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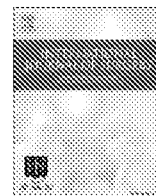
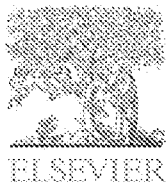
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## Laparoscopic cholecystectomy in sickle cell disease patients: Does operating time matter?

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### ABSTRACT

**Objectives:** To report the experience of performing laparoscopic cholecystectomy (LC) in patients suffering from sickle cell disease (SCD), and to assess if their postoperative complications can be minimized by shortening the operating time.

**Methods:** Strict measures were taken to minimize the operating times and duration of pneumoperitoneum in SCD patients undergoing LC. Data collected included demographics, preoperative haemoglobin, the surgical technique used, operating times, insufflation pressures, perioperative complications and hospital length of stay.

**Results:** In the 5-year period from July 2003 to June 2008, 19 patients with SCD underwent elective LC. Of these, 84% were female. The mean age was 21.5 years. The most common indication for surgery was symptomatic cholelithiasis (60%). The mean preoperative haemoglobin was 8.2 g/dL. No preoperative blood transfusions were given. Four patients had preoperative endoscopic retrograde cholangiopancreatography (ERCP). Mean operating time was 27.9 min (range 20–45 min) which is 2.5–6 times quicker than most reports in the literature. There was no conversion to open surgery. Mean hospital length of stay was 2.5 days. Postoperative complications were noted in four patients with painful crises accounting for 50%. There was no mortality.

**Conclusion:** The study suggests that if stringent measures are taken to shorten the operating time, LC can be safely and effectively performed in SCD patients with minimal perioperative complications.

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## 1. Introduction

Sickle cell disease (SCD) is a condition endemic to Africa although it is currently prevalent in many other countries due to migrant populations.<sup>1</sup> The West Indies is one of the regions where SCD is highly prevalent, owing to a large population of individuals of African lineage and diverse inter-racial mixing. Haemolytic anaemia associated with sickle cell disease predisposes these patients to an increased risk of developing pigmented gallstones which increases with age.<sup>2,3</sup> In Jamaica, 9% of children and 83% of adults with SCD suffer from cholelithiasis.<sup>4</sup> The incidence and prevalence of SCD and associated gall bladder disease have not been well documented for other countries in the Caribbean region.

Cholecystectomy is commonly performed in SCD patients for symptomatic as well as asymptomatic cholelithiasis and is the most

common surgical procedure in this cohort of patients.<sup>5</sup> They are unique surgical patients requiring closer attention to prevent perioperative complications. Hence, optimal perioperative management of SCD patients undergoing cholecystectomy has always been a contentious issue.

In the general population, the benefits of laparoscopic cholecystectomy (LC) over open cholecystectomy (OC) with respect to many aspects of perioperative outcome have been established beyond doubt.<sup>6</sup> However, in SCD patients, some studies have suggested that OC may be preferable to LC in order to minimize complications such as postoperative acute chest syndrome (ACS).<sup>7–9</sup>

Many pathophysiological changes associated with pneumoperitoneum may lead to perioperative complications, which have been well established in animal studies and in the general population.<sup>10,11</sup> However, few studies have specifically analysed the causal relationship of factors such as operating time and intra-abdominal pressure to the development of perioperative complications in SCD patients. The studies quoting a higher incidence of

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ACS in patients undergoing LC compared to OC, did report relatively longer operating times in the former.<sup>7–9</sup>

It is known that CO<sub>2</sub> insufflation during LC can result in hypercapnia and respiratory acidosis.<sup>12</sup> These changes, which could precipitate sickling in SCD, would necessarily be related to the duration of the surgery. Moreover, ACS is often most severe in the lung bases, the same regions which are underventilated during the insufflation of the peritoneal cavity in LC. We sought to minimize the diaphragmatic splinting and physiological changes that precipitate sickling by shortening the operating times and decreasing the insufflation pressures. However, it would be unethical to have a control group within the SCD patients with longer operating times and higher insufflation pressures, as this would expose patients to unnecessary risk. We hereby report our experience with 19 consecutive LCs in SCD patients.

