

# **Research Article**

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# Prophylactic cholecystectomy by low-impact laparoscopy in drepanocyte children after selective transfusion exchange: the result of a monocentric study

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# Abstract

**Background:** A monocentric study was undertaken in order to study the morbidity of cholecystectomy by low-impact laparoscopy in sickle cell children with asymptomatic vesicular lithiasis, and to bring the relevance of a clinical pathway with selective preoperative transfusion exchange in the prevention of alloimmunization. **Method:** Over a period of 7 years, between July 2011 and August 2018, 44 consecutive sickle cell children were surgically treated for their cholelithiasis. During the first phase of the study, 22 children had a systematic transfusion exchange. For the next 22 children, from January 2016, a selective transfusion exchange protocol was applied. **Results:** Microcælioscopy was converted into laparoscopy. No perioperative complication occurred in patients after a transfusion exchange. The selective exchange protocol reduced the number of transfusions by 77.28 %. Acute thoracic crisis occurred on day 1 in one of the non-transfused patients requiring postoperative transfusion. **Conclusion:** A transfusion exchange was performed selectively. Only laparoscopic cholecystectomy was performed under general anesthesia. Acute thoracic crisis occurred on day 1 in one of the non-transfused patients requiring postoperative transfusion.

**Keywords:** Prophylactic, Cholecystectomy, Low-Impact, Laparoscopy, Drepanocytechildren, Selectivetransfusion Exchange.

# INTRODUCTION

Sickle cell disease is a common monogenic disease worldwide, affecting more than 300,000 newborns each year <sup>[1]</sup>. Patients with sickle cell disease have chronic hemolytic anemia and are therefore at increased risk of cholelithiasis; In France, 80% of cases are diagnosed in the Ile-de-France and overseas territories where the frequency of the genetic trait " S " is respectively estimated at 2.2 and 5.4-11% of the population <sup>[2, 3]</sup>.

The speakers proposed cholecystectomy to patients with symptomatic or complicated vesicular lithiasis <sup>[4]</sup>. On the other hand, with regard to children with asymptomatic cholecystolithiasis in the specific case of sickle cell disease, there is still a controversy over the therapeutic behavior with very little consensual information on the prophylactic surgery of asymptomatic children as well as on the need for or not the transfusion exchange before the intervention <sup>[5, 6]</sup>.

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Since the laparoscopic approach is also practiced electively in lithiasic biliary pathology in children with sickle cell disease operated in the southern hospital center of Paris, it seemed to us interesting to approach the subject.

# MATERIAL AND METHODS

This is a retrospective and prospective study from January 1, 2011 to August 31, 2018, for a total duration of 7 years 7 months. The data come from patient records, operative reports and a data collection questionnaire. A comprehensive random sampling method was used, covering all children with sickle cell cholecystectomy. Two collection techniques have helped us in the realization of this study: the list of under 18 who underwent cholécystec tomy in the study period and from software reference (administration of care), opera (programming and archiving of the operating room activities), M-Eva (for patient monitoring, general coordination of other software and archiving).

Variables included were age, sex, weight, race, type of sickle cell disease, history of acute thoracic syndrome, baseline hemoglobin, preoperative hemoglobin, transfusion or transfusion exchange, type of anesthesia, surgical approach, operative procedure; operative time, evolution and duration of hospitalization.

# RESULTS

# Sociodemographic characteristics

# Frequency

During our study from April 6, 2011 to July 11, 2018, 7 years 3 months, 50 children benefited from laparoscopic cholecystectomy at CHSF(Centre Hospitalier Sud Francilien). 6 were eliminated for noncompliance with the inclusion criteria. Our study then focused on 44 patients. They accounted for 88% of children operated on for biliary disease, an annual frequency of about 6.1 cases / year.

# Age distribution

The average age was 11.07 years with extremes of 6 years and 17 years. The under-15s were in the majority

# **Distribution by sex**

In our series there were as many girls as boys. The sex ratio was 0.5

#### Distribution according to race

The black race is the most affected by hemolytic anemia 98%.

## **Diagnostic aspects**

# Type of hemoglobinopathy

The majority of our patients (86.4%) had homozygous sickle cell disease as shown in the table below.

