder disease	1.18	1.26	1.19	1.16	1.22	1.22	1.20	
Malignant tumor	0.48	0.44	0.42	0.38	0.38	0.38	0.42	
Benign tumor	0.20	0.19	0.19	0.19	0.18	0.18	0.18	
Other acute pancreatitis	0.33	0.27	0.22	0.19	0.17	0.16	0.15	
Other biliary tract disease	0.04	0.04	0.05	0.04	0.05	0.05	0.05	
Trauma	0.03	0.04	0.03	0.03	0.03	0.03	0.02	
Operative procedure (%)								***
Laparoscopic	90.0	90.9	91.6	92.4	93.0	93.6	94.0	
Open cholecystectomy	9.98	9.11	8.37	7.59	7.03	6.43	6.05	
Outpatient stay (%)	0.74	1.04	1.69	3.03	5.66	11.0	18.7	***
Length of stay (days)	6.54	6.3	6.12	5.81	5.5	5.14	4.72	***
Intensive care unit (%)	1.65	1.63	1.67	1.62	1.6	1.47	1.46	***
Public hospital (%)	49.9	51.1	50.8	51.5	51.8	52.7	52.5	***
Source of admission (%)								***
Acute care hospital	2.08	2.03	1.84	1.94	1.79	1.77	1.71	
Home	97.9	98.0	98.2	98.1	98.2	98.2	98.3	
Discharge disposition (%)								***
Acute care hospital	3.67	3.64	3.59	3.4	3.3	3.15	2.94	
Home	96.3	96.4	96.4	96.6	96.7	96.9	97.1	
In-hospital mortality (%)	0.45	0.48	0.47	0.42	0.42	0.39	0.39	**

** 0.001 < P < 0.01; -: P > 0.05; *: 0.01 < P < 0.05.

*** P < 0.001.

trends in cholecystectomies, and Fig. 2 shows comparison of age distribution in patients who underwent a cholecystectomy.

1.1. Indication

Overall, 589,510 patients (73.0%) underwent cholecystectomy for cholecystitis from 2008 to 2014. The rate of cholecystectomies performed for cholecystitis increased from 71.4% in 2008 to 74.0% in 2014 (Table 4). Cholecystitis was the most common primary diagnosis, followed by cholelithiasis (22.2% [22.11; 22.29]). Over the study period, there were 744,779 (92.2%) laparoscopic cholecystectomies and 62,528 (7.75%) open cholecystectomies. The proportion of laparoscopic cholecystectomy increased significantly from 90% in 2008 to 94% in 2014 ($P < 0.001$). Overall, 98% of patients undergoing cholecystectomy were admitted from home, and 2% of patients were transferred from another acute care hospital.

1.2. General trends

In the whole database, the number of stays with ICD10 codes of gallstones increased by 21.4% over the study period (2008–2014), either as associated diagnoses or as principal diagnosis (Table 5). During the same period, the raw number of cholecystectomies for gallstones or gallbladder diseases increased by 12.2% (from 107,152 in

2008, to 120,245 in 2014, Table 4). The standardized incidence ratio of those procedures increased by 9.0% (from 167.52 per 100,000 inhabitants in 2008, to 182.59 in 2014, Table 4).

1.3. Outcomes

The average inpatient hospital length of stay (LOS) was 5.71. LOS decreased significantly from 6.5 days in 2008 to 4.7 days in 2014 ($P < 0.001$). Outpatient stays increased significantly from 0.74% in 2008 to 18.7% in 2014 ($P < 0.001$, Fig. 3). During the 7-year study period, 12,784 (1.58%) patients spent at least one day in an intensive care unit. The overall in-hospital mortality was 0.43% (95%CI [0.42% to 0.45%]). In-hospital mortality significantly decreased over time from 0.45% in 2008 to 0.38% in 2014 ($P < 0.01$). In-hospital mortality was significantly higher for males (0.71%) than for females (0.29%) ($P < 0.001$). After cholecystectomy, 96.6% of patients were discharged home (Table 4).

Table 6 presents the incidence rate for the 8 most common types of complications in the 30-days period after cholecystectomy, including the stay of surgery, and readmissions, even in other hospitals, with respect to the surgical technique. The most common complications were intra-abdominal complications (23.1% for laparoscopy, 27.5% for open cholecystectomy).

