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Cholecystectomy in sickle cell disease patients: Is there more acute chest syndrome after laparoscopy? A case controlled study

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ABSTRACT

Laparoscopy is increasingly being recommended in order to reduce postoperative complications among sickle cell disease patients undergoing cholecystectomy. Acute chest syndrome is the most deadly of these complications. The purpose of this study was to assess if laparoscopic approach reduces postoperative complications related to sickle cell disease after cholecystectomy. A retrospective study of records of sickle cell patients who underwent cholecystectomy for cholelithiasis, from January 1990 to December 2005 was conducted. 136 sickle cell patients underwent surgery: 47 (34.5%) by laparoscopy and 89 (63.5%) by laparotomy. The mean operative time was 71.4 ± 18.9 min in the laparoscopy group and 61.2 ± 15.3 min in the laparotomy group (non-significant difference). The mortality was not significantly different between the two groups: one patient died in the open cholecystectomy group but no death occurred in the laparoscopic one. The morbidity related to the sickle cell disease was significantly higher in the laparoscopy group [$n = 5$ (10.5%)] than in the laparotomy group [$n = 4$ (4.5%)] ($p = 0.04$). This difference was associated with a higher rate of acute chest syndrome in the laparoscopy group [$n = 4$ (8, 5%)] compared to that in the laparotomy group [$n = 1$ (1.1%)] ($p = 0.01$). There were more complications related to sickle cell disease in the laparoscopy group due to acute chest syndrome. Thus, these data should be confirmed in further randomized studies which must be undertaken.

1. Introduction

Cholelithiasis is a frequent complication of sickle cell disease. Prevalence rate ranges from 30% to 70%.[1] Three quarter of these patients become symptomatic,[2] needing cholecystectomy. For patients free of sickle cell disease, laparoscopic approach is considered as the gold standard of cholecystectomy. For sickle cell patients, some studies have shown that laparoscopic cholecystectomy was feasible.[3–7] But patients with sickle cell disease who undergo cholecystectomy are generally considered

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to be at greater risk for perioperative complications than patients without sickle cell disease.[7,8] The most dangerous complication is the acute chest syndrome because of its high mortality rate.[8]

Although improvements have been made in perioperative management of sickle cell disease patients who undergo open cholecystectomy (oxygen therapy, hydratation, and transfusion),[7,9,10] the effect of laparoscopy in promoting acute chest syndrome has not been well studied. In fact, the insufflated CO_2 is absorbed and can lead to a metabolic acidosis which is a major cause of the red blood cells' falciformation.[11] Moreover, the increase of the intra-abdominal pressure during the laparoscopy can equally cause hypoventilation by reducing the diaphragm elevation. So, these two facts could combine and increase the risk of evolving an acute chest syndrome after laparoscopic cholecystectomy.

The aim of our study was to compare the outcome of open surgery versus laparoscopic approach in sickle cell disease patients with symptomatic cholelithiasis who underwent cholecystectomy.

2. Patients and methods

We reviewed the records of all sickle cell disease patients who underwent cholecystectomy for cholelithiasis from October 1990 to September 2005. The data were analysed by Epi Info6®. A cholecystectomy was performed in sickle cell patients with symptomatic cholelithiasis whether for biliary colic, gallbladder sludge, microlithiasis or acute cholelithiasis.

Sickle cell patients were patients who were homozygous with haemoglobin S detected by electrophoresis. With regard to the type of haemolysis, these patients were divided into two groups: those who experienced chronic haemolysis (phenotype SSFA2 and SFA2) and others who experienced acute haemolysis (phenotype SC and SAFA2). Patients with chronic haemolysis and anaemia (SSFA2 and SFA2) are considered to have more severe sickle cell disease symptoms than those with few acute haemolysis (SSFA2 and SFA2). Patients with haemoglobin AA or AS and patients with concomitant choledocotomy or bilio-intestinal diversion during cholecystectomy ($n = 4$) were excluded of the study. Records with incomplete data were also excluded ($n = 13$). Sickle cell disease–related morbidity was defined as postoperative complications directly linked to sickle cell disease. Other postoperative complications were defined as general morbidity. The choice of the approach of cholecystectomy (laparoscopy versus open cholecystectomy) was made based on discussion between the surgeon and the patient. Laparoscopy was performed with four trocars (a periumbilical trocar and three additional trocars in epigastric, right and left hypochondriac region) after creating a 12-mm Hg blinded pneumoperitoneum with a Veress needle. Each patient has had the same perioperative management, in order to avoid vaso-occlusion crisis: hyperhydratation, oxygen therapy, warming up, pain control and transfusion if needed.