## 2. Methods

LC in SCD patients was planned meticulously and the following methods were utilized to ensure a shorter operating time in these patients:

1. SCD patients were exclusively operated on by the most senior laparoscopic surgeon (first author) with an experienced assistant and a scrub nurse.
2. Residents and junior surgeons were not allowed to operate on SCD patients, despite the fact that the procedures were performed in a teaching hospital, where postgraduate residents in surgery are trained.
3. No teaching was done on SCD cases during the operation.
4. SCD patients were scheduled to have surgery second or third on the operating list. A previous LC will ensure that the laparoscopic equipment is functioning properly. This will avoid undue prolongation of the operating time due to malfunctioning equipment.
5. An ultrasonically activated scalpel (Harmonic Scalpel™) was used to obliterate the cystic artery and dissect the gall bladder off the liver, and this technique is known to shorten the operating time.<sup>13</sup>
6. Patients with suspected choledocholithiasis had preoperative ERCP and sphincterotomy thus eliminating the need for intraoperative cholangiography.

### 2.1. Other perioperative considerations

All SCD patients were admitted 1 day prior to surgery and received preoperative intravenous hydration. Preoperative haematological and biochemical investigations and abdominal ultrasounds were routinely performed.

In all the SCD patients, LC was performed with the standard four-port technique using 12 mmHg of CO<sub>2</sub> pneumoperitoneum created via an open Hassan port technique. Insufflation pressure was maintained at the minimum that would allow good exposure for a safe surgery.

All patients underwent standard general anaesthesia with controlled ventilation using an endotracheal tube. Intraoperatively they were monitored using automated non-invasive blood pressure, temperature, electrocardiography, pulse oximetry and end-tidal CO<sub>2</sub>. All patients received antibiotic prophylaxis during induction of anaesthesia. It was ensured that the patients received only warm crystalloids infusion. Postoperatively, all the patients were given intravenous fluids to maintain hydration, antibiotics, opioid analgesia, oxygen therapy and kept warm with additional blankets. Criteria for discharge included: (1) adequate pain control, (2) the ability to tolerate light diet, (3) ability to ambulate and (4)

ability to void urine. All patients were followed up in the outpatient clinic at intervals of 2, 6 and 12 weeks postoperatively.

Data recorded included demographics such as age, gender and ethnicity; clinical data included sickle cell type, preoperative steady state haemoglobin, transfusion requirements, need for ERCP, indications for surgery, severity classification of the procedure, operative time, CO<sub>2</sub> insufflation time, intra-abdominal pressures, intraoperative and postoperative complications and hospital length of stay.

### 2.2. Definitions used for data collection

- Steady state haemoglobin was defined as the average of three previous haemoglobin values taken 3 months apart.
- Severity classification of the procedure categorized patients from Class I through IV depending on the anatomy of the patient found during surgery: Class I when the anatomy was clear without any dissection, Class II when the anatomy was discernible after initial dissection, Class III when the anatomy was discernible after assiduous dissection and Class IV when the anatomy was unclear even after extensive dissection.
- Operative duration was recorded as the time from the skin incision for the first port to skin closure of the last port. The duration of pneumoperitoneum was noted as the time from the start of CO<sub>2</sub> insufflation until deflation of the peritoneum.
- Hospital length of stay was calculated from the day of admission to the day of discharge.

Specifically defined complications included painful crisis, acute chest syndrome, neurological events, renal complications and fever or infection.

- Painful crisis was defined as non-surgical pain lasting longer than 24 h requiring narcotic analgesia.
- Acute chest syndrome was defined as the presence of a new pulmonary infiltrate involving at least one full lung segment.
- A neurological event was defined as a change in neurological status accompanied by neurological findings.
- Renal complication was defined as altered biochemical renal parameters pointing to renal insufficiency, haematuria, or proteinuria.
- Fever or infection was defined as a temperature higher than 37.5 °C or documented infection lasting at least 48 h.

