Surg Endosc (2013) 27:3897–3901
DOI 10.1007/s00464-013-3005-5

Real-time near-infrared fluorescent cholangiography could shorten operative time during robotic single-site cholecystectomy

Nicolas C. Buchs · François Pugin · Dan E. Azagury · Minoa Jung · Francesco Volonte · Monika E. Hagen · Philippe Morel

Received: 27 February 2013 / Accepted: 26 April 2013 / Published online: 14 May 2013

Abstract
Background With the introduction of a new platform, robotic single-site cholecystectomy (RSSC) has been reported as feasible and safe for selected cases. In parallel, the development of real-time near-infrared fluorescent cholangiography using indocyanine green (ICG) has been seen as a help during the dissection, even if the data are still preliminary. The study purpose is to report our experience with ICG RSSC and compare the outcomes to standard RSSC.
Methods From February 2011 to December 2011, 44 selected patients underwent RSSC for symptomatic cholelithiasis. Among them, 23 (52.3 %) were included in an experimental protocol using the ICG, and the remainder (47.7 %) underwent standard RSSC. There was no randomization. The endpoints were the perioperative outcomes. This is a prospective study, approved by our local Ethics Committee.
Results There were no differences in terms of patients' characteristics, except that there were more male patients in the ICG group (47.8 vs. 9.5 %; $p = 0.008$). Regarding the surgical data, the overall operative time was shorter for the ICG group, especially for patients with a body mass index (BMI) ≤ 25 (-24 min) but without reaching statistical significance ($p = 0.06$). For BMI >25, no differences were observed. Otherwise, there were no differences in terms of conversion, complications, or length of stay between both groups.
Conclusions A RSSC with a real-time near-infrared fluorescent cholangiography can be performed safely. In addition, for selected patients with a low BMI, ICG could shorten the operative time during RSSC. Larger studies are still required before drawing definitive conclusions.

Keywords Indocyanine green · Fluorescence · Cholangiography · Single-site · Robotic · Cholecystectomy · Operative time

The introduction of single-site surgery has brought new challenges and technical difficulties [1, 2]. Among the possible indications, cholecystectomy has been seen by many as a good model for a single-site approach [3, 4]. On the other hand, the risk of bile duct injury has raised concerns. A liberal use of the critical view of safety has been therefore advocated [5], even if it is sometimes difficult to be obtained by a single-site approach. In addition, routine use of cholangiography also has been advocated to allow an early recognition of a biliary tree lesion [6, 7]. Yet, it can be difficult to perform intraoperative cholangiography during single-site cholecystectomy, and few surgeons routinely perform this examination [8].

From there, the interest for fluorescent cholangiography has increased [9–11], especially since the introduction of this technology for robotic single-site surgery. Several groups have shown interesting results, with a real-time identification of the extrahepatic biliary anatomy [12, 13]. Yet, the real utility of indocyanine green (ICG) is still debatable in daily practice. On the other hand, a quick recognition of the cystic and the common hepatic ducts, and their junction could shorten the dissection phase and operative time.

N. C. Buchs (✉) · F. Pugin · D. E. Azagury · M. Jung · F. Volonte · M. E. Hagen · P. Morel
Clinic for Visceral and Transplantation Surgery, Department of Surgery, Faculty of Medicine, University Hospital of Geneva, University of Geneva, Rue Gabriel-Perret-Gentil, 4, 1211 Geneva 14, Switzerland
e-mail: nicolas.c.buchs@hcuge.ch

The study was designed to compare the outcomes of patients who underwent robotic single-site cholecystectomy (RSSC) by a standard approach to those who benefited from a real-time near-infrared fluorescent cholangiography.