Acute chest syndrome was defined as the onset of a new lobar infiltration on chest X-ray, excluding atelectasis, accompanied by fever greater than 38.5 °C, cough, dyspnoea and commonly pleuritic pain.[11,12] Statistical analysis has compared two groups: sickle cell patients operated by laparoscopic cholecystectomy and those operated by open cholecystectomy. We first compared the epidemiological, clinical and therapeutic data to assess whether the two groups were comparable. Then, we compared the general and sickle cell disease–related morbidity and the mortality rate to assess the outcomes according to the cholecystectomy approach. This analysis was performed using the Epi Info6 software, using the χ^2, Student and Fisher non-parametric test.

3. Results

136 sickle cell patients with symptomatic cholelithiasis underwent cholecystectomy: 47 (34.5%) by laparoscopy and 89 (65.5%) by open surgery. The distribution of biological characteristics predictive of sickle cell disease severity (chronic haemolysis phenotypes and acute haemolysis phenotypes) was homogenous between laparoscopy group and open cholecystectomy group: 56.6% ($n = 28$) and 40.4% ($n = 19$) versus 67.4% ($n = 60$) and 32.6% ($n = 29$) [non-significant difference] (Table 1). The difference in clinical and paraclinical characteristic between the two groups was not significant (Table 2). So, the two groups were similar. The mean operating time was 71 ± 17 min in laparoscopy group and 62 ± 12 min in open cholecystectomy group. The mean hospital stay was, respectively, 7.7 ± 1.7 days and 6.2 ± 2.1 days. There was no death in laparoscopy group but one patient died in the other one [non-significant difference]. The death occurred after an acute haemolysis crisis. The morbidity rate non-related to the sickle cell disease was not significantly different between the laparoscopy group 27.6% ($n = 14$) and the other one 22.5% ($n = 20$) [Table 3]. But there was more sickle cell–related complications in the laparoscopy group compared to open cholecystectomy group [14.9% versus 4.5% ($p = 0.04$)] (Table 4).

4. Discussion

For sickle cell disease–free patients, laparoscopic approach is widely admitted to be the gold standard of cholecystectomy. Among sickle cell patients, the feasibility has been demonstrated by numerous studies for children and adult.[1,3,6,7,12–15] They suggested that the outcomes of the two approaches were similar.[1,3,13–15] Moreover, some of these studies reported that laparoscopic cholecystectomy for sickle cell disease

Table 1 – Characteristics of severity of the sickle cell disease

Haemoglobin type	LC ($n = 47$)	OC ($n = 89$)
SSFA2	55.3% ($n = 26$)	61.8% ($n = 55$)
SFA2	4.3% ($n = 2$)	5.6% ($n = 5$)
SAFA2	12.8% ($n = 6$)	10.1% ($n = 9$)
SC	27.6% ($n = 13$)	22.5% ($n = 20$)

LC, laparoscopy cholecystectomy; OC, open cholecystectomy. Non-significant difference.

Table 2 – Comparison of perioperative data

	CL ($n=47$)	OC ($n=89$)
Median age (yr)	25.5 ± 9.7	27.3 ± 7.1
Sex (M:F)	61.7% (29/18)	43.8% (39/50)
Hepatic colic	12.8% ($n=6$)	10.1% ($n=9$)
Cholecystitis	87.2% ($n=41$)	90% ($n=81$)
Gangrenous of the gallbladder	36.2% ($n=17$)	50.6% ($n=45$)
Haemoglobin level (g/dl)	10.7 ± 1.9	10.7 ± 1.9
Preoperative transfusion	78.7% ($n=37$)	67.4% ($n=60$)
Accidental opening of gallbladder	23.4% ($n=11$)	17.9% ($n=17.9$)
Intraoperative desaturation	2.1% ($n=1$)	3.4% ($n=3$)

LC, laparoscopy cholecystectomy; OC, open cholecystectomy.
Non-significant difference.

patients was better than open cholecystectomy in terms of postoperative pain, early deambulation and hospital stay.[1,3,6,7]