Table 2: Distribution of patients by type of	f hemoglobinopathy
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Hemoglobinopathies	Numbers	Percentage
Homozygous sickle cell disease	38	86.4
Sickle cell disease heterozygote	4	9.1
Spherocytosis	2	4.5
Total	44	100

## **History of STA**

The antecedent of STA is shown in the table below

Table 3: Distribution of patients according to antecedent STA

Antecedent	Numbers	Percentage
Absence of STA	24	54.45
Presence of STA	20	45.55
Total	44	100

#### Patient weight

The majority of patients, 39 or 88.6% have a weight between 20 and 49 kg. Only 11.4% have a weight of at least 50kg

## Level(Tx) of Hemoglobin(Hb) basic and preoperative

About half of the patients in our series had a baseline Hb above 8g / dl. No patient had a preoperative Hb level of less than 7g / dl.

#### Therapeutic aspects

# **Medical treatment**

Only the transfusion exchange was given as medical treatment to some of our patients. For this specific case there were 2 stage:

During the first phase of the study between July 2011 and December 2015; 22 children were operated including 21 cases of sickle cell disease and one case of spherocytosis. Of the 21 cases of sickle cell disease, transfusion was systematic but not performed in a single patient because of a history of a transfusion accident during her last transfusion followed by hemolytic anemia.

On the 2nd phase of the study 22 children were operated on. For this phase a protocol was instituted collegially with pediatric anesthesia and surgery services to only transfuse if history of acute thoracic syndrome and preoperative hemoglobin level  $\leq 8g$  / dl. According to this protocol, only 5 out of 22 children (22.72%) were transfused as part of the preoperative preparation and one child underwent bleeding because he had a preoperative rate of 10.5 g / dl. Thus the number of transfusions was reduced by 77.28% in this cohort.

## **Preoperative assessment**

The actual surgical treatment was performed after a preoperative assessment. The standard assessment consisted of Rhesus factor blood grouping, cardiac ultrasound and chest X-ray, blood count, prothrombin time, Kaolin partial thromboplastin time and preanesthetic consultation.

#### Surgical treatment

#### Types of anesthesia used

GA was used for all our patients. In addition, only one patient was ASA III vs 43 ASA II in our series.

# Look first

With the exception of one case in which microcœloscopy was converted into conventional laparoscopy, all the rest (43/44) benefited from laparoscopic law-impact.

## **Operative act**

Only cholecystectomy was performed in all patients in our series.

## • Duration of intervention

The average duration of intervention was 46.64 minutes with extremes of 22 and 76 minutes.

# 4. Evolution

# • Postoperative evolution

After the interventions, 42 patients (95.5%) had simple follow-ups, 2 patients (4.5%) of the complicated follow-ups. All 2 are homozygous and non-transfused sickle cell patients.

The first SS homozygote was the only ASA III in the non-transfused series because it did not have a history of acute thoracic crisis. She remained 6 days in hospitalization for thoracic syndrome occurred as of J1 postoperative. The evolution was marked by a good recovery under medical treatment of which a blood transfusion then left on D5 postoperative.

The second homozygous SS beta thalassemic non-transfused preoperatively given a transfusion accident during the last transfusion exchange. She developed a bilateral thoracic syndrome that required a transfer to postoperative J1 Kremlin Bicêtre for treatment in intensive care (With Non-Invasive Ventilation) for 7 days before its re-admission to the CHSF. During her rehospitalization, she developed infectious, respiratory and haematological instability, which necessitated a new transfer to the Necker hospital for close surveillance as of J17 postoperatively. Returned 6 days later for surveillance she came out under medical treatment the next day J24 postoperative.

## **Duration of hospitalization**

The average duration of hospitalization is 2.95 days with extremes of 2 and 6 days.

### Pathological examination of the gall bladder

Pathological examination showed lesions of chronic cholecystitis throughout our series. No signs of malignancy were observed

## DISCUSSION

In our series 88% of children operated on for cholelithiasis had hemoglobinopathy or more than  $\frac{3}{4}$  cholecystectomies performed in children. This reinforces the fact that gallstones are a frequent complication of haemoglobinopathies, as reported by most authors with a frequency generally above 50% <sup>[6-11]</sup>.