Materials and methods

From February 2011 to December 2011, 44 selected patients underwent a RSSC for symptomatic cholelithiasis. Among these 44 patients, 23 were included in an experimental protocol, using the ICG for an intraoperative fluorescent cholangiography (52.3 %). The others (47.7 %) underwent standard RSSC without ICG. There was no randomization. The choice of the technique was based on the availability of the near-infrared system. The goal of the fluorescent cholangiogram was to visualize the extrahepatic biliary anatomy, as already described [13].

The inclusion criteria were the same for both groups and included patients aged 18–80 years with symptoms consistent with gallbladder disease and gallstone confirmed by ultrasound or computer tomography, and with an American Society of Anesthesiologists score (ASA) of 1–3. The exclusion criteria were acute cholecystitis, biliary pancreatitis or suspicion of common bile duct stone and/or abnormal liver tests. Moreover, previous upper abdominal open surgery also was considered as a relative contraindication. In addition, a lack of cooperation by patient due to psychological or severe systemic illness, a history of adverse reaction to ICG, or any contraindication to ICG label also were considered reasons not to proceed with this approach [13].

The same experienced team performed all of the procedures. This is a prospective study that was approved by our local Ethics Committee. All patients enrolled in this study gave their informed consent.

Surgical technique

As already described in our preliminary experience [13–16], all the patients underwent RSSC using the da Vinci Si Surgical System (Intuitive Surgical, Intuitive Inc., CA, USA) with the new single-site platform.

For the ICG group, a 2.5-mg dose of ICG was administered intravenously during patient preparation by anesthesia, approximately 30–45 min before incision.

Except for the administration of ICG, both groups were similar in terms of surgical technique.

The operative time was defined as the time in between skin incision and skin closure, including the docking time. In the ICG group, the surgeon was authorized to switch to fluorescent mode as often as desired to clearly visualize the biliary anatomy.

A conversion was defined as the need to finish the procedure by open or laparoscopic surgery.

Statistical analysis

The results of parametric and nonparametric data were expressed as mean ± standard deviation (SD) and median (range), respectively. GraphPad Software (GraphPad, La Jolla, CA, USA) was used for all statistical analyses. Confidence intervals were set at 95 %. A two-sided p value of ≤ 0.05 was considered statistically significant. Comparisons between both groups were determined using Fisher's exact test for discrete variables and Student's t test for continuous variables.

Results

During the study period, 23 patients underwent RSSC with a real-time near-infrared fluorescent cholangiography (ICG group; 52.3 %), whereas 21 were achieved without ICG (standard group; 47.7 %). Table 1 summarizes the patients' demographics. Of note, there were more male patients in the ICG group. Otherwise, there were no differences concerning patients' characteristics between both groups.

Regarding surgical data (Table 2), the operative time was slightly shorter for the ICG group (−6 min). Yet, it was neither statistically nor clinically significant ($p = 0.38$). However, if only patients with a body mass index (BMI) ≤25

Table 1 Patients' demographics

	Overall ($n = 44$)	ICG group ($n = 23$)	Standard group ($n = 21$)	p value
Gender				0.008
Male	13	11	2	
Female	31	12	19	
Age, mean ± SD (years)	47.7 ± 11.2	47.3 ± 11	48 ± 11.7	0.84
ASA score, mean ± SD	1.7 ± 0.5	1.7 ± 0.6	1.8 ± 0.4	0.5
BMI, mean ± SD (kg/m^2)	27 ± 4.1	27 ± 4.7	27 ± 3.4	1

ICG indocyanine green, *SD* standard deviation, *ASA* American Society of Anesthesiologists score, *BMI* body mass index