However, our results showed that there were more sickle cell–related complications in laparoscopic group compared to open cholecystectomy, due to acute chest syndrome. The same results have been reported by Wales [12] and Delatte et al.[16] Wales reported acute chest syndrome in 22.7% in laparoscopic group versus 15.4% in open cholecystectomy group. In another report from Delatte et al., the incidence of acute chest syndrome was higher in laparoscopic group (10.2% versus 0.4%). These data must be taken into account in the choice of the safest approach for sickle cell patients who have to undergo surgery, having regard to the mortality rate of acute chest syndrome. In fact, acute chest syndrome is known to be the leading cause of death in sickle cell disease patients because of its high rate of mortality.[8,17–19] The effect of pneumoperitoneum in promoting acute chest syndrome is more and more understood. Polymerisation of deoxygenated sickle haemoglobin is the *primum movens* of all the illness of sickle cell disease. The polymerisation of deoxygenated sickle haemoglobin makes red blood cells less pliable and deforms some of them. These cells cannot easily negotiate capillary beds, resulting in premature haemolysis and vaso-occlusion.[11] Haemolysis and vaso-occlusion are the reasons of all the symptoms and perioperative complication such as acute chest syndrome. During the procedure of laparoscopy, the sole site of excretion of the insufflated carbon dioxide (CO_2) is the lung. Despite vigorous intraoperative hyperventilation, patients remain hyperbaric and acidotic, which cause sickle erythrocytes, thereby precipitating vaso-occlusion and acute chest syndrome.[20] In contrast to other vascular beds, the lung vasculature constrict with hypoxia, by the role of free radicals.[21] In an underventilated lung, sickle cells remain deoxygenated, that led to perioperative hypoxia, hypoperfusion and acidosis: areas of ischemia/reperfusion develop, increasing production of oxidizing molecules such as O_2^-, H_2O_2, OH radical and $ONOO^-$ leading to further inflammation, subsequent infarction and acute chest syndrome.[22] Fat embolism from bone marrow infarction during a pain crisis or infection may produce an acute chest syndrome. To decrease the rate of postoperative complications related to sickle cell disease, many improvements have been made in the preoperative management. Currently, this management includes pre-emptive erythrocyte transfusion, aggressive hydratation, and avoidance of hypoxia, pain, hypothermia and acidosis.[8–10,18,19] These precautions decrease morbidity and mortality rates according to Haberkern et al.[1] Despite these precautions, acute chest syndrome occurs in 50% of postoperative conditions. It is due to perioperative stress, hypothermia, hypoxia, acidosis and pain, which cause erythrocyte to sickle.[23] In our serie, we did not observe any deaths from acute chest syndrome, probably because of prompt treatment by transfusion and oxygen, antibiotics, effective analgesia and chest physiology. It is probably the best treatment of acute chest syndrome as reported by other authors.[16,24]

Table 3 – Postoperative complications non-related to sickle cell disease

	CL ($n=47$)	OC ($n=89$)	p
Mortality	0% ($n=0$)	1.1% ($n=1$)	0.65 (Fischer)
Morbidity non-related to SCD	27.6% ($n=14$)	22.5% ($n=20$)	0.34 (χ^2)
Fever	12.8% ($n=6$)	4.5% ($n=12$)	
Wound infection	0% ($n=0$)	0% ($n=0$)	
Abdominal infection	0% ($n=0$)	0% ($n=0$)	
Biliary fistula	0% ($n=0$)	0% ($n=0$)	
Pulmonary infection	4.2% ($n=2$)	2.2% ($n=2$)	
Urinary tract infection	2.1% ($n=1$)	2.2% ($n=2$)	
Deep vein thrombosis	0% ($n=0$)	0% ($n=0$)	

SCD, sickle cell disease.

Table 4 – Postoperative complications related to sickle cell disease

	CL ($n=47$)	OC ($n=89$)	p
Morbidity related to SCD	14.9% ($n=7$)	4.5% ($n=4$)	0.04 (Fischer test)
Acute haemolysis	4.3% ($n=2$)	3.4% ($n=3$)	
Stroke	0% ($n=0$)	0% ($n=0$)	
Acute chest syndrome	10.6% ($n=5$)	1.1% ($n=1$)	0.01 (Fischer test)

SCD, sickle cell disease.

5. Conclusion

Compared to the open approach, laparoscopy can lead to more acute chest syndrome which is the most lethal postoperative complication after abdominal surgery. These findings must be confirmed by further prospective randomized studies. As a result, in the meantime, when laparoscopy is performed, great care must be taken, such as: operating with low pressure (8–11 mm Hg), extending the hospital stay beyond 3 days because acute chest syndrome is detected typically after day 2 or day 3.[17] Patients must also have early mobilization, effective pain control and intensive spirometry in order to prevent lung complication.