## 3. Results

Between July 2003 and June 2008, 19 SCD patients with a homozygous SS genotype, had LC.

The mean age was 21.5 years (range 9–37 years) and 17 were females. The mean steady state haemoglobin was 8.2 g/dL. All the cholecystectomies were done electively for various indications. The most common indication was cholelithiasis (58%). Other indications were choledocholithiasis (15.8%), asymptomatic cholelithiasis (10.5%), acute-on-chronic cholecystitis (10.5%) and gallstone pancreatitis (5.2%).

None of the patients received preoperative transfusions. Preoperative 'endoscopic retrograde cholangiopancreatography' (ERCP) was done in four patients, three of whom had a history of worsening jaundice. All four of them had dilated common bile ducts (>7 mm diameter) on ultrasound. ERCP was successful in removing the common bile duct stones and endoscopic sphincterotomy was performed in all four patients.

According to the severity classification of the procedure, 36.8% were classified as Class I, 58% as Class II, and 5.2% as Class III.

The operative time ranged from 20 to 45 min with a mean of 27.9 min. The mean duration of pneumoperitoneum was 20.9 min.

The average intraoperative blood loss was about 50 mL. The mean hospital length of stay was 2.5 days (range 1.5–7 days).

Clinically significant complications were encountered in four patients. One patient suffered a complication secondary to a technical fault in the procedure which led to bleeding from the cystic artery; this was subsequently corrected by laparoscopic clipping of the cystic artery stump, 12 h following the first operation. Two patients had symptoms suggestive of painful vaso-occlusive crisis. Pain relief was achieved with opioids and they were discharged symptom-free, although their hospital length of stay was prolonged by 2 days. The fourth case was a 10-year old female who developed shortness of breath on the first postoperative day. She had a unilateral basal consolidation in the chest radiograph and was treated with oxygen supplementation, chest physiotherapy and antibiotics. She had complete resolution of symptoms without the need for exchange transfusion, ICU admission and/or mechanical ventilation. She remained in the hospital for 7 days postoperatively.

There was no mortality in this case series.

#### 4. Discussion

The main finding of this study is the good perioperative outcome of LC in SCD patients, with minimal complications. SCD patients have a relatively higher risk of complications such as painful crisis, ACS and haemolytic crisis during the perioperative period, which may be precipitated by hypoxia, dehydration, hypothermia, infection, severe stress and pain.<sup>14</sup>

The incidence of postoperative complications in the present study (16%) is considerably lower than an earlier study from Jamaica, which reported 38% complications and mortality in one out of 12 patients.<sup>15</sup> Painful crisis was the most common postoperative complication in the present study, while ACS was the most common complication in the Jamaican study.<sup>15</sup> Only one patient in the present study had a postoperative pulmonary complication, although this patient had an earlier episode of ACS, 3 months before the surgery.

In general, LC has been shown to be superior to OC in many respects such as less postoperative pain, shorter hospitalization, more favourable cosmetic outcome and improved postoperative pulmonary function, which is more important in SCD.<sup>16,17</sup> However, in SCD patients, some reports have suggested that an OC might have fewer complications than LC.<sup>7–9</sup> There are many possible reasons for increased perioperative morbidity following LC in SCD patients. The pathophysiological effects of CO<sub>2</sub> pneumoperitoneum in various organ systems are well documented.<sup>12</sup> These effects directly correlate with the amount of intra-abdominal pressure, duration of insufflation and the patient's position on the operating table.<sup>12</sup> The alteration in splanchnic perfusion is proportional to the intra-abdominal pressure and duration of pneumoperitoneum.<sup>12</sup> CO<sub>2</sub> insufflation may cause increased PaCO<sub>2</sub> leading to respiratory acidosis and catecholamine release.<sup>18,19</sup> Increased duration of insufflation is independently associated with an increased incidence of hypercapnia.<sup>20</sup> ACS, the most common and feared complication in a SCD patient shows a predilection for the basal lung regions, which are likely to be underventilated during the CO<sub>2</sub> pneumoperitoneum.<sup>21</sup> All the aforementioned changes associated with CO<sub>2</sub> insufflation would be more significant as the duration of CO<sub>2</sub> pneumoperitoneum increases, and may predispose SCD patients for sickling in the perioperative period, causing painful crises as well as ACS.