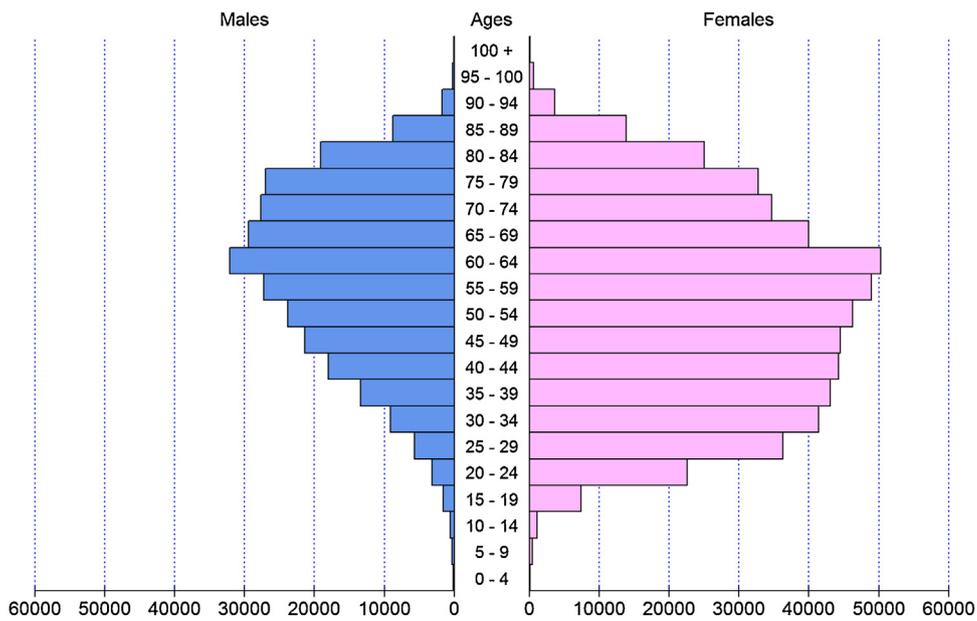


Figure 2. Age and gender distribution in patients who underwent a cholecystectomy from 2008 through 2014.

Year	Any diagnosis	Principal diagnosis
2008	221,807	171,888
2009	233,882	180,908
2010	239,931	187,493
2011	247,207	193,807
2012	255,055	199,440
2013	258,880	201,424
2014	269,279	208,591
2008–2014 trend	+21.4%	+21.4%

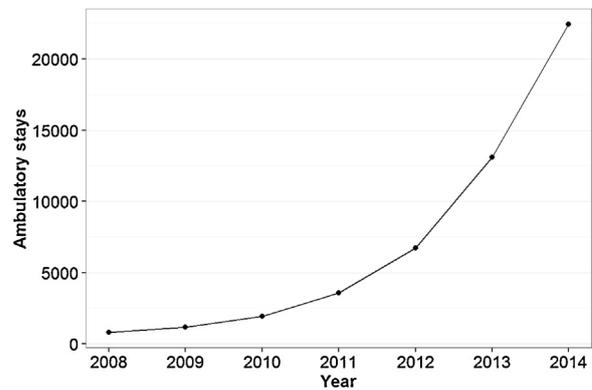


Figure 3. Trends in number of ambulatory surgeries from 2008 to 2014.

2. Discussion

In this study, we were able to examine demographic trends in cholecystectomy from 2008 to 2014 in France. The annual incidence rate of cholecystectomy increased from 167 in 2008 to 183 per 100,000 inhabitants in 2014. Our findings appear higher than in previous studies [8,9]. We observed a significant increase of the raw number of surgical procedures (+12.2%). However, this increase is lower than the increase of the number of hospital stays with a diagnosis of gallstone (+21.4%). We think that the increase of gallstones might be in relation with changes in living and eating habits in the French population. However, in the same time, the surgeons are probably less likely to operate on patients with uncertain diagnosis. We also confirmed that women clearly make up the majority of cholecystectomies. Women’s predisposition for gallstone disease has been shown in multiple studies, and increased body fat in women appeared to be associated with an increased risk of cholelithiasis [12]. Benion et al. found significant differences between men and women in the size of total bile acid and chenodeoxycholic acid pool, which could suggest a possible mechanism for the higher prevalence of gallstones among women [13]. However, in our study we found that surgery occurred for younger and younger women. Other mechanisms, probably of hormonal origin, are mentioned, such as the LPAC syndrome (low phospholipid-associated cholelithiasis) [14,15].

Cholecystitis (73.0%) and cholelithiasis (22.2%) were the most common causes of cholecystectomy in our study, but it is worth noting that the principal diagnosis is encoded after the patient discharge, according to the results of the microscopic pathology examination. In a study conducted in Sweden, the main primary diagnosis was gallbladder disease [8]. Cholelithiasis appeared to be the first primary diagnosis in a study performed in Scotland, followed by cholecystitis [16]. In our study we did not observe an increase of cholecystectomies for asymptomatic gallstones, instead, over the years, the proportion of this indication seems to decrease (23.7% in 2008 against 21.3% in 2014). But it is impossible for us to affirm that these cholecystectomies are, so far, abusive. Indeed, the final diagnosis relies on the results of the pathologic analysis, which could be in contradiction with the initial clinical and paraclinical presentation. In addition, some comorbidities and patient characteristics are not available in the PMSI, and our study did not consider hospitalizations prior to cholecystectomy, which could possibly justify cholecystectomy. Surgical techniques have been investigated in several studies. In the United States, between 78,3% and 93% of all cholecystectomy were laparoscopic [17–19]. Similar rates have been found across Europe (72% in Sweden, 93% in France, and 73% in Scotland) [20]. In the present study, we have shown that the laparoscopic

Table 6 Complications encountered by patients undergoing cholecystectomy, 2008–2014 (initial inpatient stay and within 30 days readmissions).