Table 2 Perioperative data

	Overall ($n = 44$)	ICG group ($n = 23$)	Standard group ($n = 21$)	p value
Operative time, mean ± SD (min)	88.2 ± 23.7	85.2 ± 21.5	91.5 ± 26	0.38
For BMI ≤ 25	80.4 ± 25.7	70 ± 13.1	93.7 ± 32.5	0.06
For BMI > 25	92.7 ± 21.7	95 ± 20.4	90.4 ± 23.5	0.6
Docking time, mean ± SD (min)	7.1 ± 3.9	6.2 ± 3.7	8.1 ± 3.8	0.1
Conversion	0	0	0	1
Intraoperative complication	1 (2.3 %)	1 (4.3 %)	0	1
Blood loss, mean ± SD (ml)	12.2 ± 13.4	12 ± 13.4	12.4 ± 13.6	0.92
Postoperative complication	3 (6.8 %)	2 (8.7 %)	1 (4.8 %)	1
Hospital stay, mean ± SD (days)	1.1 ± 0.7	1.1 ± 0.6	1.1 ± 0.8	1

ICG indocyanine green, *SD* standard deviation, *BMI* body mass index

were considered, the difference was clinically more relevant. Indeed, the operative time for the ICG group was almost 24 min shorter than for the standard group ($p = 0.06$). No differences were observed in patients with a BMI superior to 25 kg/m^2. In addition, the operative time was significantly shorter for low BMI in the ICG group compared with overweight BMI in the same group (−25 min; $p = 0.004$).

There was no conversion but one intraoperative complication: one intraoperative bleeding (estimation: 50 ml) occurred in an obese patient in the ICG group, requiring an additional port for a bipolar forceps. There was no intraoperative complication in the standard group. Regarding postoperative complications, there was no difference between both groups. Two patients in the ICG group were readmitted for abdominal pain, with normal ultrasonography and blood test. They were successfully treated conservatively. One patient in the standard group was readmitted for an incisional hernia 8 months after the initial surgery, requiring a laparoscopic repair. None of the intra- or postoperative complications were related to the use of ICG.

The mean hospital stay was similar between both groups.

Discussion

To the best of our knowledge, we report the first comparative study between standard RSSC and RSSC using ICG. Our results show a trend toward statistically significantly reduced operative time, especially for patients with a BMI ≤25 (−24 min). The previous experience with ICG has shown its interest for the recognition of biliary anatomy during cholecystectomy [9–11, 17]. Recently, Spinoglio et al. [12] have reported their experience with ICG and RSSC with encouraging results. They have visualized at least one biliary structure in 100 % of cases. Similar findings have been previously reported by our group [13].

However, the exact role of this new technology is still debatable. If everybody agrees to consider that fluorescent cholangiography cannot replace standard cholangiography to exclude a common bile duct stones, ICG coupled with a near infrared camera has the advantage of being nonionizing [17]. We strongly think that the exclusion criteria have to be respected, and all patients with a suspicion of common bile duct stone require intraoperative cholangiography. On the other hand, the expeditious detection of the main biliary structures seems to speed up the dissection of Calot's triangle, as we report, and should avoid a biliary injury. This new technology therefore could provide an increased level of security during RSSC. Yet, in this small series, fortunately, we did not have any biliary injury, and thus we cannot confirm this fact. However, we have demonstrated the utility of ICG to speed up the dissection, at least in patients with a low BMI. Of note, the difference disappears when patients with a BMI > 25 are considered. This fact can be easily explained by the tissue penetration ability of near-infrared light. Penetration has been showed to be limited to 5–10 mm [17, 18]. A small amount of fatty tissue surrounding the biliary structures is therefore sufficient to prevent ICG identification prior to any dissection of Calot's triangle [5, 17]. The advantage of ICG use in even only slightly obese patients might be therefore rapidly compromised.

In addition, in this series, we have shown that the use of ICG is safe. There were no differences between both groups in terms of complications and none were associated to the use of ICG. In other reports, the safety of ICG also has been demonstrated [12, 13], with a risk of anaphylactic reactions approximately of 0.003 % at doses exceeding 0.5 mg/kg [18].

