



A case series of cholecystectomy in Jamaican sickle cell disease patients - The need for a new strategy



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HIGHLIGHTS

- Morbidity rates for cholecystectomy in Jamaican sickle cell patients remain high.
- There is a trend to higher morbidity for laparoscopic over open cholecystectomy.
- Preoperative transfusion is rarely employed in this patient population.

ARTICLE INFO

Article history:

Received 20 October 2016

Received in revised form

31 January 2017

Accepted 1 February 2017

Keywords:

Sickle cell

Cholecystectomy

Outcomes

Jamaican

Gallstones

ABSTRACT

High morbidity rates related to cholecystectomy in sickle cell disease (SCD) patients have been previously reported in the region. This study serves to assess the current outcomes related to cholecystectomy in a Jamaican SCD population. **METHODS:** A retrospective chart review of SCD patients undergoing elective cholecystectomy at the University Hospital of the West Indies over a 6-year period was performed providing relevant information for analysis. Patients were grouped on an intention-to-treat basis into an open and laparoscopic group. **RESULTS:** A total of 27 patients were included (18 laparoscopic and 9 open). Both groups were matched for age, gender and steady state hemoglobin. Only one patient (in the open group) received preoperative blood transfusion. The conversion rate for laparoscopy was 28%. Operative time was significantly longer in the open group (175.3 ± 62.1 vs. 125.9 ± 54.4 min, $p = 0.0355$). Bile duct exploration was undertaken in 66.7% of patients in the open group compared to 0% in the laparoscopic group. There was no significant difference between groups with respect to hospital stay, morbidity or mortality. The overall 30-day morbidity was 48.1% with acute chest syndrome being diagnosed in 6 patients and pneumonia in 7 patients. **CONCLUSION:** Morbidity rates related to cholecystectomy in the Jamaican SCD population remain high. Further studies to evaluate the factors contributing to such high morbidity in this population are warranted, with particular focus on laparoscopic cholecystectomy. Strategies such as preoperative transfusion and prophylactic cholecystectomy also need to be evaluated and considered in this patient group.

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1. Introduction

Sickle cell disease (SCD) is a prevalent inherited haemolytic disorder that affects 1 in 150 newborns in Jamaica [1]. Owing to red blood cell haemolysis, these patients are predisposed to the development of gallstones, with rates of up to 83% in the adult population [2]. The current standard of care for the treatment of symptomatic gallstones is laparoscopic cholecystectomy [3], with

some reports suggesting that asymptomatic gallstones should be managed similarly in the sickle cell population [4].

Sickle cell patients are prone to significant morbidity and mortality related to surgery and anesthesia. Changes in temperature, oxygen tension and fluid volume related to the surgical process predispose SCD patients to red cell sickling intra- and post-operatively with consequent vaso-occlusive crises [5]. The most notable SCD-related postoperative complications include acute chest syndrome, painful crises, stroke and priapism.

International reports suggest perioperative morbidity rates of 7%–14%, most of which are SCD-specific [6–8]. Rates of acute chest syndrome have been quoted as 0.4%–10% [9]. Mortality rates of less

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than 1% have been reported from high-volume centers [10,11]. Significantly higher morbidity rates have been quoted in the Caribbean—37.5% by Plummer et al. [12] and 21% by Dan et al. [13]. No contributing factors have been elucidated to date.

With improvements in surgical and anesthetic care, greater awareness of the pathophysiology and predisposition to vaso-occlusive crises and improved perioperative patient management, we sought to assess the current outcomes for cholecystectomy in a Jamaican sickle cell disease population and to determine whether any differences in outcomes were noted based on the surgical approach.

2. Methods

This is a retrospective single-center case series of all sickle cell disease patients over 12 years of age consecutively undergoing elective cholecystectomy for confirmed gallstone disease between January 2009 and December 2014. The patients were managed at the University Hospital of the West Indies, a tertiary-level teaching hospital affiliated with the University of the West Indies. The study was conducted in accordance with the Declaration of Helsinki (research registry UIN: researchregistry2115), with ethics approval granted by the University of the West Indies/Faculty of Medical Sciences Ethics Committee (ECP 84, 15/16). The data collected through chart review were analyzed using SPSS version 18. Patients with sickle cell trait (hemoglobin AS) were excluded.

Data collection included patient demographics, phenotype, preoperative hemoglobin, surgical procedure, additional procedures, operative time, postoperative complications and hospital stay. Patients were separated into two groups – open and laparoscopic. The surgeon made the decision regarding surgical approach based on factors including need for cholangiography and common bile duct exploration.

Statistical analysis performed aimed to determine overall morbidity and mortality and the differences between groups with respect to operative time, complications and total hospital stay. Mann-Whitney U and Chi-squared tests were used for non-parametric scale and categorical variables, respectively. P value of <0.05 was considered significant. This study has been reported in line with the PROCESS Guidelines [14].

3. Results

During the 6-year study period, 27 patients were identified who met the inclusion criteria. All cases were conducted under direct supervision of a consultant surgeon. The consultant performed eight cases while the remaining 19 were performed by year 4 or 5 residents under supervision. Eighteen patients (66.7%) underwent laparoscopic cholecystectomy while an open approach was undertaken in 9 (33.3%) patients. The conversion rate for laparoscopic cholecystectomy was 27.8%. Reasons for conversion were difficult visualization due to hepatomegaly in one patient and significant scarring obscuring Calot's triangle in four patients. Symptomatic cholelithiasis and choledocholithiasis represented the main indications for cholecystectomy (Fig. 1). No patient in the cohort underwent prophylactic cholecystectomy.

The mean age of the cohort was 30.8 years, with all patients being homozygous HbSS in phenotype. The mean hemoglobin on presentation was 7.4 g/dl. Twenty-one (77.8%) patients had been admitted at least once previously with gallstone-related complications. The mean time from onset of symptoms to surgery in this cohort was 223.5 days (range: 22–1394 days).

Twenty-five of 27 (92.6%) patients had some form of duct evaluation. Fifteen (60%) patients had preoperative endoscopic or magnetic resonance cholangiopancreatography. The remainder,

including one patient who failed endoscopic retrograde cholangiopancreatography, underwent operative cholangiography ± common bile duct exploration. (Fig. 2). Fig. 3 demonstrates that all patients chosen to undergo open cholecystectomy had intraoperative duct evaluation performed compared to only one patient in the laparoscopic group. No common duct exploration was performed laparoscopically. Twenty-one (77.8%) patients had abnormal gallbladders at operation (fibrotic and contracted in 11 patients and distended with adhesions to surrounding structures in 10 patients).

There was no significant difference between groups related to baseline characteristics of age, gender, previous admissions or hemoglobin at presentation. Only one patient (3.7%) of the cohort had preoperative blood transfusion (Table 1). Operative time was significantly longer in the open group (175.3 vs. 125.9 min, p value = 0.0355). There was no statistical difference between groups with respect to hospital stay, perioperative morbidity or mortality (Table 2). The overall 30-day morbidity rate for the cohort was 48.1%. There were no intraoperative complications. Postoperative complications were predominantly medical, with acute chest syndrome and nosocomial pneumonia being the most common (Table 3). Two patients died, the causes being acute chest syndrome in one patient and cardiac failure, renal failure and sepsis in the other. The mortality rate was 7.4% (Table 2). Mean follow-up for this cohort was 6 weeks. Twenty-five percent of the cohort defaulted from follow-up prior to discharge from the surgical clinic.

4. Discussion

The present study demonstrates that laparoscopic cholecystectomy has become the predominant approach to management of gallstone disease in the Jamaican sickle cell disease population, with open cholecystectomy being reserved for patients requiring additional procedures. Although no difference in outcomes were noted between open and laparoscopic groups, the overall morbidity and mortality rates related to cholecystectomy in the Jamaican sickle cell disease population remain high at 44.4% and 7.4% respectively.

Perioperative morbidity and mortality rates higher than those noted in the general population are expected in sickle cell disease patients and are related to increased perioperative red cell sickling. Methods to reduce sickling and improve outcomes have been established over time and form an essential part of the perioperative management of a sickle cell patient. These measures include ensuring normothermia, intravenous fluid hydration, supplemental oxygen, analgesia, antibiotics and chest physiotherapy [15]. The role of perioperative blood transfusion, either simple or exchange transfusion, as well as the use of minimally invasive surgical approaches has been debated [7,16–18].

Laparoscopic cholecystectomy is the gold standard surgical approach in the general population [19]. Multiple international reports have demonstrated laparoscopic cholecystectomy to be safe and associated with low morbidity and mortality in the SCD population. Morbidity rates of 6.6%–14% [6–8] and mortality rates of 0%–1.4% have been quoted [10,11]. Early concerns related to physiologic changes and the potential for increased sickling associated with pneumoperitoneum have not been substantiated [20]. A single report has suggested an increased rate of acute chest syndrome associated with laparoscopic cholecystectomy [7]. However, the retrospective nature of the study introduced significant bias and such conclusions have also not been substantiated by other studies.

National and regional data show morbidity rates significantly higher than those reported internationally. Plummer and Dan reported morbidity rates of 35.2% and 21.1% respectively for laparoscopic cholecystectomy in SCD patients [12,13]. Admittedly, both

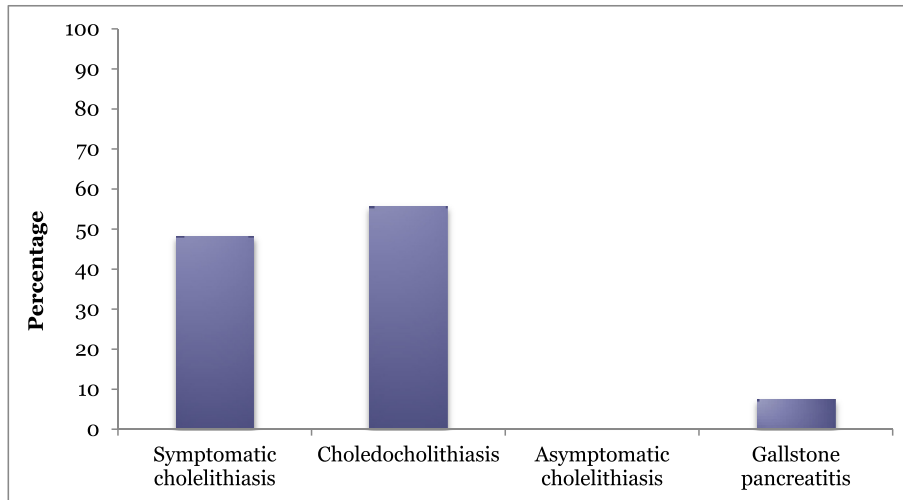


Fig. 1. Indication for elective cholecystectomy in cohort of Jamaican sickle cell disease patients.

the present study and that of Plummer et al. [12] are retrospective. As such, homogeneity in a strict perioperative protocol cannot be determined - factors which would undoubtedly influence patient outcome. Dan et al. [13], however, reported outcomes of a prospective cohort of patients who had a strict perioperative protocol instituted. Despite this, the morbidity rates were still high.

4.1. Surgical approach

In attempting to determine independent factors contributing to adverse outcomes in our patients, we evaluated the role of the open and laparoscopic surgical approach. The present study demonstrates that, despite advances in laparoscopic surgery, open cholecystectomy remains a reality in our region. The reasons appear to relate primarily to the need for additional procedures such as intraoperative cholangiography and common bile duct exploration. Although the feasibility in performing these procedures laparoscopically is well established [21,22], lack of expertise and equipment (cholangiography catheters and choledochoscopes) has limited their implementation in our institution.

There were no differences demonstrated between groups for morbidity or mortality rates in the present study. This may suggest that open cholecystectomy is a feasible alternative, particularly where lack of equipment and resources exist. With some studies suggesting poorer outcomes for laparoscopic cholecystectomy [7], a randomized trial would be justified in evaluating the optimal surgical approach in the sickle cell population.

4.2. Fetal hemoglobin

SCD patients of Caribbean descent are inherently prone to greater red cell sickling due to low fetal hemoglobin concentrations and as such, this factor may play a role in surgical outcomes. Fetal hemoglobin has been found to be protective with less sickling noted in patients with higher fetal hemoglobin concentrations [23]. Racial variations have been noted in fetal hemoglobin concentrations, with the black population having considerably lower concentrations of fetal hemoglobin compared to those of Middle Eastern or Caucasian origin. Higher rates of vasoocclusive crises and acute chest syndrome in the black SCD population have been

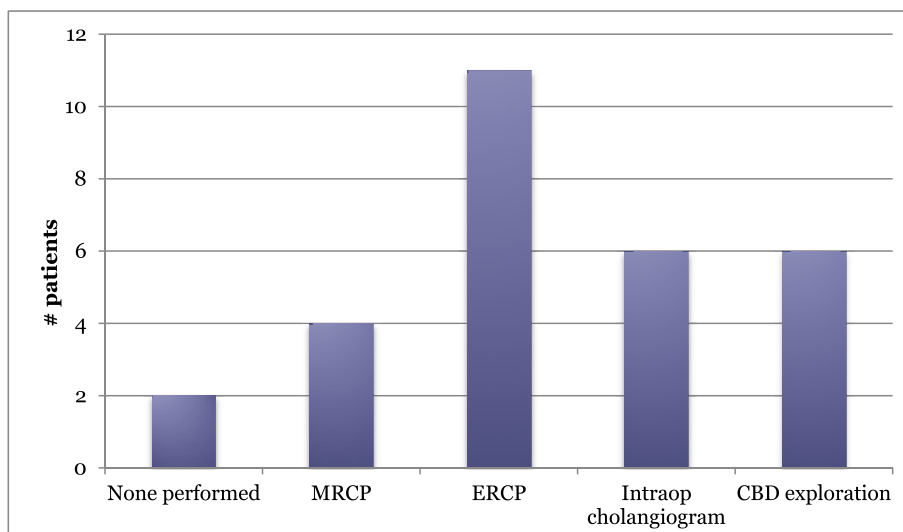


Fig. 2. Method of clearing the common bile duct in cohort of Jamaican sickle cell disease patients.

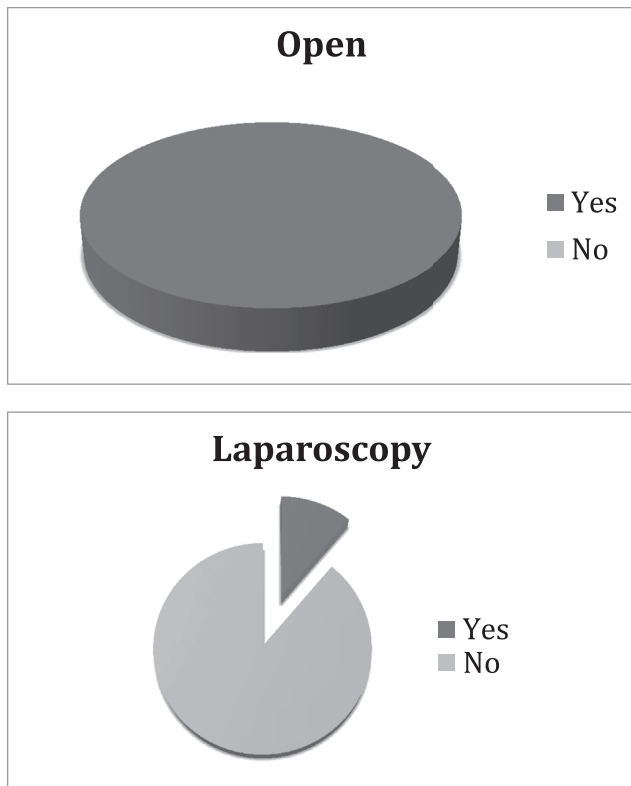


Fig. 3. Additional procedures (operative cholangiogram and/or common bile duct exploration) required according to surgical group.

attributed to low fetal hemoglobin concentrations [24,25]. Higher morbidity rates with cholecystectomy found in the black population [12,13] compared to the Middle Eastern population [6,8], where fetal hemoglobin levels are notably high [24], may support this supposition.

4.3. Preoperative transfusion

Preoperative blood transfusion, in an effort to improve oxygen delivery and reduce red cell sickling, has been explored as a measure to improve patient surgical outcomes. Studies have evaluated the effect of transfusion on outcomes, as well as the type of transfusion – conservative or aggressive (exchange transfusion).

Table 1
Baseline characteristics, according to group.

Parameter	Open	Laparoscopic	Total	P value
Age (years)	29.3 ± 14.5 (14,56)	31.5 ± 11.9 (15,64)	30.8 ± 12.6 (14,64)	NS
Female gender	5/9 (55.6%)	10/18 (55.6%)	15/27 (55.6%)	NS
Previous admissions	7/9 (77.8%)	14/18 (77.8%)	21/27 (77.8%)	NS
Haemoglobin on admission (g/dl)	7.2 ± 1.4 (5.1,9.9)	7.5 ± 1.7 (5.5,11.7)	7.4 ± 1.6 (5.1,11.7)	NS
Preoperative transfusion	1/9	0/18	1/27 (3.7%)	

Table 2
Outcome of cohort of Jamaican sickle cell disease patients, according to group.

Parameter	Open	Laparoscopic	Total	P value
Operative time (mins)	175.3 ± 62.1	125.9 ± 54.4	143 ± 59.7	0.0355
Hospital stay (days)	5.1 ± 3.1	8.8 ± 10.8	7.5 ± 9.0	NS
Intraoperative complications (n)	0	0	0	NS
Postoperative complications (n)	3	10	13 (48.1%)	NS
Death (n)	0	2	2 (7.4%)	NS

Most studies support some form of preoperative transfusion. Haberkern et al. [26] reported on 364 patients undergoing cholecystectomy. The highest rate of postoperative sickle cell events was noted in the nontransfusion group. More recently, Howard et al. [27] found significantly higher complication rates in the no-transfusion group (39%) compared to the preoperative transfusion group (15%) in their randomized trial. Aziz et al. [28] has contradicted these views by showing worse outcomes in patients undergoing preoperative transfusion (25% complication rate vs. 0% in the no-transfusion group). By instituting a strict protocol that included the use of routine prophylactic CPAP, Leff et al. [17] demonstrated that SCD patients undergoing cholecystectomy can have minimal morbidity without preoperative transfusion. No patient developed postoperative painful crises and one patient experienced acute chest syndrome in their study.

Studies evaluating the value of exchange transfusion (decreasing hemoglobin S levels) have demonstrated that a conservative approach (increasing hemoglobin levels) is sufficient in improving patient outcomes. Vichinsky et al. [9] found a higher rate of transfusion-related complications in the aggressive transfusion group (14% vs. 7%) in a randomized trial and concluded that a conservative transfusion regime was preferable.

National and regional policies do not support preoperative transfusion in SCD patients, as demonstrated by the 3.7% transfusion rate in the present study and 0% transfusion in previous regional reports [12,13]. Of note, most international reports evaluating outcomes of SCD patients undergoing cholecystectomy include preoperative transfusion with rates of 57.4%–92% [6–8,29]. Concordantly, these groups have more favorable outcomes. Further research evaluating preoperative transfusion in our SCD population would be warranted prior to making any conclusions on the independent value of such an intervention.

4.4. Prophylactic cholecystectomy

Based on the natural history of gallstones in the Jamaican SCD population showing low conversion to symptomatic cholelithiasis [30] and the recognized morbidity associated with surgery in this population, there has been a policy to offer cholecystectomy only to symptomatic patients. This is consistent with most regional and international reports that included few asymptomatic patients (0–10.5%) [12,13].

With advances in perioperative and anesthetic care, and the advantages conferred by a laparoscopic approach, the role of cholecystectomy in asymptomatic SCD patients has been recently

Table 3
Postoperative complications.

Type of complication	Nature of complication	Number of patients (n)
Surgical		
Major	Reactionary bleeding requiring reoperation	1
Minor	Surgical site infection	1
Medical		
Major	Acute Chest Syndrome	3
	Pneumonia	2
	Neurological	2
	Renal impairment	1
	Cardiac failure	1
Minor	Acute Chest Syndrome	3
	Pneumonia	5

Major: requiring ICU admission or surgery.

evaluated. Curro et al. [31] evaluated 26 asymptomatic pediatric patients who underwent prophylactic cholecystectomy or cholecystectomy when they became symptomatic. Both operative time (90 min vs. 65 min) and morbidity rates (50% vs. 12.5%) were significantly greater in the symptomatic group. Muroi et al. [4] evaluated prophylactic cholecystectomy in the adult population. Prospectively enrolled asymptomatic patients were matched with a group of symptomatic patients. Postoperative complications were less frequent (11.5% vs. 25.5%) in asymptomatic patients. Prophylactic cholecystectomy also reduced hospital stay (5.7 vs. 7.96 days).

The present study shows that 77.8% of patients presented with gallstone complications requiring at least one hospitalization prior to undergoing cholecystectomy. In addition, the average time from onset of symptoms to surgery was 223 days. This echoes a prior study from our institution that showed a mean time to surgery of 173 days after conservative management of acute cholecystitis [32]. The fact that 78% of patients in the present study had an abnormal gallbladder at surgery, representative of chronic cholecystitis, and that 80% of conversions were due to obscured anatomy exemplifies the fact that our patients are presenting and undergoing surgery late. Where significant delays and resource limitations exist (as in our population), prophylactic cholecystectomy may prove a realistic option in avoiding complications of gallstones and the morbidity and mortality associated with surgery in this group of patients. This is a promising area that requires further study, including a randomized trial.

The limitations of this study lie mainly in its retrospective nature and the small patient numbers, both of which may influence result interpretation. Despite these limitations, we believe that our results highlight the fact that perioperative outcomes in sickle cell patients can vary depending on the specific population. Additional research, particularly from regions where research is lacking, can only shed further light on the challenges facing this group of patients. It is essential that novel approaches to optimizing SCD patient outcomes be evaluated, ideally through prospective and randomized controlled trials.

5. Conclusion

SCD patients remain a vulnerable group with respect to surgery and its outcomes. Despite advancements in perioperative care and anesthesia, morbidity and mortality rates are still unacceptably high for SCD patients undergoing cholecystectomy in Jamaica. Further evaluation of the role of the surgical approach, preoperative transfusion and prophylactic cholecystectomy through randomized trials is paramount to definitively ascertaining the factors contributing to these poor outcomes and the strategies needed to improve

them.

Ethical approval

Ethics approval was given by the University Hospital of the West Indies/University of the West Indies/Faculty of Medical Sciences Ethics Committee. Reference number: ECP 84, 2015/2016.

Sources of funding

This research paper was conducted without any funding.

Author contribution

P. Leake – study design, data collection, writing.
M. Reid – study design, data analysis.
J. Plummer – study design, writing.

Conflicts of interest

No conflicts of interest.

Trial registry number

Research Registry - researchregistry1698.

Guarantor

Dr. Pierre-Anthony Leake.

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