The average age of our patients was 11.07 years with extremes of 6 years and 17 years; the under-15s were in the majority with 29.54% from 6 to 10 years and 56, 82% between 10 and 14 years. Our findings are close to those of Gumiero *et al.* <sup>[12]</sup> in Brazil who found an average age of 12.5 years (standard deviation 5) and Walker *et al.* in Jamaica <sup>[13]</sup> who reported 15% to less than 10 years and 22% between 10 and 14 years old. In the study of NZEH *et al.* <sup>[14]</sup> the youngest with cholelithiasis was 10 years old and the one with bile sludge was 5 years old. These above-mentioned data clearly indicate that lithiasis biliary pathology is developed according to age in children with sickle cell disease.

The sex ratio of 0.5 as in several studies <sup>[7, 11, 13, 15, 16]</sup> is a good example of the fact that the disease has no predominance related to sex.

We found 86.4% of homozygous sickle cell patients against 9.1% of heterozygotes.

Gumiero *et al.* <sup>[12]</sup> obtained 64% against 34% SS while B. Fall *et al.* <sup>[17]</sup> obtained 80.5% homozygotes and 19.5% heterozygotes in Senegal. These results corroborate the clinical severity and intensity of hemolysis in homozygous patients who are therefore dependent on a higher frequency of lithiasis compared to heterozygotes.

We observed the history of acute chest syndrome in 45.55% of our patients. Several studies <sup>[7, 15, 16, 18]</sup> find this antecedent and this constitutes with the vaso- occlusive crises a pre-existing entity of morbidity inherent to the sickle cell population.

In our series 52.3% of patients had a baseline hemoglobin level that did not exceed 8g / dl and this motivated a selective transfusion exchange. It should be noted that this attitude was intended to improve patients' pre- and postoperative comfort. At first systematic for a first cohort of 22 patients, this attitude was modified because of the risk of transfusion accident but also of alloimmunization; and became selective for the second cohort of 22 patients. For this cohort, the history of acute thoracic syndrome was added as the second decision criterion for transfusion exchange.

Indeed, the need for preoperative transfusion of sickle cell is still debated. Meshikes *et al.* <sup>[19]</sup> showed that transfusion for hemoglobin levels below 10 g / dl had a preventive effect on postoperative hypoxia. Rutledge *et al.* <sup>[20]</sup> have also shown that the post-transfusion elevation of hematocrit to 30% in sickle cell causes an increase in oxygen saturation and a reduction in sickling of red blood cells.

Randomized studies evaluating perioperative transfusion in homozygous sickle cell patients have shown a clear decrease in complications related to sickling of red blood cells <sup>[21-23]</sup>.

Under general anesthesia the cholecystectomy by modified microcoelioscopy (low insufflation pressure, a single optic and only the bipolar forceps to dissect and coagulate) was practiced on our 44 patients by the same surgeon except urgently with an average duration of intervention 46.64 minutes for extremes of 22 and 76 minutes. Only one conversion of microcoelioscopy into conventional laparoscopy was necessary. No conversion to laparotomy was performed in our series.

B.Fall *et al.* <sup>[17]</sup> in standard laparoscopy in sickle cell patients (pressure of 15mmHg for adults and 12mmHg for children) had an average duration of 60 minutes for extremes of 30 to 90 minutes; with a single conversion to laparotomy in a homozygous SS child to perform a hepatic jejunal anastomosis on Y-loop because of a biliary convergence wound related to a difficult dissection caused by cholecystitis lesions with inflammatory infiltration of the hepatic pedicle.

G. Curro *et al.* in Italy <sup>[9]</sup> performed standard laparoscopy also in their series without any conversion.

Nicola de'Angelis *et al.* <sup>[16]</sup> had an average duration of 28.22 minutes for microco-oscopy and 49.64 minutes for standard laparoscopy with 2 standard laparoscopic microcoelioscopy conversions due to the technical problems of the bipolar forceps via the trocar. 3mm for one and optical problems for the other.

We believe that these statistical differences can be explained by the modification of the surgical technique in our series but also the daily practical experience of each surgeon in standard laparoscopy first and then in microcooscopy.