On the other hand, the exact role of RSSC also is still under investigation. While it is clear that the robotic technology might help to perform single-site surgery [19, 20], stronger evidence is required before generalizing this

technique. During the past couple of years, several groups, including ours, have reported encouraging results with RSSC [16, 21–23]. In addition, the learning curve was reported to be shorter with the robotic technology in comparison to standard single-site laparoscopy [23, 24]. The adjunction of ICG to the three-dimensional robotic vision is certainly helpful to achieve a safe and time-efficient dissection of Calot's triangle [13], as it was already demonstrated for single-incision laparoscopic cholecystectomy [17].

Even if novel and encouraging, the data reported in this study have several limitations deserving comment. First, this is not a randomized study and the both groups were not exactly similar, at least for gender.

Secondly, the risk of bias because of the learning curve needs to be mentioned. Indeed, the patients were not operated on during the same time period. The majority of the standard patients underwent the procedure earlier in the experience. Thus, we cannot completely exclude a bias because of this learning curve. Yet, subjectively, we do have the impression that a real-time fluorescent cholangiography can speed up the operative time. The difference in terms of operative time (at least for patients with a low BMI) is clinically relevant, even if it did not reach a statistical significance. This can be explained by the small number of patients.

Finally, there was no cost analysis. Yet, even if the additional price of ICG is negligible, the total cost of the robotic system and its maintenance remain a key question for numerous institutions. On the other hand, for this specific indication, the use of ICG could speed up the dissection and thus save operative time (and potentially result in a cost benefit). However, it was beyond the scope of our study and remains mainly hypothetical.

Conclusions

A RSSC with a real-time near-infrared fluorescent cholangiography can be performed safely. In addition, for selected patients with a low BMI, ICG could fasten the operative time during RSSC. Larger studies are required before drawing definitive conclusions.

Disclosures Drs. Buchs, Pugin, Azagury, Volonte, Jung, and Morel have no conflicts of interest or financial ties to disclose. Dr. Hagen has a financial relationship with Intuitive Surgical.