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REFERENCES

1. Haberkern CM, Neumatr LD, Orringer EP, et al. Cholecystectomy in sickle cell anemia patients: perioperative outcome of 364 cases from the National Preoperative Transfusion Study. *Blood* 1997;**89**(5):1533–42.
2. Malone BS, Werlin SL. Cholecystectomy and cholelithiasis in sickle cell anemia. *Am J Dis Child* 1988;**142**: 799–800.
3. Tagge EP, Othersen HB, Jackson SM, et al. Impact of laparoscopic cholecystectomy on the management of cholelithiasis in children with sickle cell disease. *J Pediatr Surg* 1994;**29**(2):209–13.
4. Al-Mulhim AS, Al-Mulhim FM, Al-Suwaiygh AA. The role of laparoscopic cholecystectomy in the management of acute cholecystitis in patients with sickle cell disease. *Am J Surg* 2002;**183**(6):668–72.
5. Séguier-Lipszyc E, de Lagausie P, Benkerrou M, et al. Elective laparoscopic cholecystectomy. Treatment of choice for cholelithiasis in children with sickle cell disease? *Surg Endosc* 2001;**15**:301–4.
6. Vecchio R, Cacciola E, Di Martino M, et al. Laparoscopic surgery in sickle cell disease. *Surg Endosc* 2002;**16**:1807–8.
7. Bonatsos G, Birbas K, Toutouzas K, Durakis N. Laparoscopic cholecystectomy in adults with sickle cell disease. *Surg Endosc* 2001;**15**:816–9.
8. Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease. Cooperative study of sickle cell diseases. *Blood* 1995;**86**:3676–84.
9. Vichinsky EP, Neumayr LD, Earles AN, et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group. *N Engl J Med* 2000;**342**(25):1855–65.
10. Vichinsky EP, Haberkern CM, Neumayr L, et al. Comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. *N Engl J Med* 1995;**333**:206–13.
11. Serjeant GR. Sickle cell disease. *Lancet* 1997;**350**:725–30.
12. Wales PW, Carver E, Crawford MW, Kim PCW. Acute chest syndrome after abdominal surgery in children with sickle cell disease: is a laparoscopic approach better? *J Pediatr Surg* 2001; **36**(5):718–21.
13. Esposito C, Gonsalez Sabin MA, Corcione F, et al. Results and complications of laparoscopic cholecystectomy in childhood. *Surg Endosc* 2001;**15**:890–2.
14. Meshikhes A, Al-Dhurais SA, Al-Jama A, et al. Laparoscopic cholecystectomy in patients with sickle cell disease. *J R Coll Surg Ednib* 1995;**40**:383–5.
15. Duncan ND, Smith AI, McDonald AH, Mitchell DIG. Biliary surgery in sickle cell disease: the Jamaïcan experience. *J R Coll Surg Edinb* 2002;**47**(1):414–7.
16. Delatte SJ, Hebra A, Tagge E, et al. Acute chest syndrome in the postoperative sickle cell patient. *J Pediatr Surg* 1999;**34**(1):188–91.
17. Platt OS, Brambilla DJ, Rose WF, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. *N Engl J Med* 1994;**330**:1639–44.
18. Cohen AR, Martin MB, Silber JH, et al. A modified transfusion program for prevention of stoke in sickle cell disease. *Blood* 1992;**79**:1657–61.
19. Wayne AS, Kevy SV, Nathan DG. Transfusion management of sickle cell disease. *Blood* 1993;**81**:1109–23.
20. Koivusalo AM, Lindgren L. Effects of carbon dioxide pneumoperitoneum for laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2000;**44**(7):834–41.
21. Klings ES, Farber HW. Role of free radicals in the pathogenesis of acute chest syndrome in sickle cell disease. *Respir Res* 2001; **2**(5):280–5.
22. Kokoska ER, West KW, Carney DE, et al. Risk factors for acute chest syndrome in children with sickle cell disease undergoing abdominal surgery. *J Pediatr Surg* 2004;**39**(6):848–50.
23. Weil JV, Castro O, Malik AB, et al. Pathogenesis of lung disease in sickle cell hemoglobinopathies. *Am Rev Respir Dis* 1993;**148**: 249–56.
24. Crawford MW, Speakman M, Carver ED, Kim PCW. Acute chest syndrome shows a predilection for basal lung regions on the side of upper abdominal surgery. *Can J Anesth* 2004; **51**(7):707–11.