Moreover, some studies <sup>[23, 24]</sup> show that a laparoscopic low-impact cholecystectomy is associated with a decrease in postoperative morbidity related to sickle cell disease with 18.3% postoperative complications per LC versus 2.9% per impact <sup>[16]</sup>.

The postoperative morbidity in our study was 4.5% (2cas). All 2 are homozygous and non-transfused sickle cell patients who had an acute thoracic crisis postoperatively with a favorable evolution on J5 and J24 postoperatively, respectively.

In asymptomatic children as in our series; G. Curro *et al.* <sup>[9]</sup> had only minor complications including an infection of the wound in the opening of a trocar.

Miltenburg *et al.* <sup>[25]</sup> reported 52 cholecystectomies on 128 children with sickle cell disease; a morbidity of 16% for urgent cholecystectomies and 6% for elective cholecystectomy. Ditto for Suel *et al.* <sup>[18]</sup> compared 34 sickle cell children who underwent elective LC with 17 children undergoing emergency surgery and noted a significant difference related to increased morbidity if urgent surgery. Gumiero *et al.* <sup>[12]</sup> achieved a morbidity rate of 22% in children who had prophylactic surgery but a higher rate in the symptomatic children with sickle cell population. In the same series, non-operated asymptomatic patients are followed over a 7-year period without symptoms.

Apart from the sickle-cell disease field, which is a comorbidity in itself for urgent surgery, it should be noted that some authors such as Haberkern *et al.* <sup>[26]</sup> have shown that the incidence of complications in sickle cell disease was higher in non-transfused patients. as in our series. Same finding in the series of B.Fall *et al.* <sup>[17]</sup> with no complication in the transfused compared to 16.7% in the non transfused.

We believe that these statistical differences can be related to several other factors. Thus, sickle cell patients who are frequently hospitalized have a high risk of postoperative complication; similarly, CO2 insufflation in the peritoneal cavity during the LC reducing diaphragmatic clearance is at the origin of hypoventilation, thus contributing to the occurrence of postoperative vaso- occlusive attacks <sup>[27, 28]</sup>. All this seems better understood and solved by Koshy *et al.* <sup>[29]</sup> who drew up an anesthetic and surgical profile for SS and SC patients undergoing cholecystectomy. In their study there was no significant difference in the overall risk of postoperative complications in the 203 transfused versus the 13 non-transfused patients.

In our study, the average duration of hospitalization was 2.95 days with extremes of 2 and 5 days. G. Curro *et al.* <sup>[9]</sup> find an average of 3 days with extremes of 2 to 4 days. On the other hand, in symptomatic patients operated on an emergency basis, the same series records an average of 7.4 days with extremes of 4 to 10 days. This reinforces the finding that the morbidity rate is significantly proportional to the hospital stay.

## CONCLUSION

At the end of our study on " prophylactic cholecystectomy by lowimpact laparoscopy with or without transfusion exchange in children with sickle cell disease: result of a single-center study", the annual frequency was 6, 1 case / year with a sex ratio of 0.5 and an average age of our patients of 11.07 years with extremes of 6 years and 17 years. The black race is the most affected 98%. The majority of our patients (86.4%) were homozygous sickle cell patients. A transfusion exchange was performed selectively. Only laparoscopic cholecystectomy was performed under general anesthesia. The average duration of intervention was 46.64 minutes with extremes of 22 and 76 minutes. Postoperative morbidity in our study was 4.5% and a hard medium ed hospitalization of 2.95 days with extremes of 2 and 5 davs.

# **Conflict of Interest**

No conflict of interest was declared by the authors.

## **Authors Contributions**

All the authors participated actively in the realization of this work.

**ZTGJ**: Subject design and configuration, data interpretation, manuscript correction, review of the final manuscript and supervision of the work.

**MVM**: Harvesting, interpretation of data, translation of the manuscript into english and review of the final manuscript.

**AG and BAP**: Collect, analysis and interpretation of the results and review of the final manuscript.

**PJM**: Manuscript correction, interpretation of the results and review of the final manuscript.

AJJ, DFM and MDK: Manuscript correction, translation of the manuscript into english and review of the final manuscript.

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