References

1. Ayloo SM, Buchs NC, Addeo P, Giulianotti PC (2011) Laparoendoscopic single-site adjustable gastric banding: technical considerations. Surg Laparosc Endosc Percutan Tech 21(6):e295–e300
2. Ayloo SM, Buchs NC, Addeo P, Bianco FM, Giulianotti PC (2011) Traditional versus single-site placement of adjustable gastric banding: a comparative study and cost analysis. Obes Surg 21(7):815–819
3. Bucher P, Pugin F, Buchs N, Ostermann S, Charara F, Morel P (2009) Single port access laparoscopic cholecystectomy (with video). World J Surg 33(5):1015–1019
4. Bucher P, Pugin F, Buchs NC, Ostermann S, Morel P (2011) Randomized clinical trial of laparoendoscopic single-site versus conventional laparoscopic cholecystectomy. Br J Surg 98(12):1695–1702
5. Buddingh KT, Nieuwenhuijs VB, van Buuren L, Hulscher JB, de Jong JS, van Dam GM (2011) Intraoperative assessment of biliary anatomy for prevention of bile duct injury: a review of current and future patient safety interventions. Surg Endosc 25(8):2449–2461
6. Buddingh KT, Weersma RK, Savenije RA, van Dam GM, Nieuwenhuijs VB (2011) Lower rate of major bile duct injury and increased intraoperative management of common bile duct stones after implementation of routine intraoperative cholangiography. J Am Coll Surg 213(2):267–274
7. Flum DR, Dellinger EP, Cheadle A, Chan L, Koepsell T (2003) Intraoperative cholangiography and risk of common bile duct injury during cholecystectomy. JAMA 289(13):1639–1644
8. Rawlings A, Hodgett SE, Matthews BD, Strasberg SM, Quasebarth M, Brunt LM (2010) Single-incision laparoscopic cholecystectomy: initial experience with critical view of safety dissection and routine intraoperative cholangiography. J Am Coll Surg 211(1):1–7
9. Ishizawa T, Bandai Y, Kokudo N (2009) Fluorescent cholangiography using indocyanine green for laparoscopic cholecystectomy: an initial experience. Arch Surg 144(4):381–382
10. Ishizawa T, Tamura S, Masuda K, Aoki T, Hasegawa K, Imamura H, Beck Y, Kokudo N (2009) Intraoperative fluorescent cholangiography using indocyanine green: a biliary road map for safe surgery. J Am Coll Surg 208(1):e1–e4
11. Ishizawa T, Bandai Y, Hasegawa K, Kokudo N (2010) Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agents? World J Surg 34(10):2505–2506
12. Spinoglio G, Priora F, Bianchi PP, Lucido FS, Licciardello A, Maglione V, Grosso F, Quarati R, Ravazzoni F, Lenti LM (2012) Real-time near-infrared (NIR) fluorescent cholangiography in single-site robotic cholecystectomy (SSRC): a single-institutional prospective study. Surg Endosc. doi:10.1007/s00464-012-2733-2
13. Buchs NC, Hagen ME, Pugin F, Volonte F, Bucher P, Schiffer E, Morel P (2012) Intra-operative fluorescent cholangiography using indocyanine green during robotic single site cholecystectomy. Int J Med Robot 8(4):436–440
14. Iranmanesh P, Morel P, Buchs NC, Pugin F, Volonte F, Kreaden US, Hagen ME (2013) Docking of the da Vinci Si Surgical System® with single-site technology. Int J Med Robot 9(1):12–16
15. Morel P, Pugin F, Bucher P, Buchs NC, Hagen ME (2012) Robotic single-incision laparoscopic cholecystectomy. J Robot Surg 6(3):273–274
16. Morel P, Hagen ME, Bucher P, Buchs NC, Pugin F (2011) Robotic single-port cholecystectomy using a new platform: initial clinical experience. J Gastrointest Surg 15(12):2182–2186
17. Ishizawa T, Kaneko J, Inoue Y, Takemura N, Seyama Y, Aoki T, Beck Y, Sugawara Y, Hasegawa K, Harada N et al (2011) Application of fluorescent cholangiography to single-incision laparoscopic cholecystectomy. Surg Endosc 25(8):2631–2636
18. Speich R, Saesseli B, Hoffmann U, Neftel KA, Reichen J (1988) Anaphylactoid reactions after indocyanine-green administration. Ann Intern Med 109(4):345–346
19. Buchs NC, Pugin F, Volonte F, Jung M, Hagen ME, Morel P (2012) Robotic single site surgery: current practice and future developments. Rev Med Suisse 8(346):1316–1320

20. Balaphas A, Hagen ME, Buchs NC, Pugin F, Volonte F, Inan I, Morel P (2012) Robotic laparoendoscopy single site surgery: a transdisciplinary review. Int J Med Robot 9(1):1–11
21. Kroh M, El-Hayek K, Rosenblatt S, Chand B, Escobar P, Kaouk J, Chalikonda S (2011) First human surgery with a novel single-port robotic system: cholecystectomy using the da Vinci Single-Site platform. Surg Endosc 25(11):3566–3573
22. Wren SM, Curet MJ (2011) Single-port robotic cholecystectomy: results from a first human use clinical study of the new da Vinci single-site surgical platform. Arch Surg 146(10):1122–1127
23. Pietrabissa A, Sbrana F, Morelli L, Badessi F, Pugliese L, Vinci A, Klersy C, Spinoglio G (2012) Overcoming the challenges of single-incision cholecystectomy with robotic single-site technology. Arch Surg 147(8):709–714
24. Spinoglio G, Lenti LM, Maglione V, Lucido FS, Priora F, Bianchi PP, Grosso F, Quarati R (2012) Single-site robotic cholecystectomy (SSRC) versus single-incision laparoscopic cholecystectomy (SILC): comparison of learning curves. First European experience. Surg Endosc 26(6):1648–1655