Complication	Laparoscopy (% and 95%CI)		Open cholecystectomy (% and 95%CI)	
Intra-abdominal	23.09	[22.7; 23.49]	27.52	[26.52; 28.54]
Hemorrhagic	13.29	[12.97; 13.61]	13.33	[12.57; 14.11]
Infectious	7.21	[6.97; 7.46]	13.35	[12.6; 14.14]
Transfusion	3.18	[3.02; 3.35]	7.00	[6.44; 7.6]
Renal	2.92	[2.77; 3.09]	6.40	[5.86; 6.97]
Cardiac	1.86	[1.73; 1.99]	3.04	[2.66; 3.45]
Pulmonary	1.09	[1; 1.2]	2.63	[2.28; 3.02]
Anesthetic	0.18	[0.14; 0.23]	0.20	[0.11; 0.32]

procedure rate increased from 90% in 2008 to 94% in 2014. These results are consistent with many studies establishing the laparoscopic procedure as a “gold-standard” for acute cholecystitis and for symptomatic cholelithiasis [21,22]. To support this, in our research work the laparoscopic procedure was not associated with more frequent complications than open cholecystectomy, one of the reasons might be that the learning curve of the procedure is now acquired, not to mention that laparotomy surgeries are generally for patients at higher risk of complications. For example, in France, any patient under anticoagulant therapy will be operated by open surgery rather than laparoscopy.

Our study showed that the mean patient age was 55 years old. This result is consistent with prior reports where mean patient age ranged from 51 to 55 [8,11,16,18–20]. Furthermore, women were found significantly younger than men. We have several hypotheses to explain the increase in cholecystectomies performed for cholecystitis. Our main hypothesis is that the increase in the incidence of overweight and obesity in the general population may explain the increase in biliary lithiasis and thus indirectly cholecystitis. This increase would therefore be linked to a change in lifestyle. On the other hand, it is possible that the increase in health authorities’ controls may require the surgeon or pathologist to code a diagnosis of posterior cholecystitis, where the pathological result is doubtful or inconclusive. The length of stay after cholecystectomy decreased significantly from 6.5 days in 2008 to 4.7 in 2014. The mean length of stay ranges from 4.1 to 4.4 days [8,20], with longer length of stay among men and elderly patients. The decrease in length of stay could be partially related to the growth of outpatient surgery. Indeed, in 2008, 0.74% of stays were performed on an outpatient basis, while they were 18.7% in 2014. Outpatient surgery tends to be preferred due to its cost-effectiveness aspect for the management of health resources [23,24]. Moreover, many recent studies have shown its safe side [25–29], even in the children population [30]. In a study conducted in the United States on elderly patients, the most common complications were infections (7.02%), hematologic complications (4.95%), and renal complications (4.7%) [17]. The mortality rate varies across studies from 0.4% for young patients to 3.2% for elderly patient [8,16,17,20].

Incidence of gallbladder disease in France has been described by Plant et al. in 1973. To our knowledge, no study since then has described the epidemiology of cholecystectomy in the general population in France [10].

The strengths of this study include the use of a large database, which includes all cholecystectomies related to gallstones or gallbladder diseases. Because the PMSI was created primarily for reimbursement, the database is

reliable and comprehensive for surgical procedure. Many other pieces of information are usually considered reliable: age, sex, length of stay, admission, discharge, and in-hospital mortality.

There are limitations inherent to secondary use of medical administrative database. There can be coding errors regarding diagnoses and procedures. Operative details are not available. Not all the comorbidities can be coded, especially when they did not cause additional burden on the health care team. The database used did not enable to compute the delay between symptoms and surgery. In CCAM classification, there is no code for surgical conversion (from laparoscopy to open cholecystectomy), thus conversions were finally classified as open surgeries. Another limitation of this study is the absence of the cause of death in the database, such diagnosis being possibly embedded in associated diagnoses. Moreover, outcomes that did not induce secondary hospital admission were absent from the database. In addition, we could not evaluate post-operative pain and analgesia.

3. Conclusion

This is the first nationwide study since 1973 to examine patients’ characteristics and outcomes following cholecystectomy for gallstones or gallbladder disease in the French general population. It found that the incidence rate of cholecystectomies increased over time. The length of stay decreased significantly from 2008 to 2014 and the proportion of procedures performed on an outpatient basis has increased exponentially since 2008.

It would be interesting for future studies in this area to explore potential factors for increased incidence, outcomes, and post-hospital mortality. An economic approach would also complement the results of this study.

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Disclosure of interest

The authors declare that they have no competing interest.

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