Thus, a lower intra-abdominal pressure and a shorter duration of CO<sub>2</sub> insufflation may assist in limiting the extent of the pathophysiological changes and positively influence the outcome of laparoscopic surgeries.<sup>12</sup> Most SCD patients are asthenic in stature. We found that a low insufflation pressure of 12 mmHg used in the

present study provided adequate exposure in SCD patients. We could avoid higher insufflation pressures usually required in hypersthenic patients, thus minimizing diaphragmatic splinting in SCD patients.

Most notably, the studies reporting higher complication rates following LC in SCD patients also reported significantly longer operating times than the present study.<sup>7–9</sup> Using the criteria defined, we were able to achieve an operating time of 28 min which is 2.5–6 times shorter than the earlier reports (71–192 min).<sup>7–9</sup> Increased duration of surgery also means that the patient remains anaesthetized for a longer time, which increases the likelihood of lung complications and postoperative hypoxaemia.<sup>22</sup> In our view, the relatively shorter operating time in the present study could have been the paramount reason for the minimal perioperative complications, and we took strict measures to diminish the duration of surgery.

To reiterate the important point, all SCD patients were exclusively operated on by the senior and the most experienced surgeon and none was operated upon by residents or junior surgeons. This not only helped in achieving shorter operating times, but also a zero conversion to an open procedure. Of note, the previous studies which reported longer operative times for this procedure did not discuss the seniority and experience of the operating surgeon.<sup>7–9</sup>

In SCD patients, preoperative serial haemoglobin measurements, and optimization by blood transfusion when necessary, may reduce the risk of perioperative hypoxia.<sup>23</sup> Recognition of the patient's 'steady state' haemoglobin is essential to prevent unnecessary transfusion. None of the patients in the study had preoperative transfusions. We follow a conservative approach to blood transfusion. SCD patients are transfused preoperatively only if their haemoglobin levels are >1 g/dL below their known steady state values. Exchange transfusions are considered only if recommended specifically by the paediatricians or haematologists.

Adequate perioperative hydration and analgesia have been shown to decrease the rate of complications in SCD patients.<sup>5,23</sup> In the present study, all patients received adequate parenteral analgesia and intravenous fluids postoperatively until they were able to tolerate normal diet and oral pain medication. Optimization of patients' temperature is another factor which needs special attention in SCD patients. The ambient temperatures in the operating and recovery rooms are relatively colder. Additionally, general anaesthesia predisposes patients to hypothermia. Prevention of hypothermia is vital in SCD patients to minimize sickling, and this was achieved in the present study by shorter operating times, warm intravenous fluids and extra blankets.

The study from Jamaica reported that all patients underwent ERCP.<sup>12</sup> In our study, only 21% of patients had ERCP and endoscopic removal of bile duct stones by sphincterotomy prior to surgery, avoiding intraoperative cholangiography. This could have further enabled reduction in the operating times in our study.

The limitation of this study is the lack of a control group but, as mentioned earlier, it is ethically unacceptable to have this group. We suggest that in centres where the operating time for LC is significantly longer, it may be possible to record serial measurements of end-tidal CO<sub>2</sub>, PaCO<sub>2</sub> and pH and establish the possible causal relationship of these factors to perioperative complications.

In conclusion, the present study highlights a good outcome for LC in SCD patients. More pertinently, LC in these patients should be performed by a senior and experienced surgeon to achieve shorter operating times, which may be the key factor in minimizing perioperative pulmonary complications. By achieving shorter operating times at low insufflation pressures, LC could be safely and effectively done in SCD patients and should be considered the preferred alternative to the traditional open approach.

**Conflict of interest**

None of the authors has any financial disclosures; there is no conflict of interest in the publication.

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**Ethical